Clinical Study Report Appendix 16.1.9

Drug Substance MEDI7352

Study Code D5680C00002

Appendix 16.1.9
Documentation of Statistical Methods and Supporting Statistical Analysis

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NRS pain/PK/ADA/Total NGF Analysis Plan	
Drug Substance	MEDI7352
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NRS pain/PK/ADA/Total NGF Analysis Plan (Interim Analyses)

Study D5680C00002

A Randomised, Double-Blind, Placebo-Controlled, Dose-Response Study of the Efficacy and Safety of MEDI7352 in Subjects with Painful Diabetic Neuropathy

TABLE OF CONTENTS

TITLE PAGE 1
TABLE OF CONTENTS 2
INTERIM ANALYSIS SAP SIGNATURE PAGE 4
1 INTRODUCTION 5
2 EFFICACY OBJECTIVES 6
3 PK[redacted] AND IMMUNOGENICITY OBJECTIVES 6
4 PK[redacted] AND IMMUNOGENICITY ASSESSMENTS 6
5 PROCESS & DATA FLOW 7
5.1 PREMIER-SUPPLIED ANALYSES 7
5.2 INTIQUAN-SUPPLIED ANALYSES 7
6 STATISTICAL METHODS 8
6.1 NRS Pain 9
6.1.1 Data Conventions for Statistical Analysis of ePRO Pain Diary Data 9
6.1.2 Handling of Missing Diary Data 10
6.1.3 Derivation of Endpoints 11
6.1.4 Descriptive Statistics 11
6.1.5 Statistical Analysis 12
6.1.6 Updated Statistical Power Calculation 13
6.2 PK 13
6.3 Total NGF 14
6.4 Anti-drug Antibody 14
6.5 Individual Subject Profiles 14
6.6 Other Data 15
6.6.1 Subject Disposition and eligibility for statistical analysis 15
6.6.2 Demographic data 15
7 SOFTWARE DETAILS 16
8 STATISTICAL APPENDIX 16
9 REPORTING 18
10 OUTPUT SHELLS EXAMPLES 21

LIST OF TABLES

Table 1 Planned Tables 18
Table 2 Planned Figures 19

LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation or special term	Description
ADA	Anti-drug antibody
ADaM	Analysis Data Model
AZ	AstraZeneca
BLQ	Below the limit of quantification
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence interval
CPQP	Clinical Pharmacology and Quantitative Pharmacology
CTX-II	C-terminal cross-linked telopeptide of type II collagen
CXCL13	Chemokine C-X-C motif ligand 13
IA	Interim analysis
IARC	Interim Analysis Review Committee
ID	Identification
IP	Investigational product
NONMEM	Non-linear mixed effect modelling
NGF	Nerve growth factor
MAD	Multiple-ascending dose
PDN	Painful Diabetic Neuropathy
PD	Pharmacodynamic
PK	Pharmacokinetic
CCI [redacted]	
SAD	Single-ascending dose
SDTM	Study Data Tabulation Model
TNFα	Tumour necrosis factor alpha
VPC	Visual predictive check

INTERIM ANALYSIS SAP SIGNATURE PAGE

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1 INTRODUCTION

MEDI7352 is a new modality bispecific fusion protein targeting both nerve growth factor (NGF) and tumour necrosis factor alpha (TNFα) that is being developed to treat chronic pain. Both the anti-NGF and anti-TNFα pathways are precedented. This data analysis plan document provides a high-level description of the dataflow that will be followed and the outputs to be generated for the NRS pain scores, PK, ADA and total NGF variables in support of the interim analysis(es) for the Phase 2 dose response study D5680C00002 conducted with MEDI7352 in subjects with painful diabetic neuropathy. Full details of the study design can be found in the Clinical Study Protocol version 7.0 (13th April 2022).

Interim analyses are planned after approximately 60 subjects have completed at least 2 weeks of randomised treatment across placebo and MEDI7352 CCI IV dose in stage 3 of the study. Unblinded personnel who are not otherwise involved in the study conduct will prepare the data for review by an Interim Analysis Review Committee. The members of the Interim Analysis Review Committee are independent of the day-to-day study activities. The study team will remain blinded to the results of the interim analysis for the duration of the study. Firewalls will be put in place to ensure that information is not inadvertently disseminated to the blinded members of the study team. The primary aim of the interim analysis is to validate the key assumptions of the original sample size calculation, which could result in a recommendation to adjust the sample size (overall and/or to individual dose groups) or the treatment allocation ratio in stage 4 of the study. In support of the interpretation of the efficacy (NRS) data analysis, PK, ADA and total NGF data will also be analysed.

Study Description Overview

- Phase of development: Phase 2.
- Patient population: Participants with painful diabetic neuropathy.
- Study size: Approximately 272 eligible subjects will be randomly assigned to double-blind treatment with one of 4 dose levels of MEDI7352 (dependent upon stage of the study) or placebo to ensure that approximately 236 subjects are evaluable for the efficacy analysis of stages 2-4 combined.
- General design: This is a multicentre, multinational, randomised, double-blind, placebo-controlled, parallel-group study.
- Route of administration: intravenous.
- Doses investigated: CCI . Each subject will receive 6 doses, 1 dose every 2 weeks (Days 1, 14, 28, 42, 56, and 70), administered IV over a 60-minute period. Note: only CCI and CCI doses are included in the Interim Analysis (from stages 2 and 3).
- Development objectives: proof of efficacy.

2 EFFICACY OBJECTIVES

The primary objective is to assess the efficacy of MEDI7352 versus placebo on chronic pain in subjects with PDN currently taking standard of care medication for their PDN pain. A secondary objective is to characterise the dose-response relationship of MEDI7352 on chronic pain in subjects with PDN. However, this interim analysis plan will not cover the latter objective.

3 PK[redacted] AND IMMUNOGENICITY OBJECTIVES

The Pharmacokinetics, pharmacodynamic (total NGF) and immunogenicity of MEDI7352 are secondary objectives/endpoints in the study. [redacted]. A description of these objectives/endpoints is provided below.

Secondary objectives:

- To assess the PK, PD, and immunogenicity of MEDI7352 in subjects with PDN

Exploratory objectives:

[redacted]

4 PK[redacted] AND IMMUNOGENICITY ASSESSMENTS

Blood samples for determination of serum MEDI7352 concentrations and serum total NGF concentrations are collected at the following time-points:

Day 1 (pre-treatment), Day 14, Day 28, Day 42, Day 56, Day 70 (pre-dose, end of infusion, and 8 h), Day 71, Day 77, Day 84 and Early termination (if relevant).

Blood samples for determination of presence of anti MEDI7352 antibodies (ADA) are collected at the following time-points:

Baseline, Day 14, Day 28, Day 56, Day 70, Day 84 and Week 18.

Note: on dosing days, blood samples are taken prior to IP administration.

5 PROCESS & DATA FLOW

Prior to the interim database lock, it is expected that data within scope of the Interim Analysis will be cleaned and have no outstanding edit checks.

5.1 PREMIER-SUPPLIED ANALYSES

Prior to the interim analysis, a dummy run will be performed on a blinded data transfer using dummy randomization codes. This blinded analysis step will also be used by the sponsor blinded statistician to perform the sponsor QC of the primary analysis. Premier will perform their own QC as per standard operating procedures. The unblinded interim analysis will be performed by the unblinded Premier statistician. Both the blinded Premier statistician and blinded Sponsor statistician will be prohibited from access to the unblinded interim analysis.

5.2 INTIQUAN-SUPPLIED ANALYSES

Data Management and Biostatistics at PREMIER will generate datasets containing the PK, ADA (immunogenicity) and total NGF data with additional study variables (i.e. baseline weight; dosing time; treatment allocation; PK, ADA and total NGF sampling time), and a dataset containing the efficacy data (i.e. NRS scores) for the purpose of generating individual profile plots (generated by IntiQuan) in support of the main efficacy data analysis conducted by PREMIER Biostatistics. The data structure and transfer process from Premier to AZ will be detailed in a separate Data Transfer Guideline document, and control of blinding will be described in MEDI7352 Study D5680C00002 Interim Analysis Review Committee Charter.

6 STATISTICAL METHODS

Handling of missing or unquantifiable data:

Except for specific NRS pain analyses (described in section 6.1) missing data will not be imputed. PK and Total NGF data below the limit of quantification will be handled using a left censoring approach (i.e. values BLQ are defined as >=0 and <BLQ). ADA titre reported as <30 (below the minimum required dilution) is a negative result for the presence of ADA and will be treated as missing in the calculation of ADA titre summary statistics.

Populations for analysis:

Details of the populations for analysis as described in the CSP are presented below:

- Modified intent-to-treat (mITT): all randomised subjects who receive at least 1 dose of double-blind study medication and have at least 1 post-baseline NRS assessment. If a subject is randomised incorrectly or is administered the incorrect IP, analyses of the mITT population will be based on the IWRS-assigned treatment. In addition, for the purposes of the efficacy interim analysis of weekly average NRS pain score, it is also required that subjects have an evaluable 'Average Week 12 Pain NRS (LOCF)'score, which is defined as having completed two doses of IP and recorded sufficient pain NRS data for at least 2 weeks to enable the week 2 average calculation as described in section 6.1.

- Safety set: The safety population will include all subjects who receive at least 1 dose of double-blind study medication.

- PK set: all subjects for whom a PK sample was obtained and analysed.

In addition, a "Completers" set will be analysed for efficacy, defined as the subset of the mITT population who have a week 12 average NRS score.

A further subset of the mITT population "Week 6 LOCF" may be used to for efficacy analyses if the number of subjects with week 6 to week 11 NRS weekly averages (but no week 12 weekly average) is at least 20% the size of those with complete week 12 NRS averages.

For the purposes of the IA 'all PK and PD data available by the data cut-off date for the IA' will be included in the population PK and population PKPD analyses.

For the Safety set data presentations, The following clarifies how to handle the situation where a participant receives a treatment other than that to which the participant was randomised:

- If a participant randomised to placebo receives at least one dose of MEDI7352 XX µg/kg during the entire double-blind treatment period then the actual treatment arm = MEDI7352 XX, where XX corresponds to the lowest dose of MEDI7352 that the participant received during the double-blind treatment period.

- If a participant took only MEDI7352 XX µg/kg treatment during the entire double-blind treatment period, then the actual treatment arm = MEDI7352 XX, where XX corresponds to the dose of MEDI7352 that the participant took during the entire double-blind treatment period, regardless of what treatment the participant was randomized to.

- If a participant took a mix of MEDI7352 XX µg/kg treatments during the entire double-blind treatment period, then the actual treatment arm = MEDI7352 XX, where XX corresponds to the lowest dose of MEDI7352 that the participant received during the double-blind treatment period, regardless of what treatment the participant was randomized to.

6.1 NRS Pain

For all outputs the placebo group will include subjects pooled across stages 2 and 3.

6.1.1 Data Conventions for Statistical Analysis of ePRO Pain Diary Data

- 'Baseline' period: is defined as the seven day period prior to randomization i.e. Day -7 to Day -1, inclusive. A subject is considered to have a valid Baseline Pain score at study entry if there are at least 5 days of recorded diary pain scores in the 7 day period. This is consistent with the protocol inclusion criterion 9. However, for the purposes of inclusion in the statistical analysis of ePRO Pain Diary data, a subject is considered to have an evaluable baseline if they have at least 4 days out of 7 have recorded diary pain scores.
- 'Week 12' period: is defined for each subject as the seven day period ending within the protocol stipulated window (day 84 $\pm$ 3), where at least 4 days out of 7 have recorded diary pain scores. Where several such windows exist the one ending closest to day 84 will be selected. If there are two such windows that are equidistant from day 84 then the one with the largest number of diary entries will take precedence. If they have the same number of entries then the later of the two end dates will be chosen. If no such window exists then week 12 will be considered missing for the purposes of weekly average scoring. For example:

Day	77	78	79	80	81	82	83	84	85	Number non missing
7-day Window 85	Y	N	Y	Y	N	N	Y	N	Y	4
7-day Window 84	Y	N	Y	Y	N	N	Y	N	Y	3 (So technically Missing)
7-day Window 83	Y	N	Y	Y	N	N	Y	N	Y	4

In the example above, the 7 day window ending at day 84 has only 3 days of entries, so cannot be used as week 12 average. However Day 83 and day 85 have exactly 4 entries in their 7 day windows. These are equidistant from the ideal day 84, so the algorithm chooses day 85 to take the average i.e. the later of the two.

The same approach as for week 12 will be taken for weeks 2,4,6,8 and 10, but using the corresponding nominal study days and the $\pm$ 3 days visit windows as described in the protocol, as follows:

- 'Week 2' period: is defined for each subject as the seven day period ending within the protocol stipulated window (day 14 $\pm$ 3), where at least 4 days out of 7 have recorded diary pain scores.
- 'Week 4' period: is defined for each subject as the seven day period ending within the protocol stipulated window (day 28 $\pm$ 3), where at least 4 days out of 7 have recorded diary pain scores.
- 'Week 6' period: is defined for each subject as the seven day period ending within the protocol stipulated window (day 42 $\pm$ 3), where at least 4 days out of 7 have recorded diary pain scores.
- 'Week 8' period: is defined for each subject as the seven day period ending within the protocol stipulated window (day 56 $\pm$ 3), where at least 4 days out of 7 have recorded diary pain scores.
- 'Week 10' period: is defined for each subject as the seven day period ending within the protocol stipulated window (day 70 $\pm$ 3), where at least 4 days out of 7 have recorded diary pain scores.

6.1.2 Handling of Missing Diary Data

- 'Missing Baseline': Subjects with missing baseline data (i.e. zero or 1-3 days of diary pain scores will not be included in the Interim Analysis because the primary analysis is change-from-baseline.
- 'Missing Week 12': If a subject has zero or $\leq$ 3 days of diary pain data in each of the possible seven day periods ending within the protocol definition of week 12 (day 84 $\pm$ 3), then an imputed 'week 12 LOCF' will be calculated from the latest

7 'non-missing' entries of the subject's diary closest to their nominal week 12 visit (i.e. the latest 7 day period containing at least 4 NRS values), provided that this would qualify as at least 'week 2' according to the windowing definition above. Otherwise, the week 12 LOCF weekly average NRS pain score will be set to missing.

6.1.3 Derivation of Endpoints

- 'Average Baseline Pain NRS': is defined as the arithmetic average of the 'non-missing' daily pain scores within the baseline period defined above. For example, if a subject has 4 days of non-missing pain scores their average will be calculated over 4 days, not the full 7 day baseline period.
- 'Average Week 12 Pain NRS': is defined as the arithmetic average of the 'non-missing' daily pain scores within each subject's specific week 12 period defined above.
- 'Average Week 12 Pain NRS (LOCF)': is defined as the arithmetic average of the 'non-missing' daily pain scores within each subject's specific week 12 period or according to the imputed 'week 12 LOCF' approach described above.
- 'Change from Baseline to Week 12 Pain NRS': is defined for each subject as 'Average Week 12 Pain NRS' minus 'Average Baseline Pain NRS'.
- 'Change from Baseline to Week 12 Pain NRS (LOCF)': is defined for each subject as 'Average Week 12 Pain NRS (LOCF)' minus 'Average Baseline Pain NRS'.

6.1.4 Descriptive Statistics

Tables of arithmetic mean, standard deviation, minimum, maximum, median, 1st and 3rd quartiles and N, will be provided by treatment group and total, for the following NRS endpoints:

- Baseline weekly average pain NRS
- Weekly average pain NRS for weeks 2, 4, 6, 8, 10 and 12
- Change from Baseline Pain NRS to weeks 2, 4, 6, 8, 10 and 12
- Week 12 LOCF: Weekly average pain NRS and Change from Baseline

In addition, the following plots will be produced:

- Mountain plots (also known as folded empirical distribution plots) and boxplots, by treatment group, of Weekly Average and 'Change from Baseline to Week 12 Pain NRS (LOCF)' will be presented.

- Line plots of the observed Weekly Average and Change from baseline in mean Daily NRS scores for each treatment group from baseline through to the day 87 (the upper limit of the week 12 visit window), with Week 12 LOCF as an additional plotting point.

- Spaghetti/Connected line time plot of individual subjects for observed Weekly Average (these will be presented as individual profiles as in section 6.5) and Change from Baseline to week 12.

6.1.5 Statistical Analysis

ANCOVA of 'Change from Baseline to Week 12 Pain NRS (LOCF)':
The linear model will be an analysis of covariance (ANCOVA) with dependent variable 'Change from Baseline to Week 12 Pain NRS (LOCF)', and independent variables will be dose group (as a factor, with placebo group as the reference level), and 'Baseline weekly average pain NRS' as the continuous covariate. The random error is assumed to be normally and independently distributed with constant variance. The following outputs from the fitted model will be tabulated:

- Parameter estimates of the difference between each dose group and placebo, t-value, degrees of freedom, standard error, conventional 95% 2-sided and also 'Lalonde-type' asymmetric confidence intervals (i.e. lower limit of 1-sided 90% CI and upper limit of 1-sided 80% CI), and model residual standard deviation (RMSE).
- Least squares means estimates of change from baseline to week 12 for CCI [redacted] CCI [redacted] and Placebo groups, with 95% 2-sided confidence intervals. The least squares mean is a model estimate using fitted group parameter and the baseline weekly average pain NRS parameter evaluated at the grand mean over both groups.
- As a sensitivity analysis, an estimate of the treatment effect at week 12, together with 95 % 2-sided confidence intervals and also 'Lalonde-type' asymmetric confidence intervals (i.e. lower limit of 1-sided 90% CI and upper limit of 1-sided 80% CI), will also be obtained from a "Mixed Effects Repeated Measures model", which assumes a Multivariate Normal distribution across visits within patient, with a fully parameterized unstructured covariance matrix and contains treatment, baseline NRS, visit and treatment-by-visit interaction as fixed effects, using all available data (but not LOCF). If there are convergence issues then a simpler covariance structure, such as AR1 will be implemented.
- Bayesian posterior probabilities that the 'Reduction' in Week 12 Pain NRS (LOCF) of CCI [redacted] versus Placebo is (a) Greater than zero i.e. the probability of a non-zero treatment effect. (b) Greater than the target 1.25-point reduction treatment effect. Superimpose the above values on a plot of Bayesian posterior probability versus reduction on a grid ranging from zero to 2. The Bayesian

linear model will be fitted using the bfitmod function within the R Dosefinding package. Further details are included in the appendix.

6.1.6 Updated Statistical Power Calculation

The original power calculation will be re-visited using knowledge about the observed residual standard deviation (RMSE) from the CCI and CCI versus placebo ANCOVA analysis, and the observed effects of CCI and CCI versus placebo. The eMax dose response curve used for any power simulations of stage 4 data will be based upon the ED50 required to fit the observed effect of CCI at the IA and two scenarios of the CCI assumed effect size: 1) the Protocol assumed effect size of 1.25 versus placebo, and 2) the observed effect of CCI versus placebo at the IA. If the estimated ED50 is negative, then linear interpolation will be used instead of an Emax approach.

Revised power calculation will be performed as follows:

Conditional Power of Test of Dose Response Curve under original stage 4 sample size and dose allocation

The conditional power of the pre-planned final test of the dose response curve will be simulated under the above two assumptions regarding the true maximum treatment effect for CCI for data accruing after the interim analysis with sample sizes per group as per protocol and using the observed data in stage 2 and 3 combined. Further details are given in the programming appendix.

The above analyses will be performed by Premier.

6.2 PK

Pharmacokinetic data from this phase 2 study conducted in subjects with PDN will be appended to the existing PK data from other MEDI7352 studies conducted in subjects with painful osteoarthritis of the knee. Data will subsequently be analysed by population methods using nonlinear mixed-effects modelling. The existing 1-compartment population PK model with time-dependent clearance reflecting ADA-mediated elimination of the drug developed based on the SAD/MAD and phase 2B OA study data will be used as a starting point and updated as required based on the emerging new data. The analysis will be carried out using appropriate software (e.g., NONMEM, MONOLIX). The impact of prospectively selected covariates (i.e. weight), if available, on MEDI7352 exposure (e.g. clearance, volumes) will be evaluated. Population PK parameter estimates (e.g., clearance, volume, rate of absorption and bioavailability) with 95% CI from the final model will be tabulated. The uncertainty in the parameter estimates in the final model will be assessed (e.g. from the standard error estimates provided by NONMEM or from the 95% CI estimates provided by other appropriate analysis conducted using other software). Finally, the final model performance will be investigated

using a set of goodness of fit plots as well as Visual Predictive Check (VPC) method. Other evaluation methods may be used (e.g., bootstrapping) if deemed appropriate.

The above analyses will be performed by IntiQuan. Premier will supply the Serum MEDI7352 concentration dataset and ancillary variables as described in the Data Transfer Guidelines document.

6.3 Total NGF

Total NGF data collected in this phase 2 study conducted in subjects with PDN will be appended to the existing total NGF data from other MEDI7352 studies and will subsequently be analysed by population methods using nonlinear mixed-effects modelling. CCI [redacted] The existing semi-mechanistic drug-target binding population PKPD model developed based on the SAD/MAD and phase 2B OA study data will be used as a starting point and updated as required based on the emerging new data. The analysis will be carried out using appropriate software (e.g., NONMEM, MONOLIX). The impact of potential covariates (if available) on the PD parameters (e.g. maximum effect) will be evaluated, if deemed appropriate. The population PD parameter estimates with 95% CI from the final model will be tabulated. The uncertainty in the parameter estimates in the final model will be assessed (e.g. from the standard error estimates provided by NONMEM or from the 95% CI estimates provided by other appropriate analysis conducted using other software). Finally, the final model performance will be investigated using a set of goodness of fit plots as well as Visual Predictive Check (VPC) method. Other evaluation methods may be used (e.g., bootstrapping) if deemed appropriate.

The above analyses will be performed by IntiQuan.

6.4 Anti-drug Antibody

Anti-Drug Antibody response during the entire study period and at each study assessment will be summarised according to prevalence, incidence and titre value for the Safety Set.

The above analyses will be performed by Premier.

6.5 Individual Subject Profiles

Individual subject trellis-type plots presenting observed PK (concentration), ADA titre, total NGF concentration and predicted free NGF concentration profiles over time as well as individual observed daily and weekly averaged NRS score (six plots on 1 page per subject) will be generated by IntiQuan in support of the interpretation of the main efficacy data analysis conducted by PREMIER.

The time axis of each sub-plot will be in weeks. The Y-axis of each of the 6 sub-plots will be as follows:

a) Serum MEDI7352 Concentration (ng/mL) on log10 scale, with a separate plot symbol for BLOQ values.

b) ADA Titre on log scale, with a red symbol for ADA positive values and green symbol for ADA negative values

c) Serum free NGF % change from baseline (predicted) on linear scale

d) Serum total NGF concentration on log10 scale

e) NRS Daily score, values connected by lines. Reference lines for baseline average daily score and minimum daily score post-baseline.

f) Average weekly NRS score, values connected by lines. Weekly value taken from efficacy analysis approach. Reference lines for baseline average Weekly score and minimum Weekly score post-baseline.

6.6 Other Data

6.6.1 Subject Disposition and eligibility for statistical analysis

A table will be produced to show for stage 2 and 3 of the study the number of subjects:

- Screened
- Enrolled

For Total and by dose group the number of subjects:

- Randomized
- Included in the mITT population
  - Evaluable Week 12 efficacy
  - Evaluable LOCF efficacy
- Not efficacy evaluable
- Completed study
- Reasons for withdrawal

6.6.2 Demographic data

A table of arithmetic mean, standard deviation, minimum, maximum, median, 1st and 3rd quartiles and N (observed and missing), will be provided by treatment

group and total, for age. And frequency tables by treatment group and total for gender and race.

The above analyses will be performed by Premier.

7 SOFTWARE DETAILS

Efficacy: SAS version 9.4 and R version 4.2.1 will be used to create the D5680C00002 interim analysis outputs, as appropriate.

Monolix version 2019R1 (Lixoft) will be used for conducting the cross-study population analyses and R version 3.6.3 (R-project, www.r-project.org) will be used for generation of the associated outputs.

8 STATISTICAL APPENDIX

A1. Bayesian linear model to calculate posterior probabilities of the maximum treatment effect (CCI versus Placebo data) using **bFitMod** function within **DoseFinding** package

- Calculate the Least Squares Means for each dose group and their variance-covariance matrix (using package 'emmeans')
- Create indicator variable for dose: 0=Placebo and 1=CCI
- Execute **bFitMod** with:
  a. model as "linear"
  b. Independent Gaussian Priors for intercept and slope parameters: N(0,100). With starting values of 0.
  c. Lsmean Estimates and Variance-Covariance for placebo and CCI as inputs from the ANCOVA described in section 6.1.5, and
  d. simulate 100,000 draws from the posterior distribution, with seed = 301020 (to allow for independent replication).
  e. Process the saved **bFitMod** object as follows:
     - Select the 'samples' element from the saved bFitMod object
     - The 'delta' variable within the 'samples' element is the posterior value of the treatment difference between CCI and placebo
- Estimate the posterior probabilities that the treatment effect is
  a. Greater than zero

b. Greater than a 1.25-point reduction from the posterior sample of the slope parameter.

by computing the proportion of posterior 'delta' values less than zero and -1.25, respectively.

A2. Simulation of Conditional Power of the Dose Response Curve test under original stage 4 sample size and dose allocation

- There is no formula available to compute conditional power of the dose response test, therefore a simulation approach will be taken as follows:
- Calculate the residual standard deviation (RMSE) from the ANCOVA model fitted to the interim data.
- Simulate the stage 4 data for each of the four dose groups from an emax model with an appropriate ED50 and random error = residual standard deviation.

The parameters for the emax model, from which to simulate from, will be calculated (fixed) as follows:

$ED50 = 450*(Y_{IA}-Y_{450})/(Y_{450} – 450*Y_{IA}/150)$ and

$emax = Y_{450}*(ED_{50} + 450)/450$

where Y_{IA}= observed effect of CCI versus placebo, Y_{450} = one of the two scenarios of the CCI effect versus placebo.

If the estimated ED50 is negative then the data are not consistent with an Emax model therefore linear interpolation between zero and CCI will be used instead of an Emax approach for estimating the effect of the CCI dose in stage 4 as follows: Lsmean for CCI versus placebo = (CCI)*Lsmean CCI versus placebo .

The 'intercept' (E_0) of the Emax model is set to the 'intercept plus the regression term for baseline value evaluated at the average of the baseline values' from the ANCOVA model of the interim analysis. The maximum effect over placebo at the highest dose studied in stage 4 (currently planned to be CCI is set at values as specified in section 6.1.6.

The algorithm for simulating Change-from-baseline and baseline values for each subject is as follows:

- Simulate 10,000 stage 4 datasets. Each simulation consists of:
  - For each dose group, select a sample of baseline values of size as per protocol with replacement from the combined distribution of baseline values in the interim dataset.
  - For each dose group, simulate a change-from-baseline value for each subject from the simulation model conditional upon the subject's baseline value

- Combine stage 2 and 3 observed data and stage 4 simulated data and analyze using the **MCTtest** function of the **R Dosefinding** package, with the candidate models as specified in the protocol and options type=”normal”, alternative="one.sided", alpha=0.025 and addCovars = baseline.
- Output the minimum adjusted p-value of the multiplicity adjusted test

▪ Calculate conditional Power of the dose response test as 100*(number of minimum p-values < 0.025 / number of simulations)

▪ Repeat for each CCI effect scenario. If the estimated ED50 is negative then linear interpolation will be used instead of an Emax approach scenario.

9 REPORTING

In support of the interim analysis which have for primary focus efficacy, Tables and Figures will be created. In addition, results from the PK, ADA and total NGF data analysis may also be summarised in a PowerPoint presentation created by AZ CPQP/IntiQuan.

Tables and figures listed in Table 1 and Table 2, respectively, will be generated, as data permits.

Table 1 Planned Tables

Number	Description	Producer
Table 1.1.1	Demography	PREMIER
Table 1.1.2	Subject Disposition	PREMIER
Table 1.2.1	Descriptive Statistics of Weekly Average Pain NRS from Baseline and all visits to Week 12: Observed Values and Week 12 LOCF: mITT Population	PREMIER
Table 1.2.2	Descriptive Statistics of Weekly Average Pain NRS from Baseline and all visits to Week 12: Observed Values: mITT Population with week 12 NRS Weekly Averages	PREMIER
Table 1.2.3	Statistical Analysis of Change from Baseline to Week 12 Pain NRS (LOCF): ANCOVA: mITT Population	PREMIER
Table 1.2.4	Statistical Analysis of Change from Baseline to Week 12 Pain NRS: ANCOVA: mITT Population with week 12 NRS Weekly Averages	PREMIER
Table 1.2.5	Statistical Analysis of Change from Baseline to Week 12 Pain NRS: MMRM: mITT Population	PREMIER
Table A1.1	Population PK parameter estimates with 95% CI from the final PK model	IntiQuan
Table A1.2	Population PD parameter estimates with 95% CI from the final PKPD model	IntiQuan
Table A1.3	Summary of Anti-Drug Antibody responses during the study	PREMIER

Table 1 Planned Tables

Number	Description	Producer
Table A1.4	Anti-Drug Antibody results and titre summary by timepoint	PREMIER
Table A1.5	Predicted average % change from baseline in serum free NGF concentration following intravenous administration of MEDI7352 and tanezumab 2.5 and 5 mg SC	IntiQuan

Table 2 Planned Figures

Number	Description	
Figure 1.1	Mountain plot of Weekly Average to Week 12 Pain NRS (LOCF) by treatment group	PREMIER
Figure 1.2	Mountain plot of Change from Baseline to Week 12 Pain NRS (LOCF) by treatment group	PREMIER
Figure 1.3	Boxplot of Weekly Average to Week 12 Pain NRS (LOCF) by treatment group	PREMIER
Figure 1.4	Boxplot of 'Change from Baseline to Week 12 Pain NRS (LOCF)	PREMIER
Figure 1.5	Mean Weekly Average Pain NRS from Baseline to Week 12 (including Week 12 LOCF)	PREMIER
Figure 1.6	Mean Change from Baseline Pain NRS from Week 1 to Week 12 (including Week 12 LOCF)	PREMIER
Figure 1.7	Individual Spaghetti plot of Mean Weekly Average Pain NRS from Baseline to Week 12	PREMIER
Figure 1.8	Individual Spaghetti plot Change from Baseline Pain NRS from Week 1 to Week 12	PREMIER
Figure 1.9	Bayesian Predicted Probabilities of Effect Size versus Placebo	PREMIER
Figure 1.10	Conditional Power of MCP-MOD test	PREMIER
Figure A1.1	Model goodness of fit plots (population PK analysis)	IntiQuan
Figure A1.2	Visual predictive check (population PK analysis)	IntiQuan
Figure A1.3	Observed/predicted serum MEDI7352 concentration-time profiles (by participant) (population PK analysis)	IntiQuan
Figure A1.4	Observed serum MEDI7352 concentration-time profiles by ADA status (by treatment)	IntiQuan
Figure A1.5	Population mean (95% CI) serum MEDI7352 concentration-time profiles by treatment	IntiQuan
Figure A1.6	Population mean (95% CI) serum MEDI7352 concentration-time profiles by ADA status and by treatment	IntiQuan
Figure A1.7	Model goodness of fit plots (population PKPD analysis)	IntiQuan
Figure A1.8	Visual predictive check (population PKPD analysis)	IntiQuan

Table 2 Planned Figures

Number	Description	
Figure A1.9	Observed/predicted serum total NGF concentration-time profiles (by participant) (population PKPD analysis)	IntiQuan
Figure A1.10	Predicted serum free NGF concentration-time profiles (by participant) (population PKPD analysis)	IntiQuan
Figure A1.11	Observed serum total NGF concentration-time profiles by ADA status (by treatment)	IntiQuan
Figure A1.12	Predicted serum free NGF concentration-time profiles by ADA status (by treatment)	IntiQuan
Figure A1.13	Predicted median % change from baseline serum free NGF concentration-time profiles by treatment	IntiQuan
Figure A1.14	Predicted median % change from baseline serum free NGF concentration-time profiles by ADA status and by treatment	IntiQuan
Figure A1.15	Predicted median % change from baseline serum free NGF concentration-time profiles following intravenous administration of MEDI7352 and tanezumab 2.5 and 5 mg SC	IntiQuan
Figure A1.16	Individual observed serum MEDI7352 concentration, ADA titre and serum total NGF concentration profiles over time, observed daily as well as weekly averaged NRS pain scores as well as predicted serum free NGF concentration -time profiles (6 plots per participant)	IntiQuan

10 OUTPUT SHELLS EXAMPLES

The format of selected tables and figures created by Premier is described in separate documents

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Table of Contents

Approvals 2
Document History 4
Table of Contents 5
List of Tables 7
List of Figures 7
List of Abbreviations 8
1. Overview 12
2. Study Objectives and Endpoints 12
2.1. Study Objectives 12
2.1.1. Primary Objective 12
2.1.2. Secondary Objectives 12
2.1.3. Exploratory Objectives 13
2.2. Study Endpoints 13
2.2.1. Efficacy Endpoints 13
2.2.2. Safety Endpoints 14
2.2.3. Pharmacokinetic/Pharmacodynamic Variable(s) 14
2.2.4. Other Endpoints 15
3. Overall Study Design and Plan 15
3.1. Overall Design 15
3.2. Sample Size and Power 15
3.3. Study Population 16
3.4. Treatments Administered 17
3.5. Method of Assigning Subjects to Treatment Groups 17
3.6. Blinding and Unblinding 17
3.7. Schedule of Events 18
4. Statistical Analysis and Reporting 18
4.1. Introduction 18
4.2. Interim Analysis and Data Monitoring 19
5. Analysis Populations 19
6. General Issues for Statistical Analysis 20
6.1. Statistical Definitions and Algorithms 20
6.1.1. Baseline 20
6.1.2. Adjustments for Covariates 20

6.1.3. Multiple Comparisons 20
6.1.4. Handling of Dropouts or Missing Data 21
6.1.5. Analysis Visit Windows 21
6.1.6. Pooling of Sites 22
6.1.7. Efficacy Variables 22
6.1.8. Derived Variables 23
6.1.9. Data Adjustments/Handling/Conventions 25
7. Study Patients/Subjects and Demographics 26
7.1. Disposition of Patients/Subjects and Withdrawals 26
7.2. Protocol Deviations 27
7.3. Demographics and Other Baseline Characteristics 27
7.4. Exposure 28
8. Efficacy Analysis 28
8.1. Primary Efficacy Analysis 28
8.1.1. Sensitivity Analyses of the Primary Efficacy Endpoint 30
8.2. Secondary Efficacy Analysis 30
8.3. Exploratory Efficacy Analysis 31
9. Safety and Tolerability Analysis 31
9.1. Adverse Events 33
9.1.1. Adverse Events Leading to Discontinuation of IP 33
9.1.2. Deaths and Serious Adverse Events 34
9.1.3. Drug-Induced Liver Injury 34
9.1.4. Infection Risk 34
9.2. COVID-19 Vaccination and Screening 34
9.3. Clinical Laboratory Evaluations 34
9.4. Vital Signs 35
9.5. Electrocardiograms 35
9.6. Physical and Neurological Examination 36
9.7. Total Neuropathy Score-Nurse 36
9.8. Motor and Sensory Nerve Conduction Studies 36
9.9. Strength and Deep Tendon Reflexes 36
9.10. Hypersensitivity/Anaphylactic Reactions, Injection Site or Infusion Reactions 36
9.11. Prior and Concomitant Medication and Procedures 37
10. Changes from Planned Analysis 38
11. Other Planned Analysis 38

11.1. Biomarkers 38
11.2. Immunogenicity 39
11.3. Pharmacokinetic Analysis 39
12. References 40
13. Tables, Listings, and Figures 41
13.1. Demographic Data 41
13.2. Efficacy Data 42
13.3. Safety Data 43
13.4. Pharmacokinetic/Pharmacodynamic Data 46
13.5. Planned Listing Descriptions 46
13.6. Planned Figure Descriptions 48
14. Tables, Listing and Figure Shells 50
14.1. Standard Layout for all Tables, Listings, and Figures 50
15. Appendix: Calculation of Dose to achieve target effects 52

List of Tables

Table 1: Demographic Data Summary Tables and Figures 41
Table 2: Efficacy Data 42
Table 3: Safety Data 43
Table 4: Pharmacokinetic/Pharmacodynamic Data 46
Table 5: Planned Listings 46
Table 6: Planned Figures 49

List of Figures

Figure 1: Standardized Layout 51

List of Abbreviations

Abbreviation	Definition
ADA	Anti-Drug Antibody
AE	Adverse Event
AIC	Akaike Information Criterion
ALT	Alanine Aminotransferase
ANCOVA	Analysis of Covariance
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
BOCF	Baseline Observation Carried Forward
CI	Confidence Interval
CMH	Cochran-Mantel-Haenszel
COVID-19	Coronavirus Disease 2019
CSR	Clinical Study Report
DSIS	Daily Sleep Interference Scale
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
ED50, ED90	The Dose to achieve 50%, 90% of the Maximum Effect.
EMA	European Medicines Agency

Abbreviation	Definition
Emax	The Model-Based Maximum Treatment Effect Versus Placebo
ePRO	Electronic Patient-Reported Outcome System
FDA	Food and Drug Administration
gCV%	Geometric Coefficient of Variation
GEE	Generalized Estimating Equation
gmean	Geometric Mean
gSD	Geometric Standard Deviation
HL	Hy's Law
HR	Heart Rate
ICH	International Council for Harmonization
IP	Investigational Product
IV	Intravenous
IWRS	Interactive Web Response System
LLOQ	Lower Limit of Quantification
LOCF	Last Observation Carried Forward
LS	Least Squares
MCP-mod	Multiple Comparison Procedure Modelling
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified Intent-to-Treat

Abbreviation	Definition
MMRM	Mixed Effects Models Repeated Measures
NC	Not Calculable
NCA	Noncompartmental Analysis
NPS	Neuropathic Pain Scale
NQ	Not Quantifiable
NRS	Numeric Rating Scale
PD	Pharmacodynamics
PDN	Painful Diabetic Neuropathy
PGIC	Patient Global Impression of Change
CCI [redacted]	
PHT	Potential Hy's Law
PK	Pharmacokinetic
PT	Preferred Term
QTcF	QT Fridericia's Correction
CCI [redacted]	
RPOA	Rapidly Progressive Osteoarthritis
SAE	Serious Adverse Event
SAF	Safety
SAP	Statistical Analysis Plan

Abbreviation	Definition
SAS®	a Software System Used for Data Analysis
SDTM	Study Data Tabulation Model
SF-36	36-Item Short Form Health Survey
SiAP	Statistical Interim Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
TBL	Total Bilirubin
TEAE	Treatment-Emergent Adverse Event
tNGF	Total Nerve Growth Factor
TNSn	Total Neuropathy Score-Nurse
ULN	Upper Limit of Normal
ULOQ	Upper Limit of Quantification

1. Overview

This statistical analysis plan (SAP) describes the planned analysis and reporting for AstraZeneca protocol number D5680C00002 (A Randomised, Double-Blind, Placebo-Controlled, Dose-Response Study of the Efficacy and Safety of MEDI7352 in Subjects with Painful Diabetic Neuropathy), dated 13-Apr-2022 version 7.0. Reference materials for this statistical plan include the protocol and the accompanying sample data collection documents. Operational aspects related to collection and timing of planned clinical assessments are not repeated in this SAP unless relevant to the planned analysis.

The structure and content of this SAP provides sufficient detail to meet the requirements identified by the Food and Drug Administration (FDA), European Medicines Agency (EMA), and International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use: Guidance on Statistical Principles in Clinical Trials (ICH, 1998). All work planned and reported for this SAP will follow internationally accepted guidelines, published by the American Statistical Association (ASA, 2018) and the Royal Statistical Society (RSS, 2014), for ethical statistical practice.

The planned analyses identified in this SAP may be included in clinical study reports (CSRs), regulatory submissions, or future manuscripts. CCI [redacted]

The statistical plan described hereafter has been developed by blinded study team members prior to the Interim Analysis but after the Administrative Analysis has been conducted. It will be approved before final unblind, performing inferential or descriptive analysis of hard-locked data from AstraZeneca's study D5680C00002.

2. Study Objectives and Endpoints

2.1. Study Objectives

2.1.1. Primary Objective

The primary objective is to assess the efficacy of MEDI7352 versus placebo on chronic pain in subjects with painful diabetic neuropathy (PDN) currently taking standard of care medication for their PDN pain.

2.1.2. Secondary Objectives

The secondary objectives are:

- To assess the safety and tolerability of MEDI7352 in subjects with PDN
- To assess the pharmacokinetics (PK), pharmacodynamics (PD), and immunogenicity of MEDI7352 in subjects with PDN

- To characterise the dose-response relationship of MEDI7352 on chronic pain in subjects with PDN

2.1.3. Exploratory Objectives

CCI

[redacted]

2.2. Study Endpoints

2.2.1. Efficacy Endpoints

2.2.1.1. Primary Efficacy Endpoint

The primary efficacy endpoint of this study is the change in the weekly average of the average daily pain scores from the baseline week to Week 12 of MEDI7352 compared to placebo, as measured on an 11-point (0-10) numeric rating scale (NRS).

The target population is the entire patient population, i.e., the collection of all patients eligible to be included in the randomized clinical trial based on prespecified (and duly justified) inclusion/exclusion criteria.

The study was not designed using the Estimand framework. However, the following general aspects of an Estimand can be inferred: the Estimand can be generically defined as the true between-treatment difference in the target population endpoint means for the change from baseline for the Pain NRS at Week 12, while-on-treatment and regardless of prohibited or rescue medication use.

2.2.1.2. Secondary Efficacy Endpoint(s)

The secondary efficacy endpoints of this study include the following:

- Change in the weekly average of the average daily pain score, as measured on an 11-point (0-10) NRS, from baseline to Weeks 2, 4, 6, 8, and 10 of treatment and the week before the follow-up visit.
- Percentage of subjects who have achieved ≥30% and ≥50% reductions in the weekly average of the average daily pain score from baseline during Weeks 4, 8, and 12 of treatment and the week before follow-up.

- Change in Galer Neuropathic Pain Scale (NPS) from baseline to Days 28, 56, and 84 of treatment and the follow-up visit.
- Change in Daily Sleep Interference Scale (DSIS) from baseline to Days 28, 56, and 84 of treatment and the follow-up visit.
- Proportion of subjects who have 'improved', 'much improved,' or 'very much improved' relative to baseline on the Patient Global Impression of Change (PGIC) on Days 28, 56, and 84 of treatment and the follow-up visit.
- Change in the 36-item Short-Form Health Survey (SF-36) from baseline to Day 84 of treatment.
- Usage of rescue medication (yes/no) from baseline to Week 12 of treatment.

2.2.1.3. Exploratory Efficacy Endpoint(s)

CCI [redacted]

2.2.2. Safety Endpoints

The safety endpoints of this study include the following:

- Adverse events (AEs) and serious adverse events (SAEs)
- Physical and neurological examinations
- Neuropathy assessments Total Neuropathy Score-Nurse (TNSn) S
- Strength (dorsiflexion), and deep tendon reflex (knee and ankle) assessments
- Vital signs
- 12 lead digital electrocardiogram (ECGs)
- Clinical laboratory testing (hematology, chemistry, coagulation, and immunology)
- Motor and sensory nerve conduction studies
- Concomitant medications and therapies
- Injection site reactions and infusion reactions

2.2.3. Pharmacokinetic/Pharmacodynamic Variable(s)

The pharmacokinetic (PK) endpoints of the study include the MEDI7352 concentrations measurements in serum/plasma.

The pharmacodynamic (PD) endpoints of the study include total nerve growth factor (tNGF) measurements in serum/plasma.

2.2.4. Other Endpoints

The following endpoints will be assessed:

- Change in the weekly average of the average daily pain scores from the baseline week to Week 12, as measured on an 11-point (0-10) NRS, versus dose.
- Immunogenicity (ADA) assessments.

3. Overall Study Design and Plan

This is a randomised, double-blind, placebo-controlled study of MEDI7352 in subjects with moderate to severe chronic PDN persistent for 6 months or longer, not adequately controlled by standard of care treatments, caused by type 1 or type 2 diabetes mellitus. The study incorporates a screening period of up to 45 days and a 12-week double-blind treatment period during which MEDI7352 or placebo will be administered intravenously (IV) on 6 occasions, with each dose separated by 14 days. There will be a 6-week follow-up period.

3.1. Overall Design

3.2. Sample Size and Power

There will be 4 stages in the study: in the first stage, subjects will be randomly assigned to placebo or the lowest dose (CCI) until at least 10 subjects have been recruited. In the second stage, up to 30 subjects will be randomly assigned to a placebo or CCI of MEDI7352; prior to commencing the third stage, the safety and tolerability experience following administration of multiple doses of CCI in the Phase 1 study of MEDI7352 will be evaluated. In stage 3 of the study, approximately 67 subjects will be randomly assigned to placebo or CCI of MEDI7352. The third stage will include an interim analysis to enable decision making for stage 4 with respect to the sample size and dose allocation ratio. If no changes are made following the interim analysis, in stage 4 of the study, approximately 165 eligible subjects will be randomly assigned to treatment across 3 dose levels of MEDI7352 (CCI) or placebo, to ensure that approximately 236 subjects are evaluable for the efficacy analysis of stages 2 to 4 combined. The number of subjects in the fourth stage is currently planned to follow an equal treatment allocation to each of the 4 treatment groups. However, the exact number of subjects and the allocation to each dose in stage 4 will be determined after the interim analysis.

There is no formal sample size calculation for stage 1; 10 subjects in stage 1 are considered sufficient for the initial assessment of safety. The sample size for stages 2-4 combined was determined by a formal power calculation (see below) and the size of stage 3 was defined to enable decision making for the stage 4 sample size and dose allocation ratio.

This study is powered at greater than 80% to detect a statistically significant (1-sided alpha = 0.025) dose-response relationship when the true Week 12 placebo-corrected change from baseline difference at the CCI dose is 1.25 on the 11-point NRS scale (MEDI7352-placebo treatment) and the true dose-response follows a hyperbolic Emax relationship, with ED50 within the range CCI . This calculation also assumes:

- The true standard deviation (SD) is 2.4, which is based on other studies undertaken with pregabalin in PDN (Satoh et al. 2011, Lesser et al. 2004, Rosenstock et al. 2004, Tölle et al. 2008).
- The data from stages 2, 3, and 4 are combined so that the number of subjects for the dose-response analysis is 236 with the total number evaluable for placebo, CCI doses equal to 81, 37, 51, and 67, respectively. This is comprised of, assuming an overall 10% non-evaluability rate:
    - 28 out of 30 randomised in stage 2; 14 per arm
    - 60 out of 67 randomised in stage 3; 30 per arm, and
    - 148 out of 165 randomised in stage 4; 37 per arm
- The dose-response hypothesis test is multiplicity adjusted as described by Pinheiro et al. 2006 in order to control the type 1-error.

The above calculations were performed using the software R and the R-package 'DoseFinding' [https://cran.r-project.org/web/packages/DoseFinding/DoseFinding.pdf] with the following parameters:

- Population SD (of change from baseline to week 12) = 2.4
- Placebo effect = 1 point reduction in NRS and CCI effect = 2.25 reduction from baseline, ie, delta= 1.25
- Linear contrasts were determined from 5 'candidate dose' response models which are all E_{max} models with decreasing potency/increasing ED50: 7.5, 15, 30, 60, 750 µg/kg. The 5th case is essentially linear in dose. E_{max} models were chosen following the recommendations in a recent meta-analysis of dose response studies by Thomas et al., 2014.
- Power was assessed across 16 alternative true dose response curves, 12 E_{max} with ED50 ranging from 0.375 to 750 µg/kg, 3 logistic and 1 quadratic, all having a Week 12 placebo-corrected change from baseline difference at the CCI dose of 1.25.

The overall withdrawal rate is anticipated to be approximately 10%. However, since the primary analysis will use Last Observation Carried Forward (LOCF) for withdrawn subjects, and the SD estimate is taken from studies which also used the LOCF approach, the only additional subjects recruited will be to account for withdrawals in stages 2, 3, and 4 if withdrawal occurs at, or prior to, the Week 2 visit.

The number of subjects who will agree to participate in the genetic research is unknown. It is therefore not possible to establish whether sufficient data will be collected to allow a formal statistical evaluation or whether only descriptive statistics will be generated.

3.3. Study Population

Male or female (postmenopausal or surgically sterile) subjects aged ≥18 to ≤80 years with

chronic PDN persistent for 6 months or longer, not adequately controlled by standard of care treatments .

3.4. Treatments Administered

Once randomized, subjects will be dosed with either MEDI7352 or placebo on Day 1, Day 14, Day 28, Day 42, Day 56, and Day 70. MEDI7352 or placebo will be administered IV over a 60-minute period. To maintain the blind, a placebo volume equivalent to the MEDI7352 volume will be administered for each dosing.

3.5. Method of Assigning Subjects to Treatment Groups

The randomisation schedule will be computer generated using a permuted block algorithm appropriate to the treatment groups included in each stage and will randomly allocate investigational product (IP) to randomisation numbers. The randomisation numbers will be assigned sequentially through a central interactive web response system (IWRS) as subjects are entered into the study. The randomisation schedule will not be stratified, and study centre will not be a blocking factor in the randomisation schedule.

The randomisation schedule has been prepared by Premier Research before the start of the study. No one involved in the study performance will have access to the randomisation schedule before official unblinding of treatment assignment. No subject will be randomised into this study more than once.

3.6. Blinding and Unblinding

All subjects, investigators, and study personnel involved in the conduct of the study, including data management, will be blinded to treatment assignment with the exception of a specified unblinded statistician and programmer from Premier Research who will have access to the randomization code, unblinded site monitors and clinical manager from Premier Research, and the unblinded pharmacist at each study site. The unblinded study personnel will not participate in study procedures or data analysis prior to unblinding of the study data to all study related personnel. Unblinded personnel who are not otherwise involved in the study will prepare data for review and interim analysis.

Study personnel will make every effort to safeguard the integrity of the study blind to minimize bias in the conduct of the study. Treatment unblinding is discouraged if knowledge of the treatment assignment will not materially change the planned management of a medical emergency. Unblinding will be permitted in a medical emergency that requires immediate knowledge of the subject's treatment assignment.

Unblinding should be discussed in advance with the medical monitor if possible. For emergency unblinding, study personnel will use the IWRS. Only authorized users will have access to the unblinding function in the IWRS, and the IWRS will reveal the treatment information for the selected subject only. If the investigator is not able to discuss treatment unblinding in advance, then he/she must notify the medical monitor as soon as possible about the unblinding incident without revealing the subject's treatment assignment. The IWRS will also send a blinded notification to the clinical team alerting them that a break blind occurred.

The investigator or designee must record the date and reason for treatment unblinding on the appropriate electronic case report form (eCRF) for that subject. In all cases that are not emergencies, the investigator must discuss the event with the medical monitor prior to unblinding the subject's treatment assignment.

If treatment assignment is unblinded for an individual subject, study personnel will be notified of that subject's treatment assignment without unblinding the treatment assignments for the remaining subjects in the study. Thus, the overall study blind will not be compromised. If a subject's treatment assignment is unblinded, he/she will be asked to withdraw from the study. The investigator will make this decision after consultation with the medical monitor.

Overall unblinding will take place at the end of the study only after database lock has been achieved.

3.7. Schedule of Events

Please see the protocol Tables 2-1, 2-2 for a detailed schedule of events.

4. Statistical Analysis and Reporting

All efficacy and safety statistical analysis will be based on data from stages 1, 2, 3 and 4 combined, unless specified otherwise.

4.1. Introduction

Data processing, tabulation of descriptive statistics, calculation of inferential statistics, and graphical representations will primarily use SAS (release 9.4 or higher). The multiple comparison and modelling (MCP-Mod) analysis will be performed using R (release 4.2.1 or higher) and the DoseFinding package (version 1.0-3 or higher). If a use of other software is warranted, the final statistical methodology report will detail what software was used for what purposes.

Continuous (quantitative) variable summaries will include the number of subjects (n) with non-missing values, the number of missing values, arithmetic mean, SD, median, 1st, and 3rd quartiles (where applicable), minimum, and maximum.

Categorical (qualitative) variable summaries will include the frequency and percentage of subjects who are in the particular category or each possible value. In general, the denominator for the percentage calculation will be based upon the total number of subjects in the study population for the treatment group, unless otherwise specified. The denominator for by-visit displays will be the number of subjects in the relevant study population with non-missing data at each visit, unless otherwise specified.

The minimum and maximum will be reported with the same degree of precision (i.e., the same number of decimal places) as the observed data. Measures of location (mean and median) will be

reported to 1 degree of precision more than the observed data and measures of spread will be reported to 2 degrees of precision more than the observed data.

Percentages will be presented to 1 decimal place, unless otherwise specified.

Unless otherwise indicated, all statistical tests will be conducted at the 0.025 significance level using 1-tailed tests, and *P* values will be reported. For estimation purposes, 2-sided 95% confidence intervals (CI) will be presented.

Total NGF and PK concentration data will be summarized by dose as per the quantitative variables and presenting the number (n) of non-missing observations, and the n < lower limit of quantification (LLOQ). PD and PK parameters will be summarized by dose and will include the arithmetic mean, SD, geometric mean (gmean), gmean ± geometric SD, geometric coefficient of variation (gCV%), median, minimum and maximum.

4.2. Interim Analysis and Data Monitoring

Details of the interim analysis have been included in the Statistical Interim Analysis Plan (SiAP) version 1.0 dated 10-Feb-2023.

5. Analysis Populations

The following analysis populations are planned for this study:

- **Screening Population (Screened)**: All subjects who provide informed consent and/or assent and provide demographic and/or baseline screening assessments, regardless of the subject's randomisation and treatment status in the study. The Screening Set will be analysed as randomised, according to planned treatment.
- **Safety Population (SAF):** The Safety Population includes all subjects who receive at least 1 dose of double-blind study medication. The Safety Set will be analysed according to actual treatment.
- **Modified Intent-To-Treat Population (mITT):** The modified intent-to-treat population will be used for all efficacy analyses and will include all randomised subjects who receive at least 1 dose of double-blind study medication and have at least 1 daily NRS assessment while receiving double-blind treatment. The mITT Set will be analysed as randomised, according to planned treatment.
- **Pharmacokinetic Population (PK):** The PK Population will include all subjects for who a PK sample was obtained and analysed. The PK Set will be analysed according to actual treatment.

Assignment of subjects to populations will be confirmed at a blinded data review meeting to be held before the study database is locked.

If a subject is randomised incorrectly or is administered the incorrect IP, analyses of the mITT population will be based on the IWRS-assigned treatment whereas all other analyses will be based on the actual treatment.

6. General Issues for Statistical Analysis

6.1. Statistical Definitions and Algorithms

6.1.1. Baseline

For all safety endpoints, the last observation recorded prior to the first dose of treatment will be used as the baseline observation for calculations of change from baseline.

For pain diary data the baseline period is defined as the seven-day period prior to randomization, i.e., Day -7 to Day -1, inclusive. A subject is considered to have an evaluable baseline pain score if there are at least 4 days of recorded diary pain scores in the 7-day period.

6.1.2. Adjustments for Covariates

In addition to treatment group, the baseline value of the variable undergoing analysis and the co-medication type (Anticonvulsant versus Antidepressant) will be included in the analysis of covariance (ANCOVA) model as additive covariates. Co-medication type will be determined by blinded clinical review of each subject's medication record at baseline.

Covariates in the mixed effects models repeated measures (MMRM) and generalized estimating equations (GEE) analyses include those specified for the ANCOVA analyses, together with time and its interaction with dose group.

The crossing of co-medication type and median baseline pain score will be used as strata in the Cochran-Mantel-Haenszel (CMH) model tests. Assuming two co-medication types, the strata will be:

1) Anticonvulsant (Baseline NRS < Median),
2) Anticonvulsant (Baseline NRS > Median),
3) Antidepressant (Baseline NRS < Median),
4) Antidepressant (Baseline NRS > Median).

Where the median baseline NRS is calculated over all subjects.

6.1.3. Multiple Comparisons

A multiple comparison procedure modelling approach (MCP-Mod) on LOCF data will be used for primary efficacy endpoints.

No adjustments will be made for multiple comparisons outside the MCP-Mod approach.

6.1.4. Handling of Dropouts or Missing Data

For the analyses of the primary efficacy endpoints based on the mITT Population, a variety of methods will be used to deal with missing data, including:

- Primary Method: LOCF.
- Observed cases analysis.
- Baseline observation carried forward (BOCF)

Subjects with missing weekly average NRS baseline data (i.e., zero or 1-3 days of diary pain scores) will not be included in the efficacy analysis because the primary analysis is change-from-baseline. If a subject has zero or $\leq$3 days of diary pain data in each of the possible post-baseline seven day periods ending within the protocol definition of week 12 (day 84 $\pm$ 3), then an imputed 'week 12 LOCF' weekly average NRS pain score will be calculated from the latest 7 'non-missing' entries of the subject's diary closest to their nominal week 12 visit (i.e., the latest 7 day period containing at least 4 NRS values), provided that this would qualify as at least 'week 2' according to the windowing outlined in Section 6.1.5. Otherwise, the week 12 LOCF weekly average NRS pain score will be set to missing.

6.1.5. Analysis Visit Windows

Statistical analyses will be based on scheduled visits and windows as per Protocol Table 2-1: Schedule of Events. If an assessment falls between 2 windows, then the closest visit will be used only if an assessment result is not provided within that window. All other visits will be listed only as unscheduled visits. For presentation purposes these will be mapped to the visit prior and labeled, e.g., Unscheduled Visit 3.1, if Visit 3 was the closest date prior.

For pain diary data the following analysis periods will be defined:

- Week X_i: the 7-day period ending within the protocol window Day $Y_i \pm 3$ where at least 4 days out of 7 have recorded diary pain scores. Where several such windows exist the one ending closest to day Y_i will be selected. If there are two such windows that are equidistant from day Y_i, then the one with the largest number of diary entries will take precedence. If they have the same number of entries, then the later of the two end dates will be chosen. If no such window exists, then week X_i will be considered missing for the purposes of weekly average scoring.

  Where:

  - X_1=2, Y_1=14
  - X_2=4, Y_2=28
  - X_3=6, Y_3=42
  - X_4=8, Y_4=56

- X_5=10, Y_5=70
- X_6=12, Y_6=84

- The week before follow-up is defined as the 7-day period prior to the last day of pain diary data for subjects completing the study (i.e., entering in the Week 18) where at least 4 days out of 7 have recorded diary pain scores.

6.1.6. Pooling of Sites

Analysis by investigative site will not be conducted.

6.1.7. Efficacy Variables

6.1.7.1. Pain Numerical Rating Scale

Subjects will assess their perceived average neuropathic pain over the previous 24 hours using an 11-point NRS, with 0 representing no pain and 10 representing the worst pain imaginable. Subjects will be instructed to assess their average daily pain at approximately the same time every morning, and to record their response in a subject diary (ePRO).

6.1.7.2. Neuropathic Pain Scale

Subjects will assess their neuropathic pain using the Galer NPS. The NPS includes 2 descriptors of pain, including intensity and unpleasantness, and 8 descriptors that assess specific qualities of neuropathic pain: sharp, hot, dull, cold, sensitive, itchy, deep, and surface pain. Each of these 10 dimensions has a 0 to 10 NRS in which 0 is equal to no pain and 10 equals the most intense pain. There is an additional descriptor about duration and frequency of pain, which has a 1 to 3 NRS. In which 1 = I feel a background pain all the time and occasional flare-ups (breakthrough pain) some of the time, 2 = I feel a single type of pain all the time, and 3 = I feel a single type of pain only sometimes. Other times, I am pain free.

6.1.7.3. Daily Sleep Interference Scale

Subjects will assess how their neuropathic pain interferes with their sleep using the DSIS. The DSIS is an 11-point Likert scale, with 0 indicating that pain did not interfere with sleep and 10 indicating that pain completely interfered with sleep. The DSIS is completed by subjects once a day (upon awakening) to accurately capture variability in sleep interference due to pain on a daily basis, thus minimizing recall bias.

6.1.7.4. Patient Global Impression of Change

Subjects will rate their overall improvement in health status using the PGIC. The PGIC consists of a 7-point scale where 1 = “very much improved” and 7 = “very much worse.” Subjects will be asked the following question: “How would you rate your overall improvement with treatment during the clinical study?” The response options include the following:

- Very Much Improved - 1
- Much Improved - 2
- Minimally Improved - 3
- No Change - 4
- Minimally Worse - 5
- Much Worse - 6
- Very Much Worse - 7

6.1.7.5. Short-Form Health Survey

The subject's health status and quality of life will be assessed using the SF-36. The SF-36 assesses 8 health concepts: 1) limitations in physical activities because of health problems; 2) limitations in social activities because of physical or emotional problems; 3) limitations in usual role activities because of physical health problems; 4) bodily pain; 5) general mental health (psychological distress and well-being); 6) limitations in usual role activities because of emotional problems; 7) vitality (energy and fatigue); and 8) general health perceptions. The items use Likert-type scales with either 5 or 6 points, or 2 or 3 points. Scores will be derived by the validated built-in scoring tool. Higher SF-36 scores indicate a better state of health.

6.1.7.6. Rescue Medication Use

Subjects will record all rescue medications they take for neuropathic pain in a paper diary. This will be transcribed in to the eCRF collecting usage, date and time of rescue medication, medication administered, dose, frequency and route.

Subjects will be grouped by the following for rescue medication use:

- Compliant with protocol guidance on permitted therapies
- Non-compliant with protocol guidance on permitted therapies

A review of medications will be conducted at a blinded data review meeting to be held before the study database is locked.

6.1.7.7. CCI

CCI

[redacted]

6.1.8. Derived Variables

- Change from baseline = value at current time point – value at baseline.

- Reference End Date = Date of completion/discontinuation.
- Study duration = Reference end date – date of first dose of treatment + 1
- Duration of exposure (days) = min(date of last dose of treatment + 14 days or date of death) – date of first dose of treatment + 1.
- Treatment-emergent AEs (TEAEs) are defined as:
    - AEs with onset at the time of or following the start of treatment with IP and not more than 30 days after the last administration of IP, or
    - AEs starting prior to the start of treatment but increasing in severity or relationship at the time of, or following, the start of treatment with IP and not more than 30 days after the last administration of IP.
- Average Baseline Pain NRS = the arithmetic average of the 'non-missing' daily pain scores within the baseline period defined in Section 6.1.1. For example, if a subject has 5 days of non-missing pain scores their average will be calculated over 5 days, not the full 7-day baseline period.
- Average Week X Pain NRS = the arithmetic average of the 'non-missing' daily pain scores within each subject's specific week X period defined in Section 6.1.5.
- Average Week 12 Pain NRS (LOCF) = the arithmetic average of the 'non-missing' daily pain scores within each subject's specific week 12 period or according to the imputed LOCF/BOCF approach defined in Section 6.1.4.
- Change from Baseline to Week X Pain NRS = for each subject 'Average Week X Pain NRS' minus 'Average Baseline Pain NRS'.
- Change from Baseline to Week 12 Pain NRS (LOCF/BOCF) = for each subject 'Average Week 12 Pain NRS (LOCF)' minus 'Average Baseline Pain NRS'.
- Galer NPS Total Score (ranges from 0 to 100): sum of Pain Intensity, Pain Unpleasantness, Pain Sharpness, Pain Hotness, Pain Dullness, Pain Coldness, Pain Sensitivity, Pain Itching, Deep Pain Intensity, and Surface Pain Intensity (All in an 11-point NRS).
- Change from Baseline to Week X Galer NPS Total Score = for each subject 'Galer NPS Total Score' minus 'Baseline Galer NPS Total Score'.
- Total number of days rescue medication was used = End Date of Medication - Start Date of medication + 1. Each day on which rescue medication was used at least once is counted.

- Cumulative consumption (mg) of paracetamol rescue medication use = Total dose of rescue medication (mg) consumed during the days in which paracetamol was used.
- Average daily dose (mg) of paracetamol rescue medication use = Cumulative consumption of paracetamol rescue medication (mg) /total number of days paracetamol rescue medication was used.

6.1.9. Data Adjustments/Handling/Conventions

All collected data will be presented in listings. Data not subject to analysis according to this plan will not appear in any tables or graphs but will be included only in the data listings.

All *P* values will be displayed in four decimals and rounded using standard scientific notation (e.g., 0.XXXX). If a *P* value less than 0.0001 occurs it will be shown in tables as <0.0001.

AEs and medical histories will be coded using the latest version of the Medical Dictionary for Regulatory Activities (MedDRA) thesaurus available at time of programming.

If partial dates of AEs occur, the convention for replacing missing dates for the purpose of TEAE is as follows: if just day is missing then the day assigned is the first day of the month or the date of first dose (if in the same month), whichever is later; if just month is missing then the month assigned is the month of the first dose, unless that results in a date prior to the first dose in which case the month after the first dose is used; and if both month and day are missing then the month assigned is the month of the first dose and the day assigned is either the first day of the month or the first dose date, whichever is later.

If partial times occur, the convention is as follows: if the missing time occurs on the day of the first dose and both the hour and minute are missing then the time assigned is the time of the first dose, otherwise if both the hour and minute are missing and the date is not the date of first dose the time assigned is 12:00; if the date is the same as the date of the first dose and only hour is missing the hour assigned is 12 or the hour of first dose, whichever is later, and if the date is the same as the date of first dose and only the minute is missing the minute assigned is 30 or the minute of first dose, whichever is later. Otherwise the hour assigned is 12 if the hour is missing and the date is not the same as the date of first dose and the minute assigned is 30 is the the date is not the same as the date of first dose.

These conventions will be applied only to AE onset dates and times with the following precaution: if the missing date and time reflect the date and time of onset of an AE, the modified date and time will be constructed to match the first documented date/time post drug administration while preserving the order in which the AE was reported in the eCRF.

In general, for quantitative laboratory values reported as '<X' or '≤X', the LLOQ will be used for analysis (i.e., the value of X will be used in the analysis for lab values reported as '<X' or '≤X'). Similarly, for quantitative laboratory values reported as '>X' or '≥X', the upper limit of

quantification (ULOQ) will be used for analysis (i.e., the value of X will be used in the analysis for lab values reported as '>X' or '≥X').

For analysis purposes, repeat laboratory test results will not be used unless the original laboratory value is missing or indicated as invalid, in which case the first non-missing repeated laboratory value will be used for data analysis.

ADA titre reported as <30 (below the minimum required dilution) is a negative result for the presence of ADA.

For descriptive statistics of serum concentration summaries:

- At a time-point where less than or equal to 50% of the values are not quantifiable (NQ, below LLOQ), all NQ values will be set to the LLOQ, and all descriptive statistics will be calculated accordingly.
- If more than 50%, but not all, of the concentrations are NQ, the geometric mean, geometric mean ± geometric SD and gCV% will be reported as not calculable (NC). The maximum value is reported from the individual data, and the minimum and median are set as NQ.
- If all concentrations are NQ at a time-point, the geometric mean, minimum, median and maximum are reported as NQ and the gCV% and geometric mean ± geometric SD as NC.

7. Study Patients/Subjects and Demographics

7.1. Disposition of Patients/Subjects and Withdrawals

The total number of subjects for each of the following analysis populations will be presented for the Screening Population by randomized treatment group and overall:

- Screening Population
- Safety Population
- mITT Population
- Included in the mITT population
  - Evaluable Week 12 efficacy
  - Evaluable LOCF efficacy
- Not efficacy evaluable
- PK Population

For the Screening Population, disposition will include tabulation of:

- the number of screened subjects
- the number of re-screened subjects
- the number of enrolled subjects

The output will be further presented by treatment group and overall summarising:

- the number of randomized subjects

- the number of subjects who completed study treatment
- the number of completed subjects
- the number of subjects withdrawing (discontinued)
- the reasons for discontinuation from study treatment and withdrawal from the study.

For all categories of subjects by treatment group, percentages will be calculated using the number of subjects randomized as the denominator.

7.2. Protocol Deviations

Major protocol deviations, as determined by a Sponsor blinded review of the data prior to database lock and unblinding of the study will be reported in listings.

The Sponsor or designee will be responsible for producing the final deviation file. This file will be finalized prior to database lock, and all information will be included in the SDTM.DV domain (deviations domain).

All protocol deviations will be presented in a data listing, with a flag to indicate if a deviation was considered major.

A summary table by treatment group and overall will be generated based on protocol deviation severity (minor/major) and the classification of protocol using the following categories:

- Inclusion
- Exclusion
- Study drug
- Assessment – safety
- Assessment– efficacy
- Lab/endpoint data
- Visit window
- Informed consent
- Prohibited co-medication
- Overdose/misuse
- Other

7.3. Demographics and Other Baseline Characteristics

Descriptive summaries of the demographic and other baseline characteristics will be presented for all analysis populations. All demographic and baseline characteristics will be presented both overall and by treatment group.

The following demographic and baseline data will be presented in tables:

- Demographics: age, gender, ethnicity, race, height, weight, and body mass index (BMI)

- For female the number and percentage of women surgically sterile and postmenopausal will be described.
- Diagnosis of osteoarthritis: number of subjects with osteoarthritis diagnosis and area affected, clinical significance, radiological investigations, radiological significance, Kellgren-Lawrence score.

The number and percent of subjects reporting various medical histories, grouped by MedDRA system organ class (SOC) and preferred term (PT), will be tabulated by treatment group.

This analysis will be conducted for the Safety Population.

7.4. Exposure

The following parameters of study drug exposure and compliance will be summarized by treatment group for the Safety Population:

- Maximum number of doses administered
- Total duration of exposure
- Total (cumulative) dose infused

In addition, any incomplete infusions will be listed.

8. Efficacy Analysis

All efficacy variables will be summarized descriptively including number of observations, number of missing values, mean, SD, minimum, median, and maximum for continuous variables, and frequency of observations in each category and percentage for categorical variables.

Primary and secondary endpoint efficacy data will be tabulated according to the observed cases, LOCF, and BOCF approaches.

8.1. Primary Efficacy Analysis

The primary efficacy endpoint of this study is the change in the weekly average of the average daily pain scores from the baseline week to Week 12 measured on an 11-point (0-10) NRS.

MCP-Mod approach. The main statistical analysis of the primary efficacy endpoint will use the MCP-Mod approach on LOCF data, which is a well-established statistical methodology for establishing both the existence of a dose response and modelling the underlying dose-response relationship. The modelling step ('MOD' step) from the MCP-MOD approach will only be conducted if stage 4 is initiated, otherwise there would be insufficient dosing data to fit the non-linear models.

There are two steps to MCP-Mod:

1. The 'MCP' step is a rigorous method to establish presence of a dose response while protecting the type I error and, if the dose-response relationship is statistically significant, then
2. The 'MOD' step estimates the dose response function and associated model parameters.

The MCP test will use linear contrasts corresponding to the five candidate models described in Section 3.2. The test will use pre-specified model parameters and optimal contrasts for each will be generated. The hypotheses are as follows:

Null hypothesis (H_0): Optimal contrasts $\mu \geq 0$ for all models

Alternative hypothesis (H_A): Optimal contrasts $\mu < 0$ for at least one model

where μ is the true event rate.

The underlying model will be an ANCOVA with dependent variable 'change from baseline to Week 12 (LOCF)', and independent variables will include:

- dose group as a factor variable with the placebo group as the reference level
- baseline score, i.e., baseline weekly average pain (NRS), as a continuous variable
- co-medication type.

The random error is assumed to be normally and independently distributed with constant variance. The parameter estimates of the difference between each dose group and placebo, least square (LS) Means estimates of change from baseline to Week 12 for each dose, standard errors, 95% unadjusted, 'Lalonde-type' asymmetric CI (i.e., lower limit of 1-sided 90% CI and upper limit of 1-sided 80% CI), and *P* values will be presented.

If the MCP test is statistically significant, then the MOD step will select the most appropriate model from hyperbolic E_{max}, sigmoidal E_{max} or linear using the 'E_{maxlin}' approach as described by Kirby et al (2011). From this model (including the same covariates as the ANCOVA model), various estimates will be derived (together with CI) of parameters of interest such as ED50, effective dose to achieve 90% of maximum effect (ED90), dose to achieve selected target effects, and model estimates of the treatment effect at doses studied (see Appendix in Section 15).

MMRM: In addition, changes from baseline in continuous endpoints will be compared between treatment groups using mixed models repeated measures including terms for:

- co-medication type (as a factor)
- treatment (as a factor)
- time (as a factor)
- the interaction between treatment and time point
- and the baseline value of the variable undergoing analysis

The mixed model for repeated measure will use average of average daily pain score of observed data at week 2, 4, 6, 8, 10, and 12. An unstructured covariance matrix will be used to model the

within-subject errors. The Kenwards-Roger method will be used to estimate degrees of freedom. If this analysis fails to converge, a simpler structure (e.g., first-order ante-dependent or heterogeneous compound symmetry structures) will be found using Akaike information criterion (AIC).

The results will be presented using LS Means estimates, corresponding 95% CI for each treatment group and timepoint, along with the LS Means of differences with Placebo, standard error, 95% CI and p-values.

The primary efficacy analysis will be based on the mITT population.

8.1.1. Sensitivity Analyses of the Primary Efficacy Endpoint

To complement the MCP-MOD outputs, estimates and CI of each pairwise comparison versus placebo from the ANCOVA model described in the MCP step will be produced.

8.2. Secondary Efficacy Analysis

The MMRM model outlined in Section 8.1 will be applied for secondary endpoints using observed cases:

- Change in Galer NPS total score from baseline to Days 28, 56, and 84 of treatment and the follow-up visit.
- Change in DSIS from baseline to Days 28, 56, and 84 of treatment and the follow-up visit.
- Change in the eight SF-36 parameters from baseline to Day 84 of treatment.

A GEE approach for binary data will be used for the following dichotomous endpoints:

- Percentage of subjects who have achieved ≥30% reductions in the weekly average of the average daily pain score from baseline during Weeks 4, 8, and 12 of treatment and the week before follow-up.
- Percentage of subjects who have achieved ≥50% reductions in the weekly average of the average daily pain score from baseline during Weeks 4, 8, and 12 of treatment and the week before follow-up.

The GEE model specification will include a binomial distribution, a logit link function, and an unstructured covariance matrix. If this analysis fails to converge, a simpler structure (e.g. first-order autoregressive or compound symmetry structures) will be found using AIC. The model will include terms for:

- co-medication type (as a factor)
- treatment (as a factor)
- time (as a factor)
- the interaction between treatment and time

A CMH test stratified by the crossing of co-medication subgroup and median baseline pain score will also be carried out for the above dichotomous endpoints. The CMH risk difference at Week 12 will be estimated between the treatment group and placebo. The number and percentage of subjects meeting the reduction response will be displayed, along with the risk difference, 95% CI and *P* value.

The proportion of subjects who have 'improved', 'much improved,' or 'very much improved' relative to baseline on the PGIC on Days 28, 56, and 84 of treatment and the follow-up visit will be tested using a CMH statistics.

The efficacy analysis of secondary endpoints will be based on the observed cases and on the mITT population.

Usage of rescue medication (yes/no) will be summarized by dose group for each visit from baseline to Week 12 of treatment and over the whole treatment period. The following additional variables will be derived and summarised:

- Total number of days rescue medication was used.
  - Each day on which rescue medication was used at least once is counted.
- Cumulative consumption (mg) of paracetamol rescue medication use.
  - Calculated as the total dose of rescue medication (mg).
- Average daily dose (mg) of paracetamol rescue medication use.
  - Calculated as: cumulative consumption of rescue medication (mg)/total number of days rescue medication was used.

8.3. Exploratory Efficacy Analysis

CCI

[redacted]

9. Safety and Tolerability Analysis

All safety analyses will be performed on the Safety Population using descriptive statistics. Descriptive summaries by treatment group and overall will be produced. No inferential statistical tests will be performed.

The analysis of safety assessments in this study will include summaries of the following categories of safety and tolerability data collected for each patient:

- Adverse events
    - TEAEs
    - SAEs
    - Significant AEs
        - TEAEs leading to discontinuation of IP
    - AEs of Special Interest
        - Positively-adjudicated possible or probable rapidly progressive osteoarthritis (RPOA), subchondral insufficiency fractures, primary osteonecrosis, or pathological fracture
        - Infections that meet SAE and/or severe AE criteria
        - Anaphylactic reactions or infusion-related reactions that lead to permanent discontinuation of administration of IP
    - TEAEs associated with abnormal liver
    - Any deaths

Drug induced liver injuryClinical laboratory investigations

- Vital signs
- Electrocardiograms (ECG)
- COVID-19 screening
- Physical and neurological examination
- Total neuropathy score-nurse
- Motor and sensory nerve conduction studies
- Strength and deep tendon reflexes
- Hypersensitivity /Anaphylactic reactions
- Injection site or infusion reactions
- Liver diagnostic investigations, risk factors, signs and symptoms.
- Infection diagnostic investigations, risk factors, signs and symptoms.
- Prior and concomitant medications and therapies

9.1. Adverse Events

A summary table by treatment group will present the number and percent of subjects reporting:

- Any AEs
- Non-serious AEs occurring in more than 5% of subjects
- Any TEAEs
- Any SAEs
- Any TEAEs possibley related to study drug
- Any TEAEs leading to discontinuation of IP
- Any SAEs possibley related to study drug
- Life-threatenings SAEs
- SAEs resulting in death

Summaries of the incidence of TEAEs will be displayed by treatment group, by ADA status, by severity and by:

- SOC and PT
- SOC, PT, and maximum severity (mild, moderate, severe)
- SOC, PT, and maximum causality (not related, possibly related) to the study drug

In the summaries showing severity and relationship to study drug the event with the maximum severity or strongest relationship will be reported. If a particular event is missing the severity and/or relationship, then the strongest possible severity or relationship will be assumed for analysis (severity = severe, relationship = related).

In the case of multiple occurrences of the same AE within the same subject, each subject will only be counted once for each level of summarization.

All AEs will be presented in a by-treatment and by-subject listing, detailing the verbatim term given by the Investigator, the PT, SOC, onset date and time, end date and time, severity, outcome, relationship to study drug, action taken with study drug, other action taken, seriousness, and criteria for seriousness.

9.1.1. Adverse Events Leading to Discontinuation of IP

A summary of incidence rates (frequencies and percentages) of TEAEs leading to discontinuation of IP, by treatment group, SOC, and PT will be prepared. The table will also be produced separately by maximum severity and maximum causality.

A data listing of TEAEs leading to discontinuation of IP will also be provided, displaying details of the event(s) captured on the rCRF.

9.1.2. Deaths and Serious Adverse Events

Any deaths that occur during the study and serious adverse events will be listed.

A summary of incidence rates (frequencies and percentages) of SAEs by treatment group, SOC, and PT will be prepared. The table will also be produced separately for life-threatening SAEs, for SAEs with outcome death and for SAEs by relationship to study medication.

9.1.3. Drug-Induced Liver Injury

A summary of incidence rates of TEAEs associated with abnormal liver by treatment group, SOC, and PT will be prepared.

The type and the results of the liver diagnostic investigation performed will be tabulated by treatment group.

The number and percentage of subjects within each type of liver risk factors and style events will be tabulated by treatment group. Liver signs and symptoms will be presented in the same way.

9.1.4. Infection Risk

A summary of incidence rates of infections that meet SAE or severe AE criteria by treatment group, SOC, and PT will be prepared.

The type and the results of infection diagnostic investigation performed will be tabulated by treatment group.

The number and percentage of subjects within each type of infection risk factors and style events will be tabulated by treatment group. Infection signs and symptoms will be presented in the same way.

9.2. COVID-19 Vaccination and Screening

The number and percentage of fully vaccinated subjects at baseline will be summarized by treatment group.

The symptoms, tests, and results from coronavirus disease 2019 (COVID-19) screening will be tabulated for each visit by treatment group.

COVID-19 vaccination, signs, symptoms and impact will be presented in listings.

9.3. Clinical Laboratory Evaluations

Absolute values and changes from baseline will be summarized using descriptive statistics by

treatment group and visit for chemistry, hematology, coagulation, and urinalysis tests.

The number of subjects with clinical laboratory values (chemistry, hematology, coagulation, and urinalysis) categorized as below, within, or above normal ranges (or as either normal or abnormal for urinalysis variables that do not have quantitative ranges) and whether they are clinically significant or not will be tabulated for each clinical laboratory analyte by treatment group and visit. A shift table showing change from baseline in range categories for each clinical laboratory analyte will be produced by treatment group and by visit.

The number of subjects with values for Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥ 3 × upper limit of normal (ULN), and with values for total bilirubin (TBL) ≥ 2 × ULN will be summarized in AST, ALT vs. TBL shift tables to identify Potential Hy's Law (PHL) and Hy's Law (HL) cases by treatment group.

Diagnostic immunology, urine pregnancy, and urine drug tests will be presented in by-subject listings only.

All laboratory values will be displayed in the data listings and those that are outside the normal range will be flagged, along with corresponding normal ranges.

9.4. Vital Signs

Descriptive summaries of actual values and changes from baseline by treatment group, visit and time point will be presented for:

- Supine heart rate
- Supine systolic blood pressure
- Supine diastolic blood pressure
- Respiratory rate
- Body temperature
- Standing heart rate
- Standing systolic blood pressure
- Standing diastolic blood pressure

Height, weight, and BMI will be presented at baseline only.

9.5. Electrocardiograms

The number and percentage of subjects with normal, abnormal not clinically significant, and abnormal clinically significant ECG results will be summarized by treatment group and by visit.

If applicable (digital ECGs), descriptive summaries will be presented by treatment group, visit and time point (for Day 1 only) for ECG measures of PR, QRS, QT, RR intervals and for the calculated variables QTcF and HR for each treatment group and time point.

Heart rate (HR) and Fridericia's correction (QTcF) will be derived as follows:

Heart Rate (HR)	$HR = 10^3 \frac{60}{RR_{msec}}$
Fridericia's Correction (QTcF)	$QTc_f = \frac{QT_{msec}}{\sqrt[3]{RR}}$ sec

9.6. Physical and Neurological Examination

The physical and neurological examination findings will be presented in listings.

9.7. Total Neuropathy Score-Nurse

Descriptive summaries of the TNSn will be presented by treatment groups and by visit. Additionally, the number and percentage of subjects within each category (0, 1, 2, 3, and 4) for each sub-score (sensory symptom, motor symptom, autonomic symptom, pin sensibility, vibration sensibility) will be summarized by treatment group and by visit.

9.8. Motor and Sensory Nerve Conduction Studies

Amplitude, peak latency, conduction velocity, and duration of nerve action potentials will be summarized by treatment group and visit for each location and evaluation type. The number of subjects with normal and abnormal evaluation will be tabulated by treatment group and by visit.

9.9. Strength and Deep Tendon Reflexes

The number and percentage of subjects within each category of the ankle dorsiflexion strength and the deep tendon reflexes will be tabulated by treatment group and by visit .

9.10. Hypersensitivity/Anaphylactic Reactions, Injection Site or Infusion Reactions

The type and symptoms of hypersensitivity/ anaphylactic reactions will be tabulated by treatment group.

Injection site reactions will be tabulated describing the severity of pain, tenderness, erythema/redness, and induration/swelling by treatment group and by visit.

Anaphylactic reactions and infusion related reactions will be summarized in line with AEs, displayed by treatment group and by:

- SOC and PT
- SOC, PT, and maximum severity (mild, moderate, severe)

Hypersensitivity/anaphylactic and infusion related reactions will also be presented in a by-

treatment and by-subject listings, detailing type of reaction, severity grade for symptom with highest severity and onset time for hypersensitivity/anaphylactic reactions, and assessment result for injection site or infusion related reactions.

9.11. Prior and Concomitant Medication and Procedures

Prior medications will be presented separately from concomitant medications.

Medications will be coded using the latest version of the WHO Drug Dictionary.

Medications that started before first dose of study medication will be considered prior, whether they were stopped before first dose of study medication or not.

A concomitant medication is defined as any medication continuing or starting after first dose of study medication. This includes medications which start before first dose of study medication and continue while on-treatment, and medications that started after first dose of study medication.

The frequency and percentage of concomitant medications will be summarized by Anatomical Therapeutic Chemical (ATC) class 2 and preferred name by treatment groups, unless otherwise specified.

In listings, all medications will be displayed.

If the start/stop dates of a medication are partially or completely missing, then the medication will be assumed to be concomitant if it cannot be definitely shown from the start/stop dates that it was not administered while on-treatment. Missing dates will not be replaced.

Thus, the following approach will be taken for exclusion from concomitant medications because of discontinuation before start of treatment:

- If the stop day is missing but the month is complete, then the medication will be excluded from concomitant medications only if the stop month is before the month of the first dose of study medication.
- If the stop day and month are missing but the year is complete, then the medication will be excluded from concomitant medications only if the stop year is before the year of the first dose of study medication.
- If the stop date is completely missing, then the medication will not be excluded.

For concomitant medication exclusion (because of the late start after the end of the treatment period):

- If the start day is missing but the month is complete, then the medication will be excluded from concomitant medications only if the start month is after the last month of the treatment period.

- If the start day and month are missing but the year is complete, then the medication will be excluded from concomitant medications only if the start year is after the year of the treatment period.
- If the start date is completely missing, then the medication will not be excluded.

A similar approach will be used for summarizing concomitant procedures.

10. Changes from Planned Analysis

CCI [redacted]

The PK endpoints involving derivation of PK parameters for each dose and for each subject will be conducted by a population PK analysis of the data as part of a pooled data analysis instead of by a noncompartmental analysis (NCA). This will be documented in the CSR as a change in planned analysis. The pooled data analysis will be described in a separate modelling analysis plan. As a result, description of TLFs related to PK parameters are removed from this SAP.

Additional analyses with pooled site as a covariate are not going to be conducted and as such, they are removed from this SAP.

It was planned to have a supplementary analysis to the primary using an adaptive MCP-MOD method. In this analysis, stages 2+3 and stage 4 were going to be analysed separately and the results combined using an inverse-normal *P* value combination function (with weights related to the original planned sample sizes). This supplementary analysis is removed from this SAP.

The Cochran-Mantel-Haenszel test for the non-binary categorical endpoints has been extended to include the secondary endpoint of pain response.

11. Other Planned Analysis

11.1. CCI [redacted]

CCI [redacted]

11.2. Immunogenicity

Blood samples will be collected for assessment of ADA levels. Anti-Drug Antibody response during the entire study period and at each study assessment will be summarised according to ADA category and titre value for the Safety population with evaluable ADA results. A listing of the ADA test results will be produced.

For immunogenicity analysis, the presence of detectable (i.e., positive) ADAs against MEDI7352 will be reported. ADA results from each sample are reported as either positive or negative. In addition, the ADA titer result will be reported for samples confirmed positive for the presence of ADAs. A participant is defined as being ADA-positive if a positive ADA result is available at any time, including baseline and all post-baseline measurements, otherwise ADA negative.

The following ADA categories will be determined:

- ADA positive if a collected sample is tested positive at any time during the study, including baseline and/or post-baseline. (The percentage of these participants in a population is known as ADA prevalence).
- Treatment-emergent ADA positive (TE-ADA+): A positive post-baseline result and either of the following statements holds:
    - Baseline is ADA negative and at least one post-baseline assessment is ADA positive. This is called treatment-induced ADA positive.
    - Baseline is ADA positive, and the baseline titre is boosted by greater than the variability of the assay (i.e., ≥X-fold increase, commonly 4-fold) at ≥1 post-baseline timepoint. This is called treatment-boosted ADA positive.

  (The percentage of these participants in a population is known as ADA incidence)
- Only baseline positive if a collected sample is tested positive at baseline.
- Non-Treatment-emergent ADA positive (non-TE-ADA+): Participants who are ADA positive but not fulfilling the conditions for TE-ADA+.
- Treatment-emergent Persistently ADA positive: ADA negative at baseline and having at least 2 post-baseline ADA positive measurements with ≥16 weeks (112 days) between first and last positive, or an ADA positive result at the last available post-baseline assessment.
- Treatment-emergent Transiently ADA positive: ADA negative at baseline and at least one post-baseline ADA positive measurement and not fulfilling the conditions for persistently positive
- ADA positive post-baseline and positive at baseline.

11.3. Pharmacokinetic Analysis

Pharmacokinetic concentration data will be summarized using descriptive statistics by dose and treatment visit overall and by ADA status (positive/negative) presenting the number (n) of non-

missing observations, and the n < LLOQ. A figure of geometric mean (with and without gSD) serum MEDI7352 concentration over time by treatment group will be generated (overall and by ADA status (positive/negative)). Additionally, pharmacokinetic concentration data will be listed and presented graphically as spaghetti plots of individual participant profiles by treatment group and ADA status (positive/negative).

12. References

1. ICH (1998) ICH Harmonised Tripartite Guideline. Statistical Principles for Clinical Trials E9; 1998. https://database.ich.org/sites/default/files/E9_Guideline.pdf
2. ASA. (2018) Ethical Guidelines for Statistical Practice. Prepared by the Committee on Professional Ethics, April 2018. http://www.amstat.org/about/ethicalguidelines.cfm
3. RSS. (2014) The Royal Statistical Society: Code of Conduct, 2014. http://www.rss.org.uk/Images/PDF/join-us/RSS-Code-of-Conduct-2014.pdf.
4. Satoh J, Yagihashi S, Baba M, Suzuki M, Arakawa A, Yoshiyama T. Efficacy and safety evaluation of pregabalin treatment over 52 weeks in patients with diabetic neuropathic pain extended after a double-blind placebo-controlled trial. *J Diabetes Investig*. 2011;2(6):457-463. Doi: 10.1111/j.2040-1124.2011.00122.x.
5. Lesser H, Sharma U, LaMoreaux L, Poole RM. Pregabalin relieves symptoms of painful diabetic neuropathy: a randomized controlled trial. *Neurology*. 2004;63(11):2104-2110.
6. Rosenstock J, Tuchman M, LaMoreaux L, Sharma U. Pregabalin for the treatment of painful diabetic peripheral neuropathy: a double-blind, placebo-controlled trial. *Pain*. 2004;110(3):628-638.
7. Tölle T, Freynhagen R, Versavel M, Trostmann U, Young JP Jr. Pregabalin for relief of neuropathic pain associated with diabetic neuropathy: a randomized, double-blind study. *Eur J Pain*. 2008;12(2):203-213.
8. Pinheiro J, Bornkamp B, Bretz F. Design and analysis of dose-finding studies combining multiple comparisons and modelling procedures. *J Biopharm Stat*. 2006;16(5):639-656. Doi: 10.1080/10543400600860428.
9. Thomas N, Sweeney K, Somayaji V. Meta-analysis of clinical dose–response in a large drug development portfolio. *Stat Biopharm Res*. 2014;6(4):302-317. Doi: 10.1080/19466315.2014.924876.
10. Kirby S, B*rain P, Jones B. Fitting E(max) models to clinical trial dose-response data.* Pharma Stat. 2011;10(2):143-149. Doi: 10.1002/pst.432.

13. Tables, Listings, and Figures

All listings, tables, and graphs will have a header showing the sponsor company name and protocol and a footer showing the version of SAS, the file name and path, and the source of the data (eCRF page or listing number).

The following are planned summary tables for protocol number D5680C00002. The table numbers and page numbers are place holders only and will be determined when the tables are produced.

