Statistical Analysis Plan
Gamida Cell EAP

An Open Label Expanded Access Study of Omidubicel, for Allogeneic Transplantation in Patients with Hematological Malignancies

Statistical Analysis Plan

Version 1.0 11JUN2025

Table of Contents

Statistical Analysis Plan
Gamida Cell EAP

STUDY INFORMATION

Study Title	An Open Label Expanded Access Study of Omidubicel, for Allogeneic Transplantation in Patients with Hematological Malignancies
Protocol Number:	GC P#07.01.020
IND Number:	14459
Protocol Version:	1.0
Development Phase:	IIIb
Products or Interventions:	Omidubicel (formerly NiCord and CordIn)
Form/Route:	Cord transplant
Indication Studied:	Hematologic Malignancies
Sponsor:	Gamida Cell Ltd. PO Box 34670 Jerusalem 91340 Israel
Clinical Trial Initiation Date:	Study activation and enrollment opening date: 26 Jun 2020

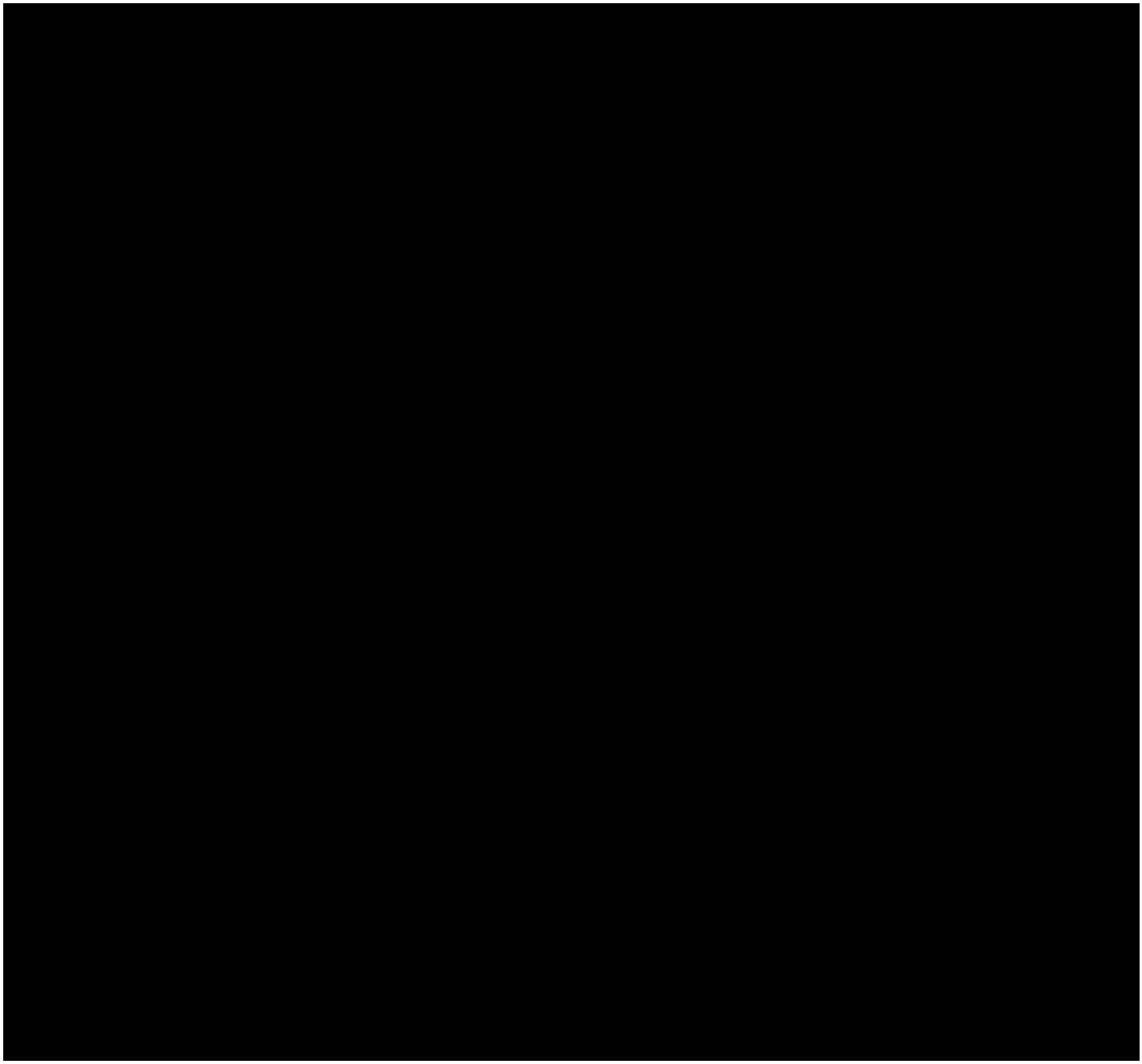
Statistical Analysis Plan
Gamida Cell EAP

VERSION HISTORY

SAP Version	Change	Rationale
1.0	Not Applicable	Original version.

Statistical Analysis Plan
Gamida Cell EAP

SIGNATURE PAGE



LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse Event
ALT/SGPT	Alanine Aminotransferase
ANC	Absolute Neutrophil Count
AST/SGOT	Aspartate Aminotransferase
CBU	Cord Blood Unit
CI	Confidence Interval
CSR	Clinical Study Report
GvHD	Graft-versus-Host-Disease
Hb	Hemoglobin
HLA	Human Leukocyte Antigen
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IQR	Interquartile Range
MedDRA	Medical Dictionary for Regulatory Activities
N	Number (typically refers to Patients)
PT	Preferred Term
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SCT	Stem Cell Transplant
SD	Standard Deviation
SOC	System Organ Class
TNC	Total Nucleated Cell
UCB	Umbilical Cord Blood
WBC	White Blood Cell

Statistical Analysis Plan
Gamida Cell EAP

1 INTRODUCTION

1.1 Purpose and Structure of the Document

The Statistical Analysis Plan (SAP) for "An Open Label Expanded Access Study of Omidubicel, for Allogeneic Transplantation in Patients with Hematological Malignancies" (GC P#07.01.020) describes and expands upon the statistical information presented in the protocol.

