

CONFIDENTIAL

STATISTICAL ANALYSIS PLAN

for 5, 6 or 7 year follow-up control after the SCHEDULE study
(SCANDINAVIAN HEART TRANSPLANT EVEROLIMUS DE NOVO STUDY WITH EARLY CNI AVOIDANCE)

Sponsor Study Code: CRAD001ANO05 / NCT02864706 (Previous CRAD001ANO026YFU)

[REDACTED]

Sponsor Novartis

Product/Compound Everolimus (Certican®)

Phase of the study IV

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ABBREVIATIONS

AE	Adverse Event
ANCOVA	Analysis of Covariance
BDI	Beck Depression Inventory
BiVad	Biventricular Assist Device
BMI	Body Mass Index
CAV	Cardiac Allograft Vasculopathy
CI	Confidence Interval
CRF	Case Report Form
CsA	Cyclosporine
CSP	Clinical Study Protocol
ECG	Electrocardiogram
ECMO	Extra Corporal Membrane Oxygenation
EQ-5D	Euro Quality of Life 5D
FF	Fractional shortening
IMP	Investigational Medicinal Product
ITT	Intention-to-Treat
IVUS	Intravascular Ultrasound
LOCF	Last Observation Carried Forward
LVAD	Left Ventricular Assist Device
LVEDD	Left Ventricular End Diastolic Dimension
LVEF	Left Ventricular Ejection Fraction
LVESD	Left Ventricular End Systolic Dimension
MedDRA	Medical Dictionary for Regulatory Activities
MDRD	Modification of Diet in Renal Disease Study Group
mGFR	measured Glomerular Filtration Rate
MMF	Mycophenolate Mofetil
MMRM	Mixed Model Repeated Measures
PPS	Per Protocol Set
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SF-36	Short Form 36
SOC	System Organ Class
VAS	Visual Analogue Scale
WHO	World Health Organization

1 INTRODUCTION

This Statistical Analysis Plan (SAP) is based on Clinical Study Protocol (CSP) final version 2.0 DK, dated 07-Jul-2016 including Amendments No. 1, dated 27-Jun-2016 and Updates to Section 4.5 as requested by the Danish Health Authority. The CSP describes the procedures for a single 5, 6 or 7 year follow-up control visit of patients that participated in the 12-month SCHEDULE-study and the following 3-year follow-up examination/visit.

2 STUDY OBJECTIVES

Purpose

To evaluate, in *de novo* heart transplant recipients, whether early initiation of everolimus and early elimination of cyclosporine (CsA), compared to standard immunosuppressive regimen including CsA can improve long-term renal function and slow down the progression of Cardiac Allograft Vasculopathy (CAV).

Aim

The major aim of this extension study is to evaluate the long-term (i.e. 5 to 7 years) effect of early initiation of everolimus and early elimination of CsA compared to standard immunosuppressive regimen including CsA on primary and secondary endpoints investigated in the SCHEDULE main study.

3 EFFICACY AND SAFETY ENDPOINTS

3.1 Primary Efficacy Endpoint

The primary endpoint is renal function as assessed by measured glomerular filtration rate (mGFR) 5-7 years after randomization.