13.1. Demographic Data

Table 1: Demographic Data Summary Tables and Figures

Table Number	Population	Table Title/Summary
Table 14.1.2	Screening	Subject Disposition
Table 14.1.3	Screen Failure	Summary of Reasons for Screening Failure
Table 14.1.4.1	Screening	Demographics and Baseline Characteristics
Table 14.1.4.2	Safety	Demographics and Baseline Characteristics
Table 14.1.4.3	mITT	Demographics and Baseline Characteristics
Table 14.1.4.4	PK	Demographics and Baseline Characteristics
Table 14.1.5.1	Screening	Osteoarthritis Characteristics
Table 14.1.5.2	Safety	Osteoarthritis Characteristics
Table 14.1.5.3	mITT	Osteoarthritis Characteristics
Table 14.1.5.4	PK	Osteoarthritis Characteristics
Table 14.1.6	Safety	Medical History by System Organ Class and Preferred Term
Table 14.1.7	Safety	Prior Medications by ATC Class and Preferred Name
Table 14.1.8	Safety	Protocol Deviations
Table 14.1.9	Safety	Overall Study Drug Exposure

13.2. Efficacy Data

Table 2: Efficacy Data

Table Number	Population	Table Title / Summary
Table 14.2.1.1.1	mITT	Daily Pain NRS: Summary Statistics (Observed Cases)
Table 14.2.1.1.2	mITT	Daily Pain NRS: Summary Statistics (LOCF)
Table 14.2.1.1.3	mITT	Daily Pain NRS: Summary Statistics (BOCF)
Table 14.2.1.2.1	mITT	Daily Pain NRS: Primary MCP-Mod Analysis (LOCF)
Table 14.2.1.2.2	mITT	Statistical Analysis of CFB to Week 12 Daily Pain NRS: Primary ANCOVA Analysis (LOCF)
Table 14.2.1.3.1	mITT	Statistical Analysis of CFB Daily Pain NRS: MMRM Analysis. (Observed Cases)
Table 14.2.1.3.2	mITT	Daily Pain NRS: Sensitivity of Primary MCP-Mod Analysis (BOCF)
Table 14.2.2.1	mITT	Galer NPS: Summary Statistics (Observed Cases)
Table 14.2.2.2	mITT	Galer NPS: MMRM Analysis (Observed Cases)
Table 14.2.3.1	mITT	DSIS: Summary Statistics (Observed Cases)
Table 14.2.3.2	mITT	DSIS: MMRM Analysis (Observed Cases)
Table 14.2.4.1	mITT	SF-36: Summary Statistics (Observed Cases)
Table 14.2.4.2	mITT	SF-36: MMRM Analysis (Observed Cases)
Table 14.2.5.1	mITT	Rescue Medication Use: Summary Statistics
Table 14.2.6.1	mITT	Daily Pain NRS Responder Analysis (≥30%): Cochran-Mantel-Haenszel (Observed Cases)
Table 14.2.6.2	mITT	Daily Pain NRS Responder Analysis (≥30%): GEE Analysis (Observed Cases)
Table 14.2.7.1	mITT	Daily Pain NRS Responder Analysis (≥50%): Cochran-Mantel-Haenszel (Observed Cases)
Table 14.2.7.2	mITT	Daily Pain NRS Responder Analysis (≥50%): GEE Analysis (Observed Cases)
Table 14.2.8.1	mITT	Patient Global Impression of Change: Summary Statistics
Table 14.2.8.2	mITT	Patient Global Impression of Change: Cochran-Mantel-Haenszel
CCI [redacted]		

13.3. Safety Data

Table 3: Safety Data

Table Number	Population	Table Title / Summary
14.3.1 Displays of Adverse Events		
Table 14.3.1.1	Safety	Summary of Overall Adverse Events
Table 14.3.1.2	Safety	Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Table 14.3.1.3	Safety	Treatment Emergent Adverse Events by Severity, System Organ Class and Preferred Term
Table 14.3.1.4	Safety	Treatment Emergent Adverse Events by Relationship to Study Medication, System Organ Class and Preferred Term
Table 14.3.1.5	Safety	Treatment Emergent Adverse Events by ADA Status Category, System Organ Class and Preferred Term
Table 14.3.1.6	Safety	Treatment Emergent Adverse Events Leading to Discontinuation of Study drug by System Organ Class and Preferred Term
Table 14.3.1.7	Safety	Non-Serious Adverse Events Occurring in More than 5% of Subjects by System Organ Class and Preferred Term
Table 14.3.1.8	Safety	Treatment Emergent Adverse Events Occurring in More than 5% of Subjects by Preferred Term
Table 14.3.1.9	Safety	Treatment Emergent Adverse Events by Preferred Term
14.3.2 Summary of Deaths, Other Serious and Significant Adverse Events		
Table 14.3.2.1.1	Safety	Serious Adverse Events by System Organ Class and Preferred Term
Table 14.3.2.1.2	Safety	Life-Threatening Serious Adverse Events by System Organ Class and Preferred Term
Table 14.3.2.1.3	Safety	Serious Adverse Events with Outcome Death by System Organ Class and Preferred Term
Table 14.3.2.1.4	Safety	Serious Adverse Events by Relationship to Study Medication, System Organ Class and Preferred Term
14.3.2.2 Displays of Significant Adverse Events and Adverse Events of Special Interest		
Table 14.3.2.2.1	Safety	Treatment Emergent Adverse Events Associated with Abnormal Liver by System Organ Class and Preferred Term
Table 14.3.2.2.2	Safety	Potential Joint Related Adverse Events of Special Interest by System Organ Class and Preferred Term
Table 14.3.2.2.3	Safety	Serious and/or severe Infections by System Organ Class and Preferred Term

Table Number	Population	Table Title / Summary
Table 14.3.2.2.4	Safety	Anaphylactic Reactions, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of IP by System Organ Class and Preferred Term
14.3.3 Narratives of Deaths and Other Serious Adverse Events		
Table 14.3.3.1	Safety	Listing of Serious Adverse Events
Table 14.3.3.2	Safety	Listing of Deaths
14.3.4 Laboratory Data Summary Tables		
Table 14.3.4.1	Safety	Descriptive Summary of Clinical Chemistry
Table 14.3.4.2	Safety	Shift Table of Clinical Chemistry Results
Table 14.3.4.3	Safety	Descriptive Summary of Hematology
Table 14.3.4.4	Safety	Shift Table of Hematology Results
Table 14.3.4.5	Safety	Descriptive Summary of Coagulation
Table 14.3.4.6	Safety	Shift Table of Coagulation Results
Table 14.3.4.7	Safety	Descriptive Summary of Urinalysis
Table 14.3.4.8	Safety	Shift Table of Urinalysis Results
Table 14.3.4.9	Safety	Maximum On-Treatment ALT and AST versus Maximum On-Treatment Total Bilirubin
14.3.6 Other Safety Data Summary Tables		
Table 14.3.5.1	Safety	Descriptive Summary of Vital Signs
Table 14.3.5.2	Safety	Descriptive Summary of ECG Data
Table 14.3.5.3	Safety	Summary of Overall Evaluation of safety ECG Data
Table 14.3.5.4	Safety	Covid-19 Screening
Table 14.3.5.5	Safety	Summary of Sub-Scores for Total Neuropathy Score-Nurse
Table 14.3.5.6	Safety	Descriptive Summary of Total Neuropathy Score-Nurse
Table 14.3.5.7	Safety	Summary of Motor and Sensory Nerve Conduction Studies
Table 14.3.5.8	Safety	Summary of Strength and Deep Tendon Reflexes
Table 14.3.5.9	Safety	Summary of Local Injection Site Reactions
Table 14.3.5.10	Safety	Summary of Anaphylactic Reactions
Table 14.3.5.11	Safety	Summary of Liver Diagnostic Investigations
Table 14.3.5.12	Safety	Summary of Liver Risk Factors and Lifestyle Events
Table 14.3.5.13	Safety	Summary of Liver Signs and Symptoms

Table Number	Population	Table Title / Summary
Table 14.3.5.14	Safety	Summary of Infection Diagnostic Investigations
Table 14.3.5.15	Safety	Summary of Infection Risk Factors and Lifestyle Events
Table 14.3.5.16	Safety	Summary of Infection Signs and Symptoms
Table 14.3.5.17	Safety	Summary of Concomitant Medications by ATC Level 2 and Preferred Term
Table 14.3.5.18	Safety	Summary of Concomitant Procedures
Table 14.3.5.19	Safety	Anti-Drug Antibody Results and Titre Summary by Timepoint
Table 14.3.5.20	Safety	Descriptive Summary of Anti-Drug Antibody Results and Titre by ADA Categories

13.4. Pharmacokinetic/Pharmacodynamic Data

Table 4: Pharmacokinetic/Pharmacodynamic Data

Table Number	Population	Table Title / Summary
14.4 Pharmacokinetic and Pharmacodynamic Data Summary Tables		
Table 14.4.1	PK	Summary of Serum MEDI7352 Concentrations
Table 14.4.2	Safety	Summary of Serum total NGF Concentrations

13.5. Planned Listing Descriptions

The following are planned data and patient/subject data listings for protocol number D5680C00002.

In general, one listing will be produced per eCRF domain. All listings will be sorted by treatment, site, and subject number. All calculated variables will be included in the listings.

In all listings a blank line will be placed between each subject. Within a data listing, if an item appears line after line (e.g., repetition of subject number), then only the first occurrence will be displayed.

In data listings, the information for one subject will be kept on one page if at all possible, rather than splitting a subject's information across pages.

Table 5: Planned Listings

Data Listing Number	Population	Data Listing Title / Summary
16.2 Subject Data Listings		
16.2.1 Subject Discontinuations/Completions		
Listing 16.2.1.1	Screening	Subject Disposition
Listing 16.2.1.2	Screening	Assignment to Analysis Populations
Listing 16.2.1.3	Safety	Reason for IP Discontinuation and Withdrawal from the Study
Listing 16.2.1.4	Screen Failure	List of Reasons for Screening Failure
Listing 16.2.1.5	Screening	Visits List and COVID-19 Impact
16.2.2 Protocol Deviations		
Listing 16.2.2.1	Screening	Subjects Not Meeting All Inclusion Criteria or Meeting any Exclusion Criteria
Listing 16.2.2.2	Safety	Protocol Deviations
16.2.3 Randomization		
Listing 16.2.3	Safety	Randomization and Treatment Group

Data Listing Number	Population	Data Listing Title / Summary
16.2 Subject Data Listings		
16.2.4 Demographic Data and Other Baseline Characteristics		
Listing 16.2.4.1	Screening	Demographic and Baseline Characteristics
Listing 16.2.4.2	Safety	Medical History
Listing 16.2.4.3	Screening	Osteoarthritis Characteristics
16.2.5 Compliance and/or Drug Concentration Data		
Listing 16.2.5.1	Safety	Study Drug Administration: Individual Doses
16.2.6 Individual Efficacy Response Data		
Listing 16.2.6.1	mITT	Daily Pain NRS
Listing 16.2.6.2	mITT	Galer NPS
Listing 16.2.6.3	mITT	DSIS
Listing 16.2.6.4	mITT	SF-36
Listing 16.2.6.5	mITT	Rescue Medication Usage
Listing 16.2.6.6	mITT	Patient Global Impression of Change
CCI		
16.2.7 Adverse Event Listings (by Patient/Subject)		
Listing 16.2.7.1	Safety	Adverse Events
Listing 16.2.7.2	Safety	Treatment Emergent Adverse Events Leading to Study Drug Discontinuation
Listing 16.2.7.3	Safety	Treatment Emergent Adverse Events Associated with Abnormal Liver
Listing 16.2.7.4	Safety	Joint Related Adverse Events of Special Interest
Listing 16.2.7.5	Safety	Serious and/or Severe Infections
Listing 16.2.7.6	Safety	Anaphylactic Reactions, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of Study Drug
16.2.8 Laboratory Values (by Patient/Subject)		
Listing 16.2.8.1	Safety	Clinical Chemistry Laboratory Evaluations
Listing 16.2.8.2	Safety	Hematology Laboratory Evaluations
Listing 16.2.8.3	Safety	Coagulation Laboratory Evaluations
Listing 16.2.8.4	Safety	Urinalysis Laboratory Evaluations
Listing 16.2.8.5	Safety	Serology Laboratory Evaluations
Listing 16.2.8.6	Safety	Pregnancy Test Results

Data Listing Number	Population	Data Listing Title / Summary
16.2 Subject Data Listings		
Listing 16.2.8.7	Safety	Drug Test Results
Listing 16.2.8.8	Safety	COVID-19 Screening
16.2.9 Other Clinical Observations and Measurements (by Patient/Subject)		
Listing 16.2.9.1	Safety	Vital Signs Measurements
Listing 16.2.9.2	Safety	ECG Results
Listing 16.2.9.3	Safety	Physical Examination Results
Listing 16.2.9.4	Safety	Neurological Examination Results
Listing 16.2.9.5	Safety	Total Neuropathy Score-Nurse
Listing 16.2.9.6	Safety	Motor and Sensory Nerve Conduction Studies
Listing 16.2.9.7	Safety	Strength and Deep Tendon Reflexes
Listing 16.2.9.8	Safety	Injection Site Reactions
Listing 16.2.9.9	Safety	Anaphylactic Reactions
Listing 16.2.9.10	Safety	Liver Diagnostic Investigations
Listing 16.2.9.11	Safety	Liver Risk Factors and Lifestyle Events
Listing 16.2.9.12	Safety	Liver Signs and Symptoms
Listing 16.2.9.13	Safety	Infection Diagnostic Investigations
Listing 16.2.9.14	Safety	Infection Risk Factors and Lifestyle Events
Listing 16.2.9.15	Safety	Infection Signs and Symptoms
Listing 16.2.9.16	Safety	Prior and Concomitant Medications
Listing 16.2.9.17	Safety	Prohibited Concomitant Medications
Listing 16.2.9.18	Safety	Concomitant Procedures
Listing 16.2.9.19	Safety	Anti-drug Antibody Test Results
16.2.10 Pharmacokinetic/Pharmacodynamic Measurements		
Listing 16.2.10.1	PK	Serum MEDI7352 Concentrations
Listing 16.2.10.2	Safety	Serum total NGF Concentrations

13.6. Planned Figure Descriptions

The following are planned summary figures for protocol number D5680C00002. The figure numbers and page numbers are place holders only and will be determined when the figures are produced.

Table 6: Planned Figures

Figure Number	Population	Figure Title/Summary
Figure 14.2.1.1	mITT	Daily Pain NRS: MCP-Mod Dose Response Model
Figure 14.2.1.2	mITT	Daily Pain NRS: Boxplots at Week 12 by Treatment Group and Missing Data Handling
Figure 14.2.1.3	mITT	Daily Pain NRS: Boxplots at Week 12 by Treatment Group and Co-Medication Subgroup
Figure 14.2.1.4	mITT	Daily Pain NRS: MMRM LS Means (95% Confidence Interval) over 12-weeks by Treatment Group (Observed Cases)
Figure 14.3.6.1.1	Safety	Vital Sign Profiles: Mean (±SD) Systolic Blood Pressure over time
Figure 14.3.6.1.2	Safety	Vital Sign Profiles: Mean (±SD) Diastolic Blood Pressure over time
Figure 14.3.6.1.3	Safety	Vital Sign Profiles: Mean (±SD) Heart Rate over time
Figure 14.3.6.1.4	Safety	Vital Sign Profiles: Mean (±SD) Respiratory Rate over time
Figure 14.3.6.1.5	Safety	Vital Sign Profiles: Mean (±SD) Temperature over time
Figure 14.4.1.1	PK	Pharmacokinetics: Line Plot of Geometric Mean (with and without gSD) Serum MEDI7352 over time
Figure 14.4.1.2	PK	Pharmacokinetics: Individual Plot of Serum MEDI7352 Concentrations over time
Figure 14.4.2.1	Safety	Pharmacodynamics: Line Plot of Geometric Mean (with and without gSD) Serum total NGF over time
Figure 14.4.2.2	Safety	Pharmacodynamics: Individual Plot of Serum total NGF over time

14. Tables, Listing and Figure Shells

14.1. Standard Layout for all Tables, Listings, and Figures

The following standard layout will be applied to all Tables, Listings, and Figures in support of this study. Note that programming notes may be added if appropriate after each table, listing and figure shell. All shells will be provided as a separate document.

Figure 1: Standardized Layout

Astra Zeneca — Page xx of xx

Protocol: D5680C00002 — Version

<Table, Listing, Figure> xx.x.x

Title of Table, Listing or Figure

Study Population and if applicable subgroup Description

Body of Table, Listing or Figure

Note: If directly Applicable

Footnote 1

Footnote 2

Footnote n

Footnote n+1 SAS program path and name Executed on ddmmmyyyy at hh:mm on data from ddmmmyyyy

15. Appendix: Calculation of Dose to achieve target effects

Although only one dose-response model type (Emax) is pre-specified in the protocol for the primary analysis, CCI [redacted]

Let us assume the R® *DoseFinding* package original parametrization for these two dose-response model functions below:

Journal of Statistical Software 9

Name	$f(d, \boldsymbol{\theta})$	$f^0(d, \boldsymbol{\theta}^*)$	(*)	(♯)
`linear`	$E_0 + \delta d$	d		
`linlog`	$E_0 + \delta \log(d + c)$	$\log(d + c)$		c
`quadratic`	$E_0 + \beta_1 d + \beta_2 d^2$	$d + \delta d^2$ if $\beta_2 < 0$	δ	
`emax`	$E_0 + E_{\max} d/(ED_{50} + d)$	$d/(ED_{50} + d)$	ED_{50}	
`logistic`	$E_0 + E_{\max}/\{1 + \exp[(ED_{50} - d)/\delta]\}$	$1/\{1 + \exp[(ED_{50} - d)/\delta]\}$	$(ED_{50}, \delta)^\top$	
`exponential`	$E_0 + E_1(\exp(d/\delta) - 1)$	$\exp(d/\delta) - 1$	δ	
`sigEmax`	$E_0 + E_{\max} d^h/(ED_{50}^h + d^h)$	$d^h/(ED_{50}^h + d^h)$	$(ED_{50}, h)^\top$	
`betaMod`	$E_0 + E_{\max} B(\delta_1, \delta_2)(d/D)^{\delta_1}(1 - d/D)^{\delta_2}$	$B(\delta_1, \delta_2)(d/D)^{\delta_1}(1 - d/D)^{\delta_2}$	$(\delta_1, \delta_2)^\top$	D

Table 1: Dose-response models implemented in the **MCPMod** package. Column (*) lists for

1. Equations for Target Dose D_Δ to achieve a Delta (Δ) versus placebo

   Emax: $TD_\Delta = ED_{50}/((E_{max}/\Delta) - 1)$, where ED_{50} and E_{max} are estimated from the fitted Emax model

   Exponential: $TD_\Delta = \delta * \log((\Delta/E_1) + 1)$, where δ and E_1 are estimated from the fitted exponential model

   (The function TD from the DoseFinding package will be used for the above)

2. Equations for Dose (ED_P) to achieve a certain proportion P of the effect of the maximum dose studied versus placebo (See DoseFinding manual page 51 where ED is 'Effective Dose')

Emax: $ED_P = (P * ED_{50} * \max(doses)) / (ED_{50} + (1-P) * \max(doses)) = (P * ED_{50} * 150) / (ED_{50} + (1-P) * 150)$

Exponential: $ED_P = \delta * \log((P * \exp(\max(doses)/\delta) + 1 - P)) = \delta * \log((P * \exp(150/\delta) + 1 - P))$

(The function ED from the DoseFinding package will be used for the above)

3. Equation for Dose (asym ED_P) to achieve a certain proportion P of the asymptotic maximum effect (E_{max}) versus placebo

Emax: asymptotic $ED_P = (P * ED_{50}) / (1-P)$

Simulation-based CI will be created for each of the above quantities from the mean and covariance matrix of the model parameters, assuming multivariate normality. Therefore 10,000 samples from the multivariate distribution will be taken, and for each simu lation the TD and ED estimates calculated. The 2.5% and 97.5% percentiles will then form the appropriate 95% two-sided CI.

Sponsor	AstraZeneca
Protocol Title:	A Randomised, Double-Blind, Placebo-Controlled, Dose-Response Study of the Efficacy and Safety of MEDI7352 in Subjects with Painful Diabetic Neuropathy
Development Phase	2
Protocol Number:	D5680C00002
Premier Research PCN:	MEDU177093
Document Version:	Final Version 1.1
Document Date:	31-Aug-2023

Approvals

Role	Signatures
Biostatistician	Print Name: PPD Biostatistician, Premier Research
	Sign Name: 
Peer Reviewer	Print Name: PPD PPD Biostatistics, Premier Research
	Sign Name: 

Role	Signatures
AstraZeneca Biostatistician	Print Name: PPD Statistical Consultant to AstraZeneca
	Sign Name: PPD
AstraZeneca Representative	Print Name: PPD PPD AstraZeneca Neuroscience
	Sign Name: PPD

Document History

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0.5	21-Apr-2023	PPD	Draft Version
0.6	24-May-2023	PPD	Draft Version
1.0	12-Jul-2023	PPD	Final Version
1.1	31-Jul-2023	PPD	Final Version

Table of Contents

Approvals 1
Document History 3
Table of Contents 4
List of Tables 6
List of Figures 6
List of Abbreviations 7
1. Overview 11
2. Study Objectives and Endpoints 11
2.1. Study Objectives 11
2.1.1. Primary Objective 11
2.1.2. Secondary Objectives 11
2.1.3. Exploratory Objectives 12
2.2. Study Endpoints 12
2.2.1. Efficacy Endpoints 12
2.2.2. Safety Endpoints 13
2.2.3. Pharmacokinetic/Pharmacodynamic Variable(s) 13
2.2.4. Other Endpoints 14
3. Overall Study Design and Plan 14
3.1. Overall Design 14
3.2. Sample Size and Power 14
3.3. Study Population 15
3.4. Treatments Administered 16
3.5. Method of Assigning Subjects to Treatment Groups 16
3.6. Blinding and Unblinding 16
3.7. Schedule of Events 17
4. Statistical Analysis and Reporting 17
4.1. Introduction 17
4.2. Interim Analysis and Data Monitoring 18
5. Analysis Populations 18
6. General Issues for Statistical Analysis 19
6.1. Statistical Definitions and Algorithms 19
6.1.1. Baseline 19
6.1.2. Adjustments for Covariates 19

6.1.3. Multiple Comparisons 19
6.1.4. Handling of Dropouts or Missing Data 20
6.1.5. Analysis Visit Windows 20
6.1.6. Pooling of Sites 21
6.1.7. Efficacy Variables 21
6.1.8. Derived Variables 23
6.1.9. Data Adjustments/Handling/Conventions 24
7. Study Patients/Subjects and Demographics 25
7.1. Disposition of Patients/Subjects and Withdrawals 25
7.2. Protocol Deviations 26
7.3. Demographics and Other Baseline Characteristics 26
7.4. Exposure 27
8. Efficacy Analysis 27
8.1. Primary Efficacy Analysis 27
8.1.1. Sensitivity Analyses of the Primary Efficacy Endpoint 29
8.2. Secondary Efficacy Analysis 29
8.3. Exploratory Efficacy Analysis 30
9. Safety and Tolerability Analysis 30
9.1. Adverse Events 32
9.1.1. Adverse Events Leading to Discontinuation of IP 32
9.1.2. Deaths and Serious Adverse Events 33
9.1.3. Drug-Induced Liver Injury 33
9.1.4. Infection Risk 33
9.2. COVID-19 Vaccination and Screening 33
9.3. Clinical Laboratory Evaluations 33
9.4. Vital Signs 34
9.5. Electrocardiograms 34
9.6. Physical and Neurological Examination 35
9.7. Total Neuropathy Score-Nurse 35
9.8. Motor and Sensory Nerve Conduction Studies 35
9.9. Strength and Deep Tendon Reflexes 35
9.10. Hypersensitivity/Anaphylactic Reactions, Injection Site or Infusion Reactions 35
9.11. Prior and Concomitant Medication and Procedures 36
10. Changes from Planned Analysis 37
11. Other Planned Analysis 37

11.1. Biomarkers 37
11.2. Immunogenicity 38
11.3. Pharmacokinetic Analysis 39
12. References 39
13. Tables, Listings, and Figures 41
13.1. Demographic Data 41
13.2. Efficacy Data 42
13.3. Safety Data 43
13.4. Pharmacokinetic/Pharmacodynamic Data 46
13.5. Planned Listing Descriptions 46
13.6. Planned Figure Descriptions 49
14. Tables, Listing and Figure Shells 51
14.1. Standard Layout for all Tables, Listings, and Figures 51
15. Appendix: Calculation of Dose to achieve target effects 53

List of Tables

Table 1: Demographic Data Summary Tables and Figures 41
Table 2: Efficacy Data 42
Table 3: Safety Data 43
Table 4: Pharmacokinetic/Pharmacodynamic Data 46
Table 5: Planned Listings 46
Table 6: Planned Figures 50

List of Figures

Figure 1: Standardized Layout 52

List of Abbreviations

Abbreviation	Definition
ADA	Anti-Drug Antibody
AE	Adverse Event
AIC	Akaike Information Criterion
ALT	Alanine Aminotransferase
ANCOVA	Analysis of Covariance
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
BOCF	Baseline Observation Carried Forward
CI	Confidence Interval
CMH	Cochran-Mantel-Haenszel
COVID-19	Coronavirus Disease 2019
CSR	Clinical Study Report
DSIS	Daily Sleep Interference Scale
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
ED50, ED90	The Dose to achieve 50%, 90% of the Maximum Effect.
EMA	European Medicines Agency

Abbreviation	Definition
Emax	The Model-Based Maximum Treatment Effect Versus Placebo
ePRO	Electronic Patient-Reported Outcome System
FDA	Food and Drug Administration
gCV%	Geometric Coefficient of Variation
GEE	Generalized Estimating Equation
gmean	Geometric Mean
gSD	Geometric Standard Deviation
HL	Hy's Law
HR	Heart Rate
ICH	International Council for Harmonization
IP	Investigational Product
IV	Intravenous
IWRS	Interactive Web Response System
LLOQ	Lower Limit of Quantification
LOCF	Last Observation Carried Forward
LS	Least Squares
MCP-mod	Multiple Comparison Procedure Modelling
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified Intent-to-Treat

Abbreviation	Definition
MMRM	Mixed Effects Models Repeated Measures
NC	Not Calculable
NCA	Noncompartmental Analysis
NPS	Neuropathic Pain Scale
NQ	Not Quantifiable
NRS	Numeric Rating Scale
PD	Pharmacodynamics
PDN	Painful Diabetic Neuropathy
PGIC	Patient Global Impression of Change
CCI [redacted]	
PHT	Potential Hy's Law
PK	Pharmacokinetic
PT	Preferred Term
QTcF	QT Fridericia's Correction
CCI [redacted]	
RPOA	Rapidly Progressive Osteoarthritis
SAE	Serious Adverse Event
SAF	Safety
SAP	Statistical Analysis Plan

Abbreviation	Definition
SAS®	a Software System Used for Data Analysis
SDTM	Study Data Tabulation Model
SF-36	36-Item Short Form Health Survey
SiAP	Statistical Interim Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
TBL	Total Bilirubin
TEAE	Treatment-Emergent Adverse Event
tNGF	Total Nerve Growth Factor
TNSn	Total Neuropathy Score-Nurse
ULN	Upper Limit of Normal
ULOQ	Upper Limit of Quantification

1. Overview

This statistical analysis plan (SAP) describes the planned analysis and reporting for AstraZeneca protocol number D5680C00002 (A Randomised, Double-Blind, Placebo-Controlled, Dose-Response Study of the Efficacy and Safety of MEDI7352 in Subjects with Painful Diabetic Neuropathy), dated 13-Apr-2022 version 7.0. Reference materials for this statistical plan include the protocol and the accompanying sample data collection documents. Operational aspects related to collection and timing of planned clinical assessments are not repeated in this SAP unless relevant to the planned analysis.

The structure and content of this SAP provides sufficient detail to meet the requirements identified by the Food and Drug Administration (FDA), European Medicines Agency (EMA), and International Conference on Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use: Guidance on Statistical Principles in Clinical Trials (ICH, 1998). All work planned and reported for this SAP will follow internationally accepted guidelines, published by the American Statistical Association (ASA, 2018) and the Royal Statistical Society (RSS, 2014), for ethical statistical practice.

The planned analyses identified in this SAP may be included in clinical study reports (CSRs), regulatory submissions, or future manuscripts. CCI [redacted]

The statistical plan described hereafter has been developed by blinded study team members prior to the Interim Analysis but after the Administrative Analysis has been conducted. It will be approved before final unblind, performing inferential or descriptive analysis of hard-locked data from AstraZeneca's study D5680C00002.

2. Study Objectives and Endpoints

2.1. Study Objectives

2.1.1. Primary Objective

The primary objective is to assess the efficacy of MEDI7352 versus placebo on chronic pain in subjects with painful diabetic neuropathy (PDN) currently taking standard of care medication for their PDN pain.

2.1.2. Secondary Objectives

The secondary objectives are:

- To assess the safety and tolerability of MEDI7352 in subjects with PDN
- To assess the pharmacokinetics (PK), pharmacodynamics (PD), and immunogenicity of MEDI7352 in subjects with PDN

- To characterise the dose-response relationship of MEDI7352 on chronic pain in subjects with PDN

2.1.3. Exploratory Objectives

CCI

[redacted]

2.2. Study Endpoints

2.2.1. Efficacy Endpoints

2.2.1.1. Primary Efficacy Endpoint

The primary efficacy endpoint of this study is the change in the weekly average of the average daily pain scores from the baseline week to Week 12 of MEDI7352 compared to placebo, as measured on an 11-point (0-10) numeric rating scale (NRS).

The target population is the entire patient population, i.e., the collection of all patients eligible to be included in the randomized clinical trial based on prespecified (and duly justified) inclusion/exclusion criteria.

The study was not designed using the Estimand framework. However, the following general aspects of an Estimand can be inferred: the Estimand can be generically defined as the true between-treatment difference in the target population endpoint means for the change from baseline for the Pain NRS at Week 12, while-on-treatment and regardless of prohibited or rescue medication use.

2.2.1.2. Secondary Efficacy Endpoint(s)

The secondary efficacy endpoints of this study include the following:

- Change in the weekly average of the average daily pain score, as measured on an 11-point (0-10) NRS, from baseline to Weeks 2, 4, 6, 8, and 10 of treatment and the week before the follow-up visit.
- Percentage of subjects who have achieved ≥30% and ≥50% reductions in the weekly average of the average daily pain score from baseline during Weeks 4, 8, and 12 of treatment and the week before follow-up.

- Change in Galer Neuropathic Pain Scale (NPS) from baseline to Days 28, 56, and 84 of treatment and the follow-up visit.
- Change in Daily Sleep Interference Scale (DSIS) from baseline to Days 28, 56, and 84 of treatment and the follow-up visit.
- Proportion of subjects who have 'improved', 'much improved,' or 'very much improved' relative to baseline on the Patient Global Impression of Change (PGIC) on Days 28, 56, and 84 of treatment and the follow-up visit.
- Change in the 36-item Short-Form Health Survey (SF-36) from baseline to Day 84 of treatment.
- Usage of rescue medication (yes/no) from baseline to Week 12 of treatment.

2.2.1.3. Exploratory Efficacy Endpoint(s)

CCI [redacted]

2.2.2. Safety Endpoints

The safety endpoints of this study include the following:

- Adverse events (AEs) and serious adverse events (SAEs)
- Physical and neurological examinations
- Neuropathy assessments Total Neuropathy Score-Nurse (TNSn) S
- Strength (dorsiflexion), and deep tendon reflex (knee and ankle) assessments
- Vital signs
- 12 lead digital electrocardiogram (ECGs)
- Clinical laboratory testing (hematology, chemistry, coagulation, and immunology)
- Motor and sensory nerve conduction studies
- Concomitant medications and therapies
- Injection site reactions and infusion reactions

2.2.3. Pharmacokinetic/Pharmacodynamic Variable(s)

The pharmacokinetic (PK) endpoints of the study include the MEDI7352 concentrations measurements in serum/plasma.

The pharmacodynamic (PD) endpoints of the study include total nerve growth factor (tNGF) measurements in serum/plasma.

2.2.4. Other Endpoints

The following endpoints will be assessed:

- Change in the weekly average of the average daily pain scores from the baseline week to Week 12, as measured on an 11-point (0-10) NRS, versus dose.
- Immunogenicity (ADA) assessments.

3. Overall Study Design and Plan

This is a randomised, double-blind, placebo-controlled study of MEDI7352 in subjects with moderate to severe chronic PDN persistent for 6 months or longer, not adequately controlled by standard of care treatments, caused by type 1 or type 2 diabetes mellitus. The study incorporates a screening period of up to 45 days and a 12-week double-blind treatment period during which MEDI7352 or placebo will be administered intravenously (IV) on 6 occasions, with each dose separated by 14 days. There will be a 6-week follow-up period.

3.1. Overall Design

3.2. Sample Size and Power

There will be 4 stages in the study: in the first stage, subjects will be randomly assigned to placebo or the lowest dose (CCI) until at least 10 subjects have been recruited. In the second stage, up to 30 subjects will be randomly assigned to a placebo or CCI of MEDI7352; prior to commencing the third stage, the safety and tolerability experience following administration of multiple doses of CCI in the Phase 1 study of MEDI7352 will be evaluated. In stage 3 of the study, approximately 67 subjects will be randomly assigned to placebo or CCI of MEDI7352. The third stage will include an interim analysis to enable decision making for stage 4 with respect to the sample size and dose allocation ratio. If no changes are made following the interim analysis, in stage 4 of the study, approximately 165 eligible subjects will be randomly assigned to treatment across 3 dose levels of MEDI7352 (CCI) or placebo, to ensure that approximately 236 subjects are evaluable for the efficacy analysis of stages 2 to 4 combined. The number of subjects in the fourth stage is currently planned to follow an equal treatment allocation to each of the 4 treatment groups. However, the exact number of subjects and the allocation to each dose in stage 4 will be determined after the interim analysis.

There is no formal sample size calculation for stage 1; 10 subjects in stage 1 are considered sufficient for the initial assessment of safety. The sample size for stages 2-4 combined was determined by a formal power calculation (see below) and the size of stage 3 was defined to enable decision making for the stage 4 sample size and dose allocation ratio.

This study is powered at greater than 80% to detect a statistically significant (1-sided alpha = 0.025) dose-response relationship when the true Week 12 placebo-corrected change from baseline difference at the CCI dose is 1.25 on the 11-point NRS scale (MEDI7352-placebo treatment) and the true dose-response follows a hyperbolic Emax relationship, with ED50 within the range 1-750 µg/kg. This calculation also assumes:

- The true standard deviation (SD) is 2.4, which is based on other studies undertaken with pregabalin in PDN (Satoh et al. 2011, Lesser et al. 2004, Rosenstock et al. 2004, Tölle et al. 2008).
- The data from stages 2, 3, and 4 are combined so that the number of subjects for the dose-response analysis is 236 with the total number evaluable for placebo, CCI [redacted] doses equal to 81, 37, 51, and 67, respectively. This is comprised of, assuming an overall 10% non-evaluability rate:
    - 28 out of 30 randomised in stage 2; 14 per arm
    - 60 out of 67 randomised in stage 3; 30 per arm, and
    - 148 out of 165 randomised in stage 4; 37 per arm
- The dose-response hypothesis test is multiplicity adjusted as described by Pinheiro et al. 2006 in order to control the type 1-error.

The above calculations were performed using the software R and the R-package 'DoseFinding' [https://cran.r-project.org/web/packages/DoseFinding/DoseFinding.pdf] with the following parameters:

- Population SD (of change from baseline to week 12) = 2.4
- Placebo effect = 1 point reduction in NRS and CCI [redacted] effect = 2.25 reduction from baseline, ie, delta= 1.25
- Linear contrasts were determined from 5 'candidate dose' response models which are all E_{max} models with decreasing potency/increasing ED50: 7.5, 15, 30, 60, 750 µg/kg. The 5th case is essentially linear in dose. E_{max} models were chosen following the recommendations in a recent meta-analysis of dose response studies by Thomas et al., 2014.
- Power was assessed across 16 alternative true dose response curves, 12 E_{max} with ED50 ranging from 0.375 to 750 µg/kg, 3 logistic and 1 quadratic, all having a Week 12 placebo-corrected change from baseline difference at the CCI [redacted] dose of 1.25.

The overall withdrawal rate is anticipated to be approximately 10%. However, since the primary analysis will use Last Observation Carried Forward (LOCF) for withdrawn subjects, and the SD estimate is taken from studies which also used the LOCF approach, the only additional subjects recruited will be to account for withdrawals in stages 2, 3, and 4 if withdrawal occurs at, or prior to, the Week 2 visit.

The number of subjects who will agree to participate in the genetic research is unknown. It is therefore not possible to establish whether sufficient data will be collected to allow a formal statistical evaluation or whether only descriptive statistics will be generated.

3.3. Study Population

Male or female (postmenopausal or surgically sterile) subjects aged ≥18 to ≤80 years with

chronic PDN persistent for 6 months or longer, not adequately controlled by standard of care treatments .

3.4. Treatments Administered

Once randomized, subjects will be dosed with either MEDI7352 or placebo on Day 1, Day 14, Day 28, Day 42, Day 56, and Day 70. MEDI7352 or placebo will be administered IV over a 60-minute period. To maintain the blind, a placebo volume equivalent to the MEDI7352 volume will be administered for each dosing.

3.5. Method of Assigning Subjects to Treatment Groups

The randomisation schedule will be computer generated using a permuted block algorithm appropriate to the treatment groups included in each stage and will randomly allocate investigational product (IP) to randomisation numbers. The randomisation numbers will be assigned sequentially through a central interactive web response system (IWRS) as subjects are entered into the study. The randomisation schedule will not be stratified, and study centre will not be a blocking factor in the randomisation schedule.

The randomisation schedule has been prepared by Premier Research before the start of the study. No one involved in the study performance will have access to the randomisation schedule before official unblinding of treatment assignment. No subject will be randomised into this study more than once.

3.6. Blinding and Unblinding

All subjects, investigators, and study personnel involved in the conduct of the study, including data management, will be blinded to treatment assignment with the exception of a specified unblinded statistician and programmer from Premier Research who will have access to the randomization code, unblinded site monitors and clinical manager from Premier Research, and the unblinded pharmacist at each study site. The unblinded study personnel will not participate in study procedures or data analysis prior to unblinding of the study data to all study related personnel. Unblinded personnel who are not otherwise involved in the study will prepare data for review and interim analysis.

Study personnel will make every effort to safeguard the integrity of the study blind to minimize bias in the conduct of the study. Treatment unblinding is discouraged if knowledge of the treatment assignment will not materially change the planned management of a medical emergency. Unblinding will be permitted in a medical emergency that requires immediate knowledge of the subject's treatment assignment.

Unblinding should be discussed in advance with the medical monitor if possible. For emergency unblinding, study personnel will use the IWRS. Only authorized users will have access to the unblinding function in the IWRS, and the IWRS will reveal the treatment information for the selected subject only. If the investigator is not able to discuss treatment unblinding in advance, then he/she must notify the medical monitor as soon as possible about the unblinding incident without revealing the subject's treatment assignment. The IWRS will also send a blinded notification to the clinical team alerting them that a break blind occurred.

The investigator or designee must record the date and reason for treatment unblinding on the appropriate electronic case report form (eCRF) for that subject. In all cases that are not emergencies, the investigator must discuss the event with the medical monitor prior to unblinding the subject's treatment assignment.

If treatment assignment is unblinded for an individual subject, study personnel will be notified of that subject's treatment assignment without unblinding the treatment assignments for the remaining subjects in the study. Thus, the overall study blind will not be compromised. If a subject's treatment assignment is unblinded, he/she will be asked to withdraw from the study. The investigator will make this decision after consultation with the medical monitor.

Overall unblinding will take place at the end of the study only after database lock has been achieved.

3.7. Schedule of Events

Please see the protocol Tables 2-1, 2-2 for a detailed schedule of events.

4. Statistical Analysis and Reporting

All efficacy and safety statistical analysis will be based on data from stages 1, 2, 3 and 4 combined, unless specified otherwise.

4.1. Introduction

Data processing, tabulation of descriptive statistics, calculation of inferential statistics, and graphical representations will primarily use SAS (release 9.4 or higher). The multiple comparison and modelling (MCP-Mod) analysis will be performed using R (release 4.2.1 or higher) and the DoseFinding package (version 1.0-3 or higher). If a use of other software is warranted, the final statistical methodology report will detail what software was used for what purposes.

Continuous (quantitative) variable summaries will include the number of subjects (n) with non-missing values, the number of missing values, arithmetic mean, SD, median, 1st, and 3rd quartiles (where applicable), minimum, and maximum.

Categorical (qualitative) variable summaries will include the frequency and percentage of subjects who are in the particular category or each possible value. In general, the denominator for the percentage calculation will be based upon the total number of subjects in the study population for the treatment group, unless otherwise specified. The denominator for by-visit displays will be the number of subjects in the relevant study population with non-missing data at each visit, unless otherwise specified.

The minimum and maximum will be reported with the same degree of precision (i.e., the same number of decimal places) as the observed data. Measures of location (mean and median) will be

reported to 1 degree of precision more than the observed data and measures of spread will be reported to 2 degrees of precision more than the observed data.

For derived data, minimum and maximum will be reported to 2 degrees of precision. Measures of location (mean and median) will be reported to 3 degree of precision, and measures of spread will be reported to 4 degrees of precision.

Percentages will be presented to 1 decimal place, unless otherwise specified.

Unless otherwise indicated, all statistical tests will be conducted at the 0.025 significance level using 1-tailed tests, and *P* values will be reported. For estimation purposes, 2-sided 95% confidence intervals (CI) will be presented.

Total NGF and PK concentration data will be summarized by dose as per the quantitative variables and presenting the number (n) of non-missing observations, and the n < lower limit of quantification (LLOQ). PD and PK parameters will be summarized by dose and will include the arithmetic mean, SD, geometric mean (gmean), gmean ± geometric SD, geometric coefficient of variation (gCV%), median, minimum and maximum.

4.2. Interim Analysis and Data Monitoring

Details of the interim analysis have been included in the Statistical Interim Analysis Plan (SiAP) version 1.0 dated 10-Feb-2023.

5. Analysis Populations

The following analysis populations are planned for this study:

- **Screening Population (Screened)**: All subjects who provide informed consent and/or assent and provide demographic and/or baseline screening assessments, regardless of the subject's randomisation and treatment status in the study. The Screening Set will be analysed as randomised, according to planned treatment.
- **Safety Population (SAF):** The Safety Population includes all subjects who receive at least 1 dose of double-blind study medication. The Safety Set will be analysed according to actual treatment.
- **Modified Intent-To-Treat Population (mITT):** The modified intent-to-treat population will be used for all efficacy analyses and will include all randomised subjects who receive at least 1 dose of double-blind study medication and have at least 1 daily NRS assessment while receiving double-blind treatment. The mITT Set will be analysed as randomised, according to planned treatment.
- **Pharmacokinetic Population (PK):** The PK Population will include all subjects for who a PK sample was obtained and analysed. The PK Set will be analysed according to actual treatment.

Assignment of subjects to populations will be confirmed at a blinded data review meeting to be

held before the study database is locked.

If a subject is randomised incorrectly or is administered the incorrect IP, analyses of the mITT population will be based on the IWRS-assigned treatment whereas all other analyses will be based on the actual treatment.

6. General Issues for Statistical Analysis

6.1. Statistical Definitions and Algorithms

6.1.1. Baseline

For all safety endpoints, the last observation recorded prior to the first dose of treatment will be used as the baseline observation for calculations of change from baseline.

For pain diary data the baseline period is defined as the seven-day period prior to randomization, i.e., Day -7 to Day -1, inclusive. A subject is considered to have an evaluable baseline pain score if there are at least 4 days of recorded diary pain scores in the 7-day period.

6.1.2. Adjustments for Covariates

In addition to treatment group, the baseline value of the variable undergoing analysis and the co-medication type (Anticonvulsant versus Antidepressant) will be included in the analysis of covariance (ANCOVA) model as additive covariates. Co-medication type will be determined by blinded clinical review of each subject's medication record at baseline.

Covariates in the mixed effects models repeated measures (MMRM) and generalized estimating equations (GEE) analyses include those specified for the ANCOVA analyses, together with time and its interaction with dose group.

The crossing of co-medication type and median baseline pain score will be used as strata in the Cochran-Mantel-Haenszel (CMH) model tests. Assuming two co-medication types, the strata will be:

1) Anticonvulsant (Baseline NRS < Median),
2) Anticonvulsant (Baseline NRS > Median),
3) Antidepressant (Baseline NRS < Median),
4) Antidepressant (Baseline NRS > Median).

Where the median baseline NRS is calculated over all subjects.

6.1.3. Multiple Comparisons

A multiple comparison procedure modelling approach (MCP-Mod) on LOCF data will be used for primary efficacy endpoints.

No adjustments will be made for multiple comparisons outside the MCP-Mod approach.

6.1.4. Handling of Dropouts or Missing Data

For the analyses of the primary efficacy endpoints based on the mITT Population, a variety of methods will be used to deal with missing data, including:

- Primary Method: LOCF.
- Observed cases analysis.
- Baseline observation carried forward (BOCF)

Subjects with missing weekly average NRS baseline data (i.e., zero or 1-3 days of diary pain scores) will not be included in the efficacy analysis because the primary analysis is change-from-baseline. If a subject has zero or $\leq$3 days of diary pain data in each of the possible post-baseline seven day periods ending within the protocol definition of week 12 (day 84 $\pm$ 3), then an imputed 'week 12 LOCF' weekly average NRS pain score will be calculated from the latest 7 'non-missing' entries of the subject's diary closest to their nominal week 12 visit (i.e., the latest 7 day period containing at least 4 NRS values), provided that this would qualify as at least 'week 2' according to the windowing outlined in Section 6.1.5. Otherwise, the week 12 LOCF weekly average NRS pain score will be set to missing.

6.1.5. Analysis Visit Windows

Statistical analyses will be based on scheduled visits and windows as per Protocol Table 2-1: Schedule of Events. If an assessment falls between 2 windows, then the closest visit will be used only if an assessment result is not provided within that window. All other visits will be listed only as unscheduled visits. For presentation purposes these will be mapped to the visit prior and labeled, e.g., Unscheduled Visit 3.1, if Visit 3 was the closest date prior.

For pain diary data the following analysis periods will be defined:

- Week X_i: the 7-day period ending within the protocol window Day $Y_i \pm 3$ where at least 4 days out of 7 have recorded diary pain scores. Where several such windows exist the one ending closest to day Y_i will be selected. If there are two such windows that are equidistant from day Y_i, then the one with the largest number of diary entries will take precedence. If they have the same number of entries, then the later of the two end dates will be chosen. If no such window exists, then week X_i will be considered missing for the purposes of weekly average scoring.

  Where:

  - X_1=2, Y_1=14
  - X_2=4, Y_2=28
  - X_3=6, Y_3=42

- X_4=8, Y_4=56
- X_5=10, Y_5=70
- X_6=12, Y_6=84

- The week before follow-up is defined as the 7-day period prior to the last day of pain diary data for subjects completing the study (i.e., entering in the Week 18) where at least 4 days out of 7 have recorded diary pain scores.

6.1.6. Pooling of Sites

Analysis by investigative site will not be conducted.

6.1.7. Efficacy Variables

6.1.7.1. Pain Numerical Rating Scale

Subjects will assess their perceived average neuropathic pain over the previous 24 hours using an 11-point NRS, with 0 representing no pain and 10 representing the worst pain imaginable. Subjects will be instructed to assess their average daily pain at approximately the same time every morning, and to record their response in a subject diary (ePRO).

6.1.7.2. Neuropathic Pain Scale

Subjects will assess their neuropathic pain using the Galer NPS. The NPS includes 2 descriptors of pain, including intensity and unpleasantness, and 8 descriptors that assess specific qualities of neuropathic pain: sharp, hot, dull, cold, sensitive, itchy, deep, and surface pain. Each of these 10 dimensions has a 0 to 10 NRS in which 0 is equal to no pain and 10 equals the most intense pain. There is an additional descriptor about duration and frequency of pain, which has a 1 to 3 NRS. In which 1 = I feel a background pain all the time and occasional flare-ups (breakthrough pain) some of the time, 2 = I feel a single type of pain all the time, and 3 = I feel a single type of pain only sometimes. Other times, I am pain free.

6.1.7.3. Daily Sleep Interference Scale

Subjects will assess how their neuropathic pain interferes with their sleep using the DSIS. The DSIS is an 11-point Likert scale, with 0 indicating that pain did not interfere with sleep and 10 indicating that pain completely interfered with sleep. The DSIS is completed by subjects once a day (upon awakening) to accurately capture variability in sleep interference due to pain on a daily basis, thus minimizing recall bias.

6.1.7.4. Patient Global Impression of Change

Subjects will rate their overall improvement in health status using the PGIC. The PGIC consists of a 7-point scale where 1 = “very much improved” and 7 = “very much worse.” Subjects will be asked the following question: “How would you rate your overall improvement with treatment

during the clinical study?" The response options include the following:

- Very Much Improved - 1
- Much Improved - 2
- Minimally Improved - 3
- No Change - 4
- Minimally Worse - 5
- Much Worse - 6
- Very Much Worse - 7

6.1.7.5. Short-Form Health Survey

The subject's health status and quality of life will be assessed using the SF-36. The SF-36 assesses 8 health concepts: 1) limitations in physical activities because of health problems; 2) limitations in social activities because of physical or emotional problems; 3) limitations in usual role activities because of physical health problems; 4) bodily pain; 5) general mental health (psychological distress and well-being); 6) limitations in usual role activities because of emotional problems; 7) vitality (energy and fatigue); and 8) general health perceptions. The items use Likert-type scales with either 5 or 6 points, or 2 or 3 points. Scores will be derived by the validated built-in scoring tool. Higher SF-36 scores indicate a better state of health.

6.1.7.6. Rescue Medication Use

Subjects will record all rescue medications they take for neuropathic pain in a paper diary. This will be transcribed in to the eCRF collecting usage, date and time of rescue medication, medication administered, dose, frequency and route.

Subjects will be grouped by the following for rescue medication use:

- Compliant with protocol guidance on permitted therapies
- Non-compliant with protocol guidance on permitted therapies

A review of medications will be conducted at a blinded data review meeting to be held before the study database is locked.

6.1.7.7. CCI

CCI

[redacted]

6.1.8. Derived Variables

- Change from baseline = value at current time point – value at baseline.
- Reference End Date = Date of completion/discontinuation.
- Study duration = Reference end date – date of first dose of treatment + 1
- Duration of exposure (days) = min(date of last dose of treatment + 14 days or date of death) – date of first dose of treatment + 1.
- Treatment-emergent AEs (TEAEs) are defined as:
    - AEs with onset at the time of or following the start of treatment with IP, or
    - AEs starting prior to the start of treatment but increasing in severity or relationship at the time of, or following, the start of treatment with IP.
- Average Baseline Pain NRS = the arithmetic average of the 'non-missing' daily pain scores within the baseline period defined in Section 6.1.1. For example, if a subject has 5 days of non-missing pain scores their average will be calculated over 5 days, not the full 7-day baseline period.
- Average Week X Pain NRS = the arithmetic average of the 'non-missing' daily pain scores within each subject's specific week X period defined in Section 6.1.5.
- Average Week 12 Pain NRS (LOCF) = the arithmetic average of the 'non-missing' daily pain scores within each subject's specific week 12 period or according to the imputed LOCF/BOCF approach defined in Section 6.1.4.
- Change from Baseline to Week X Pain NRS = for each subject 'Average Week X Pain NRS' minus 'Average Baseline Pain NRS'.
- Change from Baseline to Week 12 Pain NRS (LOCF/BOCF) = for each subject 'Average Week 12 Pain NRS (LOCF)' minus 'Average Baseline Pain NRS'.
- Galer NPS Total Score (ranges from 0 to 100): sum of Pain Intensity, Pain Unpleasantness, Pain Sharpness, Pain Hotness, Pain Dullness, Pain Coldness, Pain Sensitivity, Pain Itching, Deep Pain Intensity, and Surface Pain Intensity (All in an 11-point NRS).
- Change from Baseline to Week X Galer NPS Total Score = for each subject 'Galer NPS Total Score' minus 'Baseline Galer NPS Total Score'.
- Total number of days rescue medication was used = End Date of Medication - Start Date

of medication + 1. Each day on which rescue medication was used at least once is counted.

- Cumulative consumption (mg) of paracetamol rescue medication use = Total dose of rescue medication (mg) consumed during the days in which paracetamol was used.
- Average daily dose (mg) of paracetamol rescue medication use = Cumulative consumption of paracetamol rescue medication (mg) /total number of days paracetamol rescue medication was used.

6.1.9. Data Adjustments/Handling/Conventions

All collected data will be presented in listings. Data not subject to analysis according to this plan will not appear in any tables or graphs but will be included only in the data listings.

All *P* values will be displayed in four decimals and rounded using standard scientific notation (e.g., 0.XXXX). If a *P* value less than 0.0001 occurs it will be shown in tables as <0.0001.

AEs and medical histories will be coded using the latest version of the Medical Dictionary for Regulatory Activities (MedDRA) thesaurus available at time of programming.

If partial dates of AEs occur, the convention for replacing missing dates for the purpose of TEAE is as follows: if just day is missing then the day assigned is the first day of the month or the date of first dose (if in the same month), whichever is later; if just month is missing then the month assigned is the month of the first dose, unless that results in a date prior to the first dose in which case the month after the first dose is used; and if both month and day are missing then the month assigned is the month of the first dose and the day assigned is either the first day of the month or the first dose date, whichever is later.

If partial times occur, the convention is as follows: if the missing time occurs on the day of the first dose and both the hour and minute are missing then the time assigned is the time of the first dose, otherwise if both the hour and minute are missing and the date is not the date of first dose the time assigned is 12:00; if the date is the same as the date of the first dose and only hour is missing the hour assigned is 12 or the hour of first dose, whichever is later, and if the date is the same as the date of first dose and only the minute is missing the minute assigned is 30 or the minute of first dose, whichever is later. Otherwise the hour assigned is 12 if the hour is missing and the date is not the same as the date of first dose and the minute assigned is 30 is the the date is not the same as the date of first dose.

These conventions will be applied only to AE onset dates and times with the following precaution: if the missing date and time reflect the date and time of onset of an AE, the modified date and time will be constructed to match the first documented date/time post drug administration while preserving the order in which the AE was reported in the eCRF.

In general, for quantitative laboratory values reported as '<X' or '≤X', the LLOQ will be used

for analysis (i.e., the value of X will be used in the analysis for lab values reported as '<X' or '≤X'). Similarly, for quantitative laboratory values reported as '>X' or '≥X', the upper limit of quantification (ULOQ) will be used for analysis (i.e., the value of X will be used in the analysis for lab values reported as '>X' or '≥X').

For analysis purposes, repeat laboratory test results will not be used unless the original laboratory value is missing or indicated as invalid, in which case the first non-missing repeated laboratory value will be used for data analysis.

ADA titre reported as <30 (below the minimum required dilution) is a negative result for the presence of ADA.

For descriptive statistics of serum concentration summaries:

- At a time-point where less than or equal to 50% of the values are not quantifiable (NQ, below LLOQ), all NQ values will be set to the LLOQ, and all descriptive statistics will be calculated accordingly.
- If more than 50%, but not all, of the concentrations are NQ, the geometric mean, geometric mean ± geometric SD and gCV% will be reported as not calculable (NC). The maximum value is reported from the individual data, and the minimum and median are set as NQ.
- If all concentrations are NQ at a time-point, the geometric mean, minimum, median and maximum are reported as NQ and the gCV% and geometric mean ± geometric SD as NC.

7. Study Patients/Subjects and Demographics

7.1. Disposition of Patients/Subjects and Withdrawals

The total number of subjects for each of the following analysis populations will be presented for the Screening Population by randomized treatment group and overall:

- Screening Population
- Safety Population
- mITT Population
- Included in the mITT population
  - Evaluable Week 12 efficacy
  - Evaluable LOCF efficacy
- Not efficacy evaluable
- PK Population

For the Screening Population, disposition will include tabulation of:

- the number of screened subjects
- the number of re-screened subjects
- the number of enrolled subjects

The output will be further presented by treatment group and overall summarising:

- the number of randomized subjects
- the number of subjects who completed study treatment
- the number of completed subjects
- the number of subjects withdrawing (discontinued)
- the reasons for discontinuation from study treatment and withdrawal from the study.

For all categories of subjects by treatment group, percentages will be calculated using the number of subjects randomized as the denominator.

7.2. Protocol Deviations

Major protocol deviations, as determined by a Sponsor blinded review of the data prior to database lock and unblinding of the study will be reported in listings.

The Sponsor or designee will be responsible for producing the final deviation file. This file will be finalized prior to database lock, and all information will be included in the SDTM.DV domain (deviations domain).

All protocol deviations will be presented in a data listing, with a flag to indicate if a deviation was considered major.

A summary table by treatment group and overall will be generated based on protocol deviation severity (minor/major) and the classification of protocol using the following categories:

- Inclusion
- Exclusion
- Study drug
- Assessment – safety
- Assessment– efficacy
- Lab/endpoint data
- Visit window
- Informed consent
- Prohibited co-medication
- Overdose/misuse
- Other

7.3. Demographics and Other Baseline Characteristics

Descriptive summaries of the demographic and other baseline characteristics will be presented for all analysis populations. All demographic and baseline characteristics will be presented both overall and by treatment group.

The following demographic and baseline data will be presented in tables:

- Demographics: age, gender, ethnicity, race, height, weight, and body mass index (BMI)
- For female the number and percentage of women surgically sterile and postmenopausal will be described.
- Diagnosis of osteoarthritis: number of subjects with osteoarthritis diagnosis and area affected, clinical significance, radiological investigations, radiological significance, Kellgren-Lawrence score.

The number and percent of subjects reporting various medical histories, grouped by MedDRA system organ class (SOC) and preferred term (PT), will be tabulated by treatment group.

This analysis will be conducted for the Safety Population.

7.4. Exposure

The following parameters of study drug exposure and compliance will be summarized by treatment group for the Safety Population:

- Maximum number of doses administered
- Total duration of exposure
- Total (cumulative) dose infused

In addition, any incomplete infusions will be listed.

8. Efficacy Analysis

All efficacy variables will be summarized descriptively including number of observations, number of missing values, mean, SD, minimum, median, and maximum for continuous variables, and frequency of observations in each category and percentage for categorical variables.

Primary and secondary endpoint efficacy data will be tabulated according to the observed cases, LOCF, and BOCF approaches.

8.1. Primary Efficacy Analysis

The primary efficacy endpoint of this study is the change in the weekly average of the average daily pain scores from the baseline week to Week 12 measured on an 11-point (0-10) NRS.

MCP-Mod approach. The main statistical analysis of the primary efficacy endpoint will use the MCP-Mod approach on LOCF data, which is a well-established statistical methodology for establishing both the existence of a dose response and modelling the underlying dose-response relationship. The modelling step ('MOD' step) from the MCP-MOD approach will only be conducted if stage 4 is initiated, otherwise there would be insufficient dosing data to fit the non-linear models.

There are two steps to MCP-Mod:

1. The 'MCP' step is a rigorous method to establish presence of a dose response while protecting the type I error and, if the dose-response relationship is statistically significant, then
2. The 'MOD' step estimates the dose response function and associated model parameters.

The MCP test will use linear contrasts corresponding to the five candidate models described in Section 3.2. The test will use pre-specified model parameters and optimal contrasts for each will be generated. The hypotheses are as follows:

Null hypothesis (H_0): Optimal contrasts $\mu \geq 0$ for all models

Alternative hypothesis (H_A): Optimal contrasts $\mu < 0$ for at least one model

where μ is the true event rate.

The underlying model will be an ANCOVA with dependent variable 'change from baseline to Week 12 (LOCF)', and independent variables will include:

- dose group as a factor variable with the placebo group as the reference level
- baseline score, i.e. baseline weekly average pain (NRS), as a continuous variable
- co-medication type.

The random error is assumed to be normally and independently distributed with constant variance. The parameter estimates of the difference between each dose group and placebo, least square (LS) Means estimates of change from baseline to Week 12 for each dose, standard errors, 95% unadjusted, 'Lalonde-type' asymmetric CI (i.e., lower limit of 1-sided 90% CI and upper limit of 1-sided 80% CI), and *P* values will be presented.

If the MCP test is statistically significant, then the MOD step will select the most appropriate model from hyperbolic E_{max}, sigmoidal E_{max} or linear using the 'E_{maxlin}' approach as described by Kirby et al (2011). From this model (including the same covariates as the ANCOVA model), various estimates will be derived (together with CI) of parameters of interest such as ED50, effective dose to achieve 90% of maximum effect (ED90), dose to achieve selected target effects, and model estimates of the treatment effect at doses studied (see Appendix in Section 15).

MMRM: In addition, changes from baseline in continuous endpoints will be compared between treatment groups using mixed models repeated measures including terms for:

- co-medication type (as a factor)
- treatment (as a factor)
- time (as a factor)
- the interaction between treatment and time point
- and the baseline value of the variable undergoing analysis

The mixed model for repeated measure will use average of average daily pain score of observed data at week 2, 4, 6, 8, 10, and 12. An unstructured covariance matrix will be used to model the

within-subject errors. The Kenwards-Roger method will be used to estimate degrees of freedom. If this analysis fails to converge, a simpler structure (e.g., first-order ante-dependent or heterogeneous compound symmetry structures) will be found using Akaike information criterion (AIC).

The results will be presented using LS Means estimates, corresponding 95% CI for each treatment group and timepoint, along with the LS Means of differences with Placebo, standard error, 95% CI and p-values.

The primary efficacy analysis will be based on the mITT population.

8.1.1. Sensitivity Analyses of the Primary Efficacy Endpoint

To complement the MCP-MOD outputs, estimates and CI of each pairwise comparison versus placebo from the ANCOVA model described in the MCP step will be produced.

8.2. Secondary Efficacy Analysis

The MMRM model outlined in Section 8.1 will be applied for secondary endpoints using observed cases:

- Change in Galer NPS total score from baseline to Days 28, 56, and 84 of treatment and the follow-up visit.
- Change in DSIS from baseline to Days 28, 56, and 84 of treatment and the follow-up visit.
- Change in the eight SF-36 parameters from baseline to Day 84 of treatment.

A GEE approach for binary data will be used for the following dichotomous endpoints:

- Percentage of subjects who have achieved ≥30% reductions in the weekly average of the average daily pain score from baseline during Weeks 4, 8, and 12 of treatment and the week before follow-up.
- Percentage of subjects who have achieved ≥50% reductions in the weekly average of the average daily pain score from baseline during Weeks 4, 8, and 12 of treatment and the week before follow-up.

The GEE model specification will include a binomial distribution, a logit link function, and an unstructured covariance matrix. If this analysis fails to converge, a simpler structure (e.g. first-order autoregressive or compound symmetry structures) will be found using AIC. The model will include terms for:

- co-medication type (as a factor)
- treatment (as a factor)
- time (as a factor)
- the interaction between treatment and time

A CMH test stratified by the crossing of co-medication subgroup and median baseline pain score will also be carried out for the above dichotomous endpoints. The CMH risk difference at Week 12 will be estimated between the treatment group and placebo. The number and percentage of subjects meeting the reduction response will be displayed, along with the risk difference, 95% CI and *P* value.

The proportion of subjects who have 'improved', 'much improved,' or 'very much improved' relative to baseline on the PGIC on Days 28, 56, and 84 of treatment and the follow-up visit will be tested using a CMH statistics.

The efficacy analysis of secondary endpoints will be based on the observed cases and on the mITT population.

Usage of rescue medication (yes/no) will be summarized by dose group for each visit from baseline to Week 12 of treatment and over the whole treatment period. The following additional variables will be derived and summarised:

- Total number of days rescue medication was used.
  - Each day on which rescue medication was used at least once is counted.
- Cumulative consumption (mg) of paracetamol rescue medication use.
  - Calculated as the total dose of rescue medication (mg).
- Average daily dose (mg) of paracetamol rescue medication use.
  - Calculated as: cumulative consumption of rescue medication (mg)/total number of days rescue medication was used.

8.3. Exploratory Efficacy Analysis

CCI

[redacted]

9. Safety and Tolerability Analysis

All safety analyses will be performed on the Safety Population using descriptive statistics. Descriptive summaries by treatment group and overall will be produced. No inferential statistical tests will be performed.

The analysis of safety assessments in this study will include summaries of the following categories of safety and tolerability data collected for each patient:

- Adverse events
    - TEAEs
    - SAEs
    - Significant AEs
        - TEAEs leading to discontinuation of IP
    - AEs of Special Interest
        - Positively-adjudicated possible or probable rapidly progressive osteoarthritis (RPOA), subchondral insufficiency fractures, primary osteonecrosis, or pathological fracture
        - Infections that meet SAE and/or severe AE criteria
        - Anaphylactic reactions or infusion-related reactions that lead to permanent discontinuation of administration of IP
    - TEAEs associated with abnormal liver
    - Any deaths
    - Drug induced liver injury

Clinical laboratory investigations

- Vital signs
- Electrocardiograms (ECG)
- COVID-19 screening
- Physical and neurological examination
- Total neuropathy score-nurse
- Motor and sensory nerve conduction studies
- Strength and deep tendon reflexes
- Hypersensitivity /Anaphylactic reactions
- Injection site or infusion reactions
- Liver diagnostic investigations, risk factors, signs and symptoms.
- Infection diagnostic investigations, risk factors, signs and symptoms.
- Prior and concomitant medications and therapies

9.1. Adverse Events

A summary table by treatment group will present the number and percent of subjects reporting:

- Any AEs
- Non-serious AEs occurring in more than 5% of subjects
- Any TEAEs
- Any SAEs
- Any TEAEs possibley related to study drug
- Any TEAEs leading to discontinuation of IP
- Any SAEs possibley related to study drug
- Life-threatenings SAEs
- SAEs resulting in death

Summaries of the incidence of TEAEs will be displayed by treatment group, by ADA status, by severity and by:

- SOC and PT
- SOC, PT, and maximum severity (mild, moderate, severe)
- SOC, PT, and maximum causality (not related, possibly related) to the study drug

In the summaries showing severity and relationship to study drug the event with the maximum severity or strongest relationship will be reported. If a particular event is missing the severity and/or relationship, then the strongest possible severity or relationship will be assumed for analysis (severity = severe, relationship = related).

In the case of multiple occurrences of the same AE within the same subject, each subject will only be counted once for each level of summarization.

All AEs will be presented in a by-treatment and by-subject listing, detailing the verbatim term given by the Investigator, the PT, SOC, onset date and time, end date and time, severity, outcome, relationship to study drug, action taken with study drug, other action taken, seriousness, and criteria for seriousness.

9.1.1. Adverse Events Leading to Discontinuation of IP

A summary of incidence rates (frequencies and percentages) of TEAEs leading to discontinuation of IP, by treatment group, SOC, and PT will be prepared. The table will also be produced separately by maximum severity and maximum causality.

A data listing of TEAEs leading to discontinuation of IP will also be provided, displaying details of the event(s) captured on the rCRF.

9.1.2. Deaths and Serious Adverse Events

Any deaths that occur during the study and serious adverse events will be listed.

A summary of incidence rates (frequencies and percentages) of SAEs by treatment group, SOC, and PT will be prepared. The table will also be produced separately for life-threatening SAEs, for SAEs with outcome death and for SAEs by relationship to study medication.

9.1.3. Drug-Induced Liver Injury

A summary of incidence rates of TEAEs associated with abnormal liver by treatment group, SOC, and PT will be prepared.

The type and the results of the liver diagnostic investigation performed will be tabulated by treatment group.

The number and percentage of subjects within each type of liver risk factors and style events will be tabulated by treatment group. Liver signs and symptoms will be presented in the same way.

9.1.4. Infection Risk

A summary of incidence rates of infections that meet SAE or severe AE criteria by treatment group, SOC, and PT will be prepared.

The type and the results of infection diagnostic investigation performed will be tabulated by treatment group.

The number and percentage of subjects within each type of infection risk factors and style events will be tabulated by treatment group. Infection signs and symptoms will be presented in the same way.

9.2. COVID-19 Vaccination and Screening

The number and percentage of fully vaccinated subjects at baseline will be summarized by treatment group.

The symptoms, tests, and results from coronavirus disease 2019 (COVID-19) screening will be tabulated for each visit by treatment group.

COVID-19 vaccination, signs, symptoms and impact will be presented in listings.

9.3. Clinical Laboratory Evaluations

Absolute values and changes from baseline will be summarized using descriptive statistics by

treatment group and visit for chemistry, hematology, coagulation, and urinalysis tests.

The number of subjects with clinical laboratory values (chemistry, hematology, coagulation, and urinalysis) categorized as below, within, or above normal ranges (or as either normal or abnormal for urinalysis variables that do not have quantitative ranges) and whether they are clinically significant or not will be tabulated for each clinical laboratory analyte by treatment group and visit. A shift table showing change from baseline in range categories for each clinical laboratory analyte will be produced by treatment group and by visit.

The number of subjects with values for Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥ 3 × upper limit of normal (ULN), and with values for total bilirubin (TBL) ≥ 2 × ULN will be summarized in AST, ALT vs. TBL shift tables to identify Potential Hy's Law (PHL) and Hy's Law (HL) cases by treatment group.

Diagnostic immunology, urine pregnancy, and urine drug tests will be presented in by-subject listings only.

All laboratory values will be displayed in the data listings and those that are outside the normal range will be flagged, along with corresponding normal ranges.

9.4. Vital Signs

Descriptive summaries of actual values and changes from baseline by treatment group, visit and time point will be presented for:

- Supine heart rate
- Supine systolic blood pressure
- Supine diastolic blood pressure
- Respiratory rate
- Body temperature
- Standing heart rate
- Standing systolic blood pressure
- Standing diastolic blood pressure

Height, weight, and BMI will be presented at baseline only.

9.5. Electrocardiograms

The number and percentage of subjects with normal, abnormal not clinically significant, and abnormal clinically significant ECG results will be summarized by treatment group and by visit.

If applicable (digital ECGs), descriptive summaries will be presented by treatment group, visit and time point (for Day 1 only) for ECG measures of PR, QRS, QT, RR intervals and for the calculated variables QTcF and HR for each treatment group and time point.

Heart rate (HR) and Fridericia's correction (QTcF) will be derived as follows:

Heart Rate (HR)	$HR = 10^3 \frac{60}{RR_{msec}}$
Fridericia's Correction (QTcF)	$QTc_f = \frac{QT_{msec}}{\sqrt[3]{RR}}$ sec

9.6. Physical and Neurological Examination

The physical and neurological examination findings will be presented in listings.

9.7. Total Neuropathy Score-Nurse

Descriptive summaries of the TNSn will be presented by treatment groups and by visit. Additionally, the number and percentage of subjects within each category (0, 1, 2, 3, and 4) for each sub-score (sensory symptom, motor symptom, autonomic symptom, pin sensibility, vibration sensibility) will be summarized by treatment group and by visit.

9.8. Motor and Sensory Nerve Conduction Studies

Amplitude, peak latency, conduction velocity, and duration of nerve action potentials will be summarized by treatment group and visit for each location and evaluation type. The number of subjects with normal and abnormal evaluation will be tabulated by treatment group and by visit.

9.9. Strength and Deep Tendon Reflexes

The number and percentage of subjects within each category of the ankle dorsiflexion strength and the deep tendon reflexes will be tabulated by treatment group and by visit .

9.10. Hypersensitivity/Anaphylactic Reactions, Injection Site or Infusion Reactions

The type and symptoms of hypersensitivity/ anaphylactic reactions will be tabulated by treatment group.

Injection site reactions will be tabulated describing the severity of pain, tenderness, erythema/redness, and induration/swelling by treatment group and by visit.

Anaphylactic reactions and infusion related reactions will be summarized in line with AEs, displayed by treatment group and by:

- SOC and PT
- SOC, PT, and maximum severity (mild, moderate, severe)

Hypersensitivity/anaphylactic and infusion related reactions will also be presented in a by-

treatment and by-subject listings, detailing type of reaction, severity grade for symptom with highest severity and onset time for hypersensitivity/anaphylactic reactions, and assessment result for injection site or infusion related reactions.

9.11. Prior and Concomitant Medication and Procedures

Prior medications will be presented separately from concomitant medications.

Medications will be coded using the latest version of the WHO Drug Dictionary.

Medications that started before first dose of study medication will be considered prior, whether they were stopped before first dose of study medication or not.

A concomitant medication is defined as any medication continuing or starting after first dose of study medication. This includes medications which start before first dose of study medication and continue while on-treatment, and medications that started after first dose of study medication.

The frequency and percentage of concomitant medications will be summarized by Anatomical Therapeutic Chemical (ATC) class 2 and preferred name by treatment groups, unless otherwise specified.

In listings, all medications will be displayed.

If the start/stop dates of a medication are partially or completely missing, then the medication will be assumed to be concomitant if it cannot be definitely shown from the start/stop dates that it was not administered while on-treatment (from first exposure to treatment till last dose of study medication + 14 exposure days). Missing dates will not be replaced.

Thus, the following approach will be taken for exclusion from concomitant medications because of discontinuation before start of treatment:

- If the stop day is missing but the month is complete, then the medication will be excluded from concomitant medications only if the stop month is before the month of the first dose of study medication.
- If the stop day and month are missing but the year is complete, then the medication will be excluded from concomitant medications only if the stop year is before the year of the first dose of study medication.
- If the stop date is completely missing, then the medication will not be excluded.

For concomitant medication exclusion (because of the late start after the end of the treatment period):

- If the start day is missing but the month is complete, then the medication will be excluded from concomitant medications only if the start month is after the last month of the treatment period.

- If the start day and month are missing but the year is complete, then the medication will be excluded from concomitant medications only if the start year is after the year of the treatment period.
- If the start date is completely missing, then the medication will not be excluded.

A similar approach will be used for summarizing concomitant procedures.

10. Changes from Planned Analysis

CCI [redacted]

The PK endpoints involving derivation of PK parameters for each dose and for each subject will be conducted by a population PK analysis of the data as part of a pooled data analysis instead of by a noncompartmental analysis (NCA). This will be documented in the CSR as a change in planned analysis. The pooled data analysis will be described in a separate modelling analysis plan. As a result, description of TLFs related to PK parameters are removed from this SAP.

Additional analyses with pooled site as a covariate are not going to be conducted and as such, they are removed from this SAP.

It was planned to have a supplementary analysis to the primary using an adaptive MCP-MOD method. In this analysis, stages 2+3 and stage 4 were going to be analysed separately and the results combined using an inverse-normal *P* value combination function (with weights related to the original planned sample sizes). This supplementary analysis is removed from this SAP.

The Cochran-Mantel-Haenszel test for the non-binary categorical endpoints has been extended to include the secondary endpoint of pain response.

The definition of TEAE from the protocol has been changed in this SAP, eliminating the condition for the AE onset not being more than 30 days after the last administration of IP to be regarded as a TEAE. The change in the definition of TEAE has been made upon Sponsor request, to enable transparency, adequate safety reporting and oversight of safety profile/risks.

11. Other Planned Analysis

11.1. CCI [redacted]

CCI [redacted]

CCI

CCI

11.2. Immunogenicity

Blood samples will be collected for assessment of ADA levels. Anti-Drug Antibody response during the entire study period and at each study assessment will be summarised according to ADA category and titre value for the Safety population with evaluable ADA results. A listing of the ADA test results will be produced.

For immunogenicity analysis, the presence of detectable (i.e., positive) ADAs against MEDI7352 will be reported. ADA results from each sample are reported as either positive or negative. In addition, the ADA titer result will be reported for samples confirmed positive for the presence of ADAs. A participant is defined as being ADA-positive if a positive ADA result is available at any time, including baseline and all post-baseline measurements, otherwise ADA negative.

The following ADA categories will be determined:

- ADA positive if a collected sample is tested positive at any time during the study, including baseline and/or post-baseline. (The percentage of these participants in a population is known as ADA prevalence).
- Treatment-emergent ADA positive (TE-ADA+): A positive post-baseline result and either of the following statements holds:
    - Baseline is ADA negative and at least one post-baseline assessment is ADA positive. This is called treatment-induced ADA positive.
    - Baseline is ADA positive, and the baseline titre is boosted by greater than the variability of the assay (i.e., ≥X-fold increase, commonly 4-fold) at ≥1 post-baseline timepoint. This is called treatment-boosted ADA positive.

  (The percentage of these participants in a population is known as ADA incidence)

- Only baseline positive if a collected sample is tested positive at baseline.
- Non-Treatment-emergent ADA positive (non-TE-ADA+): Participants who are ADA positive but not fulfilling the conditions for TE-ADA+.
- Treatment-emergent Persistently ADA positive: ADA negative at baseline and having at least 2 post-baseline ADA positive measurements with ≥16 weeks (112 days) between first and last positive, or an ADA positive result at the last available post-baseline assessment.
- Treatment-emergent Transiently ADA positive: ADA negative at baseline and at least one post-baseline ADA positive measurement and not fulfilling the conditions for persistently positive

- ADA positive post-baseline and positive at baseline.

11.3. Pharmacokinetic Analysis

Pharmacokinetic concentration data will be summarized using descriptive statistics by dose and treatment visit overall and by ADA status (positive/negative) presenting the number (n) of non-missing observations, and the n < LLOQ. A figure of geometric mean (with and without gSD) serum MEDI7352 concentration over time by treatment group will be generated (overall and by ADA status (positive/negative)). Additionally, pharmacokinetic concentration data will be listed and presented graphically as spaghetti plots of individual participant profiles by treatment group and ADA status (positive/negative).

12. References

1. ICH (1998) ICH Harmonised Tripartite Guideline. Statistical Principles for Clinical Trials E9; 1998. https://database.ich.org/sites/default/files/E9_Guideline.pdf
2. ASA. (2018) Ethical Guidelines for Statistical Practice. Prepared by the Committee on Professional Ethics, April 2018. http://www.amstat.org/about/ethicalguidelines.cfm
3. RSS. (2014) The Royal Statistical Society: Code of Conduct, 2014. http://www.rss.org.uk/Images/PDF/join-us/RSS-Code-of-Conduct-2014.pdf.
4. Satoh J, Yagihashi S, Baba M, Suzuki M, Arakawa A, Yoshiyama T. Efficacy and safety evaluation of pregabalin treatment over 52 weeks in patients with diabetic neuropathic pain extended after a double-blind placebo-controlled trial. *J Diabetes Investig*. 2011;2(6):457-463. Doi: 10.1111/j.2040-1124.2011.00122.x.
5. Lesser H, Sharma U, LaMoreaux L, Poole RM. Pregabalin relieves symptoms of painful diabetic neuropathy: a randomized controlled trial. *Neurology*. 2004;63(11):2104-2110.
6. Rosenstock J, Tuchman M, LaMoreaux L, Sharma U. Pregabalin for the treatment of painful diabetic peripheral neuropathy: a double-blind, placebo-controlled trial. *Pain*. 2004;110(3):628-638.
7. Tölle T, Freynhagen R, Versavel M, Trostmann U, Young JP Jr. Pregabalin for relief of neuropathic pain associated with diabetic neuropathy: a randomized, double-blind study. *Eur J Pain*. 2008;12(2):203-213.
8. Pinheiro J, Bornkamp B, Bretz F. Design and analysis of dose-finding studies combining multiple comparisons and modelling procedures. *J Biopharm Stat*. 2006;16(5):639-656. Doi: 10.1080/10543400600860428.
9. Thomas N, Sweeney K, Somayaji V. Meta-analysis of clinical dose–response in a large drug development portfolio. *Stat Biopharm Res*. 2014;6(4):302-317. Doi: 10.1080/19466315.2014.924876.

10. Kirby S, B*rain P, Jones B. Fitting E(max) models to clinical trial dose-response data.* Pharma Stat. 2011;10(2):143-149. Doi: 10.1002/pst.432.

13. Tables, Listings, and Figures

All listings, tables, and graphs will have a header showing the sponsor company name and protocol and a footer showing the version of SAS, the file name and path, and the source of the data (eCRF page or listing number).

The following are planned summary tables for protocol number D5680C00002. The table numbers and page numbers are place holders only and will be determined when the tables are produced.

13.1. Demographic Data

Table 1: Demographic Data Summary Tables and Figures

Table Number	Population	Table Title/Summary
Table 14.1.2	Screening	Subject Disposition
Table 14.1.3	Screen Failure	Summary of Reasons for Screening Failure
Table 14.1.4.1	Screening	Demographics and Baseline Characteristics
Table 14.1.4.2	Safety	Demographics and Baseline Characteristics
Table 14.1.4.3	mITT	Demographics and Baseline Characteristics
Table 14.1.4.4	PK	Demographics and Baseline Characteristics
Table 14.1.5.1	Screening	Osteoarthritis Characteristics
Table 14.1.5.2	Safety	Osteoarthritis Characteristics
Table 14.1.5.3	mITT	Osteoarthritis Characteristics
Table 14.1.5.4	PK	Osteoarthritis Characteristics
Table 14.1.6	Safety	Medical History by System Organ Class and Preferred Term
Table 14.1.7	Safety	Prior Medications by ATC Class and Preferred Name
Table 14.1.8	Safety	Protocol Deviations
Table 14.1.9	Safety	Overall Study Drug Exposure

13.2. Efficacy Data

Table 2: Efficacy Data

Table Number	Population	Table Title / Summary
Table 14.2.1.1.1	mITT	Daily Pain NRS: Summary Statistics (Observed Cases)
Table 14.2.1.1.2	mITT	Daily Pain NRS: Summary Statistics (LOCF)
Table 14.2.1.1.3	mITT	Daily Pain NRS: Summary Statistics (BOCF)
Table 14.2.1.2.1	mITT	Daily Pain NRS: Primary MCP-Mod Analysis (LOCF)
Table 14.2.1.2.2	mITT	Statistical Analysis of CFB to Week 12 Daily Pain NRS: Primary ANCOVA Analysis (LOCF)
Table 14.2.1.3.1	mITT	Statistical Analysis of CFB Daily Pain NRS: MMRM Analysis. (Observed Cases)
Table 14.2.1.3.2	mITT	Daily Pain NRS: Sensitivity of Primary MCP-Mod Analysis (BOCF)
Table 14.2.2.1	mITT	Galer NPS: Summary Statistics (Observed Cases)
Table 14.2.2.2	mITT	Galer NPS: MMRM Analysis (Observed Cases)
Table 14.2.3.1	mITT	DSIS: Summary Statistics (Observed Cases)
Table 14.2.3.2	mITT	DSIS: MMRM Analysis (Observed Cases)
Table 14.2.4.1	mITT	SF-36: Summary Statistics (Observed Cases)
Table 14.2.4.2	mITT	SF-36: MMRM Analysis (Observed Cases)
Table 14.2.5.1	mITT	Rescue Medication Use: Summary Statistics
Table 14.2.6.1	mITT	Daily Pain NRS Responder Analysis (≥30%): Cochran-Mantel-Haenszel (Observed Cases)
Table 14.2.6.2	mITT	Daily Pain NRS Responder Analysis (≥30%): GEE Analysis (Observed Cases)
Table 14.2.7.1	mITT	Daily Pain NRS Responder Analysis (≥50%): Cochran-Mantel-Haenszel (Observed Cases)
Table 14.2.7.2	mITT	Daily Pain NRS Responder Analysis (≥50%): GEE Analysis (Observed Cases)
Table 14.2.8.1	mITT	Patient Global Impression of Change: Summary Statistics
Table 14.2.8.2	mITT	Patient Global Impression of Change: Cochran-Mantel-Haenszel
CCI [redacted]		

13.3. Safety Data

Table 3: Safety Data

Table Number	Population	Table Title / Summary
14.3.1 Displays of Adverse Events		
Table 14.3.1.1	Safety	Summary of Overall Adverse Events
Table 14.3.1.2	Safety	Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Table 14.3.1.3	Safety	Treatment Emergent Adverse Events by Severity, System Organ Class and Preferred Term
Table 14.3.1.4	Safety	Treatment Emergent Adverse Events by Relationship to Study Medication, System Organ Class and Preferred Term
Table 14.3.1.5	Safety	Treatment Emergent Adverse Events by ADA Status Category, System Organ Class and Preferred Term
Table 14.3.1.6	Safety	Treatment Emergent Adverse Events Leading to Discontinuation of Study drug by System Organ Class and Preferred Term
Table 14.3.1.7	Safety	Non-Serious Adverse Events Occurring in More than 5% of Subjects by System Organ Class and Preferred Term
Table 14.3.1.8	Safety	Treatment Emergent Adverse Events Occurring in More than 5% of Subjects by Preferred Term
Table 14.3.1.9	Safety	Treatment Emergent Adverse Events by Preferred Term
14.3.2 Summary of Deaths, Other Serious and Significant Adverse Events		
Table 14.3.2.1.1	Safety	Serious Adverse Events by System Organ Class and Preferred Term
Table 14.3.2.1.2	Safety	Life-Threatening Serious Adverse Events by System Organ Class and Preferred Term
Table 14.3.2.1.3	Safety	Serious Adverse Events with Outcome Death by System Organ Class and Preferred Term
Table 14.3.2.1.4	Safety	Serious Adverse Events by Relationship to Study Medication, System Organ Class and Preferred Term
14.3.2.2 Displays of Significant Adverse Events and Adverse Events of Special Interest		
Table 14.3.2.2.1	Safety	Treatment Emergent Adverse Events Associated with Abnormal Liver by System Organ Class and Preferred Term
Table 14.3.2.2.2	Safety	Potential Joint Related Adverse Events of Special Interest by System Organ Class and Preferred Term
Table 14.3.2.2.3	Safety	Serious and/or severe Infections by System Organ Class and Preferred Term

Table Number	Population	Table Title / Summary
Table 14.3.2.2.4	Safety	Anaphylactic Reactions, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of IP by System Organ Class and Preferred Term
14.3.3 Narratives of Deaths and Other Serious Adverse Events		
Table 14.3.3.1	Safety	Listing of Serious Adverse Events
Table 14.3.3.2	Safety	Listing of Deaths
14.3.4 Laboratory Data Summary Tables		
Table 14.3.4.1	Safety	Descriptive Summary of Clinical Chemistry
Table 14.3.4.2	Safety	Shift Table of Clinical Chemistry Results
Table 14.3.4.3	Safety	Descriptive Summary of Hematology
Table 14.3.4.4	Safety	Shift Table of Hematology Results
Table 14.3.4.5	Safety	Descriptive Summary of Coagulation
Table 14.3.4.6	Safety	Shift Table of Coagulation Results
Table 14.3.4.7	Safety	Descriptive Summary of Urinalysis
Table 14.3.4.8	Safety	Shift Table of Urinalysis Results
Table 14.3.4.9	Safety	Maximum On-Treatment ALT and AST versus Maximum On-Treatment Total Bilirubin
14.3.6 Other Safety Data Summary Tables		
Table 14.3.5.1	Safety	Descriptive Summary of Vital Signs
Table 14.3.5.2	Safety	Descriptive Summary of ECG Digital Data
Table 14.3.5.3	Safety	Summary of Overall Evaluation of Safety ECG Data
Table 14.3.5.4	Safety	Covid-19 Screening
Table 14.3.5.5	Safety	Summary of Sub-Scores for Total Neuropathy Score-Nurse
Table 14.3.5.6	Safety	Descriptive Summary of Total Neuropathy Score-Nurse
Table 14.3.5.7	Safety	Summary of Motor and Sensory Nerve Conduction Studies
Table 14.3.5.8	Safety	Summary of Strength and Deep Tendon Reflexes
Table 14.3.5.9	Safety	Summary of Local Injection Site Reactions
Table 14.3.5.10	Safety	Summary of Anaphylactic Reactions
Table 14.3.5.11	Safety	Summary of Liver Diagnostic Investigations
Table 14.3.5.12	Safety	Summary of Liver Risk Factors and Lifestyle Events
Table 14.3.5.13	Safety	Summary of Liver Signs and Symptoms

Table Number	Population	Table Title / Summary
Table 14.3.5.14	Safety	Summary of Infection Diagnostic Investigations
Table 14.3.5.15	Safety	Summary of Infection Risk Factors and Lifestyle Events
Table 14.3.5.16	Safety	Summary of Infection Signs and Symptoms
Table 14.3.5.17	Safety	Summary of Concomitant Medications by ATC Level 2 and Preferred Term
Table 14.3.5.18	Safety	Summary of Concomitant Procedures
Table 14.3.5.19	Safety	Anti-Drug Antibody Results and Titre Summary by Timepoint
Table 14.3.5.20	Safety	Descriptive Summary of Anti-Drug Antibody Results and Titre by ADA Categories

13.4. Pharmacokinetic/Pharmacodynamic Data

Table 4: Pharmacokinetic/Pharmacodynamic Data

Table Number	Population	Table Title / Summary
14.4 Pharmacokinetic and Pharmacodynamic Data Summary Tables		
Table 14.4.1	PK	Summary of Serum MEDI7352 Concentrations
Table 14.4.2	Safety	Summary of Serum total NGF Concentrations

13.5. Planned Listing Descriptions

The following are planned data and patient/subject data listings for protocol number D5680C00002.

In general, one listing will be produced per eCRF domain. All listings will be sorted by treatment, site, and subject number. All calculated variables will be included in the listings.

In all listings a blank line will be placed between each subject. Within a data listing, if an item appears line after line (e.g., repetition of subject number), then only the first occurrence will be displayed.

In data listings, the information for one subject will be kept on one page if at all possible, rather than splitting a subject's information across pages.

Table 5: Planned Listings

Data Listing Number	Population	Data Listing Title / Summary
16.2 Subject Data Listings		
16.2.1 Subject Discontinuations/Completions		
Listing 16.2.1.1	Screening	Subject Disposition
Listing 16.2.1.2	Screening	Assignment to Analysis Populations
Listing 16.2.1.3	Safety	Reason for IP Discontinuation and Withdrawal from the Study
Listing 16.2.1.4	Screen Failure	List of Reasons for Screening Failure
Listing 16.2.1.5	Screening	Visits List and COVID-19 Impact
16.2.2 Protocol Deviations		
Listing 16.2.2.1	Screening	Subjects Not Meeting All Inclusion Criteria or Meeting any Exclusion Criteria
Listing 16.2.2.2	Safety	Protocol Deviations
16.2.3 Randomization		
Listing 16.2.3	Safety	Randomization and Treatment Group

Data Listing Number	Population	Data Listing Title / Summary
16.2 Subject Data Listings		
16.2.4 Demographic Data and Other Baseline Characteristics		
Listing 16.2.4.1	Screening	Demographic and Baseline Characteristics
Listing 16.2.4.2	Safety	Medical History
Listing 16.2.4.3	Screening	Osteoarthritis Characteristics
16.2.5 Compliance and/or Drug Concentration Data		
Listing 16.2.5.1	Safety	Study Drug Administration: Individual Doses
16.2.6 Individual Efficacy Response Data		
Listing 16.2.6.1	mITT	Daily Pain NRS
Listing 16.2.6.2	mITT	Galer NPS
Listing 16.2.6.3	mITT	DSIS
Listing 16.2.6.4	mITT	SF-36
Listing 16.2.6.5	mITT	Rescue Medication Usage
Listing 16.2.6.6	mITT	Patient Global Impression of Change
CCI [redacted]		
16.2.7 Adverse Event Listings (by Patient/Subject)		
Listing 16.2.7.1	Safety	Adverse Events
Listing 16.2.7.2	Safety	Treatment Emergent Adverse Events Leading to Study Drug Discontinuation
Listing 16.2.7.3	Safety	Treatment Emergent Adverse Events Associated with Abnormal Liver
Listing 16.2.7.4	Safety	Joint Related Adverse Events of Special Interest
Listing 16.2.7.5	Safety	Serious and/or Severe Infections
Listing 16.2.7.6	Safety	Anaphylactic Reactions, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of Study Drug
16.2.8 Laboratory Values (by Patient/Subject)		
Listing 16.2.8.1	Safety	Clinical Chemistry Laboratory Evaluations
Listing 16.2.8.2	Safety	Hematology Laboratory Evaluations
Listing 16.2.8.3	Safety	Coagulation Laboratory Evaluations
Listing 16.2.8.4	Safety	Urinalysis Laboratory Evaluations
Listing 16.2.8.5	Safety	Serology Laboratory Evaluations
Listing 16.2.8.6	Safety	Pregnancy Test Results

Data Listing Number	Population	Data Listing Title / Summary
16.2 Subject Data Listings		
Listing 16.2.8.7	Safety	Drug Test Results
Listing 16.2.8.8	Safety	COVID-19 Screening
16.2.9 Other Clinical Observations and Measurements (by Patient/Subject)		
Listing 16.2.9.1	Safety	Vital Signs Measurements
Listing 16.2.9.2.1	Safety	12-Lead Digital ECG Results
Listing 16.2.9.2.2	Safety	12-Lead Safety ECG Results
Listing 16.2.9.3	Safety	Physical Examination Results
Listing 16.2.9.4	Safety	Neurological Examination Results
Listing 16.2.9.5	Safety	Total Neuropathy Score-Nurse
Listing 16.2.9.6	Safety	Motor and Sensory Nerve Conduction Studies
Listing 16.2.9.7	Safety	Strength and Deep Tendon Reflexes
Listing 16.2.9.8	Safety	Injection Site Reactions
Listing 16.2.9.9	Safety	Anaphylactic Reactions
Listing 16.2.9.10	Safety	Liver Diagnostic Investigations
Listing 16.2.9.11	Safety	Liver Risk Factors and Lifestyle Events
Listing 16.2.9.12	Safety	Liver Signs and Symptoms
Listing 16.2.9.13	Safety	Infection Diagnostic Investigations
Listing 16.2.9.14	Safety	Infection Risk Factors and Lifestyle Events
Listing 16.2.9.15	Safety	Infection Signs and Symptoms
Listing 16.2.9.16	Safety	Prior and Concomitant Medications
Listing 16.2.9.17	Safety	Prohibited Concomitant Medications
Listing 16.2.9.18	Safety	Concomitant Procedures
Listing 16.2.9.19	Safety	Anti-drug Antibody Test Results
16.2.10 Pharmacokinetic/Pharmacodynamic Measurements		
Listing 16.2.10.1	PK	Serum MEDI7352 Concentrations
Listing 16.2.10.2	Safety	Serum total NGF Concentrations

13.6. Planned Figure Descriptions

The following are planned summary figures for protocol number D5680C00002. The figure numbers and page numbers are place holders only and will be determined when the figures are produced.

Table 6: Planned Figures

Figure Number	Population	Figure Title/Summary
Figure 14.2.1.1	mITT	Daily Pain NRS: MCP-Mod Dose Response Model
Figure 14.2.1.2	mITT	Daily Pain NRS: Boxplots at Week 12 by Treatment Group and Missing Data Handling
Figure 14.2.1.3	mITT	Daily Pain NRS: Boxplots at Week 12 by Treatment Group and Co-Medication Subgroup
Figure 14.2.1.4	mITT	Daily Pain NRS: MMRM LS Means (95% Confidence Interval) over 12-weeks by Treatment Group (Observed Cases)
Figure 14.3.6.1.1	Safety	Vital Sign Profiles: Mean (±SD) Systolic Blood Pressure over time
Figure 14.3.6.1.2	Safety	Vital Sign Profiles: Mean (±SD) Diastolic Blood Pressure over time
Figure 14.3.6.1.3	Safety	Vital Sign Profiles: Mean (±SD) Heart Rate over time
Figure 14.3.6.1.4	Safety	Vital Sign Profiles: Mean (±SD) Respiratory Rate over time
Figure 14.3.6.1.5	Safety	Vital Sign Profiles: Mean (±SD) Temperature over time
Figure 14.4.1.1	PK	Pharmacokinetics: Line Plot of Geometric Mean (with and without gSD) Serum MEDI7352 over time
Figure 14.4.1.2	PK	Pharmacokinetics: Individual Plot of Serum MEDI7352 Concentrations over time
Figure 14.4.2.1	Safety	Pharmacodynamics: Line Plot of Geometric Mean (with and without gSD) Serum total NGF over time
Figure 14.4.2.2	Safety	Pharmacodynamics: Individual Plot of Serum total NGF over time

14. Tables, Listing and Figure Shells

14.1. Standard Layout for all Tables, Listings, and Figures

The following standard layout will be applied to all Tables, Listings, and Figures in support of this study. Note that programming notes may be added if appropriate after each table, listing and figure shell. All shells will be provided as a separate document.

Figure 1: Standardized Layout

Astra Zeneca — Page xx of xx

Protocol: D5680C00002 — Version

<Table, Listing, Figure> xx.x.x

Title of Table, Listing or Figure

Study Population and if applicable subgroup Description

Body of Table, Listing or Figure

Note: If directly Applicable

Footnote 1

Footnote 2

Footnote n

Footnote n+1 SAS program path and name Executed on ddmmmyyyy at hh:mm on data from ddmmmyyyy

15. Appendix: Calculation of Dose to achieve target effects

Although only one dose-response model type (Emax) is pre-specified in the protocol for the primary analysis, CCI [redacted]

Let us assume the R® *DoseFinding* package original parametrization for these two dose-response model functions below:

Journal of Statistical Software 9

Name	$f(d, \boldsymbol{\theta})$	$f^0(d, \boldsymbol{\theta}^*)$	(*)	(♯)
`linear`	$E_0 + \delta d$	d		
`linlog`	$E_0 + \delta \log(d + c)$	$\log(d + c)$		c
`quadratic`	$E_0 + \beta_1 d + \beta_2 d^2$	$d + \delta d^2$ if $\beta_2 < 0$	δ	
`emax`	$E_0 + E_{\max} d/(ED_{50} + d)$	$d/(ED_{50} + d)$	ED_{50}	
`logistic`	$E_0 + E_{\max}/\{1 + \exp[(ED_{50} - d)/\delta]\}$	$1/\{1 + \exp[(ED_{50} - d)/\delta]\}$	$(ED_{50}, \delta)^\top$	
`exponential`	$E_0 + E_1(\exp(d/\delta) - 1)$	$\exp(d/\delta) - 1$	δ	
`sigEmax`	$E_0 + E_{\max} d^h/(ED_{50}^h + d^h)$	$d^h/(ED_{50}^h + d^h)$	$(ED_{50}, h)^\top$	
`betaMod`	$E_0 + E_{\max} B(\delta_1, \delta_2)(d/D)^{\delta_1}(1 - d/D)^{\delta_2}$	$B(\delta_1, \delta_2)(d/D)^{\delta_1}(1 - d/D)^{\delta_2}$	$(\delta_1, \delta_2)^\top$	D

Table 1: Dose-response models implemented in the **MCPMod** package. Column (*) lists for

1. Equations for Target Dose D_Δ to achieve a Delta (Δ) versus placebo

   Emax: $TD_\Delta = ED_{50}/((E_{max}/\Delta) - 1)$, where ED_{50} and E_{max} are estimated from the fitted Emax model

   Exponential: $TD_\Delta = \delta * \log((\Delta/E_1) + 1)$, where δ and E_1 are estimated from the fitted exponential model

   (The function TD from the DoseFinding package will be used for the above)

2. Equations for Dose (ED_P) to achieve a certain proportion P of the effect of the maximum dose studied versus placebo (See DoseFinding manual page 51 where ED is 'Effective Dose')

Emax: $ED_P = (P * ED_{50} * \max(doses)) / (ED_{50} + (1-P) * \max(doses)) = (P * ED_{50} * 150) / (ED_{50} + (1-P) * 150)$

Exponential: $ED_P = \delta * \log((P * \exp(\max(doses)/\delta) + 1 - P)) = \delta * \log((P * \exp(150/\delta) + 1 - P))$

(The function ED from the DoseFinding package will be used for the above)

3. Equation for Dose (asym ED_P) to achieve a certain proportion P of the asymptotic maximum effect (E_{max}) versus placebo

Emax: asymptotic $ED_P = (P * ED_{50}) / (1-P)$

Simulation-based CI will be created for each of the above quantities from the mean and covariance matrix of the model parameters, assuming multivariate normality. Therefore 10,000 samples from the multivariate distribution will be taken, and for each simulation the TD and ED estimates calculated. The 2.5% and 97.5% percentiles will then form the appropriate 95% two-sided CI.

