Statistical Analysis Plan
Version 2.0
Jun 2, 2021

Protocol: PB-102-F03
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A Multi Center Extension Study of PRX-102 Administered by Intravenous Infusions Every 2 Weeks for up to 60 Months to Adult Fabry Patients

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1. ABBREVIATIONS

ADA	Anti-Drug Antibody
AE	Adverse Event
BLISS	Barisoni Lipid Inclusion Scoring System
BPI	Brief Pain Inventory
CKD	Chronic Kidney Disease
CRF	Case Report Form
CSR	Clinical Study Report
DBL	Database Lock
ECG	Electrocardiography
EF	Ejection Fraction
eGFR	Estimated Glomerular Filtration Rate
FCE	Fabry Clinical Events
FD	Fabry Disease
Gb3	Globotriaosylceramide
ICF	Informed Consent Form
IgG	Immunoglobulin G
IRR	Infusion Related Reaction
IV	Intravenous
KDIGO	Kidney Disease Improving Global Outcomes
LVM	Left Ventricular Mass
LVMI	Left Ventricular Mass Index
Lyso Gb3	Globotriaosylsphingosine
MedDRA	Medical Dictionary for Regulatory Activities
MRI	Magnetic Resonance Imaging
MSSI	Mainz Severity Score Index
PT	Preferred Term
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation

SE	Standard Error
SOC	System Organ Class
TEAE	Treatment-Emergent Adverse Event
UPCR	Urine Protein to Creatinine Ratio
WHO	World Health Organization

2. INTRODUCTION

The statistical analysis plan (SAP) contains the analysis information in detail on the definition of the analysis populations, derivation of variables, convention of analysis scope, and statistical methodology for the analyses of safety, tolerability and efficacy parameters of PRX-102 administered by intravenous infusion based on the data collected per the protocol PB-102-F03 (extension of PB-102-F01 and PB-102-F02), the phase 1/2 studies sponsored by Protalix, Ltd.

For those patients who enrolled in this extension study, the data collected in studies PB-102-F01 and PB-102-F02 will be integrated for all safety and efficacy analyses. These patients were treated for 12 months with PRX-102 (3 months in PB-102-F01 and 9 months in PB-102-F02) before being enrolled in PB-102-F03 extension study. Unless stated otherwise, the treatment duration considered in the SAP will be from the start of treatment with PRX-102 in study PB-102-F01, i.e. Visit 1 of the study PB-102-F01.

This plan follows the methods described in the study protocol and provides more specific details. In case of disagreement between the SAP and the protocol, the SAP prevails. Any changes to the analysis as described in the protocol will be documented in this SAP.

An interim analysis was performed to support a regulatory submission. The 1st version of the SAP and the interim Clinical Study Report (CSR) described the planned interim analyses. This version of the SAP describes only the planned analyses for the final analyses. This version of the SAP lists also the changes from the previous version of the SAP.

Any deviations from this SAP during the actual data analysis will be documented properly in a change request or a note-to-file document, as well as in the final CSR. The SAP will be finalized before the database lock (DBL).

3. OBJECTIVES AND ENDPOINTS

3.1. Objectives

To evaluate the ongoing safety, tolerability, and efficacy parameters of PRX-102 in adult Fabry patients who have successfully completed treatment with PRX-102 in studies PB-102-F01 and PB-102-F02.

3.2. Endpoints

3.2.1. Exploratory Efficacy Endpoints

- Plasma Globotriaosylceramide (Gb3) concentrations
- Plasma Globotriaosylsphingosine (Lyso-Gb3) concentration
- Gastrointestinal symptoms
- Estimated Glomerular Filtration Rate ($eGFR_{CKD-EPI}$)
- eGFR Slope
- Urine Protein/Creatinine Ratio (UPCR)
- Short Form Brief Pain Inventory (BPI)
- Cardiac Magnetic Resonance Imaging (MRI) assessments
- Cardiac function assessment by echocardiography and stress test.
- Mainz Severity Score Index (MSSI).
- Fabry Clinical Events (FCE)

3.2.2. Safety Endpoints

- Treatment-Emergent Adverse Events (TEAE)
- Injection site reactions
- Infusion Related Reactions (IRR)
- Clinical laboratory tests
- Physical examinations
- Electrocardiogram (ECG)
- Vital signs
- Concomitant medications
- Treatment induced Anti-PRX-102 antibodies
- Brain MRI

4. STUDY DESIGN

This is an open-label study to evaluate the ongoing safety, tolerability and efficacy parameters of PRX-102 in adult Fabry patients (≥18 years of age) who completed studies PB-102-F01 and PB-102-F02.

Patients will be enrolled to receive 1.0 mg/kg of PRX-102 as an intravenous infusion every 2 weeks (+/- 3 days) for up to 60 months and no less than 36 months.

4.1. Sample Size and Statistical Power Consideration

No formal sample size calculation has been performed for this study.
Sample size in this extension study depended upon the number of patients who completed Study PB-102-F02 and enrolled into this study.

4.2. Study Flow Chart

Activity	Screening visit (Day 1)	Infusions visits 1-131(±3days)	Visit 2 M (±6days)	Visits: 3M 9 M 15 M 21 M (±6days)	Visits: 6M 18 M 30 M 42 M 54M (±6days)	Visits : 12 M 36M 48 M (±6days)	Visits: 24 M 60M (±6 days)	3 Months after last infusion[4] (±6 days)
Review Inclusion/exclusion criteria	x							
Sign ICFs	x							
Concomitant medications[3]	x[1]	x	x	x	x	x	x	x
Vital signs[3]	x[1]	x	x	x	x	x	x	
Body weight	x[1]				x	x	x	
Physical examination	x[1]			x	x	x	x	
Adverse events assessments[3]	x[1]	x	x	x	x	x	x	x
Blood Chemistry	x[1]			x	x	x	x	
Blood count	x[1]			x	x	x	x	
Urinalysis	x[1]			x	x	x	x	
Spot urine test for proteinuria	x[1]			x	x	x	x	
Plasma Gb3 concentration	x[1]			x	x	x	x	
Plasma Lyso Gb3 concentration	x[1]			x	x	x	x	
Anti PRX-102 Antibodies (IgG)	x[1]		x	x	x	x	x	x
Electrocardiography (ECG)	x[1]				x	x	x	
Short form Brief Pain Inventory (BPI)	x[1]			x	x	x	x	
Gastrointestinal symptoms	x[1]			x	x	x	x	
Cardiac function assessment (echocardiography and stress test)						x	x	
Cardiac MRI						x	x	
Brain MRI							x	
Mainz Severity Score Index (MSSI)	x[1]				x	x	x	
IV infusion[2]		x[2]						
Plasma PRX-102 level (PK) [4]		x[4](only on infusion 1)						

[1] values for these evaluations will be transferred from Visit 20 of study PB-102-F02

[2] during all the study, infusions are administered every 2 weeks

[3] should be performed at all visits

[4] Blood sample for last PK timepoint of last infusion (Visit 20) of protocol PB-102-F02 will be drawn pre-infusion

5. ANALYSIS POPULATIONS (ANALYSIS SETS)

5.1. Safety Population

Safety population consists of all subjects who received any dose (partial or complete) of the study medication as part of PB-102-F03.