3.2 Secondary Efficacy Endpoints

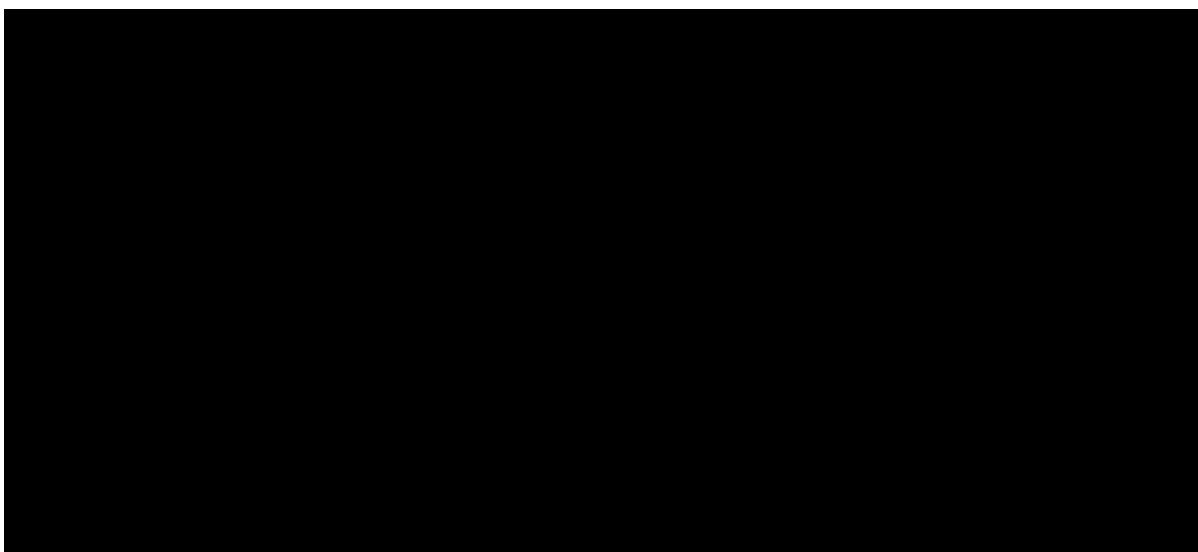
- Progression of CAV by Intravascular Ultrasound (IVUS) analysis
- Myocardial structure and function by echocardiography assessment
 - Left Ventricular End Diastolic Dimension (LVEDD) (cm)
 - Left Ventricular End Systolic Dimension (LVESD) (cm)
 - Left Ventricular Ejection Fraction (LVEF) (%)
 - Fractional shortening (FF) %
- The variables will be presented for week 2, baseline, month 12, 3-years follow-up and 5-7-years follow-up visit.
- Quality of life will be presented for pre-transplantation, month 12, 3-years follow-up, 5-7-years follow-up visit and change from pre-transplantation
 - Short Form 36 version 2 (SF-36): consists of 36 questions of health-related quality which each can take one of five responses. The 36 questions are divided

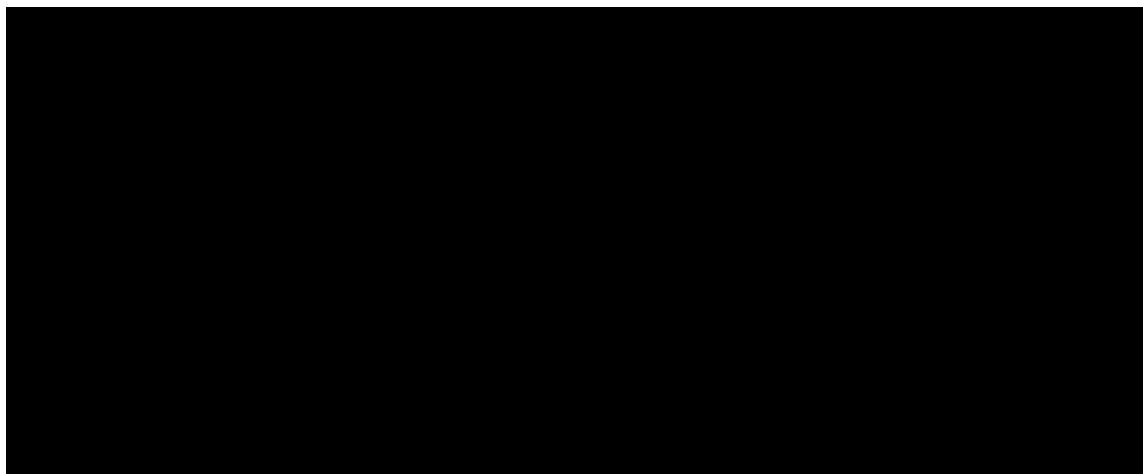
in eight dimensions; Physical Functioning, Role Physical , Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional and Mental Health. QualityMetric Health Outcomes™ Scoring Software, Based on 1998 US Norms, will be used for the calculations of the eight dimensions plus Physical Health Summary and Mental Health Summary.

- Euro Quality of Life 5D (EQ-5D): is a descriptive system of healthrelated quality of life states consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) each of which can be assessed as one of three levels of severity (no problems/some or moderate problems/extreme problems). A Visual Analogue Scale (VAS)-scale is also included in the EQ-5D questionnaire. An EQ-5D index will be calculated based on the United Kingdom TTO N3 value set. The algorithm for the EQ-5D index is received from EuroQoL Research Foundation.
- Beck Depression Inventory (BDI): the form consists of 21 questions to measure the intensity, severity, and depth of depression. The total score per patient and assessment will be between 0 to 63. The total score will be classified in two different ways according to investigator:
 - 0-9 Normal
 - 10-15 Mild
 - 16-23 Moderate
 - 24-63 Severe
 - 0-9 Normal
 - 10-15 Mild
 - 16-63 Moderate/Severe

3.3 Safety Endpoints

Number of Adverse Events (AEs)/Serious Adverse Events (SAEs).