Sponsor:	AstraZeneca
Protocol Title	A Randomised, Double-Blind, Placebo-Controlled, Dose-Response Study of the Efficacy and Safety of MEDI7352 in Subjects with Painful Diabetic Neuropathy
Development Phase	2
Protocol Numbers:	D5680C00002
Premier Research PCNs:	MEDU177093
Document Version:	Final Version 1.0
Document Date:	12-Jul-2023

Document History

Version	Date	Author	Description
0.1	24-Mar-2023	PPD	Draft Version
0.2	21-Apr-2023	PPD	Draft Version
0.3	24-May-2023	PPD	Draft Version
0.4	20-Jun-2023	PPD	Draft Version

Tables, Listings, and Figures Conventions

All listings, tables, and graphs will have a header showing the sponsor company name, protocol and version of delivery and a footer showing the version of SAS, the file name and path, and the source of the data (listing number).

The following reporting conventions will be adopted for the presentation of study data. These conventions will enhance the review process and help to standardize the presentation with common notations.

General Reporting Conventions

- All tables and data listings will be developed in landscape orientation.
- Specialized text styles, such as bolding, italics, borders, shading, and superscripted and subscripted text will not be used in tables, figures, and data listings unless they add significant value to the table, figure, or data listing.
- Only standard keyboard characters should be used in tables and data listings. Special characters, such as nonprintable control characters, printer-specific characters, or font specific characters, will not be used on a table, figure, or data listing.
- Adverse events with missing MedDRA coding will have their system organ class preferred term presented as “Not Coded” and the Preferred Term presented as verbatim in the tables. The “Not Coded” frequencies will be sorted to the end of the tables. This will only be applicable for any deliveries sent before database lock (e.g., for dry runs).
- Programming notes may be inserted into the shells, these notes will not appear in the final output.

Population Summary Conventions

- Population sizes may be presented for each classification factor as totals in the column header as (N=xx), where appropriate.
- All population summaries for categorical variables will include all categories that were planned and for which the participants may have had a response.
- All population summaries for continuous variables will include: n, mean, SD, median, quartiles, minimum, and maximum. Other summaries (e.g., number missing, geometric mean, 95% CIs, and coefficient of variation [CV] or % CV) may be used as appropriate. The precision of the maximum and minimum will match the maximum precision in the observed data and 2 decimals for derived data unless specifically mentioned in the corresponding shell. The mean and median will have 1 additional decimal place. The SD will have 2 additional decimal places. For derived data, minimum and maximum will be reported to 2 degrees of precision. Measures of location (mean and median) will be reported to 3 degree of precision, and measures of spread will be reported to 4 degrees of precision.

- All percentages are rounded and reported to a single decimal point (xx.x%). Exceptions are 0 and 100 that will be displayed as 0 and 100% respectively.

Planned Tables, Figures and Listings

- The table and listing numbers are place holders only and will be determined when the outputs are produced.
- In all listings a blank line will be placed between each participant. Within a data listing, if an item appears line after line (e.g., repetition of participant number), then only the first occurrence will be displayed.
- In data listings, the information for 1 participant will be kept on 1 page, if possible, rather than splitting a Subjects's information across pages.

Planned Table Descriptions and Shells

Number Title Population	Unique (U) or Repeated (R)
Table 14.1.2 - - Screening Population	U
Table 14.1.3 - Summary of Reasons for Screening Failure - Screen Failure Population	U
Table 14.1.4.1 - Demographics and Baseline Characteristics - Screening Population	U
Table 14.1.4.2 - Demographics and Baseline Characteristics - Safety Population	R
Table 14.1.4.3 - Demographics and Baseline Characteristics - mITT Population	R
Table 14.1.4.4 - Demographics and Baseline Characteristics - PK Population	R
Table 14.1.5.1 - Osteoarthritis Characteristics - Screening Population	U
Table 14.1.5.2 - Osteoarthritis Characteristics - Safety Population	R
Table 14.1.5.3 - Osteoarthritis Characteristics - mITT Population	R
Table 14.1.5.4 - Osteoarthritis Characteristics - PK Population	R
Table 14.1.6 - Medical History by System Organ Class and Preferred Term - Safety Population	U
Table 14.1.7 - Prior Medications by ATC Level 2 and Preferred Name - Safety Population	U
Table 14.1.8 - Protocol Deviations - Safety Population	U
Table 14.1.9 - Overall Study Drug Exposure - Safety Population	U
Table 14.2.1.1.1 - Daily Pain NRS: Summary Statistics (Observed Cases) - mITT Population	U
Table 14.2.1.1.2 - Daily Pain NRS: Summary Statistics (LOCF) - mITT Population	R
Table 14.2.1.1.3 - Daily Pain NRS: Summary Statistics (BOCF) - mITT Population	R
Table 14.2.1.2.1 - Daily Pain NRS: Primary MCP-Mod Analysis (LOCF) - mITT Population	U
Table 14.2.1.2.2 - Statistical Analysis of CFB to Week 12 Daily Pain NRS: Primary ANCOVA Analysis (LOCF) - mITT Population	U
Table 14.2.1.3.1 - Statistical Analysis of CFB Daily Pain NRS: MMRM Analysis. (Observed Cases) - mITT Population	U
Table 14.2.1.3.2 - Daily Pain NRS: Sensitivity of Primary MCP-Mod Analysis (BOCF) - mITT Population	R
Table 14.2.2.1 - Galer NPS: Summary Statistics (Observed Cases) - mITT Population	U
Table 14.2.2.2 - Galer NPS: MMRM Analysis (Observed Cases) - mITT Population	U
Table 14.2.3.1 - DSIS: Summary Statistics (Observed Cases) - mITT Population	U
Table 14.2.3.2 - DSIS: MMRM Analysis (Observed Cases) - mITT Population	U
Table 14.2.4.1 - SF-36: Summary Statistics (Observed Cases) - mITT Population	U
Table 14.2.4.2 - SF-36: MMRM Analysis (Observed Cases) - mITT Population	U
Table 14.2.5.1 - Rescue Medication Use: Summary Statistics - mITT Population	U

Number Title Population	Unique (U) or Repeated (R)
Table 14.2.6.1 - Daily Pain NRS Responder Analysis (≥30%): Cochran-Mantel Haenszel (Observed Cases) - mITT Population	U
Table 14.2.6.2 - Daily Pain NRS Responder Analysis (≥30%): GEE Analysis (Observed Cases) - mITT Population	U
Table 14.2.7.1 - Daily Pain NRS Responder Analysis (≥50%): Cochran-Mantel Haenszel (Observed Cases) - mITT Population	R
Table 14.2.7.2 - Daily Pain NRS Responder Analysis (≥50%): GEE Analysis (Observed Cases) - mITT Population	R
Table 14.2.8.1 - Patient Global Impression of Change: Summary Statistics - mITT Population	U
Table 14.2.8.2 - Patient Global Impression of Change: Cochran-Mantel Haenszel - mITT Population	U
CCI [redacted]	U
Table 14.3.1.1 - Summary of Overall Adverse Events - Safety Population	U
Table 14.3.1.2 - Treatment Emergent of Adverse Events by System Organ Class and Preferred Term - Safety Population	U
Table 14.3.1.3 - Treatment Emergent of Adverse Events by Severity, System Organ Class and Preferred Term - Safety Population	U
Table 14.3.1.4 - Treatment Emergent Adverse Events by Relationship to Study Medication, System Organ Class and Preferred Term - Safety Population	U
Table 14.3.1.5 - Treatment Emergent Adverse Events by ADA Status Category, System Organ Class and Preferred Term - Safety Population	U
Table 14.3.1.6 - Treatment Emergent Adverse Events Leading to Discontinuation of Study drug by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.1.7 - Non-Serious Adverse Events Occurring in More than 5% of Subjects by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.1.8 - Treatment Emergent Adverse Events Occurring in More than 5% of Subjects by Preferred Term - Safety Population	R
Table 14.3.1.9 - Treatment Emergent Adverse Events by Preferred Term - Safety Population	R
Table 14.3.2.1.1 - Serious Adverse Events by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.1.2 - Life-Threatening Serious Adverse Events by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.1.2 - Serious Adverse Events with Outcome Death by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.1.4 - Serious Adverse Events by Relationship to Study Medication, System Organ Class and Preferred Term - Safety Population	R
Table 14.3.3.1 - Listing of Serious Adverse Events - Safety Population	U
Table 14.3.3.2 - Listing of Deaths - Safety Population	U

Number Title Population	Unique (U) or Repeated (R)
Table 14.3.2.2.1 - Treatment Emergent Adverse Events Associated with Abnormal Liver by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.2.2 - Potential Joint Related Adverse Events of Special Interest by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.2.3 - Serious and/or severe Infections by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.2.4 - Anaphylactic Reactions, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of IP by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.4.1 - Descriptive Summary of Clinical Chemistry - Safety Population	U
Table 14.3.4.2 - Shift Table of Clinical Chemistry Results - Safety Population	U
Table 14.3.4.3 - Descriptive Summary of Hematology - Safety Population	R
Table 14.3.4.4 - Shift Table of Hematology Results - Safety Population	R
Table 14.3.4.5 - Descriptive Summary of Coagulation - Safety Population	R
Table 14.3.4.6 - Shift Table of Coagulation Results - Safety Population	R
Table 14.3.4.7 - Descriptive Summary of Urinalysis - Safety Population	U
Table 14.3.4.8 - Shift Table of Urinalysis Results - Safety Population	R
Table 14.3.4.9 - Maximum On-Treatment ALT and AST versus Maximum On-Treatment Total Bilirubin - Safety Population	U
Table 14.3.5.1 - Descriptive Summary of Vital Signs - Safety Population	U
Table 14.3.5.2 - Descriptive Summary of ECG Data - Safety Population	U
Table 14.3.5.3 - Summary of Overall Evaluation of safety ECG Data - Safety Population	U
Table 14.3.5.4 - Covid-19 Screening - Safety Population	U
Table 14.3.5.5 - Summary of Sub-Scores for Total Neuropathy Score-Nurse - Safety Population	U
Table 14.3.5.6 - Descriptive Summary of Total Neuropathy Score-Nurse - Safety Population	U
Table 14.3.5.7 - Summary of Motor and Sensory Nerve Conduction Studies - Safety Population	U
Table 14.3.5.8 - Summary of Strength and Deep Tendon Reflexes - Safety Population	U
Table 14.3.5.9 - Summary of Local Injection Site Reactions - Safety Population	U
Table 14.3.5.10 - Summary of Hypersensitivity/Anaphylactic Reactions - Safety Population	U
Table 14.3.5.11 - Summary of Liver Diagnostic Investigations - Safety Population	U
Table 14.3.5.12 - Summary of Liver Risk Factors and Lifestyle Events - Safety Population	U
Table 14.3.5.13 - Summary of Liver Signs and Symptoms - Safety Population	U
Table 14.3.5.14 - Summary of Infection Diagnostic Investigations - Safety Population	U
Table 14.3.5.15 - Summary of Infection Risk Factors and Lifestyle Events - Safety Population	U

Number Title Population	Unique (U) or Repeated (R)
Table 14.3.5.16 - Summary of Infection Signs and Symptoms - Safety Population	**U**
Table 14.3.5.17 - Summary of Concomitant Medications by ATC Level 2 and Preferred Name - Safety Population	**R**
Table 14.3.5.18 - Summary of Concomitant Procedures - Safety Population	**R**
Table 14.3.5.19 - Anti-Drug Antibody Results and Titre Summary by Timepoint - Safety Population	**U**
Table 14.3.5.20 - Descriptive Summary of Anti-Drug Antibody Results and Titre by ADA Categories - Safety Population	**U**
Table 14.4.1 - Summary of Serum MEDI7352 Concentrations - PK Population	**U**
Table 14.4.2 - Summary of Serum total NGF Concentrations - PD Population	**U**

Table Change Log

Output Number	Date of Change	Change Made By (initials)	Description/Rationale

1. Demographic Data

Table 14.1.2
Subject Disposition
Screening Population

Status	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=xx)
Screening Population [1]					xx (100%)
Enrolled Subjects					xx (xx.x %)
Re-screened Subjects	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Randomized Subjects	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Safety Population [2]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
mITT Population [3]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Evaluable Week 12 Efficacy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Evaluable LOCF Efficacy [4]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Efficacy Evaluable	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PK Population [5]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Completed Study Treatment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Discontinued Study Treatment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reason for Discontinuation:					
Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lack of Efficacy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lost to Follow-up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Non-compliance with Study Drug	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Physician Decision	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pregnancy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Progressive Disease	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Violation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Study Terminated by Sponsor	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Technical Problems	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Withdrawal by Subject	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Completed Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Withdrawn from the Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reason for Discontinuation:					
Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lack of Efficacy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lost to Follow-up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
...					

COVID-19 = Coronavirus disease 2019; LOCF = Last Observation Carried Forward; mITT = modified intent-to-treat; N = number of subjects per treatment group; PK = pharmacokinetic.
Note: Percentages are n/Number of subjects randomized*100 as displayed in column header N, except for the screened, enrolled, re-screened and randomized, where n/Number of Screening subjects*100.
[1] The Screening Population includes all subjects who provide informed consent and provide demographic and/or baseline screening assessments.
[2] The Safety Population includes all subjects who receive at least 1 dose of double-blind study medication.
[3] The mITT Population includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
[4] Subjects in the mITT Population with LOCF applied for missing efficacy data at week 12,
[5] The PK Population includes all subjects for who a pharmacokinetic sample was obtained and analyzed.

Reference Listings: 16.2.1.1, 16.2.1.2, 16.2.1.3,

Programming Notes:

- Display only reasons for early discontinuation with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.3
Summary of Reasons for Screening Failure
Screen Failure Population

	Total (N=xx)
Number of Subjects Who Don't Meet Inclusion/Exclusion Criteria	xx (xx.x%)
Reason 1	xx (xx.x%)
Reason 2	xx (xx.x%)
Reason 3	xx (xx.x%)
Reason 4	xx (xx.x%)

N = number of subjects.
Note: subject can be counted in more than one criterion.
Reference Listing 16.2.1.4

Table 14.1.4.1
Demographics and Baseline Characteristics
Screening Population

Variable Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	 CCI (N=xx)	 CCI (N=xx)	Total (N=xx)
Age (years) [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Age Category					
≥18 - <65 years	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
≥65 years	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Gender					
Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ethnicity					
Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Race					
American Indian or Alaska Native	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Black or African American	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Native Hawaiian or Other Pacific Islander	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Specified	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Screening Height (cm)					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Screening Weight (kg)					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Screening BMI (kg/m²)					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Female characteristics [2]					
Surgically sterile	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Postmenopausal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Fully vaccinated for COVID-19					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

BMI = Body Mass Index; COVID-19 = Coronavirus disease 2019; n = number of subjects by treatment group with collected parameter; N = number of subjects per treatment group; SD = standard deviation.
[1] Age was calculated as age at time of consent.
[2] Percentages are n/Number of Female subjects from Analysis Population*100
Reference Listing: 16.2.4.1

Programming Notes:

- If a variable is between 2 pages, start the variable in the second page.
- Keep all possible values for each category even if no subject.
- A column for CCI dosing (CCI [redacted] will only be added if Stage 4 is initiated.

Table 14.1.4.2
Demographics and Baseline Characteristics
Safety Population

Programming Notes:

- Same shell as Table 14.1.4.1.
- Keep all possible values for each category even if no subject.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.4.3
Demographics and Baseline Characteristics
mITT Population

Programming Notes:

- Same shell as Table 14.1.4.1.
- Keep all possible values for each category even if no subject.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.4.4
Demographics and Baseline Characteristics
PK Population

Programming Notes:

- Same shell as Table 14.1.4.1.
- Keep all possible values for each category even if no subject.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.5.1
Osteoarthritis Characteristics
Screening Population

Variable Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=xx)
Subjects diagnosed with Osteoarthritis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Joint(s)/Area(s) affected:					
Shoulder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Elbow	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hip	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Knee	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ankle	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Spine	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hands	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Feet	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Osteoarthritis clinically significant					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Radiologic investigations conducted [1]					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Plain radiography	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
MRI	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Joint(s)/Area(s) investigated:					
Shoulder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Elbow	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hip	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Knee	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ankle	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Spine	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Hands	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Feet	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Osteoarthritis radiologically significant					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Kellgren-Lawrence score reported					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No/Not applicable	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Radiologic Scoring System Used?					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

MRI = magnetic resonance imaging; N = number of subjects per treatment group.
[1] Subjects who reported more than one radiologic investigation within each category were only counted once.
Reference Listing: 16.2.4.3

Programming Notes:

- Display only Joint(s)/Areas(s) affected and investigated with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.5.2
Osteoarthritis Characteristics
Safety Population

Programming Notes:

- Same shell as Table 14.1.5.1.
- Display only Joint(s)/Areas(s) affected and investigated with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.5.3
Osteoarthritis Characteristics
mITT Population

Programming Notes:

- Same shell as Table 14.1.5.1.
- Display only Joint(s)/Areas(s) affected and investigated with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.5.4
Osteoarthritis Characteristics
PK Population

Programming Notes:

- Same shell as Table 14.1.5.1.
- Display only Joint(s)/Areas(s) affected and investigated with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.6
Medical History by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=xxx)	MEDI7352 CCI (N=xx)	 CCI (N=xx)	 CCI (N=xx)	Total (N=xxx)
Any Medical History	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
System Organ Class 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
…	…	…	…	…	…
System Organ Class n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)

N = number of subjects per treatment group.
Note: All medical history terms were coded using the Medical Dictionary for Regulatory Activities (MedDRA), version 26.0. At each level of summarization (system organ class or preferred term), subjects having more than one medical history term were counted only once. System organ class and preferred terms are sorted in descending order of frequency of Total column, and alphabetically if same frequency.

Reference Listing: 16.2.4.2

Programming Notes:

- SOC and PT texts should be in proper case in table.
- Sort SOC and PT (within SOC) in descending order of frequency in the Total column. Sort alphabetically in case of ties.
- Uncoded Medical History Events
  - When there are uncoded Medical History Events in the database, the events will be summarized with SOC and PT set to [Not Coded]. The [Not Coded] will be sorted at the end of the table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.7
Prior Medications by ATC Class and Preferred Name
Safety Population

ATC Class [1] Preferred Term	Placebo	MEDI7352			Total
		CCI	CCI	CCI	
	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Subjects with at Least One Prior Medication	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATC Level 2 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Name 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Name n	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATC Level 2 n	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Name 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Name n	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

ATC = Anatomical Therapeutic Class; N = number of subjects per treatment group.
[1] ATC Class is defined as ATC Level 2.
Note: Prior medications are defined as medications that started before first dose of study, whether they were stopped before first dose of study medication or not. All prior medications are coded using WHO drug dictionary version vMar2023. At each level of summarization (ATC Level 2 or Preferred Name), subjects who reported more than one prior medication were only counted once. ATC Level 2 and Preferred Term are sorted in in descending order of frequency of total, and alphabetically if same frequency.
Reference Listing: 16.2.9.16

Programming Notes:

- If uncoded ATC Level or Preferred Name, please put them as [Not Coded]
- ATC and Preferred Name texts should be in proper case in table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.8
Protocol Deviations
Safety Population

	Placebo	MEDI7352			Total
		CCI	CCI	CCI	
	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Subjects With Any Important Protocol Deviation/Violation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 5	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 6	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
……..					

N = number of subjects per treatment group.
Notes: Percentages are n/Number of subjects by treatment group*100.
Subjects with one or more deviations within a type of protocol deviation were counted only once.

Reference Listing 16.2.2.1

Programming Notes:

- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

2. Exposure and Compliance

Table 14.1.9
Overall Study Drug Exposure
Safety Population

Category/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=xx)
Maximum Number of Doses Administered [1]					
1 Dose	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 Doses	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 Doses	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 Doses	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
5 Doses	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
6 Doses	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total Duration of Exposure (days) [2]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Total (cumulative) dose infused (mL)					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

n = number of subjects by treatment group with collected parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Subjects are counted once for each level of dose administered.
[2] Duration of exposure (days) = min(date of last dose of treatment + 14 days or date of death) – date of first dose of treatment + 1.
Reference Listing: 16.2.5.1

Programming Notes:

- Add all categories even if count is 0.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

3. Primary Efficacy Analysis

Table 14.2.1.1.1
Daily Pain NRS: Summary Statistics (Observed Cases)
mITT Population

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=XX)
Baseline [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 2					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 2 CFB					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
…					

CFB = Change from Baseline; DPS = Daily Pain Score; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NRS = Numeric Rating Scale; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
Note: Data shown are weekly averages of the average daily pain scores on an 11-point (0-10) NRS and CFB for the same variable.
[1] Baseline is defined as the average of the 'non-missing' DPS within the seven-day period prior to randomization **i.e.,** Day -7 to Day -1, inclusive.

Reference Listing: 16.2.6.1

Programming Notes:

- Include all observed data (Not the LOCF) on weekly averages of the average daily pain scores for Baseline, Week 2, 4, 6, 8, 10, 12 and 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.1.1.2
Daily Pain NRS: Summary Statistics (LOCF)
mITT Population

Programming Notes:

- Same shell as Table 14.2.1.1.1.
- Include all observed and LOCF data on weekly averages of the average daily pain scores for Baseline, Week 2, 4, 6, 8, 10, and 12
- Add abbreviation in footnote: LOCF = Last Observation Carried Forward.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.1.1.3
Daily Pain NRS: Summary Statistics (BOCF)
mITT Population

Programming Notes:

- Same shell as Table 14.2.1.1.1.
- Include all observed and BOCF data on weekly averages of the average daily pain scores for Baseline, Week 2, 4, 6, 8, 10, and 12
- Add abbreviation in footnote: BOCF = Baseline Observation Carried Forward.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.1.2.1
Daily Pain NRS: Primary MCP-Mod Analysis (LOCF)
mITT Population

'MCP' step

Model Contrast [1]	t value	1-sided adjusted P-value [2]
Hyperbolic E_{max}		
ED50 = 7.5	xx.xx	0.xxxx
ED50 = 15	xx.xx	0.xxxx
ED50 = 30	xx.xx	0.xxxx
ED50 = 60	xx.xx	0.xxxx
ED50 = 750	xx.xx	0.xxxx
Exponential		
δ = 100	xx.xx	0.xxxx
δ = 200	xx.xx	0.xxxx

CFB = Change from Baseline; LOCF = Last Observation Carried Forward; MCP = Multiple Comparisons; Procedure; NRS = Numeric rating scale.
[1] ED50 = Effective Dose giving half of the asymptotic maximum effect.
[2] Multiplicity Adjusted P-value

'MOD' step [3]
Selected Model xxxxxxxxxx

Parameter	Estimate	95% CI of Estimate [6]
ED50	xx.x	[x.xx to x.xx]
ED90 [4]	xx.x	[x.xx to x.xx]
Asymptotic ED90 [5]	xx.x	[x.xx to x.xx]
Dose to achieve target (-1.25) effect	xx.x	[x.xx to x.xx]
Treatment effect at dose = 5 mcg	xx.x	[x.xx to x.xx]
Treatment effect at dose = 50 mcg	xx.x	[x.xx to x.xx]
Treatment effect at dose = 150 mcg	xx.x	[x.xx to x.xx]
Treatment effect at dose = 450 mcg	xx.x	[x.xx to x.xx]

CI: Confidence Interval; LOCF = Last Observation Carried Forward; MCP = Multiple Comparisons; Procedure; MOD = Modelling; NRS = Numeric rating scale.
[3] Results from the 'MOD' step will only be available in case any of the MCP tests is statistically significant.
[4] ED90 = Effective Dose giving 90% of the effect of the maximum dose studied.
[5] Asymptotic ED90 = Effective Dose giving 90% of the asymptotic maximum effect.
[6] 2.5% and 97.5% quantiles taken from 100000 samples from the multivariate normal distribution for model fitted estimates and its covariance matrix.
Reference Listing: 16.2.6.1

Programming Notes:

- The 'MOD' step will only be performed if stage 4 is initiated, otherwise there would be insufficient dosing data to fit the non-linear models.

Table 14.2.1.2.2
Statistical Analysis of CFB to Week 12 Daily Pain NRS: Primary ANCOVA Analysis (LOCF)
mITT Population

Model parameter estimates

Parameter	Estimate	t value	Degrees of freedom	Standard Error	2-sided 95% unadjusted CL	Asymmetric CL [1]	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx	[x.xx to x.xx]		
Co-Medication Type			2				0.xxxx
Baseline pain NRS	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]		0.xxxx
Active 5 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Active 150 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Active 450 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Model residual standard deviation	xx.xx						

ANCOVA = analysis of covariance; CFB = Change from Baseline;
CL = Confidence limits; LOCF = Last Observation Carried Forward; NRS = Numeric rating scale.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: ANCOVA by dose using NRS baseline value and co-medication as covariates, with CFB to Week 12 (LOCF) as dependent variable.

Least Square Means

Treatment	Number of Subjects	LS mean [3]	95% CI of LS mean
Active 450 mcg	xx	x.xx	[x.xx to x.xx]
Active 150 mcg	xx	x.xx	[x.xx to x.xx]
Active 5 mcg	xx	x.xx	[x.xx to x.xx]
Placebo	xx	x.xx	[x.xx to x.xx]

CI = Confidence interval; LOCF = Last Observation Carried Forward; LS = least square; NRS = Numeric rating scale.
[3] The LS mean is a model estimate using fitted group parameter and the baseline
weekly average pain NRS parameter evaluated at the grand mean over each group.
Reference Listing: 16.2.6.1

Programming Notes:

- Concomitant co-medication Type indicated for Painful Diabetic Neuropathy: either anticonvulsant class (pregabalin or gabapentin) or antidepressant class (duloxetine, venlafaxine, or amitriptyline).
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.1.3.1
Statistical Analysis of CFB Daily Pain NRS: MMRM Analysis. (Observed Cases)
mITT Population

Model parameter estimates

Parameter	Estimate	t value	Degrees of freedom	Standard Error	2-sided 95% unadjusted CL	Asymmetric CL [1]	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx			
Co-medication type			1				0.xxxx
Week			7				0.xxxx
Treatment			3				0.xxxx
Treatment*Week			21				0.xxxx
Baseline pain NRS	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]		0.xxxx
Active 5 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Active 150 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Active 450 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Model residual standard deviation	xx.xx						

CFB = Change from Baseline; CL = Confidence limits; MMRM = Mixed Model for Repeated Measures; NRS = Numeric rating scale.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: MMRM using Time, Treatment, Treatment*Time, NRS baseline value, and Co-medication type as covariates, with CFB as dependent variable.

Least Square Means: week xxxxx

Treatment	Number of patients	LS mean [3]	95% CI of LS mean
Active 450 mcg	xx	x.xx	[x.xx to x.xx]
Active 150 mcg	xx	x.xx	[x.xx to x.xx]
Active 5 mcg	xx	x.xx	[x.xx to x.xx]
Placebo	xx	x.xx	[x.xx to x.xx]
Active 450 mcg - Placebo	xx	x.xx	[x.xx to x.xx]
Active 150 mcg - Placebo	xx	x.xx	[x.xx to x.xx]
Active 5 mcg - Placebo	xx	x.xx	[x.xx to x.xx]

CI = Confidence interval; LS = least square; NRS = Numeric rating scale.
[3] The LS mean is a model estimate using fitted group parameter and the baseline weekly average pain NRS parameter evaluated at the grand mean over each group.
Reference Listing: 16.2.6.1

Programming Notes:

- Include LSmeans and difference in Lsmean with Placebo in repeated tables for the Treatment*Week interaction.
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.1.3.2
Daily Pain NRS: Sensitivity of Primary MCP-Mod Analysis (BOCF)
mITT Population

Programming Notes:

- Same shell as Table 14.2.1.2.1, substituting “LOCF = Last Observation Carried Forward” by “BOCF = Baseline Observation Carried Forward”.
- The MCP-MOD approach will only be performed if stage 4 is initiated, otherwise there would be insufficient dosing data to fit the non-linear models.

4. Secondary Efficacy Analysis

Table 14.2.2.1
Galer NPS: Summary Statistics (Observed Cases)
mITT Population

Parameter: xxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI [redacted] (N=xx)	MEDI7352 CCI [redacted] (N=xx)	MEDI7352 CCI [redacted] (N=xx)	Total (N=xx)
Baseline [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 4					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 4 CFB					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

…

For Pain Duration Frequency

Baseline [1]					
I feel a background pain all of the time and occasional flare-ups	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
I feel a single type of pain all the time	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
feel a single type of pain only sometimes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 4					

CFB = Change from Baseline; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NPS = Neuropathic Pain Scale; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
Note: Data shown are Pain Intensity, Unpleasantness, and Descriptor scores on an 11-point (0-10) NRS, and Pain Duration/Frequency on a 3-point NRS (1-3), plus CFB for the same variables.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Reference Listing: 16.2.6.2

Programming Notes:

- Include all observed data on Galer NPS scores for Baseline, Week 4, 8, 12, and 18.
- Repeat for the Parameters: Pain intensity, Pain Unpleasantness, Pain Sharpness, Pain Hotness, Pain Dullness, Pain Coldness, Pain Sensitivity, Pain Itching, Deep Pain Intensity, Surface Pain Intensity (All in an 11-point NRS), and Pain Duration/Frequency (in a 3-point NRS).
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.2.2
Galer NPS: MMRM Analysis (Observed Cases)
mITT Population

Model parameter estimates

Parameter	Estimate	t value	Degrees of freedom	Standard Error	2-sided 95% unadjusted CL	Asymmetric CL [1]	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx			
Co-Medication type			1				0.xxxx
Week			4				0.xxxx
Treatment			3				0.xxxx
Treatment*Week			12				0.xxxx
Baseline NPS	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]		0.xxxx
Active 5 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Active 150 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Active 450 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Model residual standard deviation	xx.xx						

CFB = Change from Baseline; CL = Confidence limits; MMRM: Mixed Model for Repeated Measures; NPS = Neuropathic Pain Scale.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: MMRM using Time, Treatment, Treatment*Time, NPS baseline value, and Co-medication type as covariates, with CFB as dependent variable.

Least Square Means: week: xxxx

Treatment	Number of patients	LS mean [3]	95% CI of LS mean
Active 450 mcg	xx	x.xx	[x.xx to x.xx]
Active 150 mcg	xx	x.xx	[x.xx to x.xx]
Active 5 mcg	xx	x.xx	[x.xx to x.xx]
Placebo	xx	x.xx	[x.xx to x.xx]
Active 450 mcg - Placebo	xx	x.xx	[x.xx to x.xx]
Active 150 mcg - Placebo	xx	x.xx	[x.xx to x.xx]
Active 5 mcg - Placebo	xx	x.xx	[x.xx to x.xx]

CI = Confidence interval; LS = least square; NPS = Neuropathic Pain Scale.
[3] The LS mean is a model estimate using fitted group parameter and the baseline NPS parameter evaluated at the grand mean over each group.
Reference Listing: 16.2.6.2

Programming Notes:

- Include Lsmeans and difference in Lsmean with Placebo in repeated tables for the Treatment*Week interaction.
- Include all observed data on Galer NPS scores for Baseline, Week 4, 8, 12, and 18.
- Analysis is done for Galer NPS Total Score.
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.3.1
DSIS: Summary Statistics (Observed Cases)
mITT Population

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=XX)
Baseline [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 4					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 4 CFB					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
…					

CFB = Change from Baseline; DSIS = Daily Sleep Interference; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
Note: Data shown are weekly averages of the average daily sleep interference scores on an 11-point (0-10) NRS and CFB for the same variable.
[1] Baseline is defined as the average of the 'non-missing' DSIS within the seven-day period prior to randomization **i.e.,** Day -7 to Day -1, inclusive.

Reference Listing: 16.2.6.3

Programming Notes:

- Include all observed data on weekly averages of the average daily Sleep Interference score for Baseline, Week 4, 8, 12, and 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.3.2
DSIS: MMRM Analysis (Observed Cases)
mITT Population

Model parameter estimates

Parameter	Estimate	t value	Degrees of freedom	Standard Error	2-sided 95% unadjusted CL	Asymmetric CL [1]	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx			
Co-medication type			1				0.xxxx
Week			4				0.xxxx
Treatment			3				0.xxxx
Treatment*Week			12				0.xxxx
Baseline DSIS	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]		0.xxxx
Active 5 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Active 150 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Active 450 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Model residual standard deviation	xx.xx						

CFB = Change from Baseline; CL = Confidence limits; MMRM: Mixed Model for Repeated Measures; DSIS = Daily Sleep Interference.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: MMRM using Time, Treatment, Treatment*Time, DSIS baseline value, and Co-medication type as covariates, with CFB as dependent variable.

Least Square Means: week xxxx

Treatment	Number of patients	LS mean [3]	95% CI of LS mean
Active 450 mcg	xx	x.xx	[x.xx to x.xx]
Active 150 mcg	xx	x.xx	[x.xx to x.xx]
Active 5 mcg	xx	x.xx	[x.xx to x.xx]
Placebo	xx	x.xx	[x.xx to x.xx]
Active 450 mcg - Placebo	xx	x.xx	[x.xx to x.xx]
Active 150 mcg - Placebo	xx	x.xx	[x.xx to x.xx]
Active 5 mcg - Placebo	xx	x.xx	[x.xx to x.xx]

CI = Confidence interval; LS = least square.
[3] The LS mean is a model estimate using fitted group parameter and the baseline weekly average DSIS parameter evaluated at the grand mean over each group.
Reference Listing: 16.2.6.1

Programming Notes:

- Include LS means and difference in LS mean with Placebo in repeated tables for the Treatment*Week interaction.
- Include all observed data on weekly average DSIS for Baseline, Week 4, 8, 12, and 18.
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.4.1
SF-36: Summary Statistics (Observed Cases)
mITT Population

Parameter: xxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=XX)
Baseline [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 12					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 12 CFB					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

...

When parameter is "Change in general Health"

Baseline [1]					
Much better now than one year ago	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Somewhat better now than one year ago	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
About the same as one year ago	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Somewhat worse now than one year ago	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Much worse now than one year ago	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 12					

CFB = Change from Baseline; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NRS = numeric rating scale; SD = standard deviation; SF-36 = 36-Item Short-Form Health Survey; Q1 = first quartile; Q3 = third quartile.
Note: Data shown are derived SF-36 scores and Change in General Health on a 5-point NRS (1-5), plus CFB for the same variables.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Reference Listing: 16.2.6.4

Programming Notes:

- Include all observed data on SF-36 scores for Baseline and Week 12.
- Repeat for the Parameters: Physical functioning, Role limitations due to physical health, Role limitations due to emotional problems, Vitality (Energy/fatigue), Emotional well-being, Social functioning, Pain and General Health (from 0 to 100), Physical Health Summary, Mental Health Summary, and Change in general Health (in a 5-point NRS).
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.4.2
SF-36: MMRM Analysis (Observed Cases)
mITT Population

Model parameter estimates: xxxxxxxx

Parameter	Estimate	t value	Degrees of freedom	Standard Error	2-sided 95% unadjusted CL	Asymmetric CL [1]	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx			
Co-medication type			xx				0.xxxx
Week			1				0.xxxx
Treatment			3				0.xxxx
Treatment*Week			3				0.xxxx
Baseline SF-36	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]		0.xxxx
Active 5 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Active 150 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Active 450 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Model residual standard deviation	xx.xx						

CFB = Change from Baseline; CL = Confidence limits; MMRM: Mixed Model for Repeated Measures; SF-36 = 36-Item Short-Form Health Survey.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: MMRM using Time, Treatment, Treatment*Time, SF-36 baseline value, and Co-medication type as covariates, with CFB as dependent variable.

Least Square Means: xxxxxxxx / week xxxx

Treatment	Number of patients	LS mean [3]	95% CI of LS mean
Active 450 mcg	xx	x.xx	[x.xx to x.xx]
Active 150 mcg	xx	x.xx	[x.xx to x.xx]
Active 5 mcg	xx	x.xx	[x.xx to x.xx]
Placebo	xx	x.xx	[x.xx to x.xx]
Active 450 mcg - Placebo	xx	x.xx	[x.xx to x.xx]
Active 150 mcg - Placebo	xx	x.xx	[x.xx to x.xx]
Active 5 mcg - Placebo	xx	x.xx	[x.xx to x.xx]

CI = Confidence interval; LS = least square.
[3] The LS mean is a model estimate using fitted group parameter and the baseline SF-36 parameter evaluated at the grand mean over each group.
Reference Listing: 16.2.6.4

Programming Notes:

- Include Lsmeans and difference in Lsmean with Placebo in repeated tables for the Treatment*Week interaction.
- Include all observed data on SF-36 scores for Baseline and Week 12.
- Repeat for the Parameters: Physical functioning, Role limitations due to physical health, Role limitations due to emotional problems, Vitality (Energy/fatigue), Emotional well-being, Social functioning, Pain and General Health. Add parameter name after ‘Model parameter estimates:’ and after ‘Least Square Means:’
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.5.1
Rescue Medication Use: Summary Statistics
mITT Population

Variable	Placebo	MEDI7352			Total
		CCI	CCI	CCI	
Statistic or Category	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Number of subjects taking any rescue medication	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number of subjects taking any permitted rescue medication	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total number of days rescue medication was used [1]					
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Cumulative consumption of Paracetamol Rescue Medication (mg) [2]					
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Paracetamol Rescue Medication Average Daily Dose (mg) [3]					
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Number of subjects taking any prohibited rescue medication	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Each day on which permitted rescue medication was used at least once is counted.
[2] Calculated as the total dose of paracetamol rescue medication (mg).
[3] Calculated as: cumulative consumption of paracetamol rescue medication (mg) /total number of days rescue medication was used.

Reference Listing: 16.2.6.5

Programming Notes:

- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.
- Refer to

Table 14.2.6.1
Daily Pain NRS Responder Analysis (≥30%): Cochran-Mantel Haenszel (Observed Cases)
mITT Population

Cochran-Mantel-Haenszel Test

Visit/ Category	Number of Subjects (%)	Risk Difference [1]	95% CI of Risk Difference	2-sided P-value [2]
Week 4				
>=30% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Week 8				
>=30% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Week 12				
>=30% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Week 18				
>=30% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx

CI = confidence interval; NRS = numeric rating scale.
[1] Common effect for the strata (co-medication type*median Baseline Pain NRS) specific risk difference, representing common difference in probability across strata.
[2] P-value < 0.05 indicates a significant association between number of subjects with >=30% decrease from Baseline and treatment across strata.
Reference Listing: 16.2.6.1

Programming notes:

- Include all observed data for Week 4, 8, 12, 18.

Table 14.2.6.2
Daily Pain NRS Responder Analysis (≥30%): GEE Analysis (Observed Cases)
mITT Population

Model parameter estimates

Parameter	Estimate	Z value	Degrees of freedom	Standard Error	2-sided 95% CL	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx		
Co-medication type			xx			0.xxxx
Week			4			0.xxxx
Treatment			3			0.xxxx
Treatment*Week			12			0.xxxx
Active 5 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	0.xxxx
Active 150 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	0.xxxx
Active 450 mcg vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	0.xxxx
Dispersion	xx.xx					

CL = Confidence limits; GEE: Generalized Estimation Equations; NRS = Numeric rating scale.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: GEE using Time, Treatment, Treatment*Time and Co-medication type as covariates, with dependent binary variable indicating whether weekly average pain NRS has >=30% decrease from Baseline.

Reference Listing: 16.2.6.1

Programming notes:

- Include all observed data for Week 4, 8, 12, and 18.
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.7.1
Daily Pain NRS Responder Analysis (≥50%): Cochran-Mantel Haenszel (Observed Cases)

mITT Population

Cochran-Mantel-Haenszel Test

Visit/ Category	Number of Subjects (%)	Risk Difference [1]	95% CI of Risk Difference	2-sided P-value [2]
Week 4				
>=50% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Week 8				
>=50% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Week 12				
>=50% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Week 18				
>=50% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx

CI = confidence interval; NRS = numeric rating scale.
[1] Common effect for the strata (co-medication type*median Baseline Pain NRS) specific risk difference, representing common difference in probability across strata.
[2] P-value < 0.05 indicates a significant association between number of subjects with >=50% decrease from Baseline and treatment across strata.
Reference Listing: 16.2.6.1

Programming notes:

- Include all observed data for Week 4, 8, 12, and 18.

Table 14.2.7.2
Daily Pain NRS Responder Analysis (≥50%): GEE Analysis (Observed Cases)
mITT Population

Programming notes:

- Same shell as Table 14.2.6.3. Change footnote in [2] as: "p-value is derived from the following model: GEE using Time, Treatment, Treatment*Time and Co-medication type as covariates, with dependent binary variable indicating whether weekly average pain NRS has >=50% decrease from Baseline".
- Include all observed data for Week 4, 8, 12, and 18.
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.8.1
Patient Global Impression of Change: Summary Statistics
mITT Population

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=XX)
Week 4					
Number of PGIC Responders	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Very Much Improved	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Much Improved	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Minimally Improved	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No change	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Minimally Worse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Much Worse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Very Much Worse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 8					
…					

N = number of subjects per treatment group; PGIC = Patient Global Impression of Change.
Note: Percentages for Number of subjects in the different improvement categories relative to baseline are n/Number of Subjects by treatment group at each visit *100.

Reference Listing: 16.2.6.6

Programming notes:

- Include all observed data on PGIC scores for Week 4, 8, 12 and 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.8.2
Patient Global Impression of Change: Cochran-Mantel Haenszel
mITT Population

Cochran-Mantel-Haenszel Test

Visit/ Category	Number of Patients (%)	Risk Difference [1]	95% CI of Risk Difference	2-sided P-value [2]
Week 4				
Improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Much Improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Very Much improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Week 8				
Improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Much Improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Very Much improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Week 12				
Improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Much Improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Very Much improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx

Week 18				
Improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Much Improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Very Much improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx

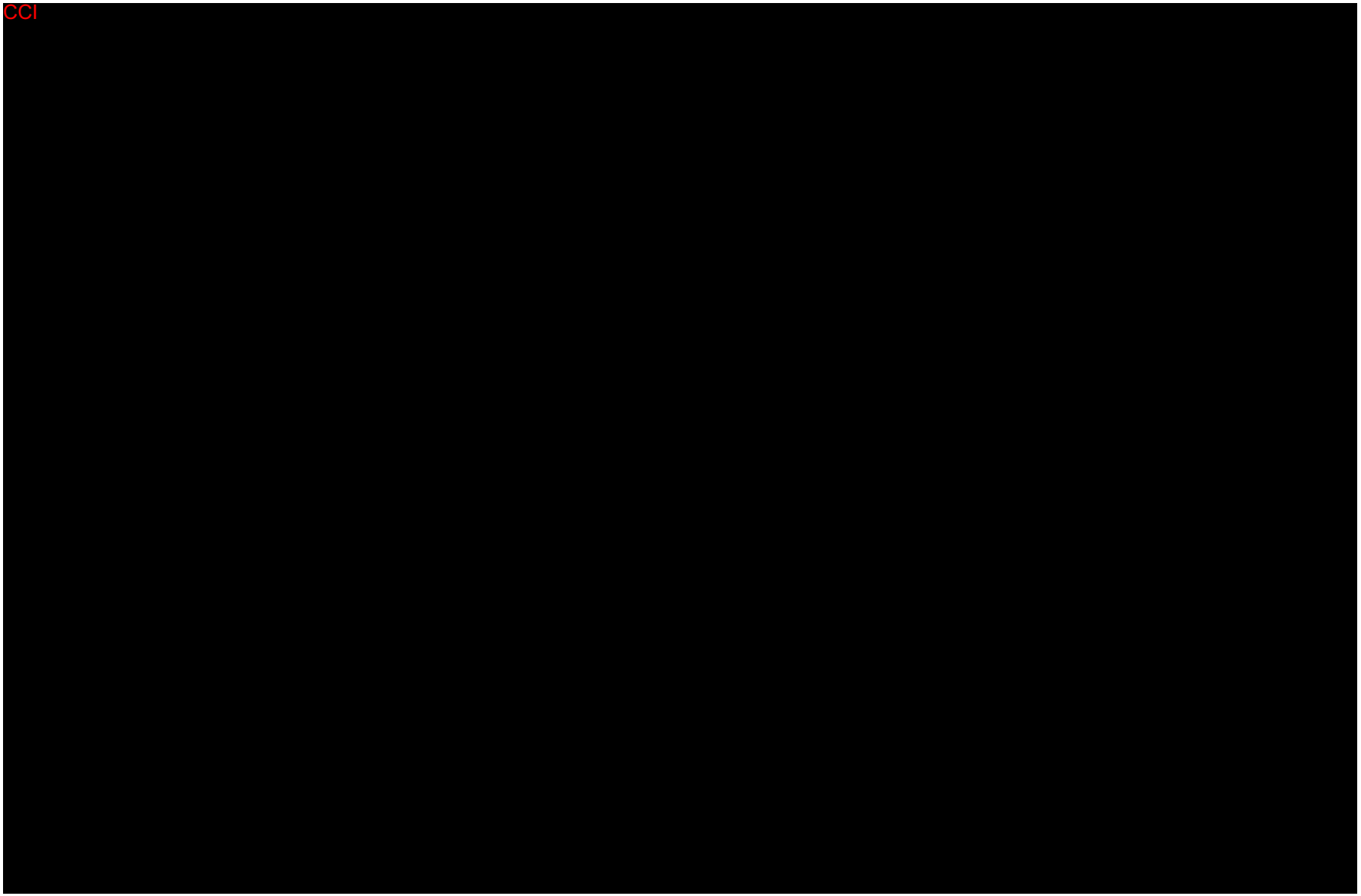
CI = confidence interval; NRS = numeric rating scale.
[1] Common effect for the strata (co-medication type*median Baseline Pain NRS) specific risk difference, representing common difference in probability across strata.
[2] P-value < 0.05 indicates a significant association between improvement relative to Baseline and treatment across strata.
Reference Listing: 16.2.6.6

Programming Notes:

- Include all observed data on PGIC scores for Week 4, 8, 12 and 18.

5. Exploratory Efficacy Analyses

CCI



CCI

[redacted]

6. Safety and Tolerability

6.1. Displays of Adverse Events

Table 14.3.1.1
Summary of Overall Adverse Events
Safety Population

Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Subjects with any AE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any TEAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any SAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any SAE possibly related to IP [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any TEAE leading to Discontinuation of IP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any TEAE related to IP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Mild related to IP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Moderate related to IP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Severe related to IP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any SAE leading to Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

AE = adverse event; IP = Investigational product, N = number of subjects per treatment group; SAE = serious adverse event; TEAE = treatment emergent adverse event.
[1] Possibly related is defined as with reasonable possibility that the AE was caused by the IP, as assessed by investigator
Note: Subjects who reported more than one adverse event within each category were only counted once. A TEAE is defined as an adverse event with an onset at the time of or following the start of treatment with IP.
Reference Listing: 16.2.7.1, 16.2.7.2, 16.2.7.3, 16.2.7.4

Programming Notes:

- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=xx)	MEDI7352 CCI (N=xx)	 CCI (N=xx)	 CCI (N=xx)	 All MEDI7352 (N=xx)	Total (N=xx)
Subjects with at Least One TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx

AE = adverse event; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects within each SOC/PT category; N = number of subjects per treatment group; IP = investigational product; PT = Preferred Term; SOC = System Organ Class; TEAE = treatment-emergent adverse event.
Note: Results are n (n/N * 100) then the total number of events.
A TEAE is defined as AE with an onset at the time of or following the start of treatment with IP.
Aes were coded using MedDRA version 26.0. Subjects are counted once for each SOC and once for each PT.
Aes are displayed by descending frequency of SOC, then descending frequency of PT within SOC, based on 'All MEDI7352' column. Table is sorted by international order for SOC of same frequency, and alphabetically for PT of same frequency.
Reference Listing: 16.2.7.1

Programming Notes:

- SOC and PT texts should be in proper case in table.
- In case a term is not coded (e.g. in a dry run) it will be labelled as “Not Coded [SOC]” and “Not Coded [PT]”, and sorted at the end of the table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.3
Treatment Emergent Adverse Events by Severity, System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term Severity	Placebo	MEDI7352				Total
		CCI	CCI	CCI	All MEDI7352	
	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Subjects with at Least One TEAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

AE = adverse event; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; ; n = number of subjects within each SOC/PT/Severity category; N = number of subjects per treatment group; PT = Preferred Term; SOC = System Organ Class; TEAE = treatment-emergent adverse event.
Note: Results are n (n/N * 100).
A TEAE is defined as an AE with an onset at the time of or following the start of treatment with IP.
Aes were coded using MedDRA version 26.0. Subjects are counted once for each SOC and once for each PT at the maximum severity.
Aes are displayed by descending frequency of SOC, then descending frequency of PT within SOC, based on 'All MEDI7352' column. Table is sorted by international order for SOC of same frequency, and alphabetically for PT of same frequency.
Reference Listing 16.2.7.1

Programming Notes:

- SOC and PT texts should be in proper case in table.
- Present only severity categories with at least one subject.
- In case a term is not coded (e.g. in a dry run) it will be labelled as “Not Coded [SOC]” and “Not Coded [PT]”, and sorted at the end of the table. SOC.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.4
Treatment Emergent Adverse Events by Relationship to Study Medication, System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term Relatedness	Placebo	MEDI7352				Total
		CCI	CCI	CCI	All MEDI7352	
	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Subjects with at Least One TEAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

…

AE = adverse event; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects within each SOC/PT/Relatedness category; N = number of subjects per treatment group; PT = Preferred Term; SOC = System Organ Class; TEAE = treatment-emergent adverse event.
[1] Related is defined as reasonable possibility that the AE was caused by investigational product, as assessed by the investigator.
Note: Results are n (n/N *100).
A TEAE is defined as an AE with an onset at the time of or following the start of treatment with IP.
Aes were coded using MedDRA version 26.0. Subjects are counted once for each SOC and once for each PT for the most related AE.
Aes are displayed by descending frequency of SOC, then descending frequency of PT within SOC, based on 'All MEDI7352' column. Table is sorted by international order for SOC of same frequency, and alphabetically for PT of same frequency.
Reference Listing 16.2.7.1

Programming Notes:

- SOC and PT texts should be in proper case in table.
- Present only severity categories with at least one subject.
- In case a term is not coded (e.g. in a dry run) it will be labelled as “Not Coded [SOC]” and “Not Coded [PT]”, and sorted at the end of the table. SOC.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.5
Treatment Emergent Adverse Events by ADA Status Category, System Organ Class and Preferred Term
Safety Population

Treatment: xxxxxxx

System Organ Class Preferred Term	ADA Negative (N=xx)	ADA Positive (N=xx)	TE-ADA Positive (N=xx)	Non-TE-ADA Positive (N=xx)	TE Persistently ADA Positive (N=xx)	TE Transiently ADA Positive (N=xx)	Post-Baseline and Baseline Positive (N=xx)	Only Baseline Positive (N=xx)
Subjects with at Least One TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx

AE = adverse event; ADA = Anti-Drug Antibodies; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; ; n = number of subjects within each SOC/PT category; N = number of subjects per ADA status category; PT = Preferred Term; SOC = System Organ Class; TEAE = treatment-emergent adverse event.
ADA categories are defined in the Statistical Analysis Plan.
Note: Results are n (n/N *100) then the total number of events.
A TEAE is defined as an AE with an onset at the time of or following the start of treatment with IP.
Aes were coded using MedDRA version 26.0. Subjects are counted once for each SOC and once for each PT.
Table is sorted by international order for SOC, and alphabetically for PT.
Reference Listing: 16.2.7.1

Programming Notes:

- SOC and PT texts should be in proper case in table.
- Repeat for Placebo, CCI and Overall.
- In case a term is not coded (e.g. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]", and sorted at the end of the table. SOC.
- A table for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.6
Treatment Emergent Adverse Events Leading to Discontinuation of Study Drug by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at Least One TEAE leading to IP discontinuation".
- Update Reference Listing to 16.2.7.2.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.7
Non-Serious Adverse Events Occurring in More than 5% of Subjects by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at Least One Non-Serious AE" and remove references to TEAEs.
- Update Reference Listing to 16.2.7.1.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.8
Treatment Emergent Adverse Events Occurring in More than 5% of Subjects by Preferred Term
Safety Population

Preferred Term	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Subjects with at Least One TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
…						

AE = adverse event; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects within each PT category; N = number of subjects per treatment group; PT = Preferred Term; TEAE = treatment-emergent adverse event.
Note: Results are n (n/Number of subjects in the Safety population within each PT*100) then the total number of events.
A TEAE is defined as AE with an onset at the time of or following the start of treatment with IP.
Aes were coded using MedDRA version 26.0. Subjects are counted once for each PT.
Aes are displayed by descending frequency of PT based on 'All MEDI7352' column, and alphabetically for PT of same frequency.
Reference Listing: 16.2.7.1

Programming Notes:

- PT texts should be in proper case in table.
- In case a term is not coded (e.g., in a dry run) it will be labelled as Not Coded [PT]", and sorted at the end of the table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.9
Treatment Emergent Adverse Events by Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.8.
- Display all TEAEs, not only the most common.
- PT texts should be in proper case in table.
- In case a term is not coded (e.g., in a dry run) it will be labelled as Not Coded [PT]", and sorted at the end of the table.
- A column for CCI dosing CCI) will only be added if Stage 4 is initiated.

6.2. Summary of Deaths and Other Serious Adverse Events

Table 14.3.2.1.1
Serious Adverse Events by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Number of Subjects with at Least One SAE", add "SAE = Serious Adverse Event" to abbreviations, and remove references to TEAEs.
- Change footnote for "Reference Table 14.3.3.1".
- A column for CCI dosing (CCI [redacted]) will only be added if Stage 4 is initiated.

Table 14.3.2.1.2
Life-Threatening Serious Adverse Events by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Number of Subjects with at Least One Life-Threatening SAE", add "SAE = Serious Adverse Event" to abbreviations, and remove references to TEAEs.
- Add "Note: Life-threatening SAEs as judged by the investigator".
- Change footnote for "Reference Table 14.3.3.1".
- A column for CCI dosing (CCI [redacted]) will only be added if Stage 4 is initiated

Table 14.3.2.1.3
Serious Adverse Events with Outcome Death by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Number of Subjects with at Least One SAE with Outcome Death", add "SAE = Serious Adverse Event" to abbreviations, and remove references to TEAEs.
- Change footnote for "Reference Table 14.3.3.2".
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.2.1.4
Serious Adverse Events by Relationship to Study Medication, System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.4. Change first row to be "Number of subjects with at Least One SAE", add "SAE = Serious Adverse Event" to abbreviations, and remove references to TEAEs.
- Change footnote for "Reference Table 14.3.3.1".
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.3.1
Listing of Serious Adverse Events
Safety Population

Subject ID/ Treatment Arm	AE ID Number	System Organ Class/ Preferred Term/ Verbatim Term	Start Date/Time (Study Day)/ End Date/Time (Study Day)	Severity/ Relationship	Outcome/ Action Taken/ Therapy?	SAE Leading to Study DC?	TEAE?	Serious Criteria
XXXXX/ XXXX	X	XXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXX	DDMMMYYYY/ HH:MM (X)/ DDMMMYYYY/ HH:MM (X)	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXXXXX/ Yes	No	No	XX
XXXXX/ XXXX	X	XXXXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXXX	DDMMMYYYY/ HH:MM (X)/ DDMONYYYY /HH:MM (X)	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXXXXX/ No	Yes	XX	XX / XXX
XXXXX/ XXXX	X	XXXXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXX	DDMONYYYY/ HH:MM (X)/ Ongoing	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXXXXX/No	No	XX	XX / XXX

DC = discontinuation; ID = identification; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; SAE = serious adverse event; TEAE = treatment emergent adverse event.
Note: Study Day = date of interest – date of first infusion. A TEAE is defined as an adverse event with an onset at the time of or following the start of treatment with IP.
SAEs were coded using MedDRA version 26.0

Programming Notes:

- If time missing, display "- -:- -".
- AE ID number represents Record position within Subject.
- If no events meet the criteria for display (i.e., no AEs occur in the study), present "No events are reported.".
- SOC & PT text should be in proper case in table.
- Sort by Treatment ID/ Subject ID / Start Date / End Date (alphabetically for SOC if same date for two events).
- In case a term is not coded (e.g.. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]". SOC and PT abbreviations should be added in this case in footnote.

Table 14.3.3.2
Listing of Deaths
Safety Population

Subject ID/ Treatment Arm	AE ID Number	System Organ Class/ Preferred Term/ Verbatim Term	Start Date/Time (Study Day)/ End Date/Time (Study Day)	Severity/ Relationship	Outcome/ Action Taken/ Therapy?	AE Leading to IP DC?	TEAE?	Serious Criteria
XXXXX/ XXXX	X	XXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXXXXX/ Yes	No	No	XX
XXXXX/ XXXX	X	XXXXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXXXX/No	Yes	XX	XX / XXX
XXXXX/ XXXX	X	XXXXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ Ongoing	XXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXXX/ No	No	XX	XX / XXX

DC = discontinuation; ID = identification; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; TEAE = treatment emergent adverse event.
Note: Study Day = date of interest – date of first infusion. A TEAE is defined as an adverse event with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0

Programming Notes:

- If time missing, display "- -:- -".
- AE ID number represents Record position within Subject.
- If no events meet the criteria for display (i.e., no AEs occur in the study), present "No events are reported.".
- SOC & PT text should be in proper case in table.
- Sort by Treatment Arm/ Subject ID / Start Date / End Date (alphabetically for SOC if same date for two events).
- In case a term is not coded (e.g., in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]". SOC and PT abbreviations should be added in this case in footnote.

6.3. Displays of Significant Adverse Events and Adverse Events of Special Interest

Table 14.3.2.2.1
Treatment Emergent Adverse Events Associated with Abnormal Liver by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at least One TEAE Associated with Abnormal Liver". Remove references to TEAEs in footnote.
- Update Reference Listing to 16.2.7.3.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.2.2.2
Potential joint Related Adverse Events of Special Interest by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at least One Potential Joint Related AESI"
- Add abbreviation for AESI = Adverse Event of Special Interest. Remove references to TEAEs in footnote.
- Update Reference Listing to 16.2.7.4
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.2.2.3
Serious and/or severe Infections by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at Least One SAE or Severe AE Related to Infection". Add "SAE = Serious Adverse Event" to abbreviations. Remove references to TEAEs in footnote.
- Update Reference Listing to 16.2.7.5.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.2.2.4
Anaphylactic Reactions, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of IP by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at Least One Anaphylactic Reaction, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of IP". Remove references to TEAEs in footnote.
- Update Reference Listing to 16.2.7.6.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

6.4. Laboratory Data

Table 14.3.4.1
Descriptive Summary of Clinical Chemistry
Safety Population

Parameter: xxxxx (unit)

Visit/ Statistic	Placebo (N=xx)	MEDI7352 [redacted] (N=xx)	MEDI7352 [redacted] (N=xx)	MEDI7352 [redacted] (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Low NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Low CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 1						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Low NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Low CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)

Day 1 CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

CFB = change from baseline; CS = clinically Significant; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NCS = not clinically significant; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Note: Percentages are n/Number of subjects by treatment group at each visit*100.
Reference Listing: 16.2.8.1

Programming Notes:

- Present only scheduled visits.
- Sort Parameters in the following Order: Albumin, Alkaline Phosphatase, Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Bicarbonate, Calcium, Chloride, Creatinine, High-Sensitivity C-Reactive Protein (hs-CRP), Estimated Glomerular Filtration Rate (eGFR by Cockcroft - Gault), Serum Glucose, Lactate Dehydrogenase (LDH), Potassium, Sodium, Total Bilirubin, Total Protein, Blood Urea Nitrogen (BUN), Uric Acid.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.4.2
Shift Table of Clinical Chemistry Results
Safety Population

Parameter (Unit)/ Visit / Post-Baseline Grade	Baseline Grade [1]									
	Placebo (N=xxx)					MEDI7352, CCI (N=xxx)				
	Low	Normal	High	Missing	Total	Low	Normal	High	Missing	Total
XXXXXX (Unit)										
Week x										
Low	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Missing	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Total	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Week x										
Low	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Missing	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Total	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
…										

n = number of subjects within each category; N = number of subjects per treatment group.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Percentages are n/Number of subjects by treatment group at each visit for the parameter*100.

Reference Listing 16.2.8.1

Programming Notes:

- Repeat above in new pages for MEDI7352, CCI , MEDI7352, CCI and All MEDI7352.
- Repeat the above for CCI dosing only if Stage 4 is initiated.
- Repeat for every scheduled visit.
- Present parameters in the same order as in Table 14.3.5.1.

Table 14.3.4.3
Descriptive Summary of Hematology
Safety Population

Programming Notes:

- Same shell as Table 14.3.5.1
- Present only scheduled visits.
- Sort Parameters in the following Order: Absolute basophil count, absolute eosinophil count, absolute lymphocytes count, Absolute Monocyte Count, Absolute Neutrophil Count, Basophils %, Eosinophils %, Hematocrit (HCT), Hemoglobin (HGB), hemoglobin A1C (HgbA1C), Lymphocytes %, mean corpuscular hemoglobin (MHC), Mean Corpuscular Hemoglobin Concentration (MCHC), Mean Corpuscular Volume (MCV), Monocytes %, Neutrophils %, Platelets, Red blood cell count (RBC), Red Cell Distribution Width, white blood cell Count (WBC).
- Update Reference listing to 16.2.8.2.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.4.4
Shift Table of Hematology Results
Safety Population

Programming Notes:

- Same shell as Table 14.3.5.2
- Repeat the shell for CCI dosing if Stage 4 is initiated.
- Repeat for every scheduled visit.
- Present parameters in the same order as in Table 14.3.5.3.
- Update Reference listing to 16.2.8.2

Table 14.3.4.5
Descriptive Summary of Coagulation
Safety Population

Programming Notes:

- Same shell as Table 14.3.5.1
- Present only scheduled visits.
- Sort Parameters in the following Order: Activated Partial Thromboplastin Clotting Time (APTT), Fibrinogen, International normalized ratio (INR), Prothrombin Time (PT).
- Update Reference listing to 16.2.8.3.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.4.6
Shift Table of Coagulation Results
Safety Population

Programming Notes:

- Same shell as Table 14.3.5.2
- Repeat for CCI dosing if Stage 4 is initiated.
- Repeat for every scheduled visit.
- Present parameters in the same order as in Table 14.3.5.4.
- Update Reference listing to 16.2.8.3.

Table 14.3.4.7
Descriptive Summary of Urinalysis
Safety Population

Parameter: xxxxx (unit)

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Low NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Low CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 1						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Low NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Low CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 1 CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

…

Repeat for all visits for Parameters: Specific Gravity and pH

Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Negative	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Positive	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
If Positive, Specify [2]						
100 mg/dL	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
250 mg/dL	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
500 mg/dL	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
>= 1000 mg/dL	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 1						
n	xx	xx	xx	xx	xx	xx
Negative	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Positive	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)

…

Repeat for all visits for Parameters: Blood, Glucose, Ketones and Protein

CFB = change from baseline; CS = clinically significant; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NCS = not clinically significant; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
[2] Percentages are n/Number of Subjects with a Positive Result*100.
Note: Percentages are n/Number of subjects by treatment group at each visit*100.
Reference Listing: 16.2.8.4

Programming Notes:

- Present only scheduled visits.
- Sort Parameters in the following Order: Blood Urine, Glucose, Ketones, pH, Protein, Specific Gravity.
- Categories for If Positive, Specify:
  - Blood, Urine: Trace, Small, Moderate.
  - Glucose: 100 mg/dL, 250 mg/dL, 500 mg/dL, >= 1000 mg/dL.
  - Ketones: Trace, 15 mg/dL.
  - Protein: Trace, 30 mg/dL, 100 mg/dL.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.4.8
Shift Table of Urinalysis Results
Safety Population

Programming Notes:

- Same shell as Table 14.3.5.2
- Repeat for CCI dosing if Stage 4 is initiated.
- Repeat for every scheduled visit.
- Present parameters in the same order as in Table 14.3.5.3.
- Update Reference listing to 16.2.8.4

Table 14.3.4.9
Maximum On-Treatment ALT and AST versus Maximum On-Treatment Total Bilirubin
Safety Population

Group	Nobs		Total Bilirubin <2 x ULN n (%)	Total Bilirubin >=2 x ULN n (%)
Placebo				
N=xxx	xxx	ALT		
		<3 x ULN	x (xx.x%)	x (xx.x%)
		>=3 - <5 x ULN	x (xx.x%)	x (xx.x%)
		>=5 - <10 x ULN	0	0
		>=10 x ULN	0	0
		AST		
		<3 x ULN	x (xx.x%)	x (xx.x%)
		>=3 - <5 x ULN	x (xx.x%)	x (xx.x%)
		>=5 - <10 x ULN	0	0
		>=10 x ULN	0	0

…
Repeat for: CCI [redacted] ***All MEDI7352***

ALT = alanine aminotransferase; AST = aspartate aminotransferase; IP = investigational product; n = number of subjects per category; N = number of subjects per treatment group; Nobs = number of subjects per treatment group with at least one post-baseline assessment on treatment; ULN = upper limit of normal.
Note: On-treatment assessments include assessments on or after the date of first dose of IP. Baseline is defined as the last observation recorded prior to the first dose of treatment.
Percentages are based on Nobs.
Reference Listing: 16.2.8.1

Programming Notes:

- Per Protocol, the elevations of ALT or AST and Total Bilirubin do not have to occur at the same time or within a specified time frame. That is the reason why the table is presented by Subject instead of by visit. So, if for example, one subject has ALT >=3 - <5 x ULN at Day 1, and TBL >=2 x ULN at Week 18, n in that cell will increase by one.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

6.5. Other Safety Data

Table 14.3.5.1
Descriptive Summary of Vital Signs
Safety Population

Parameter: xxxxx

Visit / Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1: 15 Minutes Post-Dose						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1: 15 Minutes Post-Dose CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

…

CFB = Change from Baseline; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment. Reference Listing: 16.2.9.1

Programming Notes:

- Repeat for Supine Heart Rate, Supine Systolic Blood Pressure, Supine Diastolic Blood Pressure, Respiratory Rate, Body Temperature, Standing Heart Rate, Standing Systolic Blood Pressure, Standing Diastolic Blood Pressure.
- After Week 2 (inclusive), Supine measure are taken in sitting position. We will consider them as supine (in resting position) for calculating Change from Baseline (always at supine position).
- Include the following timepoints: Baseline, Day 1: 5 Minutes Post-Dose, Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- Note that Body Tº, and standing measures are not taken on Day 1, at 15, 30 and 45 minutes post-dose.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.2
Descriptive Summary of ECG Data
Safety Population

Parameter: xxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1: 1 hour Post-Dose						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1: 1 hour Post-Dose CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
…						

CFB = Change from Baseline; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
Note: Data shown are averages of the 3 replicates taken for each parameter and timepoint, and CFB for the same variables.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.

Reference Listing: 16.2.9.2

Programming Notes:

- Repeat for PR, QRS, QT, RR, HR (Heart Rate) and QTcF taken from external data.
- Include the following timepoints: Baseline, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 4, Week, 8, Week 12, and Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.3
Summary of Overall Evaluation of Safety ECG Data
Safety Population

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Day 1: 1 hour Post-Dose						
n	xx	xx	xx	xx	xx	xx
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

CS = clinically significant; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NCS = Not clinically significant.
Note: Data are taken as the most conservative from the 3 replicates taken by timepoint.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.

Reference Listing: 16.2.9.2

Programming Notes:

- Include the following timepoints: Baseline, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 4, Week, 8, Week 12, and Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.4
Covid-19 Screening
Safety Population

Visit/ Variable Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Day 1						
Subjects Screened for COVID-19 Symptoms	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Symptoms Screened:						
Fever	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Cough	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dyspnoea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sore Throat	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Loss of Taste	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Loss of Smell	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Body Temperature Check						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Subjects with COVID-19 Swab Performed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Negative	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with COVID-19 Antibody Testing Performed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Confirmed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Suspected	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Negative	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Subjects with COVID-19 Antigen Testing Performed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Negative	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

COVID-19 = coronavirus disease 2019; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
Note: Percentages are n/Number of subjects by treatment group at each visit*100.
Reference Listing: 16.2.8.8

Programming Notes:

- Include the following timepoints: Day 1, Week 2, Week 4, Week 6, Week, 8, Week 10.
- A column for [redacted] dosing ([redacted]) will only be added if Stage 4 is initiated.

Table 14.3.5.5
Summary of Sub-Scores for Total Neuropathy Score-Nurse
Safety Population

Visit/ Variable Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
Subjects performing TNSn	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sensory Symptom Score						
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Motor Symptom Score						
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Autonomic Symptom Score						
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pin Sensibility Score						
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Vibration Sensibility Score						
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

...

N = number of subjects per treatment group; TNSn = Total Neuropathy Score-Nurse.

[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Note: Percentages for subjects performing TNSn are n/Number of subjects by treatment group at each visit*100. Percentages for each Score are n/Number of subjects by treatment group at each visit without missing score*100

Reference Listing: 16.2.9.5

Programming Notes:

- Include the following timepoints: Baseline, Day 1, Week 2, Week 4, Week 6, Week, 8, Week 10, Week 12 and Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.6
Descriptive Summary of Total Neuropathy Score-Nurse
Safety Population

Score: xxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1 CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

TNSn = Total Neuropathy Score-Nurse; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment. Reference Listing: 16.2.9.5

Programming Notes:

- Include the following timepoints: Baseline, Day 1, Week 2, Week 4, Week 6, Week, 8, Week 10, Week 12 and Week 18.
- Include the following scores: Sensory Symptom Score, Motor Symptom Score, Autonomic Symptom Score, Pin Sensibility Score, Vibration Sensibility Score, and TNSn Total.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.7
Summary of Motor and Sensory Nerve Conduction Studies
Safety Population

Parameter: xxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 18						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 18 CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Evaluation Result						
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 18						
n	xx	xx	xx	xx	xx	xx
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

CFB = Change from Baseline; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Note: Percentages are number of subjects by treatment group at each visit for each category /Number of subjects by treatment group for each visit*100
Reference Listing: 16.2.9.6

Programming Notes:

- Repeat for the following Parameters: Lower Limb - right side/Motor evaluation/Amplitude, Lower Limb - right side/Sensory evaluation/Amplitude, Lower Limb - left side/ Motor evaluation/Amplitude, Lower Limb - left side/ Sensory evaluation/Amplitude, Upper Limb - right side /Motor evaluation/Amplitude, Upper Limb - right side/ Sensory evaluation/Amplitude, Upper Limb - left side/ Motor evaluation/Amplitude, Upper Limb - left side /Sensory evaluation/Amplitude. (**Repeat the same combination of Location - Laterality/Evaluation** for Peak Latency, Conduction Velocity, Duration of action Potential).
- A column for CCI dosing (CCI [redacted]) will only be added if Stage 4 is initiated.

Table 14.3.5.8
Summary of Strength and Deep Tendon Reflexes
Safety Population

Visit/ Variable Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
Subjects performing SDTR assessment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ankle Dorsiflexion Strength						
0 - Normal Power	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1 - Mild Weakness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 - Moderate Weakness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 - Severe Weakness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 - Paralysis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Deep Tendon Reflexes						
0 - Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1 - Ankle reflex reduced	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 - Ankle reflex absent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 - Ankle reflex absent and knee reflex reduced	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 - All reflexes (both ankle and knee) absent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

n = number of subjects by treatment group at each visit for each category; N = number of subjects per treatment group; SDTR = strength and deep tendon reflexes.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Note: Percentages for each Score are n/Number of subjects by treatment group at each visit*100

Reference Listing: 16.2.9.7

Programming Notes:

- Include the following timepoints: Baseline, Day 1, Week 2, Week 4, Week 6, Week, 8, Week 10, Week 12, and Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.9
Summary of Local Injection Site Reactions
Safety Population

Visit/ Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Day 1: 15 Minutes after Start of Infusion						
Subjects with injection Site Assessed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pain						
None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tenderness						
None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Erythema/ Redness						
None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Induration/ Swelling						
None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

n = number of subjects by treatment group at each visit for each category; N = number of subjects per treatment group.
Note: Percentages for each Score are n/Number of subjects by treatment group at each visit*100
Reference Listing: 16.2.9.8

Programming Notes:

- Include the following timepoints: Day 1: 15 Minutes after Start of Infusion, Day 1: 30 Minutes after Start of Infusion, Day 1: 45 Minutes after Start of Infusion, Day 1: 60 Minutes after Start of Infusion, Day 1: 2 hours after Start of Infusion, Day 1: 4 hours after Start of Infusion, Week 2, Week 4, Week 6, Week, 8, Week 10, Week 12, and Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.10
Summary of Hypersensitivity/Anaphylactic Reactions
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with any Hypersensitivity/ Anaphylaxis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Highest Severity Grade						
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Type of Reaction						
Urticaria	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pruritus	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Rash	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Flushing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Swollen Lips, Tongue, Uvula and/or Vulva	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dyspnoea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Wheeze-Bronchospasm	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stridor	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hypoxia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hypotension	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Crampy Abdominal Pain	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Vomiting	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Diarrhoea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

N = number of subjects per treatment group.
Reference Listing: 16.2.9.9

Programming Notes:

- Display only Type of reaction with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.11
Summary of Liver Diagnostic Investigations
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Liver Diagnostics Performed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Type of Diagnostic Investigation						
Ultrasound	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
CT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
MRI/MRCP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Flushing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ERCP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
X-Ray	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tox Screening for Acetaminophen/Paracetamol	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tox Screening for Ethanol	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tox Screening, Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Specialist Consulted	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Hepatitis A	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Hepatitis B	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Hepatitis C	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Hepatitis D	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Hepatitis E	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)
Serology for Cytomegalovirus	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Epstein Barr Virus	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Autoimmune Serology	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

CT = Computerized tomography; ERCP = Endoscopic retrograde cholangiopancreatography; MRI = Magnetic resonance imaging; MRCP = Magnetic resonance cholangiopancreatography; N = number of subjects per treatment group.
Reference Listing: 16.2.9.10

Programming Notes:

- Display only Diagnostic Investigations with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.12
Summary of Liver Risk Factors and Lifestyle Events
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Liver Risk Factors Assessed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Liver Risk Factor						
Alcohol Abuse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Increased Alcohol Consumption within 1 Month of Reported Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
IV Drug Abuse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tattoo	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Acupuncture	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sexually Transmitted Diseases	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Toxic/Chemical Agent Exposure	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Travel (Areas at Risk in the Last Year)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pregnancy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Parenteral Nutrition	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Excessive Physical Exercise	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Changes Diet/Fasting Episodes/Weight Loss Diet	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Previous Drug Reaction	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Blood Transfusion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Patient Exposed to Anyone with Jaundice in the Last Month	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)
History of Hypotension	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Low Blood Pressure at Time of Event of Liver Injury and/or Abnormal Liver Laboratory Value	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
History of Liver Disease	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

IV = intravenous; N = number of subjects per treatment group.
Reference Listing: 16.2.9.10

Programming Notes:

- Display only Liver Risk Factor with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.13
Summary of Liver Signs and Symptoms
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Liver Signs/Symptoms Assessed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Liver Sign/Symptom						
Anorexia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Asthenia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pyrexia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pruritus	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Jaundice	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Arthralgia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abdominal Pain	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abdominal Tenderness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Nausea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Vomiting	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Rash	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mucosal Inflammation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Purpura	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hepatomegaly	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Splenomegaly	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)
Lymphadenopathy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ascites	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Confusional State	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Coma	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Upper Quadrant Tenderness	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)
Biliary Obstruction	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Eosinophilia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dark Urine	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

N = number of subjects per treatment group.
Reference Listing: 16.2.9.12

Programming Notes:

- Display only Liver Signs/Symptoms with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.14
Summary of Infection Diagnostic Investigations
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Infection Diagnostic Investigations	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Method						
Microscopy, Culture and Sensitivity	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serological Tests	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Nucleic Acid Based Tests	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
X-Ray	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

N = number of subjects per treatment group.
Reference Listing: 16.2.9.13

Programming Notes:

- Display only Methods with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.15
Summary of Infection Risk Factors and Lifestyle Events
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Infection Risk Factor Occurred	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Infection risk factor						
Extensive Burns within the Last Year	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tattoo, Piercing or Acupuncture within the last Year	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sexually Transmitted Diseases	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Travel to Areas at Risk of Tuberculosis or Tropical Diseases	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Infections Related to Travel	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Blood Transfusion (within the Last Year)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Exposure to Nosocomial Pathogens within the Last Year	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Contact History with Infection Source	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Previous BCG Immunization	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Evidence of BCG Scar	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tuberculin Skin or Quantiferon Test Confirms Previous Exposure or Immunity to Tuberculosis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

BCG = Bacillus Calmette-Guerin; N = number of subjects per treatment group.
Reference Listing: 16.2.9.14

Programming Notes:

- Display only infection risk factors with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.16
Summary of Infection Signs and Symptoms
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Infection Sign/Symptom Occurred	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Infection Sign/Symptoms						
Pyrexia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Headache	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Confusional State	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Convulsion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Rhinitis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Oropharyngeal Pain	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Cough	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Productive Cough	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Haemoptysis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Wheezing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dyspnoea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pleuritic Pain	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Vomiting	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Diarrhoea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Genital Discharge	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Haematuria	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dysuria	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hepatosplenomegaly	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Jaundice	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lymphadenopathy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Rash	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Petechial	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Vesicular	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Macular	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Papular	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Urticaria	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Erythema	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Blanching	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Splinter Haemorrhages	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Night sweats	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Chills	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Myalgia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Weight Decrease	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

N = number of subjects per treatment group.
Reference Listing: 16.2.9.15

Programming Notes:

- Display only infection Signs/Symptoms with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.17
Summary of Concomitant Medications by ATC Level 2 and Preferred Name
Safety Population

Programming Notes:

- Same shell as Table 14.1.7.
- Change footnote Note by: "Note: Concomitant medications are defined as medications continuing or starting on or after first dose of study medication. All concomitant medications are coded using WHO drug dictionary version vMar2023. At each level of summarization (ATC Level 2 or Preferred Name), subjects who reported more than one concomitant medication were only counted once. ATC Level 2 and Preferred Name are sorted in in descending order of frequency of total, and alphabetically if same frequency".
- If uncoded ATC Level or Preferred Name, please put them as [Not Coded]
- ATC and Preferred Name texts should be in proper case in table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.18
Summary of Concomitant Procedures
Safety Population

System Organ Class	Placebo	MEDI7352			Total
Preferred Term	(N=xxx)	CCI (N=xx)	CCI (N=xx)	CCI (N=xx)	(N=xxx)
Any Concomitant Procedure	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
System Organ Class 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
…	…	…	…	…	…
System Organ Class n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)

N = number of subjects per treatment group.
Note: All Procedure terms were coded using the Medical Dictionary for Regulatory Activities (MedDRA), version 26.0. At each level of summarization (system organ class or preferred term), subjects having more than one Procedure term were counted only once. System organ class and preferred terms are sorted in descending order of frequency of Total column, and alphabetically if same frequency.

Reference Listing: 16.2.9.18

Programming Notes:

- SOC and PT texts should be in proper case in table.
- Sort SOC and PT (within SOC) in descending order of frequency in the Total column. Sort alphabetically in case of ties.
- Uncoded Procedure events
  - When there are uncoded Procedure Events in the database, the events will be summarized with SOC and PT set to [Not Coded]. The [Not Coded] will be sorted at the end of the table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.19
Anti-Drug Antibody Results and Titre Summary by Timepoint
Safety Population

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)
Baseline [1]					
n [2]	xx	xx	xx	xx	xx
ADA Positive: n (%) [3]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 2					
n [2]	xx	xx	xx	xx	xx
ADA Positive: n (%) [3]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
…					

ADA = Anti-Drug Antibodies; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
[2] Number of subjects with at least one ADA assessment at the specific visit.
[3] Number of subjects with a positive result at the specific visit. The denominator for all percentages is the number of subjects with an ADA result for each visit.

Reference Listing: 16.2.9.19

Programming Notes:

- Keep in mind that in this table 'Total' column does not include placebo.
- Repeat for all scheduled post-baseline visits.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.20
Descriptive Summary of Anti-Drug Antibody Results and Titre by ADA Categories
Safety Population

ADA Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)
ADA positive at baseline and/or post-baseline (ADA prevalence)					
n/Nobs (%) [1] [2]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
TE-ADA positive (ADA incidence) [5]					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Treatment Induced ADA Positive					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Treatment-Boosted ADA Positive					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Non-TE-ADA Positive					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Both baseline and post-baseline positive					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Only baseline positive					
n/Nobs (%) [1] [4]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
TE-persistently ADA positive [6]					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

TE-transiently ADA positive [7]					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

ADA = Anti-Drug Antibodies; N = number of subjects per treatment group; TE-ADA = Treatment Emergent ADA; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] n represents the number of subjects satisfying the conditions of the specified ADA category
[2] Nobs represents the number of subjects with any ADA result at baseline and/or post-baseline.
[3] Nobs represents the number of subjects with an ADA result at baseline and at least one post-baseline ADA assessment.
[4] Nobs represents the number of subjects with an ADA result at baseline.
[5] TE-ADA positive is defined as either ADA negative at baseline and post-baseline ADA positive (Treatment Induced ADA Positive), or as ADA positive at baseline with pre-existing titre boosted during the study period (Treatment Induced ADA Positive). ADA incidence is the proportion of TE-ADA+ subjects in a population.
[6] ADA negative at baseline and having at least 2 post-baseline ADA positive measurements with ≥16 weeks (112 days) between first and last positive, or an ADA positive result at the last available post-baseline assessment.
[7] ADA negative at baseline and at least one post-baseline ADA positive measurement and not fulfilling the conditions for persistently positive.

Reference Listing: 16.2.9.19

Programming Notes:

- If a participant has more than 1 non-missing titre during the study, the maximum titre for each participant is summarized.
- Only present summary statistics if titre is available.
- If no positive results for a particular block of the table, then the summary statistics for the titres for that particular block would not appear.
- It is assumed that participants with a missing baseline ADA result are ADA negative at baseline.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

7. Pharmacokinetic/Pharmacodynamic Data

Table 14.4.1
Summary of Serum MEDI7352 Concentrations
PK Population

ADA Status: xxxxxxxxxx

Visit/ Statistic	MEDI7352		
	CCI (N=xx)	CCI (N=xx)	CCI (N=xx)
Baseline [1]			
n (n < LLOQ)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
gMean ± gSD	x.xx to x.xx	x.xx to x.xx	x.xx to x.xx
gCV%	xx.x	xx.x	xx.x
Median	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx
Week 2	xx (xx)	xx (xx)	xx (xx)
n (n < LLOQ)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Mean (SD)	x.xx to x.xx	x.xx to x.xx	x.xx to x.xx
gMean ± gSD	xx.x	xx.x	xx.x
gCV%	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Median	xx, xx	xx, xx	xx, xx
Min, Max			
Week 4	xx (xx)	xx (xx)	xx (xx)
n (n < LLOQ)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Mean (SD)	x.xx to x.xx	x.xx to x.xx	x.xx to x.xx
gMean ± gSD	xx.x	xx.x	xx.x
gCV%	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Median	xx, xx	xx, xx	xx, xx
Min, Max			
…			

gCV% = Geometric Coefficient of Variation (%); gMean = Geometric Mean; gSD = Geometric SD; LLOQ = Lower Limit of Quantification; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Reference Listing: 16.2.10.1

Programming Notes:

- Include the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours/ Pre-Dose, Week 11/ Pre-Dose, Week 10 + 14 Days/Pre-Dose; Week 18.
- Repeat the table for ‘ADA Positive’, ‘ADA Negative’ and ‘Overall'.
- Any values reported as NRR (not reportable) or NS (missing) will be excluded from the summary tables.
- At a time point where less than or equal to 50% of the concentration values are NQ (below LLOQ), all NQ values will be set to the LLOQ, and all descriptive statistics will be calculated accordingly.
- At a time point where more than 50% (but not all) of the values are NQ, the gmean, gmean ± gSD and gCV% will be set to NC. The maximum value will be reported from the individual data, and the minimum and median will be set to NQ.
- If all concentrations are NQ at a time point, no descriptive statistics will be calculated for that time point. The gmean, minimum, median and maximum will be reported as NQ and the gCV% and gmean ± gSD as NC.

Table 14.4.2
Summary of Serum total NGF Concentrations
Safety Population

ADA Status: xxxxxxxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	CCI (N=xx)	CCI (N=xx)
Baseline [1]				
n (n < LLOQ)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
gMean ± gSD	x.xx to x.xx	x.xx to x.xx	x.xx to x.xx	x.xx to x.xx
gCV%	xx.x	xx.x	xx.x	xx.x
Median	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Week 2				
n (n < LLOQ)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
gMean ± gSD	x.xx to x.xx	x.xx to x.xx	x.xx to x.xx	x.xx to x.xx
gCV%	xx.x	xx.x	xx.x	xx.x
Median	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Week 4				
n (n < LLOQ)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
gMean ± gSD	x.xx to x.xx	x.xx to x.xx	x.xx to x.xx	x.xx to x.xx
gCV%	xx.x	xx.x	xx.x	xx.x
Median	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
…				

gCV% = Geometric Coefficient of Variation (%); gMean = Geometric Mean; gSD = Geometric SD; LLOQ = Lower Limit of Quantification; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NGF = Nerve-Growth Factor.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Reference Listing: 16.2.10.3

Programming Notes:

- Repeat for ADA Status: “ADA Positive”, “ADA Negative” and “Overall”.
- Include the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 12; Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Planned Listing Descriptions and Shells

Number Title Population	Unique (U) or Repeated (R)
Listing 16.2.1.1 - Subject Disposition - Screening Population	U
Listing 16.2.1.2 - Assignment to Analysis Populations - Screening Population	U
Listing 16.2.1.3 - Reason for IP Discontinuation and Withdrawal from the Study - Safety Population	U
Listing 16.2.1.4 - List of Reasons for Screening Failure - Screen Failure Population	U
Listing 16.2.1.5 - Subject Visits and COVID-19 Impact - Screening Population	U
Listing 16.2.2.1 - Subjects Not Meeting All Inclusion Criteria or Meeting any Exclusion Criteria - Screening Population	U
Listing 16.2.2.2 - Protocol Deviations - Safety Population	U
Listing 16.2.3 - Randomization and Treatment Group - Safety Population	U
Listing 16.2.4.1 - Demographic and Baseline Characteristics - Screening Population	U
Listing 16.2.4.2 - Medical History - Safety Population	U
Listing 16.2.4.3 - Osteoarthritis Characteristics - Screening Population	U
Listing 16.2.5.1 - Study Drug Administration: Individual Doses - Safety Population	U
Listing 16.2.6.1 - Daily Pain NRS - mITT Population	U
Listing 16.2.6.2 - Galer NPS - mITT Population	U
Listing 16.2.6.3 - DSIS - mITT Population	U
Listing 16.2.6.4 - SF-36 - mITT Population	U
Listing 16.2.6.5 - Rescue Medication Usage - mITT Population	R
Listing 16.2.6.6 - Patient Global Impression of Change - mITT Population	U

Number Title Population	Unique (U) or Repeated (R)
CCI [redacted]	U
Listing 16.2.7.1 - Adverse Events - Safety Population	U
Listing 16.2.7.2 - Treatment Emergent Adverse Events Leading to Study Drug Discontinuation**Error! Reference source not found.** - Safety Population	R
Listing 16.2.7.3 - Treatment Emergent Adverse Events Associated with Abnormal Liver - Safety Population	R
Listing 16.2.7.4 - Joint Related Adverse Events of Special Interest - Safety Population	R
Listing 16.2.7.5 - Serious and/or Severe Infections - Safety Population	R
Listing 16.2.7.6 - Anaphylactic Reactions, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of Study Drug - Safety Population	R
Listing 16.2.8.1 - Clinical Chemistry Laboratory Evaluations - Safety Population	U
Listing 16.2.8.2 - Hematology Laboratory Evaluations - Safety Population	R
Listing 16.2.8.3 - Coagulation Laboratory Evaluations - Safety Population	R
Listing 16.2.8.4 - Urinalysis Laboratory Evaluations - Safety Population	R
Listing 16.2.8.5 - Serology Laboratory Evaluations - Safety Population	U
Listing 16.2.8.6 - Pregnancy Test Results - Safety Population	U
Listing 16.2.8.7 - Drug Test Results - Safety Population	U
Listing 16.2.8.8 - COVID-19 Screening and Vaccination - Safety Population	U
Listing 16.2.9.1 - Vital Signs Measurements - Safety Population	U
Listing 16.2.9.2 - ECG Results - Safety Population	U
Listing 16.2.9.3 - Physical Examination Results - Safety Population	U
Listing 16.2.9.4 - Neurological Examination Results - Safety Population	U
Listing 16.2.9.5 - Total Neuropathy Score-Nurse - Safety Population	U

Number Title Population	Unique (U) or Repeated (R)
Listing 16.2.9.6 - Motor and Sensory Nerve Conduction Studies - Safety Population	U
Listing 16.2.9.7 - Strength and Deep Tendon Reflexes - Safety Population	U
Listing 16.2.9.8 - Injection Site Reactions - Safety Population	U
Listing 16.2.9.9 - Hypersensitivity/Anaphylactic Reactions - Safety Population	U
Listing 16.2.9.10 - Liver Diagnostic Investigations - Safety Population	U
Listing 16.2.9.11 - Liver Risk Factors and Lifestyle Events - Safety Population	U
Listing 16.2.9.12 - Liver Signs and Symptoms - Safety Population	U
Listing 16.2.9.13 - Infection Diagnostic Investigations - Safety Population	U
Listing 16.2.9.14 - Infection Risk Factors and Lifestyle Events - Safety Population	U
Listing 16.2.9.15 - Infection Signs and Symptoms - Safety Population	U
Listing 16.2.9.16 - Prior and Concomitant Medications - Safety Population	U
Listing 16.2.9.17 - Prohibited Concomitant Medications - Safety Population	R
Listing 16.2.9.18 - Concomitant Procedures - Safety Population	R
Listing 16.2.9.19 - Anti-drug Antibody Test Results - Safety Population	U
Listing 16.2.10.1 - Serum MEDI7352 Concentrations - PK Population	U
Listing 16.2.10.2 - Serum total NGF Concentrations - PD Population	U

Listing Change Log:

Output Number	Date of Change	Change Made By (initials)	Description/Rationale

Listing 16.2.1.1
Subject Disposition
Screening Population

Subject ID	Re-screened?/ Previous Subject ID	Treatment Arm	Re-consent/ Date/Time of Initial IC/ Initial Protocol Version	Date/Time of Informed Consent	Protocol Version at consent/ Re-consent	Consent for [redacted] sample? /Date of Consent	Consent for COVID-19 Safety Measures /Date of Consent	Current Protocol version
XXXX	No	XXXX	No	DDMMMYYYY/ hh:mm	XXXX	Yes/ DDMMMYYYY	Yes/ DDMMMYYYY	XXXXX
XXXX	Yes/ XXXX	XXXX	No	DDMMMYYYY/ hh:mm	XXXX	Yes/ DDMMMYYYY	Yes/ DDMMMYYYY	XXXXX
XXXX	No	XXXX	No	DDMMMYYYY/ hh:mm	XXXX	Yes/ DDMMMYYYY	Yes/ DDMMMYYYY	XXXXX
XXXX	No	XXXX	Yes / DDMMMYYYY/hh:mm / XXXX	DDMMMYYYY/ hh:mm	XXXX	Yes/ DDMMMYYYY	No	XXXXX
XXXX	No	XXXX	No	DDMMMYYYY/ hh:mm	XXXX	No	No	XXXXX

COVID-19 = coronavirus disease 2019; IC = Informed Consent; [redacted]
.

Programming Notes:

- Sort by Treatment Arm/ Subject ID.

Listing 16.2.1.2
Assignment to Analysis Populations
Screening Population

Subject ID	Treatment Arm	Screened [1]	Randomized	SAF [2]	mITT [3]	PK [4]	Reason to Exclude from Safety [5]	Reason to Exclude from mITT [6]
XXXXXX	XXXX	Yes	No	No	No	No		
XXXXXX	XXXX	Yes	Yes	Yes	Yes	Yes		
XXXXXX	XXXX	Yes	Yes	No	No	No	XXX	
XXXXXX	XXXX	Yes	Yes	Yes	Yes	Yes		
XXXXXX	XXXX	Yes	Yes	Yes	No	No	XXX/ XXX	XXX/ XXX

mITT = Modified Intent-To-Treat Population Set; NRS = numeric rating scale; PK = pharmacokinetics; SAF = Safety Population Set.
[1] The Screening Population includes all subjects who provide informed consent and provide demographic and/or baseline screening assessments.
[2] The Safety Population includes all subjects who receive at least 1 dose of double-blind study medication.
[3] The mITT Population includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
[4] The PK Population includes all subjects for who a pharmacokinetic sample was obtained and analysed.
[5] Major deviation reason/s to exclude from Safety Population for randomized subject.
[6] Major deviation reason/s to exclude from mITT Population for randomized subject.

Programming Notes:

- If there is more than one major deviation, please concatenate with "/"
- Sort by Treatment Arm/ Subject ID.

Listing 16.2.1.3
Reason for IP Discontinuation and Withdrawal from the Study
Safety Population

Subject ID/ Treatment Arm	Study Completion Status	IP Discontinuation/ Study Withdrawal	Completion/ Discontinuation Date/Time (Study Day)	Date of Last Dose	Primary Reason for DC/ Withdrawal	Blind Broken? / Date/Time / Reason	Reason for breaking the Blind	Study Duration
XXXXXX /XXXX	Discontinued Early	IP Discontinuation	DDMMMYYYY/hh:mm (XX)		XXXXXX X	Yes / DDMMMYYYY /hh:mm	XXXXXX	XX
XXXXXX /XXXX	Discontinued Early	IP Discontinuation	DDMMMYYYY/hh:mm (XX)		XXXXXX X	No		XX
XXXXXX /XXXX	Completed		DDMMMYYYY/hh:mm (XX)	DDMMMYYYY		No		XX
XXXXXX /XXXX	Discontinued Early	Study Withdrawal	DDMMMYYYY/hh:mm		Other: XXXXXX X	No		XX
XXXXXX /XXXX	Completed		DDMMMYYYY/hh:mm (XX)	DDMMMYYYY		No		XX

DC = Discontinuation; IP = Investigational product.
[1] Any withdrawal from the study before last IP dose (Week 10) is considered an IP discontinuation.
Note: Study Day is calculated relative to the date of first dose. Study Duration = Reference end date – date of first dose of treatment + 1.

