COVER PAGE

TITLE: International, multicentre, efficacy and safety study of I10E in the maintenance treatment of patients with Chronic Inflammatory Demyelinating Polyradiculoneuropathy: Extension of PRISM study I10E-1302

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LFB BIOTECHNOLOGIES

STATISTICAL ANALYSIS PLAN

An international, multicentre, efficacy and safety study of I10E in the maintenance treatment of patients with Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP): Extension of PRISM study I10E-1302
CLINICAL TRIAL PROTOCOL: N°*I10E-1306* / EUDRACT N° 2013-005558-31
Version 5.0 dated 3 March 2017

Investigational Medicinal Product:	***I10E, a ready-to-use liquid human normal immunoglobulin for intravenous administration (IVIG), 100 mg/ml***
Indication:	***Maintenance treatment of Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP)***
Study design:	Phase III, international, multicentre, single-arm, open-label prospective study (extension of the PRISM study I10E-1302)
Sponsor:	**LFB BIOTECHNOLOGIES** 3 avenue des Tropiques BP 40305 91958 COURTABOEUF Cedex - France
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Project Statistician:	[redacted]

Clinical trial number: *I10E-1306*
Version number: 2.0
Version date: 2017-010-30
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1 LIST OF ABBREVIATIONS

Ab	Antibody
ACR	Albumin to Creatinine Ratio
AE	Adverse Event
AER	Albumin Excretion Rate
ALP	Alkaline Phosphatase
ALT	Alanine Amino Transferase
AST	Aspartate Amino Transferase
ATC	Anatomical Therapeutic Chemical
BAFF	B Cell Activating Factor
BMI	Body Mass Index
bpm	Beats per Minute
CGI	Clinical Global Impression
CI	Confidence Interval
CIDP	Chronic Inflammatory Demyelinating Polyradiculoneuropathy
CNTN1	Contactin 1
CRA	Clinical Research Associate
CRF	Case Report Form
CSA	Cross Section Area
DILI	Drug-induced Liver Injury
dps	decimal places
EOS	End of Study
FAS	Full Analysis Set
GFR	Glomerular Filtration Rate
γGT	γ Glutamyl Transferase
Hb	Hemoglobin
HBc	Hepatitis B core Antigen
HBs Ag	Hepatitis B surface Antigen

HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
ICH	International Conference on Harmonization
Ig	Immunoglobulin
IgA	Immunoglobulin A
IgG	Immunoglobulin G
IMP	Investigational Medicinal Product
INCAT	Inflammatory Neuropathy Course and Treatment
IVIG(g)	Intravenous Immunoglobulin
KM	Kaplan-Meier
kPa	Kilopascal (Pressure Unit)
LDH	Lactate Dehydrogenase
LFT	Liver Function Test
LLN	Lower Limit of Normal
LOCF	Last Observation Carry Forward
MCV	Mean Corpuscular Volume
MDRD	Modified Diet in Renal Disease
MedDRA	Medical Dictionary for Regulatory Activities
MRC	Medical Research Council
NF155	Neurofascin 155
PCR	Protein to Creatinine Ratio
PER	Protein Excretion Rate
PPS	Per Protocol Set
PT	Preferred Term
R-ODS	Rasch-built Overall Disability Scale
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System

SCIG(g)	Subcutaneous Immunoglobulin
SI	Standard International
SOC	System Organ Class
SOP	Standard Operating Procedure
SWI	Standard Working Instruction
TAAE	Temporarily Associated Adverse Event
TEAE	Treatment Emergent Adverse Event
TTS	Total Treated Set
ULN	Upper Limit of Normal
WHO	World Health Organisation

2 INTRODUCTION

2.1 STUDY OBJECTIVES

2.1.1 Primary Objective

The primary objective of this study is to assess the efficacy of I10E administered at a reduced maintenance dose in sustaining chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) response after an initial 6-month treatment in the PRISM study (I10E-1302).

2.1.2 Secondary Objective

The secondary objective of this study is to assess the safety of I10E.

2.1.3 Exploratory Objectives

The following are the exploratory objectives of the study:

- To assess a potential relationship between serum total IgG trough levels, biomarkers levels and clinical response, as assessed by neurological scales, in patients with CIDP.
- To assess a potential relationship between US coupled to neurophysiology analysis of nerves and clinical responses, as assessed by neurological scales, in patients with CIDP (ancillary study in Italy only).

2.2 STUDY DESIGN

This study is a phase III, international, multicentre, single-arm, open-label, prospective study and an extension of the PRISM study (I10E-1302).

2.3 SAMPLE SIZE

The number of patients included in this study depends on the number of responders in the I10E-1302 trial willing to participate in the extension study. Thus, no formal sample size calculation is done. The number of responders in the I10E-1302 trial is estimated to be between 15 and 30 patients.

2.4 INVESTIGATION SCHEDULE AND RANDOMISATION

The total duration of the study for a patient is approximately 48 weeks. Each patient who achieved a *response* in the I10E-1302 study, fulfils all eligibility criteria for I10E-1306 study is proposed to participate in this trial. The duration of treatment is approximately 45 weeks. A follow-up period of 3 weeks will take place after the administration of the last study drug.

Randomisation is not applicable in this single-arm study.

2.5 EVALUATION CRITERIA

2.5.1 Primary Efficacy Criterion

The primary efficacy criterion is *response* at the End of Study (EOS) visit. A patient is defined as having a *response* (or being a *responder*) if both conditions below are fulfilled:

- The patient's adjusted inflammatory neuropathy course and treatment (INCAT) disability score did not increase by more than 1 between baseline and EOS visit.
- The patient's CIDP treatment was not changed between baseline and EOS visit.