4 OVERALL STUDY DESIGN

4.1 Overview of Study Design

The 12-months SCHEDULE main study was a prospective, multi-center, randomized, controlled, parallel group, open label study in de novo heart transplant recipients. The study consisted of two study periods, period 1 (HTx to week 7-11) and period 2 (week 7-11 to Month 12). Patients fulfilling the inclusion and exclusion criteria were randomized to one of two treatment groups: (i) conventional treatment with CsA, mycophenolate mofetil (MMF), and corticosteroids (Group A), or (ii) low-dose CsA, everolimus, MMF, and corticosteroids (Group B). After period 1, CsA was discontinued in Group B (experimental set-up with off-label use of everolimus), while the standard triple-drug immunosuppressive regimen was maintained in Group A.

In the 12-month SCHEDULE-study, 115 patients were randomized and treated. The patients were recruited from six transplant centres in Norway, Sweden and Denmark. The main study was followed by a 3-year follow-up visit in which 102 of the 115 patients participated. This 5 to 7-year follow-up visit is a further longtime follow-up examination of the patients participating in the SCHEDULE main study and the 3-year follow-up visit.

After completion of the 12-month SCHEDULE study, some patients have continued on the same immunosuppression and some of the patients have switched to alternative immunosuppressive treatment.

Patients who have participated in the 12-month SCHEDULE study and the 3-year follow-up visit and who are coming for an annual 5 to 7-year follow-up visit after randomization will be asked to participate.

The patients will be allocated to the same randomization group as in the 12-month SCHEDULE study for which stratified randomization and the following four strata were applied:

- mGFR ≤60 mL/min before transplantation AND mechanical assist device, Left Ventricular Assist Device (LVAD), Biventricular Assist Device (BiVad) or Extra Corporal Membrane Oxygenation (ECMO)
- mGFR ≤60 mL /min before transplantation AND no mechanical assist device
- mGFR >60 mL /min before transplantation AND mechanical assist device
- mGFR >60 mL /min before transplantation AND no mechanical assist device

4.2 Determination of Sample Size

Not applicable for the 5 to 7-year follow-up.

5 DATA SETS TO BE ANALYSED

The following analysis sets will be used for the statistical analysis and presentation of data:

The **Safety Set** will consist of patients who:

- were included in the Safety Set in the Clinical Study Reports Addendum dated 11 August 2015 for the 3 year follow-up visit
- have at least one assessment at the 5-7-year follow-up visit

The **Intention-to-Treat (ITT)** set will consist of patients who:

- were included in the ITT in the Clinical Study Reports Addendum dated 11 August 2015 for the 3 year follow-up visit
- have at least one assessment of the efficacy variable mGFR or [REDACTED] at the 5-7-year follow-up visit

The **Per Protocol Set (PPS)** will consist of patients who:

- were included in the PPS in the Clinical Study Reports Addendum dated 11 August 2015 for the 3 year follow-up visit
- have at least one assessment of the efficacy variable mGFR or [REDACTED] at the 5-7-year follow-up visit
- are on their randomized treatment according to the CRF-page *Immunosuppressive Medications* i.e. Everolimus (without addition of CsA or Tacrolimus) or Control (Control=CsA and/or Tacrolimus without addition of Everolimus) at the 5-7-year follow-up visit
- have no major protocol deviation at the 5-7-year follow-up visit. The final criteria for PPS, regarding which protocol deviations that warrant exclusions, will be determined when all data on protocol deviations are available and will be documented in a separate document before database lock

The **Extended PPS** will consist of patients who:

- were included in the ITT in the Clinical Study Reports Addendum dated 11 August 2015 for the 3 year follow-up visit
- have at least one assessment of the efficacy variable mGFR or [REDACTED] at the 5-7-year follow-up visit
- are on their randomized treatment according to the CRF-page *Immunosuppressive Medications* i.e. Everolimus (Everolimus=Everolimus or Everolimus and CsA and/or Tacrolimus) or Control (Control= CsA and/or Tacrolimus without addition of Everolimus) at the 5-7-year follow-up visit
- have no major protocol deviation at the 5-7-year follow-up visit. The final criteria for PPS, regarding which protocol deviations that warrant exclusions, will be determined when all data on protocol deviations are available and will be documented in a separate document before database lock

The ITT is considered as the primary analysis dataset, and will be used for the primary, secondary [REDACTED] variables. The primary efficacy analysis will be repeated using the PPS and extended PPS.

Demographic presentations will be based on the safety set and on the ITT. Exposure to treatment presentations will be based on safety set, ITT, PPS and extended PPS.