This document describes all planned analyses and provides reasons and justifications for these analyses. Sample tables, listings, and figures planned for the final analyses will be presented in a separate document. Regarding the final analyses and Clinical Study Report (CSR), this SAP follows the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines, as indicated in Topic E3 (Structure and Content of Clinical Study Reports), and more generally is consistent with Topic E8 (General Considerations for Clinical Trials) and Topic E9 (Statistical Principles for Clinical Trials). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the FDA and ICH, while all work planned and reported for this SAP will follow internationally accepted guidelines published by the American Statistical Association and the Royal Statistical Society for statistical practice.

This document contains the following sections: (1) a description of the purpose and timing(s) of analyses; (2) a description of the study design, its objectives; and the variables collected/assessed to be used in analyses; (3) general statistical principles; and (4) comprehensive statistical analysis methods for study outcomes. Any deviation from this SAP will be described and justified in protocol amendments and/or in the CSR, as appropriate. The reader of this SAP is encouraged to also review the study protocol for details on conduct of the study and the operational aspects of clinical assessments.

1.2 Purpose of the Analyses

These analyses will be included in the clinical study report. No interim analysis is planned.

2 INVESTIGATIONAL PLAN

2.1 Overall Study Design and Plan

This is an open-label, non-randomized, phase IIIb clinical trial designed to evaluate a novel method of *in vitro* expanded cord blood from a single cord unit (omidubicel) in patients with hematologic malignancies.

The study will include patients with hematological malignancies for whom allogeneic stem cell transplant (SCT) is currently a recommended and potentially lifesaving treatment. The study will only enroll patients who do not have a suitably matched and readily available stem cell donor.

Once qualifying cord blood units (CBUs) have been identified and the patient (or legal guardian) signs the informed consent form (ICF), the patient is screened for the study. Eligible patients will receive omidubicel.

An umbilical cord blood (UCB) that is HLA-matched at 4-6/6 HLA class I (HLA-A & HLA-B, low resolution) and II (HLA-DRB1, high resolution) loci with the patient (There must be at least one allele match at DRB1), containing a minimum total nucleated cell count (TNC) of at least 1.8 x 10^9, at least 1.5x10^7/kg TNC and at

least 8 x 10^6 CD34+ cells (all cell doses prior to thawing) is selected and sent to a core facility to undergo CD133+ selection and expansion.

The UCB is shipped from the Cord Blood Bank to the manufacturing site, is expanded using omidubicel methodology by Gamida Cell Ltd and subsequently cryopreserved and shipped from the manufacturing site to the transplant center.

Patients will have post transplantation study visits on Days 0, 7, 14, 21, 28, 42, 100, 180, 365, 730.

2.2 Study Endpoints

Primary Endpoint
Time to neutrophil engraftment
Secondary Endpoints
Time to platelet engraftment > 20,000 cells/ul
Time to platelet engraftment > 50,000 cells/ul
Non-relapse mortality
Overall survival
Disease-free survival
Donor chimerism
Secondary graft failure
Acute graft-versus-host disease (GvHD) grade II-IV
Acute GvHD grade III-IV
Chronic GvHD
Disease relapse
Safety and Tolerability of omidubicel
Graft versus host disease-free, relapse-free survival (GRFS)
Chronic graft versus host disease-free, relapse-free survival (cGRFS)

2.3 Study Schedule of Events

Please refer to Section 7.9 of the protocol.

2.4 Statistical Considerations for the Study Design

2.4.1 Sample Size Considerations

The sample size for the study was not determined by statistical power considerations, but by an approximate estimation of the times to product licensure. In consideration of the estimated timelines to licensure, the sample size is estimated to be approximately 60 transplanted patients.

2.4.2 Allocation of Patients to Study Arms

This study is not a randomized study.

2.4.3 Blinding

This open-label study is not blinded.

3 GENERAL STATISTICAL CONSIDERATIONS

3.1 General Analysis Specifications

3.1.1 Global Analysis Principles

In the case of multiple observations for a visit, the assessment value that is closest to the planned visit date will be used in the analysis of the post transplantation records. If the assessments are equidistant to the scheduled visit, the later assessment will be used in the analysis.

Unless otherwise specified, all continuous variables will be summarized using the following statistics: n, mean, standard deviation (and/or median and quartiles or interquartile range (IQR), as appropriate), maximum, and minimum. All categorical variables will be summarized using the frequency and percentages of observed levels.

There will be no hypothesis testing.

Statistics will be based on non-missing sample sizes unless methods for analyzing the missing data have been pre-specified.

If a patient is lost to follow up, the day of loss to follow up is defined as the day after the date of last study contact.

Day 0 represents the day of transplantation.

3.1.2 Reporting Conventions

In general, all data will be listed, sorted by patient and when appropriate by time point within patient. All summary tables will be annotated with the total population size relevant to that table including any missing observations.

The mean, standard deviation, and other statistics will be reported to 1 decimal place greater than the original data. The minimum and maximum will use the same number of decimal places as the original data.

Proportions will be presented to 2 decimal places. Percentