STATISTICAL ANALYSIS PLAN

LA38-0411

The efficacy and safety of Ferriprox for the treatment of transfusional iron overload in patients with sickle cell disease or other anemias

Final Version 1.0

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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

α	Type I error rate
AE	Adverse Event
ANC	Absolute Neutrophil Count
ANCOVA	Analysis of Covariance
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical
CHQ	Child Health Questionnaire
CI	Confidence Interval
CRF	Case Report Form
CRO	Contract Research Organization
CTCAE	Common Terminology Criteria for Adverse Events
DFO	Deferoxamine
DFP	Deferiprone
DFX	Deferasirox
dw	dry weight
ECG	Electrocardiogram
eCRF	electronic Case Report Form
EDC	Electronic Data Capture
GCP	Good Clinical Practice
GGT	gamma-glutamyl transferase
Hb	Hemoglobin
HIV	Human Immunodeficiency Virus
HR	Heart rate
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ID	Identification
ITT	Intent to Treat
IVRS	Interactive Voice Response System
LIC	Liver Iron Concentration
LOCF	Last Observation Carried Forward
MDS	Myelodysplastic Syndrome
ME	Medical Event

MedDRA	Medical Dictionary for Regulatory Activities
mg	milligram
mg/g	milligram per gram
mg/kg/day	milligram/kilogram/day
mL	millilitre
MRI	Magnetic Resonance Imaging
NCI	National Cancer Institute
NDA	New Drug Application
OC	Observed Case
PP	Per-Protocol
PT	Preferred Term
RBCs	Red Blood Cells
SADR	Serious Adverse Drug Reaction
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SCD	Sickle Cell Disease
SD	Standard Deviation
SE	Standard Error
SOC	System Organ Class
SOP	Standard Operating Procedure
tid	three times a day
WHO	World Health Organization

1 INTRODUCTION

This document outlines the statistical analysis plan (SAP) for the efficacy and safety data of clinical study LA38-0411, entitled "The efficacy and safety of Ferriprox for the treatment of transfusional iron overload in patients with sickle cell disease or other anemias". The SAP for the quality of life data from SF-36 or Child Health Questionnaire (CHQ) has been prepared by QualityMetric Inc..

2 OBJECTIVES

2.1 Primary Objective

- To determine the efficacy of deferiprone vs. deferoxamine in the treatment of iron overload in patients with sickle cell disease (SCD) or other anemias.

2.2 Secondary Objectives

- To evaluate the effect of deferiprone vs. deferoxamine on the patients' quality of life;
- To evaluate the safety and tolerability of deferiprone vs. deferoxamine.

3 METHODS

3.1 Study Design

This study is a 52-week, prospective, multi-center, two-arm, randomized, open-label, parallel design study of deferiprone (Ferriprox) vs. deferoxamine.

3.2 Number of Patients

Originally, three hundred (300) male and female patients were planned to be enrolled into the study (200 patients for Ferriprox and 100 patients for deferoxamine in a 2:1 ratio for randomization). In a randomized study of two iron chelators for the treatment of iron overload in patients with sickle cell disease (Vichinsky E *et al.* 2007), mean ±SD reductions of 4.0 ± 1.5 mg/g dw and 4.5 ± 2.0 mg/g dw in LIC, as measured by SQUID, were observed (Figure 1 of the article, numerical values obtained from the authors) in patients from the baseline LIC categories of >7-14 mg/g dw or >14 mg/g dw after they were treated with 35-50 mg/kg or ≥50 mg/kg of deferoxamine respectively, for 52 weeks. Assuming the same mean reduction in LIC for Ferriprox but a higher SD of ±4.0 mg/g

dw for both treatments due to possibly higher variability associated with MRI measurement, the sample size of 300, with >80% being patients with sickle cell disease, will provide over 95% power for demonstrating non-inferiority of Ferriprox to deferoxamine in patients with sickle cell disease.

The sample size estimate is based on a non-inferiority margin of 2 mg/g dw for the reduction of LIC and α of 0.05, two-sided (or α of 0.025, one-sided). It has been reported that in a typical patient with thalassemia major, the LIC could increase by 5 mg/g dw after 1 year without chelation therapy. As the cause of iron overload is the same in thalassemia and sickle cell disease, the same increase in LIC may be expected if patients with sickle cell disease are transfused at the same rate and not treated with a chelator. Hence, the difference in reduction of LIC between deferoxamine therapy and a placebo (effect size) can be estimated to be 9 (i.e., 4 – (-5)) mg/g dw. This means that the non-inferiority margin of 2 mg/g dw would be about 20% of the effect size. With the enrolment of 300 patients, there is a greater than 99% chance (power) of occurrence of at least 1 adverse event with an anticipated incidence rate of 2%, or greater than 95% chance for an anticipated incidence rate as low as 1%.

However, patient's recruitment in this study has proceeded at a very slow pace and despite all our efforts over the past 4 years, the goal of enrolling a total of 300 patients has not been reached. A total of 213 patients (142 patients for Ferriprox and 71 patients for deferoxamine) are projected to have either completed the study or been withdrawn from the study by November 30, 2018. An interim analysis is planned to be performed on the data of these 213 patients. Based on the same values of non-inferiority margin and SD of the LIC measurement, but an α level of 0.0399, two-sided (Pocock's α spending method, see section 3.7 for details), this sample size (213 patients) will provide 89% power to demonstrate non-inferiority of Ferriprox to deferoxamine in this interim analysis, assuming no real difference in efficacy between the two treatments. For the subgroup analysis of only patients with sickle cell disease, the power will be 82% as there are 178 SCD patients (119 patients for Ferriprox and 59 patients for deferoxamine), which is approximately 84% of 213 patients. With the safety data of 213 patients, there is 98% chance (power) of occurrence of at least 1 SAE with an anticipated incidence rate of 2%, or 88% chance for an anticipated incidence rate of as low as 1%.

During this interim analysis, while patient enrollment has been put on hold, there will still be 17 patients who are on-going with their assigned drug treatment. All are projected to have completed the study by October, 2019. If the results of the interim analysis lead to the conclusion of non-inferiority of Ferriprox to deferoxamine, considerations will be given on early termination of the study, to avoid unnecessary exposure of patients to a clinical trial that has reached its objectives. The data from those patients up to the time of

study closure will be added to the interim dataset for the final statistical analysis of the study based on the same statistical analyses in this SAP.

3.3 Treatment

Baseline Phase:

During the baseline phase, patients who sign an informed consent form will undergo initial screening. On the final day of the baseline phase, patients' eligibility will be determined, based on inclusion/exclusion criteria, and qualified patients will enter the treatment phase.

Treatment Phase:

At the beginning of the treatment phase, patients will be randomized in a 2:1 ratio to receive either deferiprone or deferoxamine. The treatment phase will be 52 weeks in duration.

Deferiprone Treatment Arm:

Patients will be prescribed Ferriprox 500 mg tablets and/or 80 mg/mL oral solution, according to patient preference or product's availability, for administration three times a day (tid). The dose of Ferriprox will be based on the transfusional iron input and the severity of iron overload at baseline, and may be adjusted on the basis of the magnitude of change in iron overload during the study.

Ferriprox 25 mg/kg tid:

Patients with transfusional iron input ≤ 0.3 mg/kg/day in the 3 months prior to baseline

AND

Patients with a baseline measure of iron load of:

- Serum ferritin < 2500 µg/L

  AND

- LIC < 15 mg/g dry weight

  AND

- Cardiac T2* > 20 ms

Ferriprox 33 mg/kg tid:

Patients with a transfusional iron input > 0.3 mg/kg/day in the 3 months prior to baseline

OR

Patients with at least one baseline measure of iron load as follows:

- Serum ferritin ≥ 2500 µg/L

  OR

- LIC ≥ 15 mg/g dry weight

  OR

- Cardiac T2* ≤ 20 ms

Dosing of all patients will be initially at 15 mg/kg tid for 1 week, which will be increased to 20 mg/kg tid in Week 2 and to 25 mg/kg tid in Week 3, which will be the treatment dose for the remainder of the trial, unless a patient meets the 33 mg/kg tid dosing criteria. In that case, the dose of Ferriprox will be increased further to 33 mg/kg tid in Week 4, and this dose will be the treatment dose for the remainder of the trial.

The dose of Ferriprox will also be increased to 33 mg/kg tid at any time during the trial if the mean daily transfusional iron input increases to more than 0.3 mg/kg body weight for at least 3 consecutive months OR at Week 26 if there is less than 10% improvement from baseline to Week 26 in at least one of the measures indicative of iron overload (serum ferritin, cardiac MRI T2* or LIC).

Dose reduction recommendations will be based on regular assessment of safety markers for adverse reactions that are possibly dose dependent, such as gastrointestinal upset, increases in serum liver enzyme levels, and arthropathies.

Deferoxamine Treatment Arm:

Patients will be prescribed deferoxamine as per the approved US prescribing information at doses of 20 – 40 mg/kg/day for children (<16 years of age) and 40–50 mg/kg/day in adults (≥16 years of age) as 8 – 12 h subcutaneous infusion for 5 – 7 days per week. The dose of deferoxamine will be based on the transfusional iron input, on the severity of iron overload at baseline, and on the magnitude of its change during the study.

