Statistical Analysis Plan

NCT Number: NCT05084053

Title: A Phase 3 Study to Evaluate the Efficacy, Safety and Tolerability of TAK-771 for the Treatment of Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) and Multifocal Motor Neuropathy (MMN) in Japanese Subjects

Study Number: TAK-771-3002

Document Version and Date: Version 3.0 / 17-Oct-2024

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STATISTICAL ANALYSIS PLAN

Study Number: TAK-771-3002

A Phase 3 Study to Evaluate the Efficacy, Safety and Tolerability of TAK-771 for the Treatment of Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) and Multifocal Motor Neuropathy (MMN) in Japanese Subjects

Phase III

Version: 3.0

Date: 17-Oct-2024

Prepared by: [redacted]

Based on:

Protocol Version: Amendment 2

Protocol Date: 18-May-2022

REVISION HISTORY

Version	Approval Date	Primary Rationale for Revision
1.0	19-Aug-2021	[Not Applicable]
2.0	10-Apr-2024	Correction regarding Protocol revision (removal of unnecessary Endpoint descriptions). Corrected to match Protocol description and italicized the same description in Protocol. Added description clarifying the analysis. Added the following section: - 6.1.5 Study Information - 6.3.3 CIDP history - 6.3.4 MMN history - 6.5 Prior/Concomitant Surgeries and Procedures - 9.1.9 Missing Date Information for First Symptoms - 9.1.10 Missing Date Information for Diagnosis - 9.2 Definition of AESIs Updated the description in following section: - 1.1.2 Secondary Objectives - 1.2.2.2 Efficacy - 6.1 General Considerations - 6.1.4 Analysis Approach for Time-to-Event Variables - 6.2 Disposition of Subjects - 6.3.2 Medical History - 6.4 Medication History and Concomitant Medications - 6.4.1 Prior Medications - 6.4.2 Concomitant Medications - 6.6.1.3 Supplementary Analysis - 6.6.2 Secondary Endpoints Analysis - 6.6.3 Tertiary Endpoints Analysis - 6.7.1 Adverse Events - 6.7.1.1 Descriptive Analysis of Adverse Events per Infusion, per Subject, per Subject-Year - 6.7.2 Adverse Events of Special Interest - 6.7.3 Clinical Laboratory Evaluations - 6.7.4 Vital Signs - 6.7.7 ADA Analysis - 6.7.8 Extent of Exposure and Compliance - 6.10 Other Analyses - 8.0 CHANGES TO PROTOCOL PLANNED ANALYSES - 9.1.3 Definition of Visit Windows - 9.1.14 Character Values of Clinical Laboratory Variables

3.0	17-Oct-2024	Added description of analysis sets for Epoch 2 analysis in section 5.0. Updated description mainly to clarify the analysis in Epoch 2. In addition, in each section, added the range of Epoch 2 data to be used in the 2nd interim analysis and final analysis. Updated the description in following section: - 6.1: Added description of the start timing of each period and description of the serum IgG baseline. - 6.2: Added description to distinguish between the first 6 months in Epoch 2 and the subsequent periods. - 6.6.2-1: Added the item to be displayed in listing. - 6.6.3: Corrected a typo in an item in the PK analysis. (Changed "SD of the geometric mean" to "CV of the geometric mean") Regarding the analysis of data after day 120, a condition was added that non-relapse/worsen subjects would not be included in the analysis if there was only data for day 120 or less. - 6.7.7: Clarified definition of terms and analysis tables. - 6.7.8: Added classification of Epoch 2. - 6.10: Clarified the formula for each Epoch. Deleted the following section: - 6.6.2: "9. Change from pre-SC treatment baseline in R-ODS" in SAP v2.0 was deleted because it was a duplicate description with "6.6.2-3". Deleted unnecessary statements from section 8.0. Corrected table 6-8 in section 9.1.3. Added section 9.3.

TABLE OF CONTENTS

LIST OF IN-TEXT TABLES

ABBREVIATIONS

ADL	Activities of daily living
AE	Adverse event
AR	Adverse reaction
CI	Confidence interval
CIDP	Chronic Inflammatory Demyelinating Polyradiculoneuropathy
COVID-19	Coronavirus disease 2019
CRA	Clinical research associate
CTMS	Clinical Trial Management System
CV	Coefficient of Variation
E1INT	Epoch 1 interim
E1W1	Epoch 1 Week 1
Eo6M	End-of-Epoch 2 (6 Months)
EoE1	End-of-Epoch 1
EoE2	End-of-Epoch 2 (continued)
ECG	Electrocardiogram
FAS	Full analysis set
GNDS	Guy's Neurological Disability Scale
IgG	Immunoglobulin G
INCAT	Inflammatory Neuropathy Cause and Treatment disability score
IP	Investigation Product
IVIG	Intravenous immunoglobulin
MedDRA	Medical Dictionary for Regulatory Activities
MMN	Multifocal Motor Neuropathy
MRC	Medical Research Council
PCS	Potentially clinically significant
PK	Pharmacokinetic
PPS	Per-protocol set
PRO	Patient-reported outcomes
PT	Preferred Term (MedDRA)
R-ODS	Rasch Built Overall Disability Scale
Q1	1st quartile
Q3	3rd quartile
rHuPH20	Recombinant human hyaluronidase
SAE	Serious adverse event
SAP	Statistical analysis plan
SD	Standard deviation
SOC	System Organ Class
SYs	Subject-years
TEAE	Treatment-emergent adverse event
TIBC	Total Iron Binding Capacity

1.0 OBJECTIVES, ENDPOINTS AND ESTIMANDS

1.1 Objectives

1.1.1 Primary Objective

To evaluate the efficacy of TAK-771 in Epoch 1 as a maintenance therapy for Japanese patients with stable Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) and Multifocal Motor Neuropathy (MMN) to prevent relapse or progression of motor function.

1.1.2 Secondary Objectives

- *To assess the safety and tolerability of TAK-771 in Epoch 1 and Epoch 2 as a maintenance therapy for Japanese patients with CIDP and MMN*
- *To assess the efficacy of TAK-771 in Epoch 1 and Epoch 2*

1.1.3 Tertiary Objectives

- *To assess the serum trough levels of total immunoglobulin G (IgG)*
- *To assess the number of subjects using self-administration*

1.2 Endpoints

1.2.1 Primary Endpoints

- Cohort 1 (CIDP)

Occurrence of relapse in Epoch 1 (worsening of functional disability defined as an increase of ≥ 1 point relative to the pre-SC treatment baseline score in adjusted Inflammatory Neuropathy Cause and Treatment (INCAT) disability score)

- Cohort 2 (MMN)

Change in maximum grip strength in the more affected hand in Epoch 1 (per baseline measurement point, investigators judge which of both hands is more affected)

1.2.2 Secondary Endpoints

1.2.2.1 Safety

- *Cohort 1 (CIDP) and Cohort 2 (MMN)*
  - *Treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) regardless of causality*
  - *Causality of related SAEs and/or AEs*
  - *Serious and/or nonserious adverse reactions (ARs) plus suspected ARs**
  - *Treatment-emergent SAEs and/or AEs associated with infusions, regardless of causality*

- *Causality of related SAEs and/or AEs associated with infusions*
- *AEs temporally associated with infusions (defined as AEs occurring during or within 72 hours after completion of an infusion)*
- *Serious and/or nonserious ARs plus suspected ARs associated with infusions*
- *Treatment-emergent systemic AEs associated with infusions*
- *Treatment-emergent local infusion site reactions associated with infusions*
- *Infusions for which the infusion rate was reduced and/or the infusion was interrupted or stopped due to intolerability and/or AEs*
- *Development positive titer (≥160) binding antibodies, or develop neutralizing antibodies, to recombinant human hyaluronidase (rHuPH20)*

** In the current study, an AR/suspected AR is defined as an AE that is considered by the investigator to be possibly or probably related to investigational product (IP) administration, or for which the causality is indeterminate or missing, or that begins during infusion of IP or within 72 hours following the end of IP infusion*

1.2.2.2 Efficacy

- *Cohort 1 (CIDP)*
  - *CIDP worsening in Epoch 1 (defined as a ≥ 8 kPa decrease in the hand grip strength in the more affected hand) OR ≥ 4 points decrease in Rasch-Built Overall Disability Scale (R-ODS) relative to the pre-SC treatment baseline score at 2 consecutive time points (at the time of withdrawal from the SC treatment period)*
  - *Time to relapse in Epoch 1 and Epoch 2*
  - *Change from pre-SC treatment baseline in R-ODS score in Epoch 1*
  - *Change from baseline in an average of handgrip strength of both hands in Epoch 1*
- *Cohort 2 (MMN)*
  - *Medical Research Council (MRC) sum score in Epoch 1*
  - *Guy's Neurological Disability Scale (GNDS) in upper limb and lower limb categories in Epoch 1*
  - *Change from baseline in an average of handgrip strength of both hands in Epoch 1*

1.2.3 Tertiary Endpoints

- *Serum trough levels of total IgG*
- *Number of subjects received the study drug through self-administration*

1.3 Estimands

Table 1.a Estimand Framework

Estimand: Cohort 1 (CIDP)					
	Attributes				
Definition	Treatment	Population	Variable (or Endpoint)	Strategy for Addressing Intercurrent Event	Population-Level Summary
The primary estimand is the treatment effect of TAK-771 during Epoch 1 in targeted patient population.	The IgG dose of TAK-771 per month will be adjusted to be equivalent to subject's monthly intravenous immunoglobulin (IVIG) dose. The number of infusion visits and site visits during the SC treatment period will vary across subjects depending on whether their infusion cycles are every 2, 3, or 4 weeks.	Japanese subjects with a confirmed diagnosis of CIDP for approval (defined through appropriate inclusion/exclusion criteria) and who received TAK-771 at least once	Occurrence of relapse in Epoch 1	Early termination due to AE, Significant protocol deviation, Voluntary withdrawal, Pregnancy, CIDP relapse, start the excluded medications or non-drug therapies, termination of TAK-771 administration by investigator's determination and death are regarded as the Intercurrent Event. While on treatment strategy is used, i.e., all available INCAT data before permanent discontinuation or death are used for the analysis.	Percentage of subjects with relapse and corresponding exact 2-sided Clopper-Pearson 95% confidence interval (CI)

Table 1.b Estimand Framework

Estimand: Cohort 2 (MMN)					
	Attributes				
Definition	Treatment	Population	Variable (or Endpoint)	Strategy for Addressing Intercurrent Event	Population-Level Summary
The primary estimand is the treatment effect of TAK-771 during Epoch 1 in targeted patient population.	The IgG dose of TAK-771 per month will be adjusted to be equivalent to subject's monthly IVIG dose. The number of infusion visits and site visits during the SC treatment period will vary across subjects depending on whether their infusion cycles are every 2, 3, or 4 weeks.	Japanese subjects with a confirmed diagnosis of MMN for approval (defined through appropriate inclusion/exclusion criteria) and who received TAK-771 at least once	Change in maximum grip strength in the more affected hand in Epoch 1.	Early termination due to AE, Significant protocol deviation, Voluntary withdrawal, Pregnancy, CIDP relapse, start the excluded medications or non-drug therapies, termination of TAK-771 administration by investigator's determination and death are regarded as the Intercurrent Event. While on treatment strategy is used, i.e., all available Hand grip strength data before permanent discontinuation or death are used for the analysis.	The change from baseline to the end of study visit (the latest of E1INT or EoE1) in maximum grip strength and 2-sided 95% CI

2.0 STUDY DESIGN

This is a Phase 3, prospective, multicenter, open-label, non-controlled, single-arm study. There are two treatment Epochs, with 2 cohorts of CIDP and MMN patients in this study. A schematic of the study design is shown in Figure 6-1 of the Protocol. Investigational product administration and site visit schedule are the same in Cohort 1 and Cohort 2, but primary endpoint measurements differ.

This study will enroll subjects with a confirmed diagnosis of CIDP or MMN, who have remained on a stable dosing regimen (monthly equivalent dose of 0.4 to 2.4 g/kg BW with a dosing interval of 2 to 6 weeks) of IVIG therapy for at least 12 weeks prior to screening.

After informed consent is obtained, subjects will undergo screening and baseline procedures for the determination of eligibility and will continue to receive their own IVIG treatment at the same dose and dosing intervals prescribed prior to their entry into this study. No dosing adjustment of IVIG treatment is allowed except in cases of intolerability.

Eligible subjects will receive TAK-771 SC for a treatment period of 6 months in Epoch 1. The IgG dose of TAK-771 per month will be adjusted to be equivalent to subject's monthly IVIG dose. The number of infusion visits and site visits during the SC treatment period will vary across subjects depending on whether their infusion cycles are every 2, 3, or 4 weeks. If a subject with CIDP has met relapse criteria or a subject with MMN has been judged as being worsened by the investigator, the subject will be discontinued from the study treatment (See details in Section 7.4 of the Protocol). For safety and tolerability data, the sponsor set the minimum duration of Epoch 2 as 6 months. After the first 6 months of Epoch 2, if the subject is tolerating the drug well and voluntarily wishes to continue TAK-771 treatment, the subject can stay in the study until the commercial TAK-771 is available in each study site. After the first 6 months of Epoch 2, the investigator may adjust the dose of TAK-771 administration in every 3 months (See details in Section 6.1.1 of the Protocol). Schedule of assessments is varied across the dosing interval (See the details in Appendix A of the Protocol).

3.0 STATISTICAL HYPOTHESES AND DECISION RULES

3.1 Statistical Hypotheses

The primary objective of Epoch 1 is to evaluate the efficacy of TAK-771 as a maintenance therapy for CIDP to prevent relapse of neuromuscular disability and impairment. The following null hypothesis and alternative hypothesis will be tested as the estimated relapse rate in placebo-treated patients of 57%:

- H_0: Relapse rate >= 57%
- H_1: Relapse rate <57%

When the upper bound of exact 2-sided Clopper-Pearson 95% CI for the relapse rate will be below the threshold of 57%, H_0 will be rejected.

3.2 Statistical Decision Rules

Not applicable.

3.3 Multiplicity Adjustment

Not applicable.

4.0 SAMPLE-SIZE DETERMINATION

- *Cohort 1 (CIDP)*

The latest meta-analysis (Lewis et al., 2020 [1]) reported that 43% of placebo-treated patients showed no deterioration in 5 placebo-controlled clinical studies, hence the estimated relapse rate in placebo-treated patients of 57%. The estimated relapse rate of Cohort 1 is 12% based on the average relapse rate in 2 clinical trials (13% in ICE study and 10% in the PATH extension study). As a result, the estimated sample size to show a statistically significant (at the 2.5% level) lower relapse rate than 57% with about 90% power would be 16 CIDP patients based on an assumed TAK-771 relapse rate of 12% and assuming a 15% dropout rate using a 95% two-sided Clopper-Pearson CI. This sample size was calculated based on simulation results from 100,000 trials.