All safety analyses will be performed on this population. Demographics, baseline characteristics, medical history and compliance will be presented using this population.

5.2. Efficacy Population

Efficacy population consists of all subjects who received at least one complete dose of the study medication as part of PB-102-F03.

All exploratory efficacy analyses will be performed on this population. Since the Efficacy population and the safety population are the same, there is no need to repeat demographics, baseline characteristics, medical history and compliance on this population.

6. TREATMENT DESCRIPTIONS

Unless otherwise indicated, on the summary tables, the treatment will be identified by PRX-102 1.0 mg/kg since all subjects enrolled in this study received this dose.

7. STATISTICAL ANALYSIS METHODS AND ISSUES

7.1. Statistical Methods

Descriptive statistics, namely sample size (n), mean and its Standard Error (SE), Standard Deviation (SD), median, minimum and maximum for continuous variable. Count and percentage will be provided for categorical variable.

Due to COVID-19 pandemic, the study was prolonged for 1 patient (Enrollment ID: 26-F104), and the patients continued to have home infusions and laboratory assessments were taken in one of the visits and then as a “post COVID-19 visit”. Due to the restrictions and since the patient continued to receive the treatment under the extension study PB-102-F60 it was decided not to perform the “end of study visit” for study PB-102-F03 for this patient. AE and medications collection were continued. Two additional patients (ID: 17-F105 and

17-F118) rolled over to the extension study and the end of study visit was conducted but not all assessments specified in the protocol were performed.

Data collected as part of the prolongation will only be listed.

By visit tables will present planned visits based on the per protocol planned visits for each procedure. Outcomes of procedures which were performed in a planned visit, but the procedure was not planned for that visit, will only be listed.

In listings, visits within subjects will be shown chronologically based on the date of the visit. Unscheduled visits will be listed, and the visit column will show the visit as unscheduled, with no number.

By visit tables and listings will include data collected over three studies, each with own visit numbers and scheduling. For ease of review, visit numbers from the Study Data Tabulation Model (SDTM) will be remapped in the Analysis Data Model (ADaM) to shown consecutives visits numbers and time of visit from the beginning of Study F01. Unless otherwise specified in the shells, visits which can mapped to a month will be shown as Visit XX (Month YY) in the tables and listings and other will only show Visit XX. Appendix A (XXX) provides the mapping of the visits.

7.2. Missing Data

There will be no imputation for missing safety or efficacy endpoints except for some missing data associated with AEs which will be addressed in section 9.2.

7.3. Baseline Definition

The baseline for this extension study is defined as the baseline evaluation made in the study PB-102-F01.

7.4. Subgroup and Subset Analysis

7.4.1. Subgroups

Subgroup analysis will be conducted based on baseline characteristics and demographics for selected efficacy and safety endpoints, and will be described in the analysis section of the selected endpoints. The following subgroups will be considered:

- Gender (Male/Female).
- Fabry Disease (FD) classification (Classic/Non-Classic). In order to be classified as FD classic, a patient should have ≤ 5% mean of lab normal ranges residual enzymatic activity in plasma or leukocytes at baseline visit and at least one Fabry specific symptom: Cornea Verticillata, Acroparesthesias, and/or Angiokeratomas. In case of missing information for the symptoms or residual activity, which does not allow for clear classification as classic or non-classic, the FD classification will be missing and the subject will be excluded from the sub-group analysis (for example, if a patient meets the symptoms requirement and have a plasma residual activity of 10% but the leukocytes residual activity is missing then the classification will be missing and the patient will be excluded from the subgroup analysis. As another example, if a patient meets the symptoms requirement and have a plasma residual activity of 3% and the leukocytes residual activity is missing, it is still possible to classify the patient as Classic and the patient will be included in the subgroup analysis).

7.4.2. Subset of Treatment Duration

Since patient duration in PB-102-F03 varies, by design, it is of interest to repeat analysis for selected efficacy and safety endpoints based on patient treatment duration. This analysis is similar to subgroup analysis, but patients may belong to several duration groups, and the determination of the groups is not based on information collected prior baseline. The following 2 levels of duration will be considered: Treatment duration ≥ 3 years; Treatment duration ≥ 5 years, where treatment duration is measured from baseline of study PB-102-F01. By visits tables, for this subset, will show visits every 6 months even if the procedure is conducted more often (e.g. Plasma Lyso Gb3 concentration). For procedures which are conducted at a lower frequency (e.g.Cardiac MRI) then it will be presented by the frequency conducted.

8. DEMOGRAPHICS AND STUDY SUMMARY

8.1. Subject Disposition

The number and percentage of subjects who were enrolled to study PB-102-F03, treated, and remained in the extension study for at least 12, 24, 36, 48, and 60 months of study PB-102-F03 (equivalent to a total of PRX-102 treatment duration of 24, 36, 48, 60, 72 months, respectively) will be summarized. The number and percentage of subjects who discontinued during the extension study will also be summarized for each reason of discontinuation. The number of subjects in each of the analysis population will be presented. The number of subjects with study prolongation due to COVID-19 will be presented.

Protocol violations will be listed.

8.2. Demographics

Demographics analyses will be conducted on the safety population overall, for the two subgroups and for the treatment duration subset.

The demographics (age, gender, race, and ethnicity) will be summarized using descriptive statistics. The summary will be based on the data collected at baseline of study PB-102-F01.

The age will be determined by the date of informed consent signed for PB-102-F01 and the date of birth.

8.3. Baseline Characteristics

Baseline characteristics (based on the baseline data from study PB-102-F01) analyses will be conducted of the safety population overall, for the two subgroups and for the treatment duration subsets.

The following baseline characteristics will be summarized by descriptive statistics: weight, height, % residual enzyme activity in leukocyte (defined as the value in leukocyte × 100/83.5, where 83.5 nmol/hr/mg protein is the mean of the laboratory normal reference range), % residual enzyme activity in plasma (defined as the value in plasma ×100/12.95, where 12.95 nmol/ hr/mL is the mean of the laboratory normal reference range), eGFR,

plasma Lyso-Gb3, plasma Gb3, FD classification, UPCR categories of Kidney Disease Improving Global Outcomes (KDIGO) (see section 10.4).

8.4. Fabry Disease Medical History

The Fabry disease medical history collected in the study PB-102-F01 will be summarized by body system and conditions overall, for the two subgroups and for the treatment duration subsets, and will be conducted on the safety population.

8.5. Other Medical History

The medical history collected in the study PB-102-F01 will be summarized by Medical Dictionary for Drug Regulatory Activities (MedDRA) v15.0 coded System Organ Class (SOC) and Preferred Terms (PT) overall, for the two subgroups and for the treatment duration subsets and will be conducted on the safety population.

8.6. Treatment Compliance

Treatment compliance will be conducted on the safety population overall, for the two subgroups and for the treatment duration subsets.