Programming Notes:

- If reason for non-completion is Other, concatenate the specify text as follows: “Other: XXXXXXXXX”.
- If reason for non-completion is adverse event, concatenate with AE line number as follows: “Adverse event number X”.
- For Physician decision, screen-fail and withdrawal by subject, please provide explanation if presented on the logic “Physician decision: XXX”.
- Sort by Treatment Arm/ Subject ID.

Listing 16.2.1.4
List of Reasons for Screening Failure
Screen Failure Population

Subject ID	Treatment Arm	Screen failure Date Date/Time	Primary Reason for Screen Failure
XXXXXX	Screen Failure	DDMMMYYYY/hh:mm	XXXXXXXXX
XXXXXX	Screen Failure	DDMMMYYYY/hh:mm	XXXXXXXXX
XXXXXX	Screen Failure	DDMMMYYYY/hh:mm	
XXXXXX	Screen Failure	DDMMMYYYY/hh:mm	Other: XXXXXXXXX
XXXXXX	Screen Failure	DDMMMYYYY/hh:mm	

Programming Notes:

- If reason for non-completion is Other, concatenate the “Primary Reason for Screen Failure” text as follows: “Other: XXXXXXXXX”.
- Sort by Subject ID.

Listing 16.2.1.5
Visits List and COVID-19 Impact
Screening Population

Subject ID/ Treatment Arm	Visit Name	Visit Date (Study Day)	Is COVID-19 Pandemic Ongoing?	Impacted by COVID-19	Was visit performed? / Visit Type	Visit Performed Via	VS Data provided? / Assessments Missed?	IP dosing missed due to COVID-19 / Details	End of Treatment linked to COVID-19	Subject discontinued due to COVID-19? / Details
xxxxx/ xxxx	Visit X	DDMMM YYYY (XX)	Yes	Yes	Yes/ Delayed	On site	Y/ Efficacy	Y/ XXXX	Other: XXXX	Y/ XXXX
xxxxx/ xxxx	Visit X	DDMMM YYYY (XX)	Yes	No	Yes		N/ Safety			
xxxxx/ xxxx	Visit X	DDMMM YYYY (XX)	No	Yes	Yes	Video	N/ Efficacy, Safety	Y/ Other: XXXX		
xxxxx/ xxxx	Visit X	DDMMM YYYY (XX)	No	No	No / Missed					

COVID-19 = coronavirus disease 2019; IP = Investigational Product; VS = Vital Signs.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Visit Type: Missed, Abbreviated, Delayed.
- Visit Performed Via: Video, Phone, On Site Other: xxxxxx.
- Details on IP dosing missed: Treatment on hold due to Sponsor Decision, Subject infected with COVID-19, Subject decision, Other: xxxxxx.
- End of treatment, reason if due to COVID: Subject infected with COVID-19, Subject decision, Travel restrictions, Site closed, Study delayed/cancelled, Other: xxxxxx.
- Details on Subjects discontinuing due to COVID-19: Subject infected with COVID-19, Subject decision, End of Treatment due to Sponsor, Other: xxxxxx.
- Sort by Treatment Arm/ Subject ID.

Listing 16.2.2.1
Subjects Not Meeting All Inclusion Criteria or Meeting any Exclusion Criteria
Screening Population

Subject ID	Treatment Arm	Enrolled	Randomized	Inclusion or Exclusion	Criteria Number	Criteria Label
XXXXXX	Screen Failure	Yes	No	Inclusion	XX	XXXXXXXXXXXXXXXXXXX
		Yes	No	Exclusion	XX	XXXXXXXXXXXXXXXXXXX

Programming Notes:

- Sort by Subject ID.

Listing 16.2.2.2
Protocol Deviations
Safety Population

Subject ID	Treatment Arm	Analysis Population	Event Date (Study Day)	Event Type	Description	Category	Covid-19 Related?
XXXXXX	XXXX	Screened\RND\SAF\ mITT	DDMMMYYYY (XX)	XXXXXXXXXXX	XXXXXXX	Non-important	Y
				XXXXXXXXXXXXXX	XXXXXXXXXXXXXXX	Important	
XXXXXX	XXXX		DDMMMYYYY (XX)	XXXXXXXXXXXX	XXXXXXXXXXXXXXX XXX	XXXXX	
				XXXXXXXXXXXXXXXX	XXXXXXXXXXX	XXXXX	
XXXXXX	XXXX		DDMMMYYYY (XX)	XXXXXXXXXXXX	XXXXXXXXXXXXXXX XXX	XXXXX	

COVID-19 = Coronavirus disease 2019; mITT = Modified Intent-To-Treat Population; RND = Randomized Subjects; SAF = Safety Population.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- The structure of this listing may change depending on the information in the protocol deviations file. In the analysis population column, include only the analysis population where subject is included in.
- Sort by Treatment Arm/ Subject ID. If date is present in file, add a column for date of event and sort by date. If no date is present, sort by category with non-important first and then important.
- Event Type: Inclusion Criteria, Exclusion Criteria, Study Drug, Assessment – Safety, Assessment – Efficacy, Lab/endpoint data, Visit Window, Informed Consent, Prohibited Co-Medication, Overdose/Misuse, Other.

Listing 16.2.3
Randomization and Treatment group
Safety Population

Subject ID	Treatment Arm	Randomization Stage	Randomization Treatment	Randomization Date / Time (Study Day)	Randomization Number
XXXXXX	XXXX	Stage 1	Active [redacted]	DDMMMYYYY/hh:mm (-X)	XXXX
XXXXXX	XXXX	Stage 3	Active [redacted]	DDMMMYYYY/hh:mm (-X)	XXXX
XXXXXX	XXXX	Stage 2	Placebo	DDMMMYYYY/hh:mm (-X)	XXXX
XXXXXX	XXXX	Stage 2	Active [redacted]	DDMMMYYYY/hh:mm (-X)	XXXX
XXXXXX	XXXX	Stage 3	Placebo	DDMMMYYYY/hh:mm (-X)	XXXX

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID.

Listing 16.2.4.1
Demographic and Baseline Characteristics
Screening Population

Subject ID	Treatment Arm	Birth Date	Age (years)	Sex	Surgically sterile?/ Postmenopausal? [1]	Ethnicity	Race	Weight (kg)	Height (cm)	BMI (kg/m²)	Fully vaccinated for COVID-19?
XXX	XXX	DDMMMYYYY	XX	XX		XXXXX	XXXX	XX.X	XX.X	XX.X	Y
XXX	XXX	--MMMYYY	XX	XX	No/ Yes	XXXXX	XXXX	XX.X	XX.X	XX.X	N

COVID-19 = Coronavirus disease 2019.
Note: Height and weight are the values at Screening.
[1] Age was calculated as age at time of consent.
[2] For Female Subject Only.

Programming Notes:

- Sort by Treatment Arm/ Subject ID

Listing 16.2.4.2
Medical History
Safety Population

Subject ID	Treatment Arm	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ End Date (Study Day)/
XXXXXX	XXXX	XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)
		XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	MMMYYYY (X)/ Ongoing
		XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (X)/ Ongoing
XXXXXX	XXXX	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)

MedDRA = Medical Dictionary for Regulatory Activities.
Note: Study Day is calculated relative to the date of first dose.
Medical History were coded using MedDRA version 26.0.
Only subjects with medical history recorded are listed.

Programming Notes:

- SOC & PT text should be in proper case in listing.
- Sort by Treatment Arm/ Subject ID / Start Date / End Date of medical event.

Listing 16.2.4.3
Osteoarthritis Characteristics
Screening Population

Subject ID	Treatment Arm	Subject with OA? / Joint/ Area affected	Is OA considered CS?	Radiological Investigations Conducted? / Details	Joint Area Investigated	Is OA considered RS?	K-L Score Reported	Radiologic Scoring System / Details/ Result
XXXXXX	XXXX	Y / Shoulder	Y	Y/ Other: XXXXXX	Shoulder	Y	Grade 3	XXXXXX/ XXXXXX/ XX
XXXXXX	XXXX	Y / Ankle	N	Y / MRI	Ankle	N	N	N

CS = Clinically Significant; K-L = Kellgren-Lawrence; OA = Osteoarthritis; RS = Radiologically Significant.

.

Programming Notes:

- Sort by Treatment Arm/ Subject ID

Listing 16.2.5.1
Study Drug Administration: Individual Doses
Safety Population

Subject ID/ Treatment Arm	Visit Name	Start Date/ Time (Study Day)	End Date/ Time (Study Day)	Was Infusion Performed?/ Infusion Volume (mL)[1]/ Reason not Performed	Actually Administered Volume (mL) [2]	If Difference between [1] and [2] Volume, Reason	Any Injection Site Reactions?	Any Infusion Related Reactions	Infusion Rate (mL/ hour)	Rate Change Justification	Reason for Infusion Rate Change
XXXX/ XXXX	XXX	DDMM MYYYY /hh:mm (X)	DDMM MYYYY /hh:mm (X)	Y/ XX	XX				xx.x		
XXXX/ XXXX	XXX	DDMM MYYYY /hh:mm (X)	DDMM MYYYY /hh:mm (X)	Y/ XX	XX	XXXXX	Y	Y	xx.x	XXXXX	XXXXX XX
XXXX/ XXXX	XXX			N/ XXXXXX							

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Start Date / End Date.
- Rate Change Justification: Increased, Decreased, Interrupted.

Listing 16.2.6.1
Daily Pain NRS
mITT Population

Subject ID	Treatment Arm	Study Visit [1]	Subject Diary (ePRO) Date / Study Day	Baseline Flag [2]	DPS
XXXXXX	XXXX	Baseline	DDMMMYYYY/ (-7)	Y	X
		Baseline	DDMMMYYYY/ (-6)	Y	XX
		…	…	…	…
		Baseline	DDMMMYYYY/ (-2)	Y	XX
		Baseline	DDMMMYYYY/ (-1)	Y	XX
		…	…	…	…
		Week 2	DDMMMYYYY/ (13)		XX
		Week 2	DDMMMYYYY/ (14)		XX
		…	…	…	…
		Week X	DDMMMYYYY/ (X)		XX
		…	…	…	…
XXXXXX	XXXX	Baseline	DDMMMYYYY/ (-7)	Y	XX
		…	…	…	…

DPS = Daily Pain Score; ePRO = Electronic Patient-Reported Outcome; NRS = Numeric Rating Scale.
Note: Data shown in column 'DPS' are average daily pain scores on an 11-point (0-10) NRS. Study Day is calculated relative to the date of first dose.
[1] Study Visit is defined as the 7-day period ending within the protocol window Day ± 3, where at least 4 days out of 7 have recorded diary pain scores.
[2] Baseline is defined as the 7-day period prior to randomization **i.e.,** Day -7 to Day -1, inclusive. A subject is considered to have an evaluable baseline pain score if there are at least 5 days of recorded diary pain scores in the 7-day period.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Subject Diary Date.
- Display all measurement per Subject, starting on the Study Day = -7.
- Display Study Visit for days involved in weekly averages of the average daily pain scores for Baseline, Week 2, 4, 6, 8, 10, and 12
- Flag Baseline records only when there is at least 5 days of recorded diary pain scores in the 7-day Baseline period

Listing 16.2.6.2
Galer NPS
mITT Population

Subject ID	Treatment Arm	Parameter	Study Visit	Collection Date / Study Day	Baseline Flag [1]	NPS
XXXXXX	XXXX	Pain intensity	Baseline	DDMMMYYYY/ (X)	Y	XX
			Week 4	DDMMMYYYY/ (X)		XX
			Week 8	DDMMMYYYY/ (X)		XX
				…		XX
			Week X	DDMMMYYYY/ (X)		XX
				…		XX
		XXXX	Baseline	DDMMMYYYY/ (X)	Y	XX
		…	…	…	…	…
XXXXXX	XXXX	Pain intensity	Baseline	DDMMMYYYY/ (X)	Y	XX
			…	…	…	…
		XXXX	Week X	DDMMMYYYY/ (X)		XX
		…	…	…	…	…

NPS = Neuropathic Pain Scale; NRS = Numeric Rating Scale.
Note: Data shown in column 'NPS' are Pain Intensity, Unpleasantness, and Descriptor scores on an 11-point (0-10) NRS, and Pain Duration/Frequency on a 3-point NRS (1-3).
Study Day is calculated relative to the date of first dose.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Parameter /Collection Date.
- Keep Parameter sorting from the last bullet point in this programming notes.
- Include all observed data on Galer NPS scores for Baseline, Week 4, 8, 12, and 18.
- Repeat for the Parameters: Pain intensity, Pain Unpleasantness, Pain Sharpness, Pain Hotness, Pain Dullness, Pain Coldness, Pain Sensitivity, Pain Itching, Deep Pain Intensity, Surface Pain Intensity (All in an 11-point NRS), and Pain Duration/Frequency (in a 3-point NRS).

Listing 16.2.6.3
DSIS
mITT Population

Programming Notes:

- Same shell as Listing 16.2.6.1.
- Update footnote as:
  DSIS = Daily Sleep Interference Scale; ePRO = Electronic Patient-Reported Outcome; NRS = Numeric Rating Scale.
  Note: Data shown in column 'DSIS' are average daily Sleep Interference scores on an 11-point (0-10) NRS. Study Day is calculated relative to the date of the day of first dose.
  [1] Study Visit is defined as the seven-day period ending within the protocol window Day ± 3.
  [2] Baseline is defined as the seven-day period prior to randomization **i.e.,** Day -7 to Day -1,.
- Sort by Treatment Arm/ Subject ID / Subject Diary Date.
- Display all measurement per Subject, starting on the Study Day = -7.
- Display Study Visit for days involved in weekly averages of the average Sleep interference scores for Baseline, Week 4, 8, 12, and 18.
- Flag Baseline records only when there is at least 5 days of recorded diary Sleep interference scores in the 7-day Baseline period.

Listing 16.2.6.4
SF-36
mITT Population

Subject ID	Treatment Arm	Parameter	Item Number	Item name	Study Visit	Collection Date / Study Day	Baseline Flag [1]	SF-36
XXXXXX	XXXX	Physical functioning	3	Vigorous Activities	Baseline	DDMMMYYYY/ (X)	Y	XX
					Week 12	DDMMMYYYY/ (X)		XX
			4	Moderate Activities	Baseline	DDMMMYYYY/ (X)	Y	XX
		…	…	…	…	…	…	…
			-	Total	Baseline	DDMMMYYYY/ (X)	Y	
					Week 12	DDMMMYYYY/ (X)		XX
XXXXXX	XXXX	Role limitations due to physical health	13	Cut Amount of Time Spent on Work/Act	Baseline	DDMMMYYYY/ (X)	Y	XX
					Week 12	DDMMMYYYY/ (X)		XX
			…		…	…	..	…
…		…	…		…	…	…	…

SF-36 = 36-Item Short-Form Health Survey; NRS = Numeric Rating Scale.
Note: Data shown in column 'SF-36' are derived SF-36 scores and Change in General Health on a 5-point NRS (1-5).
Study Day is calculated relative to the date of first dose.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Parameter / Item /Collection Date.
- Keep Parameter sorting from the last bullet point in this programming notes.
- Include all data on SF-36 scores for Baseline and Week 12.
- Repeat for the Parameters: Physical functioning (items 3, 4, 5, 6, 7, 8, 9, 10, 11, 12), Role limitations due to physical health (items: 13, 14, 15, 16), Role limitations due to emotional problems (items: 17, 18, 19), Vitality (Energy/fatigue) (items: 23, 27, 29, 31), Emotional well-being (items: 24, 25, 26, 28, 30), Social functioning (20, 32), Pain (items: 21, 22) and General Health (items: 1, 33, 34, 35, 36), all with values ranging from 0 to 100. Change in general Health (in a 5-point NRS, item: 2).

Listing 16.2.6.5
Rescue Medication Usage
mITT Population

Subject ID	Treatment Arm	ATC Class (Level 2)/ Preferred Name/ Verbatim Term	Primary Indication	Start Date (Study Day)/ End Date (Study Day)	Dose (unit)	Route	Frequency
XXXXXX	XXXX	XXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	Painful Diabetic Neuropathy	--MMMYYYY (-XX)/ DDMMMYYYY (-X)	XXXX unit	XXXXXXXXX	XXXXX
	XXXX	XXXXXXXXX/ XXXXXXXXXXXXXXX/ XXXXXXXXXXX	Painful Diabetic Neuropathy	--MMMYYYY (-X)/ Ongoing	XXXX unit	XXXXXXXXX	XXXXX
	XXXX	XXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX	Painful Diabetic Neuropathy	DDMMMYYYY (X)/ DDMMMYYYY (XX)	XXXX unit	XXXXXXXXX	XXXXX

ATC = anatomical therapeutic chemical.
Note: Study Day is calculated relative to the date of first dose.
Medications were coded using WHO drug dictionary version vMar2023.

Programming Notes:

- ATC & Preferred Name text should be in proper case in table.
- Ensure proper WHO-DDE version is printed in footnote.
- Sort by subject, start date/time, end date/time, ATC level 2 & Preferred Name .
- If Dose unit, Route or Frequency is Other, display other specify text only (ie, do not display “Other: XXXXXX” but just “XXXXXX “).
- Adjust footnotes for frequency and routes as needed.
- Sort by Treatment Arm/ Subject ID / Start Date / End Date (alphabetically for ATC Class Level 2 if same date for two medications

Listing 16.2.6.6
Patient Global Impression of Change
mITT Population

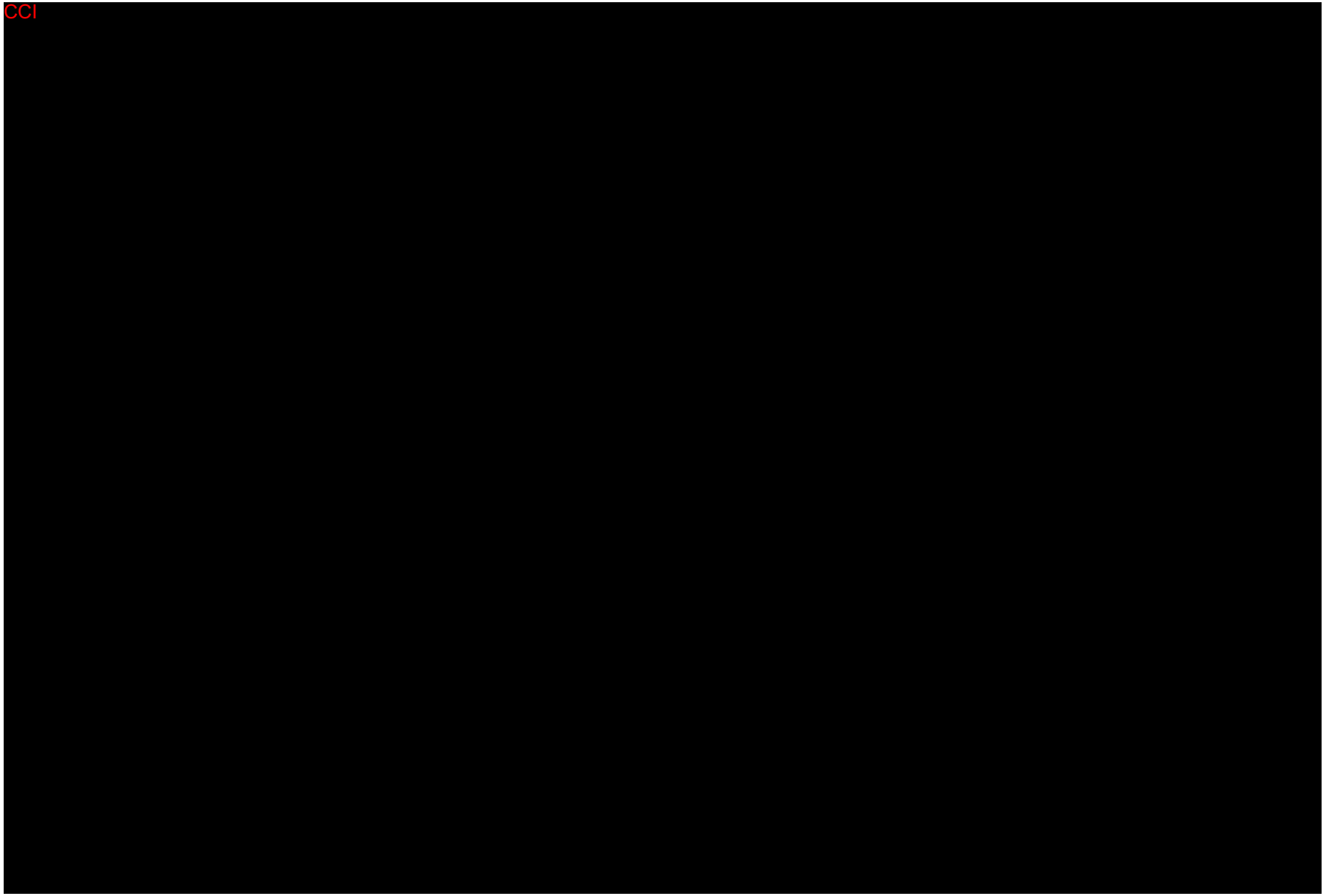
Subject ID	Treatment Arm	Study Visit	Collection Date / Study Day	PGIC
XXXXXX	XXXX	Week 4	DDMMMYYYY/ (X)	XXXXXXXX
		Week 8	DDMMMYYYY/ (X)	XXXXXXXX
		Week 12	DDMMMYYYY/ (X)	XXXXXXXX
		Week 18	DDMMMYYYY/ (X)	XXXXXXXX
XXXXXX	XXXX	Week 4	DDMMMYYYY/ (X)	XXXXXXXX
		Week 8	DDMMMYYYY/ (X)	XXXXXXXX
		Week 12	DDMMMYYYY/ (X)	XXXXXXXX
		Week 18	DDMMMYYYY/ (X)	XXXXXXXX
		…	…	…

PGIC =Patient Global Impression of Change.
Note: Data shown in column 'PGIC' are Subjects ratings about overall improvement in health status.
Study Day is calculated relative to the date of first dose.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Collection Date.
- Include all observed data on PGIC scores for Week 4, 8, 12, and 18.

CCI



CCI

CCI

Listing 16.2.7.1
Adverse Events
Safety Population

Subject ID/ Treatment Arm	AE ID Number	System Organ Class/ Preferred Term/ Verbatim Term	Start Date/Time (Study Day)/ End Date/Time (Study Day)	Severity/ Relationship	Outcome/ Action Taken/ Therapy?	AE Leading to Study DC?	TEAE	Serious/ Serious Criteria
XXXXX/ XXXX	X	XXXXXXXXXXX/ XXXXXXX/ XXXXXXX	DDMMMYYYY/HH: MM (X)/ DDMMMYYYY/HH: MM (X)	XXXXXX/ XXXXXX	XXXXXXXXX/ XXXXXXX/ Yes	No	Yes	No
XXXXX/ XXXX	X	XXXXXXXXXXX/ XXXXXXX/ XXXXXXX	DDMMMYYYY/HH: MM (X)/ DDMONYYYY/HH: MM (X)	XXXXXX/ XXXXXX	XXXXXXXXX/ XXXXXXX/ No	Yes	No	Yes / XXX
XXXXX/ XXXX	X	XXXXXXXXXXX/ XXXXXXX/ XXXXXXX	DDMONYYYY/HH: MM (X)/ Ongoing	XXXXXX/ XXXXXX	XXXXXXXXX/ XXXXXXX/ No	No	No	Yes / XXX

AE = adverse event; DC = discontinuation; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; SAE = serious adverse event; TEAE = treatment emergent adverse event.
Note: Study Day is calculated relative to the date of first dose. A TEAE is defined as an AE with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0

Programming Notes:

- If time missing, display "- -:- -".
- AE ID number represents Record position within Subject.
- If no events meet the criteria for display (i.e, no AEs occur in the study), present "No events are reported.".
- SOC & PT text should be in proper case in table.
- Sort by Treatment Arm/ Subject ID / Start Date / End Date (alphabetically for SOC if same date for two events).

In case a term is not coded (e.g. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]". SOC and PT abbreviations should be added in this case in footnote.

Listing 16.2.7.2
Treatment Emergent Adverse Events Leading to Study Drug Discontinuation
Safety Population

Programming Notes:

- Same shell as Listing 16.2.7.1.
- Update listing deleting seventh and eight columns

Listing 16.2.7.3
Treatment Emergent Adverse Events Associated with Abnormal Liver
Safety Population

Programming Notes:

- Same shell as Listing 16.2.7.1.
- Update listing deleting eighth column.

Listing 16.2.7.4
Joint Related Adverse Events of Special Interest
Safety Population

Programming Notes:

- Same shell as Listing 16.2.7.1.

Listing 16.2.7.5
Serious and/or Severe Infections
Safety Population

Programming Notes:

- Same shell as Listing 16.2.7.1.

Listing 16.2.7.6
Anaphylactic Reactions, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of Study Drug
Safety Population

Programming Notes:

- Same shell as Listing 16.2.7.1.
- Update listing by deleting seventh column.

Listing 16.2.8.1
Clinical Chemistry Laboratory Evaluations
Safety Population

Subject ID/ Treatment Arm	Parameter	Study Visit	Date/Time of Collection (Study Day)	Original Result (Unit)	Standard Results (unit)	Reference Range [1]	Baseline Flag	CFB	Results Assessment / Reason CS	Lab ID Number	Fasting Status	Comments
XXXXX/ XXXX	Chemistry panel	XXXXXX							ND: xxx			
XXXXX/ XXXX	Albumin	XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY	Y			XXXXXXX	Y	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X	H-CS / XXX	XXXXXXX	Y	XXXX
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X		XXXXXXX	Y	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X	H-NCS	XXXXXXX	N	

CFB = change from baseline; CS = clinically significant; H = High; L = Low; NCS = not clinically significant; ND = not done.
Note: Study Day is calculated relative to the date of first dose.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
[1] Reference range is used to identify potentially clinically significant laboratory values.

Programming Notes:

- Keep parameter sorting from the last bullet point below.
- For results assessment, do not populate column if result is normal.
- Sort by Treatment Arm/ Subject ID / Parameter / Date time of collection.
- If the whole panel is not done at a visit, present the information on first row of the subject under ‘Chemistry panel’ parameter and don’t present the ‘not done’ information for each parameter. Display “ND: reason why” in the result assessment column.
- Sort Parameters in the following Order: Albumin, Alkaline Phosphatase, Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Bicarbonate, Calcium, Chloride, Creatinine, High-Sensitivity C-Reactive Protein (hs-CRP), Estimated Glomerular Filtration Rate (eGFR by Cockcroft - Gault), Serum Glucose, Lactate Dehydrogenase (LDH), Potassium, Sodium, Total Bilirubin, Total Protein, Blood Urea Nitrogen (BUN), Uric Acid.

Listing 16.2.8.2
Hematology Laboratory Evaluations
Safety Population

Programming Notes:

- Same shell as Listing 16.2.8.1.
- Keep parameter sorting from the last bullet point below.
- For results assessment, do not populate column if result is normal.
- Sort by Treatment Arm/ Subject ID / Parameter / Date time of collection.
- If the whole panel is not done at a visit, present the information on first row of the subject under 'Hematology panel' parameter and don't present the 'not done' information for each parameter. Display "ND: reason why" in the result assessment column.
- Sort Parameters in the following Order: Absolute basophil count, absolute eosinophil count, absolute lymphocytes count, Absolute Monocyte Count, Absolute Neutrophil Count, Basophils %, Eosinophils %, Hematocrit (HCT), Hemoglobin (HGB), hemoglobin A1C (HgbA1C), Lymphocytes %, mean corpuscular hemoglobin (MHC), Mean Corpuscular Hemoglobin Concentration (MCHC), Mean Corpuscular Volume (MCV), Monocytes %, Neutrophils %, Platelets, Red blood cell count (RBC), Red Cell Distribution Width, white blood cell Count (WBC).

Listing 16.2.8.3
Coagulation Laboratory Evaluations
Safety Population

Programming Notes:

- Same shell as Listing 16.2.8.1.
- Keep parameter sorting from the last bullet point below.
- For results assessment, do not populate column if result is normal.
- Sort by Treatment Arm/ Subject ID / Parameter / Date time of collection.
- If the whole panel is not done at a visit, present the information on first row of the subject under 'Coagulation panel' parameter and don't present the 'not done' information for each parameter. Display "ND: reason why" in the result assessment column.
- Sort Parameters in the following Order: Activated Partial Thromboplastin Clotting Time (APTT), Fibrinogen, International normalized ratio (INR), Prothrombin Time (PT).

Listing 16.2.8.4
Urinalysis Laboratory Evaluations
Safety Population

Subject ID/ Treatment Arm	Parameter	Study Visit	Date/Time of Collection (Study Day)	Original Result (Unit)	Standard Results (unit)	Reference Range [1]	Baseline Flag	CFB	Results Assessment / Reason CS	Lab ID Number	Fasting Status	Comments
XXXXX	Urinalysis panel	XXXXXX							ND: xxx			
XXXXX	pH/ Specific Gravity	XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY	Y			XXXXXXX	Y	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X	H-CS / XXX	XXXXXXX	Y	XXXX
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X		XXXXXXX	Y	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X	H-NCS	XXXXXXX	N	
	Blood Urine/ Glucose/ Ketones/ Protein	XXXXXX	DDMMMYYYY/ HH:MM (X)	Trace			Y		H-NCS	XXXXXXX	Y	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	100 (mg/dL)	100 (mg/dL)				H-CS / XXX	XXXXXXX	Y	XXXX
		XXXXXX	DDMMMYYYY/ HH:MM (X)	Negative						XXXXXXX	N	

CFB = change from baseline; CS = clinically significant; H = High; L = Low; NCS = not clinically significant; ND = not done.
Note: Study Day is calculated relative to the date of first dose.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
[1] Reference range is used to identify potentially clinically significant laboratory values.

Programming Notes:

- Keep parameter sorting from the last bullet point below.
- For results assessment, do not populate column if result is normal.
- Sort by Treatment Arm/ Subject ID / Parameter / Date time of collection.
- If the whole panel is not done at a visit, present the information on first row of the subject under ‘Urinalysis panel’ parameter and don’t present the ‘not done’ information for each parameter. Display “ND: reason why” in the result assessment column.
- Sort Parameters in the following Order: Blood Urine, Glucose, Ketones, pH, Protein, Specific Gravity.

Listing 16.2.8.5
Serology Laboratory Evaluations
Safety Population

Subject ID	Treatment Arm	Was Serology Test Collected?	Date/Time of Collection (Study Day)	Test (Unit) [1]	Result	Lab ID Number	Fasting Status	Reason not collected	Comments
XXXX	XXXX	Yes	DDMMMYYYY Y/HH:MM (X)	Hepatitis B Ag	Negative	XXXX	Y		XXXXXXXXX
				Hepatitis C Ab	Positive	XXXX	Y		
				HIV-1/ -2 Ag	Not Done	XXXX	Y	XXXXXXX	
				Quantiferon Gold Plus NIL	X.XX (IU/mL)	XXXX	Y		

Ab = antibody; Ag = antigen; HIV = human immunodeficiency virus; TB = tuberculosis.
Note: Study Day is calculated relative to the date of first dose.
[1] if Applicable

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Date of collection / Test.
- Keep parameter sorting from the last bullet point below
- Sort Parameters in the following Order: Hepatitis B Antigen, Hepatitis C Virus Antigen, Hepatitis C Virus Antibody, HIV-1/ -2 Antigen, Quantiferon Gold Plus NIL, Quantiferon Gold Plus TB, Quantiferon Gold Plus Mitogen minus NIL, Quantiferon Gold Plus TB1 minus NIL, Quantiferon Gold Plus TB2 minus NIL

Listing 16.2.8.6
Pregnancy Test Results
Safety Population

Subject ID	Treatment Arm	Visit	Was a Urine pregnancy test performed?	Date/Time Performed (Study Day)	If not, Reason	Result
xxxxx	xxxx	xxxxx	Xxxx	Ddmmmyyyy/ hh:mm (XX)	xxxx	xxxx
		xxxxx	Xxxx	Ddmmmyyyy/ hh:mm (XX)	Other: xxxx	xxxx

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment.

Listing 16.2.8.7
Drug Test Results
Safety Population

Subject ID	Treatment Arm	Was Drug Test Performed?	Date/ Time Assessment (Study Day)	Result	Findings	Reason Test not Performed
XXXXXX	XXXX	Yes	DDMMMYYYY/ HH:MM (XX)	Negative	Negative	
XXXXXX	XXXX	Yes	DDMMMYYYY/ HH:MM (XX)	Positive	Cocaine / Opiates	

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Concatenate all findings by "/"
- Sort by Treatment Arm/ Subject ID / Date of assessment.

Listing 16.2.8.8
COVID-19 Screening
Safety Population

Subject ID/ Treatment Arm	Visit	COVID-19 Sx Screening?/Date / Time (Study Day)	Sx	Body Tº Check?/ Date/ Time (Study Day)	Body Tº (Unit)	COVID-19 swab?/ Date/ Time (Study Day)	Swab result	COVID-19 Ab testing?/ Date/ Time (Study Day)	Ab testing results	COVID-19 Ag testing?/ Date/ Time (Study Day)	Ag testing results
xxxxx/ xxxx	xxxx	Yes/ Ddmmmyyyy/ hh:mm (XX)	XXX/ XXX	Yes/ Ddmmmyyyy/ hh:mm (XX)	XX (XX)	Yes/ Ddmmmyyyy/ hh:mm (XX)	Xxxx	Yes/ Ddmmmyyyy/ hh:mm (XX)	Xxxx	Yes/ Ddmmmyyyy / hh:mm (XX)	Xxxx
	xxxx	Yes/ Ddmmmyyyy/ hh:mm (XX)	XXX	Yes/ Ddmmmyyyy/ hh:mm (XX)	XX (XX)	Yes/ Ddmmmyyyy/ hh:mm (XX)	Xxxx	Yes/ Ddmmmyyyy/ hh:mm (XX)	Xxxx	Yes/ Ddmmmyyyy / hh:mm (XX)	Xxxx

Ab = Antibody; Ag = Antigen; COVID-19 = Coronavirus disease 2019; Sx = Symptoms; Tº = Temperature.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Concatenate all Symptoms by "/"
- Sort by Treatment Arm/ Subject ID / Date of assessment

Listing 16.2.9.1
Vital Signs Measurements
Safety Population

Subject ID	Treatment Arm	Parameter	Study Visit	Position [1] / Tº Method	Date/Time of Collection (Study Day)	Original Result (Unit)	Baseline Flag	CFB
XXXXX	XXXX	Body Temperature	XXXXXX	XXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	Y	
			XXXXXX	XXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)		XX
						...		
		Resting Heat Rate	Screening	Supine	DDMMMYYYY/ HH:MM (X)	XX		
			Day 1: Pre-Dose	Supine	DDMMMYYYY/ HH:MM (X)	XX	Y	XX
			XXXXXX	Supine	DDMMMYYYY/ HH:MM (X)	XX		XX
			XXXXXX	Sitting		ND		
			XXXXXX	Sitting	DDMMMYYYY/ HH:MM (X)	XX		XX

CFB = change from baseline; ND = not done.
Note: Study Day is calculated relative to the date of first dose.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
[1] Resting position measurements encompass Sitting and Supine position measurements.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Parameter (Order in the second bullet point)/ Date time of collection.
- Repeat for Resting Heart Rate, Resting Systolic Blood Pressure, Resting Diastolic Blood Pressure, Respiratory Rate, Body Temperature, Standing Heart Rate, Standing Systolic Blood Pressure, Standing Diastolic Blood Pressure.
- After Week 2 (inclusive), Supine measure are taken in sitting position. We will consider them as supine (in resting position) for calculating Change from Baseline (always at supine position).
- Include the following timepoints: Screening, Baseline (Day 1: Pre-Dose), Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week10 + 24 hours, Week 11, Week 12, Week 18.
- Note that Body T^{o}, and standing measures are not taken on Day 1, at 15, 30 and 45 minutes post-dose.

Listing 16.2.9.2
ECG Results
Safety Population

Subject ID/ Treatment Arm	Visit	ECG Date / Time (Study Day)	Tracing	ECG Result/ Comment	PR Interval (msaec)	QRS duration (msec)	QT Interval (msec)	Heart Rate (bpm)	QTcF Interval (msec)	Reason Not Done
XXXXX	Day 1: Pre-Dose	DDMMMYYYY / HH:MM (XX)	1	Abnormal CS/ xxxx	xx	xx	xx	xx	xx	
			2	Abnormal CS/ xxxx	xx	xx	xx	xx	xx	
			3	Abnormal NCS/ xxxx	xx	xx	xx	xx	xx	
XXXXX	XXXX	DDMMMYYYY/ HH:MM (XX)	1	Normal	xx	xx	xx	xx	xx	
			2	Normal	xx	xx	xx	xx	xx	
			3	Normal	xx	xx	xx	xx	xx	

CS = clinically significant; ECG = electrocardiogram; NCS = Not clinically significant
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Date time of collection / Tracing
- Include the following timepoints: Day 1: Pre-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 4, Week, 8, Week 12, and Week 18.

Listing 16.2.9.3
Physical Examination Results
Safety Population

Subject ID	Treatment Arm	Visit	Examination Type	Exam Date/ Time (Study Day)	Body System	Result / Change from previous assessment [1]	If Abnormal, findings / Specify Changes [2]	Reason Not Done
XXXXX	XXXX	Screening	Complete	DDMMMYYYY / HH:MM (XX)	Head, Neck and Thyroid	Normal		
					Ears, Eyes, Nose and Throat	Abnormal CS	XXXXXXX	
		Day 1	Targeted	DDMMMYYYY / HH:MM (XX)	Ears, Eyes, Nose and Throat	XXXXXXXXXX	XXXXXXXX	

CS = Clinically Significant, NCS = Not Clinically Significant
Note: Study Day is calculated relative to the date of first dose.
[1] For targeted examination type: Change from previous assessment.
[2] For targeted examination type: Specify Changes.

Programming Notes:

- Keep sorting from eCRF: Head, Neck and Thyroid/ Ears, Eyes, Nose and Throat/ Chest (including breasts)/ Lungs / Heart / Lymph Nodes / Abdomen / Hepatic / Gastrointestinal / Anorectal / Genitourinary/ Skin / Musculoskeletal/Extremities / Neurological / Other.
- Complete Physical examination only at Screening, Week 12, 18 (it can also be unscheduled).
- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment / Body system

Listing 16.2.9.4
Neurological Examination Results
Safety Population

Subject ID	Treatment Arm	Visit	Exam Date/ Time (Study Day)	Body System	Result	If Abnormal, findings	Reason Not Done
XXXXX	XXXX	Screening	DDMMMYYYY / HH:MM (XX)	Mental Status	Normal		
				Cranial Nerves	Abnormal CS	XXXXXXX	
		Day 1	DDMMMYYYY / HH:MM (XX)	Cranial Nerves	XXXXXXXXXX	XXXXXXXX	

CS = Clinically Significant, NCS = Not Clinically Significant
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Keep sorting from eCRF: Mental status/ Cranial Nerves/ Motor Function/ Reflexes / Sensation and Propioception / Coordination / Other.
- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment / Body system

Listing 16.2.9.5
Total Neuropathy Score-Nurse
Safety Population

Subject ID/ Treatment Arm	Visit	Date/ Time of collection (Study Day)	Sensory Symptom Score (0–4)	Motor Symptom Score (0–4)	Autonomic Symptom Score (0–4)	Pin Sensibility Score (0–4)	Vibration Sensibility Score (0–4)	TNSn Total (0–20)	Reason Not Done
XXXXX/ XXXX	Screening	DDMMMYYYY / HH:MM (XX)	XX	XX	XX	XX	XX	XX	
	Day 1	DDMMMYYYY / HH:MM (XX)	XX	XX	XX	XX	XX	XX	
	Week 2	DDMMMYYYY / HH:MM (XX)	ND	ND	ND	ND	ND	ND	XXXXXXXXXXXXXX

ND = Not Done; TNSn = Total Neuropathy Score-Nurse.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment

Listing 16.2.9.6
Motor and Sensory Nerve Conduction Studies
Safety Population

Subject ID/ Treatment Arm	Visit	Date / Time of Collection (Study Day)	Location / Evaluation	Was Evaluation Preformed ? / Nerve	Amplitude (Motor = mV; sensory = microV) / Range	Peak Latency (msec) / Range	Conduction velocity (msec) / Range	Duration of action potential (msec) / Range	Evaluation Result	If Abnormal, Specify	Significant Changes from Baseline? / if Yes, Specify
XXXX/ XXXX	Screening	DDMMMYY YY / HH:MM (XX)	Lower Limb - right side/ Motor evaluation	Y/ XXXXXX	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	Abnormal	XXXXX	NA
			XXXXXX/ XXXXXX	Y/ XXXXXX	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	Normal		NA
			XXXXXX/ XXXXX	N							
	Week 18	DDMMMYY YY/ HH:MM (XX)	XXXXXX/ XXXXX	Y/ XXXXXX	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	Abnormal	XXXXX	N
			XXXXXX/ XXXXX	Y/ XXXXXX	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	Normal		N
			XXXXXX/ XXXXX	Y/ XXXXXX	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	Abnormal	XXXXX	Y/ XXXXXXX

NA = Not Applicable
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment / Location - Evaluation
- Keep sorting from eCRF: Lower Limb - right side/Motor evaluation, Lower Limb - right side/Sensory evaluation, Lower Limb - left side/ Motor evaluation, Lower Limb - left side/ Sensory evaluation, Upper Limb - right side /Motor evaluation, Upper Limb - right side/ Sensory evaluation, Upper Limb - left side/ Motor evaluation, Upper Limb - left side /Sensory evaluation.

Listing 16.2.9.7
Strength and Deep Tendon Reflexes
Safety Population

Subject ID	Treatment Arm	Visit	Date/ Time of collection (Study Day)	Ankle Dorsiflexion Strength	Deep Tendon Reflexes	Reason Not Done
XXXXX	XXXX	Screening	DDMMMYYYY / HH:MM (XX)	XXXX	XXXX	
		Day 1	DDMMMYYYY / HH:MM (XX)	XXXX	XXXX	
		Week 2	DDMMMYYYY / HH:MM (XX)	ND	ND	XXXXXXXXXXXXXX

ND = Not Done.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment

Listing 16.2.9.8
Injection Site Reactions
Safety Population

Subject ID	Treatment Arm	Visit	Date/ Time of Assessment (Study Day)	Pain	Tenderness	Erythema/redness	Induration/ swelling	Reason Not Done
XXXXX	XXXX	Day 1: 15 Minutes after Start of Infusion	DDMMMYYYY / HH:MM (XX)	XXXX	XXXX	XXXX	XXXX	
		Day 1: 30 Minutes after Start of Infusion	DDMMMYYYY / HH:MM (XX)	XX	XX	XX	XX	
		...						
		Week 18	DDMMMYYYY / HH:MM (XX)	ND	ND	ND	ND	XXXXXXXXXXXXXX

ND = Not Done.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment
- Include the following timepoints: Day 1: 15 Minutes after Start of Infusion, Day 1: 30 Minutes after Start of Infusion, Day 1: 45 Minutes after Start of Infusion, Day 1: 60 Minutes after Start of Infusion, Day 1: 2 hours after Start of Infusion, Day 1: 4 hours after Start of Infusion, Week 2, Week 4, Week 6, Week, 8, Week 10, Week 12, and Week 18.

Listing 16.2.9.9
Hypersensitivity/Anaphylactic Reactions
Safety Population

Subject ID	Treatment Arm	AE ID Number	Onset Date/Time (Study Day)/ Resolution Date/Time (Study Day)	Type of Reaction	Severity grade for the Symptom with Highest Severity	Onset Time for Highest Severity	Leading to IP Discontinuation?
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXX	XXXX	/HH:MM	Yes
		X	DDMMMYYYY/HH:MM (X)/ DDMONYYYY/HH:MM (X)	XXXXX			No
		...					
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ DDMONYYYY/HH:MM (X)	XXXXX	XXXX	/HH:MM	No

AE = Adverse Event.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Onset Date/Time / Resolution Date/Time / Reaction Type.
- Keep sorting from eCRF: Urticaria, Pruritus, Rash, Flushing, Swollen lips, tongue, uvula and/or vulva, Dyspnoea, Wheeze-bronchospasm, Stridor, Hypoxia, Hypotension, Crampy abdominal pain, Vomiting, Diarrhoea, Other.

Listing 16.2.9.10
Liver Diagnostic Investigations
Safety Population

Subject ID	Treatment Arm	Potential Hy's Law Case Number	Liver Diagnostic Investigation Date (Study Day)	Liver Diagnostic Investigation	Liver Diagnostic Investigation Results	Comments
XXXXX	XXXX	X	DDMMMYYYY (X)	XXXX	XXXX	XXXXX
		X	DDMMMYYYY (X)	XXXXX	XXXXX	
		...				
XXXXX	XXXX	X	DDMMMYYYY (X)	XXXXX	XXXXX	

CT = Computerized tomography; ERCP = Endoscopic retrograde cholangiopancreatography; MRI = Magnetic resonance imaging; MRCP = Magnetic resonance cholangiopancreatography.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Diagnostic Date / Liver Diagnostic Investigation.
- Keep sorting from eCRF: Ultrasound, CT, MRI/MRCP, ERCP, Liver Biopsy, X-Ray, Tox Screening for Acetaminophen/Paracetamol, Tox Screening for Ethanol, Tox Screening, Other, Specialist (e.g. Hepatologist) Consulted, Serology for Hepatitis A, Serology for Hepatitis B, Serology for Hepatitis C, Serology for Hepatitis D, Serology for Hepatitis E, for Cytomegalovirus (CMV), Serology for Epstein Barr Virus (EBV), Autoimmune Serology, Other.

Listing 16.2.9.11
Liver Risk Factors and Lifestyle Events
Safety Population

Subject ID	Treatment Arm	Potential Hy's Law Case Number	Assessment Date (Study Day)	Liver Risk Factor Start Date (Study Day)/ Liver Risk Factor Stop Date (Study Day)	Liver Risk Factor / Reference Period	Liver Risk Factor Details	Comments
XXXXX	XXXX	X	DDMMMYYYY (X)	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXX/ XXX	XXXX	XXXXX
		X	DDMMMYYYY (X)	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXXX/ XXX	XXXXX	
		...					
XXXXX	XXXX	X	DDMMMYYYY (X)	DDMMMYYYY (X)/ Ongoing	XXXXX/ XXX	XXXXX	

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Assessment Date / Liver Risk Factor Start Date / Stop Date / Liver Risk Factor.
- Keep sorting from eCRF: Alcohol Abuse, Increased Alcohol Consumption within 1 Month of Reported Event, IV Drug Abuse, Tattoo, Acupuncture, Sexually Transmitted Diseases, Toxic/Chemical Agent Exposure, Travel (Areas at Risk in the Last Year), Pregnancy, Parenteral Nutrition, Excessive Physical Exercise, Changes Diet/Fasting Episodes/Weight Loss Diet, Previous Drug Reaction (Associated with an Elevation of Liver Tests), Blood Transfusion, Subject Exposed to Anyone with Jaundice in the Last Month, History of Hypotension, Low Blood Pressure at Time of Event of Liver Injury and/or Abnormal Liver Laboratory Value, History of Liver Disease, Other.
- Concatenate comments with "/".

Listing 16.2.9.12
Liver Signs and Symptoms
Safety Population

Subject ID	Treatment Arm	Potential Hy's Law Case Number	Start Date (Study Day)/ Stop Date (Study Day)	Liver Sign/ Symptom	Intermittent
XXXXX	XXXX	X	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXX	N
		X	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXXX	N
		...			
XXXXX	XXXX	X	DDMMMYYYY (X)/ Ongoing	XXXXX	Y

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Start Date / Stop Date / Liver Sign/Symptom.
- Keep sorting from eCRF: Anorexia, Asthenia, Pyrexia, Pruritus, Jaundice, Arthralgia, Abdominal Pain, Abdominal Tenderness, Nausea, Vomiting, Rash, Mucosal Inflammation, Purpura, Hepatomegaly, Splenomegaly, Lymphadenopathy, Ascites, Confusional State, Coma, Upper Quadrant Tenderness, Biliary Obstruction, Eosinophilia, Dark Urine, Other.
- If Rash, Lymphadenopathy or Other, Concatenate Symptom with Comment as: “Rash: xxxxxx”. “Lymphadenopathy: xxxxxx”, “Other: xxxxxxxx”

Listing 16.2.9.13
Infection Diagnostic Investigations
Safety Population

Subject ID	Treatment Arm	AE ID Number	Start Date/ Time (Study Day)/ Stop Date/ Time (Study Day)	Method	Examination performed	Test Result
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXX	Y	XXXXX
		X	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X))	XXXXX	Y	XXXXX
		...				
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ Ongoing	XXXXX	N	XXXXX

AE = adverse event.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Start Date / Stop Date / Method.
- Keep sorting from eCRF: Microscopy, Culture and Sensitivity, Serological Tests, Nucleic Acid Based Tests, X-Ray, Other.

Listing 16.2.9.14
Infection Risk Factors and Lifestyle Events
Safety Population

Subject ID	Treatment Arm	AE ID Number	Start Date/ Time (Study Day)/ Stop Date/ Time (Study Day)	Infection Risk Factor	Infection Risk Occurrence	Comments
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXX	Y	XXXXX
		X	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X))	XXXXX	Y	XXXXX
		...				
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ Ongoing	XXXXX	N	Ongoing

AE = adverse event; BCG = Bacillus Calmette–Guérin.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Start Date / Stop Date / Infection Risk Factor.
- Keep sorting from eCRF: Extensive Burns within the Last Year (Thermal Burn), Tattoo, Piercing or Acupuncture within the Last Year, Sexually Transmitted Diseases, Travel to Areas at Risk of Tuberculosis or Tropical Diseases, Infections Related to Travel (e.g. Tuberculosis and Tropical Diseases), Blood Transfusion (within the Last Year), Exposure to Nosocomial Pathogens within the Last Year, Contact History with Infection Source, Previous BCG Immunization, Evidence of BCG Scar, Tuberculin Skin or Quantiferon Test Confirms Previous Exposure or Immunity to Tuberculosis.
- Fill Comment column if Infection risk factor test = Unknown Previous BCG Immunization, not done, known Sexually Transmitted Disease reference Period, or Infection risk factor specifications.

Listing 16.2.9.15
Infection Signs and Symptoms
Safety Population

Subject ID	Treatment Arm	AE ID Number	System Organ Class/ Preferred Term/ Verbatim Term	Start Date/ Time (Study Day)/ Stop Date/ Time (Study Day)	Clinical Event	Infection Sign/Symptom Occurrence	Comments
XXXXX	XXXX	X	XXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXX	Y	XXXXX
		X	XXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X))	XXXXX	Y	XXXXX
		...					
XXXXX	XXXX	X	XXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ Ongoing	XXXXX	N	Ongoing

AE = adverse event.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Start Date / Stop Date / Clinical Event.
- Keep sorting from eCRF: Pyrexia, Headache, Confusional State, Convulsion, Rhinitis, Oropharyngeal Pain, Cough, Productive Cough, Haemoptysis, Wheezing, Dyspnoea, Pleuritic Pain, Vomiting, Diarrhoea, Genital Discharge, Haematuria, Dysuria, Hepatosplenomegaly, Jaundice, Lymphadenopathy, Rash, Night sweats, Chills, Myalgia, Weight Decrease.
- Fill Comment column if Maximum Tº (Unit) available for Pyrexia, or if site for Rash or Lymphadenopathy is known.

Listing 16.2.9.16
Prior and Concomitant Medications
Safety Population

Subject ID/ Treatment Arm	Prior/ Concomitant [1]	ATC Class (Level 2)/ Preferred Name/ Verbatim Term	Given for/as	Primary Indication	Start Date (Study Day)/ End Date (Study Day)	Dose (unit)	Route	Frequency
XXXXXX / XXXX	Prior	XXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	Medical History	XXXXXXX	--MMMYYYY (-XX)/ DDMMMYYYY (-X)	XXXX unit	XXXXXX XXX	XXXXX
	Both	XXXXXXXXX/ XXXXXXXXXXXXXXX/ XXXXXXXXXXX	Prophylaxis	XXXXXXX	--MMMYYYY (-X)/ Ongoing	XXXX unit	XXXXXX XXX	XXXXX
	Concomitant	XXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX	Adverse event	XXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (XX)	XXXX unit	XXXXXX XXX	XXXXX

ATC = anatomical therapeutic chemical; WHO-DDE = World Health Organization-Drug Dictionary Enhanced.
Note: Study Day is calculated relative to the date of first dose.
Medications were coded using WHO-DDE version vMar2018.
[1] Prior medications are defined as medications that started before first dose of study, whether they were stopped before first dose of study medication or not. Concomitant medications are defined as medications starting on or after first dose of study medication Both indicates medication that was started before the day of first dose and continued after.

Programming Notes:

- ATC & Preferred Name text should be in proper case in table.
- Ensure proper WHO-DDE version is printed in footnote.
- Sort by subject, start date/time, end date/time, ATC level 2 & Preferred Name .
- If Dose unit, Route or Frequency is Other, display other specify text only (ie, do not display “Other: XXXXXX” but just “XXXXXX “).
- Adjust footnotes for frequency and routes as needed.
- Sort by Treatment ID/ Subject ID / Start Date / End Date (alphabetically for ATC Class Level 2 if same date for two medications)

Listing 16.2.9.17
Prohibited Concomitant Medications
Safety Population

Programming Notes:

- Same Shell as Listing 16.2.9.16.
- Display prohibited prior and concomitant medications provided by the Medical Coder:
- Prohibited concomitant medications:
    - NSAIDs analgesic therapies (with acetylsalicylic acid with doses >= 325 mg/day).
    - COX-2 analgesic therapies.
    - Immunotherapeutics.
    - Live viral or attenuated bacterial vaccines.
    - Oral, IV, intramuscular, or any other parenteral (other than oral) steroids (inhaled or topical steroids are permitted).
    - Biologic therapeutic agents.
- Prohibited prior and/or concomitant medications:
    - Anti-NGF therapies.
    - Anti-TNF therapies.
- ATC & PN text should be in proper case in table.
- Ensure proper WHO-DDE version is printed in footnote.
- Sort by subject, start date/time, end date/time, ATC level 2 & Preferred Name .
- If Dose unit, Route or Frequency is Other, display other specify text only (ie, do not display “Other: XXXXXX” but just “XXXXXX “).
- Adjust footnotes for frequency and routes as needed.
- Sort by subject ID / Start Date / End Date (alphabetically for ATC Class Level 2 if same date for two medications)

Listing 16.2.9.18
Concomitant Procedures
Safety Population

Subject ID	Treatment Arm	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ End Date (Study Day)	Reason for Procedure	Reason (derived verbatim term)	If Reason is Other, Specify
XXXXX	XXXX	XXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXX	
XXXXX	XXXX	XXXXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXX	
XXXXX	XXXX	XXXXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXX	DDMMMYYYY (X)/ Ongoing	OTHER	OTHER	XXXXXXXXXX

MedDRA = Medical Dictionary for Regulatory Activities.
Note: Study Day is calculated relative to the date of first dose. All Procedure terms were coded using the MedDRA version 26.0. Concomitant Procedures are defined as medications continuing or starting on or after first dose of study medication.

Programming Notes:

- SOC & PT text should be in proper case in table.
- Sort by Treatment Arm/ Subject ID / Start Date / End Date (alphabetically for SOC if same date for two events).
- In case a term is not coded (e.g. in a dry run) it will be labelled as “Not Coded [SOC]” and “Not Coded [PT]”. SOC and PT abbreviations should be added in this case in footnote.

Listing 16.2.9.19
Anti-drug Antibody Test Results
Safety Population

Subject ID	Treatment Arm	Study Visit	Date/Time of Collection (Study Day)	Screening Status Result	ADA Titer	Confirmatory Status result	Lab ID Number	Comments
XXXXX	XXXX	XXXXXX	DDMMMYYYY/ HH:MM (X)	Positive	XX	Positive	XXXXXXX	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	Positive	XX	Positive	XXXXXXX	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	Negative	XX	Negative	XXXXXXX	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	Missing		NRR	XXXXXXX	XXXX

ADA = Anti-Drug Antibodies; NA = Not Applicable; NRR = Not Reportable Result; QNS = Quantity Not Sufficient.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Collection Date.
- ADA titre reported as <30 (below the minimum required dilution) is a negative result for the presence of ADA.
- Include Following timepoints: Screening, Weeks 2, 4, 8, 10, 12, 18.

Listing 16.2.10.1
Serum MEDI7352 Concentrations
PK Population

Subject ID	Treatment Arm	Parameter	Study Visit	Date/Time of Collection (Study Day)	Result (ng/mL)	Lab ID Number	Comments
XXXXX	XXXX	MEDI7352 Concentration	XXXXXX	DDMMMYYYY/ HH:MM (X)	XX	XXXXXXX	
			XXXXXX	DDMMMYYYY/ HH:MM (X)	XX	XXXXXXX	
			XXXXXX	DDMMMYYYY/ HH:MM (X)	XX	XXXXXXX	
			XXXXXX	DDMMMYYYY/ HH:MM (X)	NRR	XXXXXXX	XXXX

NA = Not Applicable; NRR = Not Reportable Result.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Collection Date.
- Include the following timepoints: Day 1, Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours: after Week 10/ Pre-Dose, Week 11: after Week 10/ Pre-Dose, Week 10 + 14 Days: after Week 10/ Pre-Dose, Week 18.

Listing 16.2.10.2
Serum total NGF Concentrations
Safety Population

Subject ID	Treatment Arm	Parameter	Study Visit	Date/Time of Collection (Study Day)	Result (pg/mL)	Lab ID Number	Comments
XXXXX	XXXX	tNGF Concentration	XXXXXX	DDMMMYYYY/ HH:MM (X)	XX	XXXXXXX	
			XXXXXX	DDMMMYYYY/ HH:MM (X)	XX	XXXXXXX	
			XXXXXX	DDMMMYYYY/ HH:MM (X)	XX	XXXXXXX	
			XXXXXX	DDMMMYYYY/ HH:MM (X)	NS	XXXXXXX	XXXX

BLLOQ = Below the Lowest Limit of Quantitation; NA = Not Applicable; ND = Not Detected; NS = No Value due to Insufficient Volume or No Sample Received; SAT = Greater than the Top of the Standard Curve; tNGF = total Nerve-Growth Factor.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Collection Date.
- Include the following timepoints: Day 1, Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 12; Week 18.

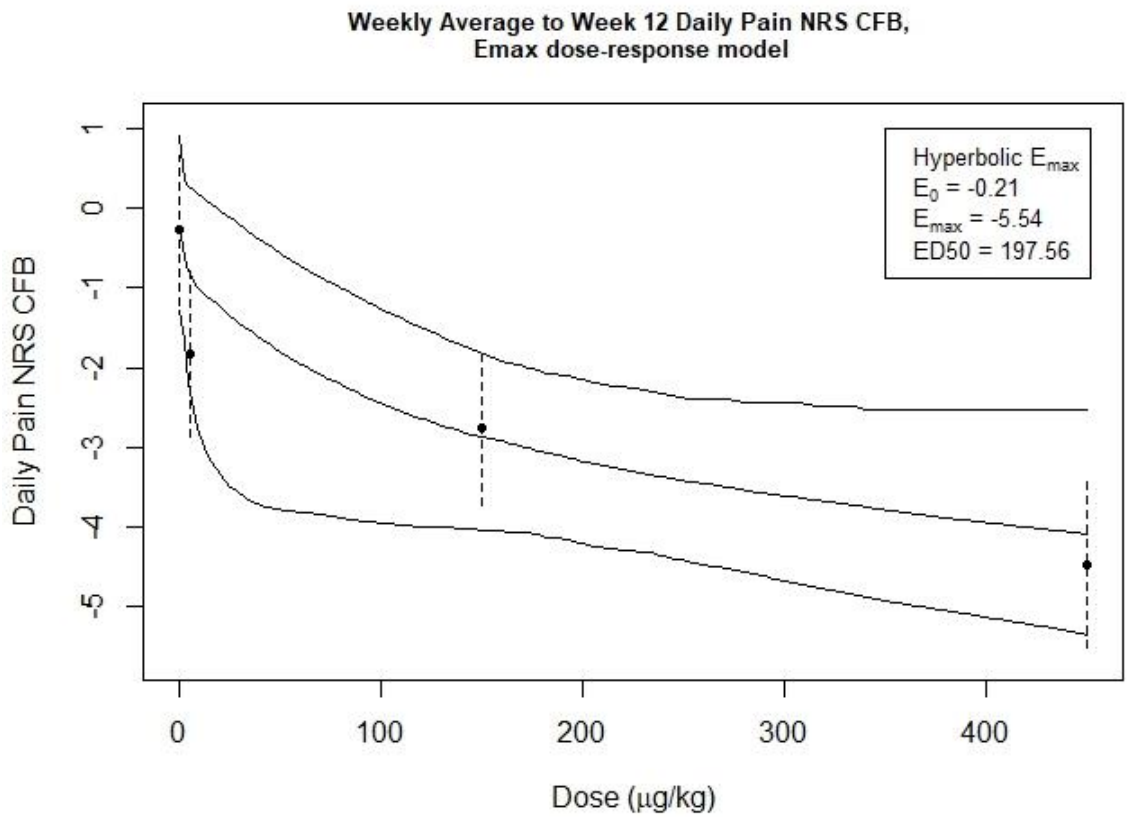
Planned Figure Descriptions and Shells

Number Title Population	Unique (U) or Repeated (R)
Figure 14.2.1.1 - Daily Pain NRS: MCP-Mod Dose Response Model - mITT Population	U
Figure 14.2.1.2 - Daily Pain NRS: Boxplots at Week 12 by Treatment Group and Missing Data Handling - mITT Population	U
Figure 14.2.1.3 - Daily Pain NRS: Boxplots at Week 12 by Treatment Group and Co-Medication Subgroup - mITT Population	R
Figure 14.2.1.4 - Daily Pain NRS: MMRM LS Means (95% Confidence Interval) over 12-weeks by Treatment Group (Observed Cases) - mITT Population	U
Figure 14.3.6.1.1 - Vital Sign Profiles: Mean (±SD) Systolic Blood Pressure over time - Safety Population	U
Figure 14.3.6.1.2 - Vital Sign Profiles: Mean (±SD) Diastolic Blood Pressure over time - Safety Population	R
Figure 14.3.6.1.3 - Vital Sign Profiles: Mean (±SD) Heart Rate over time - Safety Population	R
Figure 14.3.6.1.4 - Vital Sign Profiles: Mean (±SD) Respiratory Rate over time - Safety Population	R
Figure 14.3.6.1.5 - Vital Sign Profiles: Mean (±SD) Temperature over time - Safety Population	R
Figure 14.4.1.1 - Pharmacokinetics: Line Plot of Geometric Mean (with and without gSD) Serum MEDI7352 over time - PK Population	R
Figure 14.4.1.2 - Pharmacokinetics: Individual Plot of Serum MEDI7352 Concentrations over time - PK Population	U
Figure 14.4.2.1 - Pharmacodynamics: Line Plot of Geometric Mean (with and without gSD) total NGF over time - Safety Population	R
Figure 14.4.2.2 - Pharmacodynamics: Individual Plot of Serum total NGF over time - Safety Population	R

Figures Change Log

Output Number	Date of Change	Change Made By (initials)	Description/Rationale

Figure 14.2.1.1
Daily Pain NRS: MCP-Mod Dose Response Model
mITT Population

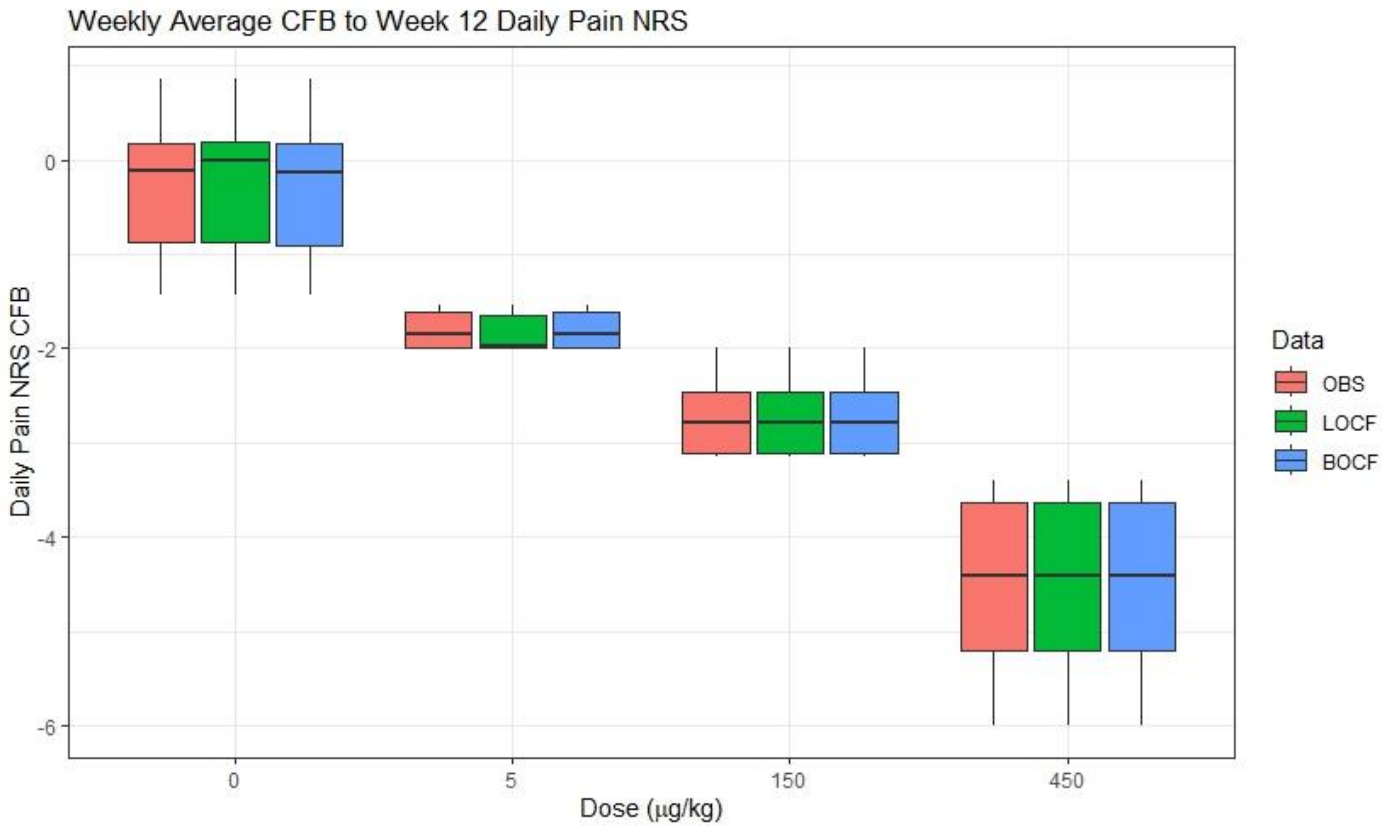


CI = Confidence Interval; CFB = Change from Baseline; DPS = Daily Pain Score; NRS = Numeric Rating Scale.
Baseline is defined as the average of the 'non-missing' DPS within the seven-day period prior to randomization i.e., Day -7 to Day -1, inclusive. Envelope depicts 95% CI of mean dose-response. Added dots are actual doses ± 95% CI.
mITT Population = includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
Reference Listing: 16.2.6.1

Programming Notes:

- Insert the following text as legend: "Weekly Average to Week 12 Daily Pain NRS CFB, xxxx dose-response model", with 'xxxx' as the selected dose-response model (e.g., Hyperbolic E_{max}).
- Dose (µg/kg) in x axis and Daily Pain NRS CFB in y axis.
- Add model parameter values as an inset plot. For e.g., Sigmoid E_{max}; E_0 = xxx, E_{max} = xxx, ED50 = xxx, λ = xxx.
- The MCP-MOD approach will only be performed if stage 4 is initiated, otherwise there would be insufficient dosing data to fit the non-linear models.

Figure 14.2.1.2
Daily Pain NRS: Boxplots at Week 12 by Treatment Group and Missing Data Handling
mITT Population



BOCF = Baseline Observation Carried Forward; CFB = Change from Baseline; DPS = Daily Pain Score; LOCF = Last Observation Carried Forward; NRS = Numeric Rating Scale; OBS = Observed Cases.
Baseline is defined as the average of the 'non-missing' DPS within the seven-day period prior to randomization i.e., Day -7 to Day -1, inclusive.
mITT Population = includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
Reference Listing: 16.2.6.1

Programming Notes:

- Insert the following text as legend: “Weekly Average CFB to Week 12 Daily Pain NRS”.
- Dose (µg/kg) and Observed/LOCF/BOCF in x axis and Daily Pain NRS CFB in y axis.
- A level for CCI dosing (CCI) will only be added if Stage 4 is initiated.

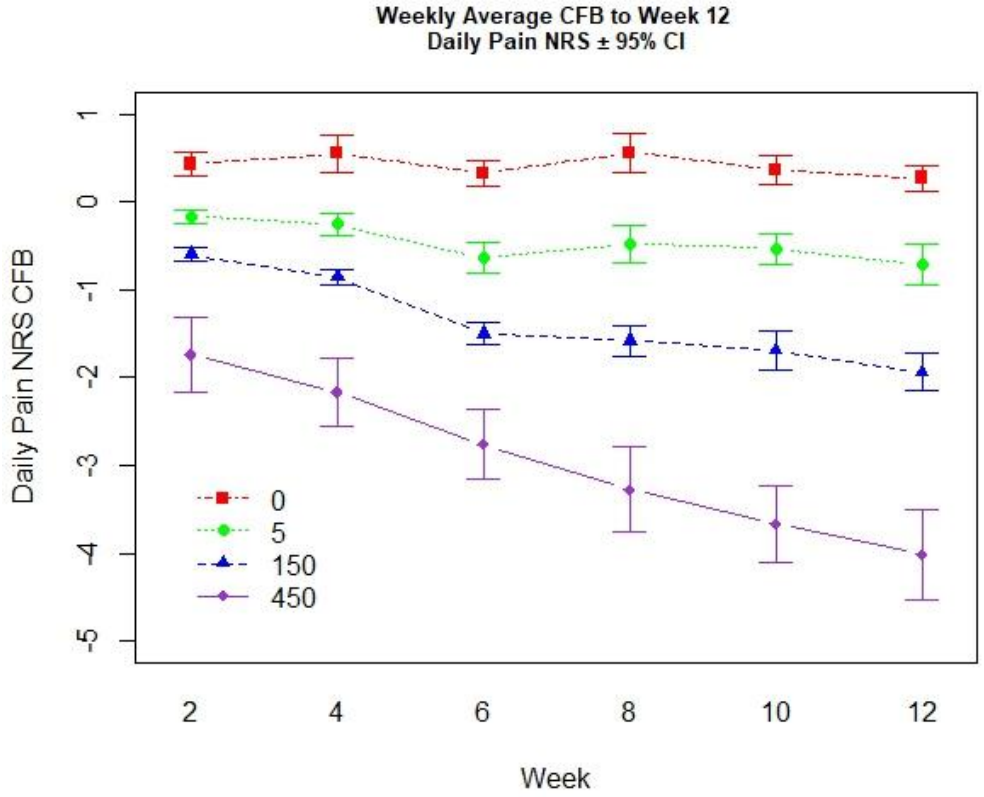
Figure 14.2.1.3
Daily Pain NRS: Boxplots at Week 12 by Treatment Group and Co-Medication Subgroup
mITT Population

CFB = Change from Baseline; DPS = Daily Pain Score; NRS = Numeric Rating Scale.
Baseline is defined as the average of the 'non-missing' DPS within the seven-day period prior to randomization i.e.,
Day -7 to Day -1, inclusive.
mITT Population = includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
Reference Listing: 16.2.6.1

Programming Notes:

- Same shell as Figure 14.2.1.2
- Insert the following text as legend: "Weekly Average CFB to Week 12 Daily Pain NRS".
- Dose (µg/kg) in x axis, Anticonvulsant/ Antidepressant/ Both/ None in right side Co-medication labels, and Daily Pain NRS CFB in y axis.
- A level for CCI dosing (between CCI) will only be added if Stage 4 is initiated.

Figure 14.2.1.4
Daily Pain NRS: MMRM LS Means (95% Confidence Interval) over 12-weeks by Treatment Group (Observed Cases)
mITT Population



CFB = Change from Baseline; CI = Confidence Interval; DPS = Daily Pain Score; LS = Least Square; MMRM = Mixed Model for Repeated Measures; NRS = Numeric Rating Scale.
Baseline is defined as the average of the 'non-missing' DPS within the seven-day period prior to randomization i.e., Day -7 to Day -1, inclusive.
mITT Population = includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
Reference Listing: 16.2.6.1

Programming Notes:

- Insert the following text as legend: "Weekly Average CFB to Week 12 Daily Pain NRS ± 95% CI".
- Week in x axis and Daily Pain NRS CFB in y axis.
- **Include a profile for each dose treatment group.**
- Include the following timepoints: Week 2, 4, 6, 8, 10, and 12.
- **Extract data for this figure from the MMRM of CFB Daily Pain NRS with Observed Cases.**
- A profile for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.3.6.1.1
Vital Sign Profiles: Mean (±SD) Systolic Blood Pressure over time
Safety Population

1H PD = 1 Hour Post-Dose; 15M PD = 15 Minutes Post-Dose; 2H PD = 2 Hours Post-Dose; 30M PD = 30 Minutes Post-Dose; 4H PD = 4 hours Post-Dose; 45M PD = 45 Minutes Post-Dose; 5M PD = 5 minutes after Infusion Completion; BASE = Baseline; D1 = Day 1; SBP = Systolic Blood Pressure; W2 = Week 2; W4 = Week 4; W6 = Week 6; W8 = Week 8; W10 = Week 10; W11 = Week 11; W12 = Week 12; W18 = Week 18.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
Reference Listing: 16.2.9.1

Programming Notes:

- Same shell as Figure 14.2.1.4
- Insert the following text as legend: “Average SBP ± Standard Deviation”.
- Study Visit in x axis and Systolic Blood Pressure (mmHg) in y axis.
- **Include a profile for Resting SBP and another for Standing SBP.**
- Include the following timepoints: Baseline, Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- Note that standing measures are not taken on Day 1, at 15, 30 and 45 minutes post-dose.
- **Make one plot for each dose treatment group, for a total of 4 plots with two profiles each.**
- A plot for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.3.6.1.2
Vital Sign Profiles: Mean (±SD) Diastolic Blood Pressure over time
Safety Population

1H PD = 1 Hour Post-Dose; 15M PD = 15 Minutes Post-Dose; 2H PD = 2 Hours Post-Dose; 30M PD = 30 Minutes Post-Dose; 4H PD = 4 hours Post-Dose; 45M PD = 45 Minutes Post-Dose; 5M PD = 5 minutes after Infusion Completion; BASE = Baseline; D1 = Day 1; DBP = Diastolic Blood Pressure; W2 = Week 2; W4 = Week 4; W6 = Week 6; W8 = Week 8; W10 = Week 10; W11 = Week 11; W12 = Week 12; W18 = Week 18.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
Reference Listing: 16.2.9.1

Programming Notes:

- Same shell as Figure 14.2.1.4
- Insert the following text as legend: “Average DBP ± Standard Deviation”.
- Study Visit in x axis and Diastolic Blood Pressure (mmHg) in y axis.
- **Include a profile for Resting DBP and another for Standing DBP.**
- Include the following timepoints: Baseline, Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- Note that standing measures are not taken on Day 1, at 15, 30 and 45 minutes post-dose.
- **Make one plot for each dose treatment group, for a total of 4 plots with two profiles each.**
- A plot for CCI dosing (CCI) will only be added if Stage 4 is initiated)

Figure 14.3.6.1.3
Vital Sign Profiles: Mean (±SD) Heart Rate over time
Safety Population

1H PD = 1 Hour Post-Dose; 15M PD = 15 Minutes Post-Dose; 2H PD = 2 Hours Post-Dose; 30M PD = 30 Minutes Post-Dose; 4H PD = 4 hours Post-Dose; 45M PD = 45 Minutes Post-Dose; 5M PD = 5 minutes after Infusion Completion; BASE = Baseline; D1 = Day 1; HR = Heart Rate; W2 = Week 2; W4 = Week 4; W6 = Week 6; W8 = Week 8; W10 = Week 10; W11 = Week 11; W12 = Week 12; W18 = Week 18.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
Reference Listing: 16.2.9.1

Programming Notes:

- Same shell as Figure 14.2.1.4
- Insert the following text as legend: “Average HR ± Standard Deviation”.
- Study Visit in x axis and Heart Rate (Beats/min) in y axis.
- **Include a profile for Resting HR and another for Standing HR.**
- Include the following timepoints: Baseline, Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- Note that standing measures are not taken on Day 1, at 15, 30 and 45 minutes post-dose.
- **Make one plot for each dose treatment group, for a total of 4 plots with two profiles each.**
- A plot for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.3.6.1.4
Vital Sign Profiles: Mean (±SD) Respiratory Rate over time
Safety Population

1H PD = 1 Hour Post-Dose; 15M PD = 15 Minutes Post-Dose; 2H PD = 2 Hours Post-Dose; 4H PD = 4 hours Post-Dose; 5M PD = 5 minutes after Infusion Completion; BASE = Baseline; D1 = Day 1; W2 = Week 2; W4 = Week 4; W6 = Week 6; W8 = Week 8; W10 = Week 10; W11 = Week 11; W12 = Week 12; W18 = Week 18.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
Reference Listing: 16.2.9.1

Programming Notes:

- Same shell as Figure 14.2.1.4
- Insert the following text as legend: “Average Respiratory Rate ± Standard Deviation”.
- Study Visit in x axis and Respiratory Rate (Breaths/min) in y axis.
- Include the following timepoints: Baseline, Day 1: 15 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- **Make one plot with 4 profiles (one for each treatment group).**
- A profile for CCI dosing (CCI) will only be added if Stage 4 is initiated.

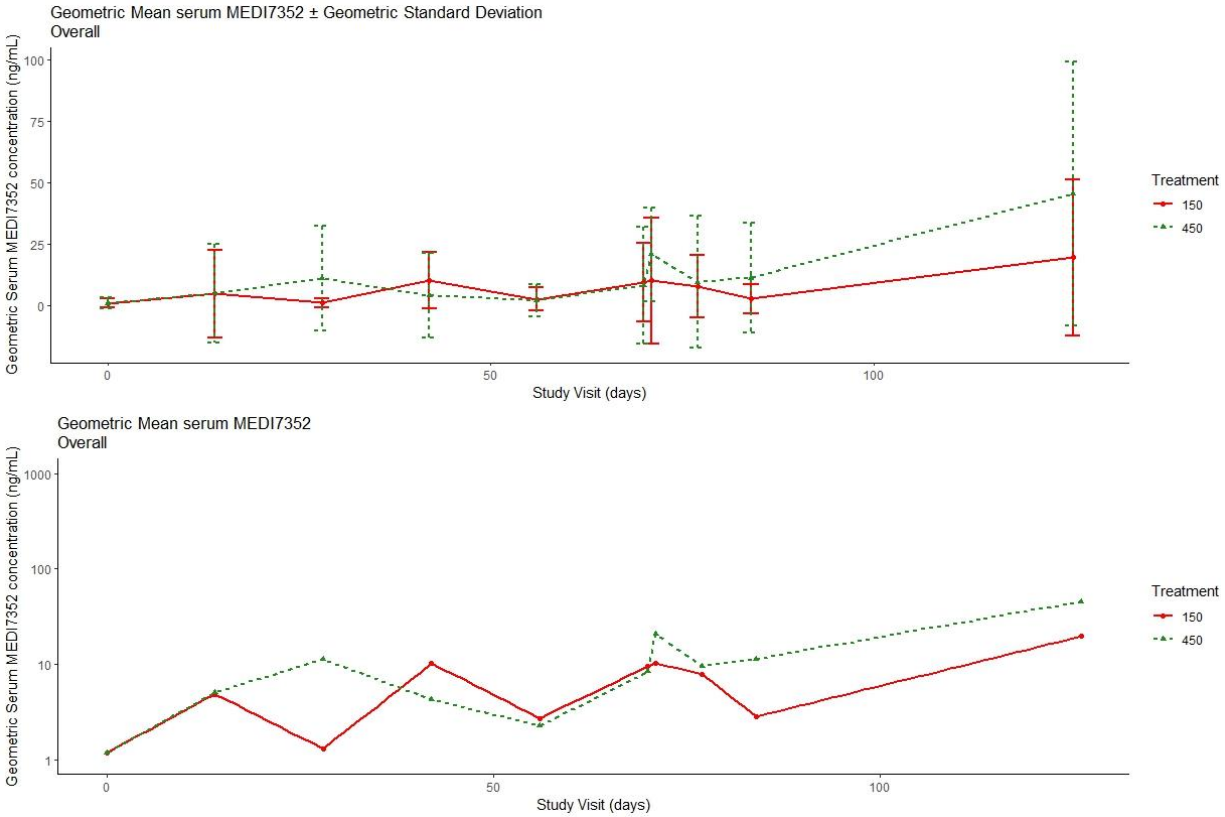
Figure 14.3.6.1.5
Vital Sign Profiles: Mean (±SD) Temperature over time
Safety Population

1H PD = 1 Hour Post-Dose; 2H PD = 2 Hours Post-Dose; 4H PD = 4 hours Post-Dose; 5M PD = 5 minutes after Infusion Completion; BASE = Baseline; D1 = Day 1; T° = Temperature; W2 = Week 2; W4 = Week 4; W6 = Week 6; W8 = Week 8; W10 = Week 10; W11 = Week 11; W12 = Week 12; W18 = Week 18.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
Reference Listing: 16.2.9.1

Programming Notes:

- Same shell as Figure 14.2.1.4
- Insert the following text as legend: "Average Body Tº ± Standard Deviation".
- Study Visit in x axis and Body Temperature (ºC) in y axis.
- Include the following timepoints: Baseline, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- **Make one plot with 4 profiles (one for each treatment group).**
- A plot for CCI dosing CCI) will only be added if Stage 4 is initiated.

Figure 14.4.1.1
Pharmacokinetics: Line Plot of Geometric Mean (with and without gSD) Serum MEDI7352 Concentrations over time
PK Population

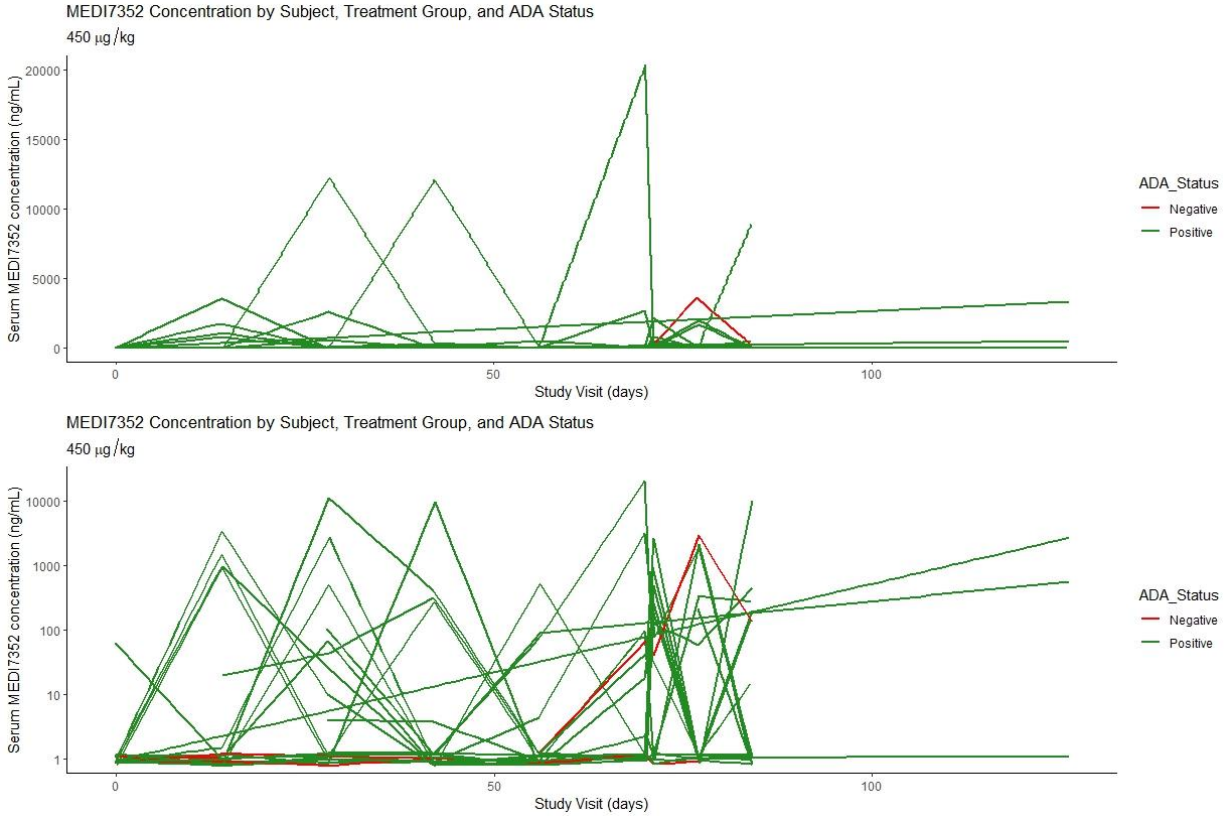


ADA = Antidrug Antibodies; gMean = Geometric Mean.
PK Population = includes all subjects for who a pharmacokinetic sample was obtained and analyzed.
ADA positive represents number of participants with at least one positive ADA result.
ADA negative represents number of participants with only negative ADA results (no positive).
Reference Listing: 16.2.10.1

Programming Notes:

- Insert the following text as upper legend: “Geometric Mean serum MEDI7352 ± Geometric Standard Deviation” for the linear plot, and “Geometric Mean serum MEDI7352” for the semi-log plot. Below legend, add legend for ADA status: “Overall”, “ADA Positive”, “ADA Negative”.
- Insert legend with different point symbols and colors for each treatment group (CCI) for the Overall plot, and a legend with different point symbols and colors for each ADA status (ADA+, ADA-) for each treatment group plot by ADA status.
- Study Visit in x axis and Serum MEDI7352 concentration (ng/mL) in y axis (**in linear and log_{10} scale, for each plot**).
- Include data from the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10: Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 10 + 14 days, Week 18.
- **Make one overall plot by treatment group, and a plot for each treatment group by ADA status for a total of 4 plots.**
- A line for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.4.1.2
Pharmacokinetics: Individual Plot of Serum MEDI7352 Concentrations over time
PK Population



ADA = Antidrug Antibodies.
PK Population = includes all subjects for who a pharmacokinetic sample was obtained and analyzed.
ADA positive represents number of participants with at least one positive ADA result.
ADA negative represents number of participants with only negative ADA results (no positive).
Reference Listing: 16.2.10.1

Programming Notes:

- Insert the following text as upper legend: "MEDI7352 Concentration by Subject, Treatment group, and ADA status". Below legend, add legend for Treatment Group: CCI
- Insert legend with different colors for each ADA status (Positive/ Negative).
- Time (days) in x axis and Serum MEDI7352 concentration (ng/mL) in y axis (**in linear and log_{10} scale, for each plot**).
- Include data from the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 10 + 14 days, Week 18.
- **Make one plot for each Treatment group (CCI), for a total of 3 plots.**
- Plots for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.4.2.1
Pharmacodynamics Line Plot of Geometric Mean (with and without gSD) Serum total NGF over time
Safety Population

ADA = Antidrug Antibodies; gMean = Geometric Mean; NGF = Nerve-Growth Factor.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
ADA positive represents number of participants with at least one positive ADA result.
ADA negative represents number of participants with only negative ADA results (no positive).
Reference Listing: 16.2.10.3

Programming Notes:

- Same shell as Figure 14.4.1.1
- Insert the following text as upper legend: “Geometric Mean total NGF ± Geometric Standard Deviation” for the linear plot, and “Geometric Mean total NGF” for the semi-log plot. Below legend, add legend for ADA status: “Overall”, “ADA Positive”, “ADA Negative”.
- Insert legend with different point symbols and colors for each treatment group (Placebo, CCI) for the Overall plot, and a legend with different point symbols and colors for each ADA status (ADA+, ADA-) for each treatment group plot by ADA status.
- Study Visit in x axis and Serum tNGF (pg/mL) in y axis (**in linear and log$_{10}$ scale for each plot**).
- Include data from the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10: Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 12, Week 18.
- **Make one overall plot by treatment group, and a plot for each treatment group by ADA status for a total of 5 plots .**
- A plot for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.4.2.2
Pharmacodynamics: Individual Plot of Serum total NGF over time
Safety Population

ADA = Antidrug Antibodies; NGF = Nerve-Growth Factor.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
ADA positive represents number of participants with at least one positive ADA result.
ADA negative represents number of participants with only negative ADA results (no positive).
Reference Listing: 16.2.10.3

Programming Notes:

- Same shell as Figure 14.4.1.2
- Insert the following text as legend: "Total NGF by Subject, Treatment group, and ADA status". Below legend, add legend for Treatment Group: CCI [redacted].
- Insert legend with different colors for each ADA status (Positive/ Negative).
- Time (days) in x axis and Serum tNGF concentration (pg/mL) in y axis (**in linear and log_{10} scale for each plot**).
- Include data from the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 12; Week 18.
- **Make one plot for each Treatment group (CCI [redacted] Placebo), for a total of 4 plots .**
- Plots for CCI [redacted] dosing (CCI [redacted]) will only be added if Stage 4 is initiated.

Sponsor:	AstraZeneca
Protocol Title	A Randomised, Double-Blind, Placebo-Controlled, Dose-Response Study of the Efficacy and Safety of MEDI7352 in Subjects with Painful Diabetic Neuropathy
Development Phase	2
Protocol Numbers:	D5680C00002
Premier Research PCNs:	MEDU177093
Document Version:	Final Version 1.1
Document Date:	31-Aug-2023

Document History

Version	Date	Author	Description
0.1	24-Mar-2023	PPD	Draft Version
0.2	21-Apr-2023	PPD	Draft Version
0.3	24-May-2023	PPD	Draft Version
1	12-Jul-2023	PPD	Final Version

Tables, Listings, and Figures Conventions

All listings, tables, and graphs will have a header showing the sponsor company name, protocol and version of delivery and a footer showing the version of SAS, the file name and path, and the source of the data (listing number).

The following reporting conventions will be adopted for the presentation of study data. These conventions will enhance the review process and help to standardize the presentation with common notations.

General Reporting Conventions

- All tables and data listings will be developed in landscape orientation.
- Specialized text styles, such as bolding, italics, borders, shading, and superscripted and subscripted text will not be used in tables, figures, and data listings unless they add significant value to the table, figure, or data listing.
- Only standard keyboard characters should be used in tables and data listings. Special characters, such as nonprintable control characters, printer-specific characters, or font specific characters, will not be used on a table, figure, or data listing.
- Adverse events with missing MedDRA coding will have their system organ class preferred term presented as "Not Coded" and the Preferred Term presented as verbatim in the tables. The "Not Coded" frequencies will be sorted to the end of the tables. This will only be applicable for any deliveries sent before database lock (e.g., for dry runs).
- Programming notes may be inserted into the shells, these notes will not appear in the final output.

Population Summary Conventions

- Population sizes may be presented for each classification factor as totals in the column header as (N=xx), where appropriate.
- All population summaries for categorical variables will include all categories that were planned and for which the participants may have had a response.
- All population summaries for continuous variables will include: n, mean, SD, median, quartiles, minimum, and maximum. Other summaries (e.g., number missing, geometric mean, 95% CIs, and coefficient of variation [CV] or % CV) may be used as appropriate. The precision of the maximum and minimum will match the maximum precision in the observed data and 2 decimals for derived data unless specifically mentioned in the corresponding shell. The mean and median will have 1 additional decimal place. The SD will have 2 additional decimal places. For derived data, minimum and maximum will be reported to 2 degrees of precision. Measures of location (mean and median) will be reported to 3 degree of precision, and measures of spread will be reported to 4 degrees of precision.

- All percentages are rounded and reported to a single decimal point (xx.x%). Exceptions are 0 and 100 that will be displayed as 0 and 100% respectively.

Planned Tables, Figures and Listings

- The table and listing numbers are place holders only and will be determined when the outputs are produced.
- In all listings a blank line will be placed between each participant. Within a data listing, if an item appears line after line (e.g., repetition of participant number), then only the first occurrence will be displayed.
- In data listings, the information for 1 participant will be kept on 1 page, if possible, rather than splitting a Subjects's information across pages.