- *Cohort 2 (MMN)*

The target number of MMN subjects was determined based on feasibility given the inclusion and exclusion criteria for this study. Multifocal motor neuropathy is less prevalent than CIDP. The annual number of MMN patients in Japan is estimated to be about 400 cases (Matsui, 2012 [2]). Five subjects are scheduled to be included in this study. Since this study is planned to be conducted in parallel with the clinical trial of maintenance therapy with CIDP patients, an effort would be made to recruit additional subjects until enrollment period of CIDP study ends, even if enrollment of 5 subjects is completed.

5.0 ANALYSIS SETS

- Enrolled Set: The Enrolled Set will consist of all subjects who signed the informed consent and not screen failed.
- Epoch 2 Entered Subjects: The Epoch 2 Entered Subjects will consist of all subjects who completed End-of-Epoch 1 visit and received the first TAK-771 administration in Epoch 2.
- *Full Analysis Set (FAS): All enrolled subjects who received TAK-771 at least once, this will be the efficacy analysis set.*

  Moreover, Epoch 2 Full Analysis Set contains subjects that meet the above criteria for Full Analysis Set in Epoch 2.
- *Safety analysis set: All enrolled subjects who received TAK-771 administration at least once, this will be the safety analysis set.*

  Moreover, Epoch 2 Safety Analysis Set contains subjects that meet the above criteria for Safety Analysis Set in Epoch 2.
- *Per Protocol Set (PPS): All enrolled subjects who received TAK-771 at least once, and had no major protocol deviations that may have a significant impact on the primary endpoint. Such protocol deviations will be determined prior to End of Epoch 1 through subject review meeting; PPS will be used for sensitivity and/or supportive analyses*

Although efficacy data will be assessed for CIDP and MMN independently, safety will be assessed as integrated data from CIDP and MMN subjects. Data for the 2 Epochs will be presented separately.

6.0 STATISTICAL ANALYSIS

6.1 General Considerations

Start of Epoch 1, End of Epoch 1/Start of Epoch 2 and End of Epoch 2 are defined as follows:

- Start of Epoch 1: Epoch 1 Week 1 (E1W1)
- End of Epoch 1/Start of Epoch 2 (6 months): End-of-Epoch 1 (EoE1) assessments are to be conducted on the day of the first infusion in the Epoch 2 (6 months). This will mark the subjects' completion of the Epoch 1.
- End of Epoch 2 (6 months): End-of-Epoch 2 (6 months) (Eo6M) assessments are to be conducted on the day of the first infusion in the Epoch 2 (continued). This will mark the subjects' completion of the Epoch 2 (6 months).
- Start of Epoch 2 (continued): It is the first infusion in the Epoch 2 (continued).
- End of Epoch 2 (continued): EoE2 (continued) will be the date of discontinuation of study at EoE2 (continued).

The start datetime of Epoch 1, Epoch 2 (6 months) and Epoch 2 (continued) will be the datetime of the first infusion (the earlier of rHuPH20 or 10% IGI) of each period.

Two formal interim data analysis and a final analysis are planned for this study. (Section 6.11)

In the second interim analysis, the analysis will be performed with data at time points up to the "Epoch 2 (6 months)", and the final analysis will include data after "Epoch 2 (continued)".

Baseline value is defined as the pre-SC treatment baseline visit value, if non-missing. If missing, then the Screening visit value will be used (if the screening visit value is non-missing). In other words, the latest available value before first SC treatment intake will be defined as baseline value.

For the lab results, baseline value is defined as the Epoch 1 Week1 (E1W1) visit value, if non-missing. If missing, then the Screening visit value will be used (if the screening visit value is non-missing).

For the serum IgG, baseline value is defined as the value collected at Baseline visit during Screening Period (according to Electronic Data Capture) even if this value is not the latest available value before first SC treatment intake.

All statistical analyses of relapse rates (primary and supplementary) will be analyzed using an exact 2-sided Clopper-Pearson 95% CI.

Unless otherwise specified, summaries of continuous variables (e.g., change from baseline) will display the following descriptive statistics: number of subjects (n), mean, median, standard deviation (SD), minimum, maximum. Means and medians and quartiles (if applicable) will be presented to 1 more decimal place than the recorded data. SDs will be presented to 2 more decimal places than the recorded data. BMI, averaged vital signs (e.g., diastolic/systolic blood pressure), and derived scores will be rounded to 1 decimal place for reporting.

Summaries of categorical and count variables will display the following: number of subjects (n), percentage (%) of subjects in the category, and number of outcomes/events/occurrences. Each summary containing a percentage will include a footnote stating the denominator that was used in calculating the percentage, unless the percentage is self-explanatory. Percentages will be presented to 1 more significant digit than the raw (actual) data. No percentages will be displayed if the number of subjects is 0.

Missing data due to the COVID-19 pandemic will not be handled any differently than missing data for other reasons.

6.1.1 Handling of Treatment Misallocations

Not applicable.

6.1.2 Analysis Approach for Continuous Variables

The corresponding analysis approach is described in Section 6.1.

6.1.3 Analysis Approach for Binary Variables

All statistical analyses of relapse rates (primary and supplementary) will be analyzed using an exact 2-sided Clopper-Pearson 95% CI.

6.1.4 Analysis Approach for Time-to-Event Variables

The corresponding analysis approach for "Time to discontinuation" is described in Section 6.2.

The corresponding analysis approach for "Time to relapse" is described in Section 6.6.2.

6.1.5 Study Information

Study Information will be presented and include the following categories:

- Date First Subject Signed Informed Consent Form
- Date of Data Cutoff
- MedDRA Dictionary Version
- WHO Drug Dictionary version
- SAS Version Used for Creating the Datasets

6.2 Disposition of Subjects

Epoch 1

Disposition summaries will be presented for overall and by cohort and will include, but are not limited to, number and percentage of subjects in the following categories, where applicable:

- Screened
- Screen failed
- Primary reason for screen failure
- Enrolled
- Received IP
- Completed Epoch 1
- Discontinued study prematurely during Epoch 1
- Primary reason for premature discontinuation during Epoch 1
- Completed Epoch 1 but not entered Epoch 2
- Primary reason for completed Epoch 1 but not entered Epoch 2
- Entered Epoch 2

Subjects who discontinued study prematurely in Epoch 1 is defined as subjects who discontinued study during Epoch 1 and did not enter Epoch 2.

Epoch 2

Disposition summaries will be presented for overall and by cohort and will include, but are not limited to, number and percentage of subjects in the following categories, where applicable:

- Entered Epoch 2
- Received IP in Epoch 2
- Completed Epoch 2 (6 months)
- Discontinued study prematurely during Epoch 2 (6 months)
- Primary reason for premature discontinuation in Epoch 2 (6 months)
- Entered Epoch 2 (continued)
- Discontinued study prematurely during Epoch 2 (continued)
- Primary reason for premature discontinuation in Epoch 2 (continued)
- Completed Epoch 2 (continued)
- Discontinued study prematurely during Epoch 2
- Primary reason for premature discontinuation in Epoch 2

The number of subjects by site will also be summarized for the Safety Analysis Set.

Subjects who discontinued study prematurely in Epoch 2 is defined as subjects who entered Epoch 2 and discontinued study prematurely. Subjects who received IP in Eo6M are defined as "Entered Epoch 2 (continued)".

Overall Discontinuation Rates will also be summarized for the Enrolled Set. An exact 2-sided Clopper-Pearson 95% CI will be used to show overall discontinuation rates. The following will be reported:

- number of subjects included in the analysis
- number (%) of subjects included in the analysis who discontinued
- estimated overall discontinuation rates and corresponding two-sided 95% CIs

Additionally, the following listings will be presented for each epoch:

- Disposition (Enrolled Set)
- Listing of all screen failures (i.e., subjects that have signed the informed consent, but did not pass screening)
- All subjects who prematurely discontinued the study will be listed for the Enrolled Set and the listing will include the primary reason for discontinuation. All AEs for subjects who prematurely discontinued will be presented.

As a further supplementary analysis, time to discontinuation for Epoch 1 and overall will be presented graphically. Time to discontinuation/completion will be calculated as:

- date of Epoch 1 discontinuation (the last assessment) /completion– date of initial dose of IP in Epoch 1 + 1 (for Epoch 1)

- date of discontinuation/completion from study (the last assessment) – date of initial dose of IP in Epoch 1 + 1 (for overall)

and all subjects will be counted as having the event (i.e. no subjects will be censored). The corresponding cumulative incidence (1-survival) function will be estimated using Kaplan-Meier curves, where the vertical axis will represent the cumulative risk of discontinuation and the number of subjects at-risk over time will be displayed.

6.2.1 Protocol deviations

Protocol deviations will be recorded in the IQVIA Clinical Trial Management System (CTMS) and will be classified as major or minor by the site staff, clinical research associate (CRA) and/or medical monitor. Such protocol deviations will be determined prior to database lock. Major/minor protocol deviations will be summarized by category, cohort and epoch for Safety Analysis Set. Protocol deviations will also be listed by subject and by site for the Safety Analysis Set.

Deviation categories will be included as part of the CTMS protocol deviations log and may include any of the following categories:

- Informed Consent Criteria
- Eligibility and Entry Criteria
- Concomitant Medication Criteria
- Laboratory Assessment Criteria
- Study Procedures Criteria
- Serious Adverse Event Criteria
- Randomization Criteria
- Visit Schedule Criteria
- Investigation Product (IP) Compliance
- Efficacy Criteria
- Administrative Criteria
- Source Document Criteria
- Regulatory or Ethics Approvals Criteria
- COVID-19
- Other Criteria

Additionally, for each epoch, a separate table and listing of protocol deviations related to the COVID-19 pandemic will be presented (Section 6.2.2). Protocol deviations which relate to the Epoch 1 Per-Protocol analysis set are described in Section 5.0.

6.2.2 COVID-19

A separate table and listing of protocol deviations related to the COVID-19 pandemic will be presented for each epoch. Missing data due to the COVID-19 pandemic will not be handled any differently than missing data for other reasons.

6.3 Demographic and Other Baseline Characteristics

6.3.1 Demographics and Baseline Characteristics

Descriptive summaries of demographic, baseline and screening characteristics will be presented separately for Epoch 1 and Epoch 2. Demographic and baseline characteristics will include age (years), age group (≤55, >55), sex, race and ethnicity. Characteristics at screening will include height (cm), weight (kg) and body mass index (kg/m^2). Demographic, baseline and screening characteristic summaries will be presented for the following analysis sets / epoch:

Epoch 1

- FAS

overall and by cohort, in addition to:

- Screen failures

Epoch 2

- FAS

overall and by cohort.

Listings of the demographic, baseline and screening characteristics will be provided for Enrolled Set.

6.3.2 Medical History

Subject medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA, version 24.0 or higher). Medical history is captured on the "MEDICAL HISTORY" eCRF form.

The number of subjects with any relevant past and current medical conditions/diseases will be tabulated by MedDRA system organ class (SOC) and preferred term (PT) for the Safety Analysis Set by each cohort. A subject will only be counted once within a particular SOC (or PT) even if he/she has multiple conditions/diseases in the same SOC (or PT). Presentation by SOC and PT will present SOC sorted alphabetically and PT within SOC by descending frequency.

Listings of medical history will be provided using the Safety Analysis Set.

6.3.3 CIDP history

Descriptive summaries of CIDP history at screening will be presented using the Safety Analysis Sets. This summary will include time since first CIDP symptoms (years), time since CIDP diagnosis (years), subject age at first diagnosis of CIDP.

Time Since First Symptoms will be calculated as follows:

Time Since First Symptoms (years) = ("Date of Informed Consent" – "Date of First Symptoms") / 365.25.

Time Since Diagnosis will be calculated as follows:

Time Since Diagnosis (years) = ("Date of Informed Consent" – "Date of Diagnosis") / 365.25.

Subject Age at First Diagnosis of CIDP will be calculated as follows:

Subject Age at First Diagnosis of CIDP (years) = ("Date of Diagnosis" – "Date of Birth") / 365.25.

Listings of CIDP history will be presented using the Safety Analysis Sets.

6.3.4 MMN history

Descriptive summaries of MMN history at screening will be presented using the Safety Analysis Sets. This summary will include time since first MMN symptoms (years), time since MMN diagnosis (years), subject age at first diagnosis of MMN.

Time Since First Symptoms will be calculated as follows:

Time Since First Symptoms (years) = ("Date of Informed Consent" – "Date of First Symptoms") / 365.25.

Time Since Diagnosis will be calculated as follows:

Time Since Diagnosis (years) = ("Date of Informed Consent" – "Date of Diagnosis") / 365.25.

Subject Age at First Diagnosis of MMN will be calculated as follows:

Subject Age at First Diagnosis of MMN (years) = ("Date of Diagnosis" – "Date of Birth") / 365.25.

Listings of MMN history will be presented using the Safety Analysis Sets.

6.4 Medication History and Concomitant Medications

Medication History and Concomitant Medications are captured on the "MEDICAL HISTORY", "MEDICATION HISTORY (IVIG)" and "CONCOMITANT MEDICATIONS" eCRF form.

Medication history and concomitant medications will be coded using the World Health Organization-Drug Dictionary (WHO-DD, Version 01MAR2021 or later).

For data presentation purposes, prior and concomitant medications are defined as follows ('time' implies date and time):

- Prior medication

  Any medication with start time prior to time of Epoch 1 IP administration.

- Concomitant medication

  Any medication with start time at or after time of Epoch 1 IP administration, OR medications with start time prior to Epoch 1 IP administration but continuing at or after Epoch 1 IP administration.

Note that medications with start time prior to time of Epoch 1 IP administration and stop time after time of Epoch 1 IP administration will be counted as both prior and concomitant medications.

For medications with partial onset times, non-missing date parts will be used to determine if the medication is a concomitant or prior medication (see Section 9.1.7). If a determination cannot be made using the non-missing date parts as to when the medication occurred relative to the date of IP administration, then the medication will be classified as concomitant medication.

6.4.1 Prior Medications

Prior medications will be provided in subject data listing only using the Safety Analysis Set.

6.4.2 Concomitant Medications

Listings of concomitant medications will be presented using the Safety Analysis Set.

6.5 Prior/Concomitant Surgeries and Procedures

Prior/Concomitant Surgeries and Procedures (simply referred to as procedures) are captured on the "PRIOR SURGERY/PROCEDURE", "CONCOMITANT PROCEDURES" eCRF form.

For data presentation purposes, prior and concomitant procedures are defined as follows ('time' implies date and time):

- Prior procedure

  Any procedures with start time prior to time of Epoch 1 IP administration.

- Concomitant procedure

  Any procedures with start time at or after time of Epoch 1 IP administration, OR procedures with start time prior to Epoch 1 IP administration but continuing at or after Epoch 1 IP administration.

Note that procedures with start time prior to time of Epoch 1 IP administration and stop time after time of Epoch 1 IP administration will be counted as both prior and concomitant procedures.

For procedures with partial onset times, non-missing date parts will be used to determine if the procedure is a concomitant or prior procedure (see Section 9.1.7). If a determination cannot be made using the non-missing date parts as to when the procedure occurred relative to the date of IP administration, then the procedure will be classified as concomitant procedure.