Safety presentations will be based on the safety set.

6 STATISTICAL AND ANALYTICAL PLANS

The planned tables and listings are presented in Appendix 1.

6.1 Changes in the Planned Analyses

Minnesota Living with Heart Failure Questionnaire was not included in the study.

6.2 Blind Review

This is an open study, however before data base lock the final decisions of patients to be included in study populations, as defined in Section 5 will be made and documented in the Pre-Analysis Review Form.

6.3 Hypotheses and Statistical Methods

6.3.1 Definitions

Baseline: Visit 6 (week 7-11)

Relative day: The relative day of an event is derived as follows:

Relative day = (Start date)-(Date of first administration of Investigational Medicinal Product (IMP))+1.

For days before the start date, calculate as Relative day = (Start date)-(Date of first administration of IMP).

Age: Date of Informed Consent at SCHEDULE main study-Birthdate

6.3.2 Summary Statistics

Data will be summarised by means of summary statistics. For continuous data, the following summary statistics will be presented: number of observations, mean value, standard deviation, minimum, first quartile, median, third quartile and maximum value. Categorical data will be presented as counts and percentages.

Summary statistics will be presented by treatment group/total and assessment visit, as applicable. Individual patient data will be listed.

6.3.3 Patient Data Listings

Data collected in the Case Report Form (CRF) will generally be listed in Appendix 16.2. CRF check questions [e.g. lab samples taken (Yes/No)] and reminders will not be listed.

Listings will be sorted by treatment group, enrollment number and randomization number.

6.3.4 Demographic and other Baseline Characteristics

Demographic data at baseline will be presented using summary statistics for the safety set and ITT.

6.3.5 Primary Efficacy analysis

The primary efficacy analysis will be based on the ITT population, the analysis will be repeated using the PPS and extended PPS.

Two-sided tests will be performed on the 5% level of significance, and 95% two-sided Confidence Interval (CI) for least square mean will be presented.

The null hypothesis is that there is no difference in the mean of mGFR between the Everolimus arm ($\mu_{\text{Everolimus}}$) and the Control arm (Control) (μ_{Control}) and the alternative hypothesis is that there is a difference between Everolimus and Control at the 5-7-years follow-up visit.

$$H_0: \mu_{\text{Everolimus}} - \mu_{\text{Control}} = 0$$

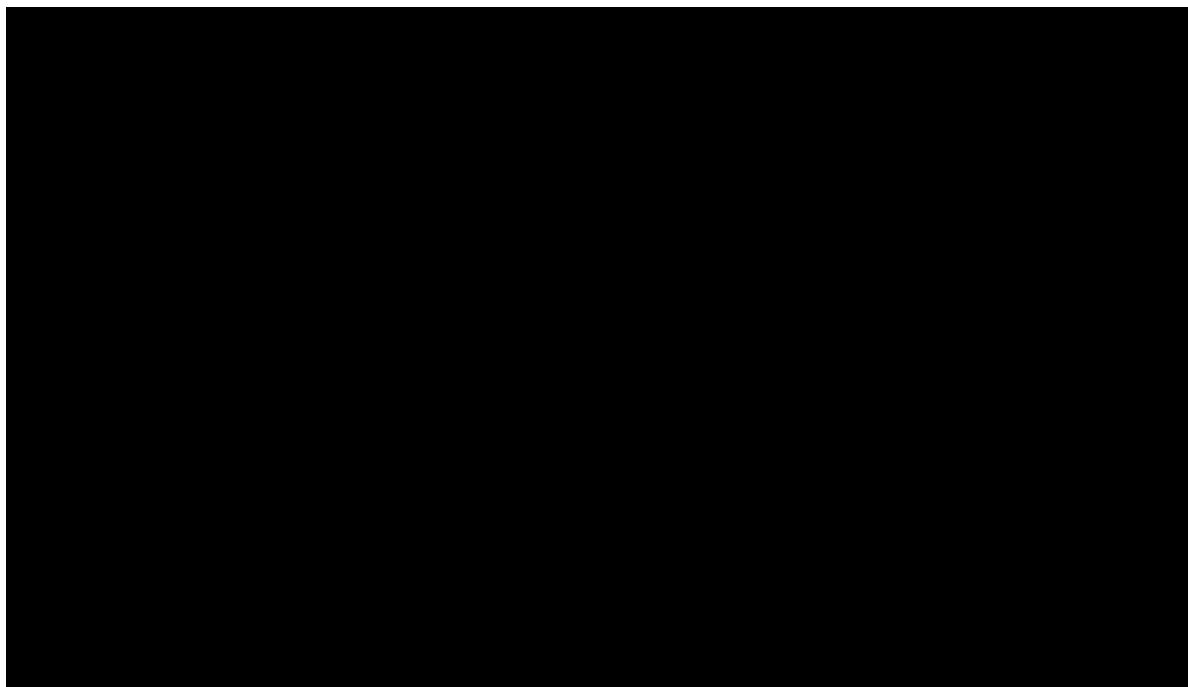
$$H_1: \mu_{\text{Everolimus}} - \mu_{\text{Control}} \neq 0$$