Planned Table Descriptions and Shells

Number Title Population	Unique (U) or Repeated (R)
Table 14.1.2 - - Screening Population	U
Table 14.1.3 - Summary of Reasons for Screening Failure - Screen Failure Population	U
Table 14.1.4.1 - Demographics and Baseline Characteristics - Screening Population	U
Table 14.1.4.2 - Demographics and Baseline Characteristics - Safety Population	R
Table 14.1.4.3 - Demographics and Baseline Characteristics - mITT Population	R
Table 14.1.4.4 - Demographics and Baseline Characteristics - PK Population	R
Table 14.1.5.1 - Osteoarthritis Characteristics - Screening Population	U
Table 14.1.5.2 - Osteoarthritis Characteristics - Safety Population	R
Table 14.1.5.3 - Osteoarthritis Characteristics - mITT Population	R
Table 14.1.5.4 - Osteoarthritis Characteristics - PK Population	R
Table 14.1.6 - Medical History by System Organ Class and Preferred Term - Safety Population	U
Table 14.1.7 - Prior Medications by ATC Level 2 and Preferred Name - Safety Population	U
Table 14.1.8 - Protocol Deviations - Safety Population	U
Table 14.1.9 - Overall Study Drug Exposure - Safety Population	U
Table 14.2.1.1.1 - Daily Pain NRS: Summary Statistics (Observed Cases) - mITT Population	U
Table 14.2.1.1.2 - Daily Pain NRS: Summary Statistics (LOCF)**Error! Reference source not found.**- mITT Population	R
Table 14.2.1.1.3 - Daily Pain NRS: Summary Statistics (BOCF) - mITT Population	R
Table 14.2.1.2.1 - Daily Pain NRS: Primary MCP-Mod Analysis (LOCF) - mITT Population	U
Table 14.2.1.2.2 - Statistical Analysis of CFB to Week 12 Daily Pain NRS: Primary ANCOVA Analysis (LOCF) - mITT Population	U
Table 14.2.1.3.1 - Statistical Analysis of CFB Daily Pain NRS: MMRM Analysis. (Observed Cases) - mITT Population	U
Table 14.2.1.3.2 - Daily Pain NRS: Sensitivity of Primary MCP-Mod Analysis (BOCF) - mITT Population	R
Table 14.2.2.1 - Galer NPS: Summary Statistics (Observed Cases) - mITT Population	U
Table 14.2.2.2 - Galer NPS: MMRM Analysis (Observed Cases) - mITT Population	U
Table 14.2.3.1 - DSIS: Summary Statistics (Observed Cases) - mITT Population	U
Table 14.2.3.2 - DSIS: MMRM Analysis (Observed Cases) - mITT Population	U
Table 14.2.4.1 - SF-36: Summary Statistics (Observed Cases) - mITT Population	U
Table 14.2.4.2 - SF-36: MMRM Analysis (Observed Cases) - mITT Population	U
Table 14.2.5.1 - Rescue Medication Use: Summary Statistics - mITT Population	U

Number Title Population	Unique (U) or Repeated (R)
Table 14.2.6.1 - Daily Pain NRS Responder Analysis (≥30%): Cochran-Mantel Haenszel (Observed Cases) - mITT Population	U
Table 14.2.6.2 - Daily Pain NRS Responder Analysis (≥30%): GEE Analysis (Observed Cases) - mITT Population	U
Table 14.2.7.1 - Daily Pain NRS Responder Analysis (≥50%): Cochran-Mantel Haenszel (Observed Cases) - mITT Population	R
Table 14.2.7.2 - Daily Pain NRS Responder Analysis (≥50%): GEE Analysis (Observed Cases) - mITT Population	R
Table 14.2.8.1 - Patient Global Impression of Change: Summary Statistics - mITT Population	U
Table 14.2.8.2 - Patient Global Impression of Change: Cochran-Mantel Haenszel - mITT Population	U
CCI [redacted]	U
Table 14.3.1.1 - Summary of Overall Adverse Events - Safety Population	U
Table 14.3.1.2 - Treatment Emergent of Adverse Events by System Organ Class and Preferred Term - Safety Population	U
Table 14.3.1.3 - Treatment Emergent of Adverse Events by Severity, System Organ Class and Preferred Term - Safety Population	U
Table 14.3.1.4 - Treatment Emergent Adverse Events by Relationship to Study Medication, System Organ Class and Preferred Term - Safety Population	U
Table 14.3.1.5 - Treatment Emergent Adverse Events by ADA Status Category, System Organ Class and Preferred Term - Safety Population	U
Table 14.3.1.6 - Treatment Emergent Adverse Events Leading to Discontinuation of Study drug by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.1.7 - Non-Serious Adverse Events Occurring in More than 5% of Subjects by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.1.8 - Treatment Emergent Adverse Events Occurring in More than 5% of Subjects by Preferred Term - Safety Population	R
Table 14.3.1.9 - Treatment Emergent Adverse Events by Preferred Term - Safety Population	R
Table 14.3.2.1.1 - Serious Adverse Events by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.1.2 - Life-Threatening Serious Adverse Events by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.1.3 - Serious Adverse Events with Outcome Death by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.1.4 - Serious Adverse Events by Relationship to Study Medication, System Organ Class and Preferred Term - Safety Population	R
Table 14.3.3.1 - Listing of Serious Adverse Events - Safety Population	U
Table 14.3.3.2 - Listing of Deaths - Safety Population	U

Number Title Population	Unique (U) or Repeated (R)
Table 14.3.2.2.1 - Treatment Emergent Adverse Events Associated with Abnormal Liver by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.2.2 - Potential Joint Related Adverse Events of Special Interest by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.2.3 - Serious and/or severe Infections by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.2.4 - Anaphylactic Reactions, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of IP by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.4.1 - Descriptive Summary of Clinical Chemistry - Safety Population	U
Table 14.3.4.2 - Shift Table of Clinical Chemistry Results - Safety Population	U
Table 14.3.4.3 - Descriptive Summary of Hematology - Safety Population	R
Table 14.3.4.4 - Shift Table of Hematology Results - Safety Population	R
Table 14.3.4.5 - Descriptive Summary of Coagulation - Safety Population	R
Table 14.3.4.6 - Shift Table of Coagulation Results - Safety Population	R
Table 14.3.4.7 - Descriptive Summary of Urinalysis - Safety Population	U
Table 14.3.4.8 - Shift Table of Urinalysis Results - Safety Population	R
Table 14.3.4.9 - Maximum On-Treatment ALT and AST versus Maximum On-Treatment Total Bilirubin - Safety Population	U
Table 14.3.5.1 - Descriptive Summary of Vital Signs - Safety Population	U
Table 14.3.5.2 - Descriptive Summary of Digital ECG Data - Safety Population	U
Table 14.3.5.3 - Summary of Overall Evaluation of safety ECG Data - Safety Population	U
Table 14.3.5.4 - Covid-19 Screening - Safety Population	U
Table 14.3.5.5 - Summary of Sub-Scores for Total Neuropathy Score-Nurse - Safety Population	U
Table 14.3.5.6 - Descriptive Summary of Total Neuropathy Score-Nurse - Safety Population	U
Table 14.3.5.7 - Summary of Motor and Sensory Nerve Conduction Studies - Safety Population	U
Table 14.3.5.8 - Summary of Strength and Deep Tendon Reflexes - Safety Population	U
Table 14.3.5.9 - Summary of Local Injection Site Reactions - Safety Population	U
Table 14.3.5.10 - Summary of Hypersensitivity/Anaphylactic Reactions - Safety Population	U
Table 14.3.5.11 - Summary of Liver Diagnostic Investigations - Safety Population	U
Table 14.3.5.12 - Summary of Liver Risk Factors and Lifestyle Events - Safety Population	U
Table 14.3.5.13 - Summary of Liver Signs and Symptoms - Safety Population	U
Table 14.3.5.14 - Summary of Infection Diagnostic Investigations - Safety Population	U
Table 14.3.5.15 - Summary of Infection Risk Factors and Lifestyle Events - Safety Population	U

Number Title Population	Unique (U) or Repeated (R)
Table 14.3.5.16 - Summary of Infection Signs and Symptoms - Safety Population	U
Table 14.3.5.17 - Summary of Concomitant Medications by ATC Level 2 and Preferred Name - Safety Population	R
Table 14.3.5.18 - Summary of Concomitant Procedures - Safety Population	R
Table 14.3.5.19 - Anti-Drug Antibody Results and Titre Summary by Timepoint - Safety Population	U
Table 14.3.5.20 - Descriptive Summary of Anti-Drug Antibody Results and Titre by ADA Categories - Safety Population	U
Table 14.4.1 - Summary of Serum MEDI7352 Concentrations - PK Population	U
Table 14.4.2 - Summary of Serum total NGF Concentrations - PD Population	U

Table Change Log

Output Number	Date of Change	Change Made By (initials)	Description/Rationale

1. Demographic Data

Table 14.1.2
Subject Disposition
Screening Population

Status	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=xx)
Screening Population [1]					xx (100%)
Screen Failures					xx (xx.x %)
Enrolled Subjects					xx (xx.x %)
Re-screened Subjects					xx (xx.x %)
Randomized Subjects	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Randomized and Not Treated Subjects	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Reason for Discontinuation					
Adverse Event	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Other	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Safety Population [2]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
mITT Population [3]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Evaluable Week 12 Efficacy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Evaluable LOCF Efficacy [4]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Efficacy Evaluable	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PK Population [5]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Completed Study Treatment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Discontinued Study Treatment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reason for Discontinuation:					
Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lack of Efficacy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lost to Follow-up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Non-compliance with Study Drug	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Physician Decision	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pregnancy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Progressive Disease	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Violation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Study Terminated by Sponsor	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Technical Problems	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Withdrawal by Subject	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sponsor Decision	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Completed Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Withdrawn from the Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reason for Discontinuation:					
Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lack of Efficacy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lost to Follow-up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
...					

COVID-19 = Coronavirus disease 2019; LOCF = Last Observation Carried Forward; mITT = modified intent-to-treat; N = number of subjects per treatment group; PK = pharmacokinetic.
Note: Percentages are n/Number of subjects randomized*100 as displayed in column header N, except for the screened, enrolled and re-screened where n/Number of Screening subjects*100, and for the randomized, where n/Number of Enrolled subjects*100.
Re-screened subjects are a subset of the Screening population.
[1] The Screening Population includes all subjects who provide informed consent and provide demographic and/or baseline screening assessments.
[2] The Safety Population includes all subjects who receive at least 1 dose of double-blind study medication.
[3] The mITT Population includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
[4] Subjects in the mITT Population with LOCF applied for missing efficacy data at week 12,
[5] The PK Population includes all subjects for who a pharmacokinetic sample was obtained and analyzed.

Reference Listings: 16.2.1.1, 16.2.1.2, 16.2.1.3,

Programming Notes:

- Display only reasons for early discontinuation with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.3
Summary of Reasons for Screening Failure
Screen Failure Population

	Total (N=xx)
Number of Subjects Who Don't Meet Inclusion/Exclusion Criteria	xx (xx.x%)
IC 01: Xxxxxxxxxxx	xx (xx.x%)
IC 02: Xxxxxxxxxxx	xx (xx.x%)
…	
EC 01: Xxxxxxxxxxx	xx (xx.x%)
EC 02: Xxxxxxxxxxx	xx (xx.x%)
…	
Number of Subjects Who are Screen Failure for other Reason than Eligibility Criteria	xx (xx.x%)

EC = exclusion criteria; IC = inclusion criteria; N = number of subjects.
Note: subject can be counted in more than one criterion.
Reference Listing 16.2.1.4

Table 14.1.4.1
Demographics and Baseline Characteristics
Screening Population

Variable Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	 CCI (N=xx)	 CCI (N=xx)	Total (N=xx)
Age (years) [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Age Category					
≥18 - <65 years	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
≥65 years	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Gender					
Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ethnicity					
Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Race					
American Indian or Alaska Native	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Black or African American	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Native Hawaiian or Other Pacific Islander	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Specified	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Screening Height (cm)					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Screening Weight (kg)					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Screening BMI (kg/m²)					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Female characteristics [2]					
Surgically sterile	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Postmenopausal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Fully vaccinated for COVID-19					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

BMI = Body Mass Index; COVID-19 = Coronavirus disease 2019; n = number of subjects by treatment group with collected parameter; N = number of subjects per treatment group; SD = standard deviation.
Note: The Screening Population includes all subjects who provide informed consent and provide demographic and/or baseline screening assessments.
[1] Age was calculated as age at time of consent.
[2] Percentages are n/Number of Female subjects from Analysis Population*100
Reference Listing: 16.2.4.1

Programming Notes:

- If a variable is between 2 pages, start the variable in the second page.
- Keep all possible values for each category even if no subject.
- A column for CCI [redacted] dosing ([redacted]) will only be added if Stage 4 is initiated.

Table 14.1.4.2
Demographics and Baseline Characteristics
Safety Population

Programming Notes:

- Same shell as Table 14.1.4.1.
- Keep all possible values for each category even if no subject.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.4.3
Demographics and Baseline Characteristics
mITT Population

Programming Notes:

- Same shell as Table 14.1.4.1.
- Keep all possible values for each category even if no subject.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.4.4
Demographics and Baseline Characteristics
PK Population

Programming Notes:

- Same shell as Table 14.1.4.1.
- Keep all possible values for each category even if no subject.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.5.1
Osteoarthritis Characteristics
Screening Population

Variable Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	 CCI (N=xx)	 CCI (N=xx)	Total (N=xx)
Subjects diagnosed with Osteoarthritis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Joint(s)/Area(s) affected:					
Shoulder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Elbow	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hip	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Knee	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ankle	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Spine	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hands	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Feet	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Osteoarthritis clinically significant					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Radiologic investigations conducted [1]					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Plain radiography	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
MRI	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Joint(s)/Area(s) investigated:					
Shoulder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Elbow	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hip	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Knee	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ankle	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Spine	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Hands	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Feet	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Osteoarthritis radiologically significant					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Kellgren-Lawrence score reported					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No/Not applicable	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Radiologic Scoring System Used?					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

MRI = magnetic resonance imaging; N = number of subjects per treatment group.
[1] Subjects who reported more than one radiologic investigation within each category were only counted once.
Reference Listing: 16.2.4.3

Programming Notes:

- Display only Joint(s)/Areas(s) affected and investigated with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.5.2
Osteoarthritis Characteristics
Safety Population

Programming Notes:

- Same shell as Table 14.1.5.1.
- Display only Joint(s)/Areas(s) affected and investigated with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.5.3
Osteoarthritis Characteristics
mITT Population

Programming Notes:

- Same shell as Table 14.1.5.1.
- Display only Joint(s)/Areas(s) affected and investigated with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.5.4
Osteoarthritis Characteristics
PK Population

Programming Notes:

- Same shell as Table 14.1.5.1.
- Display only Joint(s)/Areas(s) affected and investigated with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.6
Medical History by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=xxx)	MEDI7352 CCI (N=xx)	 CCI (N=xx)	 CCI (N=xx)	Total (N=xxx)
Any Medical History	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
System Organ Class 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
…	…	…	…	…	…
System Organ Class n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)

N = number of subjects per treatment group.
Note: All medical history terms were coded using the Medical Dictionary for Regulatory Activities (MedDRA), version 26.0. At each level of summarization (system organ class or preferred term), subjects having more than one medical history term were counted only once. System organ class and preferred terms are sorted in descending order of frequency of Total column, and alphabetically if same frequency.

Reference Listing: 16.2.4.2

Programming Notes:

- SOC and PT texts should be in proper case in table.
- Sort SOC and PT (within SOC) in descending order of frequency in the Total column. Sort alphabetically in case of ties.
- Uncoded Medical History Events
  - When there are uncoded Medical History Events in the database, the events will be summarized with SOC and PT set to [Not Coded]. The [Not Coded] will be sorted at the end of the table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.7
Prior Medications by ATC Class and Preferred Name
Safety Population

ATC Class [1] Preferred Term	Placebo	MEDI7352			Total
		CCI	CCI	CCI	
	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Subjects with at Least One Prior Medication	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATC Level 2 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Name 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Name n	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATC Level 2 n	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Name 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Name n	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

ATC = Anatomical Therapeutic Class; N = number of subjects per treatment group.
[1] ATC Class is defined as ATC Level 2.
Note: Prior medications are defined as medications that started before first dose of study, whether they were stopped before first dose of study medication or not. All prior medications are coded using WHO drug dictionary version vMar2023. At each level of summarization (ATC Level 2 or Preferred Name), subjects who reported more than one prior medication were only counted once. ATC Level 2 and Preferred Term are sorted in descending order of frequency of total, and alphabetically if same frequency.
Reference Listing: 16.2.9.16

Programming Notes:

- If uncoded ATC Level or Preferred Name, please put them as [Not Coded]
- ATC and Preferred Name texts should be in proper case in table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.8
Protocol Deviations
Safety Population

	Placebo	MEDI7352			Total
		CCI	CCI	CCI	
	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Subjects With Any Important Protocol Deviation/Violation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 5	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 6	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
……..					

N = number of subjects per treatment group.
Notes: Percentages are n/Number of subjects by treatment group*100.
Subjects with one or more deviations within a type of protocol deviation were counted only once.

Reference Listing 16.2.2.1

Programming Notes:

- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

2. Exposure and Compliance

Table 14.1.9
Overall Study Drug Exposure
Safety Population

Category/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=xx)
Maximum Number of Doses Administered [1]					
1 Dose	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 Doses	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 Doses	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 Doses	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
5 Doses	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
6 Doses	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total Duration of Exposure (days) [2]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Total (cumulative) IP volume infused (mL)					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

n = number of subjects by treatment group with collected parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Subjects are counted once for each level of dose administered.
[2] Duration of exposure (days) = min(date of last dose of treatment + 14 days or date of death) – date of first dose of treatment + 1.
Reference Listing: 16.2.5.1

Programming Notes:

- Add all categories even if count is 0.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

3. Primary Efficacy Analysis

Table 14.2.1.1.1
Daily Pain NRS: Summary Statistics (Observed Cases)
mITT Population

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=XX)
Baseline [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 2					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 2 CFB					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

…

CFB = Change from Baseline; DPS = Daily Pain Score; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NRS = Numeric Rating Scale; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
Note: Data shown are weekly averages of the average daily pain scores on an 11-point (0-10) NRS and CFB for the same variable. Total N for the mITT population = 106 at Week 2 as Subject PPD has < 4 days of diary pain data on that visit, completing the following visits till Week 12.
[1] Baseline is defined as the average of the 'non-missing' DPS within the seven-day period prior to randomization i.e., Day -7 to Day -1, inclusive.

Reference Listing: 16.2.6.1

Programming Notes:

- Include all observed data (Not the LOCF) on weekly averages of the average daily pain scores for Baseline, Week 2, 4, 6, 8, 10, 12 and 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.1.1.2
Daily Pain NRS: Summary Statistics (LOCF)
mITT Population

Programming Notes:

- Same shell as Table 14.2.1.1.1.
- Include all observed and LOCF data on weekly averages of the average daily pain scores for Baseline, Week 2, 4, 6, 8, 10, and 12
- Add abbreviation in footnote: LOCF = Last Observation Carried Forward.
- Add the following note in footnote: "LOCF applied to Week 12 only".
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.1.1.3
Daily Pain NRS: Summary Statistics (BOCF)
mITT Population

Programming Notes:

- Same shell as Table 14.2.1.1.1.
- Include all observed and BOCF data on weekly averages of the average daily pain scores for Baseline, Week 2, 4, 6, 8, 10, and 12
- Add abbreviation in footnote: BOCF = Baseline Observation Carried Forward.
- Add the following note in footnote: "BOCF applied to Week 12 only".
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.1.2.1
Daily Pain NRS: Primary MCP-Mod Analysis (LOCF)
mITT Population

'MCP' step

Model Contrast [1]	t value	1-sided adjusted P-value [2]
Hyperbolic E_{max}		
ED50 = 7.5	xx.xx	0.xxxx
ED50 = 15	xx.xx	0.xxxx
ED50 = 30	xx.xx	0.xxxx
ED50 = 60	xx.xx	0.xxxx
ED50 = 750	xx.xx	0.xxxx
Exponential		
δ = 100	xx.xx	0.xxxx
δ = 200	xx.xx	0.xxxx
Overall MCP test	xx.xx	0.xxxx

CFB = Change from Baseline; LOCF = Last Observation Carried Forward; MCP = Multiple Comparisons; Procedure; NRS = Numeric rating scale.
[1] ED50 = Effective Dose giving half of the asymptotic maximum effect.
[2] Multiplicity Adjusted P-value.

'MOD' step [3]
Selected Model xxxxxxxxxx

Parameter	Estimate	95% CI of Estimate [6]
ED50	xx.x	[x.xx to x.xx]
ED90 [4]	xx.x	[x.xx to x.xx]
Asymptotic ED90 [5]	xx.x	[x.xx to x.xx]
Dose to achieve target (-1.25) effect	xx.x	[x.xx to x.xx]
Treatment effect at dose =CCI	xx.x	[x.xx to x.xx]
Treatment effect at dose =CCI	xx.x	[x.xx to x.xx]
Treatment effect at dose =CCI	xx.x	[x.xx to x.xx]
Treatment effect at dose =CCI	xx.x	[x.xx to x.xx]

CI: Confidence Interval; LOCF = Last Observation Carried Forward; MCP = Multiple Comparisons; Procedure; MOD = Modelling; NRS = Numeric rating scale.
[3] Results from the 'MOD' step will only be available in case any of the MCP tests is statistically significant.
[4] ED90 = Effective Dose giving 90% of the effect of the maximum dose studied.
[5] Asymptotic ED90 = Effective Dose giving 90% of the asymptotic maximum effect.
[6] 2.5% and 97.5% quantiles taken from 100000 samples from the multivariate normal distribution for model fitted estimates and its covariance matrix.
Reference Listing: 16.2.6.1

Programming Notes:

- The 'MOD' step will only be performed if stage 4 is initiated, otherwise there would be insufficient dosing data to fit the non-linear models.

Table 14.2.1.2.2
Statistical Analysis of CFB to Week 12 Daily Pain NRS: Primary ANCOVA Analysis (LOCF)
mITT Population

Model parameter estimates

Parameter	Estimate	t value	Degrees of freedom	Standard Error	2-sided 95% unadjusted CL	Asymmetric CL [1]	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx	[x.xx to x.xx]		
Co-Medication Type			3				0.xxxx
Baseline pain NRS	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]		0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Model residual standard deviation	xx.xx						

ANCOVA = analysis of covariance; CFB = Change from Baseline;
CL = Confidence limits; LOCF = Last Observation Carried Forward; NRS = Numeric rating scale.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: ANCOVA by dose using NRS baseline value and co-medication as covariates, with CFB to Week 12 (LOCF) as dependent variable.

Least Square Means

Treatment	Number of Subjects	LS mean [3]	95% CI of LS mean
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
Placebo	xx	x.xx	[x.xx to x.xx]

CI = Confidence interval; LOCF = Last Observation Carried Forward; LS = least square; NRS = Numeric rating scale.
[3] The LS mean is a model estimate using fitted group parameter and the baseline weekly average pain NRS parameter evaluated at the grand mean over each group.
Reference Listing: 16.2.6.1

Programming Notes:

- Concomitant co-medication Type indicated for Painful Diabetic Neuropathy: either anticonvulsant class (pregabalin or gabapentin) or antidepressant class (duloxetine, venlafaxine, or amitriptyline).
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.1.3.1
Statistical Analysis of CFB Daily Pain NRS: MMRM Analysis. (Observed Cases)
mITT Population

Model parameter estimates

Parameter	Estimate	t value	Degrees of freedom	Standard Error	2-sided 95% unadjusted CL	Asymmetric CL [1]	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx			
Co-medication type			3				0.xxxx
Week			6				0.xxxx
Treatment			3				0.xxxx
Treatment*Week			18				0.xxxx
Baseline pain NRS	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]		0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 1 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
~~Model residual standard deviation~~	~~xx.xx~~						

CFB = Change from Baseline; CL = Confidence limits; MMRM = Mixed Model for Repeated Measures; NRS = Numeric rating scale.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: MMRM using Time, Treatment, Treatment*Time, NRS baseline value, and Co-medication type as covariates, with CFB as dependent variable.
Note: model was fitted using an unstructured covariance structure. Estimates for difference vs Placebo at Week 12.

Least Square Means: Week xxxxx

Treatment	Number of patients	LS mean [3]	95% CI of LS mean
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
Placebo	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]

CI = Confidence interval; LS = least square; NRS = Numeric rating scale.
[3] The LS mean is a model estimate using fitted group parameter and the baseline weekly average pain NRS parameter evaluated at the grand mean over each group.
Reference Listing: 16.2.6.1

Programming Notes:

- Include LSmeans and difference in LSmean with Placebo in repeated tables for the Treatment*Week interaction.
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.1.3.2
Daily Pain NRS: Sensitivity of Primary MCP-Mod Analysis (BOCF)
mITT Population

Programming Notes:

- Same shell as Table 14.2.1.2.1, substituting "LOCF = Last Observation Carried Forward" by "BOCF = Baseline Observation Carried Forward".
- The MCP-MOD approach will only be performed if stage 4 is initiated, otherwise there would be insufficient dosing data to fit the non-linear models.

4. Secondary Efficacy Analysis

Table 14.2.2.1
Galer NPS: Summary Statistics (Observed Cases)
mITT Population

Parameter: xxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=xx)
Baseline [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 4					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 4 CFB					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

...

For Pain Duration Frequency

Baseline [1]					
I feel a background pain all of the time and occasional flare-ups	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
I feel a single type of pain all the time	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
feel a single type of pain only sometimes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 4					

CFB = Change from Baseline; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NPS = Neuropathic Pain Scale; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
Note: Data shown are Pain Intensity, Unpleasantness, and Descriptor scores on an 11-point (0-10) NRS, and Pain Duration/Frequency on a 3-point NRS (1-3), plus CFB for the same variables.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Reference Listing: 16.2.6.2

Programming Notes:

- Include all observed data on Galer NPS scores for Baseline, Week 4, 8, 12, and 18.
- Repeat for the Parameters: Pain intensity, Pain Unpleasantness, Pain Sharpness, Pain Hotness, Pain Dullness, Pain Coldness, Pain Sensitivity, Pain Itching, Deep Pain Intensity, Surface Pain Intensity (All in an 11-point NRS), Galer NPS Total Score (ranging from 0 to 100), and Pain Duration/Frequency (in a 3-point NRS).
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.2.2
Galer NPS: MMRM Analysis (Observed Cases)
mITT Population

Model parameter estimates

Parameter	Estimate	t value	Degrees of freedom	Standard Error	2-sided 95% unadjusted CL	Asymmetric CL [1]	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx			
Co-Medication type			3				0.xxxx
Week			3				0.xxxx
Treatment			3				0.xxxx
Treatment*Week			9				0.xxxx
Baseline NPS	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]		0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
~~Model residual standard deviation~~	~~xx.xx~~						

CFB = Change from Baseline; CL = Confidence limits; MMRM: Mixed Model for Repeated Measures; NPS = Neuropathic Pain Scale.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: MMRM using Time, Treatment, Treatment*Time, NPS baseline value, and Co-medication type as covariates, with CFB as dependent variable.
Note: model was fitted using an unstructured covariance structure.

Least Square Means: Week: xxxx

Treatment	Number of patients	LS mean [3]	95% CI of LS mean
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
Placebo	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo	xx	x.xx	[x.xx to x.xx]

CI = Confidence interval; LS = least square; NPS = Neuropathic Pain Scale.
[3] The LS mean is a model estimate using fitted group parameter and the baseline NPS parameter evaluated at the grand mean over each group.
Reference Listing: 16.2.6.2

Programming Notes:

- Include LSmeans and difference in LSmean with Placebo in repeated tables for the Treatment*Week interaction.
- Include all observed data on Galer NPS scores for Baseline, Week 4, 8, 12, and 18.
- Analysis is done for Galer NPS Total Score.
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.3.1
DSIS: Summary Statistics (Observed Cases)
mITT Population

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=XX)
Baseline [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 4					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 4 CFB					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
…					

CFB = Change from Baseline; DSIS = Daily Sleep Interference; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
Note: Data shown are weekly averages of the average daily sleep interference scores on an 11-point (0-10) NRS and CFB for the same variable.
[1] Baseline is defined as the average of the 'non-missing' DSIS within the seven-day period prior to randomization **i.e.,** Day -7 to Day -1, inclusive.

Reference Listing: 16.2.6.3

Programming Notes:

- Include all observed data on weekly averages of the average daily Sleep Interference score for Baseline, Week 4, 8, 12, and 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.3.2
DSIS: MMRM Analysis (Observed Cases)
mITT Population

Model parameter estimates

Parameter	Estimate	t value	Degrees of freedom	Standard Error	2-sided 95% unadjusted CL	Asymmetric CL [1]	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx			
Co-medication type			3				0.xxxx
Week			3				0.xxxx
Treatment			3				0.xxxx
Treatment*Week			9				0.xxxx
Baseline DSIS	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]		0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
~~Model residual standard deviation~~	~~xx.xx~~						

CFB = Change from Baseline; CL = Confidence limits; MMRM: Mixed Model for Repeated Measures; DSIS = Daily Sleep Interference.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: MMRM using Time, Treatment, Treatment*Time, DSIS baseline value, and Co-medication type as covariates, with CFB as dependent variable.
Note: model was fitted using an unstructured covariance structure.

Least Square Means: Week xxxx

Treatment	Number of patients	LS mean [3]	95% CI of LS mean
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
Placebo	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo	xx	x.xx	[x.xx to x.xx]

CI = Confidence interval; LS = least square.
[3] The LS mean is a model estimate using fitted group parameter and the baseline weekly average DSIS parameter evaluated at the grand mean over each group.
Reference Listing: 16.2.6.3

Programming Notes:

- Include LS means and difference in LS mean with Placebo in repeated tables for the Treatment*Week interaction.
- Include all observed data on weekly average DSIS for Baseline, Week 4, 8, 12, and 18.
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.4.1
SF-36: Summary Statistics (Observed Cases)
mITT Population

Parameter: xxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=XX)
Baseline [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 12					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 12 CFB					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

...

When parameter is "Change in general Health"

Baseline [1]					
Much better now than one year ago	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Somewhat better now than one year ago	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
About the same as one year ago	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Somewhat worse now than one year ago	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Much worse now than one year ago	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 12					

CFB = Change from Baseline; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NRS = numeric rating scale; SD = standard deviation; SF-36 = 36-Item Short-Form Health Survey; Q1 = first quartile; Q3 = third quartile.
Note: Data shown are derived SF-36 scores and Change in General Health on a 5-point NRS (1-5), plus CFB for the same variables.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Reference Listing: 16.2.6.4

Programming Notes:

- Include all observed data on SF-36 scores for Baseline and Week 12.
- Repeat for the Parameters: Physical functioning, Role limitations due to physical health, Role limitations due to emotional problems, Vitality (Energy/fatigue), Emotional well-being, Social functioning, Pain and General Health (from 0 to 100), Physical Health Summary, Mental Health Summary, and Change in general Health (in a 5-point NRS).
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.4.2
SF-36: MMRM Analysis (Observed Cases)
mITT Population

Model parameter estimates: xxxxxxxx

Parameter	Estimate	t value	Degrees of freedom	Standard Error	2-sided 95% unadjusted CL	Asymmetric CL [1]	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx			
Co-medication type			3				0.xxxx
~~Week~~			~~1~~				~~0.xxxx~~
Treatment			3				0.xxxx
~~Treatment*Week~~			~~3~~				~~0.xxxx~~
Baseline SF-36	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]		0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Model residual standard deviation	xx.xx						

CFB = Change from Baseline; CL = Confidence limits; MMRM: Mixed Model for Repeated Measures; SF-36 = 36-Item Short-Form Health Survey.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: MMRM using Treatment, SF-36 baseline value, and Co-medication type as covariates, with CFB as dependent variable.
Note: model was fitted using an unstructured covariance structure.

Least Square Means: xxxxxxxx

Treatment	Number of patients	LS mean [3]	95% CI of LS mean
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
Placebo	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]

CI = Confidence interval; LS = least square.
[3] The LS mean is a model estimate using fitted group parameter and the baseline SF-36 parameter evaluated at the grand mean over each group.
Reference Listing: 16.2.6.4

Programming Notes:

- Include LSmeans and difference in LSmean with Placebo..
- Include all observed data on SF-36 scores for Baseline and Week 12.
- Repeat for the Parameters: Physical Health Summary, and Mental Health Summary Add parameter name after 'Model parameter estimates:' and after 'Least Square Means:'
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.5.1
Rescue Medication Use: Summary Statistics
mITT Population

Variable	Placebo	MEDI7352			Total
		CCI	CCI	CCI	
Statistic or Category	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Number of subjects taking any rescue medication	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number of subjects taking any permitted rescue medication	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total number of days rescue medication was used [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Cumulative consumption of Paracetamol Rescue Medication (mg) [2]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Paracetamol Rescue Medication Average Daily Dose (mg) [3]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Number of subjects taking any prohibited rescue medication	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Each day on which permitted rescue medication was used at least once is counted.
[2] Calculated as the total dose of paracetamol rescue medication (mg).
[3] Calculated as: cumulative consumption of paracetamol rescue medication (mg) /total number of days rescue medication was used.

Reference Listing: 16.2.6.5

Programming Notes:

- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.
- Refer to

Table 14.2.6.1
Daily Pain NRS Responder Analysis (≥30%): Cochran-Mantel Haenszel (Observed Cases)
mITT Population

Cochran-Mantel-Haenszel Test

Treatment/ Category	Number of Subjects (%)	Risk Difference [1]	95% CI of Risk Difference	2-sided P-value [2]
Placebo (n = xx)				
>=30% decrease from Baseline	xx (xx.x%)			
MEDI7352 CCI (n = xx)				
>=30% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI (n = xx)				
>=30% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI (n = xx)				
>=30% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx

CI = confidence interval; CMH = Cochran-Mantel-Haenszel; NRS = numeric rating scale.
[1] Common effect for the strata (co-medication type*median Baseline Pain NRS) specific risk difference, representing common difference in probability across strata of MEDI7352 dose - Placebo.
[2] P-value < 0.05 indicates a significant association between number of subjects with >=30% decrease from Baseline and treatment across strata.
Note: a separate CMH test is performed for each dose versus placebo at Week 12.
Reference Listing: 16.2.6.1

Programming notes:

- Include all observed data for Week 12.

Table 14.2.6.2
Daily Pain NRS Responder Analysis (≥30%): GEE Analysis (Observed Cases)
mITT Population

Model parameter estimates

Parameter	Estimate	Z value	Degrees of freedom	Standard Error	2-sided 95% CL	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx		
Co-medication type			3			0.xxxx
Week			3			0.xxxx
Treatment			3			0.xxxx
Treatment*Week			9			0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	0.xxxx
Dispersion	xx.xx					

CL = Confidence limits; GEE: Generalized Estimation Equations; NRS = Numeric rating scale.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: GEE using Time, Treatment, Treatment*Time and Co-medication type as covariates, with dependent binary variable indicating whether weekly average pain NRS has >=30% decrease from Baseline.
Note: model was fitted using a first-order autoregressive covariance structure. Estimates for MEDI7352 dose vs placebo and for 2-sided 95% CL displayed in odds ratio scale.

Reference Listing: 16.2.6.1

Programming notes:

- Include all observed data for Week 4, 8, 12, and 18.
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.7.1
Daily Pain NRS Responder Analysis (≥50%): Cochran-Mantel Haenszel (Observed Cases)

mITT Population

Cochran-Mantel-Haenszel Test

Treatment/ Category	Number of Subjects (%)	Risk Difference [1]	95% CI of Risk Difference	2-sided P-value [2]
Placebo (n = xx)				
>=50% decrease from Baseline	xx (xx.x%)			
MEDI7352 CCI (n = xx)				
>=50% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI (n = xx)				
>=50% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI (n = xx)				
>=50% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx

CI = confidence interval; CMH = Cochran-Mantel-Haenszel; NRS = numeric rating scale.
[1] Common effect for the strata (co-medication type*median Baseline Pain NRS) specific risk difference, representing common difference in probability across strata of MEDI7352 dose - Placebo.
[2] P-value < 0.05 indicates a significant association between number of subjects with >=50% decrease from Baseline and treatment across strata.
Note: a separate CMH test is performed for each dose versus placebo at Week 12.
Reference Listing: 16.2.6.1

Programming notes:

- Include all observed data for Week 12.

Table 14.2.7.2
Daily Pain NRS Responder Analysis (≥50%): GEE Analysis (Observed Cases)
mITT Population

Programming notes:

- Same shell as Table 14.2.6.2. Change footnote in [2] as: "p-value is derived from the following model: GEE using Time, Treatment, Treatment*Time and Co-medication type as covariates, with dependent binary variable indicating whether weekly average pain NRS has >=50% decrease from Baseline. Note: model was fitted using an unstructured covariance structure, with 'MEDI7352CCI ' and 'MEDI7352CCI treatment groups, together with co-medication categories (both types at the same time and none) dropped from the analysis to make the generalized Hessian matrix positive definite. Estimates for MEDI7352 dose vs placebo and for 2-sided 95% CL displayed in odds ratio scale.".
- Include all observed data for Week 4, 8, 12, and 18.
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.8.1
Patient Global Impression of Change: Summary Statistics
mITT Population

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=XX)
Week 4					
Number of PGIC Responders	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Very Much Improved	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Much Improved	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Minimally Improved	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No change	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Minimally Worse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Much Worse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Very Much Worse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 8					
…					

N = number of subjects per treatment group; PGIC = Patient Global Impression of Change.
Note: Percentages for Number of subjects in the different improvement categories relative to baseline are n/Number of Subjects by treatment group at each visit *100.

Reference Listing: 16.2.6.6

Programming notes:

- Include all observed data on PGIC scores for Week 4, 8, 12 and 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.8.2
Patient Global Impression of Change: Cochran-Mantel Haenszel
mITT Population

Cochran-Mantel-Haenszel Test: MEDI7352 xxx µg/kg vs Placebo

Visit/ Category	Number of Patients (%)	Risk Difference [1]	95% CI of Risk Difference	2-sided P-value [2]
Placebo, Week 4 (n = xx)				
Improved relative to Baseline	xx (xx.x%)			
MEDI7352 xxx µg/kg, Week 4 (n = xx)				
Improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Placebo, Week 4 (n = xx)				
Improved relative to Baseline	xx (xx.x%)			
MEDI7352 xxx µg/kg, Week 8 (n = xx)				
Improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Placebo, Week 12 (n = xx)				
Improved relative to Baseline	xx (xx.x%)			
MEDI7352 xxx µg/kg, Week 4 (n = xx)				
Improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx

Placebo, Week 18 (n = xx)				
Improved relative to Baseline	xx (xx.x%)			
MEDI7352 xxx µg/kg, Week 4 (n = xx)				
Improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx

CI = confidence interval; CMH = Cochran-Mantel-Haenszel; NRS = numeric rating scale.
[1] Common effect for the strata (co-medication type*median Baseline Pain NRS) specific risk difference, representing common difference in probability across strata of MEDI7352 dose - Placebo.
[2] P-value < 0.05 indicates a significant association between improvement relative to Baseline and treatment across strata.
Note: median Baseline Pain NRS was calculated from subjects having valid NRS data on at least one of the above four post-baseline visits. Note: a separate CMH test is performed for each dose versus placebo.
Reference Listing: 16.2.6.6

Programming Notes:

- Include all observed data on PGIC scores for Week 4, 8, 12 and 18.

5. Exploratory Efficacy Analyses

CCI

[redacted]

CCI

[redacted]

6. Safety and Tolerability

6.1. Displays of Adverse Events

Table 14.3.1.1
Summary of Overall Adverse Events
Safety Population

Category	Placebo (N=xx)	MEDI7352 CCI [redacted] (N=xx)	MEDI7352 CCI [redacted] (N=xx)	MEDI7352 CCI [redacted] (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Subjects with any AE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any TEAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any SAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any SAE possibly related to IP [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any TEAE leading to Discontinuation of IP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any TEAE related to IP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Mild related to IP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Moderate related to IP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Severe related to IP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any SAE leading to Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

AE = adverse event; IP = Investigational product, N = number of subjects per treatment group; SAE = serious adverse event; TEAE = treatment emergent adverse event.
[1] Possibly related is defined as with reasonable possibility that the AE was caused by the IP, as assessed by investigator.
Note: Subjects who reported more than one adverse event within each category were only counted once. A TEAE is defined as an adverse event with an onset at the time of or following the start of treatment with IP. For TEAEs categorized by severity, subjects were counted at the maximum severity.
Reference Listing: 16.2.7.1, 16.2.7.2, 16.2.7.3, 16.2.7.4

Programming Notes:

- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class	Placebo	MEDI7352				Total
		CCI	CCI	CCI	All MEDI7352	
	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Preferred Term	n (n/N * 100) m	n (n/N * 100) m	n (n/N * 100) m	n (n/N * 100) m	n (n/N * 100) m	n (n/N * 100) m
Subjects with at Least One TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx

AE = adverse event; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects within each SOC/PT category; N = number of subjects per treatment group; IP = investigational product; PT = Preferred Term; SOC = System Organ Class; TEAE = treatment-emergent adverse event.
Note: Results are n (n/N * 100) m is number of events.
A TEAE is defined as AE with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0. Subjects are counted once for each SOC and once for each PT.
AEs are displayed by descending frequency of SOC, then descending frequency of PT within SOC, based on 'All MEDI7352' column. Table is sorted by international order for SOC of same frequency, and alphabetically for PT of same frequency.
Reference Listing: 16.2.7.1

Programming Notes:

- SOC and PT texts should be in proper case in table.
- In case a term is not coded (e.g. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]", and sorted at the end of the table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.3
Treatment Emergent Adverse Events by Severity, System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term Severity	Placebo	MEDI7352				Total
		CCI	CCI	CCI	All MEDI7352	
	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Subjects with at Least One TEAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

AE = adverse event; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects within each SOC/PT/Severity category; N = number of subjects per treatment group; PT = Preferred Term; SOC = System Organ Class; TEAE = treatment-emergent adverse event.
Note: Results are n (n/N * 100).
A TEAE is defined as an AE with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0. Subjects are counted once for each SOC and once for each PT at the maximum severity.
AEs are displayed by descending frequency of SOC, then descending frequency of PT within SOC, based on 'All MEDI7352' column. Table is sorted by international order for SOC of same frequency, and alphabetically for PT of same frequency.
Reference Listing 16.2.7.1

Programming Notes:

- SOC and PT texts should be in proper case in table.
- Present only severity categories with at least one subject.
- In case a term is not coded (e.g. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]", and sorted at the end of the table. SOC.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.4
Treatment Emergent Adverse Events by Relationship to Study Medication, System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term Relatedness	Placebo	MEDI7352				Total
		CCI	CCI	CCI	All MEDI7352	
	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Subjects with at Least One TEAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

…

AE = adverse event; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects within each SOC/PT/Relatedness category; N = number of subjects per treatment group; PT = Preferred Term; SOC = System Organ Class; TEAE = treatment-emergent adverse event.
[1] Related is defined as reasonable possibility that the AE was caused by investigational product, as assessed by the investigator. If investigator's assessment is missing the event is judged as related.
Note: Results are n (n/N *100).
A TEAE is defined as an AE with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0. Subjects are counted once for each SOC and once for each PT for the most related AE.
AEs are displayed by descending frequency of SOC, then descending frequency of PT within SOC, based on 'All MEDI7352' column. Table is sorted by international order for SOC of same frequency, and alphabetically for PT of same frequency.
Reference Listing 16.2.7.1

Programming Notes:

- SOC and PT texts should be in proper case in table.
- Present only severity categories with at least one subject.
- In case a term is not coded (e.g. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]", and sorted at the end of the table. SOC.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.5
Treatment Emergent Adverse Events by ADA Status Category, System Organ Class and Preferred Term
Safety Population

Treatment: xxxxxxx

System Organ Class Preferred Term	ADA Negative (N=xx) n (n/N * 100) m	ADA Positive (N=xx) n (n/N * 100) m	TE-ADA + (N=xx) n (n/N * 100) m	Non-TE-ADA + (N=xx) n (n/N * 100) m	TE Persistently ADA + (N=xx) n (n/N * 100) m	TE Transiently ADA + (N=xx) n (n/N * 100) m	Post-Baseline and Baseline Positive (N=xx) n (n/N * 100) m	Only Baseline Positive (N=xx) n (n/N * 100) m
Subjects with at Least One TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx

AE = adverse event; ADA = Anti-Drug Antibodies; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects within each SOC/PT category; N = number of subjects per ADA status category; PT = Preferred Term; SOC = System Organ Class; TE-ADA + = Treatment emergent ADA positive; TEAE = treatment-emergent adverse event.
ADA categories are defined in the Statistical Analysis Plan.
Note: Results are n (n/N *100) m is number of events.
A TEAE is defined as an AE with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0. Subjects are counted once for each SOC and once for each PT.
Table is sorted by international order for SOC, and alphabetically for PT.
Reference Listing: 16.2.7.1

Programming Notes:

- SOC and PT texts should be in proper case in table.
- Repeat for Placebo, CCI and Overall.
- In case a term is not coded (e.g. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]", and sorted at the end of the table. SOC.
- A table for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.6
Treatment Emergent Adverse Events Leading to Discontinuation of Study Drug by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at Least One TEAE leading to IP discontinuation".
- Update Reference Listing to 16.2.7.2.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.7
Non-Serious Adverse Events Occurring in More than 5% of Subjects by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at Least One Non-Serious TEAEAE".
- Update footnote adding: "The 5% threshold for an AE to be displayed is taken from the Total column."
- Update Reference Listing to 16.2.7.1.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.8
Treatment Emergent Adverse Events Occurring in More than 5% of Subjects by Preferred Term
Safety Population

Preferred Term	Placebo (N=xx) n (n/N * 100) m	MEDI7352 CCI (N=xx) n (n/N * 100) m	MEDI7352 CCI (N=xx) n (n/N * 100) m	MEDI7352 CCI (N=xx) n (n/N * 100) m	MEDI7352 All MEDI7352 (N=xx) n (n/N * 100) m	Total (N=xx) n (n/N * 100) m
Subjects with at Least One TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
…						

AE = adverse event; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects within each PT category; N = number of subjects per treatment group; PT = Preferred Term; TEAE = treatment-emergent adverse event.
Note: Results are n (n/Number of subjects in the Safety population within each PT*100) m is number of events.
A TEAE is defined as AE with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0. Subjects are counted once for each PT.
AEs are displayed by descending frequency of PT based on 'All MEDI7352' column, and alphabetically for PT of same frequency.
The 5% threshold for a TEAE to be displayed is taken from the Total column.
Reference Listing: 16.2.7.1

Programming Notes:

- PT texts should be in proper case in table.
- In case a term is not coded (e.g., in a dry run) it will be labelled as "Not Coded [PT]" and sorted at the end of the table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.9
Treatment Emergent Adverse Events by Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.8.
- Display all TEAEs, not only the most common.
- PT texts should be in proper case in table.
- In case a term is not coded (e.g., in a dry run) it will be labelled as Not Coded [PT]", and sorted at the end of the table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

6.2. Summary of Deaths and Other Serious Adverse Events

Table 14.3.2.1.1
Serious Adverse Events by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Number of Subjects with at Least One Treatment Emergent SAE", add "SAE = Serious Adverse Event" to abbreviations.
- Change footnote for "Reference Table 14.3.3.1".
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.2.1.2
Life-Threatening Serious Adverse Events by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Number of Subjects with at Least One Life-Threatening SAE", add "SAE = Serious Adverse Event" to abbreviations.
- Add "Note: Life-threatening SAEs as judged by the investigator".
- Change footnote for "Reference Table 14.3.3.1".
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated

Table 14.3.2.1.3
Serious Adverse Events with Outcome Death by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Number of Subjects with at Least One SAE with Outcome Death", add "SAE = Serious Adverse Event" to abbreviations.
- Change footnote for "Reference Table 14.3.3.2".
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.2.1.4
Serious Adverse Events by Relationship to Study Medication, System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.4. Change first row to be "Number of subjects with at Least One Treatment Emergent SAE", add "SAE = Serious Adverse Event" to abbreviations.
- Change footnote for "Reference Table 14.3.3.1".
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.3.1
Listing of Serious Adverse Events
Safety Population

Subject ID/ Treatment Arm	AE ID Number	System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date/Time (Study Day)/ End Date/Time (Study Day)	Severity/ Relationship [1]	Outcome/ Action Taken with IP/ Therapy taken for this AE?	SAE Leading to Study DC?	TEAE?	Serious? / Serious Criteria
XXXXX/ XXXX	X	XXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXXXXX/ Yes	No	No	XX
XXXXX/ XXXX	X	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMONYYYY/HH:MM (X)	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXXXXX/ No	Yes	XX	XX / XXX
XXXXX/ XXXX	X	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXX	DDMONYYYY/HH:MM (X)/ Ongoing	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXXXXX/No	No	XX	XX / XXX

DC = discontinuation; ID = identification; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; SAE = serious adverse event; TEAE = treatment emergent adverse event.
[1] Reasonable possibility AE caused by IP as assessed by the investigator.
Note: Study Day = date of interest – date of first infusion. A TEAE is defined as an adverse event with an onset at the time of or following the start of treatment with IP.
SAEs were coded using MedDRA version 26.0

Programming Notes:

- If time missing, display "- -:- -".
- AE ID number represents Record position within Subject.
- If no events meet the criteria for display (i.e, no AEs occur in the study), present "No events are reported.".
- SOC & PT text should be in proper case in table.
- Sort by Treatment ID/ Subject ID / Start Date / End Date (alphabetically for SOC if same date for two events).
- In case a term is not coded (e.g.. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]". SOC and PT abbreviations should be added in this case in footnote.

Table 14.3.3.2
Listing of Deaths
Safety Population

Subject ID/ Treatment Arm	AE ID Number	System Organ Class/ Preferred Term/ Verbatim Term	Start Date/Time (Study Day)/ End Date/Time (Study Day)	Severity/ Relationship	Outcome/ Action Taken/ Therapy?	AE Leading to IP DC?	TEAE?	Serious? / Serious Criteria
XXXXX/ XXXX	X	XXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXXXX/ Yes	No	No	XX
XXXXX/ XXXX	X	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXXXX/No	Yes	XX	XX / XXX
XXXXX/ XXXX	X	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ Ongoing	XXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXX/ No	No	XX	XX / XXX

DC = discontinuation; ID = identification; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; TEAE = treatment emergent adverse event.
Note: Study Day = date of interest – date of first infusion. A TEAE is defined as an adverse event with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0

Programming Notes:

- If time missing, display "- -:- -".
- AE ID number represents Record position within Subject.
- If no events meet the criteria for display (i.e, no Aes occur in the study), present "No events are reported.".
- SOC & PT text should be in proper case in table.
- Sort by Treatment Arm/ Subject ID / Start Date / End Date (alphabetically for SOC if same date for two events).
- In case a term is not coded (e.g., in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]". SOC and PT abbreviations should be added in this case in footnote.

6.3. Displays of Significant Adverse Events and Adverse Events of Special Interest

Table 14.3.2.2.1
Treatment Emergent Adverse Events Associated with Abnormal Liver by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at least One TEAE Associated with Abnormal Liver".
- Update Reference Listing to 16.2.7.3.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.2.2.2
Potential joint Related Adverse Events of Special Interest by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at least One Potential Joint Related AESI"
- Add abbreviation for AESI = Adverse Event of Special Interest. Remove references to TEAEs in footnote.
- Update Reference Listing to 16.2.7.4
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.2.2.3
Serious and/or severe Infections by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at Least One SAE or Severe AE Related to Infection". Add "SAE = Serious Adverse Event" to abbreviations. Remove references to TEAEs in footnote.
- Update Reference Listing to 16.2.7.5.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.2.2.4
Anaphylactic Reactions, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of IP by System Organ Class and Preferred Term
Safety Population

System Organ Class	Placebo	MEDI7352				Total
		CCI	CCI	CCI	All MEDI7352	
Preferred Term	(N=xx) n (n/N * 100) m	(N=xx) n (n/N * 100) m	(N=xx) n (n/N * 100) m	(N=xx) n (n/N * 100) m	(N=xx) n (n/N * 100) m	(N=xx) n (n/N * 100) m
Subjects with at Least One Anaphylactic Reaction, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of IP	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Subjects with at Least One Anaphylactic Reaction, Hypersensitivity or Infusion-Related Reactions Not Leading to Discontinuation of IP [1]	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx

AE = adverse event; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects within each SOC/PT category; N = number of subjects per treatment group; IP = investigational product; PT = Preferred Term; SOC = System Organ Class; TEAE = treatment-emergent adverse event.

[1] Anaphylactic reactions, hypersensitivity or infusion-related reactions not leading to discontinuation of IP were included in table as they were categorized as AE of special interest under Protocol Amendment 4 (V5.0). Definition for AE of special interest changed from Amendment 6 (V6.0) onwards, including anaphylactic reactions, hypersensitivity or infusion-related reactions leading to permanent discontinuation of IP..
Note: Results are n (n/N * 100) m is number of events.
A TEAE is defined as AE with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0. Subjects are counted once for each SOC and once for each PT.
AEs are displayed by descending frequency of SOC, then descending frequency of PT within SOC, based on 'All MEDI7352' column. Table is sorted by international order for SOC of same frequency, and alphabetically for PT of same frequency.
Reference Listing: 16.2.7.6

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at Least One Anaphylactic Reaction, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of IP". Remove references to TEAEs in footnote.
- Update Reference Listing to 16.2.7.6.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

6.4. Laboratory Data

Table 14.3.4.1
Descriptive Summary of Clinical Chemistry
Safety Population

Parameter: xxxxx (unit)

Visit/ Statistic	Placebo (N=xx)	MEDI7352 [redacted] (N=xx)	MEDI7352 [redacted] (N=xx)	MEDI7352 [redacted] (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Low NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Low CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 1						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Low NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Low CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)

Day 1 CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

CFB = change from baseline; CS = clinically Significant; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NCS = not clinically significant; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Note: Percentages are n/Number of subjects with not missing data by treatment group at each visit*100.
Reference Listing: 16.2.8.1

Programming Notes:

- Present only scheduled visits.
- Sort Parameters in the following Order: Albumin, Alkaline Phosphatase, Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Bicarbonate, Calcium, Chloride, Creatinine, High-Sensitivity C-Reactive Protein (hs-CRP), Estimated Glomerular Filtration Rate (eGFR by Cockcroft - Gault), Serum Glucose, Lactate Dehydrogenase (LDH), Potassium, Sodium, Total Bilirubin, Total Protein, Blood Urea Nitrogen (BUN), Uric Acid.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.4.2
Shift Table of Clinical Chemistry Results
Safety Population

Parameter (Unit)/ Visit / Post-Baseline Grade	Baseline Grade [1]									
	Placebo (N=xxx)					MEDI7352, 5 µg/kg (N=xxx)				
	Low	Normal	High	Missing	Total	Low	Normal	High	Missing	Total
XXXXXX (Unit)										
Week x										
Low	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Missing	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Total	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Week x										
Low	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Missing	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Total	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
…										

n = number of subjects within each category; N = number of subjects per treatment group.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Percentages are n/Number of subjects by treatment group at each visit for the parameter*100.

Reference Listing 16.2.8.1

Programming Notes:

- Repeat above in new pages for MEDI7352, CCI MEDI7352, CCI and All MEDI7352.
- Repeat the above for CCI dosing only if Stage 4 is initiated.
- Repeat for every scheduled visit.
- Present parameters in the same order as in Table 14.3.4.1.

Table 14.3.4.3
Descriptive Summary of Hematology
Safety Population

Programming Notes:

- Same shell as Table 14.3.4.1
- Present only scheduled visits.
- Sort Parameters in the following Order: Absolute basophil count, absolute eosinophil count, absolute lymphocytes count, Absolute Monocyte Count, Absolute Neutrophil Count, Basophils %, Eosinophils %, Hematocrit (HCT), Hemoglobin (HGB), hemoglobin A1C (HgbA1C), Lymphocytes %, mean corpuscular hemoglobin (MHC), Mean Corpuscular Hemoglobin Concentration (MCHC), Mean Corpuscular Volume (MCV), Monocytes %, Neutrophils %, Platelets, Red blood cell count (RBC), Red Cell Distribution Width, white blood cell Count (WBC).
- Update Reference listing to 16.2.8.2.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.4.4
Shift Table of Hematology Results
Safety Population

Programming Notes:

- Same shell as Table 14.3.4.2
- Repeat the shell for CCI dosing if Stage 4 is initiated.
- Repeat for every scheduled visit.
- Present parameters in the same order as in Table 14.3.4.3.
- Update Reference listing to 16.2.8.2

Table 14.3.4.5
Descriptive Summary of Coagulation
Safety Population

Programming Notes:

- Same shell as Table 14.3.4.1
- Present only scheduled visits.
- Sort Parameters in the following Order: Activated Partial Thromboplastin Clotting Time (APTT), Fibrinogen, International normalized ratio (INR), Prothrombin Time (PT).
- Update Reference listing to 16.2.8.3.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.4.6
Shift Table of Coagulation Results
Safety Population

Programming Notes:

- Same shell as Table 14.3.4.2
- Repeat for CCI dosing if Stage 4 is initiated.
- Repeat for every scheduled visit.
- Present parameters in the same order as in Table 14.3.4.5.
- Update Reference listing to 16.2.8.3.

Table 14.3.4.7
Descriptive Summary of Urinalysis
Safety Population

Parameter: xxxxx (unit)

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Low NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Low CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 1						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Low NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Low CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 1 CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

…

Repeat for all visits for Parameters: Specific Gravity and pH

Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Negative	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Positive	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
If Positive, Specify [2]						
100 mg/dL	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
250 mg/dL	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
500 mg/dL	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
>= 1000 mg/dL	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 1						
n	xx	xx	xx	xx	xx	xx
Negative	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Positive	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)

…

Repeat for all visits for Parameters: Blood, Glucose, Ketones and Protein

CFB = change from baseline; CS = clinically significant; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NCS = not clinically significant; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
[2] Percentages are n/Number of Subjects with a Positive Result*100.
Note: Percentages are n/Number of subjects with not missing data by treatment group at each visit*100.
Reference Listing: 16.2.8.4

Programming Notes:

- Present only scheduled visits.
- Sort Parameters in the following Order: Blood Urine, Glucose, Ketones, pH, Protein, Specific Gravity.
- Categories for If Positive, Specify:
  - Blood, Urine: Trace, Small, Moderate.
  - Glucose: 100 mg/dL, 250 mg/dL, 500 mg/dL, >= 1000 mg/dL.
  - Ketones: Trace, 15 mg/dL, 40 mg/dL.
  - Protein: Trace, 30 mg/dL, 100 mg/dL, 300 mg/dL.

- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.4.8
Shift Table of Urinalysis Results
Safety Population

Programming Notes:

- Same shell as Table 14.3.4.2
- Repeat for CCI dosing if Stage 4 is initiated.
- Repeat for every scheduled visit.
- Present parameters in the same order as in Table 14.3.4.7.
- Update Reference listing to 16.2.8.4

Table 14.3.4.9
Maximum On-Treatment ALT and AST versus Maximum On-Treatment Total Bilirubin
Safety Population

Group	Nobs		Total Bilirubin <2 x ULN n (%)	Total Bilirubin >=2 x ULN n (%)
Placebo				
N=xxx	xxx	ALT		
		<3 x ULN	x (xx.x%)	x (xx.x%)
		>=3 - <5 x ULN	x (xx.x%)	x (xx.x%)
		>=5 - <10 x ULN	0	0
		>=10 x ULN	0	0
	xxx	AST		
		<3 x ULN	x (xx.x%)	x (xx.x%)
		>=3 - <5 x ULN	x (xx.x%)	x (xx.x%)
		>=5 - <10 x ULN	0	0
		>=10 x ULN	0	0

…
Repeat for: CCI [redacted] ***All MEDI7352***

ALT = alanine aminotransferase; AST = aspartate aminotransferase; IP = investigational product; n = number of subjects per category; N = number of subjects per treatment group; Nobs = number of subjects per treatment group with at least one post-baseline assessment on treatment; ULN = upper limit of normal.
Note: On-treatment assessments include assessments on or after the date of first dose of IP. Baseline is defined as the last observation recorded prior to the first dose of treatment.
Percentages are based on Nobs.
Reference Listing: 16.2.8.1

Programming Notes:

- Per Protocol, the elevations of ALT or AST and Total Bilirubin do not have to occur at the same time or within a specified time frame. That is the reason why the table is presented by Subject instead of by visit. So, if for example, one subject has ALT >=3 - <5 x ULN at Day 1, and TBL >=2 x ULN at Week 18, n in that cell will increase by one.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

6.5. Other Safety Data

Table 14.3.5.1
Descriptive Summary of Vital Signs
Safety Population

Parameter: xxxxx

Visit Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	 CCI (N=xx)	 CCI (N=xx)	 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1: 15 Minutes Post-Dose						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1: 15 Minutes Post-Dose CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

…

CFB = Change from Baseline; eCRF = Electronic Case Report Form; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Note: 'Day 1: 5 minutes after Infusion Completion' timepoint was only applied to subjects enrolled in Stage 1, with data collected under eCRF versions 4.0 (11DEC2018) or older.
Reference Listing: 16.2.9.1

Programming Notes:

- Repeat for Supine Heart Rate, Supine Systolic Blood Pressure, Supine Diastolic Blood Pressure, Respiratory Rate, Body Temperature, Standing Heart Rate, Standing Systolic Blood Pressure, Standing Diastolic Blood Pressure.
- After Week 2 (inclusive), Supine measure are taken in sitting position. We will consider them as supine (in resting position) for calculating Change from Baseline (always at supine position).
- Include the following timepoints: Baseline, Day 1: 5 Minutes Post-Dose, Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week 10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- Note that Body Tº, and standing measures are not taken on Day 1, at 15, 30 and 45 minutes post-dose.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.2
Descriptive Summary of Digital ECG Data
Safety Population

Parameter: xxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1: 1 hour Post-Dose						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1: 1 hour Post-Dose CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
…						

CFB = Change from Baseline; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group ; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
Note: Data shown are averages of the 3 replicates taken for each parameter and timepoint, and CFB for the same variables.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.

Reference Listing: 16.2.9.2.1

Programming Notes:

- Repeat for PR, QRS, QT, RR, HR (Heart Rate) and QTcF taken from external data.
- Include the following timepoints: Baseline, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 4, Week, 8, Week 12, and Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.3
Summary of Overall Evaluation of Safety ECG Data
Safety Population

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Day 1: 1 hour Post-Dose						
n	xx	xx	xx	xx	xx	xx
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

CS = clinically significant; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NCS = Not clinically significant.
Note: Data are taken as the most conservative from the 3 replicates taken by timepoint.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.

Reference Listing: 16.2.9.2.2

Programming Notes:

- Include the following timepoints: Baseline, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 4, Week, 8, Week 12, and Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.4
Covid-19 Screening
Safety Population

Visit/ Variable Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Day 1						
Subjects Screened for COVID-19 Symptoms	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Symptoms Screened:						
Fever	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Cough	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dyspnoea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sore Throat	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Loss of Taste	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Loss of Smell	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Body Temperature Check						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Subjects with COVID-19 Swab Performed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Negative	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with COVID-19 Antibody Testing Performed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Confirmed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Suspected	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Negative	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Subjects with COVID-19 Antigen Testing Performed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Negative	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

COVID-19 = coronavirus disease 2019; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
Note: Percentages are n/Number of subjects by treatment group at each visit*100.
Reference Listing: 16.2.8.8

Programming Notes:

- Include the following timepoints: Day 1, Week 2, Week 4, Week 6, Week, 8, Week 10.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.5
Summary of Sub-Scores for Total Neuropathy Score-Nurse
Safety Population

Visit/ Variable Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
Subjects performing TNSn	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sensory Symptom Score						
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Motor Symptom Score						
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Autonomic Symptom Score						
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pin Sensibility Score						
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Vibration Sensibility Score						
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

...

N = number of subjects per treatment group; TNSn = Total Neuropathy Score-Nurse.

[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Note: Percentages for subjects performing TNSn are n/Number of subjects by treatment group at each visit*100. Percentages for each Score are n/Number of subjects by treatment group at each visit without missing score*100

Reference Listing: 16.2.9.5

Programming Notes:

- Include the following timepoints: Baseline, Day 1, Week 2, Week 4, Week 6, Week, 8, Week 10, Week 12 and Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.6
Descriptive Summary of Total Neuropathy Score-Nurse
Safety Population

Score: xxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1 CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

TNSn = Total Neuropathy Score-Nurse; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment. Reference Listing: 16.2.9.5

Programming Notes:

- Include the following timepoints: Baseline, Day 1, Week 2, Week 4, Week 6, Week, 8, Week 10, Week 12 and Week 18.
- Include the following scores: Sensory Symptom Score, Motor Symptom Score, Autonomic Symptom Score, Pin Sensibility Score, Vibration Sensibility Score, and TNSn Total.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.7
Summary of Motor and Sensory Nerve Conduction Studies
Safety Population

Parameter: xxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 18						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 18 CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Evaluation Result						
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 18						
n	xx	xx	xx	xx	xx	xx
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

CFB = Change from Baseline; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Note: Percentages are number of subjects by treatment group at each visit for each category /Number of subjects with not missing data by treatment group for each visit*100
Reference Listing: 16.2.9.6

Programming Notes:

- Repeat for the following Parameters: Lower Limb - right side/Motor evaluation/Amplitude, Lower Limb - right side/Sensory evaluation/Amplitude, Lower Limb - left side/ Motor evaluation/Amplitude, Lower Limb - left side/ Sensory evaluation/Amplitude, Upper Limb - right side /Motor evaluation/Amplitude, Upper Limb - right side/ Sensory evaluation/Amplitude, Upper Limb - left side/ Motor evaluation/Amplitude, Upper Limb - left side /Sensory evaluation/Amplitude. (**Repeat the same combination of Location - Laterality/Evaluation** for Peak Latency, Conduction Velocity, Duration of action Potential).
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.8
Summary of Strength and Deep Tendon Reflexes
Safety Population

Visit/ Variable Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
Subjects performing SDTR assessment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ankle Dorsiflexion Strength						
0 - Normal Power	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1 - Mild Weakness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 - Moderate Weakness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 - Severe Weakness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 - Paralysis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Deep Tendon Reflexes						
0 - Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1 - Ankle reflex reduced	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 - Ankle reflex absent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 - Ankle reflex absent and knee reflex reduced	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 - All reflexes (both ankle and knee) absent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

n = number of subjects by treatment group at each visit for each category; N = number of subjects per treatment group; SDTR = strength and deep tendon reflexes.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Note: Percentages for each Score are n/Number of subjects by treatment group at each visit*100

Reference Listing: 16.2.9.7

Programming Notes:

- Include the following timepoints: Baseline, Day 1, Week 2, Week 4, Week 6, Week, 8, Week 10, Week 12, and Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.9
Summary of Local Injection Site Reactions
Safety Population

Visit/ Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Day 1: 15 Minutes after Start of Infusion						
Subjects with injection Site Assessed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pain						
None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tenderness						
None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Erythema/ Redness						
None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Induration/ Swelling						
None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

n = number of subjects by treatment group at each visit for each category; N = number of subjects per treatment group.
Note: Percentages for each Score are n/Number of subjects by treatment group at each visit*100
Reference Listing: 16.2.9.8

Programming Notes:

- Include the following timepoints: Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2, Week 4, Week 6, Week, 8, Week 10, Week 12, and Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.10
Summary of Hypersensitivity/Anaphylactic Reactions
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with any Hypersensitivity/ Anaphylaxis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Highest Severity Grade						
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Type of Reaction						
Urticaria	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pruritus	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Rash	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Flushing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Swollen Lips, Tongue, Uvula and/or Vulva	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dyspnoea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Wheeze-Bronchospasm	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stridor	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hypoxia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hypotension	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Crampy Abdominal Pain	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Vomiting	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Diarrhoea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

N = number of subjects per treatment group.
Reference Listing: 16.2.9.9

Programming Notes:

- Display only Type of reaction with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.11
Summary of Liver Diagnostic Investigations
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Liver Diagnostics Performed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Type of Diagnostic Investigation						
Ultrasound	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
CT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
MRI/MRCP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Flushing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ERCP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
X-Ray	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tox Screening for Acetaminophen/Paracetamol	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tox Screening for Ethanol	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tox Screening, Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Specialist Consulted	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Hepatitis A	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Hepatitis B	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Hepatitis C	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Hepatitis D	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Hepatitis E	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)
Serology for Cytomegalovirus	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Epstein Barr Virus	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Autoimmune Serology	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

CT = Computerized tomography; ERCP = Endoscopic retrograde cholangiopancreatography; MRI = Magnetic resonance imaging; MRCP = Magnetic resonance cholangiopancreatography; N = number of subjects per treatment group.
Reference Listing: 16.2.9.10

Programming Notes:

- Display only Diagnostic Investigations with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.12
Summary of Liver Risk Factors and Lifestyle Events
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Liver Risk Factors Assessed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Liver Risk Factor						
Alcohol Abuse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Increased Alcohol Consumption within 1 Month of Reported Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
IV Drug Abuse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tattoo	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Acupuncture	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sexually Transmitted Diseases	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Toxic/Chemical Agent Exposure	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Travel (Areas at Risk in the Last Year)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pregnancy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Parenteral Nutrition	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Excessive Physical Exercise	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Changes Diet/Fasting Episodes/Weight Loss Diet	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Previous Drug Reaction	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Blood Transfusion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Patient Exposed to Anyone with Jaundice in the Last Month	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)
History of Hypotension	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Low Blood Pressure at Time of Event of Liver Injury and/or Abnormal Liver Laboratory Value	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
History of Liver Disease	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

IV = intravenous; N = number of subjects per treatment group.
Reference Listing: 16.2.9.10

Programming Notes:

- Display only Liver Risk Factor with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.13
Summary of Liver Signs and Symptoms
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Liver Signs/Symptoms Assessed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Liver Sign/Symptom						
Anorexia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Asthenia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pyrexia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pruritus	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Jaundice	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Arthralgia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abdominal Pain	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abdominal Tenderness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Nausea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Vomiting	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Rash	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mucosal Inflammation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Purpura	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hepatomegaly	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Splenomegaly	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)
Lymphadenopathy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ascites	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Confusional State	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Coma	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Upper Quadrant Tenderness	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)
Biliary Obstruction	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Eosinophilia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dark Urine	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

N = number of subjects per treatment group.
Reference Listing: 16.2.9.12

Programming Notes:

- Display only Liver Signs/Symptoms with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.14
Summary of Infection Diagnostic Investigations
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Infection Diagnostic Investigations	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Method						
Microscopy, Culture and Sensitivity	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serological Tests	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Nucleic Acid Based Tests	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
X-Ray	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

N = number of subjects per treatment group.
Reference Listing: 16.2.9.13

Programming Notes:

- Display only Methods with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.15
Summary of Infection Risk Factors and Lifestyle Events
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Infection Risk Factor Occurred	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Infection risk factor						
Extensive Burns within the Last Year	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tattoo, Piercing or Acupuncture within the last Year	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sexually Transmitted Diseases	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Travel to Areas at Risk of Tuberculosis or Tropical Diseases	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Infections Related to Travel	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Blood Transfusion (within the Last Year)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Exposure to Nosocomial Pathogens within the Last Year	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Contact History with Infection Source	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Previous BCG Immunization	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Evidence of BCG Scar	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tuberculin Skin or Quantiferon Test Confirms Previous Exposure or Immunity to Tuberculosis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

BCG = Bacillus Calmette-Guerin; N = number of subjects per treatment group.
Reference Listing: 16.2.9.14

Programming Notes:

- Display only infection risk factors with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.16
Summary of Infection Signs and Symptoms
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Infection Sign/Symptom Occurred	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Infection Sign/Symptoms						
Pyrexia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Headache	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Confusional State	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Convulsion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Rhinitis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Oropharyngeal Pain	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Cough	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Productive Cough	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Haemoptysis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Wheezing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dyspnoea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pleuritic Pain	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Vomiting	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Diarrhoea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Genital Discharge	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Haematuria	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dysuria	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hepatosplenomegaly	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Jaundice	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lymphadenopathy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Rash	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Petechial	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Vesicular	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Macular	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Papular	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Urticaria	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Erythema	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Blanching	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Splinter Haemorrhages	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Night sweats	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Chills	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Myalgia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Weight Decrease	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

N = number of subjects per treatment group.
Reference Listing: 16.2.9.15

Programming Notes:

- Display only infection Signs/Symptoms with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.17
Summary of Concomitant Medications by ATC Level 2 and Preferred Name
Safety Population

Programming Notes:

- Same shell as Table 14.1.7.
- Change footnote Note by: "Note: Concomitant medications are defined as medications continuing or starting on or after first dose of study medication. All concomitant medications are coded using WHO drug dictionary version vMar2023. At each level of summarization (ATC Level 2 or Preferred Name), subjects who reported more than one concomitant medication were only counted once. ATC Level 2 and Preferred Name are sorted in in descending order of frequency of total, and alphabetically if same frequency".
- If uncoded ATC Level or Preferred Name, please put them as [Not Coded]
- ATC and Preferred Name texts should be in proper case in table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.18
Summary of Concomitant Procedures
Safety Population

System Organ Class Preferred Term	Placebo (N=xxx)	MEDI7352 CCI (N=xx)	 CCI (N=xx)	 CCI (N=xx)	Total (N=xxx)
Any Concomitant Procedure	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
System Organ Class 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
…	…	…	…	…	…
System Organ Class n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)

N = number of subjects per treatment group; PT = Preferred Term; SOC = System Organ Class.
Note: All Procedure terms were coded using the Medical Dictionary for Regulatory Activities (MedDRA), version 26.0. At each level of summarization (system organ class or preferred term), subjects having more than one Procedure term were counted only once. System organ class and preferred terms are sorted in descending order of frequency of Total column, and alphabetically if same frequency.
When there are uncoded Procedure Events in the database, the events will be summarized with SOC and PT set to [Not Coded]. The [Not Coded] are sorted at the end of the table.

Reference Listing: 16.2.9.18

Programming Notes:

- SOC and PT texts should be in proper case in table.
- Sort SOC and PT (within SOC) in descending order of frequency in the Total column. Sort alphabetically in case of ties.
- Uncoded Procedure events
  - When there are uncoded Procedure Events in the database, the events will be summarized with SOC and PT set to [Not Coded]. The [Not Coded] will be sorted at the end of the table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.19
Anti-Drug Antibody Results and Titre Summary by Timepoint
Safety Population

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)
Baseline [1]					
n [2]	xx	xx	xx	xx	xx
ADA Positive: n (%) [3]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 2					
n [2]	xx	xx	xx	xx	xx
ADA Positive: n (%) [3]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
…					

ADA = Anti-Drug Antibodies; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
[2] Number of subjects with at least one ADA assessment at the specific visit.
[3] Number of subjects with a positive result at the specific visit. The denominator for all percentages is the number of subjects with an ADA result for each visit.

Reference Listing: 16.2.9.19

Programming Notes:

- Keep in mind that in this table 'Total' column does not include placebo.
- Repeat for all scheduled post-baseline visits.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.20
Descriptive Summary of Anti-Drug Antibody Results and Titre by ADA Categories
Safety Population

ADA Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)
ADA positive at baseline and/or post-baseline (ADA prevalence)					
n/Nobs (%) [1] [2]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
TE-ADA positive (ADA incidence) [5]					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Treatment Induced ADA Positive					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Treatment-Boosted ADA Positive					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Non-TE-ADA Positive [6]					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Both baseline and post-baseline positive					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Only baseline positive					
n/Nobs (%) [1] [4]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
TE-persistently ADA positive [7]					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

TE-transiently ADA positive [8]					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

ADA = Anti-Drug Antibodies; N = number of subjects per treatment group; TE-ADA = Treatment Emergent ADA; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] n represents the number of subjects satisfying the conditions of the specified ADA category
[2] Nobs represents the number of subjects with any ADA result at baseline and/or post-baseline.
[3] Nobs represents the number of subjects with an ADA result at baseline and at least one post-baseline ADA assessment.
[4] Nobs represents the number of subjects with an ADA result at baseline.
[5] TE-ADA positive is defined as either ADA negative at baseline and post-baseline ADA positive (Treatment Induced ADA Positive), or as ADA positive at baseline with pre-existing titre boosted by 4-fold or greater during the study period (Treatment Induced ADA Positive). ADA incidence is the proportion of TE-ADA+ subjects in a population.
[6] ADA post-baseline positive but not fulfilling the conditions for TE-ADA+
[7] ADA negative at baseline and having at least 2 post-baseline ADA positive measurements with ≥16 weeks (112 days) between first and last positive, or an ADA positive result at the last available post-baseline assessment.
[8] ADA negative at baseline and at least one post-baseline ADA positive measurement and not fulfilling the conditions for persistently positive.

Reference Listing: 16.2.9.19

Programming Notes:

- If a participant has more than 1 non-missing titre during the study, the maximum titre for each participant is summarized.
- Only present summary statistics if titre is available.
- If no positive results for a particular block of the table, then the summary statistics for the titres for that particular block would not appear.
- It is assumed that participants with a missing baseline ADA result are ADA negative at baseline.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

7. Pharmacokinetic/Pharmacodynamic Data

Table 14.4.1
Summary of Serum MEDI7352 Concentrations
PK Population

ADA Status: xxxxxxxxxx

Visit/ Statistic	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)
Baseline [1]			
n (n < LLOQ)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
gMean [gMean ± gSD]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]
gCV%	xx.x	xx.x	xx.x
Median	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx
Week 2			
n (n < LLOQ)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
gMean [gMean ± gSD]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]
gCV%	xx.x	xx.x	xx.x
Median	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx
Week 4			
n (n < LLOQ)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
gMean [gMean ± gSD]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]
gCV%	xx.x	xx.x	xx.x
Median	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx
…			

gCV% = Geometric Coefficient of Variation (%); gMean = Geometric Mean; gSD = Geometric SD; LLOQ = Lower Limit of Quantification; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NC =not calculable; NQ = not quantifiable.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Reference Listing: 16.2.10.1

Programming Notes:

- Include the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours/ Pre-Dose, Week 11/ Pre-Dose, Week 10 + 14 Days/Pre-Dose; Week 18.
- Repeat the table for 'ADA Positive', 'ADA Negative' and 'Overall'.
- Any values reported as NRR (not reportable) or NS (missing) will be excluded from the summary tables.
- At a time point where less than or equal to 50% of the concentration values are NQ (below LLOQ), all NQ values will be set to the LLOQ, and all descriptive statistics will be calculated accordingly.
- At a time point where more than 50% (but not all) of the values are NQ, the gmean, gmean ± gSD and gCV% will be set to NC. The maximum value will be reported from the individual data, and the minimum and median will be set to NQ.
- If all concentrations are NQ at a time point, no descriptive statistics will be calculated for that time point. The gmean, minimum, median and maximum will be reported as NQ and the gCV% and gmean ± gSD as NC.

Table 14.4.2
Summary of Serum total NGF Concentrations
Safety Population

ADA Status: xxxxxxxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	CCI (N=xx)	CCI (N=xx)
Baseline [1]				
n (n < LLOQ)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
gMean [gMean ± gSD]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	
gCV%	xx.x	xx.x	xx.x	xx.x
Median	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Week 2				
n (n < LLOQ)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
gMean [gMean ± gSD]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	
gCV%	xx.x	xx.x	xx.x	xx.x
Median	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Week 4				
n (n < LLOQ)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
gMean [gMean ± gSD]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	
gCV%	xx.x	xx.x	xx.x	xx.x
Median	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
…				

gCV% = Geometric Coefficient of Variation (%); gMean = Geometric Mean; gSD = Geometric SD; LLOQ = Lower Limit of Quantification; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; ; NC = not calculable; NGF = Nerve-Growth Factor; NQ = not quantifiable.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Reference Listing: 16.2.10.3

Programming Notes:

- Repeat for ADA Status: “ADA Positive”, “ADA Negative” and “Overall”.
- Include the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 12; Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Planned Listing Descriptions and Shells

Number Title Population	Unique (U) or Repeated (R)
Listing 16.2.1.1 - Subject Disposition - Screening Population	U
Listing 16.2.1.2 - Assignment to Analysis Populations - Screening Population	U
Listing 16.2.1.3 - Reason for IP Discontinuation and Withdrawal from the Study - Safety Population	U
Listing 16.2.1.4 - List of Reasons for Screening Failure - Screen Failure Population	U
Listing 16.2.1.5 - Subject Visits and COVID-19 Impact - Screening Population	U
Listing 16.2.2.1 - Subjects Not Meeting All Inclusion Criteria or Meeting any Exclusion Criteria - Screening Population	U
Listing 16.2.2.2 - Protocol Deviations - Safety Population **Error! Reference source not found.Error! Reference source not found.Error! Reference source not found.Error! Reference source not found.Error! Reference source not found.**	U
Listing 16.2.3 - Randomization and Treatment Group - Safety Population **Error! Reference source not found.Error! Reference source not found.Error! Reference source not found.Error! Reference source not found.Error! Reference source not found.**	U
Listing 16.2.4.1 - Demographic and Baseline Characteristics - Screening Population	U
Listing 16.2.4.2 - Medical History - Safety Population	U
Listing 16.2.4.3 - Osteoarthritis Characteristics - Screening Population	U
Listing 16.2.5.1 - Study Drug Administration: Individual Doses - Safety Population	U
Listing 16.2.6.1 - Daily Pain NRS - mITT Population	U
Listing 16.2.6.2 - **Error! Reference source not found.** Galer NPS - mITT Population	U
Listing 16.2.6.3 - DSIS - mITT Population	U
Listing 16.2.6.4 - SF-36 - mITT Population	U
Listing 16.2.6.5 - Rescue Medication Usage - mITT Population	R
Listing 16.2.6.6 - Patient Global Impression of Change - mITT Population	U

Number Title Population	Unique (U) or Repeated (R)
CCI	U
Listing 16.2.7.1 - Adverse Events - Safety Population	U
Listing 16.2.7.2 - Treatment Emergent Adverse Events Leading to Study Drug Discontinuation **Error! Reference source not found.** - Safety Population	R
Listing 16.2.7.3 - Treatment Emergent Adverse Events Associated with Abnormal Liver - Safety Population	R
Listing 16.2.7.4 - Joint Related Adverse Events of Special Interest - Safety Population	R
Listing 16.2.7.5 - Serious and/or Severe Infections - Safety Population	R
Listing 16.2.7.6 - Anaphylactic Reactions, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of Study Drug - Safety Population	R
Listing 16.2.8.1 - Clinical Chemistry Laboratory Evaluations - Safety Population	U
Listing 16.2.8.2 - Hematology Laboratory Evaluations - Safety Population	R
Listing 16.2.8.3 - Coagulation Laboratory Evaluations - Safety Population	R
Listing 16.2.8.4 - Urinalysis Laboratory Evaluations - Safety Population	R
Listing 16.2.8.5 - Serology Laboratory Evaluations - Safety Population	U
Listing 16.2.8.6 - Pregnancy Test Results - Safety Population	U
Listing 16.2.8.7 - Drug Test Results - Safety Population	U
Listing 16.2.8.8 - COVID-19 Screening and Vaccination - Safety Population	U
Listing 16.2.9.1 - Vital Signs Measurements - Safety Population	U
Listing 16.2.9.2.1 - 12-Lead Digital ECG Results - Safety Population	U
Listing 16.2.9.2.2 - 12-Lead Safety ECG Results - Safety Population	U
Listing 16.2.9.3 - Physical Examination Results - Safety Population	U
Listing 16.2.9.4 - Neurological Examination Results - Safety Population	U
Listing 16.2.9.5 - Total Neuropathy Score-Nurse - Safety Population	U

Number Title Population	Unique (U) or Repeated (R)
Listing 16.2.9.6 - Motor and Sensory Nerve Conduction Studies - Safety Population	U
Listing 16.2.9.7 - Strength and Deep Tendon Reflexes - Safety Population	U
Listing 16.2.9.8 - Injection Site Reactions - Safety Population	U
Listing 16.2.9.9 - Hypersensitivity/Anaphylactic Reactions - Safety Population	U
Listing 16.2.9.10 - Liver Diagnostic Investigations - Safety Population	U
Listing 16.2.9.11 - Liver Risk Factors and Lifestyle Events - Safety Population	U
Listing 16.2.9.12 - Liver Signs and Symptoms - Safety Population	U
Listing 16.2.9.13 - Infection Diagnostic Investigations - Safety Population	U
Listing 16.2.9.14 - Infection Risk Factors and Lifestyle Events - Safety Population	U
Listing 16.2.9.15 - Infection Signs and Symptoms - Safety Population	U
Listing 16.2.9.16 - Prior and Concomitant Medications - Safety Population	U
Listing 16.2.9.17 - Prohibited Concomitant Medications - Safety Population	R
Listing 16.2.9.18 - Concomitant Procedures - Safety Population	R
Listing 16.2.9.19 - Anti-drug Antibody Test Results - Safety Population	U
Listing 16.2.10.1 - Serum MEDI7352 Concentrations - PK Population	U
Listing 16.2.10.2 - Serum total NGF Concentrations - PD Population	U

Listing Change Log:

Output Number	Date of Change	Change Made By (initials)	Description/Rationale

Listing 16.2.1.1
Subject Disposition
Screening Population

Subject ID	Re-screened?/ Previous Subject ID	Treatment Arm	Re-consent/ Date/Time of Initial IC/ Initial Protocol Version	Date/Time of Informed Consent	Protocol Version at consent/ Re-consent	Consent for [redacted] sample? /Date of Consent	Consent for COVID-19 Safety Measures /Date of Consent	Current Protocol version
XXXX	No	XXXX	No	DDMMMYYYY/ hh:mm	XXXX	Yes/ DDMMMYYYY	Yes/ DDMMMYYYY	XXXXX
XXXX	Yes/ XXXX	XXXX	No	DDMMMYYYY/ hh:mm	XXXX	Yes/ DDMMMYYYY	Yes/ DDMMMYYYY	XXXXX
XXXX	No	XXXX	No	DDMMMYYYY/ hh:mm	XXXX	Yes/ DDMMMYYYY	Yes/ DDMMMYYYY	XXXXX
XXXX	No	XXXX	Yes / DDMMMYYYY/hh:mm / XXXX	DDMMMYYYY/ hh:mm	XXXX	Yes/ DDMMMYYYY	No	XXXXX
XXXX	No	XXXX	No	DDMMMYYYY/ hh:mm	XXXX	No	No	XXXXX

COVID-19 = coronavirus disease 2019; IC = Informed Consent; [redacted]
.

Programming Notes:

- Sort by Treatment Arm/ Subject ID.

Listing 16.2.1.2
Assignment to Analysis Populations
Screening Population

Subject ID	Treatment Arm	Screened [1]	Randomized	SAF [2]	mITT [3]	PK [4]	Reason to Exclude from Safety [5]	Reason to Exclude from mITT [6]
XXXXXX	XXXX	Yes	No	No	No	No		
XXXXXX	XXXX	Yes	Yes	Yes	Yes	Yes		
XXXXXX	XXXX	Yes	Yes	No	No	No	XXX	
XXXXXX	XXXX	Yes	Yes	Yes	Yes	Yes		
XXXXXX	XXXX	Yes	Yes	Yes	No	No	XXX/ XXX	XXX/ XXX

mITT = Modified Intent-To-Treat Population Set; NRS = numeric rating scale; PK = pharmacokinetics; SAF = Safety Population Set.
[1] The Screening Population includes all subjects who provide informed consent and provide demographic and/or baseline screening assessments.
[2] The Safety Population includes all subjects who receive at least 1 dose of double-blind study medication.
[3] The mITT Population includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
[4] The PK Population includes all subjects for who a pharmacokinetic sample was obtained and analysed.
[5] Major deviation reason/s to exclude from Safety Population for randomized subject.
[6] Major deviation reason/s to exclude from mITT Population for randomized subject.

Programming Notes:

- If there is more than one major deviation, please concatenate with "/"
- Sort by Treatment Arm/ Subject ID.

Listing 16.2.1.3
Reason for IP Discontinuation and Withdrawal from the Study
Safety Population

Subject ID/ Treatment Arm	IP Discontinuation [1]/ Study Withdrawal	Completion/ Discontinuation Date (Study Day)	Date of Last Dose	Number of doses	Primary Reason for DC/ Withdrawal	Blind Broken? / Date/Time / Reason	Reason for breaking the Blind	Study Duration
XXXXXX/ XXXX	IP Discontinuation	DDMMMYYYY(XX)	DDMMMYYYY	XX	XXXXXX	Yes / DDMMMYYYY/ hh:mm	XXXXXX	XX
XXXXXX/ XXXX	IP Discontinuation	DDMMMYYYY (XX)	DDMMMYYYY	XX	XXXXXX	No		XX
XXXXXX/ XXXX	Study Withdrawal	DDMMMYYYY (XX)	DDMMMYYYY	XX	Other: XXXXXX	No		XX

DC = Discontinuation; IP = Investigational product.
[1] Any withdrawal from the study before last IP dose (Week 10) is considered an IP discontinuation.
Note: Study Day is calculated relative to the date of first dose. Study Duration = Reference end date – date of first dose of treatment + 1.

Programming Notes:

- If reason for non-completion is Other, concatenate the specify text as follows: “Other: XXXXXXXXX”.
- If reason for non-completion is adverse event, concatenate with AE line number as follows: “Adverse event number X”.
- For Physician decision, screen-fail and withdrawal by subject, please provide explanation if presented on the logic “Physician decision: XXX”.
- Do not include subjects who completed the study.
- Sort by Treatment Arm/ Subject ID.

Listing 16.2.1.4
List of Reasons for Screening Failure
Screen Failure Population

Subject ID	Treatment Arm	Screen failure Date	Primary Reason for Screen Failure
XXXXXX	Screen Failure	DDMMMYYYY	XXXXXXXXX
XXXXXX	Screen Failure	DDMMMYYYY	XXXXXXXXX
XXXXXX	Screen Failure	DDMMMYYYY	
XXXXXX	Screen Failure	DDMMMYYYY	Other: XXXXXXXXX
XXXXXX	Screen Failure	DDMMMYYYY	

Programming Notes:

- If reason for non-completion is Other, concatenate the "Primary Reason for Screen Failure" text as follows: "Other: XXXXXXXXX".
- Sort by Subject ID.

Listing 16.2.1.5
Visits List and COVID-19 Impact
Screening Population

Subject ID/ Treatment Arm	Visit Name	Visit Date (Study Day)	Is COVID-19 Pandemic Ongoing?	Impacted by COVID-19	Was visit performed? / Visit Type	Visit Performed Via	VS Data provided? / Assessments Missed?	IP dosing missed due to COVID-19 / Details	End of Treatment linked to COVID-19	Subject discontinued due to COVID-19? / Details
xxxxx/ xxxx	Visit X	DDMMM YYYY (XX)	Yes	Yes	Yes/ Delayed	On site	Y/ Efficacy	Y/ XXXX	Other: XXXX	Y/ XXXX
xxxxx/ xxxx	Visit X	DDMMM YYYY (XX)	Yes	No	Yes		N/ Safety			
xxxxx/ xxxx	Visit X	DDMMM YYYY (XX)	No	Yes	Yes	Video	N/ Efficacy, Safety	Y/ Other: XXXX		
xxxxx/ xxxx	Visit X	DDMMM YYYY (XX)	No	No	No / Missed					

COVID-19 = coronavirus disease 2019; IP = Investigational Product; VS = Vital Signs.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Visit Type: Missed, Abbreviated, Delayed.
- Visit Performed Via: Video, Phone, On Site Other: xxxxxx.
- Details on IP dosing missed: Treatment on hold due to Sponsor Decision, Subject infected with COVID-19, Subject decision, Other: xxxxxx.
- End of treatment, reason if due to COVID: Subject infected with COVID-19, Subject decision, Travel restrictions, Site closed, Study delayed/cancelled, Other: xxxxxx.
- Details on Subjects discontinuing due to COVID-19: Subject infected with COVID-19, Subject decision, End of Treatment due to Sponsor, Other: xxxxxx.
- Sort by Treatment Arm/ Subject ID/ Visit Date.

Listing 16.2.2.1
Subjects Not Meeting All Inclusion Criteria or Meeting any Exclusion Criteria
Screening Population

Subject ID	Treatment Arm	Enrolled	Randomized	Inclusion or Exclusion	Criteria Number	Criteria Label
XXXXXX	Screen Failure	Yes	No	Inclusion	XX	XXXXXXXXXXXXXXXXXXX
		Yes	No	Exclusion	XX	XXXXXXXXXXXXXXXXXXX

Programming Notes:

- Sort by Subject ID.

Listing 16.2.2.2
Protocol Deviations
Safety Population

Subject ID	Treatment Arm	Analysis Population	Event Date (Study Day)	Event Type	Description	Category	Covid-19 Related?
XXXXXX	XXXX	Screened\RND\SAF\mITT	DDMMMYYYY (XX)	XXXXXXXXXXX	XXXXXXX	Non-important	Y
				XXXXXXXXXXXXXX	XXXXXXXXXXXXXXX	Important	
XXXXXX	XXXX		DDMMMYYYY (XX)	XXXXXXXXXXX	XXXXXXXXXXXXXXX XXX	XXXXX	
				XXXXXXXXXXXXXXX	XXXXXXXXXX	XXXXX	
XXXXXX	XXXX		DDMMMYYYY (XX)	XXXXXXXXXXX	XXXXXXXXXXXXXXX XXX	XXXXX	

COVID-19 = Coronavirus disease 2019; mITT = Modified Intent-To-Treat Population; RND = Randomized Subjects; SAF = Safety Population.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- The structure of this listing may change depending on the information in the protocol deviations file. In the analysis population column, include only the analysis population where subject is included in.
- Sort by Treatment Arm/ Subject ID. If date is present in file, add a column for date of event and sort by date. If no date is present, sort by category with non-important first and then important.
- Event Type: Inclusion Criteria, Exclusion Criteria, Study Drug, Assessment – Safety, Assessment – Efficacy, Lab/endpoint data, Visit Window, Informed Consent, Prohibited Co-Medication, Overdose/Misuse, Other.

Listing 16.2.3
Randomization and Treatment group
Safety Population

Subject ID	Treatment Arm	Randomization Stage	Randomization Treatment	Randomization Date / Time (Study Day)	Randomization Number
XXXXXX	XXXX	Stage 1	Active CCI	DDMMMYYYY/hh:mm (-X)	XXXX
XXXXXX	XXXX	Stage 3	Active CCI	DDMMMYYYY/hh:mm (-X)	XXXX
XXXXXX	XXXX	Stage 2	Placebo	DDMMMYYYY/hh:mm (-X)	XXXX
XXXXXX	XXXX	Stage 2	Active CCI	DDMMMYYYY/hh:mm (-X)	XXXX
XXXXXX	XXXX	Stage 3	Placebo	DDMMMYYYY/hh:mm (-X)	XXXX

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID.

Listing 16.2.4.1
Demographic and Baseline Characteristics
Screening Population

Subject ID	Treatment Arm	Birth Date	Age (years) [1]	Sex	Surgically sterile?/ Postmenopausal? [2]	Ethnicity	Race	Weight (kg)	Height (cm)	BMI (kg/m²)	Fully vaccinated for COVID-19?
XXX	XXX	DDMMMYYY	XX	XX		XXXXX	XXXX	XX.X	XX.X	XX.X	Y
XXX	XXX	--MMMYYY	XX	XX	No/ Yes	XXXXX	XXXX	XX.X	XX.X	XX.X	N

COVID-19 = Coronavirus disease 2019.
Note: Height and weight are the values at Screening.
[1] Age was calculated as age at time of consent.
[2] For Female Subject Only.

Programming Notes:

- Sort by Treatment Arm/ Subject ID

Listing 16.2.4.2
Medical History
Safety Population

Subject ID	Treatment Arm	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ End Date (Study Day)/
XXXXXX	XXXX	XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)
		XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	MMMYYYY (X)/ Ongoing
		XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (X)/ Ongoing
XXXXXX	XXXX	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)

MedDRA = Medical Dictionary for Regulatory Activities.
Note: Study Day is calculated relative to the date of first dose.
Medical History were coded using MedDRA version 26.0.
Only subjects with medical history recorded are listed.

Programming Notes:

- SOC & PT text should be in proper case in listing.
- Sort by Treatment Arm/ Subject ID / Start Date / End Date of medical event.

Listing 16.2.4.3
Osteoarthritis Characteristics
Screening Population

Subject ID	Treatment Arm	Subject with OA? / Joint/ Area affected	Is OA considered CS?	Radiological Investigations Conducted? / Details	Joint Area Investigated	Is OA considered RS?	K-L Score Reported	Radiologic Scoring System / Details/ Result
XXXXXX	XXXX	Y / Shoulder	Y	Y/ Other: XXXXXX	Shoulder	Y	Grade 3	XXXXXX/ XXXXXX/ XX
XXXXXX	XXXX	Y / Ankle	N	Y / MRI	Ankle	N	N	N

CS = Clinically Significant; K-L = Kellgren-Lawrence; OA = Osteoarthritis; RS = Radiologically Significant.