6.5.1 Prior Procedures

Prior procedures will be provided in subject data listing only using the Safety Analysis Set.

6.5.2 Concomitant Procedures

Concomitant procedures will be provided in subject data listing only using the Safety Analysis Set.

6.6 Efficacy Analysis

6.6.1 Primary Endpoints Analysis

The following analyses will be performed in Epoch 1. The same analyses as in Epoch1 will also be performed in Epoch 2 as an exploratory analysis.

Cohort 1 (CIDP)

The primary analysis for Cohort 1 is based on occurrence of relapse (worsening of functional disability defined as an increase of ≥1 point relative to the pre-SC treatment baseline score in adjusted INCAT disability score).

An exact 2-sided Clopper-Pearson 95% CI will be used to show relapse rates, with missing outcomes imputed as no relapse. The following will be reported:

- number of subjects included in the analysis
- number (%) of subjects included in the analysis who relapsed
- estimated relapse rates and corresponding two-sided 95% CIs

The efficacy would be shown in the case that the upper bound of 95% CI for the relapse rate would be below the threshold of 57%.

Cohort 2 (MMN)

The change from baseline in maximum grip strength will be presented for more affected hand using descriptive statistics and 2-sided 95% CI based on the FAS.

6.6.1.1 Derivation of Endpoints

Cohort 1 (CIDP)

A relapse is defined as a worsening of functional disability such that there is an increase of ≥ 1 point relative to the pre-SC treatment baseline visit score in adjusted INCAT disability scores. For the primary analysis missing outcomes will be imputed as no relapse.

Adjusted INCAT disability scores are defined as follows:

Identical to INCAT score (using 10-point scale) except: INCAT upper extremity score that changed from 0 to 1 or from 1 to 0 will not be incorporated into overall INCAT score as it is not considered clinically meaningful.

The following adjusted scores are to be followed:

- An arm grade = 0 at pre-SC treatment baseline changing to arm grade = 1 at week z: adjusted scores at week z should be 0
- An arm grade = 1 at pre-SC treatment baseline changing to an arm grade = 0 at week x: adjusted scores at week x should be 1

At any time during the SC treatment period, unscheduled visit(s) may take place for a subject whose CIDP is worsening to assess whether the subject has an increase in the adjusted INCAT disability score by ≥ 1 point relative to the pre-SC treatment baseline score. INCAT assessment will be repeated during the pre-SC treatment baseline visit or early termination visit, as applicable, to confirm the subject's adjusted INCAT disability score has increased by ≥ 1 point relative to the pre-SC treatment baseline score, at which time the final determination of whether a subject has met relapse criteria will be made.

In the second interim analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2) will be used to analyze the relapse in Epoch 2.

In the final analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2 and Epoch 2 continued) will be used to analyze the relapse in Epoch 2.

Cohort 2 (MMN)

Maximum grip strength is defined as the maximum of 3 measurements for grip strength in the more affected hand at each visit.

If a subject has no available post-dose data, that subject will be excluded from the analysis.

In the second interim analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2) will be used to analyze the maximum grip strength in Epoch 2.

In the final analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2 and Epoch 2 continued) will be used to analyze the maximum grip strength in Epoch 2.

6.6.1.2 Sensitivity Analysis

Not applicable.

6.6.1.3 Supplementary Analysis

The following supplementary analyses will be performed in Epoch 1.

Cohort 1 (CIDP)

1. Changing the missing outcomes imputed as relapse.
2. Changing the strategy to address intercurrent events for the primary estimand from while on treatment to Principal stratum strategy where the stratum is restricted to subjects who did not have an intercurrent event.

3. Changing the population for the primary estimand from FAS to PPS.
4. Changing the strategy to address intercurrent events for the primary estimand from while on treatment to Composite variable strategy where all subjects are treated as "Relapse" subjects except those who have no intercurrent events and are identified to be "No Relapse" at End of Epoch 1.

As for the primary analysis, an exact 2-sided Clopper-Pearson 95% CI will be used to show relapse rates for these supplementary analyses.

Cohort 2 (MMN)

Not applicable.

6.6.2 Secondary Endpoints Analysis

All secondary endpoints analyses will be based on the FAS population. The following analyses will be performed in Epoch 1. Analysis of time to relapse will also be performed for Epoch 2. The same analyses as in Epoch1 will also be performed in Epoch 2 as an exploratory analysis.

Cohort 1 (CIDP)

1. Clinical worsening of CIDP

Clinical worsening of CIDP is defined as ≥8 kPa decrease in the hand grip strength in the more affected hand OR ≥4 points decrease in R-ODS relative to the pre-SC treatment baseline score at 2 consecutive time points (at the time of withdrawal from the SC treatment period). If 2 consecutive time points are across the different Epoch, it will be considered worsened in Epoch 1. This endpoint will be analyzed using an exact 2-sided Clopper-Pearson 95% CI, as described for the primary analysis (Section 6.6.1), with no imputation of missing values.

Additionally, the number and percentage of subjects meeting each component of worsening will be presented. A listing for worsening of functional disability will be presented for the FAS population. This Listing also displays the percentile-converted values according to the table 10 in Section 9.3.

Also perform the same analysis as above, with the following changes to the definition of Clinical worsening of CIDP.

> Modified definition: Clinical worsening of CIDP is defined as ≥8 kPa decrease in the hand grip strength in the more affected hand OR ≥4 points decrease in R-ODS relative to the pre-SC treatment baseline score at 2 consecutive time points (at the time of withdrawal from the SC treatment period). If the final time point data corresponds to *"≥8 kPa decrease in the hand grip strength in the more affected hand OR ≥4 points decrease in R-ODS relative to the pre-SC treatment baseline score "*, also treat it as Clinical worsening of CIDP.

2. Time to relapse

Time to relapse is defined as time from the date of the first SC administration of TAK-771 to the date of relapse (where relapse is defined as in Section 6.6.1.1). For subjects who relapsed in Epoch 1, time to relapse will be calculated as:

date of relapse – date of initial dose of IP in Epoch 1 + 1.

Subjects who did not relapse in Epoch 1 will be censored with time to censoring calculated as:

date of Epoch 1 discontinuation/completion – date of initial dose of IP in Epoch 1 + 1.

In the analysis through Epoch1 and Epoch2, time to relapse will be calculated as:

date of relapse – date of initial dose of IP in Epoch 1 + 1.

Subjects who did not relapse in Epoch 1 and Epoch 2 will be censored with time to censoring calculated as:

In the second interim analysis: date of discontinuation/completion of Epoch 2 (The first 6 months of Epoch 2) – date of initial dose of IP in Epoch 1 + 1.

In the final analysis: last date of discontinuation/completion of Epoch 2 (The first 6 months of Epoch 2 or Epoch 2 continued) – date of initial dose of IP in Epoch 1 + 1.

The statistics presented will include but are not limited to:

- number of subjects included in the analysis
- number of subjects with event
- number of subjects censored
- percentiles (25th, 50th and 75th, if calculable), minimum and maximum for the cumulative incidence (1-survival) function, estimated using the Kaplan-Meier method

Additionally, the cumulative incidence (1-survival) function will be estimated using Kaplan-Meier curves, where the vertical axis will represent the cumulative risk of experiencing a relapse and the number of subjects at-risk over time will be displayed.

3. Change from pre-SC treatment baseline in R-ODS

The mean change in R-ODS score, activities of daily living (ADL), from pre-SC treatment baseline will be analyzed using descriptive statistics and 2-sided 95% CI (baseline is defined in Section 6.1). The last non-missing change will be used for subjects who discontinued early. Subjects without post-baseline R-ODS data will not be included in the analysis.

Descriptive statistics (n, mean, median, SD, 1st quartile(Q1), 3rd quartile(Q3), minimum, maximum) will be presented for R-ODS and change from pre-SC treatment baseline for each visit. Additionally, the statistics reported will include but are not limited to:

- estimated change from baseline and two-sided 95% CIs

An additional plot of mean change from pre-SC treatment baseline of R-ODS by timepoint will be presented for all timepoints (weeks), using the FAS population. A listing for R-ODS score and derived endpoints will also be presented for the FAS population.

The same analyses as in Epoch1 will also be performed in Epoch 2 as an exploratory analysis.

In the second interim analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2) will be used to analyze the R-ODS in Epoch 2.

In the final analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2 and Epoch 2 continued) will be used to analyze the R-ODS in Epoch 2.

4. Change from pre-SC treatment baseline in an average of handgrip strength of both hands

The secondary endpoints associated to Cohort 1 (CIDP), change from pre-SC treatment baseline in an average of handgrip strength of both hands, will be analyzed according to the methods for the primary endpoint for Cohort 2 (MMN) (defined in Section 6.6.1).

Average of grip strength is defined as an average of the two maximum values: maximum of the 3 measurements in the more affected hand and the maximum of the 3 measurements in the less affected hand at each visit.

The same analyses as in Epoch1 will also be performed in Epoch 2 as an exploratory analysis.

In the second interim analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2) will be used to analyze the average of handgrip strength of both hands in Epoch 2.

In the final analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2 and Epoch 2 continued) will be used to analyze the average of handgrip strength of both hands in Epoch 2.

5. Change from pre-SC treatment baseline in adjusted INCAT disability score

The exploratory analyses associated to Cohort 1 (CIDP), change from pre-SC treatment baseline in adjusted INCAT disability score, will be analyzed according to the methods for the primary secondary endpoint for Cohort 2 (MMN) (defined in Section 6.6.1). Subjects without post-baseline adjusted INCAT disability score data will not be included in the analysis.

Descriptive statistics (n, mean, median, SD, Q1, Q3, minimum, maximum) will be presented for adjusted INCAT disability score and change from pre-SC treatment baseline for each visit. Additionally, the statistics reported will include but are not limited to:

- estimated change from baseline and two-sided 95% CIs

An additional plot of mean change from pre-SC treatment baseline of adjusted INCAT disability score by timepoint will be presented for all timepoints (weeks), using the FAS population. A listing for adjusted INCAT disability score will also be presented for the FAS population.

The same analyses as in Epoch1 will also be performed in Epoch 2 as an exploratory analysis.

In the second interim analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2) will be used to analyze the adjusted INCAT disability score in Epoch 2.

In the final analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2 and Epoch 2 continued) will be used to analyze the adjusted INCAT disability score in Epoch 2.

Cohort 2 (MMN)

6. GNDS in upper limb and lower limb categories

The secondary endpoints associated to Cohort 2 (MMN), GNDS in upper limb and lower limb categories, will be descriptively analyzed as a binary variable indicating whether the score of a subject increased from baseline to the value at each post baseline, with no imputation of missing values. The following will be reported:

- number of subjects and number (%) of subjects with increased score from baseline in upper limb or lower limb categories

The same analyses as in Epoch1 will also be performed in Epoch 2 as an exploratory analysis.

In the second interim analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2) will be used to analyze the GNDS in upper limb and lower limb categories in Epoch 2.

In the final analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2 and Epoch 2 continued) will be used to analyze the GNDS in upper limb and lower limb categories in Epoch 2.

7. Change from pre-SC treatment baseline in MRC sum score

The secondary endpoints associated to Cohort 2 (MMN), change from pre-SC treatment baseline in MRC sum score will also be analyzed according to the methods for the primary endpoint for Cohort 2 (MMN) (defined in Section 6.6.1).

An additional plot of mean change from pre-SC treatment baseline of MRC sum score by timepoint will be presented for all timepoints (weeks), using the FAS population. A listing for MRC sum score will also be presented for the FAS population.

The same analyses as in Epoch1 will also be performed in Epoch 2 as an exploratory analysis.

In the second interim analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2) will be used to analyze the GNDS in upper limb and lower limb categories in Epoch 2.

In the final analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2 and Epoch 2 continued) will be used to analyze the GNDS in upper limb and lower limb categories in Epoch 2.

8. Change from pre-SC treatment baseline in an average of handgrip strength of both hands

The secondary endpoints associated to Cohort 2 (MMN), change from pre-SC treatment baseline in an average of handgrip strength of both hands, will be analyzed according to the methods for the primary endpoint for Cohort 2 (MMN) (defined in Section 6.6.1).

Average of grip strength of both hands is defined as an average of the two maximum values: maximum of the 3 measurements in the more affected hand and the maximum of the 3 measurements in the less affected hand at each visit.

The same analyses as in Epoch1 will also be performed in Epoch 2 as an exploratory analysis.

In the second interim analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2) will be used to analyze the average of handgrip strength of both hands in Epoch 2.

In the final analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2 and Epoch 2 continued) will be used to analyze the average of handgrip strength of both hands in Epoch 2.

9. Change from pre-SC treatment baseline in GNDS

The secondary endpoints associated to Cohort 2 (MMN), change from pre-SC treatment baseline in GNDS, will be analyzed according to the methods for the primary endpoint for Cohort 2 (MMN)(defined in Section 6.6.1).

An additional plot of mean change from pre-SC treatment baseline of GNDS by timepoint will be presented for all timepoints (weeks), using the FAS population. A listing for GNDS score will also be presented for the FAS population.

The same analyses as in Epoch1 will also be performed in Epoch 2 as an exploratory analysis.

In the second interim analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2) will be used to analyze the GNDS in Epoch 2.

In the final analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2 and Epoch 2 continued) will be used to analyze the GNDS in Epoch 2.

6.6.2.1 Sensitivity Analysis

Not applicable.

6.6.2.2 Supplementary analysis

Not applicable.

6.6.3 Tertiary Endpoints Analysis

1. Serum trough levels of total IgG

Values below the lower limit of quantitation (LLOQ) will be considered as zero for descriptive statistics of serum trough concentrations of IgG. LLOQ for total serum trough levels of IgG is 1.72 g/L.

Epoch 1

Analyses of serum trough concentrations of IgG will include subjects in the Epoch 1 Safety Analysis Set by cohort and overall. Serum trough concentrations of IgG will be summarized

using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, maximum, geometric mean, Coefficient of Variation (CV) of the geometric mean) and 2-sided 95% CI for mean and geometric mean by timepoints and each visit. Also, change from baseline will be tabulated. Plots of individual serum trough concentrations of IgG will be presented.

In addition, the relationship between serum IgG trough levels after day 120 (every 2-week dosing Epoch 1 W27/EoE1; every 3-week dosing Epoch 1 W26/EoE1, every 4-week dosing Epoch 1 W28/EoE1) or at the time of relapse status (relapse, no relapse for CIDP)/worsening status (MMN has been judged as being worsened by Investigator) will be assessed as an exploratory analysis. Serum trough concentrations of IgG will be summarized by relapse status (for CIDP)/ worsening status (MMN has been judged as being worsened by Investigator) and using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, maximum, geometric mean, CV of the geometric mean). Also, change from baseline will be tabulated. MMN worsening is defined as "Lack of Efficacy" or "Progressive Disease" of primary reason off study treatment. For subjects who relapsed/worsened in Epoch 1, the first recorded IgG level after relapse/worsen was selected for this analysis. For subjects who did not relapse/worsen in Epoch 1, the last recorded IgG level on treatment during Epoch 1 was selected for this analysis. For subjects who did not relapse/worsen and who had no IgG results after Day 120 are not included.

Epoch 2

Analyses of serum trough concentrations of IgG for Epoch 2 will be presented for the Epoch 2 Safety Analysis Set by cohort and overall. Serum trough concentrations of IgG will be summarized using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum, maximum, geometric mean, CV of the geometric mean) and 2-sided 95% CI for mean and geometric mean by timepoints and each visit. Also, change from baseline will be tabulated. Plots of individual serum trough concentrations of IgG will be presented.

In the second interim analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2) will be used to analyze the serum trough concentrations of IgG in Epoch 2.

In the final analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2 and Epoch 2 continued) will be used to analyze the serum trough concentrations of IgG in Epoch 2.

2. Number of subjects received the study drug through self-administration.

Number and percentage of subjects received the study drug through self-administration will be summarized by cohort and epoch for Safety Analysis Set.

For calculating number of subjects received the study drug, number of subjects received the 10% IGI will be used.

Subjects received the study drug through self-administration will also be listed for the Safety Analysis Set.

In the second interim analysis, the data in Epoch 2 (The first 6 months of Epoch 2) will be used to analyze the study drug through self-administration in Epoch 2.

In the final analysis, the pre-SC treatment baseline data and the data in Epoch 2 (The first 6 months of Epoch 2 and Epoch 2 continued) will be used to analyze the study drug through self-administration in Epoch 2.

6.7 Safety Analysis

Safety analyses will be mainly presented by cohort, Epoch and overall. Analyses for clinical laboratory evaluations and vital signs will be presented by cohort and visit. Continuous data (e.g., change from baseline in a lab parameter) will be summarized using the following descriptive statistics: number of subjects (n), mean, median, SD, minimum value, maximum value.

Categorical data (e.g., occurrence of AE) will be summarized in terms of number and percentage of subjects in the category, and, where applicable, number of outcomes/events/occurrences in the category.

For analysis of "adverse events", "adverse events of special interest" and "extent of exposure and compliance", the following data will be used.

In the second interim analysis, the data in Epoch 2 (The first 6 months of Epoch 2) will be used to analyze the safety analysis in Epoch 2.

In the final analysis, the data in Epoch 2 (The first 6 months of Epoch 2 and Epoch 2 continued) will be used to analyze the safety analysis in Epoch 2.

6.7.1 Adverse Events

All AEs will be coded using MedDRA (version 24.0 or higher) and then reported by MedDRA SOC and PT, and overall. Only TEAEs will be analyzed. Non-TEAEs will be listed only.

TEAEs are defined as adverse events that occurred during or after administration of the first dose of IP. TEAEs caused in Epoch 1 are defined as AEs that occurs on or after the start of study drug administration, and before the first dose of IP in Epoch 2. TEAEs caused in Epoch 2 are defined as AEs that began during or after administration of the first dose of IP in Epoch 2.

IP-related TEAE: Any TEAE that is recorded by the investigator as "Related" to IP will be considered IP-related AE, and any AE recorded as "Not Related" will be considered unrelated AE.

TEAEs temporally associated with infusion: These are defined as AEs occurring during or within 72 hours after completion of an infusion.

Any treatment-emergent adverse events which are answered "Yes" to Infusion-Related Reaction Flag is counted as an infusion associated TEAEs.

ARs/Suspected ARs: Adverse reactions (AR) plus suspected ARs are defined as TEAEs that are considered by the investigator to be related to IP administration, or for which the causality is indeterminate or missing, or that begins during infusion of IP or within 72 hours following the end of IP infusion.

For action taken with study treatment by TEAE, both action taken with rHuPH20 and action taken with 10% IGI are collected. If "Drug Withdrawn" is selected in either rHuPH20 or 10% IGI, then the TEAE will be treated as "TEAEs leading to prematurely discontinuation".

Any TEAE with the MedDRA High-Level Group Term (HLGT) = "Administration site reactions" will be considered a local TEAE. In addition, any TEAE with Injection Site Reaction Flag = "Yes" will be considered a local TEAE. All other TEAE's will be considered a systemic AE.

The following summaries will be provided (no statistical hypothesis testing is planned):

- Number and percentage of subjects with TEAEs by SOC and PT, and overall
- Number of TEAEs: SOC and PT, and overall

The following approaches will be used, where applicable:

- Overall summary: Any TEAE, TEAE related to IP, severe TEAE, severe TEAE related to IP, serious TEAE, serious TEAE related to IP, TEAE leading to early discontinuation, TEAE leading to death, TEAE temporally associated with infusion, infusion associated TEAE, local TEAE, systemic TEAE and ARs/Suspected ARs
  - Summaries by SOC and PT: In the summaries, SOC will be sorted alphabetically, and PT will be sorted within each SOC in descending frequency in the Total column (i.e., the Total column will be sorted in descending order after the sorting by SOC and PT)
  - Summaries by Maximum Severity: Subjects with multiple events in the same category are counted only once in that category, using the event with the greatest severity. Subjects with events in more than one category are counted once in each of those categories
  - If more than 1 TEAE occurs within the same PT for the same subject, then the subject will be counted only once for that PT using the most severe and most related occurrence for the summarization by severity and by relationship to IP. For example, if a subject experienced a mild headache not related to the IP, and a moderate headache related to IP, then the subject will be counted once for headache using the moderate headache related to IP
  - In AE incidence summaries, subjects with multiple events in the same category will be counted only once in the AE category. Subjects with events in more than one category will be counted once in each of the categories
  - In AE count summaries, multiple occurrences of the same AE will be counted multiple times
  - Note that, in addition to standard AE listings, the following subject data listing will be provided per regulatory request: Subjects who prematurely discontinued from the study, and all their treatment-emergent adverse events. The listing will be based on the Enrolled Set and display demographics, first and last dose dates (if known),

withdrawal date, duration in study, primary reason for premature withdrawal, and adverse data

6.7.1.1 Descriptive Analysis of Adverse Events per Infusion, per Subject, per Subject-Year

The following summaries will be provided for Epoch 1 and overall (no statistical hypothesis testing is planned):

- Number of TEAEs per infusion, by SOC and PT
- Number of TEAEs per subject, by SOC and PT
- Number of TEAEs per 1000 subject-years, by SOC and PT

AEs per 1000 subject-years summary adjusts for differences in subjects' durations in the study and differential dropout rates between treatment groups.

For number of AEs, multiple occurrences of the same AE in the same subject will be counted multiple times.

Number of AEs and AEs per 1000 subject-years (SYs) will be provided for all AEs (if analyzable), by SOC and PT.

The following calculations apply, where applicable:

- AEs per infusion = number of AEs / total number of infusions administered of 10% IGI to subjects in the analysis set
- AE per subject = number of AEs / total number of subjects in the analysis set
- AEs per 1000 SYs in Epoch 1 = 1000 × (Total Number of AEs in Epoch 1 for all subjects / Total SYs in Epoch 1)
- Total SYs in Epoch will be calculated by summing subjects' durations in Epoch through the end of Epoch. Each subject's duration will be calculated as: (last date of Epoch – date of initial dose of IP in the Epoch + 1) / 365.25. If the subject's last date in the Epoch is missing, then the date of last dose of IP will be used if available

The following AEs will be summarized per infusion, subject, and subject year:

- Any TEAE
- Serious TEAEs
- IP-Related TEAEs
- IP-Related Serious/Non-Serious TEAEs
- TEAEs temporally associated with infusion
- Local/Systemic TEAEs
- IP-Related Local/Systemic TEAEs
- IP-Related Serious Local/Systemic TEAEs

- TEAEs That Occurred During or Within 72 Hours Post-Infusion
- ARs/Suspected ARs
- ARs/Suspected ARs temporally associated with infusion

6.7.2 Adverse Events of Special Interest

AEs of special interest will be coded using the MedDRA (version 24.0 or higher) and then reported by MedDRA PT, and overall.

Adverse events of special interest (source: Section 9.1.9.10 of the study protocol) include the followings (see Section 9.2 for details of definitions):

- Allergic reactions
  - Urticaria
  - New-onset bronchospasm
  - Oedema of tongue, lips, face (angioedema)
  - Anaphylaxis
  - Stevens-Johnson syndrome
  - Erythema multiforme
  - Toxic epidermal necrolysis
- Immune complex mediated reactions – Local
  - Induration/nodule at the site of administration that persists for more than 48 hours
  - Excessive inflammation at the site of administration - severe redness, heat, swelling, and/or pain
  - Tissue necrosis/ulceration at the site of administration
  - Dystrophic or fibrotic changes at the site of administration
  - Pigmented skin changes at the site of drug administration
- Immune complex mediated reactions – Systemic
  - Arthritis
  - Vasculitis (purpuric rash)
  - Glomerulonephritis - hematuria, red cell casts in urine, progressive renal dysfunction
- Thrombotic and Embolic Events
  - Arterial (Embolic and thrombotic events, arterial – 20000082 (SMQ))

- Venous (Embolic and thrombotic events, venous – 20000084 (SMQ))
- Vessel unspecified/unknown (Embolic and thrombotic events, vessel type unspecified and mixed arterial and venous - 20000083 (SMQ)).

The following special interest AEs will be summarized:

- Any TEAE of special interest
- TEAEs of special interest by Antibody Status (subject having elevated anti-rHuPH20 antibody titers or not).

6.7.3 Clinical Laboratory Evaluations

Clinical laboratories are not explicitly stated in the study protocol as endpoints but are included in this SAP for further assessment of the safety profile. Raw (actual) clinical laboratory values (in SI units) and changes in raw values from baseline at each post-baseline assessment time point will be summarized as continuous variables. Shift from baseline to each assessment time point will be provided for categorical variables. Results will be tabulated. The following laboratory variables/parameters will be summarized, and the data will be listed in the subject data listing, as indicated. Other than following Lab parameters will be listed only.

Hematology	The hematology panel will consist of hemoglobin, hematocrit, erythrocytes (i.e., red blood cell count), and leukocytes (i.e., [WBC]) with differential (i.e., basophils, eosinophils, lymphocytes, monocytes, neutrophils) and platelet counts, as well as absolute neutrophil count.	Summary and Listing
Clinical Chemistry	The clinical chemistry panel will consist of sodium, potassium, chloride, bicarbonate, protein, albumin, ALT, serum total bilirubin, AST, ALP, LDH, BUN, serum creatinine, creatinine phosphokinase, glucose, haptoglobin, and lipase.	Summary and Listing
Hemolytic Panel	The hemolytic panel includes Hgb, LDH, serum haptoglobin, plasma-free (unbound) Hgb, serum direct anti-globulin (direct Coombs) test, reticulocyte count, and urine hemosiderin.	Listing only
Hemoglobin A1C	HbA1c	Listing only
Serum Iron, Ferritin, and Total Iron Binding Capacity (TIBC)	Serum iron, ferritin, and TIBC	Listing only
Urinalysis	Color, specific gravity, pH, protein, glucose, ketones, bilirubin, urobilinogen, blood, nitrite, and leukocyte esterase and a microscopic examination	Listing only
Pregnancy Test	Pregnancy tests for female subjects of childbearing potential	Listing only

Summaries of shift from baseline (shift tables) will be produced for each parameter that has a reference range, using the categories: low (below the lower limit of the reference range), normal (within the reference range) and high (above the upper limit of the reference range).

In addition, shift from baseline summaries will be produced by toxicity Grade. Summaries will display number and percent of subjects whose laboratory values were assessed as Grade < 3, Grade 3, Grade 4, or missing at the pre-SC baseline, and at the post-baseline maximum Grade.

Laboratory parameters will be summarized tabularly and/or graphically using spaghetti-plots or scatterplots as follows: spaghetti-plots of clinical chemistry values by parameter and visit; scatterplots of ALT, AST, and bilirubin post-baseline versus baseline comparisons to normal range limits by parameter and visit; spaghetti-plots of hematology values by parameter and visit.

The following will be provided in subject data listings.

- Hematology values for subjects who met toxicity Grade ≥ 3 criteria for any hematology parameter
- Clinical Chemistry values for subjects who met toxicity Grade ≥ 3 criteria for any clinical chemistry parameter
- Hemolytic parameters panel for subjects who showed a reduction in Hgb level of 1g/dL or more at any time after the first full dose of IP treatment during the epoch

6.7.4 Vital Signs

Vital signs endpoints are not explicitly mentioned in the study protocol as endpoints but are included in this SAP to further assess the safety. Raw (actual) values for vital signs and their changes from baseline at each post-baseline assessment time point will be summarized by visit. Vital signs will also be summarized both graphically (spaghetti-plots).

A vital sign value will be considered potentially clinically significant (PCS) if it meets both the observed value criteria and the change from baseline criteria listed in Table 2. Number and percentage of subjects with PCS post-baseline values will be tabulated. Percentages will be calculated relative to the number of subjects with baseline and at least 1 post-baseline assessment. The numerator is the total number of subjects with at least 1 PCS post-baseline vital sign value in the specified period.

Table 2 Criteria for Potentially Clinically Significant Vital Signs

Vital Sign Parameter	Flag	Criteria [a]	
		Observed Post-Baseline Value	Change from Baseline
Systolic blood pressure (mmHg)	High	≥ 180	Increase of ≥ 20
	Low	≤ 90	Decrease of ≥ 20
Diastolic blood pressure (mmHg)	High	≥ 105	Increase of ≥ 15
	Low	≤ 50	Decrease of ≥ 15
Pulse rate (beats per minute)	High	≥ 120	Increase of ≥ 15
	Low	≤ 50	Decrease of ≥ 15

Weight (kg)	High	-	Increase of ≥ 7%
	Low	-	Decrease of ≥ 7%

[a] A post-baseline value is considered as a PCS value if it meets both criteria for observed value and change from baseline.

6.7.5 ECG

Electrocardiogram (ECG) data (overall interpretation) will be provided in subject listing only. Note that clinically significant, treatment-emergent changes in ECGs will be recorded in the study database as AEs.

6.7.6 Clinically significant, treatment-emergent changes in physical exams

Clinically significant, treatment-emergent changes in physical exams data will be listed in the subject listing only. Note that clinically significant, treatment-emergent changes in physical exams will be recorded in the study database as AEs.

6.7.7 ADA Analysis

The immunogenicity endpoints corresponding to the immunology safety objective include:

- Anti-rHuPH20 antibody (binding and/or neutralizing antibodies to rHuPH20), specifically subjects with:
  - High-binding antibodies
  - Low-binding antibodies
  - Abnormal or increased anti-rHuPH20 antibody titer
  - Elevated anti-rHuPH20 antibodies
  - Neutralizing antibodies measured
  - Positive neutralizing antibodies
  - Negative neutralizing antibodies

"Anti-rHuPH20 antibody titer ≥ 1:160" means "Positive titers (≥ 1:160)" and is described as "High-binding antibodies". "Titer < 1:160" is described as "Low-binding antibodies".

High-binding antibodies at any time: Number of subjects who had at least one anti-rHuPH20 antibody titer ≥ 1:160 during treatment.

High-binding antibodies at specific visit: Number of subjects who had anti-rHuPH20 antibody titer ≥ 1:160 at the specific visit.

Low-binding antibodies at any time: Number of subjects with anti-rHuPH20 antibody titer < 1:160 for all data during treatment.

Low-binding antibodies at specific visit: Number of subjects who had anti-rHuPH20 antibody titer <1:160 at the specific visit.

A subject is defined as having (1) abnormal or (2) increased from baseline if the subject has (1) anti-rHuPH20 antibody titer of ≥ 1:160 or (2) if anti-rHuPH20 antibody titer is higher than the greater of ≥ 1:160 of the value at baseline.

A subject is defined as having elevated anti-rHuPH20 antibody titers if the subject has two consecutive anti-rHuPH20 antibody titers of ≥ 1:160 which are elevated from the subject's baseline titers.

Antibody titers may be reported as direct titers (positive integers) or as the inverse of the amount of diluent that is required to abolish a positive test result. Subjects who have two consecutive anti-rHuPH20 antibody titers of ≥ 1:160 which are elevated from the subject's baseline titers will be classified as experiencing treatment-emergent development of anti-rHuPH20 antibodies at the first of the two time points.

Anti-rHuPH20 antibody development will be summarized (number of subjects (n), percentage (%) of subjects by category: elevated, neutralizing antibody measured, positive neutralizing antibodies, negative neutralizing antibodies, high-binding, low binding) by visit.

All treatment-emergent AEs and related AEs in subjects with "anti-rHuPH20 antibody titers ≥ 1:160" will be presented in a subject data listing. For subjects with/without "≥ 1:160 or increased from baseline in anti-rHuPH20 antibody titer", with "elevated titers", and without "anti-rHuPH20 antibody titers ≥ 1:160", all treatment-emergent AEs will be presented.

Additionally, AEs experienced by each of the titer groups will be summarized:

- Subjects with positive anti-rHuPH20 antibody titers (≥ 1:160)
  - All AEs and related AEs reported before the first positive anti-rHuPH20 antibody titers (≥ 1:160) confirmation
  - All AEs and related AEs reported after the first positive anti-rHuPH20 antibody titers (≥ 1:160) confirmation
- Subjects with any treatment emergent abnormal titer (≥ 1:160) or increased from baseline in anti-rHuPH20 antibody titer
  - All AEs and related AEs reported before any ≥ 1:160 or increased from baseline
  - All AEs and related AEs reported after any ≥ 1:160 or increased from baseline
- AEs for subjects without any treatment emergent ≥ 1:160
- AEs for subjects with elevated titers.

For TEAEs and IP-related TEAEs in subjects with "anti-rHuPH20 antibody titers ≥ 1:160", summarizes by SOC and PT (see section 6.7.1) and per Infusion, per Subject, per Subject-Year (see section 6.7.1.1).

For TEAEs in subjects with "≥ 1:160 or increased from baseline in anti-rHuPH20 antibody titer", with "elevated titers", and without "anti-rHuPH20 antibody titers ≥ 1:160", summarizes by SOC and PT and per Infusion, per Subject, per Subject-Year.

If at least 5 subjects have elevated titers, then the descriptive analysis will be conducted to assess if there is any evidence of relationship between anti-rHuPH20 antibody titer (elevated, not elevated) and the occurrence of AEs of interest. The occurrence of AEs of interest will be summarized by anti-rHuPH20 antibody titer.

In addition, the analysis of any treatment emergent abnormal titer or increased from baseline in anti-rHuPH20 antibody titer will be performed to assess if there is any evidence of relationship between anti-rHuPH20 antibody titer (elevated, not elevated) and the occurrence of AEs.

Immunology related data after IP administration will also be listed.

6.7.8 Extent of Exposure and Compliance

Exposure to IP and compliance will be summarized separately for the Epoch 1 and Epoch 2 Safety Analysis Set. Each study drug (10% IGI, rHuPH20) will be summarized separately.

The following will be presented descriptively:

- number of infusions which were interrupted/stopped/dose reduced or rate reduced

- number of infusions excluding interrupted/stopped/dose reduced or rate reduced
- number of infusions for which the infusion rate was reduced and/or the infusion was interrupted or stopped and/or dose reduced due to intolerability and/or AEs
- treatment duration (months, as defined below).

Infusion compliance is calculated as the total number of applied infusions of each study drug (10% IGI, rHuPH20) including completed, interrupted, and stopped infusions, divided by the number of expected infusions, multiplied by 100. The number of expected infusions is based on the actual number of visits. Actual number of visits means the visit up to the data cut-off or end of treatment during the epoch.

Descriptive statistics (n, mean, SD, minimum, median, and maximum) or number of subjects and percentage, as applicable, will be presented by dosing regimen, cohort and overall.

Exposure is defined as the total duration of treatment with IP (in days), calculated as:

date of last dose of IP – date of initial dose of IP + 1.

For calculating duration of treatment with IP, date of dose of 10% IGI will be used.

Treatment duration will be summarized both as a continuous variable and using the following categories:

- <1 month
- 1 - <3 months
- 3 - <6 months
- 6 - <12 months
- 12 - <18 months
- 18 - <24 months
- ≥24 months
- ≥1 month
- ≥3 months
- ≥6 months
- ≥12 months
- ≥28 months
- ≥24 months

And Summary of IP Administration will be tabulated.

The following will be presented descriptively:

- Total Number of Infusions Administered

- Number of Infusion Sites on the Body Per Infusion (1, 2, 3)
- Actual Infusion Volume (mL)
- Maximum Infusion Rate/ Site (mL/hr)
- Study Treatment Administration Performed
  (Study Subject, Investigator/Study Physician, Study Nurse, Caregiver)

Additionally, monthly dose equivalent and duration of infusion per dose of 10% IGI will be presented in Epoch 1.

Full dose is defined as the dose that is achieved after ramp-up and occurs at Epoch 1 Week 3 (Every 2 Weeks Regimen), Epoch 1 Week 5 (Every 3 Weeks Regimen) and Epoch 1 Week 8 (Every 4 Weeks Regimen).

Number of subjects who remained on study to reach full dose. Monthly Dose Equivalent (g/month) is defined as: Full dose in mL * 1g/10mL / Dose Interval in weeks * 4.348125 weeks/month and is averaged per subject. Monthly Dose Equivalent (g/kg/month) is defined as: Full dose in mL * 1g/10mL / Subject's weight in kg at baseline / Dose Interval in weeks * 4.348125 weeks/month and is averaged per subject.

Duration of infusion(s) per dose will be calculated as the sum of each infusion time for study drug per dose.

Listings of IP exposure and compliance will be provided using the Safety Analysis Set.

6.8 Pharmacokinetic, Pharmacodynamic, and Biomarker Analyses

6.8.1 Pharmacokinetic Analysis

Analyses for trough serum IgG are described in Section 6.6.3. Additional analysis may be conducted and will be described in a separate pharmacokinetic/pharmacodynamic data analysis plan if applicable.

6.8.2 Pharmacodynamic Analysis

Not applicable.

6.8.3 Biomarker Analysis

Not applicable.

6.9 Patient Reported Outcomes (PROs) and Health Care Utilization Endpoints Analysis

6.9.1 PRO Analysis

Not applicable.

6.9.2 Health Care Utilization Analysis

Not applicable.

6.10 Other Analyses

1. Time to MMN worsening

Time to MMN worsening is defined as time from the date of the first SC administration of TAK-771 to the date of MMN worsening (where MMN worsening is defined as "Lack of Efficacy" or "Progressive Disease" of primary reason off study treatment). For subjects who worsened in Epoch 1, time to MMN worsening will be calculated as:

Date of treatment end – date of initial dose of IP in Epoch 1 + 1.

Subjects who did not worsening in Epoch 1 will be censored with time to censoring calculated as:

Date of Epoch 1 discontinuation/completion – date of initial dose of IP in Epoch 1 + 1.

In the analysis through Epoch1 and Epoch2, for subjects who worsened, time to worsening will be calculated as:

In the second interim analysis: Date of treatment end of Epoch 2 (The first 6 months of Epoch 2) – date of initial dose of IP in Epoch 1 + 1.

In the final analysis: Date of treatment end of Epoch 2 (The first 6 months of Epoch 2 or Epoch 2 continued) – date of initial dose of IP in Epoch 1 + 1.

Subjects who did not worsening in Epoch 1 and Epoch 2 will be censored with time to censoring calculated as:

In the second interim analysis: Date of discontinuation/completion of Epoch 2 (The first 6 months of Epoch 2) – date of initial dose of IP in Epoch 1 + 1.

In the final analysis: Last date of discontinuation/completion of Epoch 2 (The first 6 months of Epoch 2 or Epoch 2 continued) – date of initial dose of IP in Epoch 1 + 1.

The statistics presented will include but are not limited to:

- number of subjects included in the analysis
- number of subjects with event
- number of subjects censored
- percentiles (25th, 50th and 75th, if calculable), minimum and maximum for the cumulative incidence (1-survival) function, estimated using the Kaplan-Meier method

Additionally, the cumulative incidence (1-survival) function will be estimated using Kaplan-Meier curves, where the vertical axis will represent the cumulative risk of experiencing a worsening and the number of subjects at-risk over time will be displayed.

6.11 Interim Analyses

Two formal interim data analysis to support the Japanese New Drug Application submission will be completed. Both will summarize efficacy and safety of treatment with TAK-771 in Japanese subjects with CIDP/MMN. The first interim analysis will be conducted when the last subject has reached the End of Epoch 1 visit. The second interim analysis will be conducted when the last subject has reached the visit of Week 24 in Epoch 2. The first and the second interim clinical study reports summarizing data will be prepared based on these results of analyses. No adaptive design or data monitoring committee is planned for this study.

In the first interim analysis, the analysis will be performed with data at time points up to the End of Epoch 1. The data listing will include data after the End of Epoch 1.

In the second interim analysis, the analysis will be performed with data at time points up to the Week 24 in Epoch 2. The data listing will include data after the Week24 in Epoch 2.

In the final analysis, the analysis will be performed with all Epoch 2 data.

6.12 Data Monitoring Committee/Internal Review Committee/ [Other Data Review Committees]

No Data Monitoring Committee or Internal Review Committee is planned.

7.0 REFERENCES

[1] Lewis, R. A., Cornblath, D. R., Hartung, H. P., Sobue, G., Lawo, J. P., Mielke, O., Durn, B. L., Bril, V., Merkies, I. S. J., Bassett, P., Cleasby, A. & Schaik, I. N. 2020. Placebo effect in chronic inflammatory demyelinating polyneuropathy: The PATH study and a systematic review. *Journal of the Peripheral Nervous System*, 25, 230-237.

[2] Matsui, N. 2012. Multifocal motor neuropathy: current review of epidemiology and treatment. *Rinsho shinkeigaku = Clinical neurology*, 52, 920-2.

[3] van Nes, S. I., Vanhoutte, E. K., van Doorn, P. A., Hermans, M., Bakkers, M., Kuitwaard, K., Faber, C. G. & Merkies, I. S. J. 2011. Rasch-built Overall Disability Scale (R-ODS) for immune-mediated peripheral neuropathies. *Neurology,* 76, 337-345

8.0 CHANGES TO PROTOCOL PLANNED ANALYSES

Changes to protocol-specified analyses have been made in this SAP, as follows:

- Enrolled Set was added as analysis sets
- Clinical lab assessment and vital signs are added for safety analysis.
- All efficacy endpoints will be analyzed on Epoch 1 and Epoch 2. (except for the supplemental analysis)

9.0 APPENDIX

9.1 Data Handling Conventions

9.1.1 General Data Reporting Conventions

TFLs will follow Takeda standards, where applicable, except that footnotes will be printed at the bottom of every output page. IQVIA SOPs and work instructions will apply to all statistical programming, unless otherwise specified in this SAP or the corresponding TFL shells document. Listings will be sorted by cohort, and subject identification number, unless otherwise specified. Both derived and non-derived data, if available, will be displayed in listings.

9.1.2 Definition of Baseline

Definition of baseline is described in Section 6.1.

9.1.3 Definition of Visit Windows

For statistical analysis purposes, all efficacy assessments will be assigned to an analysis visit window. Unless otherwise specified for an analysis, the following will apply:

- Assessments will be assigned based on the date the assessment was performed regardless of the completed CRF page.
- Study day will be calculated as: date of assessment – date of first dose + 1. The date of the administration 10% IGI will be used as the date of first dose.
- If two or more assessments fall within the same visit window, then the assessment that is closest to the target study day will be used for analysis. If two or more assessments are equidistant from a planned target study day, then the most recent assessment will be used for analysis.
- If there is no assessment within a visit window, then the assessment for that planned study visit will be a considered as missing.

Analysis visit windows are presented for:

- Epoch 1 Efficacy assessments:
  - 2-week regimen (Table 3)
  - 3-week regimen (Table 4)
  - 4-week regimen (Table 5)
- Epoch 2 Efficacy assessments:
  - 2-week regimen (Table 6)
  - 3-week regimen (Table 7)
  - 4-week regimen (Table 8)

Table 3 Epoch 1 Analysis Windows for Efficacy Assessments in Subjects with SC Dosing Every 2 Weeks

Analysis Visit	Epoch 1 Relative Target Day	Epoch 1 Relative Start Day	Epoch 1 Relative End Day	Other Assignment Criteria
INCAT				
SCREENING	-42 (+/-28)	-70	-18	If E1 relative day is missing and collected visit indicates SCREENING
BASELINE	-14 (+/-3)	-17	1	If E1 relative day is missing and collected visit indicates BASELINE
E1INT	105 (+/-3)	2	108	If E1 relative day is missing and collected visit indicates E1 and week number ≤ 15
EoE1	189 (+/-3)	109	E1 Last Visit	If E1 relative day is missing and collected visit indicates E1 and week number > 15
LoE1/6M				Last data among E1INT and EoE1
Hand Grip Strength, R-ODS, MRC Sum Score, GNDS				
BASELINE	-14 (+/-3)	-17	1	If E1 relative day is missing and collected visit indicates BASELINE
E1INT	105 (+/-3)	2	108	If E1 relative day is missing and collected visit indicates E1 and week number ≤ 15
EoE1	189 (+/-3)	109	E1 Last Visit	If E1 relative day is missing and collected visit indicates E1 and week number > 15
LoE1/6M				Last data among E1INT and EoE1

Table 4 Epoch 1 Analysis Windows for Efficacy Assessments in Subjects with SC Dosing Every 3 Weeks