The above between-group comparisons will be performed using an Analysis of Covariance (ANCOVA) with study treatment (Everolimus, Control) and randomization strata (mGFR above/below 60 mL/min and have/not have mechanical assist device) as classification variables. In addition, the mGFR values at baseline will be used as covariate.

All mGFR data, observed values as well as change from baseline, will be presented using summary statistics by treatment group and in total. This presentation will be given for both observed values only as well as imputed mGFR, see Section 6.6.

6.3.6 Secondary Efficacy Analyses

- The analysis of the IVUS-data will not be performed by [REDACTED]
- Echocardiography variables LVEDD, LVESD, LVEF and FF will be presented by summary statistics for observed values by treatment group and in total.
- Quality of life:
 - The eight SF-36 dimensions together with Physical Health Summary and Mental Health Summary will be presented by summary statistics for observed values and change from pre-transplantation by treatment group and in total.
 - The EQ-5D index and the VAS-scale will be presented by summary statistics for observed values and change from pre-transplantation by treatment group and in total.
 - BDI form will be presented by two shift tables. The first one showing the number of patients who changed from normal, mild, moderate or severe at pre-transplantation to normal, mild, moderate or severe at each post-transplantation time of assessment by treatment group and in total. The second will show the number of patients who changed from normal, mild, moderate/severe at pre-transplantation to normal, mild, moderate/ severe at each post-transplantation time of assessment by treatment group and in total.



6.3.8 Exposure to Treatment

The ongoing immunosuppressive treatments:

- Everolimus
- Cyclosporine (Control)
- Tacrolimus (Control)
- Prednisolone
- Mycophenolate mofetile (MMF)

will be presented by a frequency table.

The dose rate, daily dose registered in the Immunosuppressive Medication CRF-page at 5-7-years follow-up visit/time registered in the Immunosuppressive Medication CRF-page at 5-7-years follow-up visit, that was consumed by each patient will be presented in a summary table from end of main study until the 5-7-years follow-up visit. If start date is missing, end date of main study will be used (see Section 6.6).

The observed trough blood levels for Cyclosporine, Everolimus and Tacrolimus for the 5-7-years follow-up visit will be presented in a summary table.

The safety set, ITT, PPS and extended PPS population will be used and presented by treatment group and in total.

6.3.9 Concomitant Medication

All concomitant medications/therapies for the 5-7-years follow-up visit will be summarised as number of patients being treated with each type of medication/therapy classified according to ATC level 3 group text and World Health Organization (WHO) Drug Dictionary preferred name. In the summary table, each patient is only counted once for each medication, on a preferred name level.

The safety set by treatment group will be used for this presentation.

6.3.10 Adverse Events

AEs and SAEs will be coded according to the Medical Dictionary for Regulatory Activities (MedDRA) system and tabulated by System Organ Class (SOC) and by preferred term for the 5-7-years follow-up visit.

The total number of patients with at least one AE and the total number of AEs will be presented by treatment group and in total. AEs with the same preferred term will be counted only once within a patient. The SAEs will be presented in the same way as the AEs.

The safety set will be used for these presentations.

6.3.11 Other Safety Assessments

Clinical Laboratory Measurements

For the laboratory parameters presented below and assessed at the 5-7-years follow-up visit, summary statistics will be produced for observed values at pre-transplantation, transplantation, week 1, week 7-11, month 3, month 6, month 12, 3-years follow-up and 5-7-years follow-up visit. In addition, the difference from baseline to each visit at which they were assessed will be derived and presented by treatment group and in total.

Abnormal (low and high) values will be flagged in listings.

Shift tables that show the number of patients who changed from low, normal or high at baseline to low, normal or high at each post-baseline time of assessment will be presented.

In case laboratory values are below the limit of quantification, the value corresponding to the limit of quantification will be used when summarising data (e.g. if the result is <x.x then the value x.x will be used in the statistical analysis).

