ApoPharma Inc.

STATISTICAL ANALYSIS PLAN

TIRCON2012V1-EXT

Long-term Safety and Efficacy Study of Deferiprone in Patients with Pantothenate Kinase-Associated Neurodegeneration (PKAN)

Final Version 1.0

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03 APR 2018
Date (DD-MMM-YYYY)

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List of Abbreviations

%	Percentage
<	Less than
>	Greater than
≥	Greater than or equal to
≤	Less than or equal to
ADR	Adverse Drug Reaction
AE	Adverse Event
ALP	Alkaline Phosphatase
ALT	Alanine aminotransferase or serum glutamic pyruvic transaminase (SGPT)
ANC	Absolute Neutrophil Count
AR	Autoregressive of Order
AST	Aspartate aminotransferase or serum glutamic oxaloacetic transaminase (SGOT)
BAD Scale	Barry Albright Dystonia Scale
BID	Twice Daily Dosing
BUN	Blood Urea Nitrogen
cm	Centimetre
CRF	Case Report Form
DDFM	Denominator Degrees of Freedom Method
DBS	Deep Brain Stimulation
DFP	Deferiprone
DSMB	Data and Safety Monitoring Board
ECG	Electrocardiogram
eCRF	electronic Case Report Form
GGT	Gamma-glutamyl Transferase
ITT	Intent-to-treat
kg	Kilogram
KR	Kenward and Roger's method
LDH	Lactate Dehydrogenase
LSM	Least Square Mean
LV	Left Ventricular
MedDRA	The Medical Dictionary for Regulatory Activities
mg	Milligram
mmHg	Millimetres of mercury
MMRM	Mixed-Effect Model Repeated Measure
NRBC	Nucleated Red Blood Cell
OC	Observed Cases
PGI-I	Patient's Global Impression of Improvement
PKAN	Pantothenate kinase-associated neurodegeneration
PP	Per protocol
PT	Preferred Terms

SADR	Serious Adverse Drug Reaction
SAE	Serious Adverse Event
SD	Standard Deviation
SOC	System Organ Class
WBC	White Blood Cell
WHO	World Health Organization
WHODD	World Health Organization Drug Dictionary

1 Introduction

This document outlines the statistical analysis plan for the clinical trial TIRCON2012V1-EXT at ApoPharma Inc.

2 Study Objectives

2.1 Primary Objective

To evaluate the long-term safety and tolerability of deferiprone in patients with PKAN.

2.2 Secondary Objective

The secondary objectives are:

- To evaluate the change in severity of dystonia over time in patients with PKAN treated with deferiprone;
- To evaluate global improvement over time in patients with PKAN treated with deferiprone.

3 Methods

3.1 Study Design

Study TIRCON2012V1-EXT is an 18-month, multi-center, single-arm, open-label extension of study TIRCON2012V1. In the initial study, patients with a diagnosis of PKAN were being randomized in a 2:1 ratio to receive 18 months of treatment with either deferiprone or placebo, respectively. All participants who completed TIRCON2012V1 were offered the opportunity to continue in the extension study, with the final visit of the initial study being considered Visit 1 of the extension study. Patients who had been randomized to receive deferiprone in study TIRCON2012V1 continued to receive deferiprone in the extension study, while those who had been randomized to receive placebo were switched to deferiprone. Since the initial study were still in progress at the time that the first patients entered the extension study, patients and study staff remained blinded until the initial study was over as to which product was received for the previous 18 months.

In the TIRCON-EXT study, patients will have their hematology blood counts monitored weekly, and will return to the study site at 6 months (Visit 2), 12 months (Visit 3), and 18 months (Visit 4) for assessments of safety and efficacy.

3.2 Determination of Sample Size and Study Power

There was no formal sample size and power calculation for this study. All patients who completed TIRCON2012V1 study were invited to enroll in the extension study. Among the 89 subjects randomized in TIRCON2012V1 study, 76 completed the study and 68 subjects were subsequently enrolled in this extension study (44 originally randomized to the deferiprone group and 24 in the placebo group).

3.3 Analysis Populations

The following study populations will be used for analysis: Safety, Intent-to-Treat (ITT), and Per-Protocol (PP). The safety population will be used for the analysis of safety endpoints. The ITT population will represent the primary analysis population for the evaluation of efficacy endpoints, and the PP population will be the secondary efficacy analysis population.

Safety Population

The Safety population will include all patients who took at least one dose of study drug in the extension study.

ITT Population

The ITT population will include all enrolled patients who received at least one dose of study drug and have a baseline and at least one post-baseline efficacy assessment in the extension study.

PP Population

The PP population will include all enrolled patients who complete the extension study and have an efficacy assessment at the end of the study, have no major protocol violations, and have no change in DBS and baclofen pump settings or medications that could have an impact on dystonia. Prior to database lock, protocol deviations and medications that could have an impact on dystonia will be reviewed for their seriousness, and patients with major deviations will be excluded from the PP population.

3.4 Interim Analysis

No interim analysis is planned.

3.5 Missing Data Handling and Derivation Rules

For safety data analysis, no imputation will be performed on the missing data and analysis will be based on observed cases.

For efficacy endpoints, the continuous variables will be summarized and analyzed as recorded on the case report forms (CRFs). If statistically significant imbalances are detected in the incidence of changes in DBS settings and outcome impacting medication use as well as the frequency of PRN drug or rescue medication between the initial study and the extension study, a Mixed-Effect Model Repeated Measure (MMRM) model will be used as the analysis method to compare the change in score from baseline between the initial study and the extension study for patients who received placebo in initial study (TIRCON2012V1) and the analysis will be based on observed cases. If no significant imbalance was detected, the paired t-test will be used as the analysis method and the last observed data will be used.

For the efficacy analysis on all patients who received DFP during the initial and the extension study, the last observation will be used to calculate the change from baseline for patients terminated early. As a sensitivity analysis, for early termination due to worsening of disease conditions or inadequate efficacy of the drug, as indicated in the CRF, the "worst score" method will be used for data imputation. That is, for continuous variables such as BAD total score at a particular time point, the worst score of all patients will be used to impute the missing data at that time point. For categorical variable such as responder, the worst category (treatment failure) will be assigned. For missing data due to missed visit, the last observation will be used to fill the void.

For BAD total score, if one or several component scores cannot be measured, then the same component score from the last visit will be carried forward and if it is also missing, the score from the next visit will be carried backward to fill the missing component score(s) before the total score is calculated.

Date of exposure will be defined as day 1 for all duration calculations. For example, age at entry will be calculated as the integer value of the expression: (date of exposure – date of birth) / 365.25. For patients on DFP in the initial study, the date of exposure during the initial study (TIRCON2012V1) will be used while for those switched from placebo to DFP in the extension study (TIRCON2012V1-EXT), the date of exposure during the extension study will be used.

3.6 Statistical Software and Level of Significance

All statistical analyses will be performed using SAS (version 9.3 or higher) on Windows operating system. Null hypotheses tested are that there are no differences in true parameter between comparison groups, unless otherwise stated. A two-sided *p*-value of 0.05 will be used as the significance level for the determination of statistical significance in all statistical tests.

4 Statistical Analyses

The efficacy endpoints are defined as follows:

All patients:

- Change in the BAD total score from baseline (defined as prior to the start of deferiprone therapy) to Visit 4, as assessed by central evaluation of videotapes

- Proportion of patients with improved or unchanged BAD scale total score between baseline and Visit 4 (responder analysis, responders defined as change in BAD total score to be ≤0)

- Change from baseline to Visit 4 in BAD scale score per body region (eyes, mouth, neck, trunk, and each upper and lower extremity), as assessed by central evaluation of videotapes

- PGI-I score at Visit 4

- Proportion of patients showing an improvement on PGI-I at Visit 4 (responder analysis, responders are defined as patients whose conditions have not deteriorated; patients who have "no change", or are "minimally improved", "much improved" or "very much improved" in the PGI-I questionnaire at the last study visit)

The time points for these efficacy endpoints are defined as follows:

- For patients who received deferiprone in the initial study, the baseline visit of that study will be treated as the baseline visit of TIRCON2012V1-EXT as well. Thus, Visit 1 of the extension study (Week 0) will be Year 1.5 (month 18), and Visit 4 (Week 78) will be Year 3 (month 36).