A change in CIDP treatment is defined by any of the following conditions:

- Increase/decrease of the dose (g/kg) of the study treatment by 5%
- Decrease of the time between courses
- Addition of corticosteroids (equivalent of more than 10 mg/day of prednisone for more than 10 days) or immunosuppressive drugs. As this condition is not possible to derive by programming, the study physician will review all treatments with corticosteroids and immunosuppressive drugs prior to database lock and flag those who fulfil the condition
- Premature discontinuation of study drug due to insufficient response to IMP and start of other CIDP treatments such as IVIg (other than study drug), corticosteroids, immunosuppressive drugs or plasma exchange

2.5.2 Secondary Efficacy Criteria

Secondary efficacy criteria are the following:

- Change from baseline to 24 weeks (Visit V9) and EOS visit in the adjusted INCAT disability score
- Response at 24 weeks (Visit V9)
- Time to relapse
- Change from baseline to 24 weeks (Visit V9) and EOS visit in the following scores:
    - Grip strength with the Martin vigorimeter in both hands
    - Rasch-built Overall Disability Scale (R-ODS)

- Medical Research Council (MRC) 12 muscles sum score (0 to 5) and Rasch-modified MRC sum score (0 to 3)

- Percentage of patients at 24 weeks (Visit V9) and EOS visit with no requirement of change in CIDP treatment from baseline
- Change from baseline to 24 weeks (Visit V9) and EOS visit in the patient's and investigator's Clinical Global Impression (CGI)

2.5.3 Safety Criteria

The safety criteria include:

- Treatment emergent adverse events (TEAEs)
- Serious adverse events (SAEs)
- Temporarily associated adverse events (TAAEs), i.e. AEs that begin during an infusion or within 72 hours after an infusion
- Clinically significant changes from baseline in vital signs
- Clinically significant changes from baseline in laboratory parameters

2.5.4 Exploratory Criteria

The following exploratory endpoints will be considered:

Biomarker study

- Anti-Contactin 1 (CNTN1) and anti-Neurofascin 155 (NF155) antibodies titers at screening and EOS visit
- B-cell activating factor (BAFF) at EOS visit
- Complement components (C3 and C4 antigens, CH50) at EOS visit
- Serum total IgG trough levels at each visit, within 24 hours prior to study drug administration

2.6 STUDY PLAN TABLE

	Inclusion	Week 3	Week 6	Week 9	Week 12	Week 15	Week 18	Week 21	Week 24	Week 27	Week 30	Week 33	Week 36	Week 39	Week 42	Week 45	End of study (EOS)
	VISIT 1	VISIT 2	VISIT 3	VISIT 4	VISIT 5	VISIT 6	VISIT 7	VISIT 8	VISIT 9	VISIT 10	VISIT 11	VISIT 12	VISIT 13	VISIT 14	VISIT 15	VISIT 16	VISIT 17
Informed consent (before any procedure of study)	X																
Inclusion/exclusion criteria	X																
Demographics & Medical history	(X)																
Safety																	
Adverse events assessment	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Phone call 4 days (+/- 1 day) after study drug administration	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Ongoing concomitant medication	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Patient diary (delivery and verification)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Clinical assessments / Before study drug administration																	
Complete physical examination	X								X								X
Clinical examination focused on arterial or venous thromboembolic signs		X	X	X	X	X	X	X		X	X	X	X	X	X	X	
Weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Body temperature, heart rate, arterial blood pressure (systolic and diastolic)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Efficacy assessments / Before study drug administration																	
INCAT disability score	(X)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
MRC sum-score, Rash modified MRC sum-score R-ODS Grip Strength (both hands)	(X)								X								X
Patient and Investigator : CGI (Severity), CGI (Efficacy), CGI (Improvement)	(X)								X								X

Biological test Local lab / Before study drug administration	VISIT 1	VISIT 2	VISIT 3	VISIT 4	VISIT 5	VISIT 6	VISIT 7	VISIT 8	VISIT 9	VISIT 10	VISIT 11	VISIT 12	VISIT 13	VISIT 14	VISIT 15	VISIT 16	VISIT 17
Serum total IgG trough levels	(X)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urine protein reagent strip test	(X[a])	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]	X[a]
Urine Pregnancy test for female with child bearing potential	(X)																X
C3 and C4 antigens	(X)																X
Anti HBs & anti HBc Ab, HBs Ag tests, HIV and HCV tests	(X)																X
Complete blood count and differentials, haemoglobin, mean corpuscular volume, platelet count, haptoglobin,	(X)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Reticulocytes, direct Coombs test, total serum protein level	(X)																X
AST, ALT, ALP, GT	(X)																X
Creatininemia, GFR[b], total and free bilirubin[c], LDH	(X)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Serum reference sample for long term storage	(X)																X
Biological test Local lab in case of suspected clinical thrombosis																	
D-Dimers	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Biological test Local lab in case of suspected haemolysis																	
Reticulocytes, direct Coombs test	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Exploratory assessment/ Central lab/ Before study drug administration																	
Anti-CNTN1 and anti-NF155 antibodies	(X)																X
BAFF, CH50	(X)																X
Ultrasonography coupled to neurophysiology (Italian sites only)	(X)																X

(brackets) = performed for study I10E-1302

	VISIT 1	VISIT 2	VISIT 3	VISIT 4	VISIT 5	VISIT 6	VISIT 7	VISIT 8	VISIT 9	VISIT 10	VISIT 11	VISIT 12	VISIT 13	VISIT 14	VISIT 15	VISIT 16	VISIT 17
Study drug administration																	
I10E – 0.50 g/kg	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Vital signs 30-45 minutes and 60-75 hour after the start of study drug administration (each day of study drug administration)																	
Body temperature, heart rate, arterial blood pressure (systolic and diastolic)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Vital signs 30-45 min after the end of study drug administration (each day of study drug administration)																	
Body temperature, heart rate, arterial blood pressure (systolic and diastolic)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	

[a] *To be performed before study drug administration in patients who at screening in the I10E-1302 Clinical Study tested for urine protein reagent strip result "1 cross 1 (+) and/or had GFRc in the range of 60-80 mL/min/1.73m²:*

Urine protein reagent strip test result	Action
Negative or Trace	No further urine test required
1 cross (1 +) or more	Assess either AER or PER from a 24h-urine collection sampled at least 7 days after the end of the previous study drug course or assess ACR or PCR from a spot urine sample immediately following the urine protein reagent strip test (i.e. urine obtained before study drug administration). At all visits except End of Study visit: The Investigator must review these results in time prior to the next study drug administration and consider if any of the Early Discontinuation Criteria / Stopping Rules (see Section Section 5.4 of the protocol) apply.