Treatment compliance will be assessed by the percentage of the number of actual infusions out of the expected infusions during the study. The expected number of infusions is based on the patient's actual duration in the study from the baseline of study PB-102-F01. For patients whose study duration was prolonged due to COVID-19, the expected number of infusions is based on the planned duration per protocol (hence can be higher than 100%).

Compliance will be summarized using descriptive statistics. Patient compliance will be summarized also by the following categories: < 60%; ≥ 60% and < 80%; ≥80%.

9. ANALYSIS OF SAFETY ENDPOINTS

All the analyses described in this section will be conducted for the safety population.

9.1. Exposure

Two measures of exposures (in months) will be calculated for each subject: exposure to PRX-102 and exposure to PRX-102 1mg/kg.

Exposure to PRX-102

((date of last infusion) – (date of first PRX-102 infusion) + 1)*12/365.25

Exposure to PRX-102 1mg/kg

((date of last infusion) – (date of first PRX-102 1mg/kg infusion) + 1)*12/365.25

The date of first PRX-102 1mg/kg infusion will be based on information collected at both the drug administration (exposure) Case Report Form (CRF) page, and information reported by the pharmacist.

The two measures of exposure duration will be summarized by descriptive statistics overall and for the two subgroups. In addition, the cumulative exposure (over all subjects) in person-months will be provided (to PRX-102 and exposure to PRX-102 1mg/kg).

The number of partial or complete infusions that a patient received will be summarized overall and by location of administration (home/site).

9.2. Adverse Events

Adverse events (AE) will be coded by MedDRA version 15.0.

A treatment-emergent adverse event (TEAE) is defined as any AE started during or post first infusion in the study PB-102-F01.

Pre-treatment AEs include all AEs collected prior to the first PRX-102 infusion (in study PB-102-F01) and will only be listed.

The TEAE summaries described in this section will be performed for all TEAE since study PB-102-F01. The analyses will be repeated for AEs whose start date was during or after the first infusion in study PB-102-F03 (to clarify, a TEAE which started in PB-102-F02 and

was ongoing in PB-102-F03 without worsening in severity will not be included in this analysis).

All the analyses presented in this section will be conducted overall, for the two subgroups and for the treatment duration subsets.

The number and percentage of patients with at least one TEAE and the number of TEAEs will be reported in an overall table for the following parameters: Any TEAE; Related TEAEs (related TEAE are considered any TEAE reported as possibly, probably or definitely related); Mild or moderate TEAEs; Related mild or moderate TEAEs; Severe TEAEs; Related severe TEAEs; Serious TEAEs; Non-serious TEAEs; Related serious TEAEs; TEAEs leading to withdrawal; Related TEAEs leading to withdrawal; TEAEs leading to death; and related TEAEs leading to death.

The overall analysis will be repeated for injection site reactions TEAE. Identification of injection site reactions will be based on the SOC and PT in the Table 1 below.

TEAE summary tables by the MedDRA SOC and PT will present the number and percentage of subjects with at least one TEAE. These tables will be generated overall; by severity; and by relationship to study drug. Similar tables by SOC and PT will be generated for serious TEAEs overall and by relationship to study drug.

In the analysis by severity, subjects whose event was classified as “Very Severe” or “Fatal” will be presented in the “Severe” category.

In the summaries of severity and relationship to study drug, the most extreme outcome (highest severity and closest relationship to study drug) will be used for those subjects who experience the same adverse event (per PT) on more than one occasion.

Missing values associated with TEAEs will be treated as missing except for causality, intensity, and outcome of a TEAE: for these variables a “worst case” approach will be taken in the analysis. Thus:

- If the causality is missing, the TEAE will be regarded as related to the treatment
- If the intensity is missing, the intensity of the AE will be regarded as severe
- If the outcome is missing and the stop date is not provided, the outcome will be regarded as “ongoing”.

- If the seriousness is missing, all efforts should be made prior to database lock to make sure that this information is available, if still missing, the worst-case scenario will be assumed.

If there are any TEAEs leading to withdrawal or death, these cases will be presented by patient.

9.2.1. Infusion Related Reactions (IRR)

All the analysis described in this section will be performed for all IRRs since the study PB-102-F01, as well as for all IRRs reported in the study PB-102-F03 alone.

Unless specified otherwise, all the analyses presented in this section will be conducted overall, for the two subgroups and for the treatment duration subset.

IRRs are those TEAEs which occur during the infusion or within 2 hours after the completion of the infusion and their causality is definitely, probably, or possibly related.

Classification rules for assignment of patients with TEAEs during the infusion or within 2 hours after the infusion are described below.

Injection site reactions with SOC and PT listed in Table 1 are not considered IRR and should be excluded from the IRR analysis.

Table 1: Injection Site Reaction SOC and PT Not Considered as IRR

MedDRA SOC	**MedDRA Preferred Term**
General disorders and administration site conditions	Infusion site discomfort
	Injection site discomfort
	Infusion site pain
	Injection site pain
	Infusion site hematoma
	Injection site hematoma
Injury poisoning and procedural complications	Contusion
	Procedural site reaction
	Procedural pain
Vascular disorders	Vein rupture

The number and percentage of patients with at least one IRR and the number of IRRs will be reported in an overall table with the following parameters: Any IRR; Mild or

moderate IRRs; Severe IRRs; Serious IRRs; IRRs leading to withdrawal; IRRs leading to death.

An additional sub-group will be the location of administration (Home or Site). All infusions during studies PB-102-F01, PB-102-F02 and early part of PB-102-F03 were on site. Home infusions were allowed from some point during study PB-102-F03, and the location of administration was collected only from that time onwards and hence the field is the database is blank for the earlier infusions. In the analysis, all the infusion with blank location of administration in the database will be considered to take place on site. This analysis will not be repeated for the two subgroups and for the treatment duration subsets.

IRR summary tables by SOC and PT will present the number and percentage of subjects with at least one IRR. The tables for the IRRs will be presented overall and by severity.

TEAE occurring during the infusion or within 2 hours after the infusion:

To determine whether a TEAE occurred within this time frame, information collected in two CRF forms will be considered: AE form (fields of onset date and time) and Drug Administration form (fields of administration date; start and end times; question "Did the patient experience an AE during or after the infusion?" Events which meet one of the following criteria will be considered to occur during infusion or within 2 hours after the infusion:

- Date and time for both TEAE and infusion are complete, and the onset of the TEAE is during the infusion or within 2 hours from its completion (stop time), regardless of the answer to the question above;
- The answer to the question above is Yes and the date/time of the infusion or the TEAE is not complete (the question in the CRF does not limit the time frame of the TEAE to be during the infusion or within two hours, and hence in case that the date/time of the TEAE onset and infusion are complete and the TEAE is not within the timeframe, the event will not be considered even if the answer is Yes).

All other events will not be classified into this time category.

9.3. Vital Sign

The vital signs (systolic and diastolic blood pressure, pulse rate, body temperature, and respiratory rate) are collected at each infusion visit before infusion (pre-dose) and every 30 minutes during infusion (up to 6 hours) as well as at the end of observation.

Vital signs by visit and within each visit the change from the pre-dose to each time point will be summarized by descriptive statistics.

For the time points before 360 minutes, the analysis will use the nominal time in relation to the time of infusion.

In case that measurements are taken every 30 minutes or 60 minutes, but not at the planned times then only observations at 30, 60, 120… will be included in the analysis and the other will be listed (e.g. if measurements are taken at 15, 30, 45, 75, 105 minutes then the measurements at 15, 45, 75 and 105 will only be listed).

In case that patients do not tolerate the infusion, vital signs are taken every 15 minutes. These evaluations will only be listed.

In case the clinical visit lasted for more than 6 hours and vital signs were taken for more than 6 hours then these vital signs will only be listed.

9.4. Physical Examination

Physical examination results (normal / abnormal / not done) will be summarized by body system and by visit. Detail of abnormal observations will be presented in a data listing.

9.5. Clinical Laboratory Test Results

The following laboratory test results will be summarized overall by descriptive statistics at the scheduled visits, and for continuous results also including the change from baseline:

1. Hematology: Hemoglobin, Leukocytes, Platelets
2. Urinalysis: Dipstick for Presence of Blood, Glucose, Nitrite, Protein
3. Biochemistry: Alanine Transaminase, Albumin, Alkaline Phosphatase, Aspartate Aminotransferase, Bilirubin (Total), Blood Urea Nitrogen, Calcium, Creatine Kinase, Creatinine, Gamma-Glutamyl Transferase, Glucose, Lactate Dehydrogenase, Phosphate, Potassium, Protein (Total), Sodium, Uric Acid

For the parameters discussed in this section, in case that blood sample is taken twice at the same visit, this is due to mistake of the site and not due to test results that should be re-tested and hence only the results of the first blood sample (based on the time the blood sample was taken) will be listed and used in the analyses. Note that in case that a test should be repeated, this will be conducted during an unscheduled visit on another date.

All laboratory results will be listed (also parameters that are not tabulated).

Test results below the level of detection appear in the database with '<' sign. For parameters with such observations, the change from baseline will not be conducted. Descriptive statistics at a visit, for these parameters, will be based only on observation for which the observed value is above the limit of detection, and the summary will indicate the number of observations that were below the limit of detection. In the listings, these observations will be presented with the '<' sign.

9.6. Electrocardiography (ECG)

Descriptive statistics of ECG parameters (quantitative) and assessments (qualitative) will be summarized at each visit that has ECG performed. The change from baseline will be summarized as well for the ECG quantitative parameters.

9.7. Anti-PRX-102 Antibodies

A summary table for IgG Anti-Drug antibody (ADA) will present the number and percentage of patients who are positive or negative by visit. In case that IgG ADA was tested twice on the same visit (for example, due to sampling following hypersensitivity reaction) only the 1st test will be part of the IgG ADA summary by visit. The table will also show the overall ADA status post-treatment where post-treatment positive is defined as "positive" in at least one visit post baseline (stating at PB-102-F01), or "negative" if negative at all post-baseline visits, regardless of status at baseline.

Classification of ADA status to negative or positive at each visit is based on sequential evaluation as follows:

1. If the IgG screening is negative then ADA at that visit is reported as "negative" (and no more evaluations).
2. If the IgG screening is "Presumptive Positive", the next evaluation is the IgG Immunodepletion

a. If IgG Immunodepletion is negative then the ADA status at the visit is reported as “negative”
b. If IgG Immunodepletion is positive then the ADA status at the visit is reported as “positive”

Patients are considered treatment emergent ADA positive if they satisfy one of the following conditions:

1. Titer boosted: patients who were IgG positive to PRX-102 at baseline and boosted post treatment (i.e., titer increase by at least 4-fold from baseline. See Shankar et al. 2014 and FDA Guidance for Industry, January 2019: Immunogenicity Testing of Therapeutic Protein Products —Developing and Validating Assays for Anti-Drug Antibody Detection).
2. Treatment Induced: patients who were IgG negative to PRX-102 at baseline and positive in at least one timepoint post first infusion

The number and percentage of patients who are Treatment emergent ADA (yes/no) will be presented. For treatment emergent ADA, the table will indicate to which of the two groups a patient belongs (titer boosted or treatment induced).

A shift table of ADA status at baseline (positive or negative) to overall status post baseline (positive if positive in at least one visit post baseline, or negative if negative at all post-baseline visits) will be presented.

ADA status by visit, will be presented graphically for each patient.

Only patients who were tested positive for IgG ADA were further tested for Neutralizing Antibody (nAb) and other ADA characterization (i.e., IgG titer, nAb and positivity to other unique PRX-102 epitopes). These outcomes will only be listed.

Note: only data coming from serum samples can be used to determine ADA positivity as the assays were not validated for plasma. Therefore, the plasma driven data collected at Visit 2 (Week 2) of study PB-102-F01 cannot be used for the determination of ADA status, and will be excluded from the analyses.

9.8. Brain MRI

The cerebrovascular disease assessment based on the brain MRI evaluation will only be listed.

9.9. Concomitant Medication

Based on the coded data of concomitant medication using the World Health Organization (WHO) Drug Dictionary Version WHO Drug 20130901E, the data will be tabulated by count and percentage per the standardized medication name within medication class. Medication class will be listed alphabetically.

The medication listings will include a flag whether the drug was taken prior to 1st PRX-102 infusion (regardless of whether the medication was stopped before 1st PRX-102 infusion). Determination of this flag should be based on start date of the medication. In case of partial or missing start date in which it is not clear if the drug was taken prior to 1st PRX-102 infusion (e.g. only year is provided and the start year is the same as the year of 1st infusion), the end date of the medication will be used. If the end date is missing or it cannot be used then the flag will be set to No.

10. ANALYSIS OF EXPLORATORY EFFICACY ENDPOINTS

All the analyses described in this section will be conducted using the efficacy population.

10.1. Plasma Lyso-Gb3 and Gb3 Concentrations

Descriptive statistics of lyso-plasma Gb3 concentration (ng/mL), and plasma Gb3 concentration (ug/mL) will be summarized at each visit these biomarkers were collected. The absolute and percent change from baseline will be summarized as well. The actual values, absolute and percent change from baseline will be listed. In some instances, the laboratory analysed the same blood sample twice. In such situations, the average value for the patient will be used for the tables and figures, but both values will be listed.

The analyses above will be conducted overall, for the two subgroups and for the treatment duration subset.

The number and proportion of patients with a reduction of at least 25%, at least 50%, and at least 75% in plasma Lyso-Gb3 compared to baseline will be summarized at 12, 24, 36, 48, 60 and 72 months for the overall population.

The correlation coefficient between the absolute change from baseline to month 24 in plasma Lyso-Gb3 and the absolute change from baseline to month 6 in BLISS (adjudicated results reported in the CSR of the studies PB-102-F01 and PB-102-F02) will be provided. Scatter plot of the change in Lyso-Gb3 (y-axes) versus the change in BLISS (x-axis) along with a simple regression line will be presented.