Analysis Visit	Epoch 1 Relative Target Day	Epoch 1 Relative Start Day	Epoch 1 Relative End Day	Other Assignment Criteria
INCAT				
SCREENING	-42 (+/-28)	-70	-18	If E1 relative day is missing and collected visit in SCREENING
BASELINE	-14 (+/-3)	-17	1	If E1 relative day is missing and collected visit indicates BASELINE
E1INT	98 (+/-3)	2	101	If E1 relative day is missing and collected visit indicates E1 and week number ≤ 14
EoE1	182 (+/-3)	102	E1 Last Visit	If E1 relative day is missing and collected visit indicates E1 and week number > 14
LoE1/6M				Last data among E1INT and EoE1
Hand Grip Strength, R-ODS, MRC Sum Score, GNDS				
BASELINE	-14 (+/-3)	-17	1	If E1 relative day is missing and collected visit indicates BASELINE
E1INT	98 (+/-3)	2	101	If E1 relative day is missing and collected visit indicates E1 and week number ≤ 14
EoE1	182 (+/-3)	102	E1 Last Visit	If E1 relative day is missing and collected visit indicates E1 and week number > 14
LoE1/6M				Last data among E1INT and EoE1

Table 5 Epoch 1 Analysis Windows for Efficacy Assessments in Subjects with SC Dosing Every 4 Weeks

Analysis Visit	Epoch 1 Relative Target Day	Epoch 1 Relative Start Day	Epoch 1 Relative End Day	Other Assignment Criteria
INCAT				
SCREENING	-42 (+/-28)	-70	-18	If E1 relative day is missing and collected visit in SCREENING
BASELINE	-14 (+/-3)	-17	1	If E1 relative day is missing and collected visit indicates BASELINE
E1INT	112 (+/-3)	2	115	If E1 relative day is missing and collected visit indicates E1 and week number ≤ 16
EoE1	196 (+/-3)	116	E1 Last Visit	If E1 relative day is missing and collected visit indicates E1 and week number > 16
LoE1/6M				Last data among E1INT and EoE1
Hand Grip Strength, R-ODS, MRC Sum Score, GNDS				
BASELINE	-14 (+/-3)	-17	1	If E1 relative day is missing and collected visit indicates BASELINE
E1INT	112 (+/-3)	2	115	If E1 relative day is missing and collected visit indicates E1 and week number ≤ 16
EoE1	196 (+/-3)	116	E1 Last Visit	If E1 relative day is missing and collected visit indicates E1 and week number > 16
LoE1/6M				Last data among E1INT and EoE1

Table 6 Epoch 2 Analysis Windows for Efficacy Assessments (Dosing Every 2 Weeks)

Analysis Visit	Epoch 2 Relative[a] Target Day	Epoch 2 Relative Start Day	Epoch 2 Relative End Day	Other Assignment Criteria
INCAT, Hand grip strength (For MMN subjects)				
E2W4	29(+/-3)	26	43	If E2 relative day is missing and collected visit indicates E2 and week number 4
E2W8	57(+/-3)	44	71	If E2 relative day is missing and collected visit indicates E2 and week number 8
E2W12	85(+/-3)	72	99	If E2 relative day is missing and collected visit indicates E2 and week number 12
E2W16	113(+/-3)	100	127	If E2 relative day is missing and collected visit indicates E2 and week number 16
E2W20	141(+/-3)	128	155	If E2 relative day is missing and collected visit indicates E2 and week number 20
E2W24/Eo6M	169(+/-3)	156	183	If E2 relative day is missing and collected visit indicates Eo6M or (E2 and week number 24)
LoE2/6M				Last data among E2W4, E28W, E2W12, E2W16, E2W20 and E2W24/Eo6M
E2C3M	85(+/-3)	1	88	
E2C6M	169(+/-3)	89	172	
E2C9M	253(+/-3)	173	256	
E2C12M	337(+/-3)	257	340	
E2C15M	421(+/-3)	341	424	
E2C18M	505(+/-3)	425	508	
E2C21M	589(+/-3)	509	592	
E2C24M	673(+/-3)	593	676	
E2C27M	757(+/-3)	677	760	
LoE2C				Last data among E2CnM (n: 3, 6, 9, ...)
EoS				Last data throughout the study (Epoch 1 to Epoch 2)
Hand grip strength (For CIDP subjects), R-ODS, MRC sum score, GNDS				
E2W12	85(+/-3)	72	99	If E2 relative day is missing and collected visit indicates E2 and week number 12
E2W24/Eo6M	169(+/-3)	156	183	If E2 relative day is missing and collected visit indicates Eo6M or (E2 and week number 24)
LoE2/6M				Last data among E2W12 and E2W24/Eo6M
E2C3M	85(+/-3)	1	88	
E2C6M	169(+/-3)	89	172	

Table 6 Epoch 2 Analysis Windows for Efficacy Assessments (Dosing Every 2 Weeks)

Analysis Visit	Epoch 2 Relative[a] Target Day	Epoch 2 Relative Start Day	Epoch 2 Relative End Day	Other Assignment Criteria
E2C9M	253(+/-3)	173	256	
E2C12M	337(+/-3)	257	340	
E2C15M	421(+/-3)	341	424	
E2C18M	505(+/-3)	425	508	
E2C21M	589(+/-3)	509	592	
E2C24M	673(+/-3)	593	676	
E2C27M	757(+/-3)	677	760	
LoE2C				Last data among E2CnM (n: 3, 6, 9, ...)
EoS				Last data throughout the study (Epoch 1 to Epoch 2)

[a] Epoch 2 relative day for Epoch 2 until the first 6 months is based on the date of the first Epoch 2 infusion; the day of the first infusion is E2 Day 1. Epoch 2 relative day for Epoch 2 after 6 months is based on the date of the first Epoch 2 infusion of Epoch 2 after 6 months; the day of the first infusion is E2 (continued) Day 1.

Table 7 Epoch 2 Analysis Windows for Efficacy Assessments (Dosing Every 3 Weeks)

Analysis Visit	Epoch 2 Relative[a] Target Day	Epoch 2 Relative Start Day	Epoch 2 Relative End Day	Other Assignment Criteria
INCAT, Hand grip strength (For MMN subjects)				
E2W3	22(+/-3)	17	43	If E2 relative day is missing and collected visit indicates E2 and week number 3
E2W9	64(+/-3)	44	74	If E2 relative day is missing and collected visit indicates E2 and week number 9
E2W12	85(+/-3)	75	95	If E2 relative day is missing and collected visit indicates E2 and week number 12
E2W15	106(+/-3)	96	127	If E2 relative day is missing and collected visit indicates E2 and week number 15
E2W21	148(+/-3)	128	158	If E2 relative day is missing and collected visit indicates E2 and week number 21
E2W24/Eo6M	169(+/-3)	159	179	If E2 relative day is missing and collected visit indicates Eo6M or (E2 and week number 24)
LoE2/6M				Last data among E2W4, E28W, E2W12, E2W16, E2W20 and E2W24/Eo6M
E2C3M	85(+/-5)	1	90	
E2C6M	169(+/-5)	91	174	
E2C9M	253(+/-5)	175	258	
E2C12M	337(+/-5)	259	342	
E2C15M	421(+/-5)	343	426	
E2C18M	505(+/-5)	427	510	
E2C21M	589(+/-5)	511	594	
E2C24M	673(+/-5)	595	678	
E2C27M	757(+/-5)	679	762	
LoE2C				Last data among E2CnM (n: 3, 6, 9, ...)
EoS				Last data throughout the study (Epoch 1 to Epoch 2)

Table 7 Epoch 2 Analysis Windows for Efficacy Assessments (Dosing Every 3 Weeks)

Analysis Visit	Epoch 2 Relative[a] Target Day	Epoch 2 Relative Start Day	Epoch 2 Relative End Day	Other Assignment Criteria
Hand grip strength (For CIDP subjects), R-ODS, MRC sum score, GNDS				
E2W12	85(+/-5)	75	95	If E2 relative day is missing and collected visit indicates E2 and week number 12
E2W24/Eo6M	169(+/-5)	159	179	If E2 relative day is missing and collected visit indicates Eo6M or (E2 and week number 24)
LoE2/6M				Last data among E2W12 and E2W24/Eo6M
E2C3M	85(+/-5)	1	90	
E2C6M	169(+/-5)	91	174	
E2C9M	253(+/-5)	175	258	
E2C12M	337(+/-5)	259	342	
E2C15M	421(+/-5)	343	426	
E2C18M	505(+/-5)	427	510	
E2C21M	589(+/-5)	511	594	
E2C24M	673(+/-5)	595	678	
E2C27M	757(+/-5)	679	762	
LoE2C				Last data among E2CnM (n: 3, 6, 9, ...)
EoS				Last data throughout the study (Epoch 1 to Epoch 2)

[a] Epoch 2 relative day for Epoch 2 until the first 6 months is based on the date of the first Epoch 2 infusion; the day of the first infusion is E2 Day 1. Epoch 2 relative day for Epoch 2 after 6 months is based on the date of the first Epoch 2 infusion of Epoch 2 after 6 months; the day of the first infusion is E2 (continued) Day 1.

Table 8 Epoch 2 Analysis Windows for Efficacy Assessments (Dosing Every 4 Weeks)

Analysis Visit	Epoch 2 Relative[a] Target Day	Epoch 2 Relative Start Day	Epoch 2 Relative End Day	Other Assignment Criteria
INCAT, Hand grip strength (For MMN subjects)				
E2W4	29(+/-3)	26	43	If E2 relative day is missing and collected visit indicates E2 and week number 4
E2W8	57(+/-3)	44	71	If E2 relative day is missing and collected visit indicates E2 and week number 8
E2W12	85(+/-3)	72	99	If E2 relative day is missing and collected visit indicates E2 and week number 12
E2W16	113(+/-3)	100	127	If E2 relative day is missing and collected visit indicates E2 and week number 16
E2W20	141(+/-3)	128	155	If E2 relative day is missing and collected visit indicates E2 and week number 20
E2W24/Eo6M	169(+/-3)	156	183	If E2 relative day is missing and collected visit indicates Eo6M or (E2 and week number 24)
LoE2/6M				Last data among E2W4, E28W, E2W12, E2W16, E2W20 and E2W24/Eo6M
E2C3M	85(+/-7)	1	92	
E2C6M	169(+/-7)	93	176	
E2C9M	253(+/-7)	177	260	
E2C12M	337(+/-7)	261	344	
E2C15M	421(+/-7)	345	428	
E2C18M	505(+/-7)	429	512	
E2C21M	589(+/-7)	513	596	
E2C24M	673(+/-7)	597	680	
E2C27M	757(+/-7)	681	764	
LoE2C				Last data among E2CnM (n: 3, 6, 9, ...)
EoS				Last data throughout the study (Epoch 1 to Epoch 2)

Table 8 Epoch 2 Analysis Windows for Efficacy Assessments (Dosing Every 4 Weeks)

Analysis Visit	Epoch 2 Relative[a] Target Day	Epoch 2 Relative Start Day	Epoch 2 Relative End Day	Other Assignment Criteria
Hand grip strength (For CIDP subjects), R-ODS, MRC sum score, GNDS				
E2W12	85(+/-3)	72	99	If E2 relative day is missing and collected visit indicates E2 and week number 12
E2W24/Eo6M	169(+/-3)	156	183	If E2 relative day is missing and collected visit indicates Eo6M or (E2 and week number 24)
LoE2/6M				Last data among E2W12 and E2W24/Eo6M
E2C3M	85(+/-7)	1	92	
E2C6M	169(+/-7)	93	176	
E2C9M	253(+/-7)	177	260	
E2C12M	337(+/-7)	261	344	
E2C15M	421(+/-7)	345	428	
E2C18M	505(+/-7)	429	512	
E2C21M	589(+/-7)	513	596	
E2C24M	673(+/-7)	597	680	
E2C27M	757(+/-7)	681	764	
LoE2C				Last data among E2CnM (n: 3, 6, 9, ...)
EoS				Last data throughout the study (Epoch 1 to Epoch 2)

[a] Epoch 2 relative day for Epoch 2 until the first 6 months is based on the date of the first Epoch 2 infusion; the day of the first infusion is E2 Day 1. Epoch 2 relative day for Epoch 2 after 6 months is based on the date of the first Epoch 2 infusion of Epoch 2 after 6 months; the day of the first infusion is E2 (continued) Day 1.

9.1.4 Repeated or Unscheduled Assessments of Safety Parameters

If a subject has repeated assessments before initial dose of IP, then the most recent assessment value will be used as baseline in analysis/summaries involving baseline.

If a subject has repeated assessments after initial dose of IP (repeated post-baseline assessments), then the most recent assessment value will be used in analysis/summaries involving post-baseline.

Unscheduled assessments (i.e., assessments not done at a planned visit) will used only in summaries of abnormalities or toxicities (not otherwise).

All assessments, including repeated and unscheduled assessments, will be presented in the subject data listings.

9.1.5 Handling of Missing, Unused, and Spurious Data

This section provides a general plan for handling of missing data, unused and spurious data. Specifics regarding handling are addressed in specific endpoint analysis sections.

Data that appear to be spurious (e.g., outliers, incompatible with life) will be queried by Clinical Data Management and then either corrected or explained in the CSR if not correctable. Outliers will not be excluded from analysis unless otherwise specified. Any exclusion of data from analysis will be appropriately footnoted in the relevant TFLs.

9.1.6 Missing Date of Investigational Product

If the date of the last dose of IP is missing for a subject in the Safety analysis set, then all efforts will be made by the study sponsor, or on behalf of the sponsor, to obtain the date from the study investigator. If the date cannot be obtained despite all efforts, then the last visit date when IP was dispensed will be used in the calculation of treatment duration.

That is, if last dose date is missing, then last visit in Treatment Period date will be used.

9.1.7 Missing Date Information for Prior or Concomitant Medications (Therapies/Procedures)

For prior or concomitant medications (and/or therapies/procedures), incomplete (fully or partially missing) start date and/or stop date of mediation will be imputed. When the start date and the stop date are both incomplete for a subject, impute the start date first using the imputation approach described in the subsequent sections.

9.1.7.1 Incomplete Start Date

The following rules will be applied to impute the missing numerical fields. If the stop date is complete and the imputed start date is after the stop date, then the start date will be imputed using the stop date.

9.1.7.1.1 Missing Day and Month

- If the year of the incomplete start date is the same as the year of the date of the first dose of IP, then the day and month of the date of the first dose of IP will be assigned to the missing fields
- If the year of the incomplete start date is before the year of the date of the first dose of IP, then December 31 will be assigned to the missing fields
- If the year of the incomplete start date is after the year of the date of the first dose of IP, then 01 January will be assigned to the missing fields

9.1.7.1.2 Missing Month Only

- The day will be treated as missing and both month and day will be replaced according to the above procedure

9.1.7.1.3 Missing Day Only

- If the month and year of the incomplete start date are the same as the month and year of the date of the first dose of IP, then the day of the date of the first dose of IP will be assigned to the missing day
- If either the year is before the year of the date of the first dose of IP, or if both years are the same but the month is before the month of the date of the first dose of IP, then the last day of the month will be assigned to the missing day
- If either the year is after the year of the date of the first dose of IP, or if both years are the same but the month is after the month of the date of the first dose of IP, then the first day of the month will be assigned to the missing day

9.1.7.2 Incomplete Stop Date

The following rules will be applied to impute the missing numerical fields. If the date of the last dose of IP is missing, then replace it with the last visit date. If the imputed stop date is before the (imputed or non-imputed) start date, then the imputed stop date will be equal to the start date.