- For patients who received placebo in the initial study, Visit 1 of the extension study (Week 0) will be the baseline visit. Thus, Visit 4 (Week 78) will be Year 1.5 (month 18).

Patients who received placebo in initial study:

For this group only, for each measure, the changes seen between the start and completion of the initial study (TIRCON2012V1) (i.e., following 18 months on placebo) will be compared against the changes seen between the start and completion of extension study (TIRCON2012V1-EXT) (i.e., following 18 months on deferiprone), as follows:

- Comparison of change in BAD total score from baseline to completion of the initial study vs. change in BAD total score from baseline to completion of the extension study

- Comparison of the proportion of patients with improved or unchanged BAD scale total score between baseline and completion of the initial study vs. the proportion

with improved or unchanged BAD scale total score from baseline to completion of the extension study (responder analysis)

- Comparison of the change in BAD score per body region between baseline and completion of the initial study vs. change in BAD score per body region between baseline and completion of the extension study

- Comparison of PGI-I score at the completion of the initial study vs. PGI-I score at the completion of the extension study

- Comparison of the proportion of patients showing an improvement on PGI-I at completion of the initial study vs. the proportion showing an improvement at completion of the extension study (responder analysis)

The following time window will be employed to classify the efficacy data into each scheduled visit according to the time elapsed from the first medication date (date of exposure) to the assessment date:

Month 6 visit: 3 to <9 months

Month 12 visit: 9 to <15 months

Month 18 visit: 15 to <21 months

Month 24 visit: 21 to <27 months

Month 30 visit: 27 to <33 months

Month 36 visit: 33 to <39 months

The exact calculation of time elapsed from the date of exposure to the sample assessment date is: Time elapsed = (date of sample assessment) – (date of exposure) +1. The resulting time elapsed will be expressed in months and will be used for data tabulation and trend analysis. If multiple measurements for an outcome are available at the same visit for a subject, the average value will be used for that outcome for this subject at that visit.

A paired t-test will be used to assess the statistical significance of the changes in the efficacy outcomes from baseline to the end of study. For the BAD total score and for PGI-I, the proportions of patients determined to be responders at the end of study will be calculated and presented along with 95% confidence intervals.

The incidence of changes in DBS settings and outcome impacting medication use as well as the frequency of PRN drug or rescue medication use will be tabulated by visit and treatment group for patients on placebo in the initial study. The incidence of changes in DBS settings and outcome impacting medication use as well as the frequency of PRN drug or rescue medication use will be compared between the initial study and the

extension study. Continuous variables will be compared by paired t-tests while proportions by McNemar's test. If statistically significant imbalances are detected, they will be adjusted accordingly for the comparison of changes in BAD and PGI-I between the initial study and the extension study by using a MMRM model approach that is consistent with the analysis of these two efficacy measures in the initial study. The MMRM model is specified below.

The MMRM model will be applied to non-imputed data from the observed cases (OC) data set. Let y_i denote the vector of n_i continuous post-baseline measurements observed for study patient *i*. Each response (i.e., each element of y_i) will be defined as the patient's score at that occasion minus the baseline score.

The model will assume that the distribution of y_i is multivariate normal,

$$y_i \sim N(X_i\beta, \Sigma_i),$$

where X_i is a design matrix of dimensions $n_i \times p$, β is a vector of coefficients of length p, and Σ_i is an $n_i \times n_i$ covariance matrix.

The MMRM model will include baseline value of the outcome as a covariate and treatment group as the main factor in the model. A change in DBS settings or use of medications that have the potential to affect dystonia symptoms during the study may confound the treatment effect assessment (named outcome impacting medication use hereafter) for DFP vs. placebo between the initial study and the extension study for patients who were on placebo in the initial study. Hence, both variables will also be included in the MMRM model as visit-dependent covariates.

The visit-dependent covariate for DBS settings change is defined as follows: for patients with DBS at enrollment, if there is any DBS setting change since the previous visit, it will be coded as 'DBS Setting Change' for the current visit or 'No DBS Setting Change' otherwise. For example, if a patient has a DBS setting change between the outcome assessment dates at month 6 visit and month 12 visit, it will be coded as 'DBS Setting Change' for month 12 visit in the model. For those patients without DBS at enrollment, it will be coded as 'No DBS'. A discrete variable, DBSCHG, with three categories will be included in the MMRM model.

The visit-dependent covariate for the outcome impacting medication use will be defined according to whether the patient is on a regular dosing regimen or on a PRN (as needed) dosing regimen between two visits. For patients treated on a regular dosing regimen, if there is a dose change or starting of new medication since the previous visit, it will be coded as 'Yes' for the current visit and the future follow-up visits or 'No' otherwise in the model. For patients who do not use any outcome impacting medication, it will be coded as 'No'.

For patients on a PRN (as needed) dosing regimen, the visit-dependent covriate will be defined according to the treatment impact period in the following table.

Medication	Treatment impact period
Baclofen	30 days
Trihexyphenidyl	30 days
Clonazepam	30 days
Tizanidine	30 days
Botox	60 days
Tetrabenazine	90 days

If the PRN drug is started within the treatment impact period prior to the assessment date of an outcome for a visit, it will be coded as 'Yes' for that visit. If the drug is started outside this time window but is not interrupted within this period, it will also be coded as 'Yes' for that visit. Under other conditions, it will coded as 'No' in the model. A binary variable for the outcome impacting medication use, RESMED, will be included in the MMRM model.

The frequency of PRN drug or rescue medication use between two outcome assessment dates of current visit and the previous visit will also be included in the MMRM model as a quantitative visit-dependent covariate, NDRUG, for the current visit.

The MIXED procedure in SAS will be used for the MMRM model analysis. Data within each patient at different visits will be considered repeated measures. AR(1) (autoregressive of order 1) covariance structure will be used to model the correlation between repeated measures within the same patient and Kenward and Roger's method will be used to estimate the denominator degrees of freedom. The 95% confidence interval (CI) for the difference between the two treatments will be calculated by the LSMEANS statement.

A sample SAS code for the MMRM model is presented in the box below:

```
proc mixed;
  class TREAT USUBJID VISIT DBSCHG RESMED;
  model CHG=TREAT VISIT TREAT*VISIT BASE DBSCHG RESMED
NDRUG/solution ddfm=kr;
  repeated VISIT/ subject=USUBJID type=ar(1);
  lsmeans TREAT*VISIT / diff cl;
run;
```

where TREAT is the indicator variable for treatment group (DFP vs. Placebo), USUBJID represents the patient ID, VISIT is the discrete variable representing the scheduled study visit after the baseline visit, DBSCHG is the discrete variable with three categories for

DBS settings change (DBS Setting Change, No DBS Setting Change, No DBS), RESMED is the binary variable for outcome impacting medication use (Yes vs. No), CHG is the change in value of efficacy outcome from baseline to the scheduled visit, BASE is the baseline value of efficacy outcome, and NDRUG is the frequency of PRN drug or rescue medication use.

PGI-I is already a measurement of change from baseline and thus will be used directly as the outcome variable and baseline BAD score will be included as the baseline value in all models.

McNemar's test will be used to compare the proportion of responders in the initial study with the proportion of responders in the extension study.

For all patients who were on DFP in both studies, the longitudinal response profile for BAD score will be explored by a MMRM mdoel with time modelled as a continuous variable.

For this model, AR(1) (autoregressive of order 1) covariance structure will be used to model the correlation between repeated measures within the same patient and Kenward and Roger's method will be used to estimate the denominator degrees of freedom.

A sample SAS code for this MMRM model is presented in the box below:

```
proc mixed;
  class USUBJID VISIT;
  model BAD= TIME /solution ddfm=kr;
  repeated VISIT/ subject=USUBJID type=ar(1);
run;
```

where USUBJID represents the patient ID, VISIT is the discrete variable representing the scheduled study visit after the baseline visit, BAD is the value of BAD score at each time point, and TIME is the time in months at each time point corresponding to each visit.

4.1 Patient Dispositions and Drug Exposure

Patient disposition, based on the ITT population , will be summarized and presented, including the number and percentages of patients who were enrolled, completed the study, and withdrew (including reasons for withdrawals).

For each patient, the compliance on the study drug will be computed from the study drug dispensing and accountability eCRFs obtained at each visit. The extent of exposure to the study medication taken during the study and the compliance will be summarized with descriptive statistics.

The number of enrolled patients for each study site will be presented and the number of subjects included in each population will be tabulated.

4.2 Patient Characteristics

Baseline characteristics for continuous variables will be summarized by mean, standard deviation, minimum, median, and maximum values; and baseline characteristics for discrete variables will be summarized with frequency and percentages.

4.2.1 Demographics and Baseline Characteristics

Demographic data such as age, sex, ethnicity, and race will be summarized. Baseline characteristics at the initial study will also be tabulated.

4.3 Efficacy Analyses

All efficacy endpoints will be analyzed based on the ITT population. The analyses will be repeated for PP population for outcomes defined for BAD total score and PGI-I as sensitivity analyses. Detailed definition of BAD scale and PGI-I can be found in section 7.1 of the study protocol.

4.3.1 Efficacy Endpoints

<u>All patients:</u>

For the efficacy measures of BAD (total score and by body region) and PGI-I, the value at each of the measurement time points defined in section 4 will be determined and summarized using descriptive statistics for all patients on DFP treatment. Similar data will also be presented by the treatment group received in initial study.

A paired t-test will be used to assess the statistical significance of the changes in these efficacy outcomes from baseline to the end of study (Visit 4, month 18 or 36 as defined in section 4).

For the BAD total score and for PGI-I, the proportions of patients determined to be responders at the end of study (Visit 4) will be calculated and presented along with 95% confidence intervals.

The mean trajectory of BAD (total score and by body region) and PGI-I by time will be plotted. The longitudinal trend for BAD total score and by body region will be explored by the MMRM mdoel with time modelled as a continuous variable as defined in section 4 for all time points where patients were on DFP.

<u>Patients who received placebo in initial study:</u>

For the efficacy measures of BAD (total score and by body region) and PGI-I, the value at each of the measurement time points defined in section 4 will be determined and summarized using descriptive statistics for each study period.

A paired t-test will be used to compare the change in BAD (total score and by body region) between the start and completion of the initial study to that between the start and completion of the extension study. The same test will be repeated for the PGI-I data.

The incidence of changes in DBS settings and outcome impacting medication use as well as the frequency of PRN drug or rescue medication use will be tabulated and compared between the initial study and the extension study. If statistically significant imbalances are detected, they will be adjusted accordingly for the comparison of changes in BAD and PGI-I between the initial study and the extension study by using the MMRM model as defined in section 4.

For the BAD total score and for PGI-I, McNemar's test will be used to compare the proportion of responders in the initial study with the proportion of responders in the extension study.

4.3.2 Exploratory Analyses/Sensitivity Analysis

In order to explore potential differences in the change in BAD from baseline to Visit 4 and PGI-I at Visit 4 across population subgroups, subgroup analyses will be performed for the ITT population on the following factors assessed at the baseline of the initial study: Age at onset of motor symptoms (<6 years vs. ≥6 years), DBS (Deep Brain Stimulation, Yes vs. No), Region (US vs. Europe), and Duration of disease (>5 years vs. <=5 years).

Besides analysis for the ITT population, the efficacy analyses will also be repeated for outcomes defined based on BAD total score and PGI-I for the PP population as sensitivity analyses.

As a sensitivity analysis, the statistical analysis on the change in the BAD total score from baseline to Visit 4 and PGI-I at Visit 4 will be repeated with the missing data being imputed as described in section 3.5 based on the ITT population.

4.4 Safety Analyses

The safety endpoints include:

- Adverse events (AEs): Frequency, severity, time to onset, duration, and relatedness to study product
- Serious adverse events (SAEs): Frequency, severity, time to onset, duration, and relatedness to study product

- Number of discontinuations due to AEs
- Hematology assessments
- Blood chemistry assessments
- ECG assessments

All safety data collected will be presented in listings and summary tables or graphs to give an overview of the safety findings. All safety endpoints will be analyzed based on the safety population. For patients continuing on deferiprone in the extension study, this time period will be from the start of TIRCON2012V1 to the completion of TIRCON2012V1-EXT; for those who received placebo in the initial study and are switching to deferiprone in the extension study, it will be from the start to the completion of the extension study.

For those patients who do not follow the scheduled time window exactly for each visit or withdraw from the study early, the following time window will be employed to classify the safety data into each scheduled visit according to the time elapsed from the first medication date (date of exposure) to the assessment date:

Month 1.5 visit: 0.75 to <2.25 months

Month 3 visit: 2.25 to <4.5 months

Month 6 visit: 4.5 to <9 months

Month 12 visit: 9 to <15 months

Month 18 visit: 15 to <21 months

Month 24 visit: 21 to <27 months

Month 30 visit: 27 to <33 months

Month 36 visit: 33 to <39 months

4.4.1 Adverse Events

A summary table of adverse events will include the following information:

- number of patients exposed to study treatment,
- number of patients experiencing at least one AE,
- number of patients experiencing at least one severe AE,

- number of patients experiencing at least one serious AE,
- number of patients experiencing at least one drug-related AE,
- number of deaths,
- total number of patients withdrawn,
- number of withdrawals due to AEs.

All adverse experiences will be coded using MedDRA (Medical Dictionary for Regulatory Activities) and will be summarized by MedDRA System Organ Class (SOC) and Preferred Term. Adverse events will be defined as: 1) AEs that occurred or worsened (increased in intensity and/or frequency) on or after the first dose of study medication, 2) AEs with a missing start date or a stop date on or after the first dose of study medication, 3) AEs with both a missing start and stop date. Events that occur within 14 days after treatment discontinuation will also be considered AEs. Serious adverse events that occur within 30 days after treatment discontinuation will be included in the database.

Adverse events will be summarized using the total number of AEs, the total number and percent of patients who experience an AE, and the number and percent of patients who experienced an AE within each SOC (and preferred term within an SOC). The rate of each AE (per 100 patient years) will also be calculated. AEs will also be presented by intensity (mild, moderate, severe), by seriousness (serious, non-serious), and by relationship to study medication (at least possibly related, not related). The number and percentage of patients who are withdrawn from the study due to AEs will be calculated, and the AEs involved will be summarized in a frequency table. Time to onset and duration of all AEs with an incidence of >5%, and of any AEs of special interest (e.g., worsening of dystonia), will be summarized with descriptive statistics.

Patients who have experienced the same AE multiple times will be counted only once for the corresponding preferred term. Similarly, if a patient experiences multiple AEs within the same SOC, that patient will be counted only once for that SOC. AEs will be tabulated by presenting SOCs alphabetically and, within each SOC, presenting the preferred terms in decreasing order of the total number of patients who experienced each type of AE. In summaries presenting the incidence of AEs by intensity, seriousness, and relation to study medication, a patient with multiple events coded to a given preferred term or SOC will be counted only once for that preferred term or SOC according to the most severe event, the most serious event, or the event with the closest relationship to study medication.

Listings of SAEs, of withdrawals due to AEs, and of deaths will be provided separately and described in patient narratives.

4.4.2 Laboratory Data

Descriptive statistics for each clinical laboratory test will be presented for each visit as defined above for hematology and for blood biochemistry. For each test, if multiple measurements are taken on the same scheduled visit for a subject, average value will be used for this subject at that visit. According to the laboratory normal ranges, laboratory test results will be categorized as low (< lower normal limit), normal (within normal range), and high (> upper normal limit). Shift tables comparing the distributions of these three categories at baseline versus end of study for parameters of interest will be presented.

Continuous data will also be presented graphically for examination of possible trends.

Clinically significant laboratory values will be reported in the adverse event analysis.

4.4.3 Vital Signs, Weight and Height

Descriptive statistics will be presented for temperature, heart rate, respiratory rate, systolic blood pressure, diastolic blood pressure, weight, height, at baseline and each relevant visit. Data will also be presented graphically for examination of possible trends.

4.4.4 12-Lead ECG

Clinically significant ECG abnormalities will be reported. The number and percentage of patients with normal and abnormal ECG results will be provided.

Descriptive statistics will be presented for 12-lead ECG parameters at each relevant visit.

4.4.5 Treatment Compliance

Patients will be instructed on how to take the study medication. Compliance will be evaluated by calculating the volume of medication dispensed and the amount of unused drug supply remaining in the bottle. The compliance to the study medication at each visit will be summarized descriptively in a table.

4.4.6 Concomitant Medications

Medications will be coded using the World Health Organization (WHO) Drug Dictionary. Medications taken during the course of the trial (on or after the first study drug dose and before or on the study termination date) will be considered as concomitant medications. Medications started after the study termination date will not be reported in tables, but will be presented in patient data listings. Concomitant medications used to treat adverse events will be differentiated from others.

Concomitant medications will be summarized according to the preferred terms only. To count the number of patients who took a medication, a patient taking the same medication multiple times will only be counted once for that medication. Medications will be tabulated in decreasing order of the total number of patients who took each medication. In addition, the total number of patients to ever take any concomitant medications will be presented.

Concomitant medications will be presented based on the Safety population.

5 Listing of Tables and Figures

The listing of tables and figures shows the summary tables and figures that will be produced based on the statistical analysis detailed in this document. Summary tables and figures are numbered following ICH structure but the final numberings for tables and/or figures in the clinical study report can be changed if more tables and/or figures are added.

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Figure 14.3.2.11 Mean line graph for alanine transaminase (ALT) over time – safety population
Figure 14.3.2.12 Mean line graph for albumin over time – safety population
Figure 14.3.2.13 Mean line graph for blood urea nitrogen (BUN) over time – safety population
Figure 14.3.2.14 Mean line graph for calcium over time – safety population
Figure 14.3.2.15 Mean line graph for creatinine over time – safety population
Figure 14.3.2.16 Mean line graph for uric acid over time – safety population
Figure 14.3.2.17 Mean line graph for alkaline phosphatase (ALP) over time – safety population
Figure 14.3.2.18 Mean line graph for amylase over time – safety population

14.3.3 Vital signs, Weight and Height

Figure 14.3.3.1 Mean line graph for temperature over time – safety population
Figure 14.3.3.2 Mean line graph for resting heart rate over time – safety population
Figure 14.3.3.3 Mean line graph for respiration rate over time – safety population
Figure 14.3.3.4 Mean line graph for systolic blood pressure over time – safety population
Figure 14.3.3.5 Mean line graph for diastolic blood pressure over time – safety

population
Figure 14.3.3.6 Mean line graph for weight over time – safety population
Figure 14.3.3.7 Mean line graph for height over time – safety population

6 Data Listings and Individual Subject Graphs

Data listings are numbered following ICH structure. The final numberings for subject data listings in the clinical study report can be changed if more subject data listings are made in the addition to those in the SAP.

16.2 Subject Data Listings

16.2.1 Subject Disposition

16.2.1.1 Listing of Disposition

16.2.2 Protocol Deviations

16.2.2.1 Listing of Protocol Deviations

16.2.3 Subjects Excluded from the Efficacy Analysis

16.2.3.1 Assignment of Subjects to Analysis Sets

16.2.4 Demographic Data and Medical History

16.2.4.1 Listing of Informed Consent Form
16.2.4.2 Listing of Demographics
16.2.4.3 Listing of PKAN History
16.2.4.4 Listing of PKAN Symptoms
16.2.4.5 Listing of Physical Exam
16.2.4.6 Listing of Medical History

16.2.5 Compliance and/or Drug Concentration Data

16.2.5.1 Listing of Compliance
16.2.5.2 Listing of Exposure
16.2.5.3 Listing of Changes to Exposure

16.2.6 Efficacy Data

16.2.6.1 Listing of Barry Albright Dystonia (BAD) score
16.2.6.2 Listing of Patient's Global Impression of Improvement (PGI-I)

16.2.7 Adverse Events Listing

16.2.7.1 Listing of Medical Events
16.2.7.2 Listing of Adverse Events
16.2.7.3 Listing of Adverse Drug Reactions
16.2.7.4 Listing of Serious Adverse Events
16.2.7.5 Listing of Serious Adverse Drug Reactions

16.2.8 Listing of Individual Laboratory Measurements by Subjects

16.2.8.1 Listing of Hematology
16.2.8.2 Listing of Biochemistry
16.2.8.3 Listing of Urinalysis
16.2.8.4 Listing of Pregnancy Test

16.2.9 Other Listings

16.2.9.1 Listing of Vital Signs
16.2.9.2 Listing of Height and Weight
16.2.9.3 Listing of Concomitant Medications
16.2.9.4 Listing of Deep Brain Stimulator (DBS) / Baclofen Pump Setting Changes
16.2.9.5 Listing of Telephone Contacts
16.2.9.6 Listing of Bottle Numbers

16.3 Individual Subject Graphs

16.3.1 Line plot of ANC over time by patient
16.3.2 Line plot of haemoglobin over time by patient
16.3.3 Line plot of platelets over time by patient
16.3.4 Line plot of total WBC over time by patient
16.3.5 Line plot of MCV over time by patient
16.3.6 Line plot of alanine transferase over time by patient
16.3.7 Line plot of albumin over time by patient
16.3.8 Line plot of alkaline phosphatase over time by patient
16.3.9 Line plot of amylase over time by patient
16.3.10 Line plot of aspartate transaminase over time by patient
16.3.11 Line plot of total bilirubin over time by patient
16.3.12 Line plot of blood urea nitrogen over time by patient
16.3.13 Line plot of calcium over time by patient
16.3.14 Line plot of chloride over time by patient
16.3.15 Line plot of creatinine over time by patient

16.3.16 Line plot of gamma-glutamyltransferase over time by patient
16.3.17 Line plot of glucose over time by patient
16.3.18 Line plot of lactate dehydrogenase over time by patient
16.3.19 Line plot of potassium over time by patient
16.3.20 Line plot of total protein over time by patient
16.3.21 Line plot of serum ferritin over time by patient
16.3.22 Line plot of sodium over time by patient
16.3.23 Line plot of uric acid over time by patient
16.3.24 Line plot of BAD total score over time by patient
16.3.25 Line plot of PGI-I score over time by patient

7 Table Shells

The following table shells provide a framework for the display of data from this study. These tables may not be designed exactly as shown in the shells, but are intended to reflect the general layout of the data that will be included in the clinical study report. Note that 'c' in the table shells indicates an alphanumeric character and 'x' indicates a number from 0 to 9. The analysis population will be indicated at the end of table title. Some tables will be based on both ITT and PP populations, and those tables for PP population will have a 'a' added to the table number so that Table x.x for ITT population and Table x.xa for PP population. Tables generated as sensitivity analyses will have a 's' added to the table number, such as Table x.xs.

Disposition tables

Table 14.1.1 Number of patients in different populations

Population	Placebo-DFP	DFP-DFP	Overall
ITT	xx	xx	xx
PP	xx	xx	xx
Safety	xx	xx	xx

Table 14.1.2 Subject disposition – ITT population

	Placebo-DFP	DFP-DFP	Overall
Enrolled	xx	xx	xx
Exposed	xx	xx	xx
Completed	xx	xx	xx
Withdrawn	xx	xx	xx

Table 14.1.3 Subject exposure to study medication – ITT population

	Group		
	Placebo-DFP (N=xx)	DFP-DFP (N=xx)	Overall (N=xx)
Subjects Exposed	xx	xx	xx
Total Exposure (person-years)	xxx.x	xxx.x	xxx.x
Length of Exposure (years)			
Mean (SD)	xx.xx (xx.x)	xx.xx (xx.x)	xx.xx (xx.x)
Median	xx.x	xx.x	xx.x
(Min, Max)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)
Duration of Exposure [n(%)]			
>= 1 month	xx (xx)	xx (xx)	xx (xx)
>= 6 months	xx (xx)	xx (xx)	xx (xx)
Repeat for 9, 12,15, 18 months	….	….	….

Table 14.1.4 Number of patients enrolled by study site – ITT population

Country	Site	Group		
		Placebo-DFP	DFP-DFP	Overall
xxx	000x	xx	xx	xx
…	…	xx	xx	xx
Total	x	xx	xx	xx

Table 14.1.5 Summary of the reasons for not completing the study – ITT population

		Group		
		Placebo-DFP (N=xx)	DFP-DFP (N=xx)	Overall (N=xx)
Reason	Detail	n (%)	n (%)	n (%)
Adverse event	Ccccc	xx (xx)	xx (xx)	xx (xx)
	Ccccc	xx (xx)	xx (xx)	xx (xx)
Voluntary withdrawal	Ccccc	xx (xx)	xx (xx)	xx (xx)
	Ccccc	xx (xx)	xx (xx)	xx (xx)
Lost to follow up	Ccccc	xx (xx)	xx (xx)	xx (xx)
	Ccccc	xx (xx)	xx (xx)	xx (xx)
Investigator decision	Ccccc	xx (xx)	xx (xx)	xx (xx)
	Ccccc	xx (xx)	xx (xx)	xx (xx)
Protocol violation	Ccccc	xx (xx)	xx (xx)	xx (xx)
	Ccccc	xx (xx)	xx (xx)	xx (xx)
Worsening of the disease/ Lack of efficacy	Ccccc	xx (xx)	xx (xx)	xx (xx)
	Ccccc	xx (xx)	xx (xx)	xx (xx)
Other	Ccccc	xx (xx)	xx (xx)	xx (xx)
	Ccccc	xx (xx)	xx (xx)	xx (xx)
Total		xx (xx)	xx (xx)	xx (xx)

Demographics and baseline characteristics tables

Table 14.1.6 Summary of demographics data at baseline of initial study – ITT population

	Group			
	Placebo-DFP (N=xx)	DFP-DFP (N=xx)	Overall (N=xx)	DFP vs Placebo *p*-value§
Age (years) (Mean ± SD) (Minimum, Median, Maximum)	 xx.x ± xx.x (xx.x, xx.x, xx.x)	 xx.x ± xx.x (xx.x, xx.x, xx.x)	 xx.x ± xx.x (xx.x, xx.x, xx.x)	0.xxxx
Sex: n (%) Female Male	 xx (xx) xx (xx)	 xx (xx) xx (xx)	 xx (xx) xx (xx)	0.xxxx
Racial Origin: n (%) White Black Asian Native American Native Hawaiian or Other Pacific Islander Multi-Racial	 xx (xx) xx (xx) xx (xx) xx (xx) xx (xx) xx (xx)	 xx (xx) xx (xx) xx (xx) xx (xx) xx (xx) xx (xx)	 xx (xx) xx (xx) xx (xx) xx (xx) xx (xx) xx (xx)	0.xxxx
Ethnic Origin: n (%) Hispanic/Latino Other	 xx (xx) xx (xx)	 xx (xx) xx (xx)	 xx (xx) xx (xx)	0.xxxx

§ T-test for means and Fisher's exact test for percentages

Similar Table 14.1.6a will be based on PP population

Table 14.1.7 Summary of baseline characteristics at the initial study – ITT population

	Group			
	Placebo-DFP (N=xx)	DFP-DFP (N=xx)	Overall (N=xx)	DFP vs Placebo *p*-value§
Age (years) at onset of motor symptoms				0.xxxx
n	xx	xx	xx	
(Mean ± SD)	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x	
(Minimum, Median, Maximum)	(xx.x, xx.x, xx.x)	(xx.x, xx.x, xx.x)	(xx.x, xx.x, xx.x)	
Duration of disease (years)				0.xxxx
n	xx	xx	xx	
(Mean ± SD)	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x	
(Minimum, Maximum)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	
DBS: n (%)				0.xxxx
Yes	xx (xx)	xx (xx)	xx (xx)	
No	xx (xx)	xx (xx)	xx (xx)	
Baclofen pump: n (%)				0.xxxx
Yes	xx (xx)	xx (xx)	xx (xx)	
No	xx (xx)	xx (xx)	xx (xx)	
BAD				0.xxxx
n	xx	xx	xx	
(Mean ± SD)	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x	
(Minimum, Maximum)	(xx.x, xx.x)	(xx.x, xx.x)	(xx.x, xx.x)	

§ T-test for means and Fisher's exact test for percentages
Similar Table 14.1.7a will be based on PP population

Efficacy outcomes tables

Table 14.2.1.1 BAD score at each follow-up visit by treatment group in initial study – ITT population

	Visit	Placebo-DFP[§] (N=xx)	DFP-DFP[§] (N=xx)
BAD n Mean (SD) Median (Min, Max)	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 24	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 30	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)

Similar Table 14.2.1.1a will be based on PP population

§ Placebo-DFP group includes all patients who took Placebo during initial study and switched to DFP during the extension study; DFP-DFP group includes all patients who took DFP during initial study and continued on DFP during the extension study. These definitions are applicable to all tables with these treatment groups.

Table 14.2.1.2 BAD score at each follow-up visit for all patients on DFP – ITT population

	Visit	DFP[§] (N=xx)
BAD n Mean (SD) Median (Min, Max)	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 24	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 30	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x)

Similar Table 14.2.1.2a will be based on PP population

§ DFP group includes all patients who ever took DFP during initial and extension study. This definition is applicable to all tables with this treatment group.

Table 14.2.1.3 Change in BAD score at each follow-up visit by treatment group in initial study – ITT population

	Visit	Placebo-DFP (N=xx)	DFP-DFP (N=xx)
Change in BAD n Mean (SD) Median (Min, Max) *p*-value[§]	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 24	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 30	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx

	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx

§ p-value from paired t-test
Similar Table 14.2.1.3a will be based on PP population

Table 14.2.1.4 Change in BAD score from baseline at each follow-up visit for all patients on DFP – ITT population

	Visit	DFP (N=xx)
Change in BAD n Mean (SD) Median (Min, Max) *p*-value[§]	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 24	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 30	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx

	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx

§ p-value from paired t-test
Similar Table 14.2.1.4a will be based on PP population

Table 14.2.1.5 BAD score per body region at each follow-up visit by treatment group in initial study – ITT population

Body Region	Visit	Placebo-DFP (N=xx)	DFP-DFP (N=xx)
Eyes n Mean (SD) Median (Min, Max)	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 24	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 30	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
Repeat for Mouth, Neck, Trunk, Left and right upper extremity, Left and right lower extremity	…	…	…

Table 14.2.1.6 BAD score per body region at each follow-up visit for all patients on DFP – ITT population

Body Region	Visit	DFP (N=xx)
Eyes n Mean (SD) Median (Min, Max)	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 24	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 30	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
Repeat for Mouth, Neck, Trunk, Left and right upper extremity, Left and right lower extremity	…	…

Table 14.2.1.7 Change in BAD score per body region from baseline at each follow-up visit by treatment group in initial study – ITT population

	Visit	Placebo-DFP (N=xx)	DFP-DFP (N=xx)
Change in Eyes Score n Mean (SD) Median (Min, Max) *p*-value[§]	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 24	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 30	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx

	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
Repeat for Mouth, Neck, Trunk, Left and right upper extremity, Left and right lower extremity	…	…	…

§ p-value from paired t-test

Table 14.2.1.8 Change in BAD score per body region from baseline at each follow-up visit for all patients on DFP – ITT population

	Visit	DFP (N=xx)
Change in Eyes Score n Mean (SD) Median (Min, Max) *p*-value[§]	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 24	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 30	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx

	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
Repeat for Mouth, Neck, Trunk, Left and right upper extremity, Left and right lower extremity	…	…

§ p-value from paired t-test

Table 14.2.1.9 Proportions of responders in BAD total score at each follow-up visit by treatment group in initial study – ITT population

	Visit	Placebo-DFP (N=xx)	DFP-DFP (N=xx)
Responder in BAD total score n (%)	Month 6	xx (xx.x)	xx (xx.x)
	Month 12	xx (xx.x)	xx (xx.x)
	Month 18	xx (xx.x)	xx (xx.x)
	Month 24	xx (xx.x)	xx (xx.x)
	Month 30	xx (xx.x)	xx (xx.x)
	Month 36	xx (xx.x)	xx (xx.x)

Similar Table 14.2.1.9a will be based on PP population

Table 14.2.1.10 Proportions of responders in BAD total score at each follow-up visit for all patients on DFP – ITT population

	Visit	DFP (N=xx)
Responder in BAD total score n (%)	Month 6	xx (xx.x)
	Month 12	xx (xx.x)
	Month 18	xx (xx.x)
	Month 24	xx (xx.x)
	Month 30	xx (xx.x)
	Month 36	xx (xx.x)

Similar Table 14.2.1.10a will be based on PP population

Table 14.2.1.11 PGI-I score at each follow-up visit by treatment group in initial study – ITT population

	Visit	Placebo - DFP (N=xx)	DFP - DFP (N=xx)
PGI-I n Mean (SD) Median (Min, Max) *p*-value§	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 24	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 30	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx

§ p-value from paired t-test

Similar Table 14.2.1.11a will be based on PP population

Table 14.2.1.12 PGI-I score at each follow-up visit for all patients on DFP – ITT population

	Visit	DFP (N=xx)
PGI-I n Mean (SD) Median (Min, Max) *p*-value§	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 24	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 30	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx
	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx

§ p-value from paired t-test

Similar Table 14.2.1.12a will be based on PP population

Table 14.2.1.13 Proportions of responders in PGI-I at each follow-up visit by treatment group in initial study – ITT population

	Visit	Placebo-DFP (N=xx)	DFP-DFP (N=xx)
Responder in PGI-I n (%)	Month 6	xx (xx.x)	xx (xx.x)
	Month 12	xx (xx.x)	xx (xx.x)
	Month 18	xx (xx.x)	xx (xx.x)
	Month 24	xx (xx.x)	xx (xx.x)
	Month 30	xx (xx.x)	xx (xx.x)
	Month 36	xx (xx.x)	xx (xx.x)

Similar Table 14.2.1.13a will be based on PP population

Table 14.2.1.14 Proportions of responders in PGI-I at each follow-up visit for all patients on DFP – ITT population

	Visit	DFP (N=xx)
Responder in PGI-I n (%)	Month 6	xx (xx.x)
	Month 12	xx (xx.x)
	Month 18	xx (xx.x)
	Month 24	xx (xx.x)
	Month 30	xx (xx.x)
	Month 36	xx (xx.x)

Similar Table 14.2.1.14a will be based on PP population

Table 14.2.1.15 Efficacy endpoints analysis for all patients on DFP: change in value at the end of study (Visit 4) – ITT population

	Visit	Score n Mean (SD)	Change from Baseline n Mean (SD)	*p*-value[§]
BAD Total Score	Baseline	xx xx.xx (xx.x)		
	Visit 4	xx xx.xx (xx.x)	xx xx.xx (xx.x)	0.xxxx
PGI-I	Visit 4		xx xx.xx (xx.x)	0.xxxx
Eyes score	Baseline	xx xx.xx (xx.x)		
	Visit 4	xx xx.xx (xx.x)	xx xx.xx (xx.x)	0.xxxx
Repeat for other body regions	….	….	….	….

§ p-value from paired t-test
Similar Table 14.2.1.15a will be based on PP population
Similar Table 14.2.1.15s will be based on missing data imputed as sensitivity analysis

Similar Tables 14.2.1.15.1 and 14.2.1.15.2 will be based on ITT population and Age at onset of motor symptoms (Age <6 vs. Age ≥6)
Similar Tables 14.2.1.15.3 and 14.2.1.15.4 will be based on ITT population and DBS (Deep Brain Stimulation Yes vs. No)
Similar Tables 14.2.1.15.5 and 14.2.1.15.6 will be based on ITT population and Region (US vs. Europe)
Similar Tables 14.2.1.15.7 and 14.2.1.15.8 will be based on ITT population and Duration of disease at baseline (>5 years vs. <=5 years)

Table 14.2.1.16 Efficacy endpoints analysis for all patients on DFP: proportions of responders in BAD total score and PGI-I at the end of study (Visit 4) – ITT population

	Visit	(N=xx)
Responder in BAD total score n (%) (95% CI)	Visit 4	xx (xx.x) (xx.x, xx.x)
Responder in PGI-I n (%) (95% CI)	Visit 4	xx (xx.x) (xx.x, xx.x)

Similar Table 14.2.1.16a will be based on PP population
Similar Table 14.2.1.16s will be based on missing data imputed as sensitivity analysis

Table 14.2.1.17 Trend analysis by MMRM model on BAD total score and by body region for all patients – ITT population

Dependent Variable	Time slope	95% CI of the Slope	*p*-value
BAD Total Score	xx.x	(xx.xx xx.x)	0.xxxx
Eyes	xx.x	(xx.xx xx.x)	0.xxxx
Repeat for Mouth, Neck, Trunk, Left and right upper extremity, Left and right lower extremity	….	….	….

Table 14.2.2.1 BAD total score at each follow-up visit for patients on placebo in initial study – ITT population

	Visit	Placebo in TIRCON (N=xx)	DFP in TIRCON-EXT (N=xx)
BAD n Mean (SD) Median (Min, Max)	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)

Similar Table 14.2.2.1a will be based on PP population

Table 14.2.2.2 Change in BAD total score from baseline at each follow-up visit for patients on placebo in initial study – ITT population

	Visit	Placebo in TIRCON (N=xx)	DFP in TIRCON-EXT (N=xx)	DFP Vs. Placebo *p*-value§
BAD n Mean (SD) Median (Min, Max) *p*-value§	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	0.xxxx
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	0.xxxx
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	0.xxxx
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	0.xxxx

§ Paired T-test
Similar Table 14.2.2.2a will be based on PP population

Table 14.2.2.3 BAD score per body region at each follow-up visit for patients on placebo in initial study – ITT population

	Visit	Placebo in TIRCON (N=xx)	DFP in TIRCON-EXT (N=xx)
Eyes n Mean (SD) Median (Min, Max)	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
Repeat for other body regions	….	….	….

Table 14.2.2.4 Change in BAD score per body region from baseline at each follow-up visit for patients on placebo in initial study – ITT population

	Visit	Placebo in TIRCON (N=xx)	DFP in TIRCON-EXT (N=xx)	DFP Vs. Placebo *p*-value§
Eyes n Mean (SD) Median (Min, Max) *p*-value§	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	0.xxxx
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	0.xxxx
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	0.xxxx
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	0.xxxx
Repeat for other body regions	….	….	….	