Individual changes in Lyso-Gb3 and BLISS will be listed.

Mean (+/SE) Plasma Lyso-Gb3 over time will be plotted overall and by gender.

10.2. Gastrointestinal Symptoms Questionnaire

Descriptive statistics of the qualitative assessments regarding abdominal pain and diarrhea will be summarized at each visit that has the questionnaire performed. In addition, the number and proportion of patients who remained at the same category (i.e. no change in frequency or severity), improved (less severe or lower frequency) or worsened (more severe or higher frequency) will be summarized by visit.

10.3. eGFR and eGFR Slope

eGFR will be calculated based on the value of the serum creatinine values according to the CKD-EPI formula:

eGFR (mL/min/1.73 m^2) = 141 × min(Scr/κ,1)$^{\alpha}$ × max(Scr/κ, 1)$^{-1.209}$ × 0.993^{Age} × 1.018 [if female] × 1.159 [if black / African American],

where Scr is serum creatinine (mg/dL), κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1.

The age will be the actual age when the subject's serum creatinine is collected.

The annualized change in eGFR (slope) per subject will be estimated using a linear regression: eGFR = α + β × [time (year)], based on data of each individual subject on all visits starting from the baseline in study PB-102-F01, and including all collected eGFR data (scheduled and unscheduled including data collected due to prolongation due to COVID-19).

The slope β (mL/min/1.73 m^2 / year) is an estimate of the subject's annualized change in eGFR. The "[time in year]" in the formula is the time (year), from the baseline to the respective following visit, and will be estimated by (date of the visit – date of baseline)/365.25.

The eGFR listing will include also the change from baseline and the subject's annualized slope.

eGFR and eGFR change from baseline will be summarized using descriptive statistics by visit, overall, for the two subgroups and for the subset of treatment duration.

eGFR slope will be summarized using descriptive statistics overall, for the two subgroups and for the subset of treatment duration.

10.4. UPCR

Urine protein/creatinine ratio (UPCR), by spot urine test will be classified into three categories, based on the Kidney Disease Improving Global Outcomes (KDIGO) guidelines:

- Normal to mildly increased, in case UPCR < 150 mg/g,

- Moderately increased, in case 150 ≤ UPCR < 500 mg/g,
- Severely increased, in case 500 ≤ UPCR mg/g

The limit of detection for protein in the urine is 6.2 mg/dL, and in case that the protein is undetectable, the resulting UPCR is reported as < x gr/gr (calculated by 6.2 divided by the measured level of creatinine). Any such observation will be classified to one of the above categories, ignoring the '<' sign in the observation. This is considered a conservative assignment to categories.

UPCR will be summarized at each visit based on the above 3 categories overall, for the two subgroups and for the treatment duration subset.

A shift table between the 3 categories from baseline to 12, 24, 36, 48, 60 and 72 months will be presented overall.

UPCR listing will include the actual observation (i.e. '<' sign will not be removed) as well as the assigned category.

10.5. Short Form Brief Pain Inventory (BPI)

Descriptive statistics of the qualitative assessments regarding the 4 pain severity items (worst, least, right now and average), and 7 pain interference items (general activity, mood, walking ability, normal work, relations with others, sleep, and enjoyment of life) will be summarized at each visit that has BPI performed. The summaries will include also change from baseline.

The proportion of patients whose severity as reported in the "pain on the average" (question 5 in the CRF) did not change or improved compared to baseline (difference from baseline is ≤ 0) and the proportion of patients whose average pain severity deteriorated compared to baseline will be summarized by visit.

10.6. Cardiac MRI

Left ventricular mass (LVM), Left ventricular mass index (LVMI), Ejection fraction (EF) and number of left ventricular fibrotic segments will be summarized by descriptive statistics (n, mean, SE of the mean, SD, median, inter-quartile range and the range) at each visit that has cardiac MRI performed. The change from baseline will be summarized as well. The LVM and LVMI analysis will be done separately for patients who have hypertrophy at baseline and for patients who don't have this abnormality. Hypertrophy is

defined as LVMI above 91 g/m^2 for males and LVMI above 77 g/m^2 for female. The analysis will be done overall, for the two subgroups and for the treatment duration subset.

A shift from baseline to each visit in which cardiac MRI was performed in the number of left ventricular fibrosis segments (based on cardiac MRI) will be presented in a shift table.

A shift from baseline to each visit in which cardiac MRI was performed in the number of patients who have Hypertrophy (Yes / No) will be presented by gender.

10.7. Echocardiogram

Echocardiography evaluations are done with substantial variations, therefore only data listing will be provided.

Qualitative assessments (normal / other) regarding Aortic, Mitral, Tricuspid, and Pulmonic will be presented by a shift table from baseline overall.

10.8. Stress Test

Stress test qualitative evaluation (yes/no) of symptoms (chest pain, shortness of breath, dizziness, palpitations, and other), overall impression: normal stress test, target heart rate achieved and ST change will be summarized by count and percentage at each visit that has stress test performed.

In addition, for overall impression: normal stress test, a shift from baseline will be presented for each visit the stress test was performed.

10.9. Mainz Severity Score Index (MSSI)

Descriptive statistics of the qualitative assessments regarding the sign/symptom severity in general, neurological, cardiovascular, renal dysfunction, and overall score (sum of these 4 scores) will be summarized at each visit that has MSSI performed. The change from baseline will be summarize as well.

A total MSSI score < 20 is considered as mild; a score $20 \leq$ and ≤ 40 is considered moderate and > 40 is considered severe (Beck, 2006). A shift table for the overall score from baseline to each visit at which MSSI was performed between the three categories will be presented.

10.10. Fabry Clinical Events

Fabry clinical events (FCE) are classified into four categories: renal, cardiac, cerebrovascular and non-cardiac death. The adjudicated decisions will be made by the Sponsor medical monitor, based on reported adverse events and clinical information included in the data base.

The criteria for FCE are the following and based on Hopkin (2016):

1. Renal events:
    - First occurrence of either initiation or chronic dialysis (>40 days),
    - Renal transplantation.
2. Cardiac events:
    - Cardiac related death,
    - Myocardial infarction,
    - First time congestive heart failure,
    - Atrial fibrillation,
    - Ventricular tachycardia,
    - Evidence of progressive heart disease severe enough to require pacemaker,
    - Implantation of pacemaker,
    - Bypass surgery,
    - Coronary artery dilatation,
    - Implantation of defibrillator.
3. Cerebrovascular events:
    - Hemorrhagic or ischemic stroke,
    - Transient Ischemic Attack.
4. Non-cardiac related Death.

The number and percentage of patients with FCE (regardless of type of event) and by type will be presented. For the number of FCE (regardless of type of event) patients who had more than one type will be counted once.

FCE listing will show the categories by SOC and PT and the time to event measured from Visit 1.