Deferoxamine 20 mg/kg/day (children) or 40 mg/kg/day (adults):

Patients with transfusional iron input ≤ 0.3 mg/kg/day in the 3 months prior to baseline

AND

Patients with a baseline measure of iron load of:

- Serum ferritin < 2500 µg/L

  AND

- LIC < 15 mg/g dry weight

  AND

- Cardiac T2 > 20 ms

Deferoxamine up to 40 mg/kg/day (children) or 50 mg/kg/day (adults):

Patients with a transfusional iron input > 0.3 mg/kg/day in the 3 months prior to baseline

OR

Patients with at least one baseline measure of iron load as follows:

- Serum ferritin ≥ 2500 µg/L

  OR

- LIC ≥ 15 mg/g dry weight

  OR

- Cardiac T2* ≤ 20 ms

Children (<16 years of age).
The dose of deferoxamine will also be increased up to 40 mg/kg for 5 – 7 days per week at any time during the trial if the mean daily transfusional iron input increases to more than 0.3 mg/kg body weight for at least 3 consecutive months OR at Week 26 if there is less than 10% improvement from baseline to Week 26 in at least one of the measures of iron overload (serum ferritin, cardiac MRI T2* or LIC).

Adults (≥16 years of age)
The dose of deferoxamine will be increased up to 50 mg/kg for 5 – 7 days per week at any time during the trial if the mean daily transfusional iron input increases to more than 0.3 mg/kg body weight for at least 3 consecutive months OR at Week 26 if there is less than 10% improvement from baseline to Week 26 in at least one of the measures of iron overload (serum ferritin, cardiac MRI T2* or LIC).

Dose reduction recommendations will be based on regular assessment of safety markers. Efficacy, safety and tolerability evaluations will occur according to the schedule of evaluation (Table 1). Rescue medication (intravenous administration of deferoxamine or combination of 2 iron chelators: Ferriprox, deferoxamine or deferasirox) for the treatment of iron overload will not be allowed during the Treatment Phase. Should iron overload symptoms become intolerable for the patient despite dose adjustment, the Investigator should withdraw the patient from the study.
If a patient withdraws early, he or she will return to the clinic for an Early Termination Visit as soon as possible, and no later than 1 month following treatment discontinuation.

All of the efficacy and safety evaluations will be performed at the last study visit or the Early Termination visit, whichever comes first.

3.4 Study Sites and Study Duration

Study sites have been located in USA, Canada, Brazil, United Kingdom, Egypt, Saudi Arabia, Tunisia, and Turkey. Each patient is expected to participate in the study for approximately 60 weeks (from the Screening Visit to the End of Study Visit).

3.5 Schedule of Study Procedures

The efficacy and safety measurements/evaluations will be performed at visits outlined in Table 1 – Schedule of Study Procedures.

Table 1. Schedule of Study Procedures

	Baseline Phase			Treatment Phase				
STUDY PROCEDURE	**Screening/ Baseline**	**Baseline**	**Hematology Assessments [1]**	**Telephone Calls (Week 1, 2, 3)**	**Monthly Visits (Week 4, 8,16, 20, 32, 36, 44, 48)**	**Quarterly Visits (Week 12, 40)**	**Semi-Annual Visit (Week 26)**	**End of Study / Early Termination Visit[2] (Week 52)**
Informed Consent/Assent	X							
Eligibility Criteria	X							
Previous/current chelation therapy	X							
Confirmation of eligibility		X						
Demographic	X							
Randomization		X						
Medical history	X	V						R
Transfusion history	X	X						
Prior and Current medications	X	V						X
Hematology	X[3]	X[4]	X		X	X	X	X
Biochemistry	X[3,4]	V			X	X	X	X
Serum Pregnancy testing (females of childbearing potential only)	X[3]	X			X	X	X	X
Urine Pregnancy testing (females of childbearing potential only)		X						
Serology	X[3,4]	V					X	X
Urinalysis	X[3,4]	V					X	X
Physical examination	X[3,4]	V					X	X
Vital signs (including weight and height)[5]	X	X[4]			X	X	X	X
12-lead ECG	X[3,4]	V					X	X
Blood sample for genetic polymorphism of agranulocytosis (optional)		X						

	Baseline Phase				Treatment Phase			
STUDY PROCEDURE	**Screening/ Baseline**	**Baseline**	**Hematology Assessments** [1]	**Telephone Calls (Week 1, 2, 3)**	**Monthly Visits (Week 4, 8,16, 20, 32, 36, 44, 48)**	**Quarterly Visits (Week 12, 40)**	**Semi-Annual Visit (Week 26)**	**End of Study / Early Termination Visit**[2] **(Week 52)**
Contraceptive counselling	X	X			X	X	X	
Quality of Life Questionnaire (SF-36/ Child Health Questionnaire)		X					X	X
Serum Ferritin		X				X	X	X
Liver MRI/LIC	X[4,6]						X	X
Cardiac MRI T2*	X[4,6]						X	X
Dose Calculation/Verify and adjust dose level		X			X	X	X	
Contact IVRS/IWRS		X			X	X	X	X
Dispense study medication		X			X	X	X	
Dispense Patient Diary Card		X			X	X	X	
Review and Collect Diary Card					X	X	X	X
Medical events/Adverse events	X	X		X	X	X	X	X
Concomitant medications				X	X	X	X	X
Transfusion information (if applicable)[7]			X		X	X	X	X
Return used and unused study medication					X	X	X	X

X- To do, V- To verify, R- To review

1. Hematology testing is to be done weekly up to Week 26 and biweekly thereafter.
2. Early Termination: if patient withdraws from the study prior to Week 52, the patient must be seen for an early termination visit.
3. These evaluations must be done within 14 days prior to baseline visit. Females of childbearing potential must be making use of an approved birth control method at least one month prior to starting study medication.
4. Results from these tests will be considered the baseline values.
5. Height will only be measured at screening/baseline, semi-annual and Week 52 visits.
6. These evaluations must be conducted within two months prior to starting study medication
7. Collect volume of blood that the patient received during the transfusion and the mean hematocrit of the packed red blood cell units transfused.

3.6 Method of Assignment to Treatment

At the baseline visit, patients will be randomly assigned to receive Ferriprox or deferoxamine in a 2:1 ratio. Stratified randomization based on disease category (sickle cell disease vs. other anemias) and on the transfusional iron input in the 3 months prior to baseline (> 0.3 mg/kg/day vs. ≤ 0.3 mg/kg/day) will be employed to ensure that the 2:1 ratio is maintained within each of the 4 strata: 1) sickle cell disease with transfusional iron input > 0.3 mg/kg/day, 2) sickle cell disease with transfusional iron input ≤ 0.3 mg/kg/day, 3) other anemias with transfusional iron input > 0.3 mg/kg/day, and 4) other anemias with transfusional iron input ≤ 0.3 mg/kg/day. Treatment assignment and drug allocation will be performed by an Interactive Voice Response System (IVRS).

3.7 Interim Analysis

An interim analysis will be performed with the data of patients who will have either completed or been withdrawn from the study by November 30, 2018. The Pocock's α spending function (Lan and DeMets, Discrete sequential boundaries for clinical trials. Biometrika, 1983; 70:659-663) will be used for assigning α for this interim analysis. The Pocock's α spending function is:

$\alpha(t) = \alpha \times \ln [1 + (e - 1) \times t]$

where $\alpha = 0.05$ and t = information fraction

= number of patients at the interim analysis / total number of patients

= 213 patients / 300 patients

= 0.71

Substituting the values of $\alpha = 0.05$, $t = 0.71$, and $e = 2.718$ into the Pocock's α spending function gives

$\alpha(t) = 0.05 \times \ln [1 + (2.718 - 1) \times 0.71]$

$= 0.05 \times \ln [2.21978]$

$= 0.0399$

Therefore, $\alpha = 0.0399$ will be used for the interim analysis.

A study report will be prepared with the results of the interim analysis and the decision to re-start patient enrollment will be based on the advice of the Data and Safety Monitoring Board (DSMB) after their review of the interim analysis results.

4 STUDY POPULATIONS

Study populations intended for analysis will be defined as follows: Intent-to-Treat (ITT), Per-Protocol (PP), and Safety. The ITT population will represent the primary analysis population to evaluate the treatment groups on all efficacy endpoints. The primary efficacy endpoint will also be analyzed for the PP population, which is the secondary analysis population.

4.1 Intent-to-Treat Population

The ITT population will include all randomized patients who received at least one dose of study drug and have a baseline and at least one post-baseline efficacy assessment. There can be a different number of patients (N) in the ITT population for each of the four efficacy measures (LIC, serum ferritin, cardiac T2*, and quality of life) if some of the patients don't have post-baseline data on all of the three efficacy measures. All efficacy analyses will be based on the ITT population.

4.2 Per-Protocol Population

The Per-Protocol (PP) population will include all enrolled patients who will have completed the study, have no major protocol violations, and have an efficacy measure by the end of the study. Prior to database lock, major protocol violations will be determined and the affected patients will be excluded from the PP population. Major protocol violations will include (but not be limited to) the following:

- Patients who did not fulfill the LIC > 7 mg/g inclusion criterion.
- Patients who were not compliant with the treatment (< 80% compliance).
- Patients who took iron chelator medications other than the assigned study medication during the course of the study.