.

Programming Notes:

- Sort by Treatment Arm/ Subject ID

Listing 16.2.5.1
Study Drug Administration: Individual Doses
Safety Population

Subject ID/ Treatment Arm	Visit Name	Start Date/ Time (Study Day)	End Date/ Time (Study Day)	Was Infusion Performed?/ Infusion Volume (mL)[1]/ Reason not Performed	Actually Administered Volume (mL) [2]	If Difference between [1] and [2] Volume, Reason	Any Injection Site Reactions?	Any Infusion Related Reactions	Infusion Rate (mL/ hour)	Rate Change Justification	Reason for Infusion Rate Change
XXXX/ XXXX	XXX	DDMM MYYYY /hh:mm (X)	DDMM MYYYY /hh:mm (X)	Y/ XX	XX				xx.x		
XXXX/ XXXX	XXX	DDMM MYYYY /hh:mm (X)	DDMM MYYYY /hh:mm (X)	Y/ XX	XX	XXXXX	Y	Y	xx.x	XXXXX	XXXXX XX
XXXX/ XXXX	XXX			N/ XXXXXX							

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Start Date / End Date.
- Rate Change Justification: Increased, Decreased, Interrupted.

Listing 16.2.6.1
Daily Pain NRS
mITT Population

Subject ID	Treatment Arm	Study Visit [1]	Subject Diary (ePRO) Date / Study Day	Baseline Flag [2]	DPS
XXXXXX	XXXX	Baseline	DDMMMYYYY/ (-7)	Y	X
		Baseline	DDMMMYYYY/ (-6)	Y	XX
		…	…	…	…
		Baseline	DDMMMYYYY/ (-2)	Y	XX
		Baseline	DDMMMYYYY/ (-1)	Y	XX
		…	…	…	…
		Week 2	DDMMMYYYY/ (13)		XX
		Week 2	DDMMMYYYY/ (14)		XX
		…	…	…	…
		Week X	DDMMMYYYY/ (X)		XX
		…	…	…	…
XXXXXX	XXXX	Baseline	DDMMMYYYY/ (-7)	Y	XX
		…	…	…	…

DPS = Daily Pain Score; ePRO = Electronic Patient-Reported Outcome; NRS = Numeric Rating Scale.
Note: Data shown in column 'DPS' are average daily pain scores on an 11-point (0-10) NRS. Study Day is calculated relative to the date of first dose.
[1] Study Visit is defined as the 7-day period ending within the protocol window Day ± 3, where at least 4 days out of 7 have recorded diary pain scores.
[2] Baseline is defined as the 7-day period prior to randomization **i.e.,** Day -7 to Day -1, inclusive. A subject is considered to have an evaluable baseline pain score if there are at least 4 days of recorded diary pain scores in the 7-day period.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Subject Diary Date.
- Display all measurement per Subject, starting on the Study Day = -7.
- Display Study Visit for days involved in weekly averages of the average daily pain scores for Baseline, Week 2, 4, 6, 8, 10, and 12
- Flag Baseline records only when there is at least 5 days of recorded diary pain scores in the 7-day Baseline period

Listing 16.2.6.2
Galer NPS
mITT Population

Subject ID	Treatment Arm	Parameter	Study Visit	Collection Date / Study Day	Baseline Flag [1]	NPS
XXXXXX	XXXX	Pain intensity	Baseline	DDMMMYYYY/ (X)	Y	XX
			Week 4	DDMMMYYYY/ (X)		XX
			Week 8	DDMMMYYYY/ (X)		XX
				...		XX
			Week X	DDMMMYYYY/ (X)		XX
				...		XX
		XXXX	Baseline	DDMMMYYYY/ (X)	Y	XX
		...	...	...	...	...
XXXXXX	XXXX	Pain intensity	Baseline	DDMMMYYYY/ (X)	Y	XX
			...	...	...	...
		XXXX	Week X	DDMMMYYYY/ (X)		XX
		...	...	...	...	...

NPS = Neuropathic Pain Scale; NRS = Numeric Rating Scale.
Note: Data shown in column 'NPS' are Pain Intensity, Unpleasantness, and Descriptor scores on an 11-point (0-10) NRS, and Pain Duration/Frequency on a 3-point NRS (1-3).
Study Day is calculated relative to the date of first dose.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Parameter /Collection Date.
- Keep Parameter sorting from the last bullet point in this programming notes.
- Include all observed data on Galer NPS scores for Baseline, Week 4, 8, 12, and 18.
- Repeat for the Parameters: Pain intensity, Pain Unpleasantness, Pain Sharpness, Pain Hotness, Pain Dullness, Pain Coldness, Pain Sensitivity, Pain Itching, Deep Pain Intensity, Surface Pain Intensity (All in an 11-point NRS), and Pain Duration/Frequency (in a 3-point NRS).

Listing 16.2.6.3
DSIS
mITT Population

Programming Notes:

- Same shell as Listing 16.2.6.1.
- Update footnote as:
  DSIS = Daily Sleep Interference Scale; ePRO = Electronic Patient-Reported Outcome; NRS = Numeric Rating Scale.
  Note: Data shown in column 'DSIS' are daily Sleep Interference scores on an 11-point (0-10) NRS. Study Day is calculated relative to the date of the day of first dose.
  [1] Study Visit is defined as the seven-day period ending within the protocol window Day ± 3.
  [2] Baseline is defined as the seven-day period prior to randomization **i.e.,** Day -7 to Day -1,.
- Sort by Treatment Arm/ Subject ID / Subject Diary Date.
- Display all measurement per Subject, starting on the Study Day = -7.
- Display Study Visit for days involved in weekly averages of the average Sleep interference scores for Baseline, Week 4, 8, 12 , and 18.

Listing 16.2.6.4
SF-36
mITT Population

Subject ID	Treatment Arm	Parameter	Item Number	Item name	Study Visit	Collection Date / Study Day	Baseline Flag [1]	SF-36
XXXXXX	XXXX	Physical functioning	3	Vigorous Activities	Baseline	DDMMMYYYY/ (X)	Y	XX
					Week 12	DDMMMYYYY/ (X)		XX
			4	Moderate Activities	Baseline	DDMMMYYYY/ (X)	Y	XX
		…	…	…	…	…	…	…
			-	Total	Baseline	DDMMMYYYY/ (X)	Y	
					Week 12	DDMMMYYYY/ (X)		XX
XXXXXX	XXXX	Role limitations due to physical health	13	Cut Amount of Time Spent on Work/Act	Baseline	DDMMMYYYY/ (X)	Y	XX
					Week 12	DDMMMYYYY/ (X)		XX
			…		…	…	..	…
…		…	…		…	…	…	…

SF-36 = 36-Item Short-Form Health Survey; NRS = Numeric Rating Scale.
Note: Data shown in column 'SF-36' are derived SF-36 scores and Change in General Health on a 5-point NRS (1-5).
Study Day is calculated relative to the date of first dose.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Parameter / Item /Collection Date.
- Keep Parameter sorting from the last bullet point in this programming notes.
- Include all data on SF-36 scores for Baseline and Week 12.
- Repeat for the Parameters: Physical functioning (items 3, 4, 5, 6, 7, 8, 9, 10, 11, 12), Role limitations due to physical health (items: 13, 14, 15, 16), Role limitations due to emotional problems (items: 17, 18, 19), Vitality (Energy/fatigue) (items: 23, 27, 29, 31), Emotional well-being (items: 24, 25, 26, 28, 30), Social functioning (20, 32), Pain (items: 21, 22) and General Health (items: 1, 33, 34, 35, 36), all with values ranging from 0 to 100. Change in general Health (in a 5-point NRS, item: 2).

Listing 16.2.6.5
Rescue Medication Usage
mITT Population

Subject ID	Treatment Arm	ATC Class (Level 2)/ Preferred Name/ Verbatim Term	Primary Indication	Start Date (Study Day)/ End Date (Study Day)	Dose (unit)	Route	Frequency
XXXXXX	XXXX	XXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	Painful Diabetic Neuropathy	--MMMYYYY (-XX)/ DDMMMYYYY (-X)	XXXX unit	XXXXXXXXX	XXXXX
	XXXX	XXXXXXXXX/ XXXXXXXXXXXXXXX/ XXXXXXXXXXX	Painful Diabetic Neuropathy	--MMMYYYY (-X)/ Ongoing	XXXX unit	XXXXXXXXX	XXXXX
	XXXX	XXXXXXXXX/ XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX	Painful Diabetic Neuropathy	DDMMMYYYY (X)/ DDMMMYYYY (XX)	XXXX unit	XXXXXXXXX	XXXXX

ATC = anatomical therapeutic chemical.
Note: Study Day is calculated relative to the date of first dose.
Medications were coded using WHO drug dictionary version vMar2023.

Programming Notes:

- ATC & Preferred Name text should be in proper case in table.
- Ensure proper WHO-DDE version is printed in footnote.
- Sort by subject, start date/time, end date/time, ATC level 2 & Preferred Name .
- If Dose unit, Route or Frequency is Other, display other specify text only (ie, do not display “Other: XXXXXX” but just “XXXXXX “).
- Adjust footnotes for frequency and routes as needed.
- Sort by Treatment Arm/ Subject ID / Start Date / End Date (alphabetically for ATC Class Level 2 if same date for two medications

Listing 16.2.6.6
Patient Global Impression of Change
mITT Population

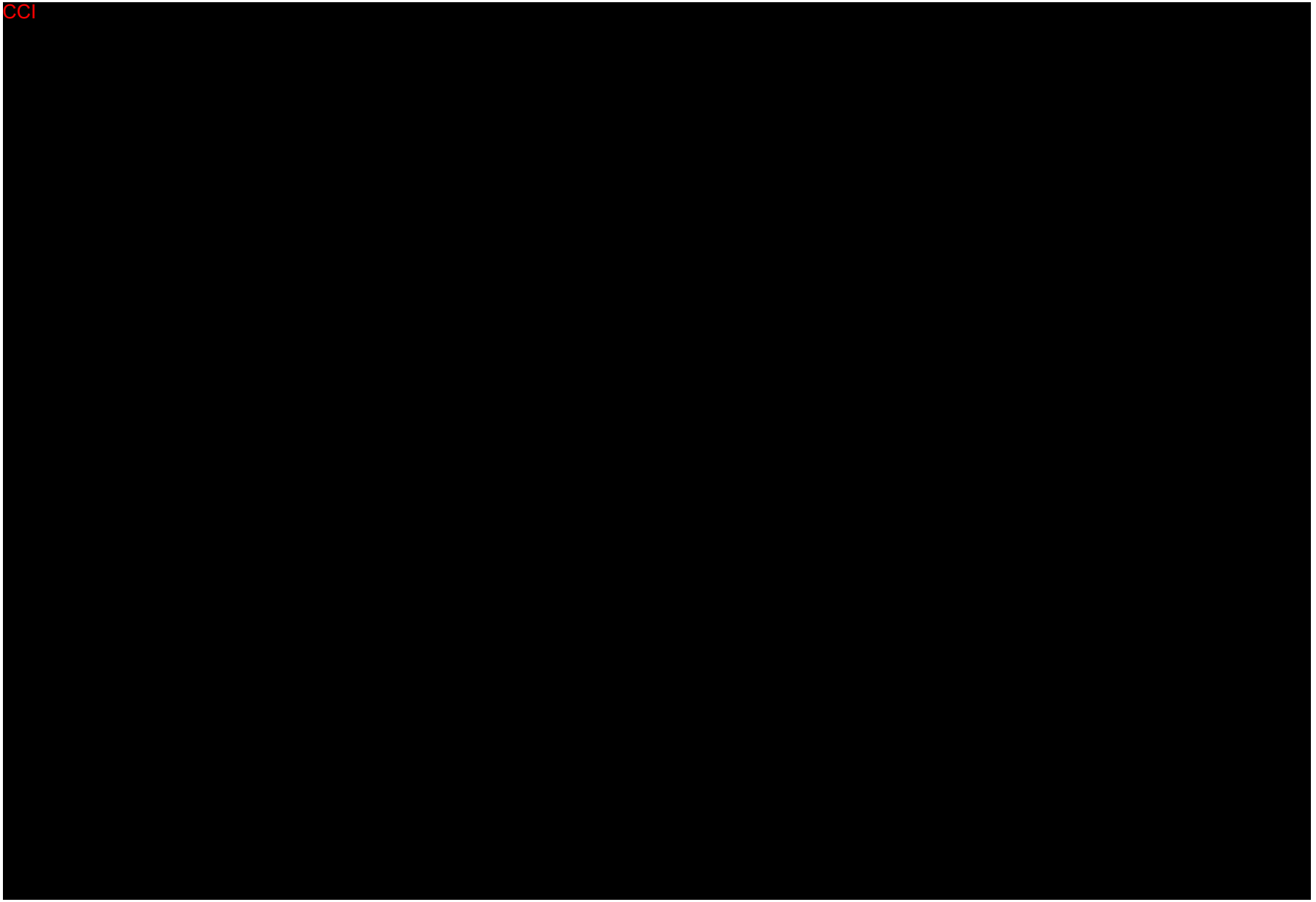
Subject ID	Treatment Arm	Study Visit	Collection Date / Study Day	PGIC
XXXXXX	XXXX	Week 4	DDMMMYYYY/ (X)	XXXXXXXX
		Week 8	DDMMMYYYY/ (X)	XXXXXXXX
		Week 12	DDMMMYYYY/ (X)	XXXXXXXX
		Week 18	DDMMMYYYY/ (X)	XXXXXXXX
XXXXXX	XXXX	Week 4	DDMMMYYYY/ (X)	XXXXXXXX
		Week 8	DDMMMYYYY/ (X)	XXXXXXXX
		Week 12	DDMMMYYYY/ (X)	XXXXXXXX
		Week 18	DDMMMYYYY/ (X)	XXXXXXXX
		...	...	...

PGIC =Patient Global Impression of Change.
Note: Data shown in column 'PGIC' are Subjects ratings about overall improvement in health status.
Study Day is calculated relative to the date of first dose.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Collection Date.
- Include all observed data on PGIC scores for Week 4, 8, 12, and 18.

CCI



CCI

[redacted]

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[redacted]

Listing 16.2.7.1
Adverse Events
Safety Population

Subject ID/ Treatment Arm	AE ID Number	System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date/Time (Study Day)/ End Date/Time (Study Day)	Severity/ Relationship [1]	Outcome/ Action Taken with IP/ Therapy taken for this AE?	AE Leading to Study DC?	TEAE	Serious? / Serious Criteria
XXXXX/ XXXX	X	XXXXXXXXXXX/ XXXXXXX/ XXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXXX/ XXXXXX	XXXXXXXXX/ XXXXXXX/ Yes	No	Yes	No
XXXXX/ XXXX	X	XXXXXXXXXXX/ XXXXXXX/ XXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMONYYYY/HH:MM (X)	XXXXXX/ XXXXXX	XXXXXXXXX/ XXXXXXX/ No	Yes	No	Yes / XXX
XXXXX/ XXXX	X	XXXXXXXXXXX/ XXXXXXX/ XXXXXXX	DDMONYYYY/HH:MM (X)/ Ongoing	XXXXXX/ XXXXXX	XXXXXXXXX/ XXXXXXX/ No	No	No	Yes / XXX

AE = adverse event; DC = discontinuation; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; SAE = serious adverse event; TEAE = treatment emergent adverse event.
[1] Reasonable possibility AE caused by IP as assessed by the investigator .
Note: Study Day is calculated relative to the date of first dose. A TEAE is defined as an AE with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0

Programming Notes:

- If time missing, display "- -:- -".
- AE ID number represents Record position within Subject.
- If no events meet the criteria for display (i.e, no AEs occur in the study), present "No events are reported.".
- SOC & PT text should be in proper case in table.
- Sort by Treatment Arm/ Subject ID / Start Date / End Date (alphabetically by SOC /PT if same date for two events).

In case a term is not coded (e.g. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]". SOC and PT abbreviations should be added in this case in footnote.

Listing 16.2.7.2
Treatment Emergent Adverse Events Leading to Study Drug Discontinuation
Safety Population

Programming Notes:

- Same shell as Listing 16.2.7.1.
- Update listing deleting seventh and eight columns

Listing 16.2.7.3
Treatment Emergent Adverse Events Associated with Abnormal Liver
Safety Population

Programming Notes:

- Same shell as Listing 16.2.7.1.
- Update listing deleting 8th column.

Listing 16.2.7.4
Joint Related Adverse Events of Special Interest
Safety Population

Programming Notes:

- Same shell as Listing 16.2.7.1.

Listing 16.2.7.5
Serious and/or Severe Infections
Safety Population

Programming Notes:

- Same shell as Listing 16.2.7.1.

Listing 16.2.7.6
Anaphylactic Reactions, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of Study Drug
Safety Population

Programming Notes:

- Same shell as Listing 16.2.7.1.
- Update footnote: Anaphylactic reactions, hypersensitivity or infusion-related reactions not leading to discontinuation of IP were included in listing as they were categorized as AE of special interest under Protocol Amendment 4 (V5.0). Definition for AE of special interest changed from Amendment 6 (V6.0) onwards, including anaphylactic reactions, hypersensitivity or infusion-related reactions leading to permanent discontinuation of IP.

Listing 16.2.8.1
Clinical Chemistry Laboratory Evaluations
Safety Population

Subject ID/ Treatment Arm	Parameter	Study Visit	Date/Time of Collection (Study Day)	Original Result (Unit)	Standard Results (unit)	Reference Range [1]	Baseline Flag	CFB	Results Assessment / Reason CS	Lab ID Number	Fasting Status	Comments
XXXXX/ XXXX	Chemistry panel	XXXXXX							ND: xxx			
XXXXX/ XXXX	Albumin	XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY	Y			XXXXXXX	Y	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X	H-CS / XXX	XXXXXXX	Y	XXXX
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X		XXXXXXX	Y	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X	H-NCS	XXXXXXX	N	

CFB = change from baseline; CS = clinically significant; H = High; L = Low; NCS = not clinically significant; ND = not done.
Note: Study Day is calculated relative to the date of first dose.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
[1] Reference range is used to identify potentially clinically significant laboratory values.

Programming Notes:

- Keep parameter sorting from the last bullet point below.
- For results assessment, do not populate column if result is normal.
- Sort by Treatment Arm/ Subject ID / Parameter / Date time of collection.
- If the whole panel is not done at a visit, present the information on first row of the subject under 'Chemistry panel' parameter and don't present the 'not done' information for each parameter. Display "ND: reason why" in the result assessment column.
- Sort Parameters in the following Order: Albumin, Alkaline Phosphatase, Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Bicarbonate, Calcium, Chloride, Creatinine, High-Sensitivity C-Reactive Protein (hs-CRP), Estimated Glomerular Filtration Rate (eGFR by Cockcroft-Gault), Serum Glucose, Lactate Dehydrogenase (LDH), Potassium, Sodium, Total Bilirubin, Total Protein, Blood Urea Nitrogen (BUN), Uric Acid.

Listing 16.2.8.2
Hematology Laboratory Evaluations
Safety Population

Programming Notes:

- Same shell as Listing 16.2.8.1.
- Keep parameter sorting from the last bullet point below.
- For results assessment, do not populate column if result is normal.
- Sort by Treatment Arm/ Subject ID / Parameter / Date time of collection.
- If the whole panel is not done at a visit, present the information on first row of the subject under 'Hematology panel' parameter and don't present the 'not done' information for each parameter. Display "ND: reason why" in the result assessment column.
- Sort Parameters in the following Order: Absolute basophil count, absolute eosinophil count, absolute lymphocytes count, Absolute Monocyte Count, Absolute Neutrophil Count, Basophils %, Eosinophils %, Hematocrit (HCT), Hemoglobin (HGB), hemoglobin A1C (HgbA1C), Lymphocytes %, mean corpuscular hemoglobin (MHC), Mean Corpuscular Hemoglobin Concentration (MCHC), Mean Corpuscular Volume (MCV), Monocytes %, Neutrophils %, Platelets, Red blood cell count (RBC), Red Cell Distribution Width, white blood cell Count (WBC).

Listing 16.2.8.3
Coagulation Laboratory Evaluations
Safety Population

Programming Notes:

- Same shell as Listing 16.2.8.1.
- Keep parameter sorting from the last bullet point below.
- For results assessment, do not populate column if result is normal.
- Sort by Treatment Arm/ Subject ID / Parameter / Date time of collection.
- If the whole panel is not done at a visit, present the information on first row of the subject under 'Coagulation panel' parameter and don't present the 'not done' information for each parameter. Display "ND: reason why" in the result assessment column.
- Sort Parameters in the following Order: Activated Partial Thromboplastin Clotting Time (APTT), Fibrinogen, International normalized ratio (INR), Prothrombin Time (PT).

Listing 16.2.8.4
Urinalysis Laboratory Evaluations
Safety Population

Subject ID/ Treatment Arm	Parameter	Study Visit	Date/Time of Collection (Study Day)	Original Result (Unit)	Standard Results (unit)	Reference Range [1]	Baseline Flag	CFB	Results Assessment / Reason CS	Lab ID Number	Fasting Status	Comments
XXXXX	Urinalysis panel	XXXXXX							ND: xxx			
XXXXX	pH/ Specific Gravity	XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY	Y			XXXXXXX	Y	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X	H-CS / XXX	XXXXXXX	Y	XXXX
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X		XXXXXXX	Y	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X	H-NCS	XXXXXXX	N	
	Blood Urine/ Glucose/ Ketones/ Protein	XXXXXX	DDMMMYYYY/ HH:MM (X)	Trace			Y		H-NCS	XXXXXXX	Y	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	100 (mg/dL)	100 (mg/dL)				H-CS / XXX	XXXXXXX	Y	XXXX
		XXXXXX	DDMMMYYYY/ HH:MM (X)	Negative						XXXXXXX	N	

CFB = change from baseline; CS = clinically significant; H = High; L = Low; NCS = not clinically significant; ND = not done.
Note: Study Day is calculated relative to the date of first dose.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
[1] Reference range is used to identify potentially clinically significant laboratory values.

Programming Notes:

- Keep parameter sorting from the last bullet point below.
- For results assessment, do not populate column if result is normal.
- Sort by Treatment Arm/ Subject ID / Parameter / Date time of collection.
- If the whole panel is not done at a visit, present the information on first row of the subject under 'Urinalysis panel' parameter and don't present the 'not done' information for each parameter. Display "ND: reason why" in the result assessment column.
- Sort Parameters in the following Order: Blood Urine, Glucose, Ketones, pH, Protein, Specific Gravity.

Listing 16.2.8.5
Serology Laboratory Evaluations
Safety Population

Subject ID	Treatment Arm	Was Serology Test Collected?	Date/Time of Collection (Study Day)	Test (Unit) [1]	Result	Lab ID Number	Fasting Status	Reason not collected	Comments
XXXX	XXXX	Yes	DDMMMYYYY Y/HH:MM (X)	Hepatitis B Ag	Negative	XXXX	Y		XXXXXXXXX
				Hepatitis C Ab	Positive	XXXX	Y		
				HIV-1/ -2 Ag	Not Done	XXXX	Y	XXXXXXX	
				Quantiferon Gold Plus NIL	X.XX (IU/mL)	XXXX	Y		

Ab = antibody; Ag = antigen; HIV = human immunodeficiency virus; TB = tuberculosis.
Note: Study Day is calculated relative to the date of first dose.
[1] if Applicable

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Date of collection / Test.
- Keep parameter sorting from the last bullet point below
- Sort Parameters in the following Order: Hepatitis B Antigen, Hepatitis C Virus Antigen, Hepatitis C Virus Antibody, HIV-1/ -2 Antigen, Quantiferon Gold Plus NIL, Quantiferon Gold Plus TB, Quantiferon Gold Plus Mitogen minus NIL, Quantiferon Gold Plus TB1 minus NIL, Quantiferon Gold Plus TB2 minus NIL

Listing 16.2.8.6
Pregnancy Test Results
Safety Population

Subject ID	Treatment Arm	Visit	Was a Urine pregnancy test performed?	Date/Time Performed (Study Day)	If not, Reason	Result
xxxxx	xxxx	xxxxx	Xxxx	Ddmmmyyyy/ hh:mm (XX)	xxxx	xxxx
		xxxxx	Xxxx	Ddmmmyyyy/ hh:mm (XX)	Other: xxxx	xxxx

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment.

Listing 16.2.8.7
Drug Test Results
Safety Population

Subject ID	Treatment Arm	Was Drug Test Performed?	Date/ Time Assessment (Study Day)	Result	Findings	Reason Test not Performed
XXXXXX	XXXX	Yes	DDMMMYYYY/ HH:MM (XX)	Negative	Negative	
XXXXXX	XXXX	Yes	DDMMMYYYY/ HH:MM (XX)	Positive	Cocaine / Opiates	

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Concatenate all findings by "/"
- Sort by Treatment Arm/ Subject ID / Date of assessment.

Listing 16.2.8.8
COVID-19 Screening
Safety Population

Subject ID/ Treatment Arm	Visit	COVID-19 Sx Screening?/Date / Time (Study Day)	Sx	Body Tº Check?/ Date/ Time (Study Day)	Body Tº (Unit)	COVID-19 swab?/ Date/ Time (Study Day)	Swab result	COVID-19 Ab testing?/ Date/ Time (Study Day)	Ab testing results	COVID-19 Ag testing?/ Date/ Time (Study Day)	Ag testing results
xxxxx/ xxxx	xxxx	Yes/ Ddmmmyyyy/ hh:mm (XX)	XXX/ XXX	Yes/ Ddmmmyyyy/ hh:mm (XX)	XX (XX)	Yes/ Ddmmmyyyy/ hh:mm (XX)	Xxxx	Yes/ Ddmmmyyyy/ hh:mm (XX)	Xxxx	Yes/ Ddmmmyyyy / hh:mm (XX)	Xxxx
	xxxx	Yes/ Ddmmmyyyy/ hh:mm (XX)	XXX	Yes/ Ddmmmyyyy/ hh:mm (XX)	XX (XX)	Yes/ Ddmmmyyyy/ hh:mm (XX)	Xxxx	Yes/ Ddmmmyyyy/ hh:mm (XX)	Xxxx	Yes/ Ddmmmyyyy / hh:mm (XX)	Xxxx

Ab = Antibody; Ag = Antigen; COVID-19 = Coronavirus disease 2019; Sx = Symptoms; Tº = Temperature.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Concatenate all Symptoms by "/"
- Sort by Treatment Arm/ Subject ID / Date of assessment

Listing 16.2.9.1
Vital Signs Measurements
Safety Population

Subject ID	Treatment Arm	Parameter	Study Visit	Position [1] / Tº Method	Date/Time of Collection (Study Day)	Original Result (Unit)	Baseline Flag	CFB
XXXXX	XXXX	Body Temperature	XXXXXX	XXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	Y	
			XXXXXX	XXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)		XX
						...		
		Resting Heat Rate	Screening	Supine	DDMMMYYYY/ HH:MM (X)	XX		
			Day 1: Pre-Dose	Supine	DDMMMYYYY/ HH:MM (X)	XX	Y	XX
			XXXXXX	Supine	DDMMMYYYY/ HH:MM (X)	XX		XX
			XXXXXX	Sitting		ND		
			XXXXXX	Sitting	DDMMMYYYY/ HH:MM (X)	XX		XX

CFB = change from baseline; eCRF = Electronic Case Report Form; ND = not done.
Note: Study Day is calculated relative to the date of first dose.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
'Day 1: 5 minutes after Infusion Completion' time point was only applied to subjects enrolled in Stage 1, with data collected under eCRF versions 4.0 (11DEC2018) or older.
[1] Resting position measurements encompass Sitting and Supine position measurements.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Parameter (Order in the second bullet point)/ Date time of collection.
- Repeat for Resting Heart Rate, Resting Systolic Blood Pressure, Resting Diastolic Blood Pressure, Respiratory Rate, Body Temperature, Standing Heart Rate, Standing Systolic Blood Pressure, Standing Diastolic Blood Pressure.
- After Week 2 (inclusive), Supine measure are taken in sitting position. We will consider them as supine (in resting position) for calculating Change from Baseline (always at supine position).
- Include the following timepoints: Screening, Baseline (Day 1: Pre-Dose), Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week 10 + 24 hours, Week 11, Week 12, Week 18.
- Note that Body T°, and standing measures are not taken on Day 1, at 15, 30 and 45 minutes post-dose.

Listing 16.2.9.2.1
12-Lead Digital ECG Results
Safety Population

Subject ID/ Treatment Arm	Visit	ECG Date / Time (Study Day)	Tracing	PR Interval (msec)	QRS duration (msec)	QT Interval (msec)	RR interval (bpm)	Heart Rate (beats/min)	QTcF Interval (msec)	Findings	Reason Not Done
XXXXX	Day 1: Pre-Dose	DDMMMYYYY / HH:MM (XX)	1	xx	xx	xx	xx	xx	xx	xx: xxxxx	
			2	xx	xx	xx	xx	xx	xx		
			3	xx	xx	xx	xx	xx	xx	xx: xxxxx	
XXXXX	XXXX	DDMMMYYYY/ HH:MM (XX)	1	xx	xx	xx	xx	xx	xx	xx: xxxxx	
			2	xx	xx	xx	xx	xx	xx		
			3	xx	xx	xx	xx	xx	xx		

CS = clinically significant; ECG = electrocardiogram; NCS = Not clinically significant
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Date time of collection / Tracing.
- For Findings, concatenate test name with test result for category "FINDINGS".
- Include the following timepoints: Day 1: Pre-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 4, Week, 8, Week 12, and Week 18.

00Listing 16.2.9.2.2
12-Lead Safety ECG Results
Safety Population

Subject ID/ Treatment Arm	Visit	ECG Date / Time (Study Day)	Tracing	ECG Result/ Comment	PR Interval (msec)	QRS duration (msec)	QTcF Interval (msec)	Reason Not Done
XXXXX	Day 1: Pre-Dose	DDMMMYYYY / HH:MM (XX)	1	Abnormal CS/ xxxx	xx	xx	xx	
			2	Abnormal CS/ xxxx	xx	xx	xx	
			3	Abnormal NCS/ xxxx	xx	xx	xx	
XXXXX	XXXX	DDMMMYYYY/ HH:MM (XX)	1	Normal	xx	xx	xx	
			2	Normal	xx	xx	xx	
			3	Normal	xx	xx	xx	

CS = clinically significant; ECG = electrocardiogram; NCS = Not clinically significant
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Date time of collection / Tracing.
- Include the following timepoints: Screening, Day 1: Pre-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 4, Week, 8, Week 12, and Week 18.

Listing 16.2.9.3
Physical Examination Results
Safety Population

Subject ID	Treatment Arm	Visit	Examination Type	Exam Date/ Time (Study Day)	Body System	Result / Change from previous assessment [1]	If Abnormal, findings / Specify Changes [2]	Reason Not Done
XXXXX	XXXX	Screening	Complete	DDMMMYYYY / HH:MM (XX)	Head, Neck and Thyroid	Normal		
					Ears, Eyes, Nose and Throat	Abnormal CS	XXXXXXX	
		Day 1	Targeted	DDMMMYYYY / HH:MM (XX)	Ears, Eyes, Nose and Throat	XXXXXXXXXX	XXXXXXXX	

CS = Clinically Significant, NCS = Not Clinically Significant
Note: Study Day is calculated relative to the date of first dose.
[1] For targeted examination type: Change from previous assessment.
[2] For targeted examination type: Specify Changes.

Programming Notes:

- Keep sorting from eCRF: Head, Neck and Thyroid/ Ears, Eyes, Nose and Throat/ Chest (including breasts)/ Lungs / Heart / Lymph Nodes / Abdomen / Hepatic / Gastrointestinal / Anorectal / Genitourinary/ Skin / Musculoskeletal/Extremities / Neurological / Other.
- Complete Physical examination only at Screening, Week 12, 18 (it can also be unscheduled).
- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment / Body system

Listing 16.2.9.4
Neurological Examination Results
Safety Population

Subject ID	Treatment Arm	Visit	Exam Date/ Time (Study Day)	Body System	Result	If Abnormal, findings	Reason Not Done
XXXXX	XXXX	Screening	DDMMMYYYY / HH:MM (XX)	Mental Status	Normal		
				Cranial Nerves	Abnormal CS	XXXXXXX	
		Day 1	DDMMMYYYY / HH:MM (XX)	Cranial Nerves	XXXXXXXXXX	XXXXXXXX	

CS = Clinically Significant, NCS = Not Clinically Significant
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Keep sorting from eCRF: Mental status/ Cranial Nerves/ Motor Function/ Reflexes / Sensation and Propioception / Coordination / Other.
- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment / Body system

Listing 16.2.9.5
Total Neuropathy Score-Nurse
Safety Population

Subject ID/ Treatment Arm	Visit	Date/ Time of collection (Study Day)	Sensory Symptom Score (0–4)	Motor Symptom Score (0–4)	Autonomic Symptom Score (0–4)	Pin Sensibility Score (0–4)	Vibration Sensibility Score (0–4)	TNSn Total (0–20)	Reason Not Done
XXXXX/ XXXX	Screening	DDMMMYYYY / HH:MM (XX)	XX	XX	XX	XX	XX	XX	
	Day 1	DDMMMYYYY / HH:MM (XX)	XX	XX	XX	XX	XX	XX	
	Week 2	DDMMMYYYY / HH:MM (XX)	ND	ND	ND	ND	ND	ND	XXXXXXXXXXXXXX

ND = Not Done; TNSn = Total Neuropathy Score-Nurse.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment

Listing 16.2.9.6
Motor and Sensory Nerve Conduction Studies
Safety Population

Subject ID/ Treatment Arm	Visit	Date / Time of Collection (Study Day)	Location / Evaluation	Was Evaluation Preformed ? / Nerve	Amplitude (Motor = mV; sensory = microV) / Range	Peak Latency (msec) / Range	Conduction velocity (msec) / Range	Duration of action potential (msec) / Range	Evaluation Result	If Abnormal, Specify/ Reason Not Done	Significant Changes from Baseline? / if Yes, Specify
XXXX/ XXXX	Screening	DDMMMYYYY / HH:MM (XX)	Lower Limb - Right Side/ Motor Evaluation	Y/ XXXXXX	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	Abnormal	XXXXX	NA
			XXXXXX/ XXXXXX	Y/ XXXXXX	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	Normal		NA
			XXXXXX/ XXXXX	N							
	Week 18	DDMMMYYYY/ HH:MM (XX)	XXXXXX/ XXXXX	Y/ XXXXXX	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	Abnormal	XXXXX	N
			XXXXXX/ XXXXX	Y/ XXXXXX	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	Normal		N
			XXXXXX/ XXXXX	Y/ XXXXXX	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	Abnormal	XXXXX	Y/ XXXXXXX

NA = Not Applicable
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment / Location - Evaluation
- Keep sorting from eCRF: Lower Limb - right side/Motor evaluation, Lower Limb - right side/Sensory evaluation, Lower Limb - left side/ Motor evaluation, Lower Limb - left side/ Sensory evaluation, Upper Limb - right side /Motor evaluation, Upper Limb - right side/ Sensory evaluation, Upper Limb - left side/ Motor evaluation, Upper Limb - left side /Sensory evaluation.

Listing 16.2.9.7
Strength and Deep Tendon Reflexes
Safety Population

Subject ID	Treatment Arm	Visit	Date/ Time of collection (Study Day)	Ankle Dorsiflexion Strength	Deep Tendon Reflexes	Reason Not Done
XXXXX	XXXX	Screening	DDMMMYYYY / HH:MM (XX)	XXXX	XXXX	
		Day 1	DDMMMYYYY / HH:MM (XX)	XXXX	XXXX	
		Week 2	DDMMMYYYY / HH:MM (XX)	ND	ND	XXXXXXXXXXXXXX

ND = Not Done.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment

Listing 16.2.9.8
Injection Site Reactions
Safety Population

Subject ID	Treatment Arm	Visit	Date/ Time of Assessment (Study Day)	Pain	Tenderness	Erythema/redness	Induration/ swelling	Reason Not Done
XXXXX	XXXX	Day 1: 15 Minutes after Start of Infusion	DDMMMYYYY / HH:MM (XX)	XXXX	XXXX	XXXX	XXXX	
		Day 1: 30 Minutes after Start of Infusion	DDMMMYYYY / HH:MM (XX)	XX	XX	XX	XX	
		...						
		Week 18	DDMMMYYYY / HH:MM (XX)	ND	ND	ND	ND	XXXXXXXXXXXXXX

ND = Not Done.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment
- Include the following timepoints: Day 1: 15 Minutes after Start of Infusion, Day 1: 30 Minutes after Start of Infusion, Day 1: 45 Minutes after Start of Infusion, Day 1: 60 Minutes after Start of Infusion, Day 1: 2 hours after Start of Infusion, Day 1: 4 hours after Start of Infusion, Week 2, Week 4, Week 6, Week, 8, Week 10, Week 12, and Week 18.

Listing 16.2.9.9
Hypersensitivity/Anaphylactic Reactions
Safety Population

Subject ID	Treatment Arm	AE ID Number	Onset Date/Time (Study Day)/ Resolution Date/Time (Study Day)	Type of Reaction	Severity grade for the Symptom with Highest Severity	Onset Time for Highest Severity	Leading to IP Discontinuation?
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXX	XXXX	/HH:MM	Yes
		X	DDMMMYYYY/HH:MM (X)/ DDMONYYYY/HH:MM (X)	XXXXX			No
		...					
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ DDMONYYYY/HH:MM (X)	XXXXX	XXXX	/HH:MM	No

AE = Adverse Event.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Onset Date/Time / Resolution Date/Time / Reaction Type.
- Keep sorting from eCRF: Urticaria, Pruritus, Rash, Flushing, Swollen lips, tongue, uvula and/or vulva, Dyspnoea, Wheeze-bronchospasm, Stridor, Hypoxia, Hypotension, Crampy abdominal pain, Vomiting, Diarrhoea, Other.

Listing 16.2.9.10
Liver Diagnostic Investigations
Safety Population

Subject ID	Treatment Arm	Potential Hy's Law Case Number	Liver Diagnostic Investigation Date (Study Day)	Liver Diagnostic Investigation	Liver Diagnostic Investigation Results	Comments
XXXXX	XXXX	X	DDMMMYYYY (X)	XXXX	XXXX	XXXXX
		X	DDMMMYYYY (X)	XXXXX	XXXXX	
		...				
XXXXX	XXXX	X	DDMMMYYYY (X)	XXXXX	XXXXX	

CT = Computerized tomography; ERCP = Endoscopic retrograde cholangiopancreatography; MRI = Magnetic resonance imaging; MRCP = Magnetic resonance cholangiopancreatography.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Diagnostic Date / Liver Diagnostic Investigation.
- Keep sorting from eCRF: Ultrasound, CT, MRI/MRCP, ERCP, Liver Biopsy, X-Ray, Tox Screening for Acetaminophen/Paracetamol, Tox Screening for Ethanol, Tox Screening, Other, Specialist (e.g. Hepatologist) Consulted, Serology for Hepatitis A, Serology for Hepatitis B, Serology for Hepatitis C, Serology for Hepatitis D, Serology for Hepatitis E, for Cytomegalovirus (CMV), Serology for Epstein Barr Virus (EBV), Autoimmune Serology, Other.

Listing 16.2.9.11
Liver Risk Factors and Lifestyle Events
Safety Population

Subject ID	Treatment Arm	Potential Hy's Law Case Number	Assessment Date (Study Day)	Liver Risk Factor Start Date (Study Day)/ Liver Risk Factor Stop Date (Study Day)	Liver Risk Factor / Reference Period	Liver Risk Factor Details	Comments
XXXXX	XXXX	X	DDMMMYYYY (X)	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXX/ XXX	XXXX	XXXXX
		X	DDMMMYYYY (X)	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXXX/ XXX	XXXXX	
		...					
XXXXX	XXXX	X	DDMMMYYYY (X)	DDMMMYYYY (X)/ Ongoing	XXXXX/ XXX	XXXXX	

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Assessment Date / Liver Risk Factor Start Date / Stop Date / Liver Risk Factor.
- Keep sorting from eCRF: Alcohol Abuse, Increased Alcohol Consumption within 1 Month of Reported Event, IV Drug Abuse, Tattoo, Acupuncture, Sexually Transmitted Diseases, Toxic/Chemical Agent Exposure, Travel (Areas at Risk in the Last Year), Pregnancy, Parenteral Nutrition, Excessive Physical Exercise, Changes Diet/Fasting Episodes/Weight Loss Diet, Previous Drug Reaction (Associated with an Elevation of Liver Tests), Blood Transfusion, Subject Exposed to Anyone with Jaundice in the Last Month, History of Hypotension, Low Blood Pressure at Time of Event of Liver Injury and/or Abnormal Liver Laboratory Value, History of Liver Disease, Other.
- Concatenate comments with "/".

Listing 16.2.9.12
Liver Signs and Symptoms
Safety Population

Subject ID	Treatment Arm	Potential Hy's Law Case Number	Start Date (Study Day)/ Stop Date (Study Day)	Liver Sign/ Symptom	Intermittent
XXXXX	XXXX	X	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXX	N
		X	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXXX	N
		...			
XXXXX	XXXX	X	DDMMMYYYY (X)/ Ongoing	XXXXX	Y

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Start Date / Stop Date / Liver Sign/Symptom.
- Keep sorting from eCRF: Anorexia, Asthenia, Pyrexia, Pruritus, Jaundice, Arthralgia, Abdominal Pain, Abdominal Tenderness, Nausea, Vomiting, Rash, Mucosal Inflammation, Purpura, Hepatomegaly, Splenomegaly, Lymphadenopathy, Ascites, Confusional State, Coma, Upper Quadrant Tenderness, Biliary Obstruction, Eosinophilia, Dark Urine, Other.
- If Rash, Lymphadenopathy or Other, Concatenate Symptom with Comment as: "Rash: xxxxxx". "Lymphadenopathy: xxxxxx", "Other: xxxxxxxx"

Listing 16.2.9.13
Infection Diagnostic Investigations
Safety Population

Subject ID	Treatment Arm	AE ID Number	Start Date/ Time (Study Day)/ Stop Date/ Time (Study Day)	Method	Examination performed	Test Result
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXX	Y	XXXXX
		X	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X))	XXXXX	Y	XXXXX
		...				
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ Ongoing	XXXXX	N	XXXXX

AE = adverse event.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Start Date / Stop Date / Method.
- Keep sorting from eCRF: Microscopy, Culture and Sensitivity, Serological Tests, Nucleic Acid Based Tests, X-Ray, Other.

Listing 16.2.9.14
Infection Risk Factors and Lifestyle Events
Safety Population

Subject ID	Treatment Arm	AE ID Number	Start Date/ Time (Study Day)/ Stop Date/ Time (Study Day)	Infection Risk Factor	Infection Risk Occurrence	Comments
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXX	Y	XXXXX
		X	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X))	XXXXX	Y	XXXXX
		...				
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ Ongoing	XXXXX	N	Ongoing

AE = adverse event; BCG = Bacillus Calmette–Guérin.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Start Date / Stop Date / Infection Risk Factor.
- Keep sorting from eCRF: Extensive Burns within the Last Year (Thermal Burn), Tattoo, Piercing or Acupuncture within the Last Year, Sexually Transmitted Diseases, Travel to Areas at Risk of Tuberculosis or Tropical Diseases, Infections Related to Travel (e.g. Tuberculosis and Tropical Diseases), Blood Transfusion (within the Last Year), Exposure to Nosocomial Pathogens within the Last Year, Contact History with Infection Source, Previous BCG Immunization, Evidence of BCG Scar, Tuberculin Skin or Quantiferon Test Confirms Previous Exposure or Immunity to Tuberculosis.
- Fill Comment column if Infection risk factor test = Unknown Previous BCG Immunization, not done, known Sexually Transmitted Disease reference Period, or Infection risk factor specifications.

Listing 16.2.9.15
Infection Signs and Symptoms
Safety Population

Subject ID	Treatment Arm	AE ID Number	System Organ Class/ Preferred Term/ Verbatim Term	Start Date/ Time (Study Day)/ Stop Date/ Time (Study Day)	Clinical Event	Infection Sign/Symptom Occurrence	Comments
XXXXX	XXXX	X	XXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXX	Y	XXXXX
		X	XXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X))	XXXXX	Y	XXXXX
		...					
XXXXX	XXXX	X	XXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ Ongoing	XXXXX	N	Ongoing

AE = adverse event.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Start Date / Stop Date / Clinical Event.
- Keep sorting from eCRF: Pyrexia, Headache, Confusional State, Convulsion, Rhinitis, Oropharyngeal Pain, Cough, Productive Cough, Haemoptysis, Wheezing, Dyspnoea, Pleuritic Pain, Vomiting, Diarrhoea, Genital Discharge, Haematuria, Dysuria, Hepatosplenomegaly, Jaundice, Lymphadenopathy, Rash, Night sweats, Chills, Myalgia, Weight Decrease.
- Fill Comment column if Maximum Tº (Unit) available for Pyrexia, or if site for Rash or Lymphadenopathy is known.

Listing 16.2.9.16
Prior and Concomitant Medications
Safety Population

Subject ID/ Treatment Arm	Prior/ Concomitant [1]	ATC Class (Level 2)/ Preferred Name/ Verbatim Term	Given for/as	Primary Indication	Start Date (Study Day)/ End Date (Study Day)	Dose (unit)	Route	Frequency
XXXXXX / XXXX	Prior	XXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	Medical History	XXXXXXX	--MMMYYYY (-XX)/ DDMMMYYYY (-X)	XXXX unit	XXXXXX XXX	XXXXX
	Both	XXXXXXXXX/ XXXXXXXXXXXXXXX/ XXXXXXXXXXX	Prophylaxis	XXXXXXX	--MMMYYYY (-X)/ Ongoing	XXXX unit	XXXXXX XXX	XXXXX
	Concomitant	XXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX	Adverse event	XXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (XX)	XXXX unit	XXXXXX XXX	XXXXX

ATC = anatomical therapeutic chemical; WHO-DDE = World Health Organization-Drug Dictionary Enhanced.
Note: Study Day is calculated relative to the date of first dose.
Medications were coded using WHO-DDE version vMar2023.
[1] Prior medications are defined as medications that started before first dose of study, whether they were stopped before first dose of study medication or not. Concomitant medications are defined as medications starting on or after first dose of study medication Both indicates medication that was started before the day of first dose and continued after.

Programming Notes:

- ATC & Preferred Name text should be in proper case in table.
- Ensure proper WHO-DDE version is printed in footnote.
- Sort by subject, start date/time, end date/time, ATC level 2 & Preferred Name .
- If Dose unit, Route or Frequency is Other, display other specify text only (ie, do not display “Other: XXXXXX” but just “XXXXXX “).
- Adjust footnotes for frequency and routes as needed.
- Sort by Treatment ID/ Subject ID / Start Date / End Date (alphabetically for ATC Class Level 2 if same date for two medications)

Listing 16.2.9.17
Prohibited Concomitant Medications
Safety Population

Programming Notes:

- Same Shell as Listing 16.2.9.16.
- Display prohibited prior and concomitant medications provided by the Medical Coder:
- Prohibited concomitant medications:
  - NSAIDs analgesic therapies (with acetylsalicylic acid with doses >= 325 mg/day).
  - COX-2 analgesic therapies.
  - Immunotherapeutics.
  - Live viral or attenuated bacterial vaccines.
  - Oral, IV, intramuscular, or any other parenteral (other than oral) steroids (inhaled or topical steroids are permitted).
  - Biologic therapeutic agents.
- Prohibited prior and/or concomitant medications:
  - Anti-NGF therapies.
  - Anti-TNF therapies.
- ATC & PN text should be in proper case in table.
- Ensure proper WHO-DDE version is printed in footnote.
- Sort by subject, start date/time, end date/time, ATC level 2 & Preferred Name .
- If Dose unit, Route or Frequency is Other, display other specify text only (ie, do not display “Other: XXXXXX” but just “XXXXXX “).
- Adjust footnotes for frequency and routes as needed.
- Sort by subject ID / Start Date / End Date (alphabetically for ATC Class Level 2 if same date for two medications)

Listing 16.2.9.18
Concomitant Procedures
Safety Population

Subject ID	Treatment Arm	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ End Date (Study Day)	Reason for Procedure	Reason (derived verbatim term)	If Reason is Other, Specify
XXXXX	XXXX	XXXXXXXXXXX/ XXXXXXXXXXXXX XXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXX	
XXXXX	XXXX	XXXXXXXXXXXXX/ XXXXXXXXXXXXX XXXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXX	
XXXXX	XXXX	XXXXXXXXXXXXX/ XXXXXXXXXXXXX XXXXXXXXXX	DDMMMYYYY (X)/ Ongoing	OTHER	OTHER	XXXXXXXXXX

MedDRA = Medical Dictionary for Regulatory Activities.
Note: Study Day is calculated relative to the date of first dose. All Procedure terms were coded using the MedDRA version 26.0. Concomitant Procedures are defined as medications continuing or starting on or after first dose of study medication.

Programming Notes:

- SOC & PT text should be in proper case in table.
- Sort by Treatment Arm/ Subject ID / Start Date / End Date (alphabetically for SOC if same date for two events).
- In case a term is not coded (e.g. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]". SOC and PT abbreviations should be added in this case in footnote.

Listing 16.2.9.19
Anti-drug Antibody Test Results
Safety Population

Subject ID	Treatment Arm	Study Visit	Date/Time of Collection (Study Day)	Screening Status Result	Confirmatory Status result	ADA Titer	Lab ID Number	Comments
XXXXX	XXXX	XXXXXX	DDMMMYYYY/ HH:MM (X)	Positive	Positive	xx	XXXXXXX	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	Positive	Positive	xx	XXXXXXX	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	Negative	Negative	xx	XXXXXXX	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	Missing	Not Reportable Result	NRR	XXXXXXX	XXXX

ADA = Anti-Drug Antibodies; NA = Not Applicable; NRR = Not Reportable Result; QNS = Quantity Not Sufficient.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Collection Date.
- ADA titre reported as <30 (below the minimum required dilution) is a negative result for the presence of ADA.
- Include Following timepoints: Screening, Weeks 2, 4, 8, 10, 12, 18.

Listing 16.2.10.1
Serum MEDI7352 Concentrations
PK Population

Subject ID	Treatment Arm	Study Visit	PK Blood Sample Collected? / Reason Not Collected	Date/Time of Collection (Study Day)	MEDI7352 Concentration (ng/mL)	Lab ID Number	Comments
XXXXX	XXXX	XXXXXX	Yes	DDMMMYYYY/ HH:MM (X)	XX	XXXXXXX	
		XXXXXX	Yes	DDMMMYYYY/ HH:MM (X)	XX	XXXXXXX	
		XXXXXX	Yes	DDMMMYYYY/ HH:MM (X)	NRR	XXXXXXX	XXXX
		XXXXXX	No / XXXXXX				

NA = Not Applicable; NRR = Not Reportable Result.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Collection Date.
- Include the following timepoints: Day 1, Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours: after Week 10/ Pre-Dose, Week 11: after Week 10/ Pre-Dose, Week 10 + 14 Days: after Week 10/ Pre-Dose, Week 18.

Listing 16.2.10.2
Serum total NGF Concentrations
Safety Population

Subject ID	Treatment Arm	Study Visit	PD Blood Sample Collected? / Reason Not Collected	Date/Time of Collection (Study Day)	Total NGF Concentration (pg/mL)	Lab ID Number	Comments
XXXXX	XXXX	XXXXXX	Yes	DDMMMYYYY/ HH:MM (X)	XX	XXXXXXX	
		XXXXXX	Yes	DDMMMYYYY/ HH:MM (X)	XX	XXXXXXX	
		XXXXXX	Yes	DDMMMYYYY/ HH:MM (X)	NS	XXXXXXX	XXXX
		XXXXXX	No / XXXXXX				

BLLOQ = Below the Lowest Limit of Quantitation; NA = Not Applicable; ND = Not Detected; NS = No Value due to Insufficient Volume or No Sample Received; PD: Pharmacodynamic; SAT = Greater than the Top of the Standard Curve; tNGF = total Nerve-Growth Factor.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Collection Date.
- Include the following timepoints: Day 1, Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 12; Week 18.

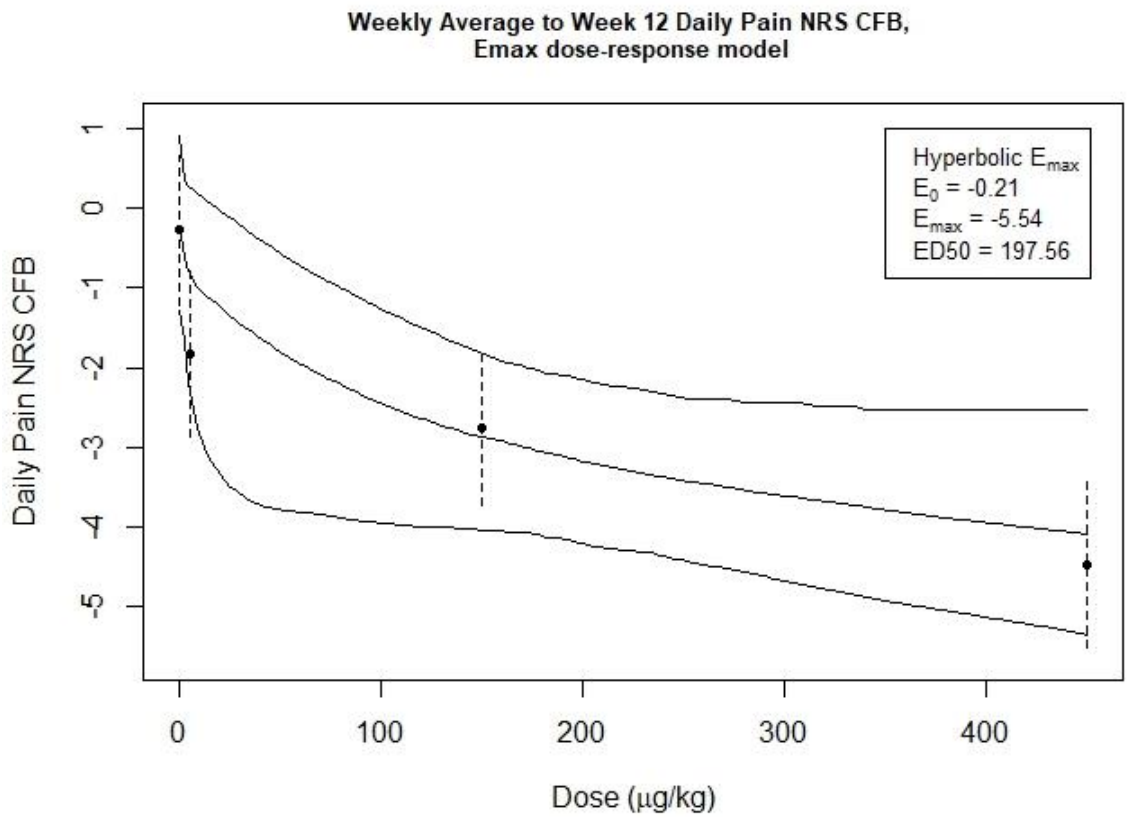
Planned Figure Descriptions and Shells

Number Title Population	Unique (U) or Repeated (R)
Figure 14.2.1.1 - Daily Pain NRS: MCP-Mod Dose Response Model - mITT Population	U
Figure 14.2.1.2 - Daily Pain NRS CFB: Boxplots at Week 12 by Treatment Group and Missing Data Handling - mITT Population	U
Figure 14.2.1.3 - Daily Pain NRS CFB: Boxplots at Week 12 by Treatment Group and Co-Medication Subgroup - mITT Population	R
Figure 14.2.1.4 - Daily Pain NRS: MMRM LS Means (95% Confidence Interval) over 12-weeks by Treatment Group (Observed Cases) - mITT Population	U
Figure 14.3.6.1.1 - Vital Sign Profiles: Mean (±SD) Systolic Blood Pressure over time - Safety Population	U
Figure 14.3.6.1.2 - Vital Sign Profiles: Mean (±SD) Diastolic Blood Pressure over time - Safety Population	R
Figure 14.3.6.1.3 - Vital Sign Profiles: Mean (±SD) Heart Rate over time - Safety Population	R
Figure 14.3.6.1.4 - Vital Sign Profiles: Mean (±SD) Respiratory Rate over time - Safety Population	R
Figure 14.3.6.1.5 - Vital Sign Profiles: Mean (±SD) Temperature over time - Safety Population	R
Figure 14.4.1.1 - Pharmacokinetics: Line Plot of Geometric Mean (with and without gSD) Serum MEDI7352 over time - PK Population	R
Figure 14.4.1.2 - Pharmacokinetics: Individual Plot of Serum MEDI7352 Concentrations over time - PK Population	U
Figure 14.4.2.1 - Pharmacodynamics: Line Plot of Geometric Mean (with and without gSD) total NGF over time - Safety Population	R
Figure 14.4.2.2 - Pharmacodynamics: Individual Plot of Serum total NGF over time - Safety Population	R

Figures Change Log

Output Number	Date of Change	Change Made By (initials)	Description/Rationale

Figure 14.2.1.1
Daily Pain NRS: MCP-Mod Dose Response Model
mITT Population

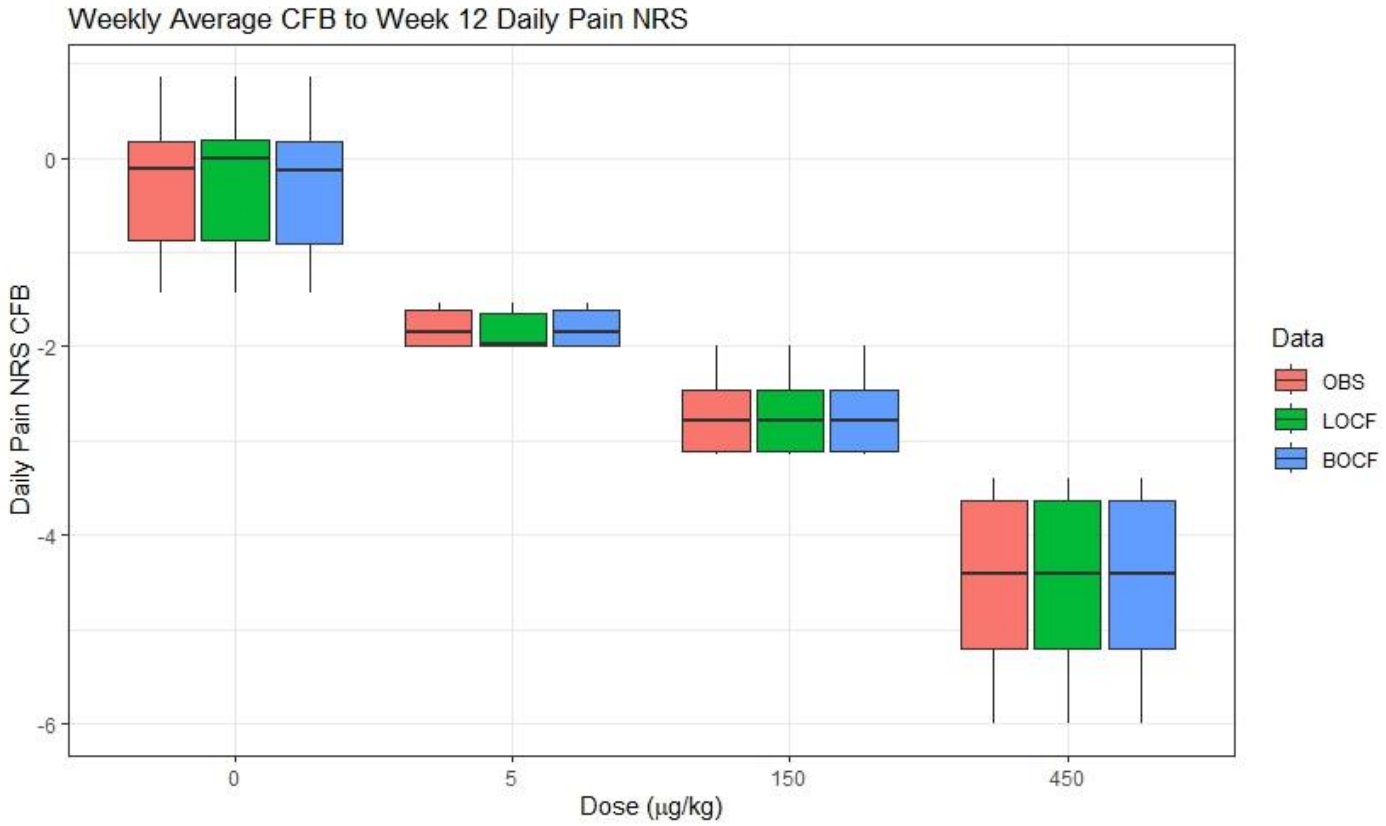


CI = Confidence Interval; CFB = Change from Baseline; DPS = Daily Pain Score; NRS = Numeric Rating Scale.
Baseline is defined as the average of the 'non-missing' DPS within the seven-day period prior to randomization i.e., Day -7 to Day -1, inclusive. Envelope depicts 95% CI of mean dose-response. Added dots are actual doses ± 95% CI.
mITT Population = includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
Reference Listing: 16.2.6.1

Programming Notes:

- Insert the following text as legend: "Weekly Average to Week 12 Daily Pain NRS CFB, xxxx dose-response model", with 'xxxx' as the selected dose-response model (e.g., Hyperbolic E_{max}).
- Dose (µg/kg) in x axis and Daily Pain NRS CFB in y axis.
- Add model parameter values as an inset plot. For e.g., Sigmoid E_{max}; E_0 = xxx, E_{max} = xxx, ED50 = xxx, λ = xxx.
- The MCP-MOD approach will only be performed if stage 4 is initiated, otherwise there would be insufficient dosing data to fit the non-linear models.

Figure 14.2.1.2
Daily Pain NRS CFB: Boxplots at Week 12 by Treatment Group and Missing Data Handling
mITT Population



BOCF = Baseline Observation Carried Forward; CFB = Change from Baseline; DPS = Daily Pain Score; LOCF = Last Observation Carried Forward; NRS = Numeric Rating Scale; OBS = Observed Cases.
Baseline is defined as the average of the 'non-missing' DPS within the seven-day period prior to randomization i.e., Day -7 to Day -1, inclusive.
mITT Population = includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
Reference Listing: 16.2.6.1

Programming Notes:

- Insert the following text as legend: “Weekly Average CFB to Week 12 Daily Pain NRS”.
- Dose (µg/kg) and Observed/LOCF/BOCF in x axis and Daily Pain NRS CFB in y axis.
- A level for CCI dosing (CCI) will only be added if Stage 4 is initiated.

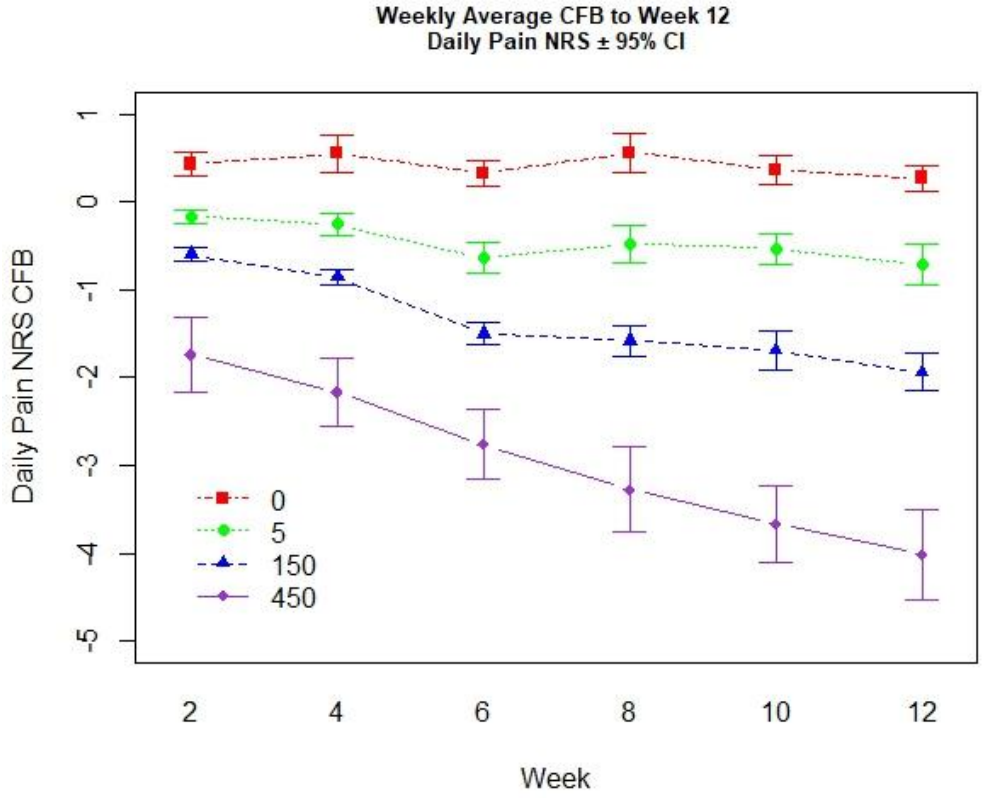
Figure 14.2.1.3
Daily Pain NRS CFB: Boxplots at Week 12 by Treatment Group and Co-Medication Subgroup
mITT Population

CFB = Change from Baseline; DPS = Daily Pain Score; NRS = Numeric Rating Scale.
Baseline is defined as the average of the 'non-missing' DPS within the seven-day period prior to randomization i.e., Day -7 to Day -1, inclusive.
mITT Population = includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
Reference Listing: 16.2.6.1

Programming Notes:

- Same shell as Figure 14.2.1.2
- Insert the following text as legend: "Weekly Average CFB to Week 12 Daily Pain NRS".
- Dose (µg/kg) in x axis, Anticonvulsant/ Antidepressant/ Both/ None in right side Co-medication labels, and Daily Pain NRS CFB in y axis.
- A level for CCI [redacted] dosing (CCI [redacted]) will only be added if Stage 4 is initiated.

Figure 14.2.1.4
Daily Pain NRS: MMRM LS Means (95% Confidence Interval) over 12-weeks by Treatment Group (Observed Cases)
mITT Population



CFB = Change from Baseline; CI = Confidence Interval; DPS = Daily Pain Score; LS = Least Square; MMRM = Mixed Model for Repeated Measures; NRS = Numeric Rating Scale.
Baseline is defined as the average of the 'non-missing' DPS within the seven-day period prior to randomization i.e., Day -7 to Day -1, inclusive.
mITT Population = includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
Reference Listing: 16.2.6.1

Programming Notes:

- Insert the following text as legend: "Weekly Average CFB to Week 12 Daily Pain NRS ± 95% CI".
- Week in x axis and Daily Pain NRS CFB in y axis.
- **Include a profile for each dose treatment group.**
- Include the following timepoints: Week 2, 4, 6, 8, 10, and 12.
- **Extract data for this figure from the MMRM of CFB Daily Pain NRS with Observed Cases.**
- A profile for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.3.6.1.1
Vital Sign Profiles: Mean (±SD) Systolic Blood Pressure over time
Safety Population

1H PD = 1 Hour Post-Dose; 15M PD = 15 Minutes Post-Dose; 2H PD = 2 Hours Post-Dose; 30M PD = 30 Minutes Post-Dose; 4H PD = 4 hours Post-Dose; 45M PD = 45 Minutes Post-Dose; 5M PD = 5 minutes after Infusion Completion; BASE = Baseline; D1 = Day 1; SBP = Systolic Blood Pressure; W2 = Week 2; W4 = Week 4; W6 = Week 6; W8 = Week 8; W10 = Week 10; W11 = Week 11; W12 = Week 12; W18 = Week 18.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
Reference Listing: 16.2.9.1

Programming Notes:

- Same shell as Figure 14.2.1.4
- Insert the following text as legend: "Average SBP ± Standard Deviation".
- Study Visit in x axis and Systolic Blood Pressure (mmHg) in y axis.
- **Include a profile for Resting SBP and another for Standing SBP.**
- Include the following timepoints: Baseline, Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week 10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- Note that standing measures are not taken on Day 1, at 15, 30 and 45 minutes post-dose.
- **Make one plot for each dose treatment group, for a total of 4 plots with two profiles each.**
- A plot for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.3.6.1.2
Vital Sign Profiles: Mean (±SD) Diastolic Blood Pressure over time
Safety Population

1H PD = 1 Hour Post-Dose; 15M PD = 15 Minutes Post-Dose; 2H PD = 2 Hours Post-Dose; 30M PD = 30 Minutes Post-Dose; 4H PD = 4 hours Post-Dose; 45M PD = 45 Minutes Post-Dose; 5M PD = 5 minutes after Infusion Completion; BASE = Baseline; D1 = Day 1; DBP = Diastolic Blood Pressure; W2 = Week 2; W4 = Week 4; W6 = Week 6; W8 = Week 8; W10 = Week 10; W11 = Week 11; W12 = Week 12; W18 = Week 18.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
Reference Listing: 16.2.9.1

Programming Notes:

- Same shell as Figure 14.2.1.4
- Insert the following text as legend: "Average DBP ± Standard Deviation".
- Study Visit in x axis and Diastolic Blood Pressure (mmHg) in y axis.
- **Include a profile for Resting DBP and another for Standing DBP.**
- Include the following timepoints: Baseline, Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week 10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- Note that standing measures are not taken on Day 1, at 15, 30 and 45 minutes post-dose.
- **Make one plot for each dose treatment group, for a total of 4 plots with two profiles each.**
- A plot for CCI dosing (CCI) will only be added if Stage 4 is initiated)

Figure 14.3.6.1.3
Vital Sign Profiles: Mean (±SD) Heart Rate over time
Safety Population

1H PD = 1 Hour Post-Dose; 15M PD = 15 Minutes Post-Dose; 2H PD = 2 Hours Post-Dose; 30M PD = 30 Minutes Post-Dose; 4H PD = 4 hours Post-Dose; 45M PD = 45 Minutes Post-Dose; 5M PD = 5 minutes after Infusion Completion; BASE = Baseline; D1 = Day 1; HR = Heart Rate; W2 = Week 2; W4 = Week 4; W6 = Week 6; W8 = Week 8; W10 = Week 10; W11 = Week 11; W12 = Week 12; W18 = Week 18.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
Reference Listing: 16.2.9.1

Programming Notes:

- Same shell as Figure 14.2.1.4
- Insert the following text as legend: "Average HR ± Standard Deviation".
- Study Visit in x axis and Heart Rate (Beats/min) in y axis.
- **Include a profile for Resting HR and another for Standing HR.**
- Include the following timepoints: Baseline, Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week 10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- Note that standing measures are not taken on Day 1, at 15, 30 and 45 minutes post-dose.
- **Make one plot for each dose treatment group, for a total of 4 plots with two profiles each.**
- A plot for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.3.6.1.4
Vital Sign Profiles: Mean (±SD) Respiratory Rate over time
Safety Population

1H PD = 1 Hour Post-Dose; 15M PD = 15 Minutes Post-Dose; 2H PD = 2 Hours Post-Dose; 4H PD = 4 hours Post-Dose; 5M PD = 5 minutes after Infusion Completion; BASE = Baseline; D1 = Day 1; W2 = Week 2; W4 = Week 4; W6 = Week 6; W8 = Week 8; W10 = Week 10; W11 = Week 11; W12 = Week 12; W18 = Week 18.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
Reference Listing: 16.2.9.1

Programming Notes:

- Same shell as Figure 14.2.1.4
- Insert the following text as legend: "Average Respiratory Rate ± Standard Deviation".
- Study Visit in x axis and Respiratory Rate (Breaths/min) in y axis.
- Include the following timepoints: Baseline, Day 1: 15 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- **Make one plot with 4 profiles (one for each treatment group).**
- A profile for CCI dosing (CCI) will only be added if Stage 4 is initiated.

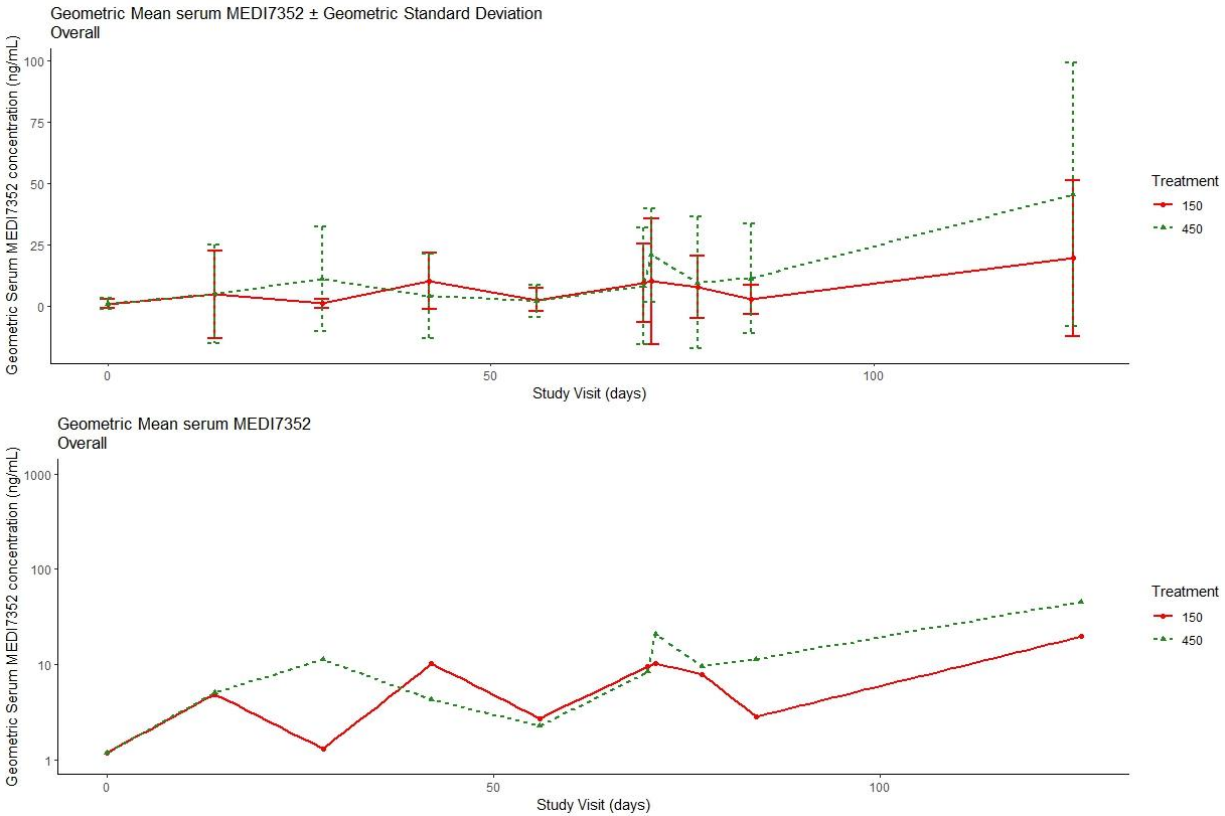
Figure 14.3.6.1.5
Vital Sign Profiles: Mean (±SD) Temperature over time
Safety Population

1H PD = 1 Hour Post-Dose; 2H PD = 2 Hours Post-Dose; 4H PD = 4 hours Post-Dose; 5M PD = 5 minutes after Infusion Completion; BASE = Baseline; D1 = Day 1; T° = Temperature; W2 = Week 2; W4 = Week 4; W6 = Week 6; W8 = Week 8; W10 = Week 10; W11 = Week 11; W12 = Week 12; W18 = Week 18.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
Reference Listing: 16.2.9.1

Programming Notes:

- Same shell as Figure 14.2.1.4
- Insert the following text as legend: "Average Body Tº ± Standard Deviation".
- Study Visit in x axis and Body Temperature (ºC) in y axis.
- Include the following timepoints: Baseline, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- **Make one plot with 4 profiles (one for each treatment group).**
- A plot for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.4.1.1
Pharmacokinetics: Line Plot of Geometric Mean (with and without gSD) Serum MEDI7352 Concentrations over Time
PK Population



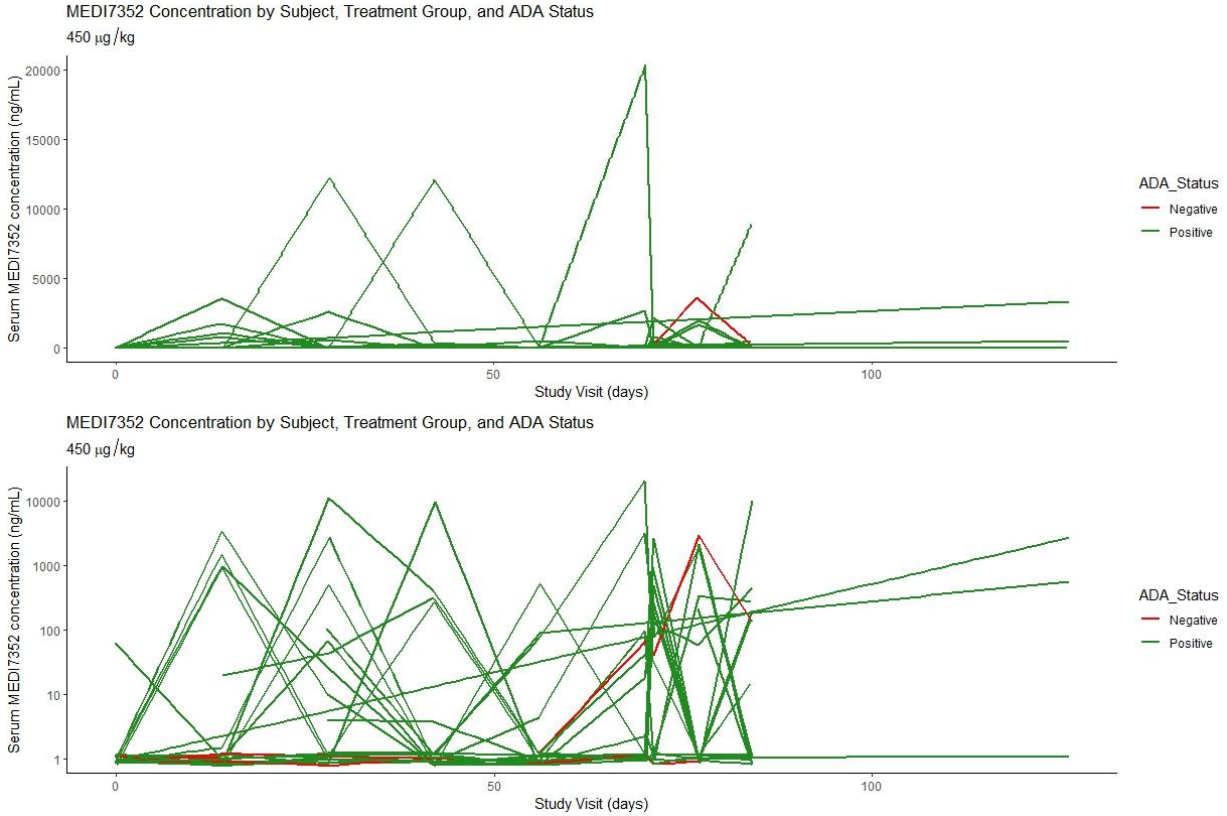
ADA = Antidrug Antibodies; gSD = Geometric Standard Deviation; LLOQ = Lower Limit of Quantification.

PK Population = includes all subjects for who a pharmacokinetic sample was obtained and analyzed.
ADA positive represents participants with at least one positive ADA result.
ADA negative represents participants with only negative ADA results (no positive).
Reference Listing: 16.2.10.1

Programming Notes:

- Insert the following text as upper legend: "Geometric Mean serum MEDI7352 ± Geometric Standard Deviation (Linear Scale)" followed by "Geometric Mean serum MEDI7352" for the linear plot, and "Geometric Mean serum MEDI7352 ± Geometric Standard Deviation (Semi-Logarithmic Scale)" followed by "Geometric Mean serum MEDI7352" for the semi-log plot. Below legend, add legend for ADA status: "Overall", "ADA Positive", "ADA Negative".
- Insert legend with different point symbols and colors for each treatment group (CCI) for the Overall plot, and a legend with different point symbols and colors for each ADA status (ADA+, ADA-) for each treatment group plot by ADA status.
- Time (Days) in x axis and Serum MEDI7352 concentration (ng/mL) in y axis (**in linear and $\log_{10}$ scale, for each plot**).
- Include data from the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10: Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 10 + 14 days, Week 18.
- **Make one overall plot by treatment group, and a plot for each treatment group by ADA status for a total of 4 plots.**
- Include a marker for LLOQ, and an inset within the plot with "LLOQ (1.00 ng/mL)".
- A line for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.4.1.2
Pharmacokinetics: Individual Plot of Serum MEDI7352 Concentrations over time
PK Population



ADA = Antidrug Antibodies; LLOQ = Lower Limit of Quantification.
PK Population = includes all subjects for who a pharmacokinetic sample was obtained and analyzed.
ADA positive represents number of participants with at least one positive ADA result.
ADA negative represents number of participants with only negative ADA results (no positive).
Reference Listing: 16.2.10.1

Programming Notes:

- Insert the following text as upper legend: "MEDI7352 Concentration by Subject, Treatment group, and ADA status" followed by "(Linear Scale)" or "(Semi-Logarithmic Scale)" depending on the plot (linear or semi-log). Below legend, add legend for Treatment Group: CCI [redacted].
- Insert legend with different colors for each ADA status (Positive/ Negative).
- Time (days) in x axis and Serum MEDI7352 concentration (ng/mL) in y axis (**in linear and log_{10} scale, for each plot**).
- Include data from the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 10 + 14 days, Week 18.
- **Make one plot for each Treatment group (CCI [redacted]), for a total of 3 plots.**
- Include a marker for LLOQ, and an inset within the plot with "LLOQ (1.00 ng/mL)".
- Plots for CCI [redacted] dosing (CCI [redacted]) will only be added if Stage 4 is initiated.

Figure 14.4.2.1
Pharmacodynamics Line Plot of Geometric Mean (with and without gSD) Serum total NGF over time
Safety Population

ADA = Antidrug Antibodies; gSD = Geometric Standard Deviation; LLOQ = Lower Limit of Quantification, NGF = Nerve-Growth Factor.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
ADA positive represents participants with at least one positive ADA result.
ADA negative represents participants with only negative ADA results (no positive).
Reference Listing: 16.2.10.3

Programming Notes:

- Same shell as Figure 14.4.1.1
- Insert the following text as upper legend: "Geometric Mean Serum Concentration of tNGF ± Geometric Standard Deviation (Linear Scale)" followed by "Geometric Mean Serum Concentration of tNGF" for the linear plot, and "Geometric Mean Serum Concentration of tNGF (Semi-Logarithmic Scale)" followed by "Geometric Mean Serum Concentration of tNGF" for the semi-log plot. Below legend, add legend for ADA status: "Overall", "ADA Positive", "ADA Negative".
- Insert legend with different point symbols and colors for each treatment group (Placebo, CCI) for the Overall plot, and a legend with different point symbols and colors for each ADA status (ADA+, ADA-) for each treatment group plot by ADA status.
- Time (Days) in x axis and Serum tNGF Concentration (pg/mL) in y axis (**in linear and log$_{10}$ scale for each plot**).
- Include data from the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10: Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 12, Week 18.
- **Make one overall plot by treatment group, and a plot for each treatment group by ADA status for a total of 5 plots .**
- Include a marker for LLOQ, and an inset within the plot with "LLOQ (10.00 pg/mL)".
- A plot for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.4.2.2
Pharmacodynamics: Individual Plot of Serum total NGF over time
Safety Population

ADA = Antidrug Antibodies; LLOQ = Lower Limit of Quantification; NGF = Nerve-Growth Factor.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
ADA positive represents number of participants with at least one positive ADA result.
ADA negative represents number of participants with only negative ADA results (no positive).
Reference Listing: 16.2.10.3

Programming Notes:

- Same shell as Figure 14.4.1.2
- Insert the following text as legend: "Total NGF by Subject, Treatment group, and ADA status" followed by "(Linear Scale)" or "(Semi-Logarithmic Scale)" depending on the plot (linear or semi-log). Below legend, add legend for Treatment Group: CCI [redacted].
- Insert legend with different colors for each ADA status (Positive/ Negative).
- Time (days) in x axis and Serum tNGF concentration (pg/mL) in y axis (**in linear and log_{10} scale for each plot**).
- Include data from the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 12; Week 18.
- **Make one plot for each Treatment group (**CCI [redacted] **Placebo), for a total of 4 plots.**
- Include a marker for LLOQ, and an inset within the plot with "LLOQ (10.00 pg/mL)".
- Plots for CCI [redacted] dosing (CCI [redacted]) will only be added if Stage 4 is initiated.

Sponsor:	AstraZeneca
Protocol Title	A Randomised, Double-Blind, Placebo-Controlled, Dose-Response Study of the Efficacy and Safety of MEDI7352 in Subjects with Painful Diabetic Neuropathy
Development Phase	2
Protocol Numbers:	D5680C00002
Premier Research PCNs:	MEDU177093
Document Version:	Final Version 1.2
Document Date:	04-Oct-2023

Document History

Version	Date	Author	Description
0.1	24-Mar-2023	PPD	Draft Version
0.2	21-Apr-2023	PPD	Draft Version
0.3	24-May-2023	PPD	Draft Version
1	12-Jul-2023	PPD	Final Version
1.1	31-Aug_2023	PPD	Final Version

Tables, Listings, and Figures Conventions

All listings, tables, and graphs will have a header showing the sponsor company name, protocol and version of delivery and a footer showing the version of SAS, the file name and path, and the source of the data (listing number).

The following reporting conventions will be adopted for the presentation of study data. These conventions will enhance the review process and help to standardize the presentation with common notations.

General Reporting Conventions

- All tables and data listings will be developed in landscape orientation.
- Specialized text styles, such as bolding, italics, borders, shading, and superscripted and subscripted text will not be used in tables, figures, and data listings unless they add significant value to the table, figure, or data listing.
- Only standard keyboard characters should be used in tables and data listings. Special characters, such as nonprintable control characters, printer-specific characters, or font specific characters, will not be used on a table, figure, or data listing.
- Adverse events with missing MedDRA coding will have their system organ class preferred term presented as "Not Coded" and the Preferred Term presented as verbatim in the tables. The "Not Coded" frequencies will be sorted to the end of the tables. This will only be applicable for any deliveries sent before database lock (e.g., for dry runs).
- Programming notes may be inserted into the shells, these notes will not appear in the final output.

Population Summary Conventions

- Population sizes may be presented for each classification factor as totals in the column header as (N=xx), where appropriate.
- All population summaries for categorical variables will include all categories that were planned and for which the participants may have had a response.
- All population summaries for continuous variables will include: n, mean, SD, median, quartiles, minimum, and maximum. Other summaries (e.g., number missing, geometric mean, 95% CIs, and coefficient of variation [CV] or % CV) may be used as appropriate. The precision of the maximum and minimum will match the maximum precision in the observed data and 2 decimals for derived data unless specifically mentioned in the corresponding shell. The mean and median will have 1 additional decimal place. The SD will have 2 additional decimal places. For derived data, minimum and maximum will be reported to 2 degrees of precision. Measures of location (mean and median) will be reported to 3 degree of precision, and measures of spread will be reported to 4 degrees of precision.

- All percentages are rounded and reported to a single decimal point (xx.x%). Exceptions are 0 and 100 that will be displayed as 0 and 100% respectively.

Planned Tables, Figures and Listings

- The table and listing numbers are place holders only and will be determined when the outputs are produced.
- In all listings a blank line will be placed between each participant. Within a data listing, if an item appears line after line (e.g., repetition of participant number), then only the first occurrence will be displayed.
- In data listings, the information for 1 participant will be kept on 1 page, if possible, rather than splitting a Subjects's information across pages.

Planned Table Descriptions and Shells

Number Title Population	Unique (U) or Repeated (R)
Table 14.1.2 - - Screening Population	U
Table 14.1.3 - Summary of Reasons for Screening Failure - Screen Failure Population	U
Table 14.1.4.1 - Demographics and Baseline Characteristics - Screening Population	U
Table 14.1.4.2 - Demographics and Baseline Characteristics - Safety Population	R
Table 14.1.4.3 - Demographics and Baseline Characteristics - mITT Population	R
Table 14.1.4.4 - Demographics and Baseline Characteristics - PK Population	R
Table 14.1.5.1 - Osteoarthritis Characteristics - Screening Population	U
Table 14.1.5.2 - Osteoarthritis Characteristics - Safety Population	R
Table 14.1.5.3 - Osteoarthritis Characteristics - mITT Population	R
Table 14.1.5.4 - Osteoarthritis Characteristics - PK Population	R
Table 14.1.6 - Medical History by System Organ Class and Preferred Term - Safety Population	U
Table 14.1.7 - Prior Medications by ATC Level 2 and Preferred Name - Safety Population	U
Table 14.1.8 - Protocol Deviations - Safety Population	U
Table 14.1.9 - Overall Study Drug Exposure - Safety Population	U
Table 14.2.1.1.1 - Daily Pain NRS: Summary Statistics (Observed Cases) - mITT Population	U
Table 14.2.1.1.2 - Daily Pain NRS: Summary Statistics (LOCF)**Error! Reference source not found.**- mITT Population	R
Table 14.2.1.1.3 - Daily Pain NRS: Summary Statistics (BOCF) - mITT Population	R
Table 14.2.1.2.1 - Daily Pain NRS: Primary MCP-Mod Analysis (LOCF) - mITT Population	U
Table 14.2.1.2.2 - Statistical Analysis of CFB to Week 12 Daily Pain NRS: Primary ANCOVA Analysis (LOCF) - mITT Population	U
Table 14.2.1.3.1 - Statistical Analysis of CFB Daily Pain NRS: MMRM Analysis. (Observed Cases) - mITT Population	U
Table 14.2.1.3.2 - Daily Pain NRS: Sensitivity of Primary MCP-Mod Analysis (BOCF) - mITT Population	R
Table 14.2.2.1 - Galer NPS: Summary Statistics (Observed Cases) - mITT Population	U
Table 14.2.2.2 - Galer NPS: MMRM Analysis (Observed Cases) - mITT Population	U
Table 14.2.3.1 - DSIS: Summary Statistics (Observed Cases) - mITT Population	U
Table 14.2.3.2 - DSIS: MMRM Analysis (Observed Cases) - mITT Population	U
Table 14.2.4.1 - SF-36: Summary Statistics (Observed Cases) - mITT Population	U
Table 14.2.4.2 - SF-36: MMRM Analysis (Observed Cases) - mITT Population	U
Table 14.2.5.1 - Rescue Medication Use: Summary Statistics - mITT Population	U

Number Title Population	Unique (U) or Repeated (R)
Table 14.2.6.1.1 - Daily Pain NRS Responder Analysis (≥30%): Cochran-Mantel Haenszel (Observed Cases) - mITT Population	U
Table 14.2.6.1.2 - Daily Pain NRS Responder Analysis (≥30%): Cochran-Mantel Haenszel (Observed Cases): All Visits - mITT Population	CCI
Table 14.2.6.2 - Daily Pain NRS Responder Analysis (≥30%): GEE Analysis (Observed Cases) - mITT Population	U
Table 14.2.7.1.1 - Daily Pain NRS Responder Analysis (≥50%): Cochran-Mantel Haenszel (Observed Cases) - mITT Population	R
Table 14.2.7.1.2 - Daily Pain NRS Responder Analysis (≥50%): Cochran-Mantel Haenszel (Observed Cases): All Visits - mITT Population	CCI
Table 14.2.7.2 - Daily Pain NRS Responder Analysis (≥50%): GEE Analysis (Observed Cases) - mITT Population	R
Table 14.2.8.1 - Patient Global Impression of Change: Summary Statistics - mITT Population	U
Table 14.2.8.2 - Patient Global Impression of Change: Cochran-Mantel Haenszel - mITT Population	U
CCI	U
Table 14.3.1.1 - Summary of Overall Adverse Events - Safety Population	U
Table 14.3.1.2 - Treatment Emergent of Adverse Events by System Organ Class and Preferred Term - Safety Population	U
Table 14.3.1.3 - Treatment Emergent of Adverse Events by Severity, System Organ Class and Preferred Term - Safety Population	U
Table 14.3.1.4 - Treatment Emergent Adverse Events by Relationship to Study Medication, System Organ Class and Preferred Term - Safety Population	U
Table 14.3.1.5 - Treatment Emergent Adverse Events by ADA Status Category, System Organ Class and Preferred Term - Safety Population	U
Table 14.3.1.6 - Treatment Emergent Adverse Events Leading to Discontinuation of Study drug by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.1.7 - Non-Serious Adverse Events Occurring in More than 5% of Subjects by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.1.8 - Treatment Emergent Adverse Events Occurring in More than 5% of Subjects by Preferred Term - Safety Population	R
Table 14.3.1.9 - Treatment Emergent Adverse Events by Preferred Term - Safety Population	R
Table 14.3.2.1.1 - Serious Adverse Events by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.1.2 - Life-Threatening Serious Adverse Events by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.1.3 - Serious Adverse Events with Outcome Death by System Organ Class and Preferred Term - Safety Population	R

Number Title Population	Unique (U) or Repeated (R)
Table 14.3.2.1.4 - Serious Adverse Events by Relationship to Study Medication, System Organ Class and Preferred Term - Safety Population	R
Table 14.3.3.1 - Listing of Serious Adverse Events - Safety Population	U
Table 14.3.3.2 - Listing of Deaths - Safety Population	U
Table 14.3.2.2.1 - Treatment Emergent Adverse Events Associated with Abnormal Liver by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.2.2 - Potential Joint Related Adverse Events of Special Interest by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.2.3 - Serious and/or severe Infections by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.2.2.4 - Anaphylactic Reactions, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of IP by System Organ Class and Preferred Term - Safety Population	R
Table 14.3.4.1 - Descriptive Summary of Clinical Chemistry - Safety Population	U
Table 14.3.4.2 - Shift Table of Clinical Chemistry Results - Safety Population	U
Table 14.3.4.3 - Descriptive Summary of Hematology - Safety Population	R
Table 14.3.4.4 - Shift Table of Hematology Results - Safety Population	R
Table 14.3.4.5 - Descriptive Summary of Coagulation - Safety Population	R
Table 14.3.4.6 - Shift Table of Coagulation Results - Safety Population	R
Table 14.3.4.7 - Descriptive Summary of Urinalysis - Safety Population	U
Table 14.3.4.8 - Shift Table of Urinalysis Results - Safety Population	R
Table 14.3.4.9 - Maximum On-Treatment ALT and AST versus Maximum On-Treatment Total Bilirubin - Safety Population	U
Table 14.3.5.1 - Descriptive Summary of Vital Signs - Safety Population	U
Table 14.3.5.2 - Descriptive Summary of Digital ECG Data - Safety Population	U
Table 14.3.5.3 - Summary of Overall Evaluation of safety ECG Data - Safety Population	U
Table 14.3.5.4 - Covid-19 Screening - Safety Population	U
Table 14.3.5.5 - Summary of Sub-Scores for Total Neuropathy Score-Nurse - Safety Population	U
Table 14.3.5.6 - Descriptive Summary of Total Neuropathy Score-Nurse - Safety Population	U
Table 14.3.5.7.1 - Summary of Motor and Sensory Nerve Conduction Studies - Safety Population	U
Table 14.3.5.7.2 - Shift Table of Motor and Sensory Nerve Conduction Results - Safety Population	CCI
Table 14.3.5.8 - Summary of Strength and Deep Tendon Reflexes - Safety Population	U
Table 14.3.5.9 - Summary of Local Injection Site Reactions - Safety Population	U

Number Title Population	Unique (U) or Repeated (R)
Table 14.3.5.10 - Summary of Hypersensitivity/Anaphylactic Reactions - Safety Population	U
Table 14.3.5.11 - Summary of Liver Diagnostic Investigations - Safety Population	U
Table 14.3.5.12 - Summary of Liver Risk Factors and Lifestyle Events - Safety Population	U
Table 14.3.5.13 - Summary of Liver Signs and Symptoms - Safety Population	U
Table 14.3.5.14 - Summary of Infection Diagnostic Investigations - Safety Population	U
Table 14.3.5.15 - Summary of Infection Risk Factors and Lifestyle Events - Safety Population	U
Table 14.3.5.16 - Summary of Infection Signs and Symptoms - Safety Population	U
Table 14.3.5.17 - Summary of Concomitant Medications by ATC Level 2 and Preferred Name - Safety Population	R
Table 14.3.5.18 - Summary of Concomitant Procedures - Safety Population	R
Table 14.3.5.19 - Anti-Drug Antibody Results and Titre Summary by Timepoint - Safety Population	U
Table 14.3.5.20 - Descriptive Summary of Anti-Drug Antibody Results and Titre by ADA Categories - Safety Population	U
Table 14.4.1 - Summary of Serum MEDI7352 Concentrations - PK Population	U
Table 14.4.2 - Summary of Serum total NGF Concentrations - PD Population	U

Table Change Log

Output Number	Date of Change	Change Made By (initials)	Description/Rationale

1. Demographic Data

Table 14.1.2
Subject Disposition
Screening Population

Status	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=xx)
Screening Population [1]					xx (100%)
Screen Failures					xx (xx.x %)
Enrolled Subjects					xx (xx.x %)
Re-screened Subjects					xx (xx.x %)
Randomized Subjects	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Randomized and Not Treated Subjects	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Reason for Discontinuation					
Adverse Event	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Other	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Safety Population [2]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
mITT Population [3]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Evaluable Week 12 Efficacy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Evaluable LOCF Efficacy [4]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Efficacy Evaluable	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PK Population [5]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Completed Study Treatment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Discontinued Study Treatment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reason for Discontinuation:					
Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lack of Efficacy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lost to Follow-up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Non-compliance with Study Drug	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Physician Decision	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pregnancy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Progressive Disease	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Violation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Study Terminated by Sponsor	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Technical Problems	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Withdrawal by Subject	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sponsor Decision	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Completed Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Withdrawn from the Study	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Reason for Discontinuation:					
Adverse Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lack of Efficacy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lost to Follow-up	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
...					