[b] *According to MDRD calculation*

[c] *Total bilirubin in all patients; if total bilirubin > ULN, free bilirubin will be assessed from the same blood sample, as total bilirubin*

3 GENERAL STATISTICAL CONSIDERATIONS

As this study is an extension study, some of the patient data are only collected in the I10E-1302 study (e.g. demography). The necessary information for the analyses of this study are obtained by combining the necessary information from the database of I10E-1302 and I10E-1306. The details about which data are to be taken from I10E-1302 are given in the respective analyses within this Statistical Analysis Plan (SAP).

3.1 DESCRIPTION OF VARIABLES

Continuous data will be described using number of valid observations, number of missing observations, mean, standard deviation, median, quartiles, minimum and maximum.

Categorical data will be described using number of missing observations, number of valid observations per category and percentage. Number of missing observations will not be taken into account for the calculation of percentages.

For descriptive statistics, the following number of decimal places (dps) will generally be applied:

- 3 dps for values in [0, 0.9995)
- 2 dps for values in [0.9995, 9.995)
- 1 dp for values in [9.995, 99.95)
- 0 dp for values ≥99.95

For negative values the same rule will be followed using the absolute value.

For original case report form (CRF) variables the minimum and maximum will use to the same number of dps as the raw data. Statistics on count variables (e.g. number of infusions) will generally be presented with 1 dp while the minimum and maximum will be presented without dp. Percentages will be presented with 1 dp. Exceptions from these rules might be applied when necessary.

3.2 HANDLING OF MISSING DATA AND OUTLIERS

Regarding the primary criterion, a patient will be also considered as a non-responder if the patient is withdrawn due to lack of efficacy of the treatment (insufficient response to the investigational medicinal product [IMP]). If the INCAT score at EOS visit is missing, then the Last Observation Carried Forward (LOCF) approach will be applied and the last available adjusted INCAT disability score will replace the missing value at EOS visit.

The LOCF approach will also be used to handle the missing data of secondary endpoints.

When AEs are documented in the diary, date-time of AE onset may be missing or incomplete. As a result, it might not be possible to determine if the AE started between the start of an infusion until 72 hours after the end of the infusion (Temporally Associated AE [TAAE]). In such cases, the response to the question "Did the

AE start within 72 hours of an infusion" will be used for determining if the AE is temporally associated to an infusion or not.

Partial dates of first symptoms and partial dates of diagnosis (collected in the I10E-1302 study) will be imputed by 15 if only the day is unknown and by 1st July if day and month are unknown. No imputation will be done if the year is unknown.

For the calculation of duration of AEs, partial start and end dates will be imputed with the first and last possible date within the period defined by the partial date, respectively. In general, no calculation of duration will be made if either the start date or stop date is missing, i.e., can't be imputed using pre-determined rules.

No other general rules for the replacement of missing data are planned.

Data listings will always show the original CRF reported values and not the imputed values.

3.3 Handling of Local Laboratory Data

Given that local laboratories were utilized for the study, laboratory results standardization may be utilized. This will proceed as follows. Denote by R_U and R_T the untransformed result and transformed result, respectively, and (I_L, I_H) and (S_L, S_H) are the investigators' and standard lower and upper limits of normality, respectively, then the transformed laboratory result can be derived using the expression

$$R_T = S_L + \frac{R_U - I_L}{I_H - I_L}(S_H - S_L).$$

Note that conversion to SI units of the untransformed result will precede the standardization process. The transformed result will be used for descriptive summaries and displays for observed and change values. If standardization is not utilized, then the untransformed result will be used for descriptive summaries and displays for observed and change values. In either case, summaries and displays for laboratory categories such as abnormalities based on L (below LLN), N (between LLN and ULN) and H (above ULN) classifications will use the classifications based on the untransformed result.

Final decision on laboratory results standardization will be made prior to database lock and will be contingent on the evaluation of the sparseness of laboratory data, the completeness of the local laboratories' normal ranges, and the choice of the standard normal ranges.

3.4 Multiplicity Issues, Subgroup Analysis, Interim Analysis, Blinding and Randomisation

This study is purely descriptive and no hypotheses are tested. No multiplicity issues are present.

No subgroup analyses and no interim analyses are planned.

Likewise, blinding and randomisation is not applicable in this single-arm trial.

3.5 Definition of the Protocol Deviations and Populations

3.5.1 Populations

The definition of analysis sets is as follows:

- Total Treated Set (TTS): all patients who received at least one administration of the study drug.
- Full Analysis Set (FAS): all TTS patients having an available assessment of the primary efficacy criterion.
- Per Protocol Set (PPS): all FAS patients without any major deviations from protocol.

If a patient is treated with a non-permitted treatment during the study period, specifically those that confound efficacy evaluation, then all efficacy variables measured after the intake of these not-allowed treatments will be censored for the efficacy analyses. Censoring of measurements will be done up to a reasonable window from the start time of a prohibited treatment where the window is determined according to the half-life of the not- allowed treatment. The window will be adjudicated prior to database lock.

The TTS will be used for the analysis of safety data.

The FAS will be used for the primary analysis of efficacy data and the PPS to test its robustness.

3.5.2 Protocol Deviations

The protocol deviations and corresponding categories are defined in the protocol deviation specifications as well as their consequence for the inclusion in the different analysis sets. The following protocol deviations categories will be studied:

- Deviations regarding inclusion criteria
- Deviations regarding exclusion criteria
- Deviations regarding the study drug
- Deviations regarding safety assessments
- Deviations regarding assessment of laboratory parameters (including biomarkers)
- Deviations regarding visit windows
- Deviations regarding informed consent
- Deviations regarding forbidden treatments during the study

- Deviations regarding overdose/misuse of study drug
- Other deviations
- Deviations regarding the primary efficacy endpoint
- Deviations regarding other efficacy endpoints
- Deviations regarding exploratory endpoints
- Deviations regarding the ancillary study
- Deviations regarding study material

In addition to these protocol deviations, other protocol deviations may be reported by the clinical research associate (CRA).

All the protocol deviations which occurred during the study will be examined during the final data review meeting. All adjudicated protocol deviations will be presented in data listings.

4 STATISTICAL ANALYSIS

4.1 DISPOSITION OF PATIENTS

In order to describe the population, descriptive statistics (number, or number and percentages) will be provided for the following:

- Patients screened (patients who signed informed consent)
- Patients enrolled
- Patients with a screening failure
- Patients who received study treatment (TTS)
  - Patients participating in the ancillary study
  - Patients who completed the study
  - Patients withdrawn early from the study and reasons for study discontinuation [AE, Protocol deviation, Withdrawal of consent, Lost to follow-up, Insufficient response to IMP, Other]

  Patients withdrawn early due to insufficient response of IMP with reason for insufficient response (INCAT, MRC sum score, R-ODS, Grip strength, CGI-Patient, CGI-Investigator, Clinical examination, Premature termination of IMP) and follow-up treatment (IVIg, Corticosteroids, Immunomodulatory or immunosuppressive agent or Other)
- Patients included in the FAS
- Patients included in the PPS

A separate in-text summary table will be produced to contain the following information: patients who received at least one dose of IMP in I10E-1302; non-responders in I10E-1302; responders in the study; and patients who discontinued. An in-text listing with all patients who were discontinued due to "Insufficient response to the IMP" may be produced. The said listing will contain identifiable relapse risk information based on review of efficacy and safety information.

Except for patients enrolled and patients with a screening failure, percentages will be calculated using the number of patients of the TTS as the denominator. For screen failure patients, a listing will be produced with the reason for screening failure and the specifications provided by the investigator. For patients who discontinued the study, a listing will be produced with the reasons of study discontinuation and the specifications provided by the investigator.

4.2 Protocol Deviations

The absolute number of deviations as well as the number and percentage of patients with at least one protocol deviations will be tabulated by deviation category and by the classification into Minor/Major. Deviation details will be provided in a listing.

4.3 Demographic and Baseline Characteristics

Unless otherwise specified, the baseline value is defined as the last available value before the first IMP course in I10E-1306. The baseline value might therefore come either from the last visit in the I10E-1302 study or the first visit in the I10E-1306 study.

The following characteristics will be summarized in subjects of the TTS. If the FAS significantly differs from the TTS, the characteristics will also be summarized on the FAS.

Parameter	**Data origin**
• Demographic characteristics: Age (years), Gender, Race, and Ethnicity (if collected)	I10E-1302
• Clinical examination:	
o Weight (kg), Height (cm) and Body Mass Index (kg/m²)	I10E-1302
• History of CIDP disease:	
o Time since the date of first symptoms	I10E-1302
o Time since the date of diagnosis	I10E-1302
o Time between first symptoms and diagnosis	I10E-1302
o Diagnostic categories of CIDP	I10E-1302
o Clinical criteria of CIDP (typical / atypical)	I10E-1302

- Electrophysiological criteria of definite CIDP — I10E-1302
- Supportive criteria of CIDP — I10E-1302
- Current INCAT disability score (arms, legs and global non-adjusted INCAT scores and global adjusted INCAT score) — I10E-1306

- Prior medications
  - Prior medications will be presented by therapeutic subgroup (level 2) and chemical subgroup (level 4) according to version WHO_DDE_B2_DECEMBER_1_2014 of the World Health Organization's (WHO) Anatomical Therapeutic Chemical (ATC) classification system. — I10E-1302

    The term "prior medication" refers to any prior medication of the I10E-1302 study plus all concomitant medication given during the I10E-1302 study which ended before the first visit of the I10E-1306 study.
- Medical and surgical history
  - Medical and surgical history will be classified by PT and SOC using the version 17.1 of the Medical Dictionary for Regulatory Activities (MedDRA). — I10E-1302

    The term "Medical and surgical history" refers to any medical and surgical history of the I10E-1302 study plus all adverse events which occurred in the I10E-1302 study.

A listing of prior CIDP treatment(s) since diagnosis [e.g., intravenous Ig (IVIg), subcutaneous Ig (SCIg), corticosteroids, and immunomodulatory or immunosuppressant agents] will be produced. The listing information will include patient status (naïve/in relapse), dosing information (start/stop times, duration, time since last dose), and reason for stopping (as applicable). As subsequent treatment periods with IVIg, corticosteroids and immunomodulatory or immunosuppressant agents might be reported under the category *Other* in the CRF, the reported treatments in this category will be classified into IVIg, corticosteroids, immunomodulatory or immunosuppressant agents and other. A listing with other treatments and their duration will be presented.

4.4 CONCOMITANT TREATMENTS

Prior medications are any medications the patient received up to 8 months before screening or judged relevant by the Investigator. Thus, a prior medication is defined as a medication with a date of screening ≤ start date + 8 months. If a medication has a partial start date, the earliest possible date within the partial date is used.

Concomitant medications are any medications the patient received at any time during the study, i.e. from screening to EOS visit. Thus a concomitant medication is defined as a medication with a treatment period which has at least one day in common with the period date of screening to EOS visit, i.e.

- Date of screening ≤ Start date of medication ≤ Date of EOS visit or

- Date of screening ≤ End date of medication ≤ Date of EOS visit or
- Start date of medication ≤ Date of screening and Date of EOS visit ≤ End date of medication

If a medication has a partial start date or end date, the earliest possible date within the partial start date is used and the last possible date within the partial end date.

Prior and concomitant medications will be summarized using TTS and will be classified according to version WHO_DDE_B2_DECEMBER_1_2014 of the WHO ATC classification system. Separate tables will be produced for prior and concomitant medications presenting the number and percentage of patients with at least one medication by therapeutic subgroup (level 2) and chemical subgroup (level 4). The tables will be sorted by decreasing incidence of therapeutic subgroup and by decreasing incidence of chemical subgroup within therapeutic subgroup.

4.5 COMPLIANCE

Study treatment compliance will be summarized using the TTS. Treatment compliance will be presented at the patient level as described below. The term *Planned* refers to the treatment dose and frequency planned at enrollment. The term *Prescribed* refers to the treatment dose and frequency reported at each IMP course and infusion.

Compliance will be described at the course level using the following criteria:

- Prescribed course dose (g/kg) = Theoretical course dose (g/kg)
  Theoretical course dose is defined according to the protocol as 0.5 g/kg.
- Time since previous course = 3 weeks ± 7 days
- Courses administered within 1 to 2 days
- Duration of the flow rate of the first course infusion remains unchanged for at least 25 minutes
- Flow rate of the first infusion of a course ≤0.5 mL/kg/h

Compliance will be described by patients using the following criterion:

- Total patient compliance: A patient is compliant if all courses of the patient are compliant.