Only the primary efficacy measure, which is LIC, will be performed with the PP population.

4.3 Safety Population

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

5. HANDLING OF MISSING DATA

In the efficacy analyses, for patients who were terminated from the study prior to Month 12, if their last efficacy measures were obtained within 30 days of Month 12, the data obtained will be treated as the Month 12 data. For early termination that occurred outside this window, the last observation carried forward (LOCF) method will be used to fill the missing data when the early termination was not caused by worsening of disease conditions or inadequate efficacy of the drug. For early termination due to worsening

of disease conditions or inadequate efficacy of the drug, as judged by assessing the AE log, the "worst value" method will be used. That is, the worst value of all patients from the corresponding treatment group will be used to impute the missing data at that time point. For missing data due to missed visit, the LOCF method will be used to fill the void.

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

6 PATIENT DISPOSTION AND BASELINE CHARACTERISTICS

A two-sided p-value of 0.05 will be used as the significance level for the determination of statistical significance in the statistical tests with the data from patient disposition and baseline characteristics.

6.1 Patient Disposition

Patient disposition will be summarized with the number and percent of patients who were enrolled, received at least one dose of study medication, completed the study, and were withdrawn from the study (including reasons for withdrawals). The proportions of drop-outs will be compared between the Ferriprox group and the deferoxamine group using Fisher's exact test.

6.2 Demographics

Demographics data such as age, sex, ethnicity, and race will be summarized by treatment group with descriptive statistics (mean, standard deviation, minimum, and maximum) for continuous variables and with frequency tables for discrete variables.

6.3 LIC, Cardiac MRI T2*, and Serum Ferritin at Baseline

The baseline data of LIC, cardiac MRI T2*, and serum ferritin will be summarized using descriptive statistics by treatment group. If there are multiple baseline values, then the value that was measured closest prior to the treatment will consider to be the baseline value.

6.4 Prior and Concomitant Medications

Prior and concomitant medications will be coded and classified by the Anatomical Therapeutic Chemical (ATC) coding scheme of the World Health Organization (WHO), using the WHO Drug Dictionary Format B – March 2018 or newer. The number and percent of patients who took a concomitant medication in each treatment group will be presented using frequency tables.

6.5 Medical History

Medical history for current and historical diagnoses and co-morbidities will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) Version 21.0 or higher and summarized by treatment group. They will be displayed by MedDRA System Organ Class (SOC) and Preferred Term (PT) and current status will be derived as "Resolved" if the stop date is reported and "Ongoing" if the stop data is missing, and will be presented in descending order of the most frequent Ongoing PT.

6.6 Physical Examinations

A physical examination including head, ears, eyes, nose, throat, neck, respiratory system, general appearance, cardiovascular system, abdominal system, skin, and nervous system will be conducted and any clinically significant findings will be recorded on the medical history log (if the findings are of a pre-existing condition) and the medical events log (if the findings are new untoward medical occurrence or worsening of a pre-existing condition that occurs after ICF singing but before dosing).

6.7 Vital Signs, Weight and Height

Vital signs (temperature, resting heart rate, respiration, and blood pressure), weight and height at baseline will be summarized using descriptive statistics by treatment group.

7 EFFICAY ANALYSES

All statistical analyses will be performed using SAS (version 9.3 or higher) on the Windows operating system.

7.1 Primary Efficacy Endpoint

Primary efficacy endpoint is the change from baseline to Week 52 in LIC. Primary efficacy endpoint will be compared between the two treatment groups using an analysis of covariance (ANCOVA) model including treatment variable as the main factor, and overall average transfusional iron input during the study, baseline LIC, and stratification factors (disease category and transfusional iron input in the 3 months prior to baseline) as covariates. The 96.01% ($1 - \alpha$, where $\alpha = 0.0399$ based on the Pocock's α spending function for interim analysis) confidence interval (CI) of the difference (Ferriprox minus deferoxamine) in change of LIC from baseline to Week 52 (i.e., Week 52 minus baseline) between the two treatment groups

will be computed. For the demonstration of non-inferiority, the upper limit of the 96.01% CI should be no more than 2 mg/g dw.

The following SAS codes of MIXED procedure will be used to produce the differences in Least Squares (LS) Mean of change in LIC at Month 6 and Month 12 between Ferriprox and deferoxamine groups and the corresponding 96.01% confidence intervals. In the mixed model, AR (1) (autoregressive of order 1) will be used for the covariance structure, and Kenward and Roger's method will be used to estimate the denominator degrees of freedom (SAS model statement option, DDFM = KR).

```
proc mixed data=LIC;
  class patient treat disease prior_iron month
  model LIC_change = treat overall_iron base_LIC disease prior_iron
                     month treat*month / noint solution ddfm=kr;
  repeated month / subject=patient(treat) type=ar(1);
  lsmeans treat*month;
  estimate 'Ferriprox - Deferoxamine at Month 6'  treat -1 1
  treat*month -1 0 1 0 / cl alpha=0.0399;
  estimate 'Ferriprox - Deferoxamine at Month 12' treat -1 1
  treat*month 0 -1 0 1 / cl alpha=0.0399;
run;
```

Definition of the variables in the statistical model:

LIC_change	: Change in LIC from baseline to Week 5
treat	: Ferriprox or Deferoxamine
month	: Duration of treatment in month
overall_iron	: Overall total transfusional iron input (mg/kg/day) during the study
base_LIC	: LIC at baseline
disease	: Sickle cell disease or other anemias
prior_iron	: transfusional iron input in 3 months prior to baseline (≤0.3mg/kg/day or >0.3 mg/kg/day)

7.2 Secondary Efficacy Endpoints

- Change from baseline to Week 52 in patient-reported quality of life (SF-36 or Child Health Questionnaire);
- Change from baseline to Week 52 in cardiac MRI T2*;
- Change from baseline to Week 52 in serum ferritin.

- Detailed information on the statistical analyses of the SF-36 or CHQ data is in a separate SAP prepared by QualityMetric Inc..
- The changes from baseline to Week 52 in cardiac MRI T2* and serum ferritin will be compared between the two treatment groups, using an ANCOVA model including treatment variable as the

main factor, and overall average transfusional iron input during the study, baseline cardiac MRI T2* or serum ferritin, and stratification factors (disease category and transfusional iron input in the 3 months prior to baseline) as covariates. As with LIC, the 96.01% CI of the difference between the two treatment groups will be computed for both cardiac MRI T2* and serum ferritin. The cardiac MRI T2* data will be log-transformed before any statistical evaluation. Since cardiac MRI T2* will be measured at baseline, Week 26, and Week 52 as with LIC, the SAS codes for LIC data, with the exception of baseline MRI T2* instead of baseline LIC being included as the covariate, will be used for cardiac MRI T2* data as well.

- The following SAS codes of MIXED procedure will be used to produce the differences in Least Squares (LS) Mean of change in serum ferritin at Months 3, 6, 9, and 12 between Ferriprox and deferoxamine groups and the corresponding 96.01% confidence intervals.

```
proc mixed data=SF;
  class patient treat disease prior_iron month;
  model SF_change = treat overall_iron base_SF disease prior_iron
                    month treat*month /
  noint solution ddfm=kr;
  repeated month / subject=patient(treat) type=ar(1);
  lsmeans treat*month;
  estimate 'Ferriprox - Deferoxamine at Month 3'  treat -1 1
  treat*month -1 0 0 0 1 0 0 0 / cl alpha=0.0399;
  estimate 'Ferriprox - Deferoxamine at Month 6'  treat -1 1
  treat*month 0 -1 0 0 0 1 0 0 / cl alpha=0.0399;
  estimate 'Ferriprox - Deferoxamine at Month 9'  treat -1 1
  treat*month 0 0 -1 0 0 0 1 0 / cl alpha=0.0399;
  estimate 'Ferriprox - Deferoxamine at Month 12' treat -1 1
  treat*month 0 0 0 -1 0 0 0 1 / cl alpha=0.0399;
run;
```

Definition of the variables in the statistical model:

SF_change	: Change in SF from baseline to Week 5
treat	: Ferriprox or Deferoxamine
month	: Duration of treatment in month
overall_iron	: Overall total transfusional iron input (mg/kg/day) during the study
base_LIC	: LIC at baseline
disease	: Sickle cell disease or other anemias
prior_iron	: transfusional iron input in 3 months prior to baseline (≤0.3mg/kg/day or >0.3 mg/kg/day)

7.3 Trend Analysis for LIC, cardiac MRI T2*, and Serum Ferritin

The longitudinal data of LIC, cardiac MRI T2*, and serum ferritin will be analyzed for time trend by using PROC MIXED procedure in SAS. The observed data of LIC, log-transformed cardiac MRI T2*, and serum ferritin will be used in this analysis. The following two statistical models will be fitted:

- Model 1: Efficacy value = Intercept + Treatment + Time + Treatment × Time
- Model 2: Efficacy value = Intercept + Treatment + Time

Treatment will be treated as a categorical variable, and Time will be the time in month at each time point. Model 1 is the full model with the main effect of Treatment and Time, and the interaction effect of Treatment × Time. Model 2 is the reduced model with the main effect of Treatment and Time without the interaction term. If the interaction of Treatment × Time in Model 1 is not significant ($p > 0.05$), the reduced Model 2 will be used as the final model for trend analysis.