Clinical chemistry/Biochemistry	Lipid profile	Hematology	Urinalysis
Serum creatinine	Total Cholesterol	Hemoglobin	Albumin/Creatinine ratio
S-Sodium	LDL- Cholesterol	Leucocytes	
Potassium	HDL- Cholesterol	Platelet count	
Alanine	Triglycerides (TG)		
Aminotransferase (ALAT)			
Aspartate			
Aminotransferase (ASAT)			
Urea			
Uric Acid			
Albumin			
HbA1c			
NT-proBNP			
Troponin-T			
C-reactive protein (CRP)			

Vital Signs

The vital signs parameters (height, weight, Body Mass Index (BMI), heart rate, systolic and diastolic blood pressure) will be presented at pre-transplantation, transplantation, week 1, week 4, week 7-11, month 3, month 6, month 9, month 12, 3-years follow-up and 5-7-years follow-up visit by summary statistics for observed values and change from pre-transplantation by treatment group and in total.

Electrocardiogram

The Electrocardiogram (ECG) parameters (heart rate, PQ-time and QRS) will be presented at transplantation, week 7-11, month 12, 3-years follow-up and 5-7-years follow-up visit by summary statistics for observed values by treatment group and in total.

Type of rhythm will be presented by a shift table showing the number of patients who changed from Sinus rhythm, Other or NA/ND/UNK at baseline to Sinus rhythm, Other or NA/ND/UNK at each post-baseline time of assessment by treatment group.

Cardiac Rejections

The number of patients with at least one cardiac rejection (grade I-III): cellular, humoral or mixed, will be presented by treatment group for three periods: during the main study, between main study to 3-years follow-up and between 3-years follow-up to 5-7-years follow-up.

Also the total number of cardiac rejection (grade I-III): cellular, humoral or mixed, and the total number of treated cardiac rejection will be presented by treatment group for the three periods.

Information regarding mixed cardiac rejection was only collected for during the main study and 3-years follow-up. During main study and at the 3-years follow-up visit, date of when a biopsy performed was collected. A biopsy confirmed rejection within 13 days from previous biopsy confirmed rejection was considered the same event. Thus, the same rejection could go on for several weeks.

6.4 Level of Significance, Multiple Comparisons and Multiplicity

The primary comparison will be performed on one single variable at one single occasion no adjustment of the statistical significance level will be made for multiple analyses. [REDACTED]

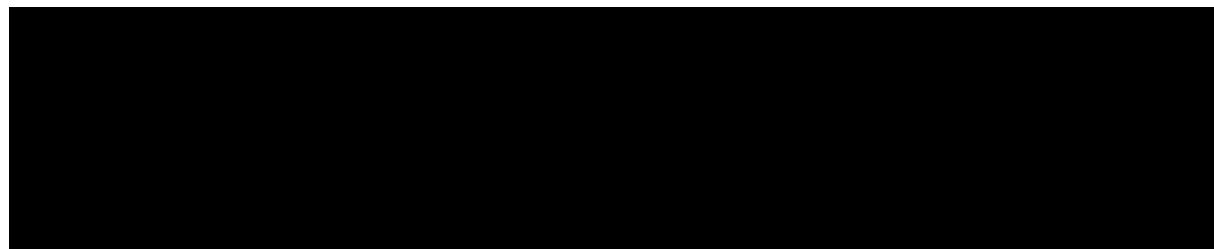
6.5 Adjustment for Covariates

Baseline measurement for mGFR will be used as covariate and stratum as classification variable in the ANCOVA.

6.6 Handling of Dropouts and Missing Data

Outliers will be included in summary tables, and will not be handled separately.

[REDACTED]

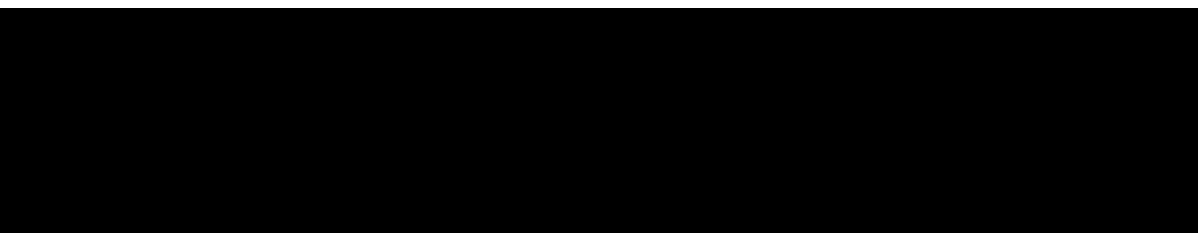


Exposure of immunosuppressive treatments: If start date and/or end date is incomplete after Data Management processing, the following will be assigned for the missing **start** date:

- if no field is available: Month 12 (Visit 11) date of main study will be imputed
- if only the year is available: Day “01” and month of “July” will be imputed
- if the month and year are available: Day “15” will be imputed
- if start date is before transplantation date (Visit 2) will be imputed

The following will be assigned for the missing **end** date:

- if no field is available, i.e. the treatment is ongoing: 5-7-years follow-up date will be imputed
- if only the year is available: Day “01” and month of “July” will be imputed
- if the month and year are available: Day “15” will be imputed



6.8 Examination of Subgroups

No subgroups were planned for the study.

6.9 Interim Analysis

No interims analysis was planed for the study.

6.10 Data Monitoring

Not applicable.

7 REFERENCES

1. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med, 1999; 130: 461-70.
2. Siddiqui O, Hung HM, O'Neill R, MMRM vs. LOCF: A comprehensive comparison based in simulation study and 25 NDA datasets. J Biopharm Stat 2009; 19(2): 227-46.
3. Mallinckrodt CH, Lane P, Schnell D, Peng Y, Mancuso J. Recommendations for the primary analysis of continuous endpoint in longitudinal clinical trials. The Drug Information Journal 2008; 42: 303-319.

APPENDIX 1

7.1 Tables to be Produced for the Clinical Study Report (Section 14 according to ICH E3)

(Table numbers refer to Section numbers in ICH E3)

14.1 DEMOGRAPHIC DATA

- Patient Disposition in Analysis Sets and Reason for Exclusions (All included patients)
- Patient Discontinuation (All included patients)
- Number of Patients by Visit (Safety)
- Demographics: Age, Race and Sex (Safety, ITT)

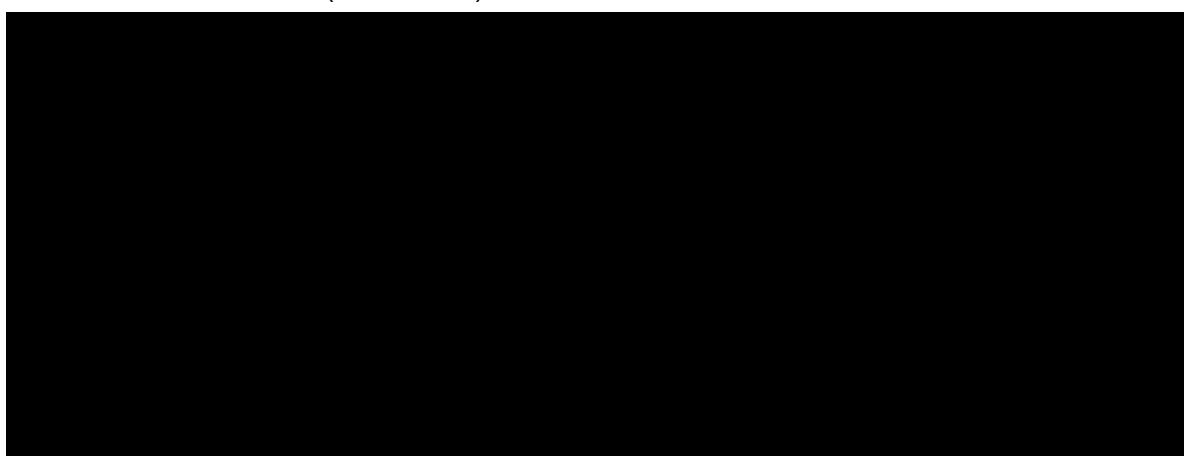
14.2 EFFICACY DATA

Primary (ITT [PPS, extended PPS])

mGFR (mL/min/1.73m²) 5-7-years Follow-Up (ANCOVA, CI, p-value, summary statistics including imputed values (or if not imputed the observed value will be used) and changes from baseline by treatment group and total)

Secondary (ITT)

- *IVUS – Not done by [REDACTED]*
- Echocardiography (the variables LVEDD, LVESD, LVEF and FF, summary statistics for observed values by treatment group and total)
- Quality of life:
 - SF-36: Physical Health Summary, Mental Health Summary, Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional, Mental Health (summary statistics for observed values and change from pre-transplantation by treatment group and total)
 - EQ-5D index and VAS (summary statistics for observed values and change from pre-transplantation by treatment group and total)
 - BDI form (shift tables)



14.3 SAFETY DATA

(Safety presentations will be based on the Safety set if not other is stated below)