11. CHANGES FROM PROTOCOL

- Changes to list of endpoints: proteinuria was changed to UPCR; FCE was not planned and added (as safety at the interim analysis and in this version as efficacy); IRR was added as a safety endpoint; Vital signs and concomitant medications were planned in the protocol but not listed in the list of endpoints
- The Per-Protocol population was removed
- For all continuous efficacy endpoints, percent change from baseline was planned. This was revised, and for some endpoints the change from baseline is considered. For some other, only shift tables are considered
- Interquartile range was removed and only maximum and minimum are shown
- AE were planned to be presented by treatment group. No separation for previous dose is done in this version
- Hypersensitivity is evaluated as part of IRR and not by itself
- Shift tables were planned for all laboratory values – for some safety parameters shift tables are presented. For other, only descriptive statistics by visits.

12. CHANGES FROM PREVIOUS VERSION OF SAP

- Completer population that was used to support regulatory submission was removed
- A subgroup of FD classification and subsets of treatment duration were added. Analyses on subgroups is performed on selected endpoints only
- The information presented at the disposition was updated and the SAP was updated to account for the impact of COVID-19
- The list of baseline characteristics was revised
- The definition of compliance was updated to reflect that this is a final analysis
- Analysis of TEAE by time category is removed. Time category is only used to identify IRR
- Several Notes-To-File were issued after the interim DBL and documented changes to the analysis. The changes are now documented in this SAP
- Definition of FCE was updated from the SAP
- Additional analyses of ASA were added
- Shift tables for some of the efficacy and safety endpoints were removed
- Exposure by race was removed

- Handling of UPCR when the protein level is below the limit of detection was revied from the note to file
- Rules to classify TEAE within two hours of infusion were revised

13. REFERENCES

Beck M. *The Mainz Severity Score Index (MSSI): development and validation of a system for scoring the signs and symptoms of Fabry disease.* Acta Pediatrica (2006): Suppl 451: 43-46.

Du Bois D, Du Bois EF. *A formula to estimate the approximate surface area if height and weight be known*. Archives of Internal Medicine (1916): 17 (6): 863-71.

Hopkin R.J et al. *Risk factors for severe clinical events in male and female patients with Fabry disease treated with agalsidase beta enzyme replacement therapy: Data from the Fabry Registry.* Molecular Genetics and Metabolism (2016) 119: 151-159.

14. LIST OF TABLES AND DATA LISTINGS

14.1. Statistical Tables

The statistical tables will be generated using SAS version 9.4. Sample size (n) will be presented by whole number. The mean and its standard error, standard deviation and median will be rounded and presented to one decimal place than the data collected. Minimum and maximum will be presented with the same number of decimal places as the data collected.

The count will be the whole number. The percentage will be rounded and presented to one decimal place.

Number	Title	Population
14.1.1	Disposition of Subjects	All
14.1.2.1	Demographics Overall and by Gender	Safety
14.1.2.2	Demographics by FD Classification and by Treatment Duration	Safety
14.1.3.1	Treatment Compliance Overall and by Gender	Safety
14.1.3.2	Treatment Compliance by FD Classification and by Treatment Duration	
14.1.4.1	Baseline Characteristics Overall and by Gender	Safety
14.1.4.2	Baseline Characteristics by FD Classification and by Treatment Duration	Safety
14.1.5.1.1	Fabry Disease Medical History Overall and by Gender	Safety
14.1.5.1.2	Fabry Disease Medical History by FD Classification and by Treatment Duration	Safety
14.1.5.2.1	Other Medical History Overall and by Gender	Safety
14.1.5.2.2	Other Medical History by FD Classification and by Treatment Duration	Safety
14.2.1.1.1	Plasma Lyso-Gb3 Concentrations Overall and by Gender	Efficacy
14.2.1.1.2	Plasma Lyso-Gb3 Concentrations by FD Classification	Efficacy
14.2.1.1.3	Plasma Lyso-Gb3 Concentrations by Treatment Duration	Efficacy
14.2.1.2	Plasma Lyso-Gb3 Concentrations - Number of Subjects with ≥ 25%, ≥ 50%, and ≥ 75% Reduction from Baseline	Efficacy
14.2.1.3	Correlation Between Change in BLISS from Baseline to Month 6 and Change in Plasma Lyso-Gb3 from Baseline to Month 24	Efficacy
14.2.2.1	Plasma Gb3 Concentrations Overall and by Gender	Efficacy
14.2.2.2	Plasma Gb3 Concentrations by FD Classification	Efficacy
14.2.2.3	Plasma Gb3 Concentrations by Treatment Duration	Efficacy
14.2.3.1	Gastrointestinal Symptoms Questionnaire	Efficacy
14.2.3.2	Gastrointestinal Symptoms Questionnaire – Proportion who Improved, Worsened or Unchanged Compared to Baseline	Efficacy

14.2.4.1.1	eGFR Overall and by Gender	Efficacy
14.2.4.1.2	eGFR by FD Classification	Efficacy
14.2.4.1.3	eGFR by Treatment Duration	Efficacy
14.2.4.2.1	eGFR Slope Overall and by Gender	Efficacy
14.2.4.2.2	eGFR Slope by FD Classification and by Treatment Duration	Efficacy
14.2.5.1	UPCR Categories Overall and by Gender	Efficacy
14.2.5.2	UPCR Categories by FD Classification	Efficacy
14.2.5.3	UPCR Categories by Treatment Duration	Efficacy
14.2.5.4	UPCR – Shift from Baseline	Efficacy
14.2.6.1	Short Form Brief Pain Inventory (BPI)	Efficacy
14.2.6.2	Short Form Brief Pain Inventory (BPI) – "Pain on The Average" - Improvement or No Change Compared to Baseline	Efficacy
14.2.7.1.1	Cardiac MRI Overall and by Gender	Efficacy
14.2.7.1.2	Cardiac MRI by FD Classification and by Treatment Duration	Efficacy
14.2.7.2	Cardiac MRI – Shift from Baseline in the Number of Left Ventricular Fibrosis Segments	Efficacy
14.2.7.3	Cardiac MRI – Shift from Baseline in the Number of patients who have Hypertrophy	Efficacy
14.2.8	Echocardiogram Qualitative Assessments – Shift Table for	Efficacy
14.2.9.1	Stress Test Qualitative Assessments	Efficacy
14.2.9.2	Stress Test for Overall Impression – Shift from Baseline	Efficacy
14.2.10.1	Mainz Severity Score Index (MSSI)	Efficacy
14.2.10.2	Mainz Severity Score Index (MSSI) Overall Score - Shift from Baseline	Efficacy
14.2.11	Number of Subjects with Fabry Clinical Events	Efficacy
14.3.1.1.1	Exposure Duration Overall and by Gender	Safety
14.3.1.1.2	Exposure Duration by FD Classification	Safety
14.3.1.2	Number of infusions Overall and by Location of Administration	Safety
14.3.2.1.1	Number of Subjects with TEAE Overall and by Gender	Safety
14.3.2.1.2	Number of Subjects with TEAE by FD Classification	Safety
14.3.2.1.3	Number of Subjects with TEAE by Treatment Duration	Safety
14.3.2.2.1	Number of TEAE Overall and by Gender	Safety
14.3.2.2.2	Number of TEAE by FD Classification	Safety
14.3.2.2.3	Number of TEAE by Treatment Duration	Safety
14.3.2.3	Summary of Injection Site Reaction TEAE	Safety
14.3.2.4.1	Number of Subjects with TEAE by MedDRA SOC and PT Overall and by Gender	Safety
14.3.2.4.2	Number of Subjects with TEAE by MedDRA SOC and PT by FD Classification	Safety
14.3.2.4.3	Number of Subjects with TEAE by MedDRA SOC and PT by Treatment Duration	Safety
14.3.2.5.1	Number of Subjects with TEAE by MedDRA SOC, PT and	Safety