The following SAS codes will be used:

```
proc mixed data=efficacy_data;
  class patient treat;
  model measure = treat month treat*month / solution ddfm=kr;
  repeated / subject=patient(treat) type=ar(1);
run;
```

Definition of the variables in the statistical model:
measure: LIC or log-transformed cardiac MRI T2*, or SF
treat : Ferriprox or Deferoxamine
month : Duration of treatment in month

7.4 Subgroup Analysis

The comparison of the two treatment groups for the primary and secondary efficacy endpoints will be performed by disease type. The same ANCOVA models without disease factor as used in the main analyses will be used.

- Patients with sickle cell disease (SCD) only
- Non- SCD patients.

7.5 Sensitivity Analysis

Sensitivity analyses will be performed on the primary efficacy measure, LIC. As a sensitivity analysis, the missing data imputation will be repeated with the LOCF method being used for all drop-out patients in the deferoxamine group and the "worst value" method being used for all drop-out patients in the Ferriprox group. This imputation approach will result in the worst case scenario for the Ferrirox group. In addition, the primary efficacy analysis will be repeated on a dataset involving only patients who have at least 6-month LIC data in the ITT population to assess the impact of early patient withdrawal on the results of the ITT analysis.

7.6 Exploratory Analysis

The following success criteria in LIC were used for the submission of Exjade's NDA.

LIC at Baseline	Success, if LIC at the last measure is
2 to < 7 mg Fe/g dw	1 to < 7 mg Fe/g dw
≥ 7 to < 10 mg Fe/g dw	1 to 7 mg Fe/g dw
≥ 10 mg Fe/g dw	Decrease in LIC ≥ 3 mg Fe/g dw

The success rates for Ferriprox and deferoxamine groups will be calculated based on these success criteria and will be compared using Fisher's exact test. It is noted that there should be no patients in the first category of 2 to < 7 mg Fe/g dw at baseline LIC because one of the inclusion criteria for this study is baseline LIC >7 mg/g dw (measured by MRI).

In addition to the statistical analyses that have been specified in the SAP, any other exploratory analyses will be performed, if warranted, as post hoc analyses.

8 SAFETY ANALYSES

The safety data for continuous variables will be summarized using descriptive statistics, and the safety data for discrete variables will be presented as frequency tables.

The safety analyses will be performed by disease category as well: SCD patients and non-SCD patients.

8.1 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 (and reason for withdrawal)
- number of withdrawals due to an AE

Adverse events will be coded using MedDRA. Adverse events are defined as AEs that occurred or worsened (increased in severity and/or frequency) on or after the first dose of study medication. Serious adverse events (SAEs) that occurred within 14 days after treatment discontinuation will be considered to be SAEs. Serious adverse events that occurred within 30 days after treatment discontinuation will be included in the database.

Adverse events will be summarized by treatment group using the total number of AEs and total exposure to the treatment, 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). AEs will also be presented by severity (mild, moderate, severe), by seriousness (serious, non-serious) and by relationship to study medication (at least possibly related, not related). The number of patients withdrawn will also be presented.

To count the number of patients who experienced each AE, patients who experienced the same AE multiple times will only be counted 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 presenting the SOC alphabetically, and within each SOC, preferred terms will be presented in decreasing order of the total number of patients who experienced each AE. In summaries presenting the

incidence of AEs by severity, seriousness, and relation to study medication, a patient with multiple events coded to a given preferred term or SOC will be counted 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.

A listing of serious adverse events and a listing of withdrawals due to AEs will be presented. Patient deaths will be listed separately and discussed with patient narratives.

8.2 Physical Examination

A physical examination including head, ears, eyes, nose, throat, neck, respiratory system, general appearance, cardiovascular system, abdominal system, skin, and nervous system will be conducted any clinically significant findings will be recorded as adverse events.

8.3 Vital Signs, Weight and Height

Descriptive statistics will be presented for temperature, resting heart rate, respiratory rate, systolic blood pressure, diastolic blood pressure, weight and height at each visit. Changes from baseline to each follow-up assessment will be also summarized using descriptive statistics by treatment group.

8.4 12-Lead ECG

ECG data will be summarized using descriptive statistics at each assessment by treatment group. Change from baseline to each follow-up assessment will be also summarized using descriptive statistics by treatment group. Shift tables for clinically significant abnormality between baseline and the last assessment will be constructed by treatment group.

8.5 Biochemistry, Hematology and Urinalysis

All analyses of laboratory data will be based on the planned visits. Laboratory data collected at unscheduled visits will be available in the data listings but not included in summary tables.

Descriptive statistics for each clinical laboratory test will be presented for each scheduled visit. Change from baseline to each follow-up assessment will be also presented. 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 treatment will be presented.

Urinalysis assessments will consist of pH, specific gravity, ketones, blood, glucose, and protein. The raw data listings for each individual patient will be produced for further evaluation, whenever needed.

Clinically significant laboratory values will be reported as AEs.

8.6 Concomitant Medications

Medications will be coded using the 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 AEs will be differentiated from others.
Concomitant medications will be summarized by preferred term only. To count the number of patients who took a medication, a patient who took 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.

8.7 Pregnancy test

Any female patients with positive pregnancy test during the study period will be listed by treatment group.

9 OTHER ANALYSES

9.1 Drug Exposure

The total daily dose taken during the study will be summarized with descriptive statistics by treatment group.

9.2 Treatment compliance

Patients will be instructed on how to take the study medication. A medication usage diary card will be provided to the patients by the study staff. Patients will record the number of tablets or volume of oral solution taken, or the volume of injection solution administered and the time of injection. For Ferriprox, compliance will be evaluated monthly by the Investigator or delegate by monthly pill counts or volume of drug returned by the patient. For deferoxamine, compliance will be evaluated by the number of infusions performed, which will be recorded monthly through the use of infusion pumps that keep records of those numbers, and by physical assessment of the infusion sites. Reasons for non-compliance with the treatment will be recorded in the source document and in the eCRFs. Compliance reported in the eCRF will be based on the patient's diary and compliance calculation. If compliance is greater than 100% and the patient reports taking all doses as prescribed, compliance will be reported as 100% in the eCRF.

Compliance ≤80% and an over-compliance of ≥120% will be reported as a protocol deviation. The number and percent of patients who had compliance ≤80% or ≥120% during the study will be presented by treatment group.

9.3 Transfusional Iron Input

It is noted that transfusional iron input (mg/kg/day) for the 3 months prior to baseline, which is one of the stratification factors of randomization in this study, has been calculated, for example, as follow:

Assumption: 1 mg iron / 1 mL packed Red Blood Cells (pRBCs)

			If partial or exchange transfusions		
Type of transfusion	**Volume of blood transfused (mL)**	**Average mean hematocrit of pRBC transfused (%) for the site**	**Volume of blood removed (mL)**	**Average mean hematocrit of pRBC removed (%) for the site (**as we do not collect hematocrit, we use hemoglobin*3 = hematocrit as assumption**)**	**Iron in pRBC** (volume blood transfused*mean hematocrit transfused – volume blood removed*mean hematocrit removed)
Simple	1200	65			780
Exchange	1250	65	1016	80	0
Partial exchange	2500	65	1000	80	825
Simple	1000	65			650
				Total iron transfused	2255 mg
				Body weight at baseline	54 kg
				3 months*30.5 days	91.5 days

Hence, transfusional iron input (mg/kg/day) for the 3 months = 2255 mg/54 kg/91.5 days = 0.46 mg/kg/day.

Transfusional iron input will be calculated monthly during the study in the same way above. Overall total transfusional iron input (mg/kg/day) during the study will be calculated by summing up monthly transfusional iron input. As the total transfusional iron input depends on the length of time a patient remains in the study, the total transfusional iron input will be divided by the total number of days involved in the months where blood transfusion data was obtained and will be compared between the two treatment groups; the same data will be used for the ANCOVA.

14 SUMMARY TABLES AND FIGURES

Summary tables and figures are numbered following ICH structure.

Note: The final numberings for tables and/or figures in the clinical study report can be changed if more tables and/or figures are made in the addition to those in the SAP.

TABLES

14.1 Demographics and Baseline Data

Table 14.1.1 Patient disposition
Table 14.1.2 Number of patients in the efficacy and safety populations
Table 14.1.3 Number of patients by study site
Table 14.1.4 Reasons for not completing the study
Table 14.1.5 Demographics data
Table 14.1.6 Liver iron concentration (LIC), cardiac MRI T2*, serum ferritin at baseline
Table 14.1.7 Prior chelation therapy
Table 14.1.8 Transfusion iron input (mg/kg/day) in the 3 months prior to baseline
Table 14.1.9 Medical history
Table 14.1.10 Vital signs at baseline
Table 14.1.11 Weight and height at baseline

14.2 Efficacy Analyses

Note: Similar tables will be produced for SCD patients only and Non-SCD patients.