COVID-19 = Coronavirus disease 2019; LOCF = Last Observation Carried Forward; mITT = modified intent-to-treat; N = number of subjects per treatment group; PK = pharmacokinetic.
Note: Percentages are n/Number of subjects randomized*100 as displayed in column header N, except for the screened, enrolled and re-screened where n/Number of Screening subjects*100, and for the randomized, where n/Number of Enrolled subjects*100.
Re-screened subjects are a subset of the Screening population.
[1] The Screening Population includes all subjects who provide informed consent and provide demographic and/or baseline screening assessments.
[2] The Safety Population includes all subjects who receive at least 1 dose of double-blind study medication.
[3] The mITT Population includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
[4] Subjects in the mITT Population with LOCF applied for missing efficacy data at week 12,
[5] The PK Population includes all subjects for who a pharmacokinetic sample was obtained and analyzed.

Reference Listings: 16.2.1.1, 16.2.1.2, 16.2.1.3,

Programming Notes:

- Display only reasons for early discontinuation with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.3
Summary of Reasons for Screening Failure
Screen Failure Population

	Total (N=xx)
Number of Subjects Who Don't Meet Inclusion/Exclusion Criteria	xx (xx.x%)
IC 01: Xxxxxxxxxxx	xx (xx.x%)
IC 02: Xxxxxxxxxxx	xx (xx.x%)
…	
EC 01: Xxxxxxxxxxx	xx (xx.x%)
EC 02: Xxxxxxxxxxx	xx (xx.x%)
…	
Number of Subjects Who are Screen Failure for other Reason than Eligibility Criteria	xx (xx.x%)

EC = exclusion criteria; IC = inclusion criteria; N = number of subjects.
Note: subject can be counted in more than one criterion.
Reference Listing 16.2.1.4

Table 14.1.4.1
Demographics and Baseline Characteristics
Screening Population

Variable Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	 CCI (N=xx)	 CCI (N=xx)	Total (N=xx)
Age (years) [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Age Category					
≥18 - <65 years	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
≥65 years	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Gender					
Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ethnicity					
Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Hispanic or Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Race					
American Indian or Alaska Native	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Black or African American	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Native Hawaiian or Other Pacific Islander	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Specified	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Screening Height (cm)					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Screening Weight (kg)					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Screening BMI (kg/m²)					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Female characteristics [2]					
Surgically sterile	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Postmenopausal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Fully vaccinated for COVID-19					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

BMI = Body Mass Index; COVID-19 = Coronavirus disease 2019; n = number of subjects by treatment group with collected parameter; N = number of subjects per treatment group; SD = standard deviation.
Note: The Screening Population includes all subjects who are enrolled and provide informed consent and demographic and/or baseline screening assessments.
[1] Age was calculated as age at time of consent.
[2] Percentages are n/Number of Female subjects from Analysis Population*100
Reference Listing: 16.2.4.1

Programming Notes:

- If a variable is between 2 pages, start the variable in the second page.
- Keep all possible values for each category even if no subject.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.4.2
Demographics and Baseline Characteristics
Safety Population

Programming Notes:

- Same shell as Table 14.1.4.1.
- Keep all possible values for each category even if no subject.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.4.3
Demographics and Baseline Characteristics
mITT Population

Programming Notes:

- Same shell as Table 14.1.4.1.
- Keep all possible values for each category even if no subject.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.4.4
Demographics and Baseline Characteristics
PK Population

Programming Notes:

- Same shell as Table 14.1.4.1.
- Keep all possible values for each category even if no subject.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.5.1
Osteoarthritis Characteristics
Screening Population

Variable Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	 CCI (N=xx)	 CCI (N=xx)	Total (N=xx)
Subjects diagnosed with Osteoarthritis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Joint(s)/Area(s) affected:					
Shoulder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Elbow	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hip	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Knee	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ankle	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Spine	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hands	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Feet	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Osteoarthritis clinically significant					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Radiologic investigations conducted [1]					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Plain radiography	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
MRI	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Joint(s)/Area(s) investigated:					
Shoulder	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Elbow	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hip	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Knee	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ankle	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Spine	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Hands	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Feet	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Osteoarthritis radiologically significant					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Kellgren-Lawrence score reported					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Grade 4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No/Not applicable	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Radiologic Scoring System Used?					
Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

MRI = magnetic resonance imaging; N = number of subjects per treatment group.
[1] Subjects who reported more than one radiologic investigation within each category were only counted once.
Reference Listing: 16.2.4.3

Programming Notes:

- Display only Joint(s)/Areas(s) affected and investigated with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.5.2
Osteoarthritis Characteristics
Safety Population

Programming Notes:

- Same shell as Table 14.1.5.1.
- Display only Joint(s)/Areas(s) affected and investigated with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.5.3
Osteoarthritis Characteristics
mITT Population

Programming Notes:

- Same shell as Table 14.1.5.1.
- Display only Joint(s)/Areas(s) affected and investigated with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.5.4
Osteoarthritis Characteristics
PK Population

Programming Notes:

- Same shell as Table 14.1.5.1.
- Display only Joint(s)/Areas(s) affected and investigated with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.6
Medical History by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Placebo (N=xxx)	MEDI7352 CCI (N=xx)	 CCI (N=xx)	 CCI (N=xx)	Total (N=xxx)
Any Medical History	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
System Organ Class 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
…	…	…	…	…	…
System Organ Class n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)

N = number of subjects per treatment group.
Note: All medical history terms were coded using the Medical Dictionary for Regulatory Activities (MedDRA), version 26.0. At each level of summarization (system organ class or preferred term), subjects having more than one medical history term were counted only once. System organ class and preferred terms are sorted in descending order of frequency of Total column, and alphabetically if same frequency.

Reference Listing: 16.2.4.2

Programming Notes:

- SOC and PT texts should be in proper case in table.
- Sort SOC and PT (within SOC) in descending order of frequency in the Total column. Sort alphabetically in case of ties.
- Uncoded Medical History Events
  - When there are uncoded Medical History Events in the database, the events will be summarized with SOC and PT set to [Not Coded]. The [Not Coded] will be sorted at the end of the table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.7
Prior Medications by ATC Class and Preferred Name
Safety Population

ATC Class [1] Preferred Term	Placebo	MEDI7352			Total
		CCI	CCI	CCI	
	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Subjects with at Least One Prior Medication	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATC Level 2 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Name 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Name n	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATC Level 2 n	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Name 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Name n	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

ATC = Anatomical Therapeutic Class; N = number of subjects per treatment group.
[1] ATC Class is defined as ATC Level 2.
Note: Prior medications are defined as medications that started before first dose of study, whether they were stopped before first dose of study medication or not. All prior medications are coded using WHO drug dictionary version vMar2023. At each level of summarization (ATC Level 2 or Preferred Name), subjects who reported more than one prior medication were only counted once. ATC Level 2 and Preferred Term are sorted in descending order of frequency of total, and alphabetically if same frequency.
Reference Listing: 16.2.9.16

Programming Notes:

- If uncoded ATC Level or Preferred Name, please put them as [Not Coded]
- ATC and Preferred Name texts should be in proper case in table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.1.8
Protocol Deviations
Safety Population

	Placebo	MEDI7352			Total
		CCI	CCI	CCI	
	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Subjects With Any Important Protocol Deviation/Violation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 5	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Protocol Deviation Type 6	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
……..					

N = number of subjects per treatment group.
Notes: Percentages are n/Number of subjects by treatment group*100.
Subjects with one or more deviations within a type of protocol deviation were counted only once.

Reference Listing 16.2.2.1

Programming Notes:

- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

2. Exposure and Compliance

Table 14.1.9
Overall Study Drug Exposure
Safety Population

Category/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=xx)
Maximum Number of Doses Administered [1]					
1 Dose	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 Doses	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 Doses	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 Doses	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
5 Doses	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
6 Doses	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total Duration of Exposure (days) [2]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Total (cumulative) IP volume infused (mL)					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

n = number of subjects by treatment group with collected parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Subjects are counted once for each level of dose administered.
[2] Duration of exposure (days) = min(date of last dose of treatment + 14 days or date of death) – date of first dose of treatment + 1.
Reference Listing: 16.2.5.1

Programming Notes:

- Add all categories even if count is 0.
- A column for [redacted] dosing ([redacted]) will only be added if Stage 4 is initiated.

3. Primary Efficacy Analysis

Table 14.2.1.1.1
Daily Pain NRS: Summary Statistics (Observed Cases)
mITT Population

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=XX)
Baseline [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 2					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 2 CFB					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

…

CFB = Change from Baseline; DPS = Daily Pain Score; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NRS = Numeric Rating Scale; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
Note: Data shown are weekly averages of the average daily pain scores on an 11-point (0-10) NRS and CFB for the same variable. Total N for the mITT population = 106 at Week 2 as Subject CCI has < 4 days of diary pain data on that visit, completing the following visits till Week 12.
[1] Baseline is defined as the average of the 'non-missing' DPS within the seven-day period prior to randomization i.e., Day -7 to Day -1, inclusive.

Reference Listing: 16.2.6.1

Programming Notes:

- Include all observed data (Not the LOCF) on weekly averages of the average daily pain scores for Baseline, Week 2, 4, 6, 8, 10, 12 and 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.1.1.2
Daily Pain NRS: Summary Statistics (LOCF)
mITT Population

Programming Notes:

- Same shell as Table 14.2.1.1.1.
- Include all observed and LOCF data on weekly averages of the average daily pain scores for Baseline, Week 2, 4, 6, 8, 10, and 12
- Add abbreviation in footnote: LOCF = Last Observation Carried Forward.
- Add the following note in footnote: "LOCF applied to Week 12 only".
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.1.1.3
Daily Pain NRS: Summary Statistics (BOCF)
mITT Population

Programming Notes:

- Same shell as Table 14.2.1.1.1.
- Include all observed and BOCF data on weekly averages of the average daily pain scores for Baseline, Week 2, 4, 6, 8, 10, and 12
- Add abbreviation in footnote: BOCF = Baseline Observation Carried Forward.
- Add the following note in footnote: "BOCF applied to Week 12 only".
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.1.2.1
Daily Pain NRS: Primary MCP-Mod Analysis (LOCF)
mITT Population

Primary 'MCP' step Model Contrast [1]	t value	1-sided adjusted P-value [2]
Hyperbolic E_{max}		
ED50 = 7.5	xx.xx	0.xxxx
ED50 = 15	xx.xx	0.xxxx
ED50 = 30	xx.xx	0.xxxx
ED50 = 60	xx.xx	0.xxxx
ED50 = 750	xx.xx	0.xxxx
Primary Overall MCP test		

CFB = Change from Baseline; LOCF = Last Observation Carried Forward; MCP = Multiple Comparisons; Procedure; NRS = Numeric rating scale.
[1] ED50 = Effective Dose giving half of the asymptotic maximum effect.
[2] Multiplicity Adjusted P-value.
Reference Listing: 16.2.6.1


CCI

'MOD' step [3]
Selected Model xxxxxxxxxx

Parameter	Estimate	95% CI of Estimate [6]
ED50	xx.x	[x.xx to x.xx]
ED90 [4]	xx.x	[x.xx to x.xx]
Asymptotic ED90 [5]	xx.x	[x.xx to x.xx]
Dose to achieve target (-1.25) effect	xx.x	[x.xx to x.xx]
Treatment effect at dose =CCI	xx.x	[x.xx to x.xx]
Treatment effect at dose =CCI	xx.x	[x.xx to x.xx]
Treatment effect at dose =CCI	xx.x	[x.xx to x.xx]
Treatment effect at dose =CCI	xx.x	[x.xx to x.xx]

CI: Confidence Interval; LOCF = Last Observation Carried Forward; MCP = Multiple Comparisons; Procedure; MOD = Modelling; NRS = Numeric rating scale.
[3] Results from the 'MOD' step will only be available in case any of the MCP tests is statistically significant.
[4] ED90 = Effective Dose giving 90% of the effect of the maximum dose studied.
[5] Asymptotic ED90 = Effective Dose giving 90% of the asymptotic maximum effect.
[6] 2.5% and 97.5% quantiles taken from 100000 samples from the multivariate normal distribution for model fitted estimates and its covariance matrix.
Reference Listing: 16.2.6.1

Programming Notes:

- The 'MOD' step will only be performed if stage 4 is initiated, otherwise there would be insufficient dosing data to fit the non-linear models.

Table 14.2.1.2.2
Statistical Analysis of CFB to Week 12 Daily Pain NRS: Primary ANCOVA Analysis (LOCF)
mITT Population

Model parameter estimates

Parameter	Estimate	t value	Degrees of freedom	Standard Error	2-sided 95% unadjusted CL	Asymmetric CL [1]	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx	[x.xx to x.xx]		
Co-Medication Type			3				0.xxxx
Baseline pain NRS	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]		0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Model residual standard deviation	xx.xx						

ANCOVA = analysis of covariance; CFB = Change from Baseline;
CL = Confidence limits; LOCF = Last Observation Carried Forward; NRS = Numeric rating scale.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: ANCOVA by dose using NRS baseline value and co-medication as covariates, with CFB to Week 12 (LOCF) as dependent variable.

Least Square Means

Treatment	Number of Subjects	LS mean [3]	95% CI of LS mean
Placebo	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]

CI = Confidence interval; LOCF = Last Observation Carried Forward; LS = least square; NRS = Numeric rating scale.
[3] The LS mean is a model estimate using fitted group parameter and the baseline
weekly average pain NRS parameter evaluated at the grand mean over each group.
Reference Listing: 16.2.6.1

Programming Notes:

- Concomitant co-medication Type indicated for Painful Diabetic Neuropathy: either anticonvulsant class (pregabalin or gabapentin) or antidepressant class (duloxetine, venlafaxine, or amitriptyline).
- Rows for [redacted] dosing ([redacted]) will only be added if Stage 4 is initiated.

Table 14.2.1.3.1
Statistical Analysis of CFB Daily Pain NRS: MMRM Analysis. (Observed Cases)
mITT Population

Model parameter estimates

Parameter	Estimate	t value	Degrees of freedom	Standard Error	2-sided 95% unadjusted CL	Asymmetric CL [1]	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx			
Co-medication type			3				0.xxxx
Week			6				0.xxxx
Treatment			3				0.xxxx
Treatment*Week			18				0.xxxx
Baseline pain NRS	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]		0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
~~Model residual standard deviation~~	~~xx.xx~~						

CFB = Change from Baseline; CL = Confidence limits; MMRM = Mixed Model for Repeated Measures; NRS = Numeric rating scale.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: MMRM using Time, Treatment, Treatment*Time, NRS baseline value, and Co-medication type as covariates, with CFB as dependent variable.
Note: model was fitted using an unstructured covariance structure. Estimates for difference vs Placebo at Week 12.

Least Square Means: Week xxxxx

Treatment	Number of patients	LS mean [3]	95% CI of LS mean
Placebo	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]

CI = Confidence interval; LS = least square; NRS = Numeric rating scale.
[3] The LS mean is a model estimate using fitted group parameter and the baseline weekly average pain NRS parameter evaluated at the grand mean over each group.
Reference Listing: 16.2.6.1

Programming Notes:

- Include LSmeans and difference in LSmean with Placebo in repeated tables for the Treatment*Week interaction.
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.1.3.2
Daily Pain NRS: Sensitivity of Primary MCP-Mod Analysis (BOCF)
mITT Population

Programming Notes:

- Same shell as Table 14.2.1.2.1, substituting "LOCF = Last Observation Carried Forward" by "BOCF = Baseline Observation Carried Forward".
- The MCP-MOD approach will only be performed if stage 4 is initiated, otherwise there would be insufficient dosing data to fit the non-linear models.

4. Secondary Efficacy Analysis

Table 14.2.2.1
Galer NPS: Summary Statistics (Observed Cases)
mITT Population

Parameter: xxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=xx)
Baseline [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 4					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 4 CFB					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

...

For Pain Duration Frequency

Baseline [1]					
I feel a background pain all of the time and occasional flare-ups	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
I feel a single type of pain all the time	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
feel a single type of pain only sometimes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 4					

CFB = Change from Baseline; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NPS = Neuropathic Pain Scale; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
Note: Data shown are Pain Intensity, Unpleasantness, and Descriptor scores on an 11-point (0-10) NRS, and Pain Duration/Frequency on a 3-point NRS (1-3), plus CFB for the same variables.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Reference Listing: 16.2.6.2

Programming Notes:

- Include all observed data on Galer NPS scores for Baseline, Week 4, 8, 12, and 18.
- Repeat for the Parameters: Pain intensity, Pain Unpleasantness, Pain Sharpness, Pain Hotness, Pain Dullness, Pain Coldness, Pain Sensitivity, Pain Itching, Deep Pain Intensity, Surface Pain Intensity (All in an 11-point NRS), Galer NPS Total Score (ranging from 0 to 100), and Pain Duration/Frequency (in a 3-point NRS).
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.2.2
Galer NPS: MMRM Analysis (Observed Cases)
mITT Population

Model parameter estimates

Parameter	Estimate	t value	Degrees of freedom	Standard Error	2-sided 95% unadjusted CL	Asymmetric CL [1]	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx			
Co-Medication type			3				0.xxxx
Week			3				0.xxxx
Treatment			3				0.xxxx
Treatment*Week			9				0.xxxx
Baseline NPS	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]		0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
~~Model residual standard deviation~~	~~xx.xx~~						

CFB = Change from Baseline; CL = Confidence limits; MMRM: Mixed Model for Repeated Measures; NPS = Neuropathic Pain Scale.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: MMRM using Time, Treatment, Treatment*Time, baseline total NPS score value, and Co-medication type as covariates, with total NPS score CFB as dependent variable.
Note: model was fitted using an unstructured covariance structure.

Least Square Means: Week: xxxx

Treatment	Number of patients	LS mean [3]	95% CI of LS mean
Placebo	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]

CI = Confidence interval; LS = least square; NPS = Neuropathic Pain Scale.
[3] The LS mean is a model estimate using fitted group parameter and the baseline total NPS score evaluated at the grand mean over each group.
Reference Listing: 16.2.6.2

Programming Notes:

- Include LSmeans and difference in LSmean with Placebo in repeated tables for the Treatment*Week interaction.
- Include all observed data on Galer NPS scores for Baseline, Week 4, 8, 12, and 18.
- Analysis is done for Galer NPS Total Score.
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.3.1
DSIS: Summary Statistics (Observed Cases)
mITT Population

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=XX)
Baseline [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 4					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 4 CFB					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
…					

CFB = Change from Baseline; DSIS = Daily Sleep Interference; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
Note: Data shown are weekly averages of the average daily sleep interference scores on an 11-point (0-10) NRS and CFB for the same variable.
[1] Baseline is defined as the average of the 'non-missing' DSIS within the seven-day period prior to randomization **i.e.,** Day -7 to Day -1, inclusive.

Reference Listing: 16.2.6.3

Programming Notes:

- Include all observed data on weekly averages of the average daily Sleep Interference score for Baseline, Week 4, 8, 12, and 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.3.2
DSIS: MMRM Analysis (Observed Cases)
mITT Population

Model parameter estimates

Parameter	Estimate	t value	Degrees of freedom	Standard Error	2-sided 95% unadjusted CL	Asymmetric CL [1]	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx			
Co-medication type			3				0.xxxx
Week			3				0.xxxx
Treatment			3				0.xxxx
Treatment*Week			9				0.xxxx
Baseline DSIS	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]		0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
~~Model residual standard deviation~~	~~xx.xx~~						

CFB = Change from Baseline; CL = Confidence limits; MMRM: Mixed Model for Repeated Measures; DSIS = Daily Sleep Interference.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: MMRM using Time, Treatment, Treatment*Time, DSIS baseline value, and Co-medication type as covariates, with CFB as dependent variable.
Note: model was fitted using an unstructured covariance structure.

Least Square Means: Week xxxx

Treatment	Number of patients	LS mean [3]	95% CI of LS mean
Placebo	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]

CI = Confidence interval; LS = least square.
[3] The LS mean is a model estimate using fitted group parameter and the baseline weekly average DSIS parameter evaluated at the grand mean over each group.
Reference Listing: 16.2.6.3

Programming Notes:

- Include LS means and difference in LS mean with Placebo in repeated tables for the Treatment*Week interaction.
- Include all observed data on weekly average DSIS for Baseline, Week 4, 8, 12, and 18.
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.4.1
SF-36: Summary Statistics (Observed Cases)
mITT Population

Parameter: xxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=XX)
Baseline [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 12					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 12 CFB					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

...

When parameter is "Change in general Health"

Baseline [1]					
Much better now than one year ago	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Somewhat better now than one year ago	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
About the same as one year ago	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Somewhat worse now than one year ago	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Much worse now than one year ago	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 12					

CFB = Change from Baseline; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NRS = numeric rating scale; SD = standard deviation; SF-36 = 36-Item Short-Form Health Survey; Q1 = first quartile; Q3 = third quartile.
Note: Data shown are derived SF-36 scores and Change in General Health on a 5-point NRS (1-5), plus CFB for the same variables.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Reference Listing: 16.2.6.4

Programming Notes:

- Include all observed data on SF-36 scores for Baseline and Week 12.
- Repeat for the Parameters: Physical functioning, Role limitations due to physical health, Role limitations due to emotional problems, Vitality (Energy/fatigue), Emotional well-being, Social functioning, Pain and General Health (from 0 to 100), Physical Health Summary, Mental Health Summary, and Change in general Health (in a 5-point NRS).
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.4.2
SF-36: MMRM Analysis (Observed Cases)
mITT Population

Model parameter estimates: xxxxxxxx

Parameter	Estimate	t value	Degrees of freedom	Standard Error	2-sided 95% unadjusted CL	Asymmetric CL [1]	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx			
Co-medication type			3				0.xxxx
~~Week~~			~~1~~				~~0.xxxx~~
Treatment			3				0.xxxx
~~Treatment*Week~~			~~3~~				~~0.xxxx~~
Baseline SF-36	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]		0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	[x.xx to x.xx]	0.xxxx
Model residual standard deviation	xx.xx						

CFB = Change from Baseline; CL = Confidence limits; MMRM: Mixed Model for Repeated Measures; SF-36 = 36-Item Short-Form Health Survey.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: MMRM using Treatment, SF-36 baseline value, and Co-medication type as covariates, with CFB as dependent variable.
Note: model was fitted using an unstructured covariance structure.

Least Square Means: xxxxxxxx

Treatment	Number of patients	LS mean [3]	95% CI of LS mean
Placebo	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI	xx	x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]
MEDI7352 CCI - Placebo		x.xx	[x.xx to x.xx]

CI = Confidence interval; LS = least square.
[3] The LS mean is a model estimate using fitted group parameter and the baseline SF-36 parameter evaluated at the grand mean over each group.
Reference Listing: 16.2.6.4

Programming Notes:

- Include LSmeans and difference in LSmean with Placebo..
- Include all observed data on SF-36 scores for Baseline and Week 12.
- Repeat for the Parameters: Physical Health Summary, and Mental Health Summary Add parameter name after 'Model parameter estimates:' and after 'Least Square Means:'
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.5.1
Rescue Medication Use: Summary Statistics
mITT Population

Variable	Placebo	MEDI7352			Total
		CCI	CCI	CCI	
Statistic or Category	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Number of subjects taking any rescue medication	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Number of subjects taking any permitted rescue medication	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Total number of days rescue medication was used [1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Cumulative consumption of Paracetamol Rescue Medication (mg) [2]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Paracetamol Rescue Medication Average Daily Dose (mg) [3]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Number of subjects taking any prohibited rescue medication	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Each day on which permitted rescue medication was used at least once is counted.
[2] Calculated as the total dose of paracetamol rescue medication (mg).
[3] Calculated as: cumulative consumption of paracetamol rescue medication (mg) /total number of days rescue medication was used.

Reference Listing: 16.2.6.5

Programming Notes:

- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.
- Refer to

Table 14.2.6.1.1
Daily Pain NRS Responder Analysis (≥30%): Cochran-Mantel Haenszel (Observed Cases)
mITT Population

Cochran-Mantel-Haenszel Test

Treatment/ Category	Number of Subjects (%)	Risk Difference [1]	95% CI of Risk Difference	2-sided P-value [2]
Placebo (n = xx)				
>=30% decrease from Baseline	xx (xx.x%)			
MEDI7352 CCI (n = xx)				
>=30% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI (n = xx)				
>=30% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI (n = xx)				
>=30% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx

CI = confidence interval; CMH = Cochran-Mantel-Haenszel; NRS = numeric rating scale.
[1] Common effect for the strata (co-medication type*median Baseline Pain NRS) specific risk difference, representing common difference in probability across strata of MEDI7352 dose - Placebo.
[2] P-value < 0.05 indicates a significant association between number of subjects with >=30% decrease from Baseline and treatment across strata.
Note: a separate CMH test is performed for each dose versus placebo at Week 12.
Reference Listing: 16.2.6.1

Programming notes:

- Include all observed data for Week 12.

Table 14.2.6.1.2
Daily Pain NRS Responder Analysis (≥30%): Cochran-Mantel Haenszel (Observed Cases): All Visits
mITT Population

Cochran-Mantel-Haenszel Test: MEDI7352 xxx µg/kg vs Placebo

Visit/ Category	Number of Patients (%)	Risk Difference [1]	95% CI of Risk Difference	2-sided P-value [2]
Placebo, Week 4 (n = xx)				
>=30% decrease from Baseline	xx (xx.x%)			
MEDI7352 xxx µg/kg, Week 4 (n = xx)				
>=30% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Placebo, Week 4 (n = xx)				
>=30% decrease from Baseline	xx (xx.x%)			
MEDI7352 xxx µg/kg, Week 8 (n = xx)				
>=30% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Placebo, Week 12 (n = xx)				
>=30% decrease from Baseline	xx (xx.x%)			
MEDI7352 xxx µg/kg, Week 4 (n = xx)				
>=30% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx

Placebo, Week 18 (n = xx)				
>=30% decrease from Baseline	xx (xx.x%)			
MEDI7352 xxx µg/kg, Week 4 (n = xx)				
>=30% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx

CI = confidence interval; CMH = Cochran-Mantel-Haenszel; NRS = numeric rating scale.
[1] Common effect for the strata (co-medication type*median Baseline Pain NRS) specific risk difference, representing common difference in probability across strata of MEDI7352 dose - Placebo.
[2] P-value < 0.05 indicates a significant association between number of subjects with >=30% decrease from Baseline and treatment across strata.
Note: a separate CMH test is performed for each dose versus placebo.
Reference Listing: 16.2.6.1

Programming Notes:

CCI [redacted]

- Include all observed data for Week 4, 8, 12, and 18.

Table 14.2.6.2
Daily Pain NRS Responder Analysis (≥30%): GEE Analysis (Observed Cases)
mITT Population

Model parameter estimates: Week X

Parameter	Estimate	Z value	Degrees of freedom	Standard Error	2-sided 95% CL	2-sided P-value [2]
Intercept	xx.xx	xx.xx		xx.xxx		
Co-medication type			3			0.xxxx
Week			3			0.xxxx
Treatment			3			0.xxxx
Treatment*Week			9			0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI vs Placebo	xx.xx	xx.xx	1	xx.xxx	[x.xx to x.xx]	0.xxxx
Dispersion	xx.xx					

CL = Confidence limits; GEE: Generalized Estimation Equations; NRS = Numeric rating scale.
[1] Lower limit of 1-sided 90% CL and upper limit of 1-sided 80% CL.
[2] P-value is derived from the following model: GEE using Time, Treatment, Treatment*Time and Co-medication type as covariates, with dependent binary variable indicating whether weekly average pain NRS has >=30% decrease from Baseline.
Note: model was fitted using a first-order autoregressive covariance structure. Estimates for MEDI7352 dose vs placebo and for 2-sided 95% CL displayed in odds ratio scale.

Reference Listing: 16.2.6.1

Programming notes:

- Include all observed data for Week 4, 8, 12, and 18.
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.7.1.1
Daily Pain NRS Responder Analysis (≥50%): Cochran-Mantel Haenszel (Observed Cases)

mITT Population

Cochran-Mantel-Haenszel Test

Treatment/ Category	Number of Subjects (%)	Risk Difference [1]	95% CI of Risk Difference	2-sided P-value [2]
Placebo (n = xx)				
>=50% decrease from Baseline	xx (xx.x%)			
MEDI7352 CCI (n = xx)				
>=50% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI (n = xx)				
>=50% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
MEDI7352 CCI (n = xx)				
>=50% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx

CI = confidence interval; CMH = Cochran-Mantel-Haenszel; NRS = numeric rating scale.
[1] Common effect for the strata (co-medication type*median Baseline Pain NRS) specific risk difference, representing common difference in probability across strata of MEDI7352 dose - Placebo.
[2] P-value < 0.05 indicates a significant association between number of subjects with >=50% decrease from Baseline and treatment across strata.
Note: a separate CMH test is performed for each dose versus placebo at Week 12.
Reference Listing: 16.2.6.1

Programming notes:

- Include all observed data for Week 12.

Table 14.2.7.1.2
Daily Pain NRS Responder Analysis (≥50%): Cochran-Mantel Haenszel (Observed Cases): All Visits
mITT Population

Cochran-Mantel-Haenszel Test: MEDI7352 xxx µg/kg vs Placebo

Visit/ Category	Number of Patients (%)	Risk Difference [1]	95% CI of Risk Difference	2-sided P-value [2]
Placebo, Week 4 (n = xx)				
>=50% decrease from Baseline	xx (xx.x%)			
MEDI7352 xxx µg/kg, Week 4 (n = xx)				
>=50% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Placebo, Week 4 (n = xx)				
>=50% decrease from Baseline	xx (xx.x%)			
MEDI7352 xxx µg/kg, Week 8 (n = xx)				
>=50% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Placebo, Week 12 (n = xx)				
>=50% decrease from Baseline	xx (xx.x%)			
MEDI7352 xxx µg/kg, Week 4 (n = xx)				
>=50% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx

Placebo, Week 18 (n = xx)				
>=50% decrease from Baseline	xx (xx.x%)			
MEDI7352 xxx µg/kg, Week 4 (n = xx)				
>=50% decrease from Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx

CI = confidence interval; CMH = Cochran-Mantel-Haenszel; NRS = numeric rating scale.
[1] Common effect for the strata (co-medication type*median Baseline Pain NRS) specific risk difference, representing common difference in probability across strata of MEDI7352 dose - Placebo.
[2] P-value < 0.05 indicates a significant association between number of subjects with >=50% decrease from Baseline and treatment across strata.
Note: a separate CMH test is performed for each dose versus placebo.
Reference Listing: 16.2.6.1

Programming Notes:

CCI [redacted]

- Include all observed data for Week 4, 8, 12, and 18.

Table 14.2.7.2
Daily Pain NRS Responder Analysis (≥50%): GEE Analysis (Observed Cases)
mITT Population

Programming notes:

- Same shell as Table 14.2.6.2. Change footnote in [2] as: "p-value is derived from the following model: GEE using Time, Treatment, Treatment*Time and Co-medication type as covariates, with dependent binary variable indicating whether weekly average pain NRS has >=50% decrease from Baseline. Note: model was fitted using an unstructured covariance structure, with 'MEDI7352 CCI ' and 'MEDI7352 CCI treatment groups, together with co-medication categories (both types at the same time and none) dropped from the analysis to make the generalized Hessian matrix positive definite. Estimates for MEDI7352 dose vs placebo and for 2-sided 95% CL displayed in odds ratio scale.".
- Include all observed data for Week 4, 8, 12, and 18.
- Rows for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.8.1
Patient Global Impression of Change: Summary Statistics
mITT Population

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	Total (N=XX)
Week 4					
Number of PGIC Responders	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Very Much Improved	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Much Improved	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Minimally Improved	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
No change	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Minimally Worse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Much Worse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Very Much Worse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 8					
…					

N = number of subjects per treatment group; PGIC = Patient Global Impression of Change.
Note: Percentages for Number of subjects in the different improvement categories relative to baseline are n/Number of Subjects by treatment group at each visit *100.

Reference Listing: 16.2.6.6

Programming notes:

- Include all observed data on PGIC scores for Week 4, 8, 12 and 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.2.8.2
Patient Global Impression of Change: Cochran-Mantel Haenszel
mITT Population

Cochran-Mantel-Haenszel Test: MEDI7352 xxx µg/kg vs Placebo

Visit/ Category	Number of Patients (%)	Risk Difference [1]	95% CI of Risk Difference	2-sided P-value [2]
Placebo, Week 4 (n = xx)				
Improved relative to Baseline	xx (xx.x%)			
MEDI7352 xxx µg/kg, Week 4 (n = xx)				
Improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Placebo, Week 4 (n = xx)				
Improved relative to Baseline	xx (xx.x%)			
MEDI7352 xxx µg/kg, Week 8 (n = xx)				
Improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx
Placebo, Week 12 (n = xx)				
Improved relative to Baseline	xx (xx.x%)			
MEDI7352 xxx µg/kg, Week 4 (n = xx)				
Improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx

Placebo, Week 18 (n = xx)				
Improved relative to Baseline	xx (xx.x%)			
MEDI7352 xxx µg/kg, Week 4 (n = xx)				
Improved relative to Baseline	xx (xx.x%)	x.xx	[x.xx to x.xx]	0.xxxx

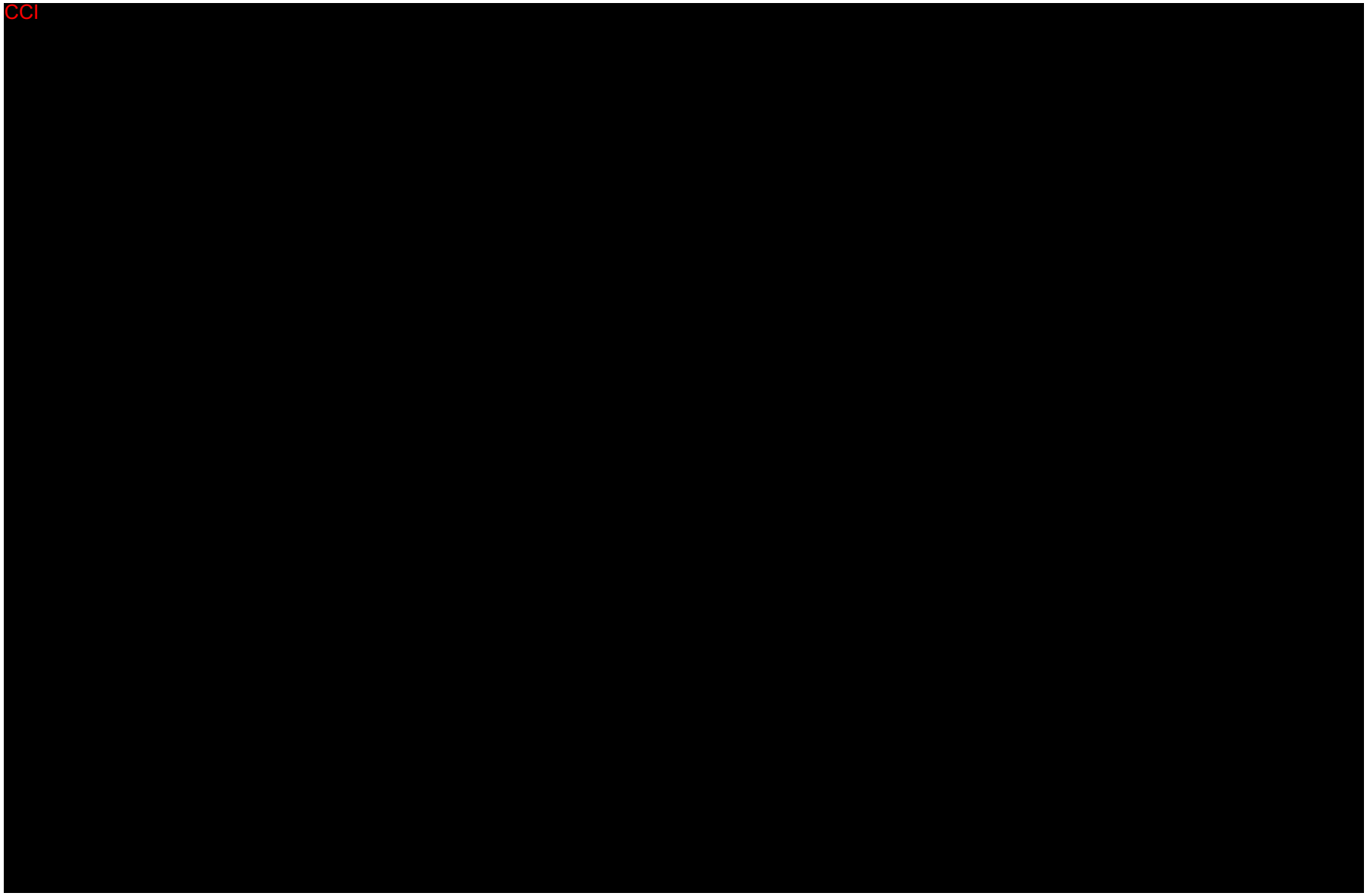
CI = confidence interval; CMH = Cochran-Mantel-Haenszel; NRS = numeric rating scale.
[1] Common effect for the strata (co-medication type*median Baseline Pain NRS) specific risk difference, representing common difference in probability across strata of MEDI7352 dose - Placebo.
[2] P-value < 0.05 indicates a significant association between improvement relative to Baseline and treatment across strata.
Note: median Baseline Pain NRS was calculated from subjects having valid NRS data on at least one of the above four post-baseline visits. Note: a separate CMH test is performed for each dose versus placebo.
Reference Listing: 16.2.6.6

Programming Notes:

- Include all observed data on PGIC scores for Week 4, 8, 12 and 18.

5. Exploratory Efficacy Analyses

CCI



CCI

6. Safety and Tolerability

6.1. Displays of Adverse Events

Table 14.3.1.1
Summary of Overall Adverse Events
Safety Population

Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Subjects with any AE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any TEAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any SAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any SAE possibly related to IP [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any TEAE leading to Discontinuation of IP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any TEAE related to IP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Mild related to IP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Moderate related to IP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAE categorized as Severe related to IP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with any SAE leading to Death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

AE = adverse event; IP = Investigational product, N = number of subjects per treatment group; SAE = serious adverse event; TEAE = treatment emergent adverse event.
[1] Possibly related is defined as with reasonable possibility that the AE was caused by the IP, as assessed by investigator.
Note: Subjects who reported more than one adverse event within each category were only counted once. A TEAE is defined as an adverse event with an onset at the time of or following the start of treatment with IP. For TEAEs categorized by severity, subjects were counted at the maximum severity.
Reference Listing: 16.2.7.1, 16.2.7.2, 16.2.7.3, 16.2.7.4

Programming Notes:

- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class	Placebo	MEDI7352				Total
		CCI	CCI	CCI	All MEDI7352	
	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Preferred Term	n (n/N * 100) m	n (n/N * 100) m	n (n/N * 100) m	n (n/N * 100) m	n (n/N * 100) m	n (n/N * 100) m
Subjects with at Least One TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx

AE = adverse event; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects within each SOC/PT category; N = number of subjects per treatment group; IP = investigational product; PT = Preferred Term; SOC = System Organ Class; TEAE = treatment-emergent adverse event.
Note: Results are n (n/N * 100) m is number of events.
A TEAE is defined as AE with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0. Subjects are counted once for each SOC and once for each PT.
AEs are displayed by descending frequency of SOC, then descending frequency of PT within SOC, based on 'All MEDI7352' column. Table is sorted by international order for SOC of same frequency, and alphabetically for PT of same frequency.
Reference Listing: 16.2.7.1

Programming Notes:

- SOC and PT texts should be in proper case in table.
- In case a term is not coded (e.g. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]", and sorted at the end of the table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.3
Treatment Emergent Adverse Events by Severity, System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term Severity	Placebo	MEDI7352				Total
		CCI	CCI	CCI	All MEDI7352	
	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Subjects with at Least One TEAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

AE = adverse event; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects within each SOC/PT/Severity category; N = number of subjects per treatment group; PT = Preferred Term; SOC = System Organ Class; TEAE = treatment-emergent adverse event.
Note: Results are n (n/N * 100).
A TEAE is defined as an AE with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0. Subjects are counted once for each SOC and once for each PT at the maximum severity.
AEs are displayed by descending frequency of SOC, then descending frequency of PT within SOC, based on 'All MEDI7352' column. Table is sorted by international order for SOC of same frequency, and alphabetically for PT of same frequency.
Reference Listing 16.2.7.1

Programming Notes:

- SOC and PT texts should be in proper case in table.
- Present only severity categories with at least one subject.
- In case a term is not coded (e.g. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]", and sorted at the end of the table. SOC.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.4
Treatment Emergent Adverse Events by Relationship to Study Medication, System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term Relatedness	Placebo	MEDI7352				Total
		CCI	CCI	CCI	All MEDI7352	
	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)	(N=xx)
Subjects with at Least One TEAE	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
System Organ Class 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Preferred Term 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

…

AE = adverse event; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects within each SOC/PT/Relatedness category; N = number of subjects per treatment group; PT = Preferred Term; SOC = System Organ Class; TEAE = treatment-emergent adverse event.
[1] Related is defined as reasonable possibility that the AE was caused by investigational product, as assessed by the investigator. If investigator's assessment is missing the event is judged as related.
Note: Results are n (n/N *100).
A TEAE is defined as an AE with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0. Subjects are counted once for each SOC and once for each PT for the most related AE.
AEs are displayed by descending frequency of SOC, then descending frequency of PT within SOC, based on 'All MEDI7352' column. Table is sorted by international order for SOC of same frequency, and alphabetically for PT of same frequency.
Reference Listing 16.2.7.1

Programming Notes:

- SOC and PT texts should be in proper case in table.
- Present only severity categories with at least one subject.
- In case a term is not coded (e.g. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]", and sorted at the end of the table. SOC.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.5
Treatment Emergent Adverse Events by ADA Status Category, System Organ Class and Preferred Term
Safety Population

Treatment: xxxxxxx

System Organ Class Preferred Term	ADA Negative (N=xx) n (n/N * 100) m	ADA Positive (N=xx) n (n/N * 100) m	TE-ADA + (N=xx) n (n/N * 100) m	Non-TE-ADA + (N=xx) n (n/N * 100) m	TE Persistently ADA + (N=xx) n (n/N * 100) m	TE Transiently ADA + (N=xx) n (n/N * 100) m	Post-Baseline and Baseline Positive (N=xx) n (n/N * 100) m	Only Baseline Positive (N=xx) n (n/N * 100) m
Subjects with at Least One TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx

AE = adverse event; ADA = Anti-Drug Antibodies; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects within each SOC/PT category; N = number of subjects per ADA status category; PT = Preferred Term; SOC = System Organ Class; TE-ADA + = Treatment emergent ADA positive; TEAE = treatment-emergent adverse event.
ADA categories are defined in the Statistical Analysis Plan.
Note: Results are n (n/N *100) m is number of events.
A TEAE is defined as an AE with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0. Subjects are counted once for each SOC and once for each PT.
Table is sorted by international order for SOC, and alphabetically for PT.
Reference Listing: 16.2.7.1

Programming Notes:

- SOC and PT texts should be in proper case in table.
- Repeat for Placebo, CCI and Overall.
- In case a term is not coded (e.g. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]", and sorted at the end of the table. SOC.
- A table for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.6
Treatment Emergent Adverse Events Leading to Discontinuation of Study Drug by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at Least One TEAE leading to IP discontinuation".
- Update Reference Listing to 16.2.7.2.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.7
Non-Serious Adverse Events Occurring in More than 5% of Subjects by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at Least One Non-Serious TEAEAE".
- Update footnote adding: "The 5% threshold for an AE to be displayed is taken from the Total column."
- Update Reference Listing to 16.2.7.1.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.8
Treatment Emergent Adverse Events Occurring in More than 5% of Subjects by Preferred Term
Safety Population

Preferred Term	Placebo (N=xx) n (n/N * 100) m	MEDI7352 CCI (N=xx) n (n/N * 100) m	MEDI7352 CCI (N=xx) n (n/N * 100) m	MEDI7352 CCI (N=xx) n (n/N * 100) m	MEDI7352 All MEDI7352 (N=xx) n (n/N * 100) m	Total (N=xx) n (n/N * 100) m
Subjects with at Least One TEAE	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
…						

AE = adverse event; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects within each PT category; N = number of subjects per treatment group; PT = Preferred Term; TEAE = treatment-emergent adverse event.
Note: Results are n (n/Number of subjects in the Safety population within each PT*100) m is number of events.
A TEAE is defined as AE with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0. Subjects are counted once for each PT.
AEs are displayed by descending frequency of PT based on 'All MEDI7352' column, and alphabetically for PT of same frequency.
The 5% threshold for a TEAE to be displayed is taken from the Total column.
Reference Listing: 16.2.7.1

Programming Notes:

- PT texts should be in proper case in table.
- In case a term is not coded (e.g., in a dry run) it will be labelled as "Not Coded [PT]" and sorted at the end of the table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.1.9
Treatment Emergent Adverse Events by Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.8.
- Display all TEAEs, not only the most common.
- PT texts should be in proper case in table.
- In case a term is not coded (e.g., in a dry run) it will be labelled as Not Coded [PT]", and sorted at the end of the table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

6.2. Summary of Deaths and Other Serious Adverse Events

Table 14.3.2.1.1
Serious Adverse Events by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Number of Subjects with at Least One Treatment Emergent SAE", add "SAE = Serious Adverse Event" to abbreviations.
- Change footnote for "Reference Table 14.3.3.1".
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.2.1.2
Life-Threatening Serious Adverse Events by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Number of Subjects with at Least One Life-Threatening SAE", add "SAE = Serious Adverse Event" to abbreviations.
- Add "Note: Life-threatening SAEs as judged by the investigator".
- Change footnote for "Reference Table 14.3.3.1".
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated

Table 14.3.2.1.3
Serious Adverse Events with Outcome Death by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Number of Subjects with at Least One SAE with Outcome Death", add "SAE = Serious Adverse Event" to abbreviations.
- Change footnote for "Reference Table 14.3.3.2".
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.2.1.4
Serious Adverse Events by Relationship to Study Medication, System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.4. Change first row to be "Number of subjects with at Least One Treatment Emergent SAE", add "SAE = Serious Adverse Event" to abbreviations.
- Change footnote for "Reference Table 14.3.3.1".
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.3.1
Listing of Serious Adverse Events
Safety Population

Subject ID/ Treatment Arm	AE ID Number	System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date/Time (Study Day)/ End Date/Time (Study Day)	Severity/ Relationship [1]	Outcome/ Action Taken with IP/ Therapy taken for this AE?	SAE Leading to Study DC?	TEAE?	Serious? / Serious Criteria
XXXXX/ XXXX	X	XXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXXXXX/ Yes	No	No	XX
XXXXX/ XXXX	X	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMONYYYY/HH:MM (X)	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXXXXX/ No	Yes	XX	XX / XXX
XXXXX/ XXXX	X	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXX	DDMONYYYY/HH:MM (X)/ Ongoing	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXXXXX/No	No	XX	XX / XXX

DC = discontinuation; ID = identification; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; SAE = serious adverse event; TEAE = treatment emergent adverse event.
[1] Reasonable possibility AE caused by IP as assessed by the investigator.
Note: Study Day = date of interest – date of first infusion. A TEAE is defined as an adverse event with an onset at the time of or following the start of treatment with IP.
SAEs were coded using MedDRA version 26.0

Programming Notes:

- If time missing, display "- -:- -".
- AE ID number represents Record position within Subject.
- If no events meet the criteria for display (i.e, no AEs occur in the study), present "No events are reported.".
- SOC & PT text should be in proper case in table.
- Sort by Treatment ID/ Subject ID / Start Date / End Date (alphabetically for SOC if same date for two events).
- In case a term is not coded (e.g.. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]". SOC and PT abbreviations should be added in this case in footnote.

Table 14.3.3.2
Listing of Deaths
Safety Population

Subject ID/ Treatment Arm	AE ID Number	System Organ Class/ Preferred Term/ Verbatim Term	Start Date/Time (Study Day)/ End Date/Time (Study Day)	Severity/ Relationship	Outcome/ Action Taken/ Therapy?	AE Leading to IP DC?	TEAE?	Serious? / Serious Criteria
XXXXX/ XXXX	X	XXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXXXX/ Yes	No	No	XX
XXXXX/ XXXX	X	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXXXX/No	Yes	XX	XX / XXX
XXXXX/ XXXX	X	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ Ongoing	XXXXXXXX/ XXXXXXXX	XXXXXXXXXX/ XXXXXXX/ No	No	XX	XX / XXX

DC = discontinuation; ID = identification; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; TEAE = treatment emergent adverse event.
Note: Study Day = date of interest – date of first infusion. A TEAE is defined as an adverse event with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0

Programming Notes:

- If time missing, display "- -:- -".
- AE ID number represents Record position within Subject.
- If no events meet the criteria for display (i.e, no Aes occur in the study), present "No events are reported.".
- SOC & PT text should be in proper case in table.
- Sort by Treatment Arm/ Subject ID / Start Date / End Date (alphabetically for SOC if same date for two events).
- In case a term is not coded (e.g., in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]". SOC and PT abbreviations should be added in this case in footnote.

6.3. Displays of Significant Adverse Events and Adverse Events of Special Interest

Table 14.3.2.2.1
Treatment Emergent Adverse Events Associated with Abnormal Liver by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at least One TEAE Associated with Abnormal Liver".
- Update Reference Listing to 16.2.7.3.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.2.2.2
Potential joint Related Adverse Events of Special Interest by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at least One Potential Joint Related AESI"
- Add abbreviation for AESI = Adverse Event of Special Interest. Remove references to TEAEs in footnote.
- Update Reference Listing to 16.2.7.4
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.2.2.3
Serious and/or severe Infections by System Organ Class and Preferred Term
Safety Population

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at Least One SAE or Severe AE Related to Infection". Add "SAE = Serious Adverse Event" to abbreviations. Remove references to TEAEs in footnote.
- Update Reference Listing to 16.2.7.5.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.2.2.4
Anaphylactic Reactions, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of IP by System Organ Class and Preferred Term
Safety Population

System Organ Class	Placebo	MEDI7352				Total
		CCI	CCI	CCI	All MEDI7352	
Preferred Term	(N=xx) n (n/N * 100) m	(N=xx) n (n/N * 100) m	(N=xx) n (n/N * 100) m	(N=xx) n (n/N * 100) m	(N=xx) n (n/N * 100) m	(N=xx) n (n/N * 100) m
Subjects with at Least One Anaphylactic Reaction, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of IP	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Subjects with at Least One Anaphylactic Reaction, Hypersensitivity or Infusion-Related Reactions Not Leading to Discontinuation of IP [1]	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx

AE = adverse event; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; n = number of subjects within each SOC/PT category; N = number of subjects per treatment group; IP = investigational product; PT = Preferred Term; SOC = System Organ Class; TEAE = treatment-emergent adverse event.

[1] Anaphylactic reactions, hypersensitivity or infusion-related reactions not leading to discontinuation of IP were included in table as they were categorized as AE of special interest under Protocol Amendment 4 (V5.0). Definition for AE of special interest changed from Amendment 6 (V6.0) onwards, including anaphylactic reactions, hypersensitivity or infusion-related reactions leading to permanent discontinuation of IP..
Note: Results are n (n/N * 100) m is number of events.
A TEAE is defined as AE with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0. Subjects are counted once for each SOC and once for each PT.
AEs are displayed by descending frequency of SOC, then descending frequency of PT within SOC, based on 'All MEDI7352' column. Table is sorted by international order for SOC of same frequency, and alphabetically for PT of same frequency.
Reference Listing: 16.2.7.6

Programming Notes:

- Same shell as Table 14.3.1.2. Change first row to be "Subjects with at Least One Anaphylactic Reaction, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of IP". Remove references to TEAEs in footnote.
- Update Reference Listing to 16.2.7.6.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

6.4. Laboratory Data

Table 14.3.4.1
Descriptive Summary of Clinical Chemistry
Safety Population

Parameter: xxxxx (unit)

Visit/ Statistic	Placebo (N=xx)	MEDI7352 [redacted] (N=xx)	MEDI7352 [redacted] (N=xx)	MEDI7352 [redacted] (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Low NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Low CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 1						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Low NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Low CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)

Day 1 CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

CFB = change from baseline; CS = clinically Significant; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NCS = not clinically significant; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Note: Percentages are n/Number of subjects with not missing data by treatment group at each visit*100.
Reference Listing: 16.2.8.1

Programming Notes:

- Present only scheduled visits.
- Sort Parameters in the following Order: Albumin, Alkaline Phosphatase, Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Bicarbonate, Calcium, Chloride, Creatinine, High-Sensitivity C-Reactive Protein (hs-CRP), Estimated Glomerular Filtration Rate (eGFR by Cockcroft - Gault), Serum Glucose, Lactate Dehydrogenase (LDH), Potassium, Sodium, Total Bilirubin, Total Protein, Blood Urea Nitrogen (BUN), Uric Acid.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.4.2
Shift Table of Clinical Chemistry Results
Safety Population

Parameter (Unit)/ Visit / Post-Baseline Grade	Baseline Grade [1]									
	Placebo (N=xxx)					MEDI7352, CCI (N=xxx)				
	Low	Normal	High	Missing	Total	Low	Normal	High	Missing	Total
XXXXXX (Unit)										
Week x										
Low	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Missing	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Total	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Week x										
Low	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Missing	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Total	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
…										

n = number of subjects within each category; N = number of subjects per treatment group.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Percentages are n/Number of subjects by treatment group at each visit for the parameter*100.

Reference Listing 16.2.8.1

Programming Notes:

- Repeat above in new pages for MEDI7352, CCI MEDI7352, CCI and All MEDI7352.
- Repeat the above for CCI dosing only if Stage 4 is initiated.
- Repeat for every scheduled visit.
- Present parameters in the same order as in Table 14.3.4.1.

Table 14.3.4.3
Descriptive Summary of Hematology
Safety Population

Programming Notes:

- Same shell as Table 14.3.4.1
- Present only scheduled visits.
- Sort Parameters in the following Order: Absolute basophil count, absolute eosinophil count, absolute lymphocytes count, Absolute Monocyte Count, Absolute Neutrophil Count, Basophils %, Eosinophils %, Hematocrit (HCT), Hemoglobin (HGB), hemoglobin A1C (HgbA1C), Lymphocytes %, mean corpuscular hemoglobin (MHC), Mean Corpuscular Hemoglobin Concentration (MCHC), Mean Corpuscular Volume (MCV), Monocytes %, Neutrophils %, Platelets, Red blood cell count (RBC), Red Cell Distribution Width, white blood cell Count (WBC).
- Update Reference listing to 16.2.8.2.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.4.4
Shift Table of Hematology Results
Safety Population

Programming Notes:

- Same shell as Table 14.3.4.2
- Repeat the shell for CCI dosing if Stage 4 is initiated.
- Repeat for every scheduled visit.
- Present parameters in the same order as in Table 14.3.4.3.
- Update Reference listing to 16.2.8.2

Table 14.3.4.5
Descriptive Summary of Coagulation
Safety Population

Programming Notes:

- Same shell as Table 14.3.4.1
- Present only scheduled visits.
- Sort Parameters in the following Order: Activated Partial Thromboplastin Clotting Time (APTT), Fibrinogen, International normalized ratio (INR), Prothrombin Time (PT).
- Update Reference listing to 16.2.8.3.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.4.6
Shift Table of Coagulation Results
Safety Population

Programming Notes:

- Same shell as Table 14.3.4.2
- Repeat for CCI dosing if Stage 4 is initiated.
- Repeat for every scheduled visit.
- Present parameters in the same order as in Table 14.3.4.5.
- Update Reference listing to 16.2.8.3.

Table 14.3.4.7
Descriptive Summary of Urinalysis
Safety Population

Parameter: xxxxx (unit)

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Low NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Low CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 1						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Low NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Low CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 1 CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

…

Repeat for all visits for Parameters: Specific Gravity and pH

Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Negative	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Positive	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
If Positive, Specify [2]						
100 mg/dL	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
250 mg/dL	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
500 mg/dL	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
>= 1000 mg/dL	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 1						
n	xx	xx	xx	xx	xx	xx
Negative	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Positive	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High NCS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
High CS	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)

…

Repeat for all visits for Parameters: Blood, Glucose, Ketones and Protein

CFB = change from baseline; CS = clinically significant; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NCS = not clinically significant; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
[2] Percentages are n/Number of Subjects with a Positive Result*100.
Note: Percentages are n/Number of subjects with not missing data by treatment group at each visit*100.
Reference Listing: 16.2.8.4

Programming Notes:

- Present only scheduled visits.
- Sort Parameters in the following Order: Blood Urine, Glucose, Ketones, pH, Protein, Specific Gravity.
- Categories for If Positive, Specify:
  - Blood, Urine: Trace, Small, Moderate.
  - Glucose: 100 mg/dL, 250 mg/dL, 500 mg/dL, >= 1000 mg/dL.
  - Ketones: Trace, 15 mg/dL, 40 mg/dL.
  - Protein: Trace, 30 mg/dL, 100 mg/dL, 300 mg/dL.

- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.4.8
Shift Table of Urinalysis Results
Safety Population

Programming Notes:

- Same shell as Table 14.3.4.2
- Repeat for CCI dosing if Stage 4 is initiated.
- Repeat for every scheduled visit.
- Present parameters in the same order as in Table 14.3.4.7.
- Update Reference listing to 16.2.8.4

Table 14.3.4.9
Maximum On-Treatment ALT and AST versus Maximum On-Treatment Total Bilirubin
Safety Population

Group	Nobs		Total Bilirubin <2 x ULN n (%)	Total Bilirubin >=2 x ULN n (%)
Placebo				
N=xxx	xxx	ALT		
		<3 x ULN	x (xx.x%)	x (xx.x%)
		>=3 - <5 x ULN	x (xx.x%)	x (xx.x%)
		>=5 - <10 x ULN	0	0
		>=10 x ULN	0	0
	xxx	AST		
		<3 x ULN	x (xx.x%)	x (xx.x%)
		>=3 - <5 x ULN	x (xx.x%)	x (xx.x%)
		>=5 - <10 x ULN	0	0
		>=10 x ULN	0	0

…
Repeat for: CCI [redacted] ***All MEDI7352***

ALT = alanine aminotransferase; AST = aspartate aminotransferase; IP = investigational product; n = number of subjects per category; N = number of subjects per treatment group; Nobs = number of subjects per treatment group with at least one post-baseline assessment on treatment; ULN = upper limit of normal.
Note: On-treatment assessments include assessments on or after the date of first dose of IP. Baseline is defined as the last observation recorded prior to the first dose of treatment.
Percentages are based on Nobs.
Reference Listing: 16.2.8.1

Programming Notes:

- Per Protocol, the elevations of ALT or AST and Total Bilirubin do not have to occur at the same time or within a specified time frame. That is the reason why the table is presented by Subject instead of by visit. So, if for example, one subject has ALT >=3 - <5 x ULN at Day 1, and TBL >=2 x ULN at Week 18, n in that cell will increase by one.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

6.5. Other Safety Data

Table 14.3.5.1
Descriptive Summary of Vital Signs
Safety Population

Parameter: xxxxx

Visit Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	 CCI (N=xx)	 CCI (N=xx)	 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1: 15 Minutes Post-Dose						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1: 15 Minutes Post-Dose CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

…

CFB = Change from Baseline; eCRF = Electronic Case Report Form; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Note: 'Day 1: 5 minutes after Infusion Completion' timepoint was only applied to subjects enrolled in Stage 1, with data collected under eCRF versions 4.0 (11DEC2018) or older.
Reference Listing: 16.2.9.1

Programming Notes:

- Repeat for Supine Heart Rate, Supine Systolic Blood Pressure, Supine Diastolic Blood Pressure, Respiratory Rate, Body Temperature, Standing Heart Rate, Standing Systolic Blood Pressure, Standing Diastolic Blood Pressure.
- After Week 2 (inclusive), Supine measure are taken in sitting position. We will consider them as supine (in resting position) for calculating Change from Baseline (always at supine position).
- Include the following timepoints: Baseline, Day 1: 5 Minutes Post-Dose, Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week 10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- Note that Body Tº, and standing measures are not taken on Day 1, at 15, 30 and 45 minutes post-dose.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.2
Descriptive Summary of Digital ECG Data
Safety Population

Parameter: xxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1: 1 hour Post-Dose						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1: 1 hour Post-Dose CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
…						

CFB = Change from Baseline; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group ; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
Note: Data shown are averages of the 3 replicates taken for each parameter and timepoint, and CFB for the same variables.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.

Reference Listing: 16.2.9.2

Programming Notes:

- Repeat for PR, QRS, QT, RR, HR (Heart Rate) and QTcF taken from external data.
- Include the following timepoints: Baseline, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 4, Week, 8, Week 12, and Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.3
Summary of Overall Evaluation of Safety ECG Data
Safety Population

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Day 1: 1 hour Post-Dose						
n	xx	xx	xx	xx	xx	xx
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

CS = clinically significant; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NCS = Not clinically significant.
Note: Data are taken as the most conservative from the 3 replicates taken by timepoint.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.

Reference Listing: 16.2.9.2

Programming Notes:

- Include the following timepoints: Baseline, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 4, Week, 8, Week 12, and Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.4
Covid-19 Screening
Safety Population

Visit/ Variable Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Day 1						
Subjects Screened for COVID-19 Symptoms	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Symptoms Screened:						
Fever	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Cough	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dyspnoea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sore Throat	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Loss of Taste	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Loss of Smell	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Body Temperature Check						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Subjects with COVID-19 Swab Performed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Negative	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Subjects with COVID-19 Antibody Testing Performed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Confirmed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Suspected	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Negative	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Subjects with COVID-19 Antigen Testing Performed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Positive	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
COVID-19 Negative	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

COVID-19 = coronavirus disease 2019; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
Note: Percentages for COVID-19 screened subjects are n/Number of subjects by treatment group*100. Percentages for symptoms/test results are n/Number of subjects by treatment group at each visit without missing result*100.
Reference Listing: 16.2.8.8

Programming Notes:

- Include the following timepoints: Day 1, Week 2, Week 4, Week 6, Week, 8, Week 10.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.5
Summary of Sub-Scores for Total Neuropathy Score-Nurse
Safety Population

Visit/ Variable Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
Subjects performing TNSn	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sensory Symptom Score						
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Motor Symptom Score						
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Autonomic Symptom Score						
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pin Sensibility Score						
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Vibration Sensibility Score						
0	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
...						

N = number of subjects per treatment group; TNSn = Total Neuropathy Score-Nurse.

[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Note: Percentages for subjects performing TNSn are n/Number of subjects by treatment group*100. Percentages for each Score are n/Number of subjects by treatment group at each visit without missing score*100.

Reference Listing: 16.2.9.5

Programming Notes:

- Include the following timepoints: Baseline, Day 1, Week 2, Week 4, Week 6, Week, 8, Week 10, Week 12 and Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.6
Descriptive Summary of Total Neuropathy Score-Nurse
Safety Population

Score: xxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Day 1 CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

TNSn = Total Neuropathy Score-Nurse; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment. Reference Listing: 16.2.9.5

Programming Notes:

- Include the following timepoints: Baseline, Day 1, Week 2, Week 4, Week 6, Week, 8, Week 10, Week 12 and Week 18.
- Include the following scores: Sensory Symptom Score, Motor Symptom Score, Autonomic Symptom Score, Pin Sensibility Score, Vibration Sensibility Score,

and TNSn Total.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.7.1
Summary of Motor and Sensory Nerve Conduction Studies
Safety Population

Parameter: xxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 18						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 18 CFB						
n	xx	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Evaluation Result						
Baseline [1]						
n	xx	xx	xx	xx	xx	xx
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 18						
n	xx	xx	xx	xx	xx	xx
Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abnormal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

CFB = Change from Baseline; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Note: Percentages are number of subjects by treatment group at each visit for each category /Number of subjects with not missing data by treatment group for each visit*100.
Reference Listing: 16.2.9.6

Programming Notes:

CCI [redacted]

- Repeat for the following Parameters: Lower Limb - Right Side/Fibular Nerve/Motor Evaluation/Amplitude (mV), Lower Limb - Right Side/Tibial Nerve/Motor Evaluation/Amplitude (mV), Lower Limb - Right Side/Sural Nerve/Sensory Evaluation/Amplitude (uV), Lower Limb - Left Side/Fibular Nerve/Motor Evaluation/Amplitude (mV), Lower Limb - Left Side/Tibial Nerve/Motor Evaluation/Amplitude (mV), Lower Limb - Left Side/Sural Nerve/Sensory Evaluation/Amplitude (uV), Upper Limb - Right Side/Medial Nerve/Motor Evaluation/Amplitude (mV), Upper Limb - Right Side/Ulnar Nerve/Motor Evaluation/Amplitude (mV), Upper Limb - Right Side/Medial Nerve/Sensory Evaluation/Amplitude (mV), Upper Limb - Right Side/Ulnar Nerve/Sensory Evaluation/Amplitude (mV), Upper Limb - Left Side/Medial Nerve/Motor Evaluation/Amplitude (mV), Upper Limb - Left Side/Ulnar Nerve/Motor Evaluation/Amplitude (mV), Upper Limb - Left Side/Medial Nerve/Sensory Evaluation/Amplitude (mV), Upper Limb - Left Side/Ulnar Nerve/Sensory Evaluation/Amplitude (mV), Lower Limb - Right Side/Fibular Nerve/Motor Evaluation/Conduction Velocity (msec), Lower Limb - Right Side/Tibial Nerve/Motor Evaluation/Conduction Velocity (msec), Lower Limb - Right Side/Sural Nerve/Sensory Evaluation/Conduction Velocity (msec), Lower Limb - Left Side/Fibular Nerve/Motor Evaluation/Conduction Velocity (msec), Lower Limb - Left Side/Tibial Nerve/Motor Evaluation/Conduction Velocity (msec), Lower Limb - Left Side/Sural Nerve/Sensory Evaluation/Conduction Velocity (msec), Upper Limb - Right Side/Medial Nerve/Motor Evaluation/Conduction Velocity (msec), Upper Limb - Right Side/Ulnar Nerve/Motor Evaluation/Conduction Velocity (msec). Upper Limb - Right Side/Medial Nerve/Sensory Evaluation/Conduction Velocity (msec), Upper Limb - Right Side/Ulnar Nerve/Sensory Evaluation/Conduction Velocity (msec), Upper Limb - Left Side/Medial Nerve/Motor Evaluation/Conduction Velocity (msec), Upper Limb - Left Side/Ulnar Nerve/Motor Evaluation/Conduction Velocity (msec), Upper Limb - Left Side/Medial Nerve/Sensory Evaluation/Conduction Velocity

(msec), Upper Limb - Left Side/Ulnar Nerve/Sensory Evaluation/Conduction Velocity (msec), Lower Limb - Right Side/Fibular Nerve/Motor Evaluation/Duration of Action Potential (msec), Lower Limb - Right Side/Tibial Nerve/Motor Evaluation/Duration of Action Potential (msec), Lower Limb - Right Side/Sural Nerve/Sensory Evaluation/Duration of Action Potential (msec), Lower Limb - Left Side/Fibular Nerve/Motor Evaluation/Duration of Action Potential (msec), Lower Limb - Left Side/Tibial Nerve/Motor Evaluation/Duration of Action Potential (msec), Lower Limb - Left Side/Sural Nerve/Sensory Evaluation/Duration of Action Potential (msec), Upper Limb - Right Side/Medial Nerve/Motor Evaluation/Duration of Action Potential (msec), Upper Limb - Right Side/Ulnar Nerve/Motor Evaluation/Duration of Action Potential (msec), Upper Limb - Right Side/Medial Nerve/Sensory Evaluation/Duration of Action Potential (msec), Upper Limb - Right Side/Ulnar Nerve/Sensory Evaluation/Duration of Action Potential (msec), Upper Limb - Left Side/Medial Nerve/Motor Evaluation/Duration of Action Potential (msec), Upper Limb - Left Side/Ulnar Nerve/Motor Evaluation/Duration of Action Potential (msec), Upper Limb - Left Side/Medial Nerve/Sensory Evaluation/Duration of Action Potential (msec), Upper Limb - Left Side/Ulnar Nerve/Sensory Evaluation/Duration of Action Potential (msec), Lower Limb - Right Side/Fibular Nerve/Motor Evaluation/Peak Latency (msec), Lower Limb - Right Side/Tibial Nerve/Motor Evaluation/Peak Latency (msec), Lower Limb - Right Side/Sural Nerve/Sensory Evaluation/Peak Latency (msec), Lower Limb - Left Side/Fibular Nerve/Motor Evaluation/Peak Latency (msec), Lower Limb - Left Side/Tibial Nerve/Motor Evaluation/Peak Latency (msec), Lower Limb - Left Side/Sural Nerve/Sensory Evaluation/Peak Latency (msec), Upper Limb - Right Side/Medial Nerve/Motor Evaluation/Peak Latency (msec), Upper Limb - Right Side/Ulnar Nerve/Motor Evaluation/Peak Latency (msec), Upper Limb - Right Side/Medial Nerve/Sensory Evaluation/Peak Latency (msec), Upper Limb - Right Side/Ulnar Nerve/Sensory Evaluation/Peak Latency (msec), Upper Limb - Left Side/Medial Nerve/Motor Evaluation/Peak Latency (msec), Upper Limb - Left Side/Ulnar Nerve/Motor Evaluation/Peak Latency (msec), Upper Limb - Left Side/Medial Nerve/Sensory Evaluation/Peak Latency (msec), Upper Limb - Left Side/Ulnar Nerve/Sensory Evaluation/Peak Latency (msec).

- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.7.2
Shift Table of Motor and Sensory Nerve Conduction Results
Safety Population

Parameter (Unit)/ Visit / Post-Baseline Grade	Baseline Grade [1]							
	Placebo (N=xxx)				MEDI7352, CCI (N=xxx)			
	Normal	Abnormal	Missing	Total	Normal	Abnormal	Missing	Total
XXXXXX (Unit)								
Week 18								
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Abnormal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Missing	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Total	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
XXXXXX (Unit)								
Week 18								
Normal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Abnormal	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Missing	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Total	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
…								

n = number of subjects within each category; N = number of subjects per treatment group.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Percentages are n/Number of subjects by treatment group at each visit for the parameter*100.

Reference Listing 16.2.9.6

Programming Notes:

CCI

- Repeat above in new pages for MEDI7352, CCI MEDI7352, CCI and All MEDI7352.
- Repeat the above for CCI dosing only if Stage 4 is initiated.
- Repeat for every scheduled visit.
- Present parameters in the same order as in Table 14.3.5.7.1.

Table 14.3.5.8
Summary of Strength and Deep Tendon Reflexes
Safety Population

Visit/ Variable Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Baseline [1]						
Subjects performing SDTR assessment	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ankle Dorsiflexion Strength						
0 - Normal Power	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1 - Mild Weakness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 - Moderate Weakness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 - Severe Weakness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 - Paralysis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Deep Tendon Reflexes						
0 - Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
1 - Ankle reflex reduced	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
2 - Ankle reflex absent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
3 - Ankle reflex absent and knee reflex reduced	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
4 - All reflexes (both ankle and knee) absent	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

n = number of subjects by treatment group at each visit for each category; N = number of subjects per treatment group; SDTR = strength and deep tendon reflexes.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Note: Percentages for subjects performing SDTR assessment are n/Number of subjects by treatment group*100. Percentages for each Score are n/Number of subjects by treatment group at each visit*100.

Reference Listing: 16.2.9.7

Programming Notes:

- Include the following timepoints: Baseline, Day 1, Week 2, Week 4, Week 6, Week, 8, Week 10, Week 12, and Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.9
Summary of Local Injection Site Reactions
Safety Population

Visit/ Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Day 1: 15 Minutes after Start of Infusion						
Subjects with injection Site Assessed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pain						
None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tenderness						
None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Erythema/ Redness						
None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Induration/ Swelling						
None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

n = number of subjects by treatment group at each visit for each category; N = number of subjects per treatment group.
Note: Percentages for subjects performing injection site assessment are n/Number of subjects by treatment group*100. Percenta ges for each Score are n/Number of subjects by treatment group at each visit*100. Subject PPD suffered an injection site reaction starting on 25MAR2019 and ending on 23APR2019, spanning Study visits Week 8, 10 and 12. However, injection site assessment was not performed on this subject till Week 18, existing high possibility for symptoms to have receded by then.
Reference Listing: 16.2.9.8

Programming Notes:

- Include the following timepoints: Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2, Week 4, Week 6, Week, 8, Week 10, Week 12, and Week 18.
- A column for CCI dosing CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.10
Summary of Hypersensitivity/Anaphylactic Reactions
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with any Hypersensitivity/ Anaphylaxis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Highest Severity Grade						
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Type of Reaction						
Urticaria	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pruritus	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Rash	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Flushing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Swollen Lips, Tongue, Uvula and/or Vulva	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dyspnoea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Wheeze-Bronchospasm	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Stridor	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hypoxia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hypotension	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Crampy Abdominal Pain	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Vomiting	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Diarrhoea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…						

N = number of subjects per treatment group.
Reference Listing: 16.2.9.9

Programming Notes:

- Display only Type of reaction with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.11
Summary of Liver Diagnostic Investigations
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Liver Diagnostics Performed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Type of Diagnostic Investigation						
Ultrasound	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
CT	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
MRI/MRCP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Flushing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ERCP	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
X-Ray	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tox Screening for Acetaminophen/Paracetamol	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tox Screening for Ethanol	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tox Screening, Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Specialist Consulted	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Hepatitis A	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Hepatitis B	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Hepatitis C	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Hepatitis D	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Hepatitis E	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)
Serology for Cytomegalovirus	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serology for Epstein Barr Virus	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Autoimmune Serology	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

CT = Computerized tomography; ERCP = Endoscopic retrograde cholangiopancreatography; MRI = Magnetic resonance imaging; MRCP = Magnetic resonance cholangiopancreatography; N = number of subjects per treatment group.
Reference Listing: 16.2.9.10

Programming Notes:

- Display only Diagnostic Investigations with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.12
Summary of Liver Risk Factors and Lifestyle Events
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Liver Risk Factors Assessed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Liver Risk Factor						
Alcohol Abuse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Increased Alcohol Consumption within 1 Month of Reported Event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
IV Drug Abuse	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tattoo	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Acupuncture	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sexually Transmitted Diseases	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Toxic/Chemical Agent Exposure	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Travel (Areas at Risk in the Last Year)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pregnancy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Parenteral Nutrition	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Excessive Physical Exercise	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Changes Diet/Fasting Episodes/Weight Loss Diet	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Previous Drug Reaction	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Blood Transfusion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Patient Exposed to Anyone with Jaundice in the Last Month	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)
History of Hypotension	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Low Blood Pressure at Time of Event of Liver Injury and/or Abnormal Liver Laboratory Value	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
History of Liver Disease	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

IV = intravenous; N = number of subjects per treatment group.
Reference Listing: 16.2.9.10

Programming Notes:

- Display only Liver Risk Factor with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.13
Summary of Liver Signs and Symptoms
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Liver Signs/Symptoms Assessed	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Liver Sign/Symptom						
Anorexia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Asthenia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pyrexia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pruritus	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Jaundice	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Arthralgia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abdominal Pain	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Abdominal Tenderness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Nausea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Vomiting	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Rash	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mucosal Inflammation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Purpura	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hepatomegaly	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Splenomegaly	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)
Lymphadenopathy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Ascites	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Confusional State	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Coma	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Upper Quadrant Tenderness	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)	xx xx.x%)
Biliary Obstruction	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Eosinophilia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dark Urine	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

N = number of subjects per treatment group.
Reference Listing: 16.2.9.12

Programming Notes:

- Display only Liver Signs/Symptoms with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.14
Summary of Infection Diagnostic Investigations
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Infection Diagnostic Investigations	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Method						
Microscopy, Culture and Sensitivity	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serological Tests	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Nucleic Acid Based Tests	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
X-Ray	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Other	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

N = number of subjects per treatment group.
Reference Listing: 16.2.9.13

Programming Notes:

- Display only Methods with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.15
Summary of Infection Risk Factors and Lifestyle Events
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Infection Risk Factor Occurred	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Infection risk factor						
Extensive Burns within the Last Year	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tattoo, Piercing or Acupuncture within the last Year	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Sexually Transmitted Diseases	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Travel to Areas at Risk of Tuberculosis or Tropical Diseases	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Infections Related to Travel	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Blood Transfusion (within the Last Year)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Exposure to Nosocomial Pathogens within the Last Year	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Contact History with Infection Source	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Previous BCG Immunization	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Evidence of BCG Scar	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Tuberculin Skin or Quantiferon Test Confirms Previous Exposure or Immunity to Tuberculosis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

BCG = Bacillus Calmette-Guerin; N = number of subjects per treatment group.
Reference Listing: 16.2.9.14

Programming Notes:

- Display only infection risk factors with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.16
Summary of Infection Signs and Symptoms
Safety Population

Statistic or Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)	Total (N=xx)
Subjects with Infection Sign/Symptom Occurred	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Infection Sign/Symptoms						
Pyrexia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Headache	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Confusional State	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Convulsion	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Rhinitis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Oropharyngeal Pain	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Cough	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Productive Cough	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Haemoptysis	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Wheezing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dyspnoea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pleuritic Pain	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Vomiting	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Diarrhoea	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Genital Discharge	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Haematuria	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Dysuria	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Hepatosplenomegaly	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Jaundice	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Lymphadenopathy	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Rash	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Petechial	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Vesicular	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Macular	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Papular	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Urticaria	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Erythema	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Blanching	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Splinter Haemorrhages	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Night sweats	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Chills	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Myalgia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Weight Decrease	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

N = number of subjects per treatment group.
Reference Listing: 16.2.9.15

Programming Notes:

- Display only infection Signs/Symptoms with non-missing value.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.17
Summary of Concomitant Medications by ATC Level 2 and Preferred Name
Safety Population

Programming Notes:

- Same shell as Table 14.1.7.
- Change footnote Note by: "Note: Concomitant medications are defined as medications continuing or starting on or after first dose of study medication. All concomitant medications are coded using WHO drug dictionary version vMar2023. At each level of summarization (ATC Level 2 or Preferred Name), subjects who reported more than one concomitant medication were only counted once. ATC Level 2 and Preferred Name are sorted in in descending order of frequency of total, and alphabetically if same frequency".
- If uncoded ATC Level or Preferred Name, please put them as [Not Coded]
- ATC and Preferred Name texts should be in proper case in table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.18
Summary of Concomitant Procedures
Safety Population

System Organ Class Preferred Term	Placebo (N=xxx)	MEDI7352 CCI (N=xx)	 CCI (N=xx)	 CCI (N=xx)	Total (N=xxx)
Any Concomitant Procedure	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
System Organ Class 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
…	…	…	…	…	…
System Organ Class n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term 1	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)
Preferred Term n	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)	xx (xx.x %)

N = number of subjects per treatment group; PT = Preferred Term; SOC = System Organ Class.
Note: All Procedure terms were coded using the Medical Dictionary for Regulatory Activities (MedDRA), version 26.0. At each level of summarization (system organ class or preferred term), subjects having more than one Procedure term were counted only once. System organ class and preferred terms are sorted in descending order of frequency of Total column, and alphabetically if same frequency.
When there are uncoded Procedure Events in the database, the events will be summarized with SOC and PT set to [Not Coded]. The [Not Coded] are sorted at the end of the table.

Reference Listing: 16.2.9.18

Programming Notes:

- SOC and PT texts should be in proper case in table.
- Sort SOC and PT (within SOC) in descending order of frequency in the Total column. Sort alphabetically in case of ties.
- Uncoded Procedure events
  - When there are uncoded Procedure Events in the database, the events will be summarized with SOC and PT set to [Not Coded]. The [Not Coded] will be sorted at the end of the table.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.19
Anti-Drug Antibody Results and Titre Summary by Timepoint
Safety Population

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)
Baseline [1]					
n [2]	xx	xx	xx	xx	xx
ADA Positive: n (%) [3]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 2					
n [2]	xx	xx	xx	xx	xx
ADA Positive: n (%) [3]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
…					

ADA = Anti-Drug Antibodies; N = number of subjects per treatment group; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
[2] Number of subjects with at least one ADA assessment at the specific visit.
[3] Number of subjects with a positive result at the specific visit. The denominator for all percentages is the number of subjects with an ADA result for each visit.

Reference Listing: 16.2.9.19

Programming Notes:

- Keep in mind that in this table 'Total' column does not include placebo.
- Repeat for all scheduled post-baseline visits.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Table 14.3.5.20
Descriptive Summary of Anti-Drug Antibody Results and Titre by ADA Categories
Safety Population

ADA Category	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	All MEDI7352 (N=xx)
ADA positive at baseline and/or post-baseline (ADA prevalence)					
n/Nobs (%) [1] [2]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
TE-ADA positive (ADA incidence) [5]					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Treatment Induced ADA Positive					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Treatment-Boosted ADA Positive					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Non-TE-ADA Positive [6]					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Both baseline and post-baseline positive					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Only baseline positive					
n/Nobs (%) [1] [4]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
TE-persistently ADA positive [7]					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

TE-transiently ADA positive [8]					
n/Nobs (%) [1] [3]	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)	xx/xxx (xx.x%)
Maximum ADA Titre					
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Q1, Q3	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

ADA = Anti-Drug Antibodies; N = number of subjects per treatment group; TE-ADA = Treatment Emergent ADA; SD = standard deviation; Q1 = first quartile; Q3 = third quartile.
[1] n represents the number of subjects satisfying the conditions of the specified ADA category
[2] Nobs represents the number of subjects with any ADA result at baseline and/or post-baseline.
[3] Nobs represents the number of subjects with an ADA result at baseline and at least one post-baseline ADA assessment.
[4] Nobs represents the number of subjects with an ADA result at baseline.
[5] TE-ADA positive is defined as either ADA negative at baseline and post-baseline ADA positive (Treatment Induced ADA Positive), or as ADA positive at baseline with pre-existing titre boosted by 4-fold or greater during the study period (Treatment-boosted ADA Positive). ADA incidence is the proportion of TE-ADA+ subjects in a population.
[6] ADA post-baseline positive but not fulfilling the conditions for TE-ADA+
[7] ADA negative at baseline and having at least 2 post-baseline ADA positive measurements with ≥16 weeks (112 days) between first and last positive, or an ADA positive result at the last available post-baseline assessment.
[8] ADA negative at baseline and at least one post-baseline ADA positive measurement and not fulfilling the conditions for persistently positive.

Reference Listing: 16.2.9.19

Programming Notes:

- If a participant has more than 1 non-missing titre during the study, the maximum titre for each participant is summarized.
- Only present summary statistics if titre is available.
- If no positive results for a particular block of the table, then the summary statistics for the titres for that particular block would not appear.
- It is assumed that participants with a missing baseline ADA result are ADA negative at baseline.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

7. Pharmacokinetic/Pharmacodynamic Data

Table 14.4.1
Summary of Serum MEDI7352 Concentrations
PK Population

ADA Status: xxxxxxxxxx

Visit/ Statistic	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)
Baseline [1]			
n (n < LLOQ)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
gMean [gMean ± gSD]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]
gCV%	xx.x	xx.x	xx.x
Median	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx
Week 2			
n (n < LLOQ)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
gMean [gMean ± gSD]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]
gCV%	xx.x	xx.x	xx.x
Median	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx
Week 4			
n (n < LLOQ)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
gMean [gMean ± gSD]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]
gCV%	xx.x	xx.x	xx.x
Median	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx
…			

gCV% = Geometric Coefficient of Variation (%); gMean = Geometric Mean; gSD = Geometric SD; LLOQ = Lower Limit of Quantification; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; NC =not calculable; NQ = not quantifiable.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Note: serum MEDI7352 concentration units = ng/mL
Reference Listing: 16.2.10.1

Programming Notes:

- Include the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours/ Pre-Dose, Week 11/ Pre-Dose, Week 10 + 14 Days/Pre-Dose; Week 18.
- Repeat the table for 'ADA Positive', 'ADA Negative' and 'Overall'.
- Any values reported as NRR (not reportable) or NS (missing) will be excluded from the summary tables.
- At a time point where less than or equal to 50% of the concentration values are NQ (below LLOQ), all NQ values will be set to the LLOQ, and all descriptive statistics will be calculated accordingly.
- At a time point where more than 50% (but not all) of the values are NQ, the gmean, gmean ± gSD and gCV% will be set to NC. The maximum value will be reported from the individual data, and the minimum and median will be set to NQ.
- If all concentrations are NQ at a time point, no descriptive statistics will be calculated for that time point. The gmean, minimum, median and maximum will be reported as NQ and the gCV% and gmean ± gSD as NC.

Table 14.4.2
Summary of Serum total NGF Concentrations
Safety Population

ADA Status: xxxxxxxxxx

Visit/ Statistic	Placebo (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)	MEDI7352 CCI (N=xx)
Baseline [1]				
n (n < LLOQ)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
gMean [gMean ± gSD]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	
gCV%	xx.x	xx.x	xx.x	xx.x
Median	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Week 2				
n (n < LLOQ)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
gMean [gMean ± gSD]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	
gCV%	xx.x	xx.x	xx.x	xx.x
Median	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Week 4				
n (n < LLOQ)	xx (xx)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
gMean [gMean ± gSD]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	x.xx [x.xx to x.xx]	
gCV%	xx.x	xx.x	xx.x	xx.x
Median	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x	xx.x, xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
…				

gCV% = Geometric Coefficient of Variation (%); gMean = Geometric Mean; gSD = Geometric SD; LLOQ = Lower Limit of Quantification; n = number of subjects by treatment group at each visit for the parameter; N = number of subjects per treatment group; ; NC =not calculable; NGF = Nerve-Growth Factor; NQ = not quantifiable.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.
Note: serum total NGF concentration units = pg/mL
Reference Listing: 16.2.10.2

Programming Notes:

- Repeat for ADA Status: “ADA Positive”, “ADA Negative” and “Overall”.
- Include the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 12; Week 18.
- A column for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Planned Listing Descriptions and Shells

Number Title Population	Unique (U) or Repeated (R)
Listing 16.2.1.1 - Subject Disposition - Screening Population	U
Listing 16.2.1.2 - Assignment to Analysis Populations - Screening Population	U
Listing 16.2.1.3 - Reason for IP Discontinuation and Withdrawal from the Study - Safety Population	U
Listing 16.2.1.4 - List of Reasons for Screening Failure - Screen Failure Population	U
Listing 16.2.1.5 - Subject Visits and COVID-19 Impact - Screening Population	U
Listing 16.2.2.1 - Subjects Not Meeting All Inclusion Criteria or Meeting any Exclusion Criteria - Screening Population	U
Listing 16.2.2.2 - Protocol Deviations - Safety Population **Error! Reference source not found.Error! Reference source not found.Error! Reference source not found.Error! Reference source not found.Error! Reference source not found.**	U
Listing 16.2.3 - Randomization and Treatment Group - Safety Population **Error! Reference source not found.Error! Reference source not found.Error! Reference source not found.Error! Reference source not found.Error! Reference source not found.**	U
Listing 16.2.4.1 - Demographic and Baseline Characteristics - Screening Population	U
Listing 16.2.4.2 - Medical History - Safety Population	U
Listing 16.2.4.3 - Osteoarthritis Characteristics - Screening Population	U
Listing 16.2.5.1 - Study Drug Administration: Individual Doses - Safety Population	U
Listing 16.2.6.1 - Daily Pain NRS - mITT Population	U
Listing 16.2.6.2 - **Error! Reference source not found.** Galer NPS - mITT Population	U
Listing 16.2.6.3 - DSIS - mITT Population	U
Listing 16.2.6.4 - SF-36 - mITT Population	U
Listing 16.2.6.5 - Rescue Medication Usage - mITT Population	R
Listing 16.2.6.6 - Patient Global Impression of Change - mITT Population	U

Number Title Population	Unique (U) or Repeated (R)
CCI	U
Listing 16.2.7.1 - Adverse Events - Safety Population	U
Listing 16.2.7.2 - Treatment Emergent Adverse Events Leading to Study Drug Discontinuation **Error! Reference source not found.** - Safety Population	R
Listing 16.2.7.3 - Treatment Emergent Adverse Events Associated with Abnormal Liver - Safety Population	R
Listing 16.2.7.4 - Joint Related Adverse Events of Special Interest - Safety Population	R
Listing 16.2.7.5 - Serious and/or Severe Infections - Safety Population	R
Listing 16.2.7.6 - Anaphylactic Reactions, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of Study Drug - Safety Population	R
Listing 16.2.8.1 - Clinical Chemistry Laboratory Evaluations - Safety Population	U
Listing 16.2.8.2 - Hematology Laboratory Evaluations - Safety Population	R
Listing 16.2.8.3 - Coagulation Laboratory Evaluations - Safety Population	R
Listing 16.2.8.4 - Urinalysis Laboratory Evaluations - Safety Population	R
Listing 16.2.8.5 - Serology Laboratory Evaluations - Safety Population	U
Listing 16.2.8.6 - Pregnancy Test Results - Safety Population	U
Listing 16.2.8.7 - Drug Test Results - Safety Population	U
Listing 16.2.8.8 - COVID-19 Screening and Vaccination - Safety Population	U
Listing 16.2.9.1 - Vital Signs Measurements - Safety Population	U
Listing 16.2.9.2.1 - 12-Lead Digital ECG Results - Safety Population	U
Listing 16.2.9.2.2 - 12-Lead Safety ECG Results - Safety Population	U
Listing 16.2.9.3 - Physical Examination Results - Safety Population	U
Listing 16.2.9.4 - Neurological Examination Results - Safety Population	U
Listing 16.2.9.5 - Total Neuropathy Score-Nurse - Safety Population	U

Number Title Population	Unique (U) or Repeated (R)
Listing 16.2.9.6 - Motor and Sensory Nerve Conduction Studies - Safety Population	U
Listing 16.2.9.7 - Strength and Deep Tendon Reflexes - Safety Population	U
Listing 16.2.9.8 - Injection Site Reactions - Safety Population	U
Listing 16.2.9.9 - Hypersensitivity/Anaphylactic Reactions - Safety Population	U
Listing 16.2.9.10 - Liver Diagnostic Investigations - Safety Population	U
Listing 16.2.9.11 - Liver Risk Factors and Lifestyle Events - Safety Population	U
Listing 16.2.9.12 - Liver Signs and Symptoms - Safety Population	U
Listing 16.2.9.13 - Infection Diagnostic Investigations - Safety Population	U
Listing 16.2.9.14 - Infection Risk Factors and Lifestyle Events - Safety Population	U
Listing 16.2.9.15 - Infection Signs and Symptoms - Safety Population	U
Listing 16.2.9.16 - Prior and Concomitant Medications - Safety Population	U
Listing 16.2.9.17 - Prohibited Concomitant Medications - Safety Population	R
Listing 16.2.9.18 - Concomitant Procedures - Safety Population	R
Listing 16.2.9.19 - Anti-drug Antibody Test Results - Safety Population	U
Listing 16.2.10.1 - Serum MEDI7352 Concentrations - PK Population	U
Listing 16.2.10.2 - Serum total NGF Concentrations - PD Population	U

Listing Change Log:

Output Number	Date of Change	Change Made By (initials)	Description/Rationale

Listing 16.2.1.1
Subject Disposition
Screening Population

Subject ID	Re-screened?/ Previous Subject ID	Treatment Arm	Re-consent/ Date/Time of Initial IC/ Initial Protocol Version	Date/Time of Informed Consent	Protocol Version at consent/ Re-consent	Consent for [redacted] sample? /Date of Consent	Consent for COVID-19 Safety Measures /Date of Consent	Current Protocol version
XXXX	No	XXXX	No	DDMMMYYYY/ hh:mm	XXXX	Yes/ DDMMMYYYY	Yes/ DDMMMYYYY	XXXXX
XXXX	Yes/ XXXX	XXXX	No	DDMMMYYYY/ hh:mm	XXXX	Yes/ DDMMMYYYY	Yes/ DDMMMYYYY	XXXXX
XXXX	No	XXXX	No	DDMMMYYYY/ hh:mm	XXXX	Yes/ DDMMMYYYY	Yes/ DDMMMYYYY	XXXXX
XXXX	No	XXXX	Yes / DDMMMYYYY/hh:mm / XXXX	DDMMMYYYY/ hh:mm	XXXX	Yes/ DDMMMYYYY	No	XXXXX
XXXX	No	XXXX	No	DDMMMYYYY/ hh:mm	XXXX	No	No	XXXXX

COVID-19 = coronavirus disease 2019; IC = Informed Consent; [redacted]
.