	Severity Overall	
14.3.2.5.2	Number of Subjects with TEAE by MedDRA SOC, PT and Severity by Gender	Safety
14.3.2.5.3	Number of Subjects with TEAE by MedDRA SOC, PT and Severity by FD Classification	Safety
14.3.2.5.4	Number of Subjects TEAE by MedDRA SOC, PT and Severity by Treatment Duration	Safety
14.3.2.6.1	Number of Subjects with TEAE by MedDRA SOC, PT and Relationship to Study Drug Overall and by Gender	Safety
14.3.2.6.2	Number of Subjects with TEAE by MedDRA SOC, PT and Relationship to Study Drug by FD Classification	Safety
14.3.2.6.3	Number of Subjects with TEAE by MedDRA SOC, PT and Relationship to Study Drug by Treatment Duration	Safety
14.3.2.7.1	Number of Subjects with Serious TEAE by MedDRA SOC, PT Overall and by Gender	Safety
14.3.2.7.2	Number of Subjects with Serious TEAE by MedDRA SOC, PT by FD Classification	Safety
14.3.2.7.3	Number of Subjects with Serious TEAE by MedDRA SOC, PT by Treatment Duration	Safety
14.3.2.8.1	Number of Subjects with Serious TEAE by MedDRA SOC, PT and Relationship to Study Drug Overall and by Gender	Safety
14.3.2.8.2	Number of Subjects with Serious TEAE by MedDRA SOC, PT and Relationship to Study Drug by FD Classification	Safety
14.3.2.8.3	Number of Subjects with Serious TEAE by MedDRA SOC, PT and Relationship to Study Drug by Treatment Duration	Safety
14.3.2.9.1	Number of Subjects with IRR Overall and by Gender	Safety
14.3.2.9.2	Number of Subjects with IRR by FD Classification	Safety
14.3.2.9.3	Number of Subjects with IRR by Treatment Duration	Safety
14.3.2.10.1	Number of IRR Overall and by Gender	Safety
14.3.2.10.2	Number of IRR by FD Classification	Safety
14.3.2.10.3	Number of IRR by Treatment Duration	Safety
14.3.2.11	Summary of IRR by Location of Administration	Safety
14.3.2.12.1	Number of Subjects with IRR by MedDRA SOC and PT Overall and by Gender	Safety
14.3.2.12.2	Number of Subjects with IRR by MedDRA SOC and PT by FD Classification	Safety
14.3.2.12.3	Number of Subjects with IRR by MedDRA SOC and PT by Treatment Duration	Safety
14.3.2.13.1	Number of Subjects with IRR by MedDRA SOC, PT and Severity Overall	Safety
14.3.2.13.2	Number of Subjects with IRR by MedDRA SOC, PT and Severity by Gender	Safety
14.3.2.13.3	Number of Subjects with IRR by MedDRA SOC, PT and Severity by FD Classification	Safety
14.3.2.13.4	Number of Subjects with IRR by MedDRA SOC, PT and Severity by Treatment Duration	Safety

14.3.3	Vital Signs	Safety
14.3.4	Physical Examinations	Safety
14.3.5.1	Laboratory Test Results – Biochemistry	Safety
14.3.5.2	Laboratory Test Results – Hematology	Safety
14.3.5.3	Laboratory Test Results – Urinalysis	Safety
14.3.5.4.1	Anti-PRX-102 Antibodies	Safety
14.3.5.4.2	Anti-PRX-102 Antibodies – Shift from Baseline	Safety
14.3.6.1	Electrocardiography (ECG) Quantitative Parameters	Safety
14.3.6.2	Electrocardiography (ECG) Qualitative Parameters	Safety
14.3.7	Concomitant Medications	Safety

14.2. Figures

Number	Title	Population
15.2.1	Change in Plasma Lyso-Gb3 from Baseline to Month 24 versus Change in Kidney Gb3-BLISS from Baseline to Month 6	Efficacy
15.2.2	Mean Plasma Lyso Gb3 Over Time by Gender and Overall	Efficacy
15.3.1	Anti-Drug Antibody Status by Visit	Safety

14.3. Data Listings

Data listings will be sorted by the subject ID.

Number	Title
1	Subject Disposition
2	Demographics
3	Concomitant Medications
4.1	Fabry Disease Medical History
4.2	Other Medical History
5	Vital Signs
6	Physical Examination
7.1	Laboratory Test Results - Biochemistry
7.2	Laboratory Test Results - Hematology
7.3	Laboratory Test Results - Anti-PRX-102 Antibodies (IgG)
7.4.1	Laboratory Test Results – Plasma Lyso-Gb3 and Gb3 Concentration including Change from Baseline
7.4.2	Plasma Lyso-Gb3 Concentrations and Change from Baseline To Month 24 Versus Change from baseline to Month 6 in BLISS
7.5	Laboratory Test Results - Spot Urine
7.6	Laboratory Test Results - Urinalysis (Dipstick)
7.7	eGFR and eGFR Slope
8	Electrocardiography (ECG)
9.1	Treatment Emergent Adverse Events
9.2	Pre-treatment Adverse Events
9.3	Infusion Related Reactions

Number	Title
9.4	Treatment Emergent Adverse Events Leading to Withdrawal or Death
9.5	Fabry Clinical Events
10	Exposure - Treatment
11.1	Brain MRI
11.2	Cardiac MRI
11.3	Echocardiogram
11.4	Stress Test
12.1	Short Brief Pain Inventory (BPI)
12.2	Gastrointestinal Symptoms
12.3	Mainz Severity Score Index (MSSI)
13	Protocol Deviations
14	Body Measurements
15	Treatment Compliance

Tables and listings shells will be provided in a separate document.