14.2.1 LIC

Table 14.2.1.1 LIC at each assessment
Table 14.2.1.2 Change in LIC at each follow-up assessment
Table 14.2.1.3 LS Means of change in LIC from ANCOVA model at each follow-up assessment
Table 14.2.1.4 Trend analysis for LIC over time

14.2.2 Cardiac MRI T2*

Table 14.2.2.1 Cardiac MRI T2* at each assessment
Table 14.2.2.2 Change cardiac MRI T2* at each follow-up assessment
Table 14.2.2.3 LS Means of change in cardiac MRI T2* from ANCOVA model at each follow-up assessment
Table 14.2.2.4 Trend analysis for cardiac MRI T2* over time

14.2.3 Serum Ferritin

Table 14.2.3.1 Serum ferritin at each assessment
Table 14.2.3.2 Change in serum ferritin at each follow-up assessment
Table 14.2.3.3 LS Means of change in serum ferritin from ANCOVA model at each follow-up assessment
Table 14.2.3.4 Trend analysis for serum ferritin over time

14.3 Safety Analyses

Note: Similar tables will be produced for SCD patients only and Non-SCD patients.

14.3.1 Adverse Events

Table 14.3.1.1 Overall summary of adverse events
Table 14.3.1.2 Adverse events
Table 14.3.1.3 Most common adverse events (≥5% in total)
Table 14.3.1.4 Adverse drug reactions
Table 14.3.1.5 Most common adverse drug reactions (≥5% in total)
Table 14.3.1.6 Serious adverse events
Table 14.3.1.7 Serious adverse drug reactions
Table 14.3.1.8 Adverse events by causality

14.3.2 Vital Signs

Table 14.3.2.1 Temperature at each assessment
Table 14.3.2.2 Change in temperature from baseline to each follow-up assessment
Note: Similar tables will be produced for resting heart rate, respiration, systolic blood pressure, and diastolic blood pressure.

14.3.3 Weight and Height

Table 14.3.3.1 Weight at each assessment
Table 14.3.3.2 Change in weight from baseline to last assessment
Table 14.3.3.1 Height at each assessment
Table 14.3.3.2 Change in height from baseline to last assessment

14.3.4 Concomitant Medications

Table 14.3.4.1 Concomitant medications

14.3.5 12-Lead ECG

Table 14.3.5.1 Heart rate of 12-Lead ECG at each assessment
Table 14.3.5.2 Change in heart rate of 12-Lead ECG from baseline to each follow-up assessment
Note: Similar tables will be produced for PR, QRS, QT, QTcF, and QTcB.

Table 14.3.5.3 Shift table for clinically significant abnormality for 12-Lead ECG: Feriprox group
Table 14.3.5.4 Shift table for clinically significant abnormality for 12-Lead ECG: Deferoxaome group

14.3.6 Laboratory Data

14.3.6.1 Hematology

Table 14.3.6.1.1 Hemoglobin at each assessment
Table 14.3.6.1.2 Change in hemoglobin from baseline to each follow-up assessment
Table 14.3.6.1.3 Shift table for hemoglobin in abnormal range at baseline vs. last assessment: Ferriprox group
Table 14.3.6.1.4 Shift table for hemoglobin in abnormal range at baseline vs. last assessment: Deferoxamine group
Note: Similar tables will be produced for total white blood cell (WBC), absolute neutrophil count (ANC), and platelets.

14.3.6.2 Biochemistry

Table 14.3.6.2.1 Total protein at each assessment
Table 14.3.6.2.2 Change in total protein from baseline to each follow-up assessment
Table 14.3.6.2.3 Shift table for total protein in abnormal range at baseline vs. last assessment: Ferriprox group
Table 14.3.6.2.4 Shift table for total protein in abnormal range at baseline vs. last assessment: Deferoxamine group
Note: Similar tables will be produced for GGT, lactate dehydrogenase (LDH), sodium, potassium, chloride, glucose (fasting at screening visit only), total, direct and indirect bilirubin, AST, ALT, albumin; blood urea nitrogen, calcium, creatinine, uric acid, alkaline phosphatase, and amylase.

14.3.6.3 Serology

Table 14.3.6.3.1 HIV at each assessment
Note: Similar tables will be produce for Hepatitis B and C.

14.3.7 Pregnancy test

Table 14.3.7.1 List of patients with positive pregnancy test during the study

14.4 Treatment compliance

Table 14.4.1 Treatment compliance at each visit

14.5 Transfusion information

Table 14.5.1 Mean transfusional iron input (mg/kg/day) during the study

14.6 Total daily dose

Table 14.6.1 Summary of total daily dose

FIGURES

14.2 Efficacy

Figure 14.2.1 Mean line graph for LIC over time
Figure 14.2.2 Mean line graph for cardiac MRI T2* over time
Figure 14.2.3 Mean line graph for serum ferritin over time
Figure 14.2.4 Bar graph for the change in LIC from baseline to the end of study
Figure 14.2.5 Bar graph for the change in cardiac MRI T2* from baseline to the end of study
Figure 14.2.6 Bar graph for the change in serum ferritin from baseline to the end of study

14.3 Safety

14.3.1 Hematology

Figure 14.3.1.1 Mean line graph for hemoglobin over visit
Figure 14.3.1.2 Proportion of patients with abnormal hemoglobin at each assessment
Note: Similar graphs will be produced for total white blood cell (WBC), absolute neutrophil count (ANC), and platelets.

14.3.2 Biochemistry

Figure 14.3.2.1 Mean line graph for total protein over visit
Figure 14.3.2.2 Proportion of patients with abnormal total protein at each assessment
Note: Similar tables will be produced for GGT, lactate dehydrogenase (LDH), sodium, potassium, chloride, glucose (fasting at screening visit only), total, direct and indirect bilirubin, AST, ALT, albumin; blood urea nitrogen, calcium, creatinine, uric acid, alkaline phosphatase, and amylase.

16 DATA LISTINGS

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

16.2 Patient Data Listings

16.2.1 Listing of informed consent
16.2.2 Listing of demographics
16.2.3 Listing of primary diagnosis
16.2.4 Listing of prior chelation
16.2.5 Listing of hydroxyurea history
16.2.6 Listing of transfusion history
16.2.7 Listing of vital signs including height, weight
16.2.8 Listing of physical examination
16.2.9 Listing of 12-lead electrocardiogram
16.2.10 Listing of urinalysis
16.2.11 Listing of hematology
16.2.12 Listing of blood sample collection dates
16.2.13 Listing of LIC
16.2.14 Listing of cardiac MRI T2*
16.2.15 Listing of chemistry
16.2.16 Listing of serology
16.2.17 Listing of pregnancy
16.2.18 Listing of urine microscopy
16.2.19 Listing of blood sample for genetic polymorphism
16.2.20 Listing of randomization
16.2.21 Listing of serum ferritin
16.2.22 Listing of dose verification
16.2.23 Listing of disposition

16.2.24 Listing of compliance
16.2.25 Listing of medical history
16.2.26 Listing of medication
16.2.27 Listing of medical events
16.2.28 Listing of adverse events
16.2.29 Listing of exposure – DFP
16.2.30 Listing of exposure – DFO
16.2.31 Listing of local labs
16.2.32 Listing of transfusion information
16.2.33 Listing of SAEs
16.2.34 Listing of withdrawals due to AEs

17 TABLE SHELLS

The following table shells provide a framework for the display of data from this study. These tables may not be produced 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.

If the same data points are collected at more than one visit, the results will be summarized in Table x.x for baseline, x.x-1 for visit 1, x.x-2 for visit 2 and so on.

Table 14.1.1 Patient disposition

	Treatment		
	Deferiprone	Deferoxamine	P-value (Fisher's exact test)
Randomized	xxx	xxx	
Exposed*	xxx (xx%)	xxx (xx%)	0.xxxx
Completed*	xxx (xx%)	xxx (xx%)	0.xxxx
Withdrawn*	xxx (xx%)	xxx (xx%)	0.xxxx

Data source: 16.2.23 Listing of disposition
Note: *Percentages are based on the number of randomized patients in each treatment group.

Table 14.1.2 Number of patients in the ITT, PP, and safety populations

		Treatment	
		Deferiprone	Deferoxamine
ITT population	LIC	xxx	xxx
	Serum Ferritin	xxx	xxx
	Cardiac MRI T2*	xxx	xxx
PP population	LIC	xxx	xxx
	Serum Ferritin	xxx	xxx
	Cardiac MRI T2*	xxx	xxx
Safety population		xxx	xxx

Data source: 16.2.20 Listing of randomization

Table 14.1.3 Number of patients by study site

	Treatment	
Study Site	Deferiprone	Deferoxamine
001	xxx	xxx
002	xxx	xxx
…	…	…
Total	xxx	xxx

Data source: 16.2.2 Listing of demographics

Table 14.1.4 Reasons for not completing the study

		Treatment		
		Deferiprone	Deferoxamine	P-value (Fisher's exact test)
N (%)		xx (100)	xx (100)	
Reason	Detail			
Adverse event	Ccccc	xx (xx)	xx (xx)	0.xxxx
	Ccccc	xx (xx)	xx (xx)	
Voluntary withdrawal	Ccccc	xx (xx)	xx (xx)	0.xxxx
	Ccccc	xx (xx)	xx (xx)	
Lost to follow-up	Ccccc	xx (xx)	xx (xx)	0.xxxx
	Ccccc	xx (xx)	xx (xx)	
Investigator decision	Ccccc	xx (xx)	xx (xx)	0.xxxx
	Ccccc	xx (xx)	xx (xx)	
Protocol violation	Ccccc	xx (xx)	xx (xx)	0.xxxx
	Ccccc	xx (xx)	xx (xx)	
Other	Ccccc	xx (xx)	xx (xx)	0.xxxx
	Ccccc	xx (xx)	xx (xx)	
Total		xx (xx)	xx (xx)	

Data source: 16.2.23 Listing of disposition

Table 14.1.5 Demographics data

	Treatment		
	Deferiprone	Deferoxamine	
N	Xxx	xxx	p-value§
Age (years): Mean ± SD (Min, Max)	 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)	0.xxxx
Ethnic Origin: n (%) Hispanic/Latino Other	 xx (xx) xx (xx)	 xx (xx) xx (xx)	0.xxxx
Racial Origin: n (%) White Black Asian Native American Native Hawaiian/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)	0.xxxx

§ T-test for age; Fisher's exact test for sex, ethnic origin, and racial origin
Data source: 16.2.2 Listing of demographics

Table 14.1.6 LIC, cardiac MRI T2*, and serum ferritin at baseline

	Treatment		
	Deferiprone	Deferoxamine	
N	xxx	xxx	
	Mean ± SD (Min, Max)	Mean ± SD (Min, Max)	P-value (t-test)
LIC (mg/g dw)	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx
Cardiac MRI T2* (ms)	xx.x ± xx.x (xx.x, x.xx)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx
Serum Ferritin (µg/L)	xxxx ± xxxx (xxxx, xxxx)	xxxx ± xxxx (xxxx, xxxx)	0.xxxx

Data source: 16.2.13 Listing of LIC, 16.2.14 Listing of cardiac MRI T2*, 16.2.21 Listing of serum ferritin

Table 14.1.7 Prior chelation therapy

	Treatment	
	Deferiprone	Deferoxamine
Deferiprone	xx (xx%)	xx (xx%)
Deferoxamine	xx (xx%)	xx (xx%)
Deferasirox	xx (xx%)	xx (xx%)

Data source: 16.2.4 Listing of prior chelation

Table 14.1.8 Transfusion iron input (mg/kg/day) in the 3 months prior to baseline

	Treatment		
	Deferiprone	Deferoxamine	
	Mean ± SD (Min, Max)	Mean ± SD (Min, Max)	P-value (T-test)
Transfusion iron input (mg/kg/day)	x.xx ± x.xx (x.xx, x.xx)	x.xx ± x.xx (x.xx, x.xx)	0.xxxx

Data source: 16.2.6 Listing of transfusion history

Table 14.1.9 Medical history

	Treatment			
	Deferiprone		Deferoxamine	
N	xxx		xxx	
Illness/Event by MedDRA Primary System Organ Class and Preferred Term	Resolved n (%)	Ongoing n (%)	Resolved n (%)	Ongoing n (%)
cccccc	xx (xx)	xx (xx)	xx (xx)	xx (xx)
cccccc	xx (xx)	xx (xx)	xx (xx)	xx (xx)
cccccc	xx (xx)	xx (xx)	xx (xx)	xx (xx)
cccccc	xx (xx)	xx (xx)	xx (xx)	xx (xx)

Data source: 16.2.25 Listing of medical history

Table 14.1.10 Vital signs at baseline

	Treatment		
	Deferiprone	Deferoxamine	
N	xxx	xxx	
Vital Sign:	Mean ± SD (Min, Max)	Mean ± SD (Min, Max)	P-value (T-test)
Temperature (ºC)	xx.x ± xx.x (xx, xx)	xx.x ± xx.x (xx, xx)	0.xxxx
Resting Heart Rate (/min)	xxx.x ± xxx.x (xxx, xxx)	xxx.x ± xxx.x (xxx, xxx)	0.xxxx
Respiration (/min)	xx.x ± xx.x (xx, xx)	xx.x ± xx.x (xx, xx)	0.xxxx
Systolic Blood Pressure (mmHg)	xxx.x ± xxx.x (xxx, xxx)	xxx.x ± xxx.x (xxx, xxx)	0.xxxx
Diastolic Blood Pressure (mmHg)	xxx.x ± xxx.x (xxx, xxx)	xxx.x ± xxx.x (xxx, xxx)	0.xxxx

Data source: 16.2.7 Listing of vital signs including height and weight

Table 14.1.12 Weight and height at baseline

	Treatment		
	Deferiprone	Deferoxamine	
N	xxx	xxx	
	Mean ± SD (Min, Max)	Mean ± SD (Min, Max)	P-value (T-test)
Weight (kg)	xx.x ± xx.x (xx, xx)	xx.x ± xx.x (xx, xx)	0.xxxx
Height (cm)	xxx.x ± xxx.x (xxx, xxx)	xxx.x ± xxx.x (xxx, xxx)	0.xxxx

§For patients who had separate screening and baseline visits, height was measured only at screening
Data source: 16.2.7 Listing of vital signs including height and weight

Table 14.2.1.1 LIC at each assessment

		Treatment		
		Deferiprone	Deferoxamine	
N		xxx	xxx	P-value (T-test)
	Visit	Mean ± SD (Min, Max)	Mean ± SD (Min, Max)	
LIC (mg/g dw)	Baseline	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx .
	Month 6	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx
	Month 12	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx

Data source: 16.2.13 Listing of LIC

Table 14.2.1.2 Change in LIC at each follow-up assessment

		Treatment		
Test	Visit	Deferiprone	Deferoxamine	
N		xxx	xxx	P-value (T-test)
Change in LIC (mg/g dw) Mean ± SD (Min, Max)	Month 6	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx
	Month 12	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx

Data source: 16.2.13 Listing of LIC

Table 14.2.1.3 LS Means of change in LIC from ANCOVA model at each follow-up assessment

		Treatment			
		Deferiprone	Deferoxamine	Deferiprone minus Deferoxamine	96.01% C.I.
N		xxx	xxx	xxx	
	Visit	LS Mean ± SE	LS Mean ± SE	LS Mean ± SE	
LIC (mg/g dw)	Month 6	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x	(xx.x, xx.x)
	Month 12	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x	(xx.x, xx.x)

Data source: 16.2.13 Listing of LIC

Table 14.2.1.4 Trend analysis for LIC over time

	Deferiprone	Deferoxamine	Deferiprone minus Deferoxamine	P-value
Slope: Mean ± SE	xx.x ± xx.x	xx.x ± xx.x	xx. x ± xx.x	0.xxxx

Data source: 16.2.13 Listing of LIC

Table 14.2.1.5 Success rate in LIC based on the submission of Exjade's NDA.

	Treatment		
	Deferiprone	Deferoxamine	P-value (Fisher's exact test)
Success rate	xx.x %	xx.x%	0.xxxx

Data source: 16.2.13 Listing of LIC

Table 14.2.2.1 Cardiac MRI T2* at each assessment

		Treatment		
		Deferiprone	Deferoxamine	
N		xxx	xxx	P-value (T-test)
	Visit	Mean ± SD (Min, Max)	Mean ± SD (Min, Max)	
Cardiac MRI T2* (ms)	Baseline	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx .
	Month 6	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx
	Month 12	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx

Data source: 16.2.14 Listing of cardiac MRI T2*

Table 14.2.2.2 Change in cardiac MRI T2* at each follow-up assessment

		Treatment		
Test	Visit	Deferiprone	Deferoxamine	
N		xxx	xxx	P-value (T-test)
Change in cardiac MRI T2* (ms) Mean ± SD (Min, Max)	Month 6	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx
	Month 12	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx

Data source: 16.2.14 Listing of cardiac MRI T2*

Table 14.2.2.3 LS Means of change in cardiac MRI T2* from ANCOVA model at each follow-up assessment

		Treatment			
		Deferiprone	Deferoxamine	Deferiprone minus Deferoxamine	96.01% C.I.
N		Xxx	xxx	xxx	
	Visit	LS Mean ± SE	LS Mean ± SE	LS Mean ± SE	
Cardiac MRI T2* (ms)	Month 6	xx.x ± xx.x	xx.x ± xx.x	(xx.x, xx.x)	(xx.x, xx.x)
	Month 12	xx.x ± xx.x	xx.x ± xx.x	(xx.x, xx.x)	(xx.x, xx.x)

Data source: 16.2.14 Listing of cardiac MRI T2*

Table 14.2.2.4 Trend analysis for cardiac MRI T2* over time

	Deferiprone	Deferoxamine	Deferiprone minus Deferoxamine	P-value
Slope: Mean ± SE	xx.x ± xx.x	xx.x ± xx.x	xx. x ± xx.x	0.xxxx

Data source: 16.2.14 Listing of cardiac MRI T2*

Table 14.2.3.1 Serum ferritin each assessment

		Treatment		
		Deferiprone	Deferoxamine	
N		xxx	xxx	P-value (T-test)
	Visit	Mean ± SD (Min, Max)	Mean ± SD (Min, Max)	
Serum Ferritin (µg/L)	Baseline	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx .
	Month 3	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx
	Month 6	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx
	Month 9	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx
	Month 12	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx

Data source: 16.2.21 Listing of serum ferritin

Table 14.2.3.2 Change in serum ferritin at each follow-up assessment

		Treatment		
Test	Visit	Deferiprone	Deferoxamine	
N		xxx	xxx	P-value (T-test)
Change in serum ferritin (µg/L) Mean ± SD (Min, Max)	Month 3	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx
	Month 6	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx
	Month 9	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx
	Month 12	xx.x ± xx.x (xx.x, xx.x)	xx.x ± xx.x (xx.x, xx.x)	0.xxxx

Data source: 16.2.21 Listing of serum ferritin

Table 14.2.3.3 LS Means of change in serum ferritin from ANCOVA model at each follow-up assessment

		Treatment			
		Deferiprone	Deferoxamine	Deferiprone minus Deferoxamine	96.01% CI
N		Xxx	xxx	xxx	
	Visit	LS Mean ± SE	LS Mean ± SE	LS Mean ± SE	
Serum ferritin (µg/L)	Month 3	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x	(xx.x, xx.x)
	Month 6	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x	(xx.x, xx.x)
	Month 9	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x	(xx.x, xx.x)
	Month 12	xx.x ± xx.x	xx.x ± xx.x	xx.x ± xx.x	(xx.x, xx.x)

Data source: 16.2.21 Listing of serum ferritin

Table 14.2.3.4 Trend analysis for serum ferritin over time

	Deferiprone	Deferoxamine	Deferiprone minus Deferoxamine	P-value
Slope: Mean ± SE	xx.x ± xx.x	xx.x ± xx.x	xx. x ± xx.x	0.xxxx

Data source: 16.2.21 Listing of serum ferritin

Table 14.3.1.1 Overall summary of adverse events

	Treatment		
	Deferiprone	Deferoxamine	
N	xxx	xxx	P-value
Number of patients experiencing at least one AE	xx (xx%)	xx (xx%)	0.xxxx
Number of patients experiencing at least one severe AE	xx (xx%)	xx (xx%)	0.xxxx
Number of patients experiencing at least one serious AE	xx (xx%)	xx (xx%)	0.xxxx
Number of patients experiencing at least one related* AE	xx (xx%)	xx (xx%)	0.xxxx
Number of patient deaths	xx (xx%)	xx (xx%)	0.xxxx
Number of patient withdrawals due to AEs	xx (xx%)	xx (xx%)	0.xxxx

*Includes possibly, probably, and definitely related. Worst case scenario of causality between the investigator and company's assessment.
Data source: 16.2.28 Listing of adverse events

Table14.3.1.2 Adverse events

	Treatment		
	Deferiprone (N=xxx)	Deferoxamine (N=xxx)	
	Exposure (patient-years): x.xx	Exposure (patient-years):x.xx	
	Total Events: xxx	Total Events: xxx	
System Organ Class Preferred Term	n Patients (%)	n Patients (%)	P-value (Fisher's exact test)
CCCCCC	x (x.x)	x (x.x)	0.xxxx
Cccccc	x (x.x)	x (x.x)	0.xxxx
Cccccc	x (x.x)	x (x.x)	0.xxxx
Cccccc	x (x.x)	x (x.x)	0.xxxx
……..	……..	……..	……..

Note: Similar tables will be produced from Table 14.3.1.3 to Table 14.3.1.7
Data source: 16.2.28 Listing of adverse events

Table 14.3.1.8 Adverse events by causality

		Treatment	
		Deferiprone (N=xxx)	Deferoxamine (N=xxx)
System Organ Class Preferred Term	Relatedness (worst case)	Patients reporting (n=xx)	Patients reporting (n=xx)
CCCCCCCC		x (x.x)	x (x.x)
cccccc	Not Related	x (x.x)	x (x.x)
	Related*	x (x.x)	x (x.x)
cccccc	Not Related	x (x.x)	x (x.x)
	Related*	x (x.x)	x (x.x)
……	…….	…..	…..

*Possibly, Probably, or Definitely Related
Data source: 16.2.28 Listing of adverse events

Table 14.3.2.1 Temperature at each assessment

	Treatment				
	Deferiprone		Deferoxamine		
Visit	N	Mean ± SD (Min, Max)	N	Mean ± SD (Min, Max)	P-value (T-test)
Baseline	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 1	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 2	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 3	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 4	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
…	…	…	…	…	…
Month 10	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 11	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 12	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx

Note: Similar tables will be produced for resting heart rate, respiration, systolic and diastolic blood pressures.
Data source: 16.2.7 Listing of vital signs including height and weight

Table 14.3.2.2 Change in temperature from baseline to each follow-up assessment

	Treatment				
	Deferiprone		Deferoxamine		
Visit	N	Mean ± SD (Min, Max)	N	Mean ± SD (Min, Max)	P-value (T-test)
Month 1	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 2	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 3	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 4	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
…	…	…	…	…	…
Month 10	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 11	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 12	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx

Note: Similar tables will be produced for resting heart rate, respiration, systolic and diastolic blood pressures.
Data source: 16.2.7 Listing of vital signs including height and weight

Table 14.3.3.1 Weight (kg) at each assessment

	Treatment				
	Deferiprone		Deferoxamine		
Visit	N	Mean ± SD (Min, Max)	N	Mean ± SD (Min, Max)	P-value (T-test)
Baseline	xxx	xxx ± xxx (xxx, xxx)	xxx	xxx ± xxx (xxx, xxx)	0.xxxx
Month 1	xxx	xxx ± xxx (xxx, xxx)	xxx	xxx ± xxx (xxx, xxx)	0.xxxx
Month 2	xxx	xxx ± xxx (xxx, xxx)	xxx	xxx ± xxx (xxx, xxx)	0.xxxx
Month 3	xxx	xxx ± xxx (xxx, xxx)	xxx	xxx ± xxx (xxx, xxx)	0.xxxx
Month 4	xxx	xxx ± xxx (xxx, xxx)	xxx	xxx ± xxx (xxx, xxx)	0.xxxx
…	…	…	…	…	…
Month 10	xxx	xxx ± xxx (xxx, xxx)	xxx	xxx ± xxx (xxx, xxx)	0.xxxx
Month 11	xxx	xxx ± xxx (xxx, xxx)	xxx	xxx ± xxx (xxx, xxx)	0.xxxx
Month 12	xxx	xxx ± xxx (xxx, xxx)	xxx	xxx ± xxx (xxx, xxx)	0.xxxx

Data source: 16.2.7 Listing of vital signs including height and weight

Table 14.3.3.2 Change in weight from baseline to last assessment

		Treatment		
		Deferiprone	Deferoxamine	
	N	xxx	xxx	P-value (T-test)
Change in weight (kg) Mean ± SD (Min, Max)	Baseline	xxx.x ± xxx.x (xxx, xxx)	xxx.x ± xxx.x (xxx, xxx)	0.xxxx
	Last assessment	xxx.x ± xxx.x (xxx, xxx)	xxx.x ± xxx.x (xxx, xxx)	0.xxxx
	Change at last assessment	xxx.x ± xxx.x (xxx, xxx)	xxx.x ± xxx.x (xxx, xxx)	0.xxxx

Data source: 16.2.7 Listing of vital signs including height and weight

Table 14.3.3.1 Height (cm) at each assessment

	Treatment				
	Deferiprone		Deferoxamine		
Visit	N	Mean ± SD (Min, Max)	N	Mean ± SD (Min, Max)	P-value (T-test)
Baseline	xxx	xxx ± xxx (xxx, xxx)	xxx	xxx ± xxx (xxx, xxx)	0.xxxx
Week 26	xxx	xxx ± xxx (xxx, xxx)	xxx	xxx ± xxx (xxx, xxx)	0.xxxx
Week 52	xxx	xxx ± xxx (xxx, xxx)	xxx	xxx ± xxx (xxx, xxx)	0.xxxx

Data source: 16.2.7 Listing of vital signs including height and weight

Table 14.3.3.4 Change in height from baseline to last assessment

		Treatment		
		Deferiprone	Deferoxamine	
	N	xxx	xxx	P-value (T-test)
Height (cm): Mean ± SD (Min, Max)	Baseline	xxx.x ± xxx.x (xxx, xxx)	xxx.x ± xxx.x (xxx, xxx)	0.xxxx
	Last assessment	xxx.x ± xxx.x (xxx, xxx)	xxx.x ± xxx.x (xxx, xxx)	0.xxxx
	Change at last assessment	xxx.x ± xxx.x (xxx, xxx)	xxx.x ± xxx.x (xxx, xxx)	0.xxxx

Data source: 16.2.7 Listing of vital signs including height and weight

Table 14.3.4.1 Concomitant medications

	Treatment		
	Deferiprone (N)	Deferoxamine (N)	
	Exposure (patient-years): x.xx	Exposure (patient-years): x.xx	
	Total Patients Reporting: xx	Total Patients Reporting: xx	
Preferred Name	n Patients (%)	n Patients (%)	
cccccc	x (x.x)	x (x.x)	
cccccc	x (x.x)	x (x.x)	
cccccc	x (x.x)	x (x.x)	
……..	……..	……..	