- 14.3.1.x Summary of Adverse Events
- 14.3.1.x Adverse Events by System Organ Class and Preferred term
- 14.3.1.x Summary of Serious Adverse Events
- 14.3.1.x Serious Adverse Events by System Organ Class and Preferred term
- 14.3.2 Listings of Deaths, Other Serious and Significant Adverse Events
- (14.3.3 *this title is reserved for narratives*)
- 14.3.4.x Abnormal Laboratory Value Listing (low and high, if reference values available)
- 14.3.4.x Other Relevant Laboratory Analyses:
 - Clinical chemistry/Biochemistry (summary statistics for observed values and change from baseline by treatment group and total values)
 - Lipid profile (summary statistics for observed values and change from baseline by treatment group and total values)
 - Hematology (summary statistics for observed values and change from baseline by treatment group and total values)
 - Urinalysis (summary statistics for observed values and change from baseline by treatment group and total values)
 - Shift Tables Clinical chemistry/Biochemistry
 - Shift Tables Lipid profile
 - Shift Tables Hematology
 - Shift Tables Urinalysis
- 14.3.5.x Extent of Exposure (Safety set, ITT, PPS, extended PPS)
 - Ongoing Immunosuppressive Treatments at 5-7-years Follow-Up (frequency table)
 - Dose Rate of Immunosuppressive Treatments from the End of the Main Study to the 5-7-years Follow-Up Visit (summary statistics)
 - Trough Blood Levels at 5-7-years Follow-Up (summary statistics for observed values)
- 14.3.6 Vital signs (summary statistics for observed values and change from pre-transplantation by treatment group and in total)
- 14.3.7.x ECG (summary statistics for observed values)
 - Shift ECG for Type of Rhythm

14.3.8.x Cardiac Rejections (frequency table by treatment group)

- Number of patients with at least one cardiac rejection (grade I-III): cellular, humoral or mixed (for three periods: during the main study, between main study to 3-years follow-up and between 3-years follow-up to 5-7-years follow-up)
- Total number of cardiac rejection grade I-III (cellular, humoral or mixed, for three periods: during the main study, between main study to 3-years follow-up and between 3-years follow-up to 5-7-years follow-up)
- Total number of treated cardiac rejection grade I-III (for three periods: during the main study, between main study to 3-years follow-up and between 3-years follow-up to 5-7-years follow-up)

14.3.9 Concomitant Medication at 5-7-years Follow-Up Visit

7.2 Graphs (Section 14.2-14.3 in ICH E3)

None

7.3 Listings of Individual Patient Data and other Information to be Produced for the Clinical Study Report (Sections 16.1 and 16.2 according to ICH E3)

(Listing numbers refer to Appendix number in ICH E3. CRF check questions/reminders will not be listed.)

- 16.1.7 Randomisation Scheme (*Copy of List, included in CSR for 12 Months*)
- 16.2.1.x Discontinued Patients, Reason for Discontinuation (from 3-years follow-up to 5-7 follow-up visit)
- 16.2.1.x Visit Dates and Other Important Dates
- 16.2.1.x *Study Termination – Not Applicable*
- 16.2.2 Protocol Deviations
- 16.2.3.x Patients Excluded from the Efficacy Analysis (Evaluable, Reason for Evaluable Classification)
- 16.2.3.x Treatment Allocation and Evaluable for All Patients
- 16.2.4.x Demographic Data
- 16.2.4.x Inclusion Criteria Not Met and Exclusion Criteria Met
- 16.2.5 Compliance and/or Drug Concentration Data
 - Immunosuppressive Medications
 - Immunosuppressive Level
- 16.2.6 Individual Efficacy Response Data
 - mGFR (mL/min/1.73m²)
 - IVUS (performed yes/no and date)
 - Echocardiography

- SF-36
- EQ-5D
- BDI form
- [REDACTED]

16.2.7 Adverse Event Listings by SOC, Preferred Term, Treatment, Patient

16.2.8.x Listing of Reference Ranges

16.2.8.x Listing of Individual Laboratory Measurements by Patient (abnormal values should be flagged)

- Clinical chemistry/Biochemistry
- Lipid profile
- Hematology
- Urinalysis

16.2.8.x Listing of Relevant Comments Regarding Laboratory Values

16.2.9 Vital Signs

16.2.10 ECG

16.2.11 Cardiac Rejections

- Main Study and 3-years Follow-Up
- 5-7-years Follow-Up

16.2.12 Concomitant Medications

7.4 US Archival Listings (Appendix 16.4 according to ICH E3)

None.