If imputation of an incomplete stop date is required for calculating duration, and both the start date and the stop date are incomplete for a subject, then the start date will be imputed first.

A completely missing stop date will be interpreted as ongoing.

9.1.7.2.1 Missing Day and Month

- If the year of the incomplete stop date is the same as the year as of the date of the last dose of IP, then the day and month of the date of the last dose of IP will be assigned to the missing fields
- If the year of the incomplete stop date is before the year of the date of the last dose of IP, then 31 December will be assigned to the missing fields

- If the year of the incomplete stop date is after the year of the date of the last dose of IP, then 01 January will be assigned to the missing fields

9.1.7.2.2 Missing Month Only

- The day will be treated as missing and both month and day will be replaced according to the above procedure

9.1.7.2.3 Missing Day Only

- If the month and year of the incomplete stop date are the same as the month and year of the date of the last dose of IP, then the day of the date of the last dose of IP will be assigned to the missing day
- If the year is before the year of the date of the last dose of IP, or if both years are the same but the month is before the month of the date of the last dose of IP, then the last day of the month will be assigned to the missing day
- If the year is after the year of the last dose of IP, or if both years are the same but the month is after the month of the date of the last dose of IP, then the first day of the month will be assigned to the missing day

9.1.8 Missing Date Information for Adverse Events

The following approaches will be applied:

- To facilitate categorization of AEs as treatment emergent, imputation of dates can be used
- If an AE start date is completely missing, then the AE will be considered treatment-emergent in Epoch 1
- For AEs with partial start dates, non-missing date parts will be used to determine if the AE is treatment-emergent or not. If a determination cannot be made using the non-missing date parts as to when the AE occurred relative to IP (eg, AE start year and month are the same as the year and month of the first dose of IP), then the AE will be classified as treatment-emergent
- For AEs, the default is to only impute incomplete (i.e., partially missing) start dates. Incomplete stop dates may also be imputed when calculation of the duration of an AE is required per the protocol
- If imputation of an incomplete stop date is required, and both the start date and the stop date are incomplete for a subject, impute the start date first

9.1.8.1 Incomplete Start Date

Rules in Section 9.1.7.1 apply.

9.1.8.2 Incomplete Stop Date

Rules in Section 9.1.7.2 apply.

9.1.9 Missing Date Information for First Symptoms

Incomplete (fully or partially missing) date of first symptoms will be imputed. Rules in Section 9.1.7.1 apply.

9.1.10 Missing Date Information for Diagnosis

Incomplete (fully or partially missing) date of diagnosis will be imputed. Rules in Section 9.1.7.1 apply.

9.1.11 Missing Severity Assessment for Adverse Events

If severity is missing for an AE starting prior to the date of the first dose of IP, then a severity of "Mild" will be assigned. If the severity is missing for an AE starting on or after the date of the first dose of IP, then a severity of "Severe" will be assigned.

If a subject experiences more than one AE categorized under the same preferred term, where one of them is categorized as "severe" and one of them is categorized as "unknown", then the severity of this AE will be counted as "severe".

If a subject experiences more than one AE categorized under the same preferred term, where one of them is categorized as "mild" or "moderate" and one of them is categorized as "unknown", then the severity of this AE will be counted as "unknown".

The imputed values for severity assessment will be used for summaries, while both the actual and the imputed values will be used in subject data listings.

9.1.12 Missing Seriousness of Adverse Events

AEs of unknown seriousness will be tabulated as SAEs in summaries; however, every effort will be made to avoid study data lock with AEs for which a determination of seriousness is missing.

9.1.13 Missing Relationship to Investigational Product for Adverse Events

If the relationship to IP is missing for an AE starting on or after the date of the first dose of IP, then a causality of "related" will be assigned. The imputed values for relationship to IP will be used for incidence summaries, while both the actual and the imputed values will be presented in data listings.

9.1.14 Character Values of Clinical Laboratory Variables

Laboratory measurements will be presented in SI units, unless otherwise specified for an analysis. If a laboratory result is expected to have a numeric value, but the data which are received include a special character such as ">" or "<", then the result will be assumed to lie outside the range of quantitation (example: if the data is < 30 or <= 30, the result will assume to be 29).

Tables based on a dichotomous or categorical grouping, including but not limited to shift tables, will place such data appropriately prior to removal of the special character, so that particularly low or high values remain recognized as such. For quantitative summaries by time-point or visit, the numeric part of such a result will be used, unless the table is designed to include explicit tabulation of results that are outside the range of quantitation.

9.2 Definition of AESIs

Definition information for AESIs in MedDRA ver.26.0 is provided in the following tables. Since there is no change in the definition of AESIs in table 9 between MedDRA ver. 26.0 and ver. 27.0, the same definitions will also be used in MedDRA ver. 27.0.

Table 9 Adverse Events of Special Interest

Display Category	Display Term	AEDECOD in Upper Case	PT Code (MedDRA ver.26.0)	Additional Conditions
Allergic Reactions	Urticaria	URTICARIA	10046735	
	New-onset bronchospasm	BRONCHOSPASM	10006482	
	Oedema of tongue, lips, face (angioedema)	Refer to Table 9.1 : Oedema of tongue, lips, face (angioedema)		
	Anaphylaxis	Refer to Table 9.2 : Anaphylaxis		
	Stevens-Johnson syndrome	STEVENS-JOHNSON SYNDROME	10042033	
	Erythema multiforme	ERYTHEMA MULTIFORME	10015218	
	Toxic epidermal necrolysis	TOXIC EPIDERMAL NECROLYSIS	10044223	
Immune complex mediated reactions - Local	Persistent induration or nodule	Refer to Table 9.3 : Persistent induration or nodule		Duration > 48 hours (> 2 days)
	Excessive inflammation	Refer to Table 9.4 : Excessive inflammation		Severity = "SEVERE"
	Tissue necrosis/ulceration at the site of administration	Refer to Table 9.5 : Tissue necrosis/ulceration		
	Dystrophic or fibrotic changes at the site of administration	Refer to Table 9.6 : Dystrophic or fibrotic changes		
	Pigmented skin changes at the site of drug administration	Refer to Table 9.7 :Pigmented skin changes		
Immune complex mediated reactions - Systemic	Arthritis	ARTHRITIS	10003246	
	Vasculitis (purpuric rash)	VASCULITIS	10047115	
		Refer to Table 9.8 : Rash		
		Refer to Table 9.9 : Purpura		
	Glomerulonephritis	HAEMATURIA	10018867	
		Refer to Table 9.10 : Nephritis		

Table 9 Adverse Events of Special Interest

Display Category	Display Term	AEDECOD in Upper Case	PT Code (MedDRA ver.26.0)	Additional Conditions
Thrombotic/embolic events	Arterial	Refer to Table 9.11 : Arterial		
	Venous	Refer to Table 9.12 : Venous		
	Vessel unspecified/unknown	Refer to Table 9.13 : Vessel unspecified/unknown		

Table 9.1 Oedema of tongue, lips, face (angioedema)

AEDECOD	PT Code
Angioedema	10002424
Face oedema	10016029
Lip oedema	10024558
Tongue oedema	10043967

Table 9.2 Anaphylaxis

AEDECOD	PT Code
Anaphylactic reaction	10002198
Anaphylactic shock	10002199

Table 9.3 Persistent induration or nodule

AEDECOD	PT Code
Injection site induration	10022075
Infusion site induration	10053482
Administration site induration	10075939
Injection site nodule	10057880
Infusion site nodule	10065484
Administration site nodule	10075765

Table 9.4 Excessive inflammation

AEDECOD	PT Code
Injection site inflammation	10022078
Infusion site inflammation	10056270
Injection site joint inflammation	10064111
Administration site inflammation	10074704
Administration site joint inflammation	10075946
Infusion site joint inflammation	10076074
Injection site joint swelling	10049260
Injection site swelling	10053425
Infusion site swelling	10053505
Administration site swelling	10075107
Infusion site joint swelling	10076078
Injection site pain	10022086
Injection site joint pain	10049261
Infusion site pain	10053483
Administration site pain	10058049
Administration site joint pain	10075948

Table 9.5 Tissue necrosis/ulceration

AEDECOD	PT Code
Injection site necrosis	10022082
Infusion site necrosis	10065478
Administration site necrosis	10075956
Injection site ulcer	10022105
Infusion site ulcer	10054995
Administration site ulcer	10075108

Table 9.6 Dystrophic or fibrotic changes

AEDECOD	PT Code
Injection site fibrosis	10022064
Infusion site fibrosis	10065462
Administration site fibrosis	10075934
Injection site dysaesthesia	10069124
Administration site dysaesthesia	10075930
Infusion site dysaesthesia	10076067

Table 9.7 Pigmented skin changes

AEDECOD	PT Code
Injection site discolouration	10051572
Infusion site discolouration	10065460
Administration site discolouration	10075098

Table 9.8 Rash

AEDECOD	PT Code
Rash	10037844
Rash erythematous	10037855
Rash follicular	10037857
Rash macular	10037867
Rash maculo-papular	10037868
Rash morbilliform	10037870
Rash neonatal	10037871
Rash papular	10037876
Rash papulosquamous	10037879
Rash pruritic	10037884
Rash scarlatiniform	10037890
Rash vesicular	10037898
Systemic lupus erythematosus rash	10042946
Vasculitic rash	10047111
Rash maculovesicular	10050004
Mucocutaneous rash	10056671
Rash rubelliform	10057984
Exfoliative rash	10064579
Butterfly rash	10067982
Paraneoplastic rash	10074687
Nodular rash	10075807
Heliotrope rash	10081454

Table 9.9 Purpura

AEDECOD	PT Code
Henoch-Schonlein purpura	10019617
Purpura	10037549
Purpura fulminans	10037556
Purpura neonatal	10037557
Purpura senile	10037560
Vascular purpura	10047097
Palpable purpura	10056872
Chronic pigmented purpura	10072726
Hypergammaglobulinaemic purpura of Waldenstrom	10086403

Table 9.10 Nephritis

AEDECOD	PT Code
Glomerulonephritis	10018364
Glomerulonephritis rapidly progressive	10018378
Lupus nephritis	10025140
Fibrillary glomerulonephritis	10068279
Tubulointerstitial nephritis and uveitis syndrome	10069034
Henoch-Schonlein purpura nephritis	10069440
Chronic autoimmune glomerulonephritis	10073016
Autoimmune nephritis	10077087
Immune-mediated nephritis	10083070

Table 9.11 Arterial

AEDECOD in Upper Case	PT Code
CAROTID ENDARTERECTOMY	10007692
RETINAL ARTERY EMBOLISM	10038826
ARTERECTOMY WITH GRAFT REPLACEMENT	10003140
HYPOTHENAR HAMMER SYNDROME	10063518
CEREBRAL ARTERY THROMBOSIS	10008092
PERIPHERAL ARTERIAL OCCLUSIVE DISEASE	10062585
MESENTERIC ARTERY THROMBOSIS	10027397
COELIAC ARTERY OCCLUSION	10069696
ARTERIAL GRAFT	10061655
CAPSULAR WARNING SYNDROME	10067744
PERIPHERAL ARTERIAL REOCCLUSION	10069379
MESENTERIC ARTERY EMBOLISM	10027395
AORTIC BYPASS	10057617
ENDARTERECTOMY	10014648
ACUTE AORTIC SYNDROME	10074337
CEREBRAL HYPOPERFUSION	10065384
TRUNCUS COELIACUS THROMBOSIS	10062363
FEMORAL ARTERY EMBOLISM	10068365
PERIPHERAL ARTERY THROMBOSIS	10072564
SUPERIOR MESENTERIC ARTERY SYNDROME	10054156
STROKE IN EVOLUTION	10059613
CORONARY ARTERY EMBOLISM	10011084
ATHERECTOMY	10063025
ILIAC ARTERY OCCLUSION	10064601
ATRIAL APPENDAGE CLOSURE	10079735
CAROTID ARTERY OCCLUSION	10048964
ARTERIAL OCCLUSIVE DISEASE	10062599
MESENTERIC ARTERY STENT INSERTION	10071261
INTRAOPERATIVE CEREBRAL ARTERY OCCLUSION	10056382
ARTERIOGRAM ABNORMAL	10061659
CEREBRAL ARTERY EMBOLISM	10008088
HEPATIC ARTERY EMBOLISM	10019635
AMAUROSIS	10001902
ARTERIOGRAM CAROTID ABNORMAL	10003195
SPINAL ARTERY EMBOLISM	10049440
SUBCLAVIAN ARTERY OCCLUSION	10069695
THROMBOEMBOLECTOMY	10064958

Table 9.11 Arterial

AEDECOD in Upper Case	PT Code
CAROTID ARTERY STENT INSERTION	10066102
PERIPHERAL ENDARTERECTOMY	10072560
SPLENIC EMBOLISM	10068677
SPINAL ARTERY THROMBOSIS	10071316
AORTIC EMBOLUS	10002897
PERIPHERAL ARTERY BYPASS	10072561
PERIPHERAL ARTERY STENT INSERTION	10072562
RETINAL ARTERY THROMBOSIS	10038831
CAROTID ARTERY THROMBOSIS	10007688
ANGIOPLASTY	10002475
BASAL GANGLIA INFARCTION	10069020
CORONARY ARTERIAL STENT INSERTION	10052086
HEPATIC ARTERY THROMBOSIS	10019636
CEREBELLAR ARTERY OCCLUSION	10053633
THROMBOTIC MICROANGIOPATHY	10043645
MESENTERIC ARTERIOSCLEROSIS	10065560
AORTIC THROMBOSIS	10002910
CAROTID ARTERIAL EMBOLUS	10007684
MYOCARDIAL INFARCTION	10028596
ARTERIAL THROMBOSIS	10003178
TRANSIENT ISCHAEMIC ATTACK	10044390
PULMONARY ENDARTERECTOMY	10072893
MYOCARDIAL NECROSIS	10028602
POSTINFARCTION ANGINA	10058144
STRESS CARDIOMYOPATHY	10066286
CEREBROVASCULAR STENOSIS	10061751
INTRA-AORTIC BALLOON PLACEMENT	10052989
CAROTID ARTERY BYPASS	10053003
HEPATIC ARTERY OCCLUSION	10051991
SPLENIC ARTERY THROMBOSIS	10074600
AMAUROSIS FUGAX	10001903
SILENT MYOCARDIAL INFARCTION	10049768
PERCUTANEOUS CORONARY INTERVENTION	10065608
CEREBELLAR ARTERY THROMBOSIS	10008023
VERTEBRAL ARTERY OCCLUSION	10048965
ARTERECTOMY	10071026
ACUTE MYOCARDIAL INFARCTION	10000891