Non-compliant courses and infusions will be listed by patient showing all of the above criteria. The criterion leading to non-compliance will be flagged.

4.6 EFFICACY ANALYSES

The efficacy analyses will be performed on the FAS. The analyses of the primary endpoint will be repeated on the PPS as sensitivity analysis (only if the PPS is different from the FAS).

If a patient is treated with a non-permitted treatment during the study period, then all efficacy variables measured after the intake of these not-allowed treatments will be censored for the efficacy analyses. Assessments of primary and secondary criteria after a forbidden treatment will be flagged in all listings.

The following treatments are not allowed during the study.

- Plasma exchange, blood products or derivatives other than the study drug.
- Immunomodulatory or immunosuppressant agents (e.g. including but not limited to cyclophosphamide, cyclosporine, interferon-α, interferon-β1a, anti-CD20, alemtuzumab, aziathioprine, etanercept, mycophenolate mofetil, methotrexate and haemotopoeitic stem cell transplantation).
- Oral or systemic corticosteroids if administered with an increasing dosage or introduced at a dose higher than 10 mg daily prednisolone or equivalent. Topical corticosteroids are permitted.
- Loop diuretics administered during the last 24 hours before an IVIg infusion.

4.6.1 Primary Efficacy Endpoint

The primary efficacy criterion is *response* of the patients at EOS visit. A patient is defined as having a *response* (or being a *responder*) both conditions below are fulfilled.

- The patient's adjusted INCAT disability score did not increase by more than 1 between baseline and EOS visit.
- The patient's CIDP treatment was not changed between baseline and EOS visit.

A change in CIDP treatment is defined by any of the following conditions:

- Increase/decrease of the dose (g/kg) of the study treatment by 5%
- Decrease of the time between courses
- Addition of corticosteroids (equivalent of more than 10 mg/day of prednisone for more than 10 days) or immunosuppressive drugs. As this condition is not possible to derive by programming, the study physician will review all treatments with corticosteroids and immunosuppressive drugs prior to database lock and flag those who fulfil the condition
- Premature discontinuation of study drug due to insufficient response to IMP and start of other CIDP treatments such as IVIg (other than study drug), corticosteroids, immunosuppressive drugs or plasma exchange

The primary analysis of the primary efficacy criterion will be done using the baseline and last available assessment of the adjusted INCAT disability score after the first study drug administration. That is, if the score at EOS visit is missing, then the Last Observation Carried Forward (LOCF) approach will be applied and the last available adjusted INCAT disability score will replace the missing value at EOS visit.

Similarly, if the assessment of the adjusted INCAT disability score is censored due to an intake of a forbidden treatment, the adjusted INCAT disability score from the last assessment before the intake of the forbidden treatment is used as replacement for the assessment of the EOS visit.

The number and percentage of Responders at EOS will be presented with descriptive statistics. The associated exact 95% Clopper-Pearson confidence interval (CI) will be calculated for the proportion of Responders.

The primary analysis will be performed using the FAS and a sensitivity analysis will be performed using the PPS.

4.6.2 Secondary Efficacy Endpoints

The following secondary efficacy endpoints will be studied.

1) Adjusted INCAT disability score

   The adjusted INCAT disability score will be presented with descriptive statistics at each visit. The change from baseline in the adjusted INCAT disability score will be analysed at 24 weeks and EOS visit.

   Several graphics will be produced:

   - Boxplots over time of a) the at-visit values and b) change from baseline
   - Waterfall plots faceted by visit of a) the at-visit values and b) change from baseline

2) Time to relapse

   Relapse is defined as as one of the following conditions:

   - Adjusted INCAT disability score increase by 1 point compared to baseline

     AND

     Judging on the clinical examination and/or the neurological scales assessments, the Investigator considers change in patient's treatment is mandatory: increase in IVIg dosage, increase or initiation of a corticotherapy, immunosuppressive therapy, plasma exchange.
   - Adjusted INCAT disability score increase by at least 2 points compared to baseline.

   Time to relapse (measured from the first IMP infusion in I10E-1306) will be analysed using a Kaplan-Meier (KM) method. Patients without relapse will be considered censored at their last assessment of the INCAT disability score. Patients with a forbidden treatment intake before a relapse will be considered censored at the date of the first intake of a forbidden treatment.

   KM estimates of the mean, the median as well as for the first and third quartile will be provided together with their associated 95% confidence interval. A KM-plot will be provided showing the incidence of relapse over time. Time of censoring will be displayed in the graph. A table will be included below the graph showing the number of patients "at risk" (i.e. without relapse), the number of patients with a relapse and the number of censored patients at the time points 0, 12, 24, 36 and 48 weeks.

   Descriptive statistics will be provided for the time to relapse on the subset of patients with relapse until EOS.

3) Grip strength (kPa) with the Martin vigorimeter in both hands

Grip strength (actual and normalized according to the healthy population) will be presented with descriptive statistics at baseline, week 24 and EOS for the dominant hand and the non-dominant hand side by side. The change from baseline in grip strength for the dominant hand and the non-dominant hand will be analysed at 24 weeks and at the EOS visit. The assessment at screening will be used for the determination of the dominant hand.

4) Rasch-built Overall Disability Scale (R-ODS)

R-ODS will be presented with descriptive statistics at baseline, week 24 and EOS visit. The change from baseline in R-ODS will be analysed at 24 weeks and at the EOS visit.

For the endpoints 1), 3), and 4) the Hodges-Lehmann estimator and the associated 95% confidence interval will be calculated for all at-visit values as well as for the change from baseline. The change from baseline for these endpoints will be tested using a Wilcoxon signed-rank test. All statistical tests will be descriptive and will use a two-sided significance level of α=5%.

Results for response rate at 24 weeks, MRC 12 muscles sum score, Rasch-modified MRC sum score, Percentage of patients without change in CIDP treatment from baseline to 24 weeks and EOS visit, and patient and investigator CGI will be presented in listings..

4.7 SAFETY ANALYSES

Safety analyses will be conducted on the TTS.