Programming Notes:

- Sort by Treatment Arm/ Subject ID.

Listing 16.2.1.2
Assignment to Analysis Populations
Screening Population

Subject ID	Treatment Arm	Screened [1]	Randomized	SAF [2]	mITT [3]	PK [4]	Reason to Exclude from Safety [5]	Reason to Exclude from mITT [6]
XXXXXX	XXXX	Yes	No	No	No	No		
XXXXXX	XXXX	Yes	Yes	Yes	Yes	Yes		
XXXXXX	XXXX	Yes	Yes	No	No	No	XXX	
XXXXXX	XXXX	Yes	Yes	Yes	Yes	Yes		
XXXXXX	XXXX	Yes	Yes	Yes	No	No	XXX/ XXX	XXX/ XXX

mITT = Modified Intent-To-Treat Population Set; NRS = numeric rating scale; PK = pharmacokinetics; SAF = Safety Population Set.
[1] The Screening Population includes all subjects who provide informed consent and provide demographic and/or baseline screening assessments.
[2] The Safety Population includes all subjects who receive at least 1 dose of double-blind study medication.
[3] The mITT Population includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
[4] The PK Population includes all subjects for who a pharmacokinetic sample was obtained and analysed.
[5] Major deviation reason/s to exclude from Safety Population for randomized subject.
[6] Major deviation reason/s to exclude from mITT Population for randomized subject.

Programming Notes:

- If there is more than one major deviation, please concatenate with "/"
- Sort by Treatment Arm/ Subject ID.

Listing 16.2.1.3
Reason for IP Discontinuation and Withdrawal from the Study
Safety Population

Subject ID/ Treatment Arm	IP Discontinuation [1]/ Study Withdrawal	Completion/ Discontinuation Date (Study Day)	Date of Last Dose	Number of doses	Primary Reason for DC/ Withdrawal	Blind Broken? / Date/Time / Reason	Reason for breaking the Blind	Study Duration
XXXXXX/ XXXX	IP Discontinuation	DDMMMYYYY(XX)	DDMMMYYYY	XX	XXXXXX	Yes / DDMMMYYYY/ hh:mm	XXXXXX	XX
XXXXXX/ XXXX	IP Discontinuation	DDMMMYYYY (XX)	DDMMMYYYY	XX	XXXXXX	No		XX
XXXXXX/ XXXX	Study Withdrawal	DDMMMYYYY (XX)	DDMMMYYYY	XX	Other: XXXXXX	No		XX

DC = Discontinuation; IP = Investigational product.
[1] Any withdrawal from the study before last IP dose (Week 10) is considered an IP discontinuation.
Note: Study Day is calculated relative to the date of first dose. Study Duration = Reference end date – date of first dose of treatment + 1.

Programming Notes:

- If reason for non-completion is Other, concatenate the specify text as follows: “Other: XXXXXXXXX”.
- If reason for non-completion is adverse event, concatenate with AE line number as follows: “Adverse event number X”.
- For Physician decision, screen-fail and withdrawal by subject, please provide explanation if presented on the logic “Physician decision: XXX”.
- Do not include subjects who completed the study.
- Sort by Treatment Arm/ Subject ID.

Listing 16.2.1.4
List of Reasons for Screening Failure
Screen Failure Population

Subject ID	Treatment Arm	Screen failure Date	Primary Reason for Screen Failure
XXXXXX	Screen Failure	DDMMMYYYY	XXXXXXXXX
XXXXXX	Screen Failure	DDMMMYYYY	XXXXXXXXX
XXXXXX	Screen Failure	DDMMMYYYY	
XXXXXX	Screen Failure	DDMMMYYYY	Other: XXXXXXXXX
XXXXXX	Screen Failure	DDMMMYYYY	

Programming Notes:

- If reason for non-completion is Other, concatenate the "Primary Reason for Screen Failure" text as follows: "Other: XXXXXXXXX".
- Sort by Subject ID.

Listing 16.2.1.5
Visits List and COVID-19 Impact
Screening Population

Subject ID/ Treatment Arm	Visit Name	Visit Date (Study Day)	Is COVID-19 Pandemic Ongoing?	Impacted by COVID-19	Was visit performed? / Visit Type	Visit Performed Via	VS Data provided? / Assessments Missed?	IP dosing missed due to COVID-19 / Details	End of Treatment linked to COVID-19	Subject discontinued due to COVID-19? / Details
xxxxx/ xxxx	Visit X	DDMMM YYYY (XX)	Yes	Yes	Yes/ Delayed	On site	Y/ Efficacy	Y/ XXXX	Other: XXXX	Y/ XXXX
xxxxx/ xxxx	Visit X	DDMMM YYYY (XX)	Yes	No	Yes		N/ Safety			
xxxxx/ xxxx	Visit X	DDMMM YYYY (XX)	No	Yes	Yes	Video	N/ Efficacy, Safety	Y/ Other: XXXX		
xxxxx/ xxxx	Visit X	DDMMM YYYY (XX)	No	No	No / Missed					

COVID-19 = coronavirus disease 2019; IP = Investigational Product; VS = Vital Signs.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Visit Type: Missed, Abbreviated, Delayed.
- Visit Performed Via: Video, Phone, On Site Other: xxxxxx.
- Details on IP dosing missed: Treatment on hold due to Sponsor Decision, Subject infected with COVID-19, Subject decision, Other: xxxxxx.
- End of treatment, reason if due to COVID: Subject infected with COVID-19, Subject decision, Travel restrictions, Site closed, Study delayed/cancelled, Other: xxxxxx.
- Details on Subjects discontinuing due to COVID-19: Subject infected with COVID-19, Subject decision, End of Treatment due to Sponsor, Other: xxxxxx.
- Sort by Treatment Arm/ Subject ID/ Visit Date.

Listing 16.2.2.1
Subjects Not Meeting All Inclusion Criteria or Meeting any Exclusion Criteria
Screening Population

SubjectID	Treatment Arm	Enrolled	Randomized	Inclusion or Exclusion	Criteria Number	Criteria Label
XXXXXX	Screen Failure	Yes	No	Inclusion	XX	XXXXXXXXXXXXXXXXXXX
		Yes	No	Exclusion	XX	XXXXXXXXXXXXXXXXXXX

Programming Notes:

- Sort by Subject ID.

Listing 16.2.2.2
Protocol Deviations
Safety Population

Subject ID	Treatment Arm	Analysis Population	Event Date (Study Day)	Event Type	Description	Category	Covid-19 Related?
XXXXXX	XXXX	Screened\RND\SAF\mITT	DDMMMYYYY (XX)	XXXXXXXXXXX	XXXXXXX	Non-important	Y
				XXXXXXXXXXXXXX	XXXXXXXXXXXXXXX	Important	
XXXXXX	XXXX		DDMMMYYYY (XX)	XXXXXXXXXXX	XXXXXXXXXXXXXXX XXX	XXXXX	
				XXXXXXXXXXXXXXX	XXXXXXXXXX	XXXXX	
XXXXXX	XXXX		DDMMMYYYY (XX)	XXXXXXXXXXX	XXXXXXXXXXXXXXX XXX	XXXXX	

COVID-19 = Coronavirus disease 2019; mITT = Modified Intent-To-Treat Population; RND = Randomized Subjects; SAF = Safety Population.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- The structure of this listing may change depending on the information in the protocol deviations file. In the analysis population column, include only the analysis population where subject is included in.
- Sort by Treatment Arm/ Subject ID. If date is present in file, add a column for date of event and sort by date. If no date is present, sort by category with non-important first and then important.
- Event Type: Inclusion Criteria, Exclusion Criteria, Study Drug, Assessment – Safety, Assessment – Efficacy, Lab/endpoint data, Visit Window, Informed Consent, Prohibited Co-Medication, Overdose/Misuse, Other.

Listing 16.2.3
Randomization and Treatment group
Safety Population

Subject ID	Treatment Arm	Randomization Stage	Randomization Treatment	Randomization Date / Time (Study Day)	Randomization Number
XXXXXX	XXXX	Stage 1	Active CCI	DDMMMYYYY/hh:mm (-X)	XXXX
XXXXXX	XXXX	Stage 3	Active CCI	DDMMMYYYY/hh:mm (-X)	XXXX
XXXXXX	XXXX	Stage 2	Placebo	DDMMMYYYY/hh:mm (-X)	XXXX
XXXXXX	XXXX	Stage 2	Active CCI	DDMMMYYYY/hh:mm (-X)	XXXX
XXXXXX	XXXX	Stage 3	Placebo	DDMMMYYYY/hh:mm (-X)	XXXX

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID.

Listing 16.2.4.1
Demographic and Baseline Characteristics
Screening Population

Subject ID	Treatment Arm	Birth Date	Age (years) [1]	Sex	Surgically sterile?/ Postmenopausal? [2]	Ethnicity	Race	Weight (kg)	Height (cm)	BMI (kg/m²)	Fully vaccinated for COVID-19?
XXX	XXX	DDMMMYYY	XX	XX		XXXXX	XXXX	XX.X	XX.X	XX.X	Y
XXX	XXX	--MMMYYY	XX	XX	No/ Yes	XXXXX	XXXX	XX.X	XX.X	XX.X	N

COVID-19 = Coronavirus disease 2019.
Note: Height and weight are the values at Screening.
[1] Age was calculated as age at time of consent.
[2] For Female Subject Only.

Programming Notes:

- Sort by Treatment Arm/ Subject ID

Listing 16.2.4.2
Medical History
Safety Population

Subject ID	Treatment Arm	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ End Date (Study Day)/
XXXXXX	XXXX	XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)
		XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	MMMYYYY (X)/ Ongoing
		XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	DDMMMYYYY (X)/ Ongoing
XXXXXX	XXXX	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)

MedDRA = Medical Dictionary for Regulatory Activities.
Note: Study Day is calculated relative to the date of first dose.
Medical History were coded using MedDRA version 26.0.
Only subjects with medical history recorded are listed.

Programming Notes:

- SOC & PT text should be in proper case in listing.
- Sort by Treatment Arm/ Subject ID / Start Date / End Date of medical event.

Listing 16.2.4.3
Osteoarthritis Characteristics
Screening Population

Subject ID	Treatment Arm	Subject with OA? / Joint/ Area affected	Is OA considered CS?	Radiological Investigations Conducted? / Details	Joint Area Investigated	Is OA considered RS?	K-L Score Reported	Radiologic Scoring System / Details/ Result
XXXXXX	XXXX	Y / Shoulder	Y	Y/ Other: XXXXXX	Shoulder	Y	Grade 3	XXXXXX/ XXXXXX/ XX
XXXXXX	XXXX	Y / Ankle	N	Y / MRI	Ankle	N	N	N

CS = Clinically Significant; K-L = Kellgren-Lawrence; OA = Osteoarthritis; RS = Radiologically Significant.

.

Programming Notes:

- Sort by Treatment Arm/ Subject ID

Listing 16.2.5.1
Study Drug Administration: Individual Doses
Safety Population

Subject ID/ Treatment Arm	Visit Name	Start Date/ Time (Study Day)	End Date/ Time (Study Day)	Was Infusion Performed?/ Infusion Volume (mL)[1]/ Reason not Performed	Actually Administered Volume (mL) [2]	If Difference between [1] and [2] Volume, Reason	Any Injection Site Reactions?	Any Infusion Related Reactions	Infusion Rate (mL/ hour)	Rate Change Justification	Reason for Infusion Rate Change
XXXX/ XXXX	XXX	DDMM MYYYY /hh:mm (X)	DDMM MYYYY /hh:mm (X)	Y/ XX	XX				xx.x		
XXXX/ XXXX	XXX	DDMM MYYYY /hh:mm (X)	DDMM MYYYY /hh:mm (X)	Y/ XX	XX	XXXXX	Y	Y	xx.x	XXXXX	XXXXX XX
XXXX/ XXXX	XXX			N/ XXXXXX							

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Start Date / End Date.
- Rate Change Justification: Increased, Decreased, Interrupted.

Listing 16.2.6.1
Daily Pain NRS
mITT Population

Subject ID	Treatment Arm	Study Visit [1]	Subject Diary (ePRO) Date / Study Day	Baseline Flag [2]	DPS
XXXXXX	XXXX	Baseline	DDMMMYYYY/ (-7)	Y	X
		Baseline	DDMMMYYYY/ (-6)	Y	XX
		…	…	…	…
		Baseline	DDMMMYYYY/ (-2)	Y	XX
		Baseline	DDMMMYYYY/ (-1)	Y	XX
		…	…	…	…
		Week 2	DDMMMYYYY/ (13)		XX
		Week 2	DDMMMYYYY/ (14)		XX
		…	…	…	…
		Week X	DDMMMYYYY/ (X)		XX
		…	…	…	…
XXXXXX	XXXX	Baseline	DDMMMYYYY/ (-7)	Y	XX
		…	…	…	…

DPS = Daily Pain Score; ePRO = Electronic Patient-Reported Outcome; NRS = Numeric Rating Scale.
Note: Data shown in column 'DPS' are average daily pain scores on an 11-point (0-10) NRS. Study Day is calculated relative to the date of first dose.
[1] Study Visit is defined as the 7-day period ending within the protocol window Day ± 3, where at least 4 days out of 7 have recorded diary pain scores.
[2] Baseline is defined as the 7-day period prior to randomization **i.e.,** Day -7 to Day -1, inclusive. A subject is considered to have an evaluable baseline pain score if there are at least 4 days of recorded diary pain scores in the 7-day period.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Subject Diary Date.
- Display all measurement per Subject, starting on the Study Day = -7.
- Display Study Visit for days involved in weekly averages of the average daily pain scores for Baseline, Week 2, 4, 6, 8, 10, and 12
- Flag Baseline records only when there is at least 5 days of recorded diary pain scores in the 7-day Baseline period

Listing 16.2.6.2
Galer NPS
mITT Population

Subject ID	Treatment Arm	Parameter	Study Visit	Collection Date / Study Day	Baseline Flag [1]	NPS
XXXXXX	XXXX	Pain intensity	Baseline	DDMMMYYYY/ (X)	Y	XX
			Week 4	DDMMMYYYY/ (X)		XX
			Week 8	DDMMMYYYY/ (X)		XX
				...		XX
			Week X	DDMMMYYYY/ (X)		XX
				...		XX
		XXXX	Baseline	DDMMMYYYY/ (X)	Y	XX
		...	...	...	...	...
XXXXXX	XXXX	Pain intensity	Baseline	DDMMMYYYY/ (X)	Y	XX
			...	...	...	...
		XXXX	Week X	DDMMMYYYY/ (X)		XX
		...	...	...	...	...

NPS = Neuropathic Pain Scale; NRS = Numeric Rating Scale.
Note: Data shown in column 'NPS' are Pain Intensity, Unpleasantness, and Descriptor scores on an 11-point (0-10) NRS, and Pain Duration/Frequency on a 3-point NRS (1-3).
Study Day is calculated relative to the date of first dose.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Parameter /Collection Date.
- Keep Parameter sorting from the last bullet point in this programming notes.
- Include all observed data on Galer NPS scores for Baseline, Week 4, 8, 12, and 18.
- Repeat for the Parameters: Pain intensity, Pain Unpleasantness, Pain Sharpness, Pain Hotness, Pain Dullness, Pain Coldness, Pain Sensitivity, Pain Itching, Deep Pain Intensity, Surface Pain Intensity (All in an 11-point NRS), and Pain Duration/Frequency (in a 3-point NRS).

Listing 16.2.6.3
DSIS
mITT Population

Programming Notes:

- Same shell as Listing 16.2.6.1.
- Update footnote as:
  DSIS = Daily Sleep Interference Scale; ePRO = Electronic Patient-Reported Outcome; NRS = Numeric Rating Scale.
  Note: Data shown in column 'DSIS' are daily Sleep Interference scores on an 11-point (0-10) NRS. Study Day is calculated relative to the date of the day of first dose.
  [1] Study Visit is defined as the seven-day period ending within the protocol window Day ± 3.
  [2] Baseline is defined as the seven-day period prior to randomization **i.e.,** Day -7 to Day -1,.
- Sort by Treatment Arm/ Subject ID / Subject Diary Date.
- Display all measurement per Subject, starting on the Study Day = -7.
- Display Study Visit for days involved in weekly averages of the average Sleep interference scores for Baseline, Week 4, 8, 12 , and 18.

Listing 16.2.6.4
SF-36
mITT Population

Subject ID	Treatment Arm	Parameter	Item Number	Item name	Study Visit	Collection Date / Study Day	Baseline Flag [1]	SF-36
XXXXXX	XXXX	Physical functioning	3	Vigorous Activities	Baseline	DDMMMYYYY/ (X)	Y	XX
					Week 12	DDMMMYYYY/ (X)		XX
			4	Moderate Activities	Baseline	DDMMMYYYY/ (X)	Y	XX
		...	...	...	...	...	...	...
			-	Total	Baseline	DDMMMYYYY/ (X)	Y	
					Week 12	DDMMMYYYY/ (X)		XX
XXXXXX	XXXX	Role limitations due to physical health	13	Cut Amount of Time Spent on Work/Act	Baseline	DDMMMYYYY/ (X)	Y	XX
					Week 12	DDMMMYYYY/ (X)		XX
			...		...	...	..	...
...		...	...		...	...	...	...

SF-36 = 36-Item Short-Form Health Survey; NRS = Numeric Rating Scale.
Note: Data shown in column 'SF-36' are derived SF-36 scores and Change in General Health on a 5-point NRS (1-5).
Study Day is calculated relative to the date of first dose.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Parameter / Item /Collection Date.
- Keep Parameter sorting from the last bullet point in this programming notes.
- Include all data on SF-36 scores for Baseline and Week 12.
- Repeat for the Parameters: Physical functioning (items 3, 4, 5, 6, 7, 8, 9, 10, 11, 12), Role limitations due to physical health (items: 13, 14, 15, 16), Role limitations due to emotional problems (items: 17, 18, 19), Vitality (Energy/fatigue) (items: 23, 27, 29, 31), Emotional well-being (items: 24, 25, 26, 28, 30), Social functioning (20, 32), Pain (items: 21, 22) and General Health (items: 1, 33, 34, 35, 36), all with values ranging from 0 to 100. Change in general Health (in a 5-point NRS, item: 2).

Listing 16.2.6.5
Rescue Medication Usage
mITT Population

Subject ID	Treatment Arm	ATC Class (Level 2)/ Preferred Name/ Verbatim Term	Primary Indication	Start Date (Study Day)/ End Date (Study Day)	Dose (unit)	Route	Frequency
XXXXXX	XXXX	XXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	Painful Diabetic Neuropathy	--MMMYYYY (-XX)/ DDMMMYYYY (-X)	XXXX unit	XXXXXXXXX	XXXXX
	XXXX	XXXXXXXXX/ XXXXXXXXXXXXXXX/ XXXXXXXXXXX	Painful Diabetic Neuropathy	--MMMYYYY (-X)/ Ongoing	XXXX unit	XXXXXXXXX	XXXXX
	XXXX	XXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX	Painful Diabetic Neuropathy	DDMMMYYYY (X)/ DDMMMYYYY (XX)	XXXX unit	XXXXXXXXX	XXXXX

ATC = anatomical therapeutic chemical.
Note: Study Day is calculated relative to the date of first dose.
Medications were coded using WHO drug dictionary version vMar2023.

Programming Notes:

- ATC & Preferred Name text should be in proper case in table.
- Ensure proper WHO-DDE version is printed in footnote.
- Sort by subject, start date/time, end date/time, ATC level 2 & Preferred Name .
- If Dose unit, Route or Frequency is Other, display other specify text only (ie, do not display “Other: XXXXXX” but just “XXXXXX “).
- Adjust footnotes for frequency and routes as needed.
- Sort by Treatment Arm/ Subject ID / Start Date / End Date (alphabetically for ATC Class Level 2 if same date for two medications

Listing 16.2.6.6
Patient Global Impression of Change
mITT Population

Subject ID	Treatment Arm	Study Visit	Collection Date / Study Day	PGIC
XXXXXX	XXXX	Week 4	DDMMMYYYY/ (X)	XXXXXXXX
		Week 8	DDMMMYYYY/ (X)	XXXXXXXX
		Week 12	DDMMMYYYY/ (X)	XXXXXXXX
		Week 18	DDMMMYYYY/ (X)	XXXXXXXX
XXXXXX	XXXX	Week 4	DDMMMYYYY/ (X)	XXXXXXXX
		Week 8	DDMMMYYYY/ (X)	XXXXXXXX
		Week 12	DDMMMYYYY/ (X)	XXXXXXXX
		Week 18	DDMMMYYYY/ (X)	XXXXXXXX
		...	...	...

PGIC =Patient Global Impression of Change.
Note: Data shown in column 'PGIC' are Subjects ratings about overall improvement in health status.
Study Day is calculated relative to the date of first dose.
[1] Baseline is defined as the last observation recorded prior to the first dose of treatment.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Collection Date.
- Include all observed data on PGIC scores for Week 4, 8, 12, and 18.

CCI

[redacted]

CCI

Listing 16.2.7.1
Adverse Events
Safety Population

Subject ID/ Treatment Arm	AE ID Number	System Organ Class/ Preferred Term/ Verbatim Term	AE Start Date/Time (Study Day)/ End Date/Time (Study Day)	Severity/ Relationship [1]	Outcome/ Action Taken with IP/ Therapy taken for this AE?	AE Leading to Study DC?	TEAE	Serious? / Serious Criteria
XXXXX/ XXXX	X	XXXXXXXXXXX/ XXXXXXX/ XXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXXX/ XXXXXX	XXXXXXXXX/ XXXXXXX/ Yes	No	Yes	No
XXXXX/ XXXX	X	XXXXXXXXXXX/ XXXXXXX/ XXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMONYYYY/HH:MM (X)	XXXXXX/ XXXXXX	XXXXXXXXX/ XXXXXXX/ No	Yes	No	Yes / XXX
XXXXX/ XXXX	X	XXXXXXXXXXX/ XXXXXXX/ XXXXXXX	DDMONYYYY/HH:MM (X)/ Ongoing	XXXXXX/ XXXXXX	XXXXXXXXX/ XXXXXXX/ No	No	No	Yes / XXX

AE = adverse event; DC = discontinuation; IP = investigational product; MedDRA = Medical Dictionary for Regulatory Activities; SAE = serious adverse event; TEAE = treatment emergent adverse event.
[1] Reasonable possibility AE caused by IP as assessed by the investigator .
Note: Study Day is calculated relative to the date of first dose. A TEAE is defined as an AE with an onset at the time of or following the start of treatment with IP.
AEs were coded using MedDRA version 26.0

Programming Notes:

- If time missing, display "- -:- -".
- AE ID number represents Record position within Subject.
- If no events meet the criteria for display (i.e, no AEs occur in the study), present "No events are reported.".
- SOC & PT text should be in proper case in table.
- Sort by Treatment Arm/ Subject ID / Start Date / End Date (alphabetically by SOC /PT if same date for two events).

In case a term is not coded (e.g. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]". SOC and PT abbreviations should be added in this case in footnote.

Listing 16.2.7.2
Treatment Emergent Adverse Events Leading to Study Drug Discontinuation
Safety Population

Programming Notes:

- Same shell as Listing 16.2.7.1.
- Update listing deleting seventh and eight columns

Listing 16.2.7.3
Treatment Emergent Adverse Events Associated with Abnormal Liver
Safety Population

Programming Notes:

- Same shell as Listing 16.2.7.1.
- Update listing deleting 8th column.

Listing 16.2.7.4
Joint Related Adverse Events of Special Interest
Safety Population

Programming Notes:

- Same shell as Listing 16.2.7.1.

Listing 16.2.7.5
Serious and/or Severe Infections
Safety Population

Programming Notes:

- Same shell as Listing 16.2.7.1.

Listing 16.2.7.6
Anaphylactic Reactions, Hypersensitivity or Infusion-Related Reactions Leading to Discontinuation of Study Drug
Safety Population

Programming Notes:

- Same shell as Listing 16.2.7.1.
- Update footnote: Anaphylactic reactions, hypersensitivity or infusion-related reactions not leading to discontinuation of IP were included in listing as they were categorized as AE of special interest under Protocol Amendment 4 (V5.0). Definition for AE of special interest changed from Amendment 6 (V6.0) onwards, including anaphylactic reactions, hypersensitivity or infusion-related reactions leading to permanent discontinuation of IP.

Listing 16.2.8.1
Clinical Chemistry Laboratory Evaluations
Safety Population

Subject ID/ Treatment Arm	Parameter	Study Visit	Date/Time of Collection (Study Day)	Original Result (Unit)	Standard Results (unit)	Reference Range [1]	Baseline Flag	CFB	Results Assessment / Reason CS	Lab ID Number	Fasting Status	Comments
XXXXX/ XXXX	Chemistry panel	XXXXXX							ND: xxx			
XXXXX/ XXXX	Albumin	XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY	Y			XXXXXXX	Y	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X	H-CS / XXX	XXXXXXX	Y	XXXX
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X		XXXXXXX	Y	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X	H-NCS	XXXXXXX	N	

CFB = change from baseline; CS = clinically significant; H = High; L = Low; NCS = not clinically significant; ND = not done.
Note: Study Day is calculated relative to the date of first dose.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
[1] Reference range is used to identify potentially clinically significant laboratory values.

Programming Notes:

- Keep parameter sorting from the last bullet point below.
- For results assessment, do not populate column if result is normal.
- Sort by Treatment Arm/ Subject ID / Parameter / Date time of collection.
- If the whole panel is not done at a visit, present the information on first row of the subject under 'Chemistry panel' parameter and don't present the 'not done' information for each parameter. Display "ND: reason why" in the result assessment column.
- Sort Parameters in the following Order: Albumin, Alkaline Phosphatase, Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Bicarbonate, Calcium, Chloride, Creatinine, High-Sensitivity C-Reactive Protein (hs-CRP), Estimated Glomerular Filtration Rate (eGFR by Cockcroft-Gault), Serum Glucose, Lactate Dehydrogenase (LDH), Potassium, Sodium, Total Bilirubin, Total Protein, Blood Urea Nitrogen (BUN), Uric Acid.

Listing 16.2.8.2
Hematology Laboratory Evaluations
Safety Population

Programming Notes:

- Same shell as Listing 16.2.8.1.
- Keep parameter sorting from the last bullet point below.
- For results assessment, do not populate column if result is normal.
- Sort by Treatment Arm/ Subject ID / Parameter / Date time of collection.
- If the whole panel is not done at a visit, present the information on first row of the subject under 'Hematology panel' parameter and don't present the 'not done' information for each parameter. Display "ND: reason why" in the result assessment column.
- Sort Parameters in the following Order: Absolute basophil count, absolute eosinophil count, absolute lymphocytes count, Absolute Monocyte Count, Absolute Neutrophil Count, Basophils %, Eosinophils %, Hematocrit (HCT), Hemoglobin (HGB), hemoglobin A1C (HgbA1C), Lymphocytes %, mean corpuscular hemoglobin (MHC), Mean Corpuscular Hemoglobin Concentration (MCHC), Mean Corpuscular Volume (MCV), Monocytes %, Neutrophils %, Platelets, Red blood cell count (RBC), Red Cell Distribution Width, white blood cell Count (WBC).

Listing 16.2.8.3
Coagulation Laboratory Evaluations
Safety Population

Programming Notes:

- Same shell as Listing 16.2.8.1.
- Keep parameter sorting from the last bullet point below.
- For results assessment, do not populate column if result is normal.
- Sort by Treatment Arm/ Subject ID / Parameter / Date time of collection.
- If the whole panel is not done at a visit, present the information on first row of the subject under 'Coagulation panel' parameter and don't present the 'not done' information for each parameter. Display "ND: reason why" in the result assessment column.
- Sort Parameters in the following Order: Activated Partial Thromboplastin Clotting Time (APTT), Fibrinogen, International normalized ratio (INR), Prothrombin Time (PT).

Listing 16.2.8.4
Urinalysis Laboratory Evaluations
Safety Population

Subject ID/ Treatment Arm	Parameter	Study Visit	Date/Time of Collection (Study Day)	Original Result (Unit)	Standard Results (unit)	Reference Range [1]	Baseline Flag	CFB	Results Assessment / Reason CS	Lab ID Number	Fasting Status	Comments
XXXXX	Urinalysis panel	XXXXXX							ND: xxx			
XXXXX	pH/ Specific Gravity	XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY	Y			XXXXXXX	Y	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X	H-CS / XXX	XXXXXXX	Y	XXXX
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X		XXXXXXX	Y	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	XX (XX)	XX - YY		XX.X	H-NCS	XXXXXXX	N	
	Blood Urine/ Glucose/ Ketones/ Protein	XXXXXX	DDMMMYYYY/ HH:MM (X)	Trace			Y		H-NCS	XXXXXXX	Y	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	100 (mg/dL)	100 (mg/dL)				H-CS / XXX	XXXXXXX	Y	XXXX
		XXXXXX	DDMMMYYYY/ HH:MM (X)	Negative						XXXXXXX	N	

CFB = change from baseline; CS = clinically significant; H = High; L = Low; NCS = not clinically significant; ND = not done.
Note: Study Day is calculated relative to the date of first dose.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
[1] Reference range is used to identify potentially clinically significant laboratory values.

Programming Notes:

- Keep parameter sorting from the last bullet point below.
- For results assessment, do not populate column if result is normal.
- Sort by Treatment Arm/ Subject ID / Parameter / Date time of collection.
- If the whole panel is not done at a visit, present the information on first row of the subject under 'Urinalysis panel' parameter and don't present the 'not done' information for each parameter. Display "ND: reason why" in the result assessment column.
- Sort Parameters in the following Order: Blood Urine, Glucose, Ketones, pH, Protein, Specific Gravity.

Listing 16.2.8.5
Serology Laboratory Evaluations
Safety Population

Subject ID	Treatment Arm	Was Serology Test Collected?	Date/Time of Collection (Study Day)	Test (Unit) [1]	Result	Lab ID Number	Fasting Status	Reason not collected	Comments
XXXX	XXXX	Yes	DDMMMYYYY Y/HH:MM (X)	Hepatitis B Ag	Negative	XXXX	Y		XXXXXXXXX
				Hepatitis C Ab	Positive	XXXX	Y		
				HIV-1/ -2 Ag	Not Done	XXXX	Y	XXXXXXX	
				Quantiferon Gold Plus NIL	X.XX (IU/mL)	XXXX	Y		

Ab = antibody; Ag = antigen; HIV = human immunodeficiency virus; TB = tuberculosis.
Note: Study Day is calculated relative to the date of first dose.
[1] if Applicable

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Date of collection / Test.
- Keep parameter sorting from the last bullet point below
- Sort Parameters in the following Order: Hepatitis B Antigen, Hepatitis C Virus Antigen, Hepatitis C Virus Antibody, HIV-1/ -2 Antigen, Quantiferon Gold Plus NIL, Quantiferon Gold Plus TB, Quantiferon Gold Plus Mitogen minus NIL, Quantiferon Gold Plus TB1 minus NIL, Quantiferon Gold Plus TB2 minus NIL

Listing 16.2.8.6
Pregnancy Test Results
Safety Population

Subject ID	Treatment Arm	Visit	Was a Urine pregnancy test performed?	Date/Time Performed (Study Day)	If not, Reason	Result
xxxxx	xxxx	xxxxx	Xxxx	Ddmmmyyyy/ hh:mm (XX)	xxxx	xxxx
		xxxxx	Xxxx	Ddmmmyyyy/ hh:mm (XX)	Other: xxxx	xxxx

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment.

Listing 16.2.8.7
Drug Test Results
Safety Population

Subject ID	Treatment Arm	Was Drug Test Performed?	Date/ Time Assessment (Study Day)	Result	Findings	Reason Test not Performed
XXXXXX	XXXX	Yes	DDMMMYYYY/ HH:MM (XX)	Negative	Negative	
XXXXXX	XXXX	Yes	DDMMMYYYY/ HH:MM (XX)	Positive	Cocaine / Opiates	

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Concatenate all findings by "/"
- Sort by Treatment Arm/ Subject ID / Date of assessment.

Listing 16.2.8.8
COVID-19 Screening
Safety Population

Subject ID/ Treatment Arm	Visit	COVID-19 Sx Screening?/Date / Time (Study Day)	Sx	Body Tº Check?/ Date/ Time (Study Day)	Body Tº (Unit)	COVID-19 swab?/ Date/ Time (Study Day)	Swab result	COVID-19 Ab testing?/ Date/ Time (Study Day)	Ab testing results	COVID-19 Ag testing?/ Date/ Time (Study Day)	Ag testing results
xxxxx/ xxxx	xxxx	Yes/ Ddmmmyyyy/ hh:mm (XX)	XXX/ XXX	Yes/ Ddmmmyyyy/ hh:mm (XX)	XX (XX)	Yes/ Ddmmmyyyy/ hh:mm (XX)	Xxxx	Yes/ Ddmmmyyyy/ hh:mm (XX)	Xxxx	Yes/ Ddmmmyyyy / hh:mm (XX)	Xxxx
	xxxx	Yes/ Ddmmmyyyy/ hh:mm (XX)	XXX	Yes/ Ddmmmyyyy/ hh:mm (XX)	XX (XX)	Yes/ Ddmmmyyyy/ hh:mm (XX)	Xxxx	Yes/ Ddmmmyyyy/ hh:mm (XX)	Xxxx	Yes/ Ddmmmyyyy / hh:mm (XX)	Xxxx

Ab = Antibody; Ag = Antigen; COVID-19 = Coronavirus disease 2019; Sx = Symptoms; Tº = Temperature.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Concatenate all Symptoms by "/"
- Sort by Treatment Arm/ Subject ID / Date of assessment

Listing 16.2.9.1
Vital Signs Measurements
Safety Population

Subject ID	Treatment Arm	Parameter	Study Visit	Position [1] / Tº Method	Date/Time of Collection (Study Day)	Original Result (Unit)	Baseline Flag	CFB
XXXXX	XXXX	Body Temperature	XXXXXX	XXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)	Y	
			XXXXXX	XXXX	DDMMMYYYY/ HH:MM (X)	XX (XX)		XX
						...		
		Resting Heat Rate	Screening	Supine	DDMMMYYYY/ HH:MM (X)	XX		
			Day 1: Pre-Dose	Supine	DDMMMYYYY/ HH:MM (X)	XX	Y	XX
			XXXXXX	Supine	DDMMMYYYY/ HH:MM (X)	XX		XX
			XXXXXX	Sitting		ND		
			XXXXXX	Sitting	DDMMMYYYY/ HH:MM (X)	XX		XX

CFB = change from baseline; eCRF = Electronic Case Report Form; ND = not done.
Note: Study Day is calculated relative to the date of first dose.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
'Day 1: 5 minutes after Infusion Completion' time point was only applied to subjects enrolled in Stage 1, with data collected under eCRF versions 4.0 (11DEC2018) or older.
[1] Resting position measurements encompass Sitting and Supine position measurements.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Parameter (Order in the second bullet point)/ Date time of collection.
- Repeat for Resting Heart Rate, Resting Systolic Blood Pressure, Resting Diastolic Blood Pressure, Respiratory Rate, Body Temperature, Standing Heart Rate, Standing Systolic Blood Pressure, Standing Diastolic Blood Pressure.
- After Week 2 (inclusive), Supine measure are taken in sitting position. We will consider them as supine (in resting position) for calculating Change from Baseline (always at supine position).
- Include the following timepoints: Screening, Baseline (Day 1: Pre-Dose), Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week 10 + 24 hours, Week 11, Week 12, Week 18.
- Note that Body T°, and standing measures are not taken on Day 1, at 15, 30 and 45 minutes post-dose.

Listing 16.2.9.2.1
12-Lead Digital ECG Results
Safety Population

Subject ID/ Treatment Arm	Visit	ECG Date / Time (Study Day)	Tracing	PR Interval (msec)	QRS duration (msec)	QT Interval (msec)	RR interval (bpm)	Heart Rate (beats/min)	QTcF Interval (msec)	Findings	Reason Not Done
XXXXX	Day 1: Pre-Dose	DDMMMYYYY / HH:MM (XX)	1	xx	xx	xx	xx	xx	xx	xx: xxxxx	
			2	xx	xx	xx	xx	xx	xx		
			3	xx	xx	xx	xx	xx	xx	xx: xxxxx	
XXXXX	XXXX	DDMMMYYYY/ HH:MM (XX)	1	xx	xx	xx	xx	xx	xx	xx: xxxxx	
			2	xx	xx	xx	xx	xx	xx		
			3	xx	xx	xx	xx	xx	xx		

CS = clinically significant; ECG = electrocardiogram; NCS = Not clinically significant
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Date time of collection / Tracing.
- For Findings, concatenate test name with test result for category "FINDINGS".
- Include the following timepoints: Day 1: Pre-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 4, Week, 8, Week 12, and Week 18.

00Listing 16.2.9.2.2
12-Lead Safety ECG Results
Safety Population

Subject ID/ Treatment Arm	Visit	ECG Date / Time (Study Day)	Tracing	ECG Result/ Comment	PR Interval (msec)	QRS duration (msec)	QTcF Interval (msec)	Reason Not Done
XXXXX	Day 1: Pre-Dose	DDMMMYYYY / HH:MM (XX)	1	Abnormal CS/ xxxx	xx	xx	xx	
			2	Abnormal CS/ xxxx	xx	xx	xx	
			3	Abnormal NCS/ xxxx	xx	xx	xx	
XXXXX	XXXX	DDMMMYYYY/ HH:MM (XX)	1	Normal	xx	xx	xx	
			2	Normal	xx	xx	xx	
			3	Normal	xx	xx	xx	

CS = clinically significant; ECG = electrocardiogram; NCS = Not clinically significant
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Date time of collection / Tracing.
- Include the following timepoints: Screening, Day 1: Pre-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 4, Week, 8, Week 12, and Week 18.

Listing 16.2.9.3
Physical Examination Results
Safety Population

Subject ID	Treatment Arm	Visit	Examination Type	Exam Date/ Time (Study Day)	Body System	Result / Change from previous assessment [1]	If Abnormal, findings / Specify Changes [2]	Reason Not Done
XXXXX	XXXX	Screening	Complete	DDMMMYYYY / HH:MM (XX)	Head, Neck and Thyroid	Normal		
					Ears, Eyes, Nose and Throat	Abnormal CS	XXXXXXX	
		Day 1	Targeted	DDMMMYYYY / HH:MM (XX)	Ears, Eyes, Nose and Throat	XXXXXXXXXX	XXXXXXXX	

CS = Clinically Significant, NCS = Not Clinically Significant
Note: Study Day is calculated relative to the date of first dose.
[1] For targeted examination type: Change from previous assessment.
[2] For targeted examination type: Specify Changes.

Programming Notes:

- Keep sorting from eCRF: Head, Neck and Thyroid/ Ears, Eyes, Nose and Throat/ Chest (including breasts)/ Lungs / Heart / Lymph Nodes / Abdomen / Hepatic / Gastrointestinal / Anorectal / Genitourinary/ Skin / Musculoskeletal/Extremities / Neurological / Other.
- Complete Physical examination only at Screening, Week 12, 18 (it can also be unscheduled).
- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment / Body system

Listing 16.2.9.4
Neurological Examination Results
Safety Population

Subject ID	Treatment Arm	Visit	Exam Date/ Time (Study Day)	Body System	Result	If Abnormal, findings	Reason Not Done
XXXXX	XXXX	Screening	DDMMMYYYY / HH:MM (XX)	Mental Status	Normal		
				Cranial Nerves	Abnormal CS	XXXXXXX	
		Day 1	DDMMMYYYY / HH:MM (XX)	Cranial Nerves	XXXXXXXXXX	XXXXXXXX	

CS = Clinically Significant, NCS = Not Clinically Significant
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Keep sorting from eCRF: Mental status/ Cranial Nerves/ Motor Function/ Reflexes / Sensation and Propioception / Coordination / Other.
- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment / Body system

Listing 16.2.9.5
Total Neuropathy Score-Nurse
Safety Population

Subject ID/ Treatment Arm	Visit	Date/ Time of collection (Study Day)	Sensory Symptom Score (0–4)	Motor Symptom Score (0–4)	Autonomic Symptom Score (0–4)	Pin Sensibility Score (0–4)	Vibration Sensibility Score (0–4)	TNSn Total (0–20)	Reason Not Done
XXXXX/ XXXX	Screening	DDMMMYYYY / HH:MM (XX)	XX	XX	XX	XX	XX	XX	
	Day 1	DDMMMYYYY / HH:MM (XX)	XX	XX	XX	XX	XX	XX	
	Week 2	DDMMMYYYY / HH:MM (XX)	ND	ND	ND	ND	ND	ND	XXXXXXXXXXXXXX

ND = Not Done; TNSn = Total Neuropathy Score-Nurse.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment

Listing 16.2.9.6
Motor and Sensory Nerve Conduction Studies
Safety Population

Subject ID/ Treatment Arm	Visit	Date / Time of Collection (Study Day)	Location / Evaluation	Was Evaluation Preformed ? / Nerve	Amplitude (Motor = mV; sensory = microV) / Range	Peak Latency (msec) / Range	Conduction velocity (msec) / Range	Duration of action potential (msec) / Range	Evaluation Result	If Abnormal, Specify/ Reason Not Done	Significant Changes from Baseline? / if Yes, Specify
XXXX/ XXXX	Screening	DDMMMYY YY / HH:MM (XX)	Lower Limb - Right Side/ Motor Evaluation	Y/ XXXXXX	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	Abnormal	XXXXX	
			XXXXXX/ XXXXXX	Y/ XXXXXX	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	Normal		NA
			XXXXXX/ XXXXX	N							NA
	Week 18	DDMMMYY YY/ HH:MM (XX)	XXXXXX/ XXXXX	Y/ XXXXXX	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	Abnormal	XXXXX	
			XXXXXX/ XXXXX	Y/ XXXXXX	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	Normal		N
			XXXXXX/ XXXXX	Y/ XXXXXX	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	xx [x.xx to x.xx]	Abnormal	XXXXX	N
											Y/ XXXXXXX

NA = Not Applicable
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment / Location - Evaluation
- Keep sorting from eCRF: Lower Limb - right side/Motor evaluation, Lower Limb - right side/Sensory evaluation, Lower Limb - left side/ Motor evaluation, Lower Limb - left side/ Sensory evaluation, Upper Limb - right side /Motor evaluation, Upper Limb - right side/ Sensory evaluation, Upper Limb - left side/ Motor evaluation, Upper Limb - left side /Sensory evaluation.

Listing 16.2.9.7
Strength and Deep Tendon Reflexes
Safety Population

Subject ID	Treatment Arm	Visit	Date/ Time of collection (Study Day)	Ankle Dorsiflexion Strength	Deep Tendon Reflexes	Reason Not Done
XXXXX	XXXX	Screening	DDMMMYYYY / HH:MM (XX)	XXXX	XXXX	
		Day 1	DDMMMYYYY / HH:MM (XX)	XXXX	XXXX	
		Week 2	DDMMMYYYY / HH:MM (XX)	ND	ND	XXXXXXXXXXXXXX

ND = Not Done.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment

Listing 16.2.9.8
Injection Site Reactions
Safety Population

Subject ID	Treatment Arm	Visit	Date/ Time of Assessment (Study Day)	Pain	Tenderness	Erythema/redness	Induration/ swelling	Reason Not Done
XXXXX	XXXX	Day 1: 15 Minutes after Start of Infusion	DDMMMYYYY / HH:MM (XX)	XXXX	XXXX	XXXX	XXXX	
		Day 1: 30 Minutes after Start of Infusion	DDMMMYYYY / HH:MM (XX)	XX	XX	XX	XX	
		...						
		Week 18	DDMMMYYYY / HH:MM (XX)	ND	ND	ND	ND	XXXXXXXXXXXXXX

ND = Not Done.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Visit / Date of assessment
- Include the following timepoints: Day 1: 15 Minutes after Start of Infusion, Day 1: 30 Minutes after Start of Infusion, Day 1: 45 Minutes after Start of Infusion, Day 1: 60 Minutes after Start of Infusion, Day 1: 2 hours after Start of Infusion, Day 1: 4 hours after Start of Infusion, Week 2, Week 4, Week 6, Week, 8, Week 10, Week 12, and Week 18.

Listing 16.2.9.9
Hypersensitivity/Anaphylactic Reactions
Safety Population

Subject ID	Treatment Arm	AE ID Number	Onset Date/Time (Study Day)/ Resolution Date/Time (Study Day)	Type of Reaction	Severity grade for the Symptom with Highest Severity	Onset Time for Highest Severity	Leading to IP Discontinuation?
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXX	XXXX	/HH:MM	Yes
		X	DDMMMYYYY/HH:MM (X)/ DDMONYYYY/HH:MM (X)	XXXXX			No
		...					
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ DDMONYYYY/HH:MM (X)	XXXXX	XXXX	/HH:MM	No

AE = Adverse Event.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Onset Date/Time / Resolution Date/Time / Reaction Type.
- Keep sorting from eCRF: Urticaria, Pruritus, Rash, Flushing, Swollen lips, tongue, uvula and/or vulva, Dyspnoea, Wheeze-bronchospasm, Stridor, Hypoxia, Hypotension, Crampy abdominal pain, Vomiting, Diarrhoea, Other.

Listing 16.2.9.10
Liver Diagnostic Investigations
Safety Population

Subject ID	Treatment Arm	Potential Hy's Law Case Number	Liver Diagnostic Investigation Date (Study Day)	Liver Diagnostic Investigation	Liver Diagnostic Investigation Results	Comments
XXXXX	XXXX	X	DDMMMYYYY (X)	XXXX	XXXX	XXXXX
		X	DDMMMYYYY (X)	XXXXX	XXXXX	
		...				
XXXXX	XXXX	X	DDMMMYYYY (X)	XXXXX	XXXXX	

CT = Computerized tomography; ERCP = Endoscopic retrograde cholangiopancreatography; MRI = Magnetic resonance imaging; MRCP = Magnetic resonance cholangiopancreatography.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Diagnostic Date / Liver Diagnostic Investigation.
- Keep sorting from eCRF: Ultrasound, CT, MRI/MRCP, ERCP, Liver Biopsy, X-Ray, Tox Screening for Acetaminophen/Paracetamol, Tox Screening for Ethanol, Tox Screening, Other, Specialist (e.g. Hepatologist) Consulted, Serology for Hepatitis A, Serology for Hepatitis B, Serology for Hepatitis C, Serology for Hepatitis D, Serology for Hepatitis E, for Cytomegalovirus (CMV), Serology for Epstein Barr Virus (EBV), Autoimmune Serology, Other.

Listing 16.2.9.11
Liver Risk Factors and Lifestyle Events
Safety Population

Subject ID	Treatment Arm	Potential Hy's Law Case Number	Assessment Date (Study Day)	Liver Risk Factor Start Date (Study Day)/ Liver Risk Factor Stop Date (Study Day)	Liver Risk Factor / Reference Period	Liver Risk Factor Details	Comments
XXXXX	XXXX	X	DDMMMYYYY (X)	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXX/ XXX	XXXX	XXXXX
		X	DDMMMYYYY (X)	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXXX/ XXX	XXXXX	
		...					
XXXXX	XXXX	X	DDMMMYYYY (X)	DDMMMYYYY (X)/ Ongoing	XXXXX/ XXX	XXXXX	

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Assessment Date / Liver Risk Factor Start Date / Stop Date / Liver Risk Factor.
- Keep sorting from eCRF: Alcohol Abuse, Increased Alcohol Consumption within 1 Month of Reported Event, IV Drug Abuse, Tattoo, Acupuncture, Sexually Transmitted Diseases, Toxic/Chemical Agent Exposure, Travel (Areas at Risk in the Last Year), Pregnancy, Parenteral Nutrition, Excessive Physical Exercise, Changes Diet/Fasting Episodes/Weight Loss Diet, Previous Drug Reaction (Associated with an Elevation of Liver Tests), Blood Transfusion, Subject Exposed to Anyone with Jaundice in the Last Month, History of Hypotension, Low Blood Pressure at Time of Event of Liver Injury and/or Abnormal Liver Laboratory Value, History of Liver Disease, Other.
- Concatenate comments with "/".

Listing 16.2.9.12
Liver Signs and Symptoms
Safety Population

Subject ID	Treatment Arm	Potential Hy's Law Case Number	Start Date (Study Day)/ Stop Date (Study Day)	Liver Sign/ Symptom	Intermittent
XXXXX	XXXX	X	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXX	N
		X	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXXX	N
		...			
XXXXX	XXXX	X	DDMMMYYYY (X)/ Ongoing	XXXXX	Y

Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Start Date / Stop Date / Liver Sign/Symptom.
- Keep sorting from eCRF: Anorexia, Asthenia, Pyrexia, Pruritus, Jaundice, Arthralgia, Abdominal Pain, Abdominal Tenderness, Nausea, Vomiting, Rash, Mucosal Inflammation, Purpura, Hepatomegaly, Splenomegaly, Lymphadenopathy, Ascites, Confusional State, Coma, Upper Quadrant Tenderness, Biliary Obstruction, Eosinophilia, Dark Urine, Other.
- If Rash, Lymphadenopathy or Other, Concatenate Symptom with Comment as: "Rash: xxxxxx". "Lymphadenopathy: xxxxxx", "Other: xxxxxxxx"

Listing 16.2.9.13
Infection Diagnostic Investigations
Safety Population

Subject ID	Treatment Arm	AE ID Number	Start Date/ Time (Study Day)/ Stop Date/ Time (Study Day)	Method	Examination performed	Test Result
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXX	Y	XXXXX
		X	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X))	XXXXX	Y	XXXXX
		...				
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ Ongoing	XXXXX	N	XXXXX

AE = adverse event.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Start Date / Stop Date / Method.
- Keep sorting from eCRF: Microscopy, Culture and Sensitivity, Serological Tests, Nucleic Acid Based Tests, X-Ray, Other.

Listing 16.2.9.14
Infection Risk Factors and Lifestyle Events
Safety Population

Subject ID	Treatment Arm	AE ID Number	Start Date/ Time (Study Day)/ Stop Date/ Time (Study Day)	Infection Risk Factor	Infection Risk Occurrence	Comments
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXX	Y	XXXXX
		X	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X))	XXXXX	Y	XXXXX
		...				
XXXXX	XXXX	X	DDMMMYYYY/HH:MM (X)/ Ongoing	XXXXX	N	Ongoing

AE = adverse event; BCG = Bacillus Calmette–Guérin.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Start Date / Stop Date / Infection Risk Factor.
- Keep sorting from eCRF: Extensive Burns within the Last Year (Thermal Burn), Tattoo, Piercing or Acupuncture within the Last Year, Sexually Transmitted Diseases, Travel to Areas at Risk of Tuberculosis or Tropical Diseases, Infections Related to Travel (e.g. Tuberculosis and Tropical Diseases), Blood Transfusion (within the Last Year), Exposure to Nosocomial Pathogens within the Last Year, Contact History with Infection Source, Previous BCG Immunization, Evidence of BCG Scar, Tuberculin Skin or Quantiferon Test Confirms Previous Exposure or Immunity to Tuberculosis.
- Fill Comment column if Infection risk factor test = Unknown Previous BCG Immunization, not done, known Sexually Transmitted Disease reference Period, or Infection risk factor specifications.

Listing 16.2.9.15
Infection Signs and Symptoms
Safety Population

Subject ID	Treatment Arm	AE ID Number	System Organ Class/ Preferred Term/ Verbatim Term	Start Date/ Time (Study Day)/ Stop Date/ Time (Study Day)	Clinical Event	Infection Sign/Symptom Occurrence	Comments
XXXXX	XXXX	X	XXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X)	XXXXX	Y	XXXXX
		X	XXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ DDMMMYYYY/HH:MM (X))	XXXXX	Y	XXXXX
		...					
XXXXX	XXXX	X	XXXXXXXXXXX/ XXXXXXXXXXXXXX XXXXXXXXXXX	DDMMMYYYY/HH:MM (X)/ Ongoing	XXXXX	N	Ongoing

AE = adverse event.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Start Date / Stop Date / Clinical Event.
- Keep sorting from eCRF: Pyrexia, Headache, Confusional State, Convulsion, Rhinitis, Oropharyngeal Pain, Cough, Productive Cough, Haemoptysis, Wheezing, Dyspnoea, Pleuritic Pain, Vomiting, Diarrhoea, Genital Discharge, Haematuria, Dysuria, Hepatosplenomegaly, Jaundice, Lymphadenopathy, Rash, Night sweats, Chills, Myalgia, Weight Decrease.
- Fill Comment column if Maximum Tº (Unit) available for Pyrexia, or if site for Rash or Lymphadenopathy is known.

Listing 16.2.9.16
Prior and Concomitant Medications
Safety Population

Subject ID/ Treatment Arm	Prior/ Concomitant [1]	ATC Class (Level 2)/ Preferred Name/ Verbatim Term	Given for/as	Primary Indication	Start Date (Study Day)/ End Date (Study Day)	Dose (unit)	Route	Frequency
XXXXXX / XXXX	Prior	XXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXX	Medical History	XXXXXXX	--MMMYYYY (-XX)/ DDMMMYYYY (-X)	XXXX unit	XXXXXX XXX	XXXXX
	Both	XXXXXXXXX/ XXXXXXXXXXXXXXX/ XXXXXXXXXXX	Prophylaxis	XXXXXXX	--MMMYYYY (-X)/ Ongoing	XXXX unit	XXXXXX XXX	XXXXX
	Concomitant	XXXXXXXXX/ XXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXX	Adverse event	XXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (XX)	XXXX unit	XXXXXX XXX	XXXXX

ATC = anatomical therapeutic chemical; WHO-DDE = World Health Organization-Drug Dictionary Enhanced.
Note: Study Day is calculated relative to the date of first dose.
Medications were coded using WHO-DDE version vMar2023.
[1] Prior medications are defined as medications that started before first dose of study, whether they were stopped before first dose of study medication or not. Concomitant medications are defined as medications starting on or after first dose of study medication Both indicates medication that was started before the day of first dose and continued after.

Programming Notes:

- ATC & Preferred Name text should be in proper case in table.
- Ensure proper WHO-DDE version is printed in footnote.
- Sort by subject, start date/time, end date/time, ATC level 2 & Preferred Name .
- If Dose unit, Route or Frequency is Other, display other specify text only (ie, do not display “Other: XXXXXX” but just “XXXXXX “).
- Adjust footnotes for frequency and routes as needed.
- Sort by Treatment ID/ Subject ID / Start Date / End Date (alphabetically for ATC Class Level 2 if same date for two medications)

Listing 16.2.9.17
Prohibited Concomitant Medications
Safety Population

Programming Notes:

- Same Shell as Listing 16.2.9.16.
- Display prohibited prior and concomitant medications provided by the Medical Coder:
- Prohibited concomitant medications:
  - NSAIDs analgesic therapies (with acetylsalicylic acid with doses >= 325 mg/day).
  - COX-2 analgesic therapies.
  - Immunotherapeutics.
  - Live viral or attenuated bacterial vaccines.
  - Oral, IV, intramuscular, or any other parenteral (other than oral) steroids (inhaled or topical steroids are permitted).
  - Biologic therapeutic agents.
- Prohibited prior and/or concomitant medications:
  - Anti-NGF therapies.
  - Anti-TNF therapies.
- ATC & PN text should be in proper case in table.
- Ensure proper WHO-DDE version is printed in footnote.
- Sort by subject, start date/time, end date/time, ATC level 2 & Preferred Name .
- If Dose unit, Route or Frequency is Other, display other specify text only (ie, do not display “Other: XXXXXX” but just “XXXXXX “).
- Adjust footnotes for frequency and routes as needed.
- Sort by subject ID / Start Date / End Date (alphabetically for ATC Class Level 2 if same date for two medications)

Listing 16.2.9.18
Concomitant Procedures
Safety Population

Subject ID	Treatment Arm	System Organ Class/ Preferred Term/ Verbatim Term	Start Date (Study Day)/ End Date (Study Day)	Reason for Procedure	Reason (derived verbatim term)	If Reason is Other, Specify
XXXXX	XXXX	XXXXXXXXXXX/ XXXXXXXXXXXXX XXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXX	
XXXXX	XXXX	XXXXXXXXXXXXX/ XXXXXXXXXXXXX XXXXXXXXXXXX	DDMMMYYYY (X)/ DDMMMYYYY (X)	XXXXXXXXX/ XXXXXXXX	XXXXXXXXXX	
XXXXX	XXXX	XXXXXXXXXXXXX/ XXXXXXXXXXXXX XXXXXXXXXX	DDMMMYYYY (X)/ Ongoing	OTHER	OTHER	XXXXXXXXXX

MedDRA = Medical Dictionary for Regulatory Activities.
Note: Study Day is calculated relative to the date of first dose. All Procedure terms were coded using the MedDRA version 26.0. Concomitant Procedures are defined as medications continuing or starting on or after first dose of study medication.

Programming Notes:

- SOC & PT text should be in proper case in table.
- Sort by Treatment Arm/ Subject ID / Start Date / End Date (alphabetically for SOC if same date for two events).
- In case a term is not coded (e.g. in a dry run) it will be labelled as "Not Coded [SOC]" and "Not Coded [PT]". SOC and PT abbreviations should be added in this case in footnote.

Listing 16.2.9.19
Anti-drug Antibody Test Results
Safety Population

Subject ID	Treatment Arm	Study Visit	Date/Time of Collection (Study Day)	Screening Status Result	Confimatory Status result	ADA Titer	Lab ID Number	Comments
XXXXX	XXXX	XXXXXX	DDMMMYYYY/ HH:MM (X)	Positive	Positive	xx	XXXXXXX	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	Positive	Positive	xx	XXXXXXX	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	Negative	Negative	xx	XXXXXXX	
		XXXXXX	DDMMMYYYY/ HH:MM (X)	Missing	Not Reportable Result	NRR	XXXXXXX	XXXX

ADA = Anti-Drug Antibodies; NA = Not Applicable; NRR = Not Reportable Result; QNS = Quantity Not Sufficient.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Collection Date.
- ADA titre reported as <30 (below the minimum required dilution) is a negative result for the presence of ADA.
- Include Following timepoints: Screening, Weeks 2, 4, 8, 10, 12, 18.

Listing 16.2.10.1
Serum MEDI7352 Concentrations
PK Population

Subject ID	Treatment Arm	Study Visit	PK Blood Sample Collected? / Reason Not Collected	Date/Time of Collection (Study Day)	MEDI7352 Concentration (ng/mL)	Lab ID Number	Comments
XXXXX	XXXX	XXXXXX	Yes	DDMMMYYYY/ HH:MM (X)	XX	XXXXXXX	
		XXXXXX	Yes	DDMMMYYYY/ HH:MM (X)	XX	XXXXXXX	
		XXXXXX	Yes	DDMMMYYYY/ HH:MM (X)	NRR	XXXXXXX	XXXX
		XXXXXX	No / XXXXXX				

NA = Not Applicable; NRR = Not Reportable Result.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Collection Date.
- Include the following timepoints: Day 1, Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours: after Week 10/ Pre-Dose, Week 11: after Week 10/ Pre-Dose, Week 10 + 14 Days: after Week 10/ Pre-Dose, Week 18.

Listing 16.2.10.2
Serum total NGF Concentrations
Safety Population

Subject ID	Treatment Arm	Study Visit	PD Blood Sample Collected? / Reason Not Collected	Date/Time of Collection (Study Day)	Total NGF Concentration (pg/mL)	Lab ID Number	Comments
XXXXX	XXXX	XXXXXX	Yes	DDMMMYYYY/ HH:MM (X)	XX	XXXXXXX	
		XXXXXX	Yes	DDMMMYYYY/ HH:MM (X)	XX	XXXXXXX	
		XXXXXX	Yes	DDMMMYYYY/ HH:MM (X)	NS	XXXXXXX	XXXX
		XXXXXX	No / XXXXXX				

BLLOQ = Below the Lowest Limit of Quantitation; NA = Not Applicable; ND = Not Detected; NS = No Value due to Insufficient Volume or No Sample Received; PD: Pharmacodynamic; SAT = Greater than the Top of the Standard Curve; tNGF = total Nerve-Growth Factor.
Note: Study Day is calculated relative to the date of first dose.

Programming Notes:

- Sort by Treatment Arm/ Subject ID / Collection Date.
- Include the following timepoints: Day 1, Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 12; Week 18.

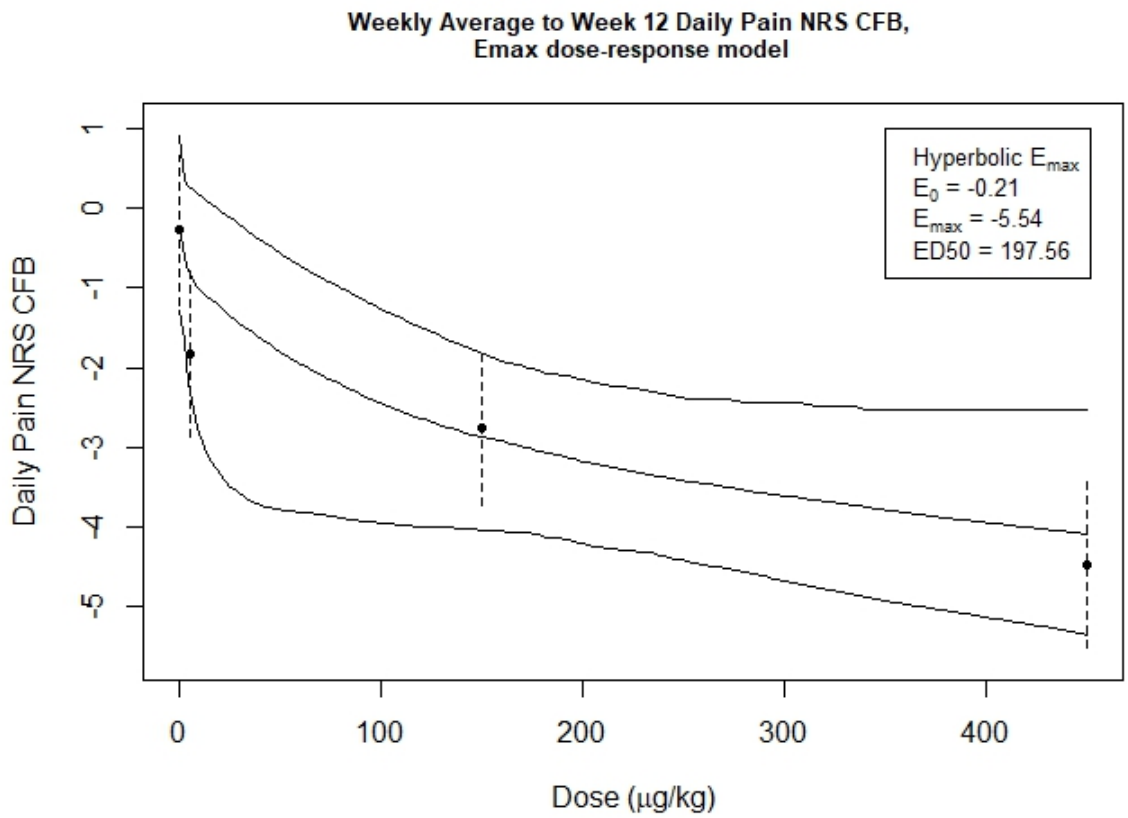
Planned Figure Descriptions and Shells

Number Title Population	Unique (U) or Repeated (R)
Figure 14.2.1.1 - Daily Pain NRS: MCP-Mod Dose Response Model - mITT Population	U
Figure 14.2.1.2 - Daily Pain NRS CFB: Boxplots at Week 12 by Treatment Group and Missing Data Handling - mITT Population	U
Figure 14.2.1.3.1 - Daily Pain NRS CFB: Boxplots at Week 12 by Treatment Group and Co-Medication Subgroup - mITT Population	R
Figure 14.2.1.3.2 - Daily Pain NRS CFB: Boxplots at Week 12 by Treatment Group and Co-Medication Subgroup, Including Opioids - mITT Population	CCI
Figure 14.2.1.4 - Daily Pain NRS: MMRM LS Means (95% Confidence Interval) over 12-weeks by Treatment Group (Observed Cases) - mITT Population	U
Figure 14.3.6.1.1 - Vital Sign Profiles: Mean (±SD) Systolic Blood Pressure over time - Safety Population	U
Figure 14.3.6.1.2 - Vital Sign Profiles: Mean (±SD) Diastolic Blood Pressure over time - Safety Population	R
Figure 14.3.6.1.3 - Vital Sign Profiles: Mean (±SD) Heart Rate over time - Safety Population	R
Figure 14.3.6.1.4 - Vital Sign Profiles: Mean (±SD) Respiratory Rate over time - Safety Population	R
Figure 14.3.6.1.5 - Vital Sign Profiles: Mean (±SD) Temperature over time - Safety Population	R
Figure 14.4.1.1 - Pharmacokinetics: Line Plot of Geometric Mean (with and without gSD) Serum MEDI7352 over time - PK Population	R
Figure 14.4.1.2 - Pharmacokinetics: Individual Plot of Serum MEDI7352 Concentrations over time - PK Population	U
Figure 14.4.2.1 - Pharmacodynamics: Line Plot of Geometric Mean (with and without gSD) total NGF over time - Safety Population	R
Figure 14.4.2.2 - Pharmacodynamics: Individual Plot of Serum total NGF over time - Safety Population	R

Figures Change Log

Output Number	Date of Change	Change Made By (initials)	Description/Rationale

Figure 14.2.1.1
Daily Pain NRS: MCP-Mod Dose Response Model
mITT Population

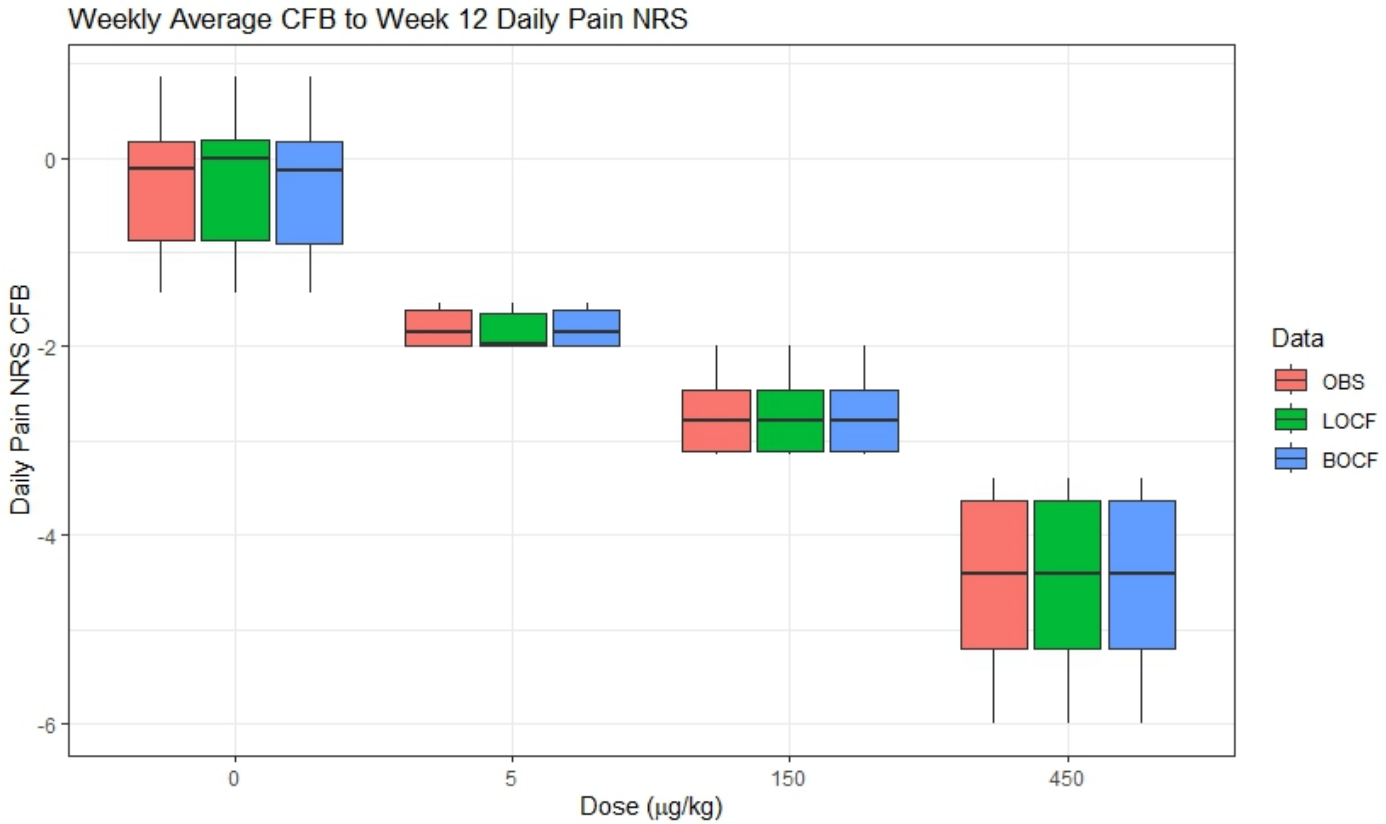


CI = Confidence Interval; CFB = Change from Baseline; DPS = Daily Pain Score; NRS = Numeric Rating Scale.
Baseline is defined as the average of the 'non-missing' DPS within the seven-day period prior to randomization i.e., Day -7 to Day -1, inclusive. Envelope depicts 95% CI of mean dose-response. Added dots are actual doses ± 95% CI.
mITT Population = includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
Reference Listing: 16.2.6.1

Programming Notes:

- Insert the following text as legend: "Weekly Average to Week 12 Daily Pain NRS CFB, xxxx dose-response model", with 'xxxx' as the selected dose-response model (e.g., Hyperbolic E_{max}).
- Dose (µg/kg) in x axis and Daily Pain NRS CFB in y axis.
- Add model parameter values as an inset plot. For e.g., Sigmoid E_{max}; E_0 = xxx, E_{max} = xxx, ED50 = xxx, λ = xxx.
- The MCP-MOD approach will only be performed if stage 4 is initiated, otherwise there would be insufficient dosing data to fit the non-linear models.

Figure 14.2.1.2
Daily Pain NRS CFB: Boxplots at Week 12 by Treatment Group and Missing Data Handling
mITT Population



BOCF = Baseline Observation Carried Forward; CFB = Change from Baseline; DPS = Daily Pain Score; LOCF = Last Observation Carried Forward; NRS = Numeric Rating Scale; OBS = Observed Cases.
Baseline is defined as the average of the 'non-missing' DPS within the seven-day period prior to randomization i.e., Day -7 to Day -1, inclusive.
mITT Population = includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
Reference Listing: 16.2.6.1

Programming Notes:

- Insert the following text as legend: “Weekly Average CFB to Week 12 Daily Pain NRS”.
- Dose (µg/kg) and Observed/LOCF/BOCF in x axis and Daily Pain NRS CFB in y axis.
- A level for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.2.1.3.1
Daily Pain NRS CFB: Boxplots at Week 12 by Treatment Group and Co-Medication Subgroup
mITT Population

CFB = Change from Baseline; DPS = Daily Pain Score; NRS = Numeric Rating Scale.
Baseline is defined as the average of the 'non-missing' DPS within the seven-day period prior to randomization i.e., Day -7 to Day -1, inclusive.
mITT Population = includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
Reference Listing: 16.2.6.1

Programming Notes:

- Same shell as Figure 14.2.1.2
- Insert the following text as legend: "Weekly Average CFB to Week 12 Daily Pain NRS".
- Dose (µg/kg) in x axis, Anticonvulsant/ Antidepressant/ Both/ None in right side Co-medication labels, and Daily Pain NRS CFB in y axis.
- A level for CCI [redacted] dosing CCI [redacted]) will only be added if Stage 4 is initiated.

Figure 14.2.1.3.2
Daily Pain NRS CFB: Boxplots at Week 12 by Treatment Group and Co-Medication Subgroup, Including Opioids
mITT Population

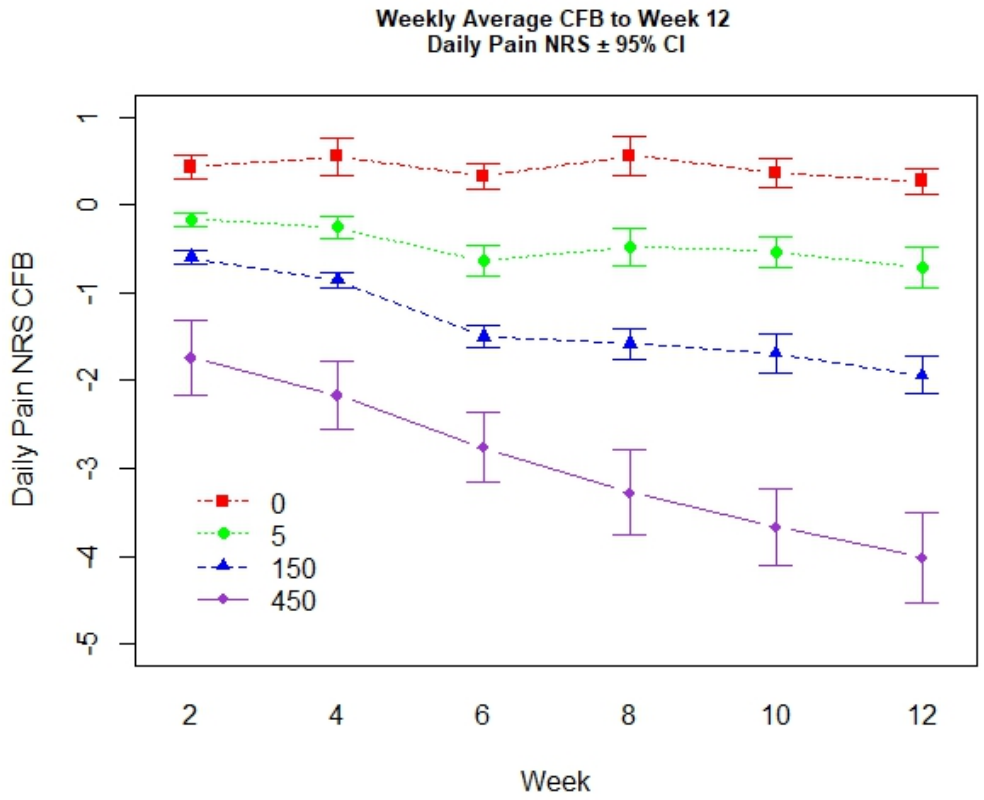
BOTH = Anticonvulsant and Antidepressant; CFB = Change from Baseline; DPS = Daily Pain Score; NRS = Numeric Rating Scale.
Baseline is defined as the average of the 'non-missing' DPS within the seven-day period prior to randomization i.e.,
Day -7 to Day -1, inclusive.
mITT Population = includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
Reference Listing: 16.2.6.1

Programming Notes:

CCI [redacted]

- Same shell as Figure 14.2.1.2
- Insert the following text as legend: "Weekly Average CFB to Week 12 Daily Pain NRS".
- Dose (µg/kg) in x axis, Anticonvulsant/ Antidepressant/ Both/ Opioid/ None in right side Co-medication labels, and Daily Pain NRS CFB in y axis.
- A level for CCI [redacted] dosing (CCI [redacted]) will only be added if Stage 4 is initiated.

Figure 14.2.1.4
Daily Pain NRS: MMRM LS Means (95% Confidence Interval) over 12-weeks by Treatment Group (Observed Cases)
mITT Population



CFB = Change from Baseline; CI = Confidence Interval; DPS = Daily Pain Score; LS = Least Square; MMRM = Mixed Model for Repeated Measures; NRS = Numeric Rating Scale.
Baseline is defined as the average of the 'non-missing' DPS within the seven-day period prior to randomization i.e., Day -7 to Day -1, inclusive.

mITT Population = includes all subjects in the Safety Population who have at least 1 daily NRS assessment while receiving double-blind treatment.
Reference Listing: 16.2.6.1

Programming Notes:

- Insert the following text as legend: "Weekly Average CFB to Week 12 Daily Pain NRS ± 95% CI".
- Week in x axis and Daily Pain NRS CFB in y axis.
- **Include a profile for each dose treatment group.**
- Include the following timepoints: Week 2, 4, 6, 8, 10, and 12.
- **Extract data for this figure from the MMRM of CFB Daily Pain NRS with Observed Cases.**
- A profile for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.3.6.1.1
Vital Sign Profiles: Mean (±SD) Systolic Blood Pressure over time
Safety Population

1H PD = 1 Hour Post-Dose; 15M PD = 15 Minutes Post-Dose; 2H PD = 2 Hours Post-Dose; 30M PD = 30 Minutes Post-Dose; 4H PD = 4 hours Post-Dose; 45M PD = 45 Minutes Post-Dose; 5M PD = 5 minutes after Infusion Completion; BASE = Baseline; D1 = Day 1; SBP = Systolic Blood Pressure; W2 = Week 2; W4 = Week 4; W6 = Week 6; W8 = Week 8; W10 = Week 10; W11 = Week 11; W12 = Week 12; W18 = Week 18.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
Reference Listing: 16.2.9.1

Programming Notes:

- Same shell as Figure 14.2.1.4
- Insert the following text as legend: "Average SBP ± Standard Deviation".
- Study Visit in x axis and Systolic Blood Pressure (mmHg) in y axis.
- **Include a profile for Resting SBP and another for Standing SBP.**
- Include the following timepoints: Baseline, Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week 10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- Note that standing measures are not taken on Day 1, at 15, 30 and 45 minutes post-dose.
- **Make one plot for each dose treatment group, for a total of 4 plots with two profiles each.**
- A plot for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.3.6.1.2
Vital Sign Profiles: Mean (±SD) Diastolic Blood Pressure over time
Safety Population

1H PD = 1 Hour Post-Dose; 15M PD = 15 Minutes Post-Dose; 2H PD = 2 Hours Post-Dose; 30M PD = 30 Minutes Post-Dose; 4H PD = 4 hours Post-Dose; 45M PD = 45 Minutes Post-Dose; 5M PD = 5 minutes after Infusion Completion; BASE = Baseline; D1 = Day 1; DBP = Diastolic Blood Pressure; W2 = Week 2; W4 = Week 4; W6 = Week 6; W8 = Week 8; W10 = Week 10; W11 = Week 11; W12 = Week 12; W18 = Week 18.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
Reference Listing: 16.2.9.1

Programming Notes:

- Same shell as Figure 14.2.1.4
- Insert the following text as legend: "Average DBP ± Standard Deviation".
- Study Visit in x axis and Diastolic Blood Pressure (mmHg) in y axis.
- **Include a profile for Resting DBP and another for Standing DBP.**
- Include the following timepoints: Baseline, Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week 10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- Note that standing measures are not taken on Day 1, at 15, 30 and 45 minutes post-dose.
- **Make one plot for each dose treatment group, for a total of 4 plots with two profiles each.**
- A plot for CCI dosing (CCI) will only be added if Stage 4 is initiated)

Figure 14.3.6.1.3
Vital Sign Profiles: Mean (±SD) Heart Rate over time
Safety Population

1H PD = 1 Hour Post-Dose; 15M PD = 15 Minutes Post-Dose; 2H PD = 2 Hours Post-Dose; 30M PD = 30 Minutes Post-Dose; 4H PD = 4 hours Post-Dose; 45M PD = 45 Minutes Post-Dose; 5M PD = 5 minutes after Infusion Completion; BASE = Baseline; D1 = Day 1; HR = Heart Rate; W2 = Week 2; W4 = Week 4; W6 = Week 6; W8 = Week 8; W10 = Week 10; W11 = Week 11; W12 = Week 12; W18 = Week 18.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
Reference Listing: 16.2.9.1

Programming Notes:

- Same shell as Figure 14.2.1.4
- Insert the following text as legend: "Average HR ± Standard Deviation".
- Study Visit in x axis and Heart Rate (Beats/min) in y axis.
- **Include a profile for Resting HR and another for Standing HR.**
- Include the following timepoints: Baseline, Day 1: 15 Minutes Post-Dose, Day 1: 30 Minutes Post-Dose, Day 1: 45 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week 10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- Note that standing measures are not taken on Day 1, at 15, 30 and 45 minutes post-dose.
- **Make one plot for each dose treatment group, for a total of 4 plots with two profiles each.**
- A plot for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.3.6.1.4
Vital Sign Profiles: Mean (±SD) Respiratory Rate over time
Safety Population

1H PD = 1 Hour Post-Dose; 15M PD = 15 Minutes Post-Dose; 2H PD = 2 Hours Post-Dose; 4H PD = 4 hours Post-Dose; 5M PD = 5 minutes after Infusion Completion; BASE = Baseline; D1 = Day 1; W2 = Week 2; W4 = Week 4; W6 = Week 6; W8 = Week 8; W10 = Week 10; W11 = Week 11; W12 = Week 12; W18 = Week 18.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
Reference Listing: 16.2.9.1

Programming Notes:

- Same shell as Figure 14.2.1.4
- Insert the following text as legend: "Average Respiratory Rate ± Standard Deviation".
- Study Visit in x axis and Respiratory Rate (Breaths/min) in y axis.
- Include the following timepoints: Baseline, Day 1: 15 Minutes Post-Dose, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- **Make one plot with 4 profiles (one for each treatment group).**
- A profile for CCI dosing (CCI) will only be added if Stage 4 is initiated.

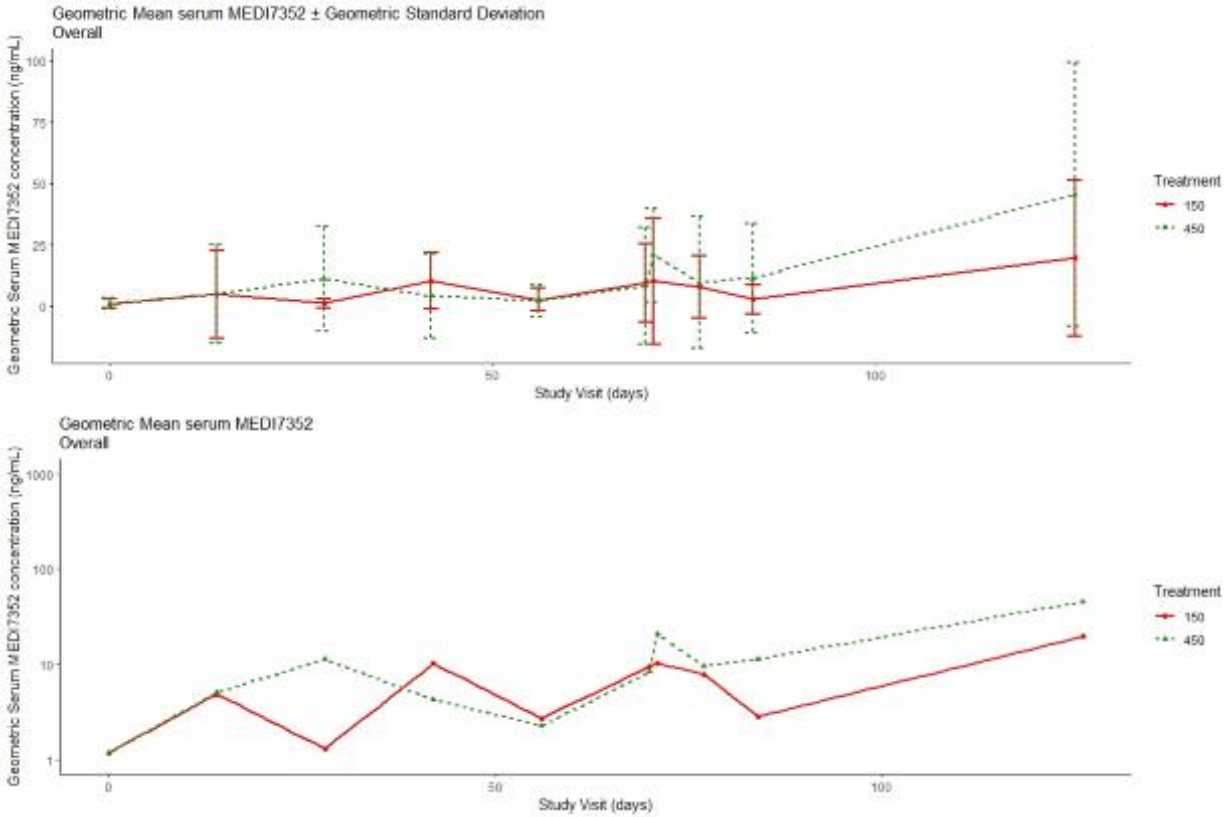
Figure 14.3.6.1.5
Vital Sign Profiles: Mean (±SD) Temperature over time
Safety Population

1H PD = 1 Hour Post-Dose; 2H PD = 2 Hours Post-Dose; 4H PD = 4 hours Post-Dose; 5M PD = 5 minutes after Infusion Completion; BASE = Baseline; D1 = Day 1; T° = Temperature; W2 = Week 2; W4 = Week 4; W6 = Week 6; W8 = Week 8; W10 = Week 10; W11 = Week 11; W12 = Week 12; W18 = Week 18.
Baseline is defined as the last observation recorded prior to the first dose of treatment.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
Reference Listing: 16.2.9.1

Programming Notes:

- Same shell as Figure 14.2.1.4
- Insert the following text as legend: "Average Body Tº ± Standard Deviation".
- Study Visit in x axis and Body Temperature (ºC) in y axis.
- Include the following timepoints: Baseline, Day 1: 1 hour Post-Dose, Day 1: 2 hours Post-Dose, Day 1: 4 hours Post-Dose, Week 2: Pre-Dose, Week 2: 5 minutes after Infusion Completion, Week 4: Pre-Dose, Week 4: 5 minutes after Infusion Completion, Week 6: Pre-Dose, Week 6: 5 minutes after Infusion Completion, Week 8: Pre-Dose, Week 8: 5 minutes after Infusion Completion, Week 10: Pre-Dose, Week 10: 5 minutes after Infusion Completion, Week10 + 24 hours, Week 11, Week 12, Week 18. (Do not include Screening records).
- **Make one plot with 4 profiles (one for each treatment group).**
- A plot for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.4.1.1
Pharmacokinetics: Line Plot of Geometric Mean (with and without gSD) Serum MEDI7352 Concentrations over Time
PK Population



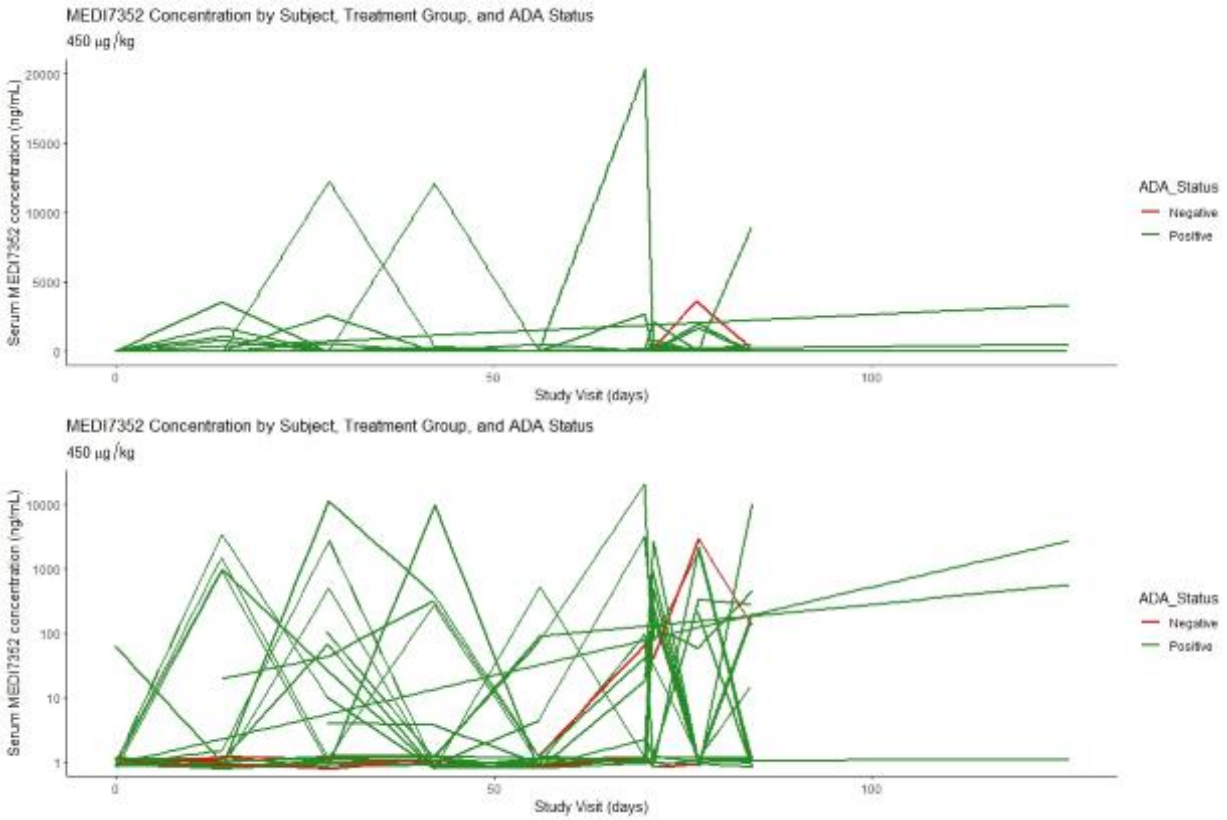
ADA = Antidrug Antibodies; gSD = Geometric Standard Deviation; LLOQ = Lower Limit of Quantification.

PK Population = includes all subjects for who a pharmacokinetic sample was obtained and analyzed.
ADA positive represents number of participants with at least one positive ADA result.
ADA negative represents number of participants with only negative ADA results (no positive).
Reference Listing: 16.2.10.1

Programming Notes:

- Insert the following text as upper legend: "Geometric Mean serum MEDI7352 ± Geometric Standard Deviation (Linear Scale)" for the linear plot, and "Geometric Mean serum MEDI7352 (Semi-Logarithmic Scale)" for the semi-log plot. Below legend, add legend for ADA status: "Overall", "ADA Positive", "ADA Negative".
- Insert legend with different point symbols and colors for each treatment group (CCI) for the Overall plot, and a legend with different point symbols and colors for each ADA status (ADA+, ADA-) for each treatment group plot by ADA status.
- Study Day in x axis and Serum MEDI7352 concentration (ng/mL) in y axis (**in linear and log_{10} scale, for each plot**).
- Include data from the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10: Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 10 + 14 days, Week 18.
- **Make one overall plot by treatment group, and a plot for each treatment group by ADA status for a total of 4 plots.**
- Include a marker for LLOQ, and an inset within the plot with "LLOQ (1.00 ng/mL)".
- A line for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.4.1.2
Pharmacokinetics: Individual Plot of Serum MEDI7352 Concentrations over time
PK Population



ADA = Antidrug Antibodies; LLOQ = Lower Limit of Quantification.
PK Population = includes all subjects for who a pharmacokinetic sample was obtained and analyzed.
ADA positive represents number of participants with at least one positive ADA result.
ADA negative represents number of participants with only negative ADA results (no positive).
Reference Listing: 16.2.10.1

Programming Notes:

- Insert the following text as upper legend: "MEDI7352 Concentration by Subject, Treatment group, and ADA status" followed by "(Linear Scale)" or "(Semi-Logarithmic Scale)" depending on the plot (linear or semi-log). Below legend, add legend for Treatment Group: CCI [redacted].
- Insert legend with different colors for each ADA status (Positive/ Negative).
- Time (days) in x axis and Serum MEDI7352 concentration (ng/mL) in y axis (**in linear and log_{10} scale, for each plot**).
- Include data from the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 10 + 14 days, Week 18.
- **Make one plot for each Treatment group (CCI [redacted]), for a total of 3 plots.**
- Include a marker for LLOQ, and an inset within the plot with "LLOQ (1.00 ng/mL)".
- Plots for CCI [redacted] dosing (CCI [redacted]) will only be added if Stage 4 is initiated.

Figure 14.4.2.1
Pharmacodynamics Line Plot of Geometric Mean (with and without gSD) Serum total NGF over time
Safety Population

ADA = Antidrug Antibodies; gSD = Geometric Standard Deviation; LLOQ = Lower Limit of Quantification, NGF = Nerve-Growth Factor.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
ADA positive represents number of participants with at least one positive ADA result.
ADA negative represents number of participants with only negative ADA results (no positive).
Reference Listing: 16.2.10.3

Programming Notes:

- Same shell as Figure 14.4.1.1
- Insert the following text as upper legend: "Geometric Mean Serum Concentration of tNGF ± Geometric Standard Deviation (Linear Scale)" for the linear plot, and "Geometric Mean Serum Concentration of tNGF (Semi-Logarithmic Scale)" for the semi-log plot. Below legend, add legend for ADA status: "Overall", "ADA Positive", "ADA Negative".
- Insert legend with different point symbols and colors for each treatment group (Placebo, CCI) for the Overall plot, and a legend with different point symbols and colors for each ADA status (ADA+, ADA-) for each treatment group plot by ADA status.
- Study Day in x axis and Serum tNGF Concentration (pg/mL) in y axis (**in linear and log$_{10}$ scale for each plot**).
- Include data from the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10: Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 12, Week 18.
- **Make one overall plot by treatment group, and a plot for each treatment group by ADA status for a total of 5 plots .**
- Include a marker for LLOQ, and an inset within the plot with "LLOQ (10.00 pg/mL)".
- A plot for CCI dosing (CCI) will only be added if Stage 4 is initiated.

Figure 14.4.2.2
Pharmacodynamics: Individual Plot of Serum total NGF over time
Safety Population

ADA = Antidrug Antibodies; LLOQ = Lower Limit of Quantification; NGF = Nerve-Growth Factor.
Safety Population = includes all subjects who receive at least 1 dose of double-blind study medication.
ADA positive represents number of participants with at least one positive ADA result.
ADA negative represents number of participants with only negative ADA results (no positive).
Reference Listing: 16.2.10.3

Programming Notes:

- Same shell as Figure 14.4.1.2
- Insert the following text as legend: "Total NGF by Subject, Treatment group, and ADA status" followed by "(Linear Scale)" or "(Semi-Logarithmic Scale)" depending on the plot (linear or semi-log). Below legend, add legend for Treatment Group: CCI [redacted].
- Insert legend with different colors for each ADA status (Positive/ Negative).
- Time (days) in x axis and Serum tNGF concentration (pg/mL) in y axis (**in linear and $\log_{10}$ scale for each plot**).
- Include data from the following timepoints: Baseline (Day 1), Week 2, Week 4, Week 6, Week 8, Week 10: Pre-Dose, Week 10; Before End of Infusion, Week 10: 8 Hours after Infusion, Week 10 + 24 hours, Week 11, Week 12; Week 18.
- **Make one plot for each Treatment group (CCI [redacted] Placebo), for a total of 4 plots.**
- Include a marker for LLOQ, and an inset within the plot with "LLOQ (10.00 pg/mL)".
- Plots for CCI [redacted] dosing (CCI [redacted]) will only be added if Stage 4 is initiated.