Table 9.11 Arterial

AEDECOD in Upper Case	PT Code
BRACHIOCEPHALIC ARTERY OCCLUSION	10069694
CORONARY ARTERY BYPASS	10011077
PENILE ARTERY OCCLUSION	10068035
CEREBROVASCULAR INSUFFICIENCY	10058842
BLINDNESS TRANSIENT	10005184
VERTEBRAL ARTERY THROMBOSIS	10057777
POPLITEAL ARTERY ENTRAPMENT SYNDROME	10071642
CORONARY ENDARTERECTOMY	10011101
CORONARY VASCULAR GRAFT OCCLUSION	10075162
AORTIC SURGERY	10061651
CORONARY ARTERY REOCCLUSION	10053261
SUBCLAVIAN ARTERY THROMBOSIS	10042334
BASILAR ARTERY THROMBOSIS	10063093
PULMONARY ARTERY THROMBOSIS	10037340
CORONARY REVASCULARISATION	10049887
LACUNAR INFARCTION	10051078
PRECEREBRAL ARTERY THROMBOSIS	10074717
CORONARY ARTERY OCCLUSION	10011086
AORTOGRAM ABNORMAL	10057794
RENAL ARTERY OCCLUSION	10048988
ISCHAEMIC CEREBRAL INFARCTION	10060840
PULMONARY ARTERY THERAPEUTIC PROCEDURE	10063731
MESENTERIC ARTERIAL OCCLUSION	10027394
RENAL ARTERY ANGIOPLASTY	10057493
CORONARY ARTERY THROMBOSIS	10011091
ILIAC ARTERY EMBOLISM	10021338
CORONARY ANGIOPLASTY	10050329
CAROTID ANGIOPLASTY	10071260
CEREBRAL ARTERY OCCLUSION	10008089
ATHEROSCLEROTIC PLAQUE RUPTURE	10076604
ARTERIAL STENT INSERTION	10061657
MESENTERIC ARTERY STENOSIS	10027396
THROMBOTIC THROMBOCYTOPENIC PURPURA	10043648
PERIPHERAL ARTERY ANGIOPLASTY	10057518
RETINAL ARTERY OCCLUSION	10038827
ARTERIAL THERAPEUTIC PROCEDURE	10052949
ARTERIAL BYPASS OPERATION	10056418

Table 9.11 Arterial

AEDECOD in Upper Case	PT Code
ISCHAEMIC STROKE	10061256
PRECEREBRAL ARTERY OCCLUSION	10036511
EMBOLIA CUTIS MEDICAMENTOSA	10058729
EMBOLISM ARTERIAL	10014513
POST PROCEDURAL MYOCARDIAL INFARCTION	10066592
RENAL EMBOLISM	10063544
PERIPHERAL EMBOLISM	10061340
LERICHE SYNDROME	10024242
SUBCLAVIAN ARTERY EMBOLISM	10042332
RENAL ARTERY THROMBOSIS	10038380
VISUAL ACUITY REDUCED TRANSIENTLY	10047532
PERIPHERAL ARTERY OCCLUSION	10057525
PAPILLARY MUSCLE INFARCTION	10033697
BASILAR ARTERY OCCLUSION	10048963

Table 9.12 Venous

AEDECOD in Upper Case	PT Code
RETINAL VEIN OCCLUSION	10038907
CEREBRAL VENOUS SINUS THROMBOSIS	10083037
VENOGRAM ABNORMAL	10047209
PORTAL VEIN CAVERNOUS TRANSFORMATION	10073979
PORTAL VEIN OCCLUSION	10058989
VENOUS OPERATION	10062175
OBSTETRICAL PULMONARY EMBOLISM	10029925
BUDD-CHIARI SYNDROME	10006537
POST THROMBOTIC SYNDROME	10048591
VENOUS THROMBOSIS	10047249
PULMONARY THROMBOSIS	10037437
PULMONARY VEIN OCCLUSION	10068690
VENOOCCLUSIVE DISEASE	10062173
VENOUS REPAIR	10052964
POSTOPERATIVE THROMBOSIS	10050902
CAVERNOUS SINUS THROMBOSIS	10007830
VENOUS RECANALISATION	10068605
HEPATIC VEIN THROMBOSIS	10019713
THROMBOPHLEBITIS MIGRANS	10043581
DEEP VEIN THROMBOSIS POSTOPERATIVE	10066881
MESENTERIC VENOUS OCCLUSION	10027403
PULMONARY VENO-OCCLUSIVE DISEASE	10037458
SPLENIC VEIN OCCLUSION	10068122
EMBOLISM VENOUS	10014522
TRANSVERSE SINUS THROMBOSIS	10044457
SI QIII TIII PATTERN	10068479
SPLENIC VEIN THROMBOSIS	10041659
VENA CAVA FILTER REMOVAL	10074397
VENOOCCLUSIVE LIVER DISEASE	10047216
RENAL VEIN THROMBOSIS	10038548
VENOUS THROMBOSIS NEONATAL	10064602
POST PROCEDURAL PULMONARY EMBOLISM	10063909
VENOUS THROMBOSIS IN PREGNANCY	10067030
ILIAC VEIN OCCLUSION	10058992
RENAL VEIN EMBOLISM	10038547
VENOUS THROMBOSIS LIMB	10061408

Table 9.12 Venous

AEDECOD in Upper Case	PT Code
THROMBOPHLEBITIS	10043570
RENAL VEIN OCCLUSION	10056293
PELVIC VENOUS THROMBOSIS	10034272
PENILE VEIN THROMBOSIS	10034324
OVARIAN VEIN THROMBOSIS	10072059
JUGULAR VEIN OCCLUSION	10076835
VENA CAVA THROMBOSIS	10047195
MAHLER SIGN	10075428
PHLEBECTOMY	10048874
VENOUS STENT INSERTION	10063389
PULMONARY MICROEMBOLI	10037421
SUPERIOR SAGITTAL SINUS THROMBOSIS	10042567
SUPERIOR VENA CAVA SYNDROME	10042569
VENA CAVA EMBOLISM	10047193
INFERIOR VENA CAVAL OCCLUSION	10058987
JUGULAR VEIN THROMBOSIS	10023237
PULMONARY EMBOLISM	10037377
VENA CAVA FILTER INSERTION	10048932
COMPRESSION GARMENT APPLICATION	10079209
PULMONARY VENOUS THROMBOSIS	10037459
CATHETERISATION VENOUS	10052698
SUPERFICIAL VEIN THROMBOSIS	10086210
PORTAL VEIN THROMBOSIS	10036206
POSTPARTUM VENOUS THROMBOSIS	10036300
HEPATIC VEIN OCCLUSION	10058991
SUPERIOR VENA CAVA OCCLUSION	10058988
OPHTHALMIC VEIN THROMBOSIS	10074349
OBSTRUCTIVE SHOCK	10073708
RETINAL VEIN THROMBOSIS	10038908
THROMBOPHLEBITIS NEONATAL	10043586
INFERIOR VENA CAVA SYNDROME	10070911
THROMBOSIS CORPORA CAVERNOSA	10067270
PULMONARY INFARCTION	10037410
SUBCLAVIAN VEIN THROMBOSIS	10049446
HOMANS' SIGN POSITIVE	10051031
VENOUS OCCLUSION	10058990
THROMBOSED VARICOSE VEIN	10043605

Table 9.12 Venous

AEDECOD in Upper Case	PT Code
AXILLARY VEIN THROMBOSIS	10003880
DEEP VEIN THROMBOSIS	10051055
PAGET-SCHROETTER SYNDROME	10050216
MAY-THURNER SYNDROME	10069727
CEREBRAL VENOUS THROMBOSIS	10008138
BRACHIOCEPHALIC VEIN OCCLUSION	10076837
MESENTERIC VEIN THROMBOSIS	10027402
CENTRAL VENOUS CATHETERISATION	10053377

Table 9.13 Vessel unspecified/unknown

AEDECOD in Upper Case	PT Code
HEPATIC INFARCTION	10019680
ARTERIOVENOUS FISTULA OCCLUSION	10058562
VASCULAR GRAFT OCCLUSION	10049060
PNEUMATIC COMPRESSION THERAPY	10059829
ARTERIOVENOUS FISTULA THROMBOSIS	10003192
TESTICULAR INFARCTION	10043337
SPLENIC INFARCTION	10041648
CEREBROSPINAL THROMBOTIC TAMPONADE	10052173
DEVICE EMBOLISATION	10074896
PARAPLEGIA	10033892
CEREBRAL INFARCTION FOETAL	10008119
TUMOUR EMBOLISM	10045168
CEREBROVASCULAR ACCIDENT	10008190
STOMA SITE THROMBOSIS	10074515
THROMBECTOMY	10043530
INTRACARDIAC THROMBUS	10048620
HEMIPLEGIA	10019468
CEREBRAL CONGESTION	10076929
CEREBELLAR INFARCTION	10008034
PARAPARESIS	10033885
PLACENTAL INFARCTION	10064620
PARESIS	10033985
PERIPHERAL REVASCULARISATION	10053351
QUADRIPLEGIA	10037714

Table 9.13 Vessel unspecified/unknown

AEDECOD in Upper Case	PT Code
THALAMIC INFARCTION	10064961
GRAFT THROMBOSIS	10051269
EMBOLISM	10061169
CARDIAC VENTRICULAR THROMBOSIS	10053994
INNER EAR INFARCTION	10070754
PITUITARY INFARCTION	10035092
VASCULAR STENT THROMBOSIS	10063934
CORONARY BYPASS THROMBOSIS	10059025
INSTILLATION SITE THROMBOSIS	10073625
ULTRASOUND DOPPLER ABNORMAL	10045413
FOETAL CEREBROVASCULAR DISORDER	10053601
INCISION SITE VESSEL OCCLUSION	10076839
ATRIAL THROMBOSIS	10048632
CEREBRAL THROMBOSIS	10008132
APPLICATION SITE THROMBOSIS	10076026
EMBOLIC STROKE	10014498
ADRENAL THROMBOSIS	10075178
BRAIN STEM INFARCTION	10006147
HAEMORRHAGIC CEREBRAL INFARCTION	10019005
VASCULAR GRAFT THROMBOSIS	10069922
MEDICAL DEVICE SITE THROMBOSIS	10076145
MESENTERIC VASCULAR OCCLUSION	10074583
DIRECTIONAL DOPPLER FLOW TESTS ABNORMAL	10013048
VACCINATION SITE THROMBOSIS	10076190
INFUSION SITE THROMBOSIS	10065489
EMBOLIC CEREBRAL INFARCTION	10060839
THROMBOSIS	10043607
CEREBRAL ISCHAEMIA	10008120
IMPLANT SITE THROMBOSIS	10063868
HAEMORRHAGIC TRANSFORMATION STROKE	10055677
MESENTERIC VASCULAR INSUFFICIENCY	10027401
VASODILATION PROCEDURE	10058794
POSTPARTUM THROMBOSIS	10077022
OPTIC NERVE INFARCTION	10030936
THROMBOTIC STROKE	10043647
HAEMORRHOIDS THROMBOSED	10019023
HAEMORRHAGIC INFARCTION	10019013

Table 9.13 Vessel unspecified/unknown

AEDECOD in Upper Case	PT Code
BONE INFARCTION	10049824
INTRACARDIAC MASS	10066087
INJECTION SITE THROMBOSIS	10022104
CEREBRAL INFARCTION	10008118
VASCULAR GRAFT	10067740
EMBOLIC PNEUMONIA	10065680
CEREBROVASCULAR OPERATION	10051902
CEREBROVASCULAR DISORDER	10008196
ANGIOGRAM ABNORMAL	10060956
THYROID INFARCTION	10043742
MICROEMBOLISM	10073734
INFARCTION	10061216
ADMINISTRATION SITE THROMBOSIS	10075968
VASCULAR STENT OCCLUSION	10077143
DISSEMINATED INTRAVASCULAR COAGULATION IN NEWBORN	10013443
HAEMORRHAGIC STROKE	10019016
VASCULAR STENT INSERTION	10063382
PROSTHETIC VESSEL IMPLANTATION	10068628
SPLENIC THROMBOSIS	10074601
COLLATERAL CIRCULATION	10069729
QUADRIPARESIS	10049680
THROMBOSIS MESENTERIC VESSEL	10043626
THROMBOTIC CEREBRAL INFARCTION	10067347
UMBILICAL CORD OCCLUSION	10076714
CEREBELLAR EMBOLISM	10067167
DEVICE OCCLUSION	10064685
VESSEL PUNCTURE SITE OCCLUSION	10076838
MONOPLEGIA	10027926
HEPATIC VASCULAR THROMBOSIS	10074494
DISSEMINATED INTRAVASCULAR COAGULATION	10013442
RETINAL INFARCTION	10051742
BRAIN STEM STROKE	10068644
CEREBRAL SEPTIC INFARCT	10070671
VISUAL MIDLINE SHIFT SYNDROME	10066856
MONOPARESIS	10027925
INTESTINAL INFARCTION	10022657
ULTRASONIC ANGIOGRAM ABNORMAL	10061604

Table 9.13 Vessel unspecified/unknown

AEDECOD in Upper Case	PT Code
BRAIN STEM EMBOLISM	10074422
THROMBOLYSIS	10043568
RENAL VASCULAR THROMBOSIS	10072226
RETINAL VASCULAR THROMBOSIS	10062108
THROMBOSIS PROPHYLAXIS	10043634
SURGICAL VASCULAR SHUNT	10058408
SHUNT THROMBOSIS	10059054
RENAL INFARCT	10038470
PORTAL SHUNT	10036204
PARADOXICAL EMBOLISM	10066059
CEREBROVASCULAR ACCIDENT PROPHYLAXIS	10049165
SPINAL CORD INFARCTION	10058571
VESSEL PUNCTURE SITE THROMBOSIS	10070649
ANGIOGRAM PERIPHERAL ABNORMAL	10057517
CHOROIDAL INFARCTION	10057403
VASCULAR OPERATION	10049071
POST PROCEDURAL STROKE	10066591
THROMBOANGIITIS OBLITERANS	10043540
HEPARIN-INDUCED THROMBOCYTOPENIA	10062506
BRAIN STEM THROMBOSIS	10062573
SHUNT OCCLUSION	10040621
TUMOUR THROMBOSIS	10068067
UMBILICAL CORD THROMBOSIS	10071652
ANGIOGRAM CEREBRAL ABNORMAL	10052906
THROMBOSIS IN DEVICE	10062546
DIPLEGIA	10013033
BASAL GANGLIA STROKE	10071043
HEMIPARESIS	10019465
PANCREATIC INFARCTION	10068239

9.3 Assignment of R-ODS Centile Metric Scores

Derive the R-ODS score converted to a percentage value for CIDP according to the table below for listing.

Table 10 R-ODS Score Conversion

R-ODS Total Score (R-ODS summed raw score)	Centile Metric
Value where PARAMCD = "SIRODS"	Value where Derived PARAMCD = "CRODS"
0	0
1	6
2	11
3	14
4	16
5	19
6	21
7	22
8	24
9	26
10	27
11	28
12	30
13	31
14	32
15	34
16	35
17	36
18	37
19	39
20	40
21	41
22	42
23	43
24	45
25	46
26	47
27	48
28	50
29	51
30	52
31	54
32	55
33	57
34	58
35	60
36	61
37	63

38	65
39	67
40	69
41	71
42	73
43	76
44	80
45	83
46	88
47	93
48	100

9.4 Analysis Software

All statistical analyses will be performed using SAS, Version 9.4 or higher.