4.7.1 Extent of Exposure

Patient level analyses

The extent of exposure to IMPs will be summarized on the patient level using the following variables:

- Duration of study participation (m) from signing of informed consent to EOS: (EOS visit date – date of informed consent + 1) / 30.4375
- Duration of treatment exposure (m) from the first day of IMP administration to EOS: (EOS visit date – date of first IMP infusion + 1) / 30.4375
- Average course frequency:

  $\frac{1}{n_C}\sum_{j=1}^{n_C}\left(\text{start date of course}_{j+1} - \text{start date of course}_j\right)$, with n_C the number of courses of the patient

  For the last course, the date of the EOS visit will be used as the *start date of course* n_C+1.
- Total number of courses
- Average number of infusions per course: $\frac{1}{n_C}\sum_{j=1}^{n_C}(\text{number of infusions at course } j)$
- Total number of infusions $\sum_{j=1}^{n_C}(\text{number of infusions at course } j)$
- Cumulative dose over all infusions (g and g/kg): $\sum_{j=1}^{n_C}\sum_{k=1}^{n_{I_j}}(\text{dose at infusion } k \text{ of course } j)$, with n_{I_j} the number of infusions at course j of the patient

- Average dose per course (g and g/kg): $\frac{1}{n_C}\sum_{j=1}^{n_C}\sum_{k=1}^{n_{I_j}}(\text{dose at infusion } k \text{ of course } j)$
- Maximum dose over all infusions (g and g/kg)
- Maximum flow rate over all infusions (mL/kg/h)

Course level analyses

The extent of exposure to IMPs will be summarized on the course level using the following variables:

- Total number of infusions
- Course dose (g and g/kg)
- Average dose per infusion (g and g/kg): $\frac{1}{n_I}\sum_{k=1}^{n_I}(\text{dose at infusion } k)$, with n_I the number of infusions of the course
- Initial flow rate of the first course infusion (mL/kg/h)
- Duration of initial flow rate of the first course infusion (min)
- Maximum flow rate over all infusions (mL/kg/h)
- Duration of the course (day)

Infusion level analyses

The extent of exposure to IMPs will be summarized on the infusion level using the following variables:

- Dose (g and g/kg)
- Initial flow rate (mL/kg/h)
- Maximum flow rate (mL/kg/h)
- Number of flow rate changes
- Duration of the infusion (min)

In all three analysis levels, dose (g and g/kg) will be derived based on the prescribed administered volume reported in the CRF:

- Dose (g) = Daily volume administered (mL) * batch concentration (i.e. 0.1 g/L)
- Dose (g/kg) = Daily volume administered (mL) * batch concentration (i.e. 0.1 g/L) / body weight (kg) at the start of the course

A listing will be provided with the presented variables of each analysis level (patient, course, infusion).

4.7.2 Adverse Events

All AEs occurring during the study will be classified by preferred term (PT) and system organ class (SOC) using the version 17.1 of the Medical Dictionary for Regulatory Activities (MedDRA).

- Seriousness *Serious* if one of the follow-ups is serious / *Non-serious* otherwise

• Seriousness criterion	For each of the criteria listed below: *Yes* if at least one of the follow-ups had *Yes* for the corresponding criterion / *No* otherwise o *Results in death* o *Life-threatening* o *In patient hospitalisation or prolongation of existing hospitalisation* o *Persistent or significant disability / incapacity* o *Congenital anomaly / birth defect* o *Important medical event*
• Start date time	Start date time of the first follow-up
• End date time	End date time of the last follow-up
• Ongoing	*Yes* if last sequence follow-up is ongoing / *No* otherwise
• Did the AE start within 72h after an infusion?	*Yes* if the first follow-up started within the first 72h after an infusion / *No* otherwise
• Intensity	maximum(Intensity of follow-ups) Increasing order of importance: *Mild / Moderate / Severe*
• Action taken	maximum(Action taken of follow-ups) Increasing order of importance: *None / Dose changed / Interruption of IMP / Discontinuation of IMP*
• Corrective medication	*Yes* if at least one of the follow-ups had a corrective medication / *No* otherwise
• Relationship to study drug	*Yes* if at least one of the follow-ups had a relationship to study drug assessed as *Yes / No* otherwise
• Outcome	maximum(Outcome of corresponding follow-ups) Increasing order of importance: *Unknown / Recovered without sequela / Recovered with sequelae / Recovering / Not recovered / Fatal*

AEs will be classified as I10E-1302 AEs or treatment emergent AEs (TEAEs) according to the date of onset:

- I10E-1302 AEs are defined as events with a date-time of onset before the start date-time of the first infusion in I10E-1306.
- TEAEs are defined as events with a date-time of onset on or after the start date-time of the first infusion in I10E-1306.

Treatment Emergent Adverse Events (TEAE)

The following rules for the derivation of the TEAE status will be used in the order of display.

1. If the date-time of the AE onset is known: TEAE = "Yes" if AE onset date-time ≥ start date-time of first IMP infusion / "No" otherwise.

2. If the date-time of the AE onset is not known but the complete date of the AE onset is known:

   - TEAE = "Yes" if AE onset date > start date of first IMP infusion.
   - TEAE = "Yes" if AE onset date = start date of first IMP infusion and investigator's assessment of the time of onset ≠ "Before infusion".
   - TEAE = "No" otherwise.

3. If the date of AE onset is a partial date and the investigator's assessment of the time of onset is not missing: TEAE = "Yes" if investigator's assessment of the time of onset "During infusion", "≤72h" or ">72h".

4. If the date of AE onset is a partial date and the investigator's assessment of the time of onset is missing:

   - TEAE = "Yes" if last possible date in the period defined by the partial date ≥ start date of first IMP infusion / "No" if the last possible date in the period defined by the partial date < start date of first IMP infusion.

5. TEAE = "Yes" otherwise.

A summary of the total number of AEs, and number and percentage of patients with at least one AE will be presented. This summary will include:

- All TEAEs
- TEAEs by seriousness criterion
- TEAEs by drug relationship
- TEAEs by temporal association with infusion (TEAE within the 72h after an infusion Yes/No)
- TEAEs by severity (Mild / Moderate / Severe)
- TEAEs by Action taken with IMP (None / Dose reduced / Dose increased / Discontinuation of IMP / Interruption of IMP)
- TEAEs by outcome (Resolved without sequelae / Resolved with sequelae / Not recovered / Recovering / Fatal / Unknown)

A similar summary table will be produced for TAAEs as well as drug related TEAEs.