15. APPENDIX: MAPPING OF SCHEDULED VISITS IN F01/F02/F03

Visitnum (SDTM)	Analysis Visit (ADaM)	Study
Screening	Screening	F01
Visit 1	Visit 1	F01
Visit 2	Visit 2	F01
Visit 3	Visit 3 (Month 1)	F01
Visit 4	Visit 4	F01
Visit 5	Visit 5 (Month 2)	F01
Visit 6	Visit 6	F01
Visit 7	Visit 7 (Month 3)	F01
Visit 1	Visit 8	F02
Visit 2	Visit 9 (Month 4)	F02
Visit 3	Visit 10	F02
Visit 4	Visit 11 (Month 5)	F02
Visit 5	Visit 12	F02
Visit 6	Visit 13	F02
Visit 7	Visit 14 (Month 6)	F02
Visit 8	Visit 15	F02
Visit 9	Visit 16 (Month 7)	F02
Visit 10	Visit 17	F02
Visit 11	Visit 18 (Month 8)	F02
Visit 12	Visit 19	F02
Visit 13	Visit 20 (Month 9)	F02
Visit 14	Visit 21	F02

Visit 15	Visit 22 (Month 10)	F02
Visit 16	Visit 23	F02
Visit 17	Visit 24 (Month 11)	F02
Visit 18	Visit 25	F02
Visit 19	Visit 26	F02
Visit 20	Visit 27 (Month 12)	F02
Visit 1	Visit 28	F03
Visit 2	Visit 29	F03
Visit 3	Visit 30 (Month 13)	F03
Visit 4	Visit 31	F03
Visit 5 (Month 2)	Visit 32 (Month 14)	F03
Visit 6	Visit 33	F03
VISIT 7 (month 3)	Visit 34 (Month 15)	F03
Visit 8	Visit 35	F03
Visit 9	Visit 36 (Month 16)	F03
Visit 10	Visit 37	F03
Visit 11	Visit 38 (Month 17)	F03
Visit 12	Visit 39	F03
Visit 13	Visit 40	F03
VISIT 14 (month 6)	Visit 41 (Month 18)	F03
Visit 15	Visit 42	F03
Visit 16	Visit 43 (Month 19)	F03
Visit 17	Visit 44	F03
Visit 18	Visit 45 (Month 20)	F03
Visit 19	Visit 46	F03
VISIT 20 (month 9)	Visit 47 (Month 21)	F03
VISIT 21	Visit 48	F03
Visit 22	Visit 49 (Month 22)	F03
Visit 23	Visit 50	F03
Visit 24	Visit 51 (Month 23)	F03
Visit 25	Visit 52	F03
Visit 26	Visit 53	F03
VISIT 27 (month 12)	Visit 54 (Month 24)	F03
Visit 28	Visit 55	F03
Visit 29	Visit 56 (Month 25)	F03
Visit 30	Visit 57	F03
Visit 31	Visit 58 (Month 26)	F03
Visit 32	Visit 59	F03
VISIT 33 (month 15)	Visit 60 (Month 27)	F03
Visit 34	Visit 61	F03
Visit 35	Visit 62 (Month 28)	F03
Visit 36	Visit 63	F03
Visit 37	Visit 64 (Month 29)	F03
Visit 38	Visit 65	F03

Visit 39	Visit 66	F03
Visit 40 (month 18)	Visit 67 (Month 30)	F03
Visit 41	Visit 68	F03
Visit 42	Visit 69 (Month 31)	F03
Visit 43	Visit 70	F03
Visit 44	Visit 71 (Month 32)	F03
Visit 45	Visit 72	F03
VISIT 46 (month 21)	Visit 73 (Month 33)	F03
Visit 47	Visit 74	F03
Visit 48	Visit 75 (Month 34)	F03
Visit 49	Visit 76	F03
Visit 50	Visit 77 (Month 35)	F03
Visit 51	Visit 78	F03
Visit 52	Visit 79	F03
VISIT 53 (month 24)	Visit 80 (Month 36)	F03
Visit 54	Visit 81	F03
Visit 55	Visit 82 (Month 37)	F03
Visit 56	Visit 83	F03
Visit 57	Visit 84 (Month 38)	F03
Visit 58	Visit 85	F03
Visit 59	Visit 86 (Month 39)	F03
Visit 60	Visit 87	F03
Visit 61	Visit 88 (Month 40)	F03
Visit 62	Visit 89	F03
Visit 63	Visit 90 (Month 41)	F03
Visit 64	Visit 91	F03
Visit 65	Visit 92	F03
VISIT 66 (month 30)	Visit 93 (Month 42)	F03
Visit 67	Visit 94	F03
Visit 68	Visit 95 (Month 43)	F03
Visit 69	Visit 96	F03
Visit 70	Visit 97 (Month 44)	F03
Visit 71	Visit 98	F03
Visit 72	Visit 99 (Month 45)	F03
Visit 73	Visit 100	F03
Visit 74	Visit 101 (Month 46)	F03
Visit 75	Visit 102	F03
Visit 76	Visit 103 (Month 47)	F03
Visit 77	Visit 104	F03
Visit 78	Visit 105	F03
VISIT 79 (month 36)	Visit 106 (Month 48)	F03
Visit 80	Visit 107	F03
Visit 81	Visit 108 (Month 49)	F03
Visit 82	Visit 109	F03

Visit 83	Visit 110 (Month 50)	F03
Visit 84	Visit 111	F03
Visit 85	Visit 112 (Month 51)	F03
Visit 86	Visit 113	F03
Visit 87	Visit 114 (Month 52)	F03
Visit 88	Visit 115	F03
Visit 89	Visit 116 (Month 53)	F03
Visit 90	Visit 117	F03
Visit 91	Visit 118	F03
VISIT 92 (month 42)	Visit 119 (Month 54)	F03
Visit 93	Visit 120	F03
Visit 94	Visit 121 (Month 55)	F03
Visit 95	Visit 122	F03
Visit 96	Visit 123 (Month 56)	F03
Visit 97	Visit 124	F03
Visit 98	Visit 125 (Month 57)	F03
Visit 99	Visit 126	F03
Visit 100	Visit 127 (Month 58)	F03
Visit 101	Visit 128	F03
Visit 102	Visit 129 (Month 59)	F03
Visit 103	Visit 130	F03
Visit 104	Visit 131	F03
Visit 105 (month 48)	Visit 132 (Month 60)	F03
Visit 106	Visit 133	F03
Visit 107	Visit 134 (Month 61)	F03
Visit 108	Visit 135	F03
Visit 109	Visit 136 (Month 62)	F03
Visit 110	Visit 137	F03
Visit 111	Visit 138 (Month 63)	F03
Visit 112	Visit 139	F03
Visit 113	Visit 140 (Month 64)	F03
Visit 114	Visit 141	F03
Visit 115	Visit 142 (Month 65)	F03
Visit 116	Visit 143	F03
Visit 117	Visit 144	F03
VISIT 118 (month 54)	Visit 145 (Month 66)	F03
Visit 119	Visit 146	F03
Visit 120	Visit 147 (Month 67)	F03
Visit 121	Visit 148	F03
Visit 122	Visit 149 (Month 68)	F03
Visit 123	Visit 150	F03
Visit 124	Visit 151 (Month 69)	F03
Visit 125	Visit 152	F03
Visit 126	Visit 153 (Month 70)	F03

Visit 127	Visit 154	F03
Visit 128	Visit 155 (Month 71)	F03
Visit 129	Visit 156	F03
Visit 130	Visit 157	F03
VISIT 131 (month 60)	Visit 158 (Month 72)	F03