§ Paired T-test

Table 14.2.2.5 Proportions of responders in BAD total score at each follow-up visit for patients on placebo in initial study – ITT population

	Visit	Placebo in TIRCON (N=xx)	DFP in TIRCON-EXT (N=xx)	DFP Vs. Placebo *p*-value§
Responder in BAD total score n (%)	Month 6	xx (xx.x)	xx (xx.x)	0.xxxx
	Month 12	xx (xx.x)	xx (xx.x)	0.xxxx
	Month 18	xx (xx.x)	xx (xx.x)	0.xxxx

§ McNemar's test

Similar Table 14.2.2.5a will be based on PP population

Table 14.2.2.6 PGI-I score at each follow-up visit for patients on placebo in initial study – ITT population

	Visit	Placebo in TIRCON (N=xx)	DFP in TIRCON-EXT (N=xx)	DFP Vs. Placebo *p*-value§
PGI-I n Mean (SD) Median (Min, Max) *p*-value§	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	0.xxxx
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	0.xxxx
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	0.xxxx

§ Paired T-test

Similar Table 14.2.2.6a will be based on PP population

Table 14.2.2.7 Proportions of responders in PGI-I at each follow-up visit for patients on placebo in initial study – ITT population

	Visit	Placebo in TIRCON (N=xx)	DFP in TIRCON-EXT (N=xx)	DFP Vs. Placebo *p*-value§
Responder in PGI-I n (%)	Month 6	xx (xx.x)	xx (xx.x)	0.xxxx
	Month 12	xx (xx.x)	xx (xx.x)	0.xxxx
	Month 18	xx (xx.x)	xx (xx.x)	0.xxxx

§ McNemar's test

Similar Table 14.2.2.7a will be based on PP population

Table 14.2.2.8 Summary of DBS settings change and medication use with a potential outcome impact for patients on placebo in initial study – ITT population

Visit		Group	
		Placebo in TIRCON (N=xx)	DFP in TIRCON-EXT (N=xx)
Month 6	DBS Settings: n (%) DBS Setting Change No DBS Setting Change No DBS	 xx (xx) xx (xx) xx (xx)	 xx (xx) xx (xx) xx (xx)
	Outcome Impacting Medication Use: n (%) Yes No	 xx (xx) xx (xx)	 xx (xx) xx (xx)
	Frequency of PRN drug or rescue medication use (Mean ± SD) Median (Minimum, Maximum)	 xx ± xx.x xx (xx, xx)	 xx ± xx.x xx (xx, xx)
Repeat for other visits	…	…	…
Overall	…	…	…

Table 14.2.2.9 Efficacy endpoints analysis with MMRM model: Least square mean (LSM) change in score from baseline to Visit 4 for patients on placebo in initial study – ITT population

	Visit	Placebo in TIRCON (N=xx)	DFP in TIRCON-EXT (N=xx)	DFP - Placebo LSM Difference (95% CI)	*p*-value
BAD	Change from baseline to Visit 4 Mean (SD)	xx.xx (xx.x)	xx.xx (xx.x)	xx (xx.x xx.x)	0.xxxx
PGI-I	Score at Visit 4 Mean (SD)	xx.xx (xx.x)	xx.xx (xx.x)	xx (xx.x xx.x)	0.xxxx
BAD Eyes	Change from baseline to Visit 4 Mean (SD)	xx.xx (xx.x)	xx.xx (xx.x)	xx (xx.x xx.x)	0.xxxx
Repeat for other body regions	….	….	….	….	….

Table 14.2.3.1 Comparison of change in BAD total score from baseline to month 18 for patients on DFP in initial study and patients on placebo in initial study but switched to DFP in the extension study – ITT population

	Visit	DFP in TIRCON (N=xx)	DFP in TIRCON-EXT (N=xx)	*p*-value[§]
BAD n Mean (SD) Median (Min, Max) *p*-value[§]	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	xx xx.xx (xx.x) xx.x (xx.x, xx.x)	
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	0.xxxx
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	0.xxxx
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	xx xx.xx (xx.x) xx.x (xx.x, xx.x) 0.xxxx	0.xxxx

§ T-test

Safety outcomes tables

Table 14.3.1.1 Overall summary of adverse events – safety population

	Treatment Group
	DFP (N=xx)
Number of subjects with at least one AE	xx (xx%)
Number of subjects with at least one SAE	xx (xx%)
Number of subjects with at least one severe AE	xx (xx%)
Number of subjects with at least one ADR	xx (xx%)
Number of deaths	xx (xx%)
Number of subject withdrawn	xx (xx%)
Number of subject withdrawals due to AE	xx (xx%)

Table 14.3.1.2 Summary of adverse events – safety population

	DFP	
	Exposure (subject-years): x.xx	
	Total Subjects Exposed: xx	
	Total Events: xxx	
	Total Subjects Reporting: xx	
System Organ Class Preferred Term	N Subjects (%)	N Events (Rate/100 patient years)
CCCCCC	x (x.x)	x (x.xx)
Ccccc	x (x.x)	x (x.xx)
Ccccc	x (x.x)	x (x.xx)
Ccccc	x (x.x)	x (x.xx)
……..	x (x.x)	x (x.xx)

Table 14.3.1.3 Summary of adverse events related to iron deficiency – safety population

	DFP	
	Exposure (subject-years): x.xx	
	Total Subjects Exposed: xx	
	Total Events: xxx	
	Total Subjects Reporting: xx	
Preferred Term	N Subjects (%)	N Events (Rate/100 patient years)
Cccccc	x (x.x)	x (x.xx)
Cccccc	x (x.x)	x (x.xx)
Cccccc	x (x.x)	x (x.xx)
……..	x (x.x)	x (x.xx)

Table 14.3.1.4 Summary of adverse events related to PKAN – safety population

	DFP	
	Exposure (subject-years): x.xx	
	Total Subjects Exposed: xx	
	Total Events: xxx	
	Total Subjects Reporting: xx	
Preferred Term	N Subjects (%)	N Events (Rate/100 patient years)
Cccccc	x (x.x)	x (x.xx)
Cccccc	x (x.x)	x (x.xx)
Cccccc	x (x.x)	x (x.xx)
……..	x (x.x)	x (x.xx)

Table 14.3.1.5 All adverse events by severity – safety population

	DFP					
	Mild		Moderate		Severe	
	Exposure (subject-years): x.xx		Exposure (subject-years): x.xx		Exposure (subject-years): x.xx	
	Total Subjects Exposed: xx		Total Subjects Exposed: xx		Total Subjects Exposed: xx	
	Total Events: xxx		Total Events: xxx		Total Events: xxx	
	Total Subjects Reporting: xx		Total Subjects Reporting: xx		Total Subjects Reporting: xx	
System Organ Class Preferred Term	N Subjects (%)	N Events (Rate/100 patient years)	N Subjects (%)	N Events (Rate/100 patient years)	N Subjects (%)	N Events (Rate/100 patient years)
CCCCCC	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)
Cccccc	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)
Cccccc	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)
Cccccc	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)
……..	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)

Table 14.3.1.6 All adverse events by seriousness – safety population

	DFP			
	Non-serious		Serious	
	Exposure (subject-years): x.xx		Exposure (subject-years): x.xx	
	Total Subjects Exposed: xx		Total Subjects Exposed: xx	
	Total Events: xxx		Total Events: xxx	
	Total Subjects Reporting: xx		Total Subjects Reporting: xx	
System Organ Class Preferred Term	N Subjects (%)	N Events (Rate/100 patient years)	N Subjects (%)	N Events (Rate/100 patient years)
CCCCCC	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)
Cccccc	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)
Cccccc	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)
Cccccc	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)
……..	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)