All TEAEs, SAEs and drug-related AEs will be summarized by SOC and PT, showing number of TEAEs, and number and percentage of patients with at least one TEAE, sorted by decreasing incidence of SOC and PT within SOC. Summary of TEAEs will also be presented by relevant subgroups (e.g., by age group [using

median as cut point], sex, race [white and non-white]/ethnicity [Hispanic or Latino and not Hispanic or Latino], and BMI [using median as cut point]). The rate of TEAEs by course and by infusion will be calculated as the absolute number of TEAEs divided by the number of courses and number of infusions, respectively and will be presented in the same manner.

Duration of TEAEs will be calculated as AE end date – AE start date + 1 and presented with descriptive statistics on recovered AEs (i.e. AEs with an outcome of "Recovered without sequelae" or "Recovered with sequelae"). Statistical unit of analysis will be the individual recovered TEAE. No imputation will be performed for the purposes of computing duration.

The time between the last administration of IMP to the onset of the TEAE will be calculated as AE start date – Date of previous IMP infusion and will be presented with descriptive statistics using the individual TEAE as statistical unit.

All SAEs, drug related AEs, AEs leading to dose changes or discontinuation of IMP, and other significant AEs will be listed.

Time of onset since last administration for most common TEAEs (those which occurred in at least 10% of the patients) will be presented by patient status (naïve/pre-treated) and by course number. Summary statistics including 95% confidence intervals will be calculated for each TEAE preferred term.

I10E-1302 AEs will be listed by patient.

Temporally Associated Adverse Events (TAAEs)

The following rules for the derivation of the TAAE status will be used in the order of display.

1. If the exact date-time of the AE onset is known this information will be used: TAAE = "Yes" if AE onset date-time ≥ start date-time of previous IMP infusion and (AE onset date-time – end date-time of previous IMP infusion) ≤ 72 hours / "No" otherwise".
2. If the exact date-time of onset is not known and the investigator's assessment of the time of onset is not missing: TAAE = "Yes" if investigator's assessment of AE onset time is either "During infusion" or "≤72h" / "No" otherwise".
3. If the exact date-time of onset is not known, the investigator's assessment of the time of onset is missing and the exact date of onset of the AE is known: TAAE = "Yes" if AE onset date is on the same day than an IMP infusion or within 3 days after an infusion / "No" otherwise".
4. TAAE = "No" otherwise.

The same analyses as for TEAEs will be repeated for the TAAEs, i.e. AEs which started within 72 hours of an infusion. For the determination if an AE started within the 72 hours of an infusion the date-time of onset of the AE outweighs the investigator's answer to the question if the AE occurred *Before infusion / During infusion / Within 72 hours after end of infusion / More than 72 hours after end of infusion*. The investigator's answer to this question is only considered for the determination of TAAE if the date-time of AE onset is not precise enough to make a clear decision (i.e. time missing and date on the same date as an infusion or three days after the end of the previous infusion, incomplete date of onset).

The summary table on TAAEs will be presented twice:

- Using the patient as statistical unit
- Using the individual infusion as statistical unit

4.7.3 Other Safety Endpoints

Unless otherwise specified, the baseline value is defined as the last available value before the first IMP course in I10E-1306. The baseline value might therefore come either from the last visit in the I10E-1302 study or the first visit in the I10E-1306 study.

- Laboratory data

  All laboratory values will be reported in standard international (SI) units. Summary displays for laboratory safety data (hematology and chemistry) will be produced by visit for both observed and change from baseline values of the different laboratory analyses. Laboratory tests taken only at screening, those in case of a qualifying event (e.g., thrombosis or haemolysis), and urine protein reagent strip test results will be presented in the laboratory listings. The following clinical parameters will be summarized:

  Hematology:
  - Complete blood count + differentials, hemoglobin (Hb), mean corpuscular volume (MCV), platelets count
  - Haptoglobin

  Biochemistry:
  - Creatininemia, glomerular filtration rate according to MDRD
  - LDH
  - Total and free bilirubin (total bilirubin in all patients; if total bilirubin > ULN, free bilirubin will be assessed from the same blood sample, as total bilirubin)
  - AST, ALT, alkaline phosphatase (ALP), γGT
  - Total serum protein level
  - Serum IgA levels

  Laboratory values will be classified as normal, low, or high based on standardized normal ranges. Laboratory categories will be expressed in terms of the L (below lower limit of normal [LLN]), N (between LLN and ULN) and H (above ULN) classifications for numerical measurements and normal, abnormal for categorical measurements. The number and percentage of patients with abnormal values

will be summarized for each laboratory parameter by visit. These summaries will include the number and percentage of patients with "any pre-treatment visit" and "any on-treatment visit post baseline" abnormality for each parameter. These displays will ensure that all abnormal values will be captured.

LNH shifts in clinical laboratory values (hematology and chemistry) from baseline to each visit post first dosing will be summarized by visit. Patients with values outside the normal range will be flagged.

Hy's Law, Temple's Corollary and Elevated Liver Function Test (LFT) Results

Incidence of patients with liver function test results satisfying the drug-induced liver injury (DILI) criterion defined as (> 3xULN for ALT/AST, > 2xULN for total bilirubin and ≤ 2xULN for ALP at the same time-point) will be presented by visit. According to Hy's Law, a pure DILI case leading to jaundice, without a hepatic transplant, has a case fatality rate of 10% to 50%.

Incidence of patients with liver function test results satisfying Temple's criterion defined as (> 3xULN for ALT/AST, ≤ 2xULN for total bilirubin and ≤ 2xULN for ALP at the same time-point) will be presented by visit.

In addition, incidence of elevated liver function test results will be presented at each visit by elevation criterion. Elevation criteria are given as follows:

- ALT (ULN - ≤ 3xULN, > 3xULN - ≤ 5xULN, > 5xULN)
- AST (ULN - ≤ 3xULN, > 3xULN - ≤ 5xULN, > 5xULN)
- Total Bilirubin (ULN - ≤ 2xULN, > 2xULN)
- ALP (ULN - ≤ 2xULN, > 2xULN)

A scatter plot of the values at the EOS assessment as well as the minimum and maximum values of each patient during the treatment follow-up against the values at baseline will be prepared for each parameter. The first diagonal will be displayed by a dotted line.