Data source: 16.2.26 Listing of medication

Table 14.3.5.1 Heart rate of 12-lead ECG at each assessment

	Treatment				
Heart Rate (bpm)	Deferiprone		Deferoxamine		P-value (T-test)
	N	Mean ± SD (Min, Max)	N	Mean ± SD (Min, Max)	
Baseline	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 6	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 12	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx

Note: Similar tables will be produced for PR (ms), QRS (ms), QT (ms), QTcF (ms), and QTcB (ms), respectively.
Data source: 16.2.9 Listing of 12-lead electrocardiogram

Table 14.3.5.2 Change in heart rate of 12-lead ECG at each follow-up assessment

	Treatment				
Heart Rate (bpm)	Deferiprone		Deferoxamine		P-value (T-test)
	N	Mean ± SD (Min, Max)	N	Mean ± SD (Min, Max)	
Month 6	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 12	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx

Note: Similar tables will be produced for PR (ms), QRS (ms), QT (ms), QTcF (ms), and QTcB (ms), respectively.
Data source: 16.2.9 Listing of 12-lead electrocardiogram

Table 14.3.5.3 Shift table for clinically significant abnormality for 12-lead ECG: Deferiprone group

		Last Assessment		
	n (%)	Normal	Abnormal	P-value (McNemar's test)
Baseline	Normal	xx (xx)	xx (xx)	0.xxxx
	Abnormal	xx (xx)	xx (xx)	

P-value = Data source: 16.2.9 Listing of 12-lead electrocardiogram

Table 14.3.5.4 Shift table for clinically significant abnormality for 12-lead ECG: Deferoxamine group

		Last Assessment		
	n (%)	Normal	Abnormal	P-value (McNemar's test)
Baseline	Normal	xx (xx)	xx (xx)	0.xxxx
	Abnormal	xx (xx)	xx (xx)	

P-value = Data source: 16.2.9 Listing of 12-lead electrocardiogram

Table 14.3.6.1.1 Hemoglobin at each assessment

	Treatment				
Hemoglobin	Deferiprone		Deferoxamine		P-value (T-test)
Visit	N	Mean ± SD (Min, Max)	N	Mean ± SD (Min, Max)	0.xxxx
Baseline	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Week 1	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Week 2	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Week 3	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Week 4	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
…	…	…	…	…	…
Week 49	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Week 50	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Week 51	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Week 52	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx

Note: Similar tables will be produced for total white blood cell (WBC), absolute neutrophil count (ANC), and platelets.
Data source: 16.2.11 Listing of hematology

Table 14.3.6.1.2 Change in hemoglobin at each follow-up assessment

	Treatment				
Hemoglobin	Deferiprone		Deferoxamine		P-value (T-test)
Visit	N	Mean ± SD (Min, Max)	N	Mean ± SD (Min, Max)	0.xxxx
Week 1	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Week 2	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Week 3	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Week 4	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
…	…	…	…	…	…
Week 49	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Week 50	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Week 51	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Week 52	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx

Note: Similar tables will be produced for total white blood cell (WBC), absolute neutrophil count (ANC), and platelets.

Data source: 16.2.11 Listing of hematology

Table 14.3.6.1.3 Shift table for hemoglobin in abnormal range at baseline vs last assessment: Deferiprone group

		Last Assessment			
	n (%)	Low	Normal	High	P-value (McNemar's test)
Baseline	Low	xx (xx)	xx (xx)	xx (xx)	0.xxxx
	Normal	xx (xx)	xx (xx)	xx (xx)	
	High	xx (xx)	xx (xx)	xx (xx)	

Note: Similar tables will be produced for total white blood cell (WBC), absolute neutrophil count (ANC), and platelets.
Data source: 16.2.11 Listing of hematology

Table 14.3.6.1.4 Shift table for hemoglobin in abnormal range at baseline vs last assessment: Deferoxamine group

		Last Assessment			
	n (%)	Low	Normal	High	P-value (McNemar's test)
Baseline	Low	xx (xx)	xx (xx)	xx (xx)	0.xxxx
	Normal	xx (xx)	xx (xx)	xx (xx)	
	High	xx (xx)	xx (xx)	xx (xx)	

Note: Similar tables will be produced for total white blood cell (WBC), absolute neutrophil count (ANC), and platelets.
Data source: 16.2.11 Listing of hematology

Table 14.3.6.2.1 Total protein at each assessment

	Treatment				
Hemoglobin	Deferiprone		Deferoxamine		P-value (T-test)
Visit	N	Mean ± SD (Min, Max)	N	Mean ± SD (Min, Max)	0.xxxx
Baseline	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 1	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 2	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 3	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 4	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
…	…	…	…	…	…
Month 10	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 11	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 12	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx

Note: Similar tables will be produced for GGT, lactate dehydrogenase (LDH), sodium, potassium, chloride, glucose (fasting at screening visit only), total, direct and indirect bilirubin, AST, ALT, albumin; blood urea nitrogen, calcium, creatinine, uric acid, alkaline phosphatase, and amylase.
Data source: 16.2.15 Listing of chemistry

Table 14.3.6.2.2 Change in total protein at each follow-up assessment

	Treatment				
Hemoglobin	Deferiprone		Deferoxamine		P-value (T-test)
Visit	N	Mean ± SD (Min, Max)	N	Mean ± SD (Min, Max)	0.xxxx
Month 1	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 2	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 3	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 4	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
…	…	…	…	…	…
Month 10	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 11	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx
Month 12	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx

Note: Similar tables will be produced for GGT, lactate dehydrogenase (LDH), sodium, potassium, chloride, glucose (fasting at screening visit only), total, direct and indirect bilirubin, AST, ALT, albumin; blood urea nitrogen, calcium, creatinine, uric acid, alkaline phosphatase, and amylase.
Data source: 16.2.15 Listing of chemistry

Table 14.3.6.2.3 Shift table for total protein in abnormal range at baseline vs last assessment: Deferiprone group

		Last Assessment			
	n (%)	Low	Normal	High	P-value (McNemar's test)
Baseline	Low	xx (xx)	xx (xx)	xx (xx)	0.xxxx
	Normal	xx (xx)	xx (xx)	xx (xx)	
	High	xx (xx)	xx (xx)	xx (xx)	

Note: Similar tables will be produced for GGT, lactate dehydrogenase (LDH), sodium, potassium, chloride, glucose (fasting at screening visit only), total, direct and indirect bilirubin, AST, ALT, albumin; blood urea nitrogen, calcium, creatinine, uric acid, alkaline phosphatase, and amylase.
Data source: 16.2.15 Listing of chemistry

Table 14.3.6.2.4 Shift table for total protein in abnormal range at baseline vs last assessment: Deferoxamine group

		Last Assessment			
	n (%)	Low	Normal	High	P-value (McNemar's test)
Baseline	Low	xx (xx)	xx (xx)	xx (xx)	0.xxxx
	Normal	xx (xx)	xx (xx)	xx (xx)	
	High	xx (xx)	xx (xx)	xx (xx)	

Note: Similar tables will be produced for GGT, lactate dehydrogenase (LDH), sodium, potassium, chloride, glucose (fasting at screening visit only), total, direct and indirect bilirubin, AST, ALT, albumin; blood urea nitrogen, calcium, creatinine, uric acid, alkaline phosphatase, and amylase.
Data source: 16.2.15 Listing of chemistry

Table 14.3.6.3.1 HIV Antibody at each assessment

	Treatment				
	Deferiprone		Deferoxamine		P-value (Fisher's exact test)
	Positive N (%)	Negative N (%)	Positive N (%)	Negative N (%)	
Baseline	xx (xx)	xx (xx)	xx (xx)	xx (xx)	0xxxx
Week 26	xx (xx)	xx (xx)	xx (xx)	xx (xx)	0.xxxx
Week 52	xx (xx)	xx (xx)	xx (xx)	xx (xx)	0.xxxx

Note: Similar tables will be produced for Hepatitis B and C.
Data source: 16.2.16 Listing of serology

Table 14.3.7.1 Female patients with positive pregnancy test during the study

	Treatment	
Pregnancy test: Positive	Deferiprone	Deferoxamine
Patient ID	xxxxxx xxxxxx xxxxxx xxxxxx ……	xxxxxx xxxxxx xxxxxx xxxxxx ……

Data source: 16.2.17 Listing of pregnancy

Table 14.3.8.1 The number and percent of patients who had compliance ≤80% or ≥120% during the study

	Treatment				
	Deferiprone		Deferoxamine		
Compliance	N	Percent	N	Percent	P-value (Fisher's exact test)
< 80%	xx	xx.x%	xx	xx.x%	0.xxxx
> 120%	xx	xx.x%	xx	xx.x%	0.xxxx

Data source: 16.2.24 Listing of compliance

Table 14.5.1 Transfusional iron input (mg/kg/day) during the study

	Treatment				
	Deferiprone		Deferoxamine		
	N	Mean ± SD (Min, Max)	N	Mean ± SD (Min, Max)	P-value (T-test)
Transfusional iron input (mg/kg/day)	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)	0.xxxx

Data source: 16.2.32 Listing of transfusion information

Table 14.6.1 Summary of total daily dose

	Treatment			
	Deferiprone		Deferoxamine	
	N	Mean ± SD (Min, Max)	N	Mean ± SD (Min, Max)
Total daily dose (mg/kg/day)	xxx	xx.x ± xx.x (xx, xx)	xxx	xx.x ± xx.x (xx, xx)

Data source: 16.2.22 Listing of dose verification