Table 14.3.1.7 All adverse events by relatedness to study medication – safety population

	DFP			
	Related		Unrelated	
	Exposure (subject-years): x.xx		Exposure (subject-years): x.xx	
	Total Subjects Exposed: xx		Total Subjects Exposed: xx	
	Total Events: xxx		Total Events: xxx	
	Total Subjects Reporting: xx		Total Subjects Reporting: xx	
System Organ Class Preferred Term	N Subjects (%)	N Events (Rate/100 patient years)	N Subjects (%)	N Events (Rate/100 patient years)
CCCCCC	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)
Cccccc	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)
Cccccc	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)
Cccccc	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)
……..	x (x.x)	x (x.xx)	x (x.x)	x (x.xx)

Table 14.3.1.8 Summary of most common (>5%) adverse drug reactions – safety population

	DFP			
	Exposure (subject-years): x.xx			
	Total Subjects Exposed: xx			
	Total Events: xxx			
	Total Subjects Reporting: xx			
System Organ Class Preferred Term	N Subjects (%)	N Events (Rate/100 patient years)	Time to onset (Days) Mean (SD) Median (Min, Max)	Duration (Days) Mean (SD) Median (Min, Max)
CCCCCC	x (x.x)	x (x.xx)	xx.xx (xx.x) xx.x (xx.x, xx.x)	xx.xx (xx.x) xx.x (xx.x, xx.x)
Cccccc	x (x.x)	x (x.xx)	xx.xx (xx.x) xx.x (xx.x, xx.x)	xx.xx (xx.x) xx.x (xx.x, xx.x)
……..	x (x.x)	x (x.xx)	xx.xx (xx.x) xx.x (xx.x, xx.x)	xx.xx (xx.x) xx.x (xx.x, xx.x)

Table 14.3.2.1.1 Hematology at each visit – safety population

Test	Visit	DFP (N=xx)
Hemoglobin (g/L) n Mean (SD) Median (Min, Max)	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 1.5	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 3	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 24	xx xx.xx (xx.x) xx.x (xx.x, xx.x)

	Month 30	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
Repeat for other hematology parameters	…	…

Table 14.3.2.1.2 Hematology analysis: change in value at the end of study (Visit 4) – safety population

	Visit	n Mean (SD)	Change from Baseline n Mean (SD)	*p*-value§
Hemoglobin (g/L)	Baseline	xx xx.xx (xx.x)		
	Visit 4	xx xx.xx (xx.x)	xx xx.xx (xx.x)	0.xxxx
Repeat for other hematology parameters	….	….	….	….

§ p-value from paired t-test

Table 14.3.2.1.3 Shift table comparing three laboratory value categories at baseline and end of study: Hematology – safety population

Laboratory Test	Treatment	Baseline	End of study			Total
			Low	Normal	High	
Hemoglobin	DFP	Low	xx	xx	xx	xx
		Normal	xx	xx	xx	xx
		High	xx	xx	xx	xx
		Total	xx	xx	xx	xx
Repeat for other tests of interest						

Table 14.3.2.2.1 Blood biochemistry at each visit – safety population

Test	Visit	DFP (N=xx)
Seum Ferritin (ug/L) n Mean (SD) Median (Min, Max)	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 1.5	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 3	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 24	xx xx.xx (xx.x) xx.x (xx.x, xx.x)

	Month 30	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
Repeat for other biochemistry parameters	…	…

Table 14.3.2.2.2 Blood biochemistry analysis: change in value at the end of study (Visit 4) – safety population

	Visit	n Mean (SD)	Change from Baseline n Mean (SD)	*p*-value§
Seum Ferritin (ug/L)	Baseline	xx xx.xx (xx.x)		
	Visit 4	xx xx.xx (xx.x)	xx xx.xx (xx.x)	0.xxxx
Repeat for other biochemistry parameters	….	….	….	….

§ p-value from paired t-test

Table 14.3.2.2.3 Shift table comparing three laboratory value categories at baseline and end of study: Blood biochemistry – safety population

Laboratory Test	Treatment	Baseline	End of study			Total
			Low	Normal	High	
Seum Ferritin	DFP	Low	xx	xx	xx	xx
		Normal	xx	xx	xx	xx
		High	xx	xx	xx	xx
		Total	xx	xx	xx	xx
Repeat for other tests of interest						

Table 14.3.2.3.1 Proportions of abnormal urinalysis results in each visit – safety population

Test	Visit	DFP (N=xx)
Abnormal Urinalysis n Abnormal (n (%))	Baseline	xx xx (xx)
	Month 1.5	xx xx (xx)
	Month 3	xx xx (xx)
	Month 6	xx xx (xx)
	Month 12	xx xx (xx)
	Month 18	xx xx (xx)
	Month 24	xx xx (xx)
	Month 30	xx xx (xx)
	Month 36	xx xx (xx)

Table 14.3.3.1 Summary of vital signs at each visit – safety population

Test	Visit	DFP (N=xx)
Resting Heart Rate n Mean (SD) Median (Min, Max)	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 1.5	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 3	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 24	xx xx.xx (xx.x) xx.x (xx.x, xx.x)

	Month 30	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
Repeat for respiratory rate, systolic blood pressure, diastolic blood pressure	…	…

Table 14.3.3.2 Summary of weight at each visit – safety population

Test	Visit	DFP (N=xx)
Weight n Mean (SD) Median (Min, Max)	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 1.5	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 3	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 24	xx xx.xx (xx.x) xx.x (xx.x, xx.x)

	Month 30	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x)

Table 14.3.3.3 Summary of height at each visit – safety population

Test	Visit	DFP (N=xx)
Height n Mean (SD) Median (Min, Max)	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x)

Table 14.3.4.1 Summary of 12-lead ECG parameters at each visit – safety population

Test	Visit	DFP (N=xx)
Heart Rate (bpm) n Mean (SD) Median (Min, Max)	Baseline	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
Repeat for PR Interval, QRS Interval, QT Interval, QTcB Interval,and QTcF Interval	…	…

Table 14.3.4.2 Proportions of normal and abnormal ECG results in each visit – safety population

Test	Visit	DFP (N=xx)
ECG n Abnormal (n (%)) Normal (n (%))	Baseline	xx xx (xx) xx (xx)
	Month 18	xx xx (xx) xx (xx)
	Month 36	xx xx (xx) xx (xx)

Table 14.3.5.1 Treatment compliance (%) by visit – safety population

Parameter	Visit	DFP (N=xx)
Compliance (%) n Mean (SD) Median (Min, Max)	Month 1.5	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 3	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 6	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 12	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 18	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 24	xx xx.xx (xx.x) xx.x (xx.x, xx.x)
	Month 30	xx xx.xx (xx.x) xx.x (xx.x, xx.x)

	Month 36	xx xx.xx (xx.x) xx.x (xx.x, xx.x)

Table 14.3.6.1 Concomitant Medications – safety population

	DFP
	Exposure (subject-years): x.xx
	Total Subjects Exposed: xx
	Total Subjects Reporting: xx
Preferred Name	N Subjects (%)
Cccccc	x (x.x)
Cccccc	x (x.x)
……..	x (x.x)

Table 14.3.6.2 Rescue Medications – safety population

	DFP
	Exposure (subject-years): x.xx
	Total Subjects Exposed: xx
	Total Subjects Reporting: xx
Preferred Name	N Subjects (%)
Baclofen	x (x.x)
Diazepam	x (x.x)
……..	x (x.x)

Table 14.3.6.3 PRN Medications – safety population

	DFP
	Exposure (subject-years): x.xx
	Total Subjects Exposed: xx
	Total Subjects Reporting: xx
Preferred Name	N Subjects (%)
Botulinum toxin type A	x (x.x)
Baclofen	x (x.x)
Clonazepam	x (x.x)
……..	x (x.x)