Laboratory test results will be listed, including all abnormalities, clinically significant or not. Pregnancy status and test results will also be listed, including the method of contraception used (if any).

- Vital Signs

Vital signs parameters including systolic and diastolic blood pressure (mmHg), heart rate (bpm), weight, and body temperature (°C) (calculated value according to the way the temperature was measured) will be summarized.

  - Patient level analyses

Descriptive statistics of vital sign values will be presented for the following time points.

a) Visit 1 may be taken from (I10E-1302)
b) Before first infusion
c) 30-45 min and 60-75 min after the start of the first infusion
d) 30-45 min after the end of the first infusion
e) EOS

Change from time point b) will be presented for time points c) to e). The minimum and maximum of each parameter during the patient's treatment follow-up will be presented.

A scatter plot of the values at the end of study assessment as well as the minimum and maximum values of each patient during the treatment follow-up against the values at baseline will be prepared for each parameter. The first diagonal will be displayed by a dotted line.

- Infusion level analyses

  Vital sign results will be presented in listings using the following time points.

  a) Before the start of the course (only first infusion of a course)
  b) 30-45 min and 60-75 min after the start of the infusion
  c) 30-45 min after the end of the infusion

  The listings will also include change from before start of the course to time points b) and c).

All abnormalities, clinically significant or not, will be listed in both patient level and course/infusion level formats.

- Thrombo-embolic physical examination

  Number and percentage of patients with at least one abnormal thrombo-embolic sign will be presented by visit together with the absolute number of signs for the following:

  - Arterial thrombo-embolic signs
  - Venous thrombo-embolic signs

- Complete physical examination

  Physical examination results will be listed.

4.8 PHARMACOKINETICS

Not Applicable.

4.9 EXPLORATORY ANALYSES

The following exploratory endpoints will be listed by visit using FAS.

1) Anti-CNTN1 and anti-NF155 antibodies titers at EOS visit
2) BAFF and complement components (C3 and C4 antigens, CH50) at EOS visit
3) Serum total IgG trough levels at least 24 hours prior each study drug administration

In addition, a listing of patients included in the ultrasonography ancillary study will be provided. The listing will include information on the consent date for the ancillary study and whether data were collected (Yes/No).

4.10 CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSIS

Early assessment of study results showed a remarkable percentage of patients who demonstrate CIDP relapse at the tested lower dose. It was decided then to early terminate the study in the interest of the patients and according to good clinical practices. This rationalized the presentation of the efficacy results to focus on key efficacy endpoints.

Results for response rate at 24 weeks, MRC 12 muscles sum score, Rasch-modified MRC sum score, Percentage of patients without change in CIDP treatment from baseline to 24 weeks and EOS visit, and patient and investigator CGI will be presented in listings.

Patient level and course/infusion level information will be provided for exposure, laboratory, and vital signs parameters.

Analysis of laboratory data may involve standardization procedure contingent on the evaluation of the sparseness of laboratory data, the completeness of the local laboratories' normal ranges, and the choice of the standard normal ranges prior to database lock. Liver function test results will be examined to identify Hy's Law, Temple's Corollary, and elevated test result cases.

Analysis of biomarker data will not be performed. Instead the data will be listed using FAS.

Planned analysis associated with the ultrasonography ancillary study will not be performed due to non-collection of required data.

5 APPENDICES

5.1 STATISTICAL SOFTWARE

Statistical analyses will be conducted on LFB server using SAS version 9.1.3 under Windows server 2012 R2.

5.2 STANDARD OPERATING PROCEDURES

The following Standard Operating Procedures will be followed:

- LFB SOP 203/05919 Statistical Analysis Plan
- LFB SOP 204/06045 Statistical Analysis Plan Template
- LFB SOP 203/05921 Statistical Programming
- LFB SOP 203/05924 Statistical Analysis
- LFB SOP 203/05897 Controlled Version of Study Documents
- LFB SOP 203/05926 Quality Control of Statistical Documents

5.3 AUDIT AND QUALITY CONTROL

5.3.1 Audit

An audit/inspection may be carried out by qualified Sponsor staff, by subcontracted auditors or by representatives of national or foreign Competent Authorities to ensure that the study is conducted as per protocol and in accordance with regulatory requirements, and to ensure the validity of the data.

5.3.2 Quality Control

A detail validation plan will be created describing quality control steps for analysis datasets, tables, listings and graphs.

5.4 STATISTICAL REVIEW

Statistical review of analysis datasets, tables, listings and graphs will be performed to ensure the accuracy and completeness of the data. The outcome of review will be documented using quality control sheets.

5.5 BIBLIOGRAPHY

Guideline (SWI) for Biostatistics and Statistical Programming

ICH E3 "Structure and Content of Clinical Study Reports"

ICH E9 "Statistical Principles of Clinical Trials"

5.6 BASIC DERIVED VARIABLES

5.6.1 Safety

Adverse Event Duration

The duration of AEs will be calculated as:

AE Duration (d) = AE stop date – AE start date + 1

Similar formula will be used for any duration-related calculations.

Time to AE onset

The time to onset of an AE since the previous infusion will be calculated as:

Time to AE onset (d) = AE start date – Date of previous IMP infusion + 1

Similar formula will be used for any time to event-related calculations.

Estimated GFR (MDRD Equation)

$$GFR\ (mL/min/1.73\ m^2) = 175 \times (Scr)^{-1.154} \times (Age)^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if African American})$$

Source: https://www.niddk.nih.gov/health-information/communication-programs/nkdep/laboratory-evaluation/glomerular-filtration-rate/estimating

5.6.2 Exposure

$$\text{Actual administered dose (g)} = \frac{\text{Batch titer (g/200mL)} \times \text{Volume infused (ml)}}{200}$$

5.6.3 Other Characteristics

Age at screening

Age at screening (years) = (Date of informed consent – Date of Birth + 1) / 365.25

Body Mass Index (BMI)

BMI (kg/m^2) = Weight (kg) / (Height (m) x Height (m))

Disability Scores

INCAT/Adjusted INCAT disability score = arm disability score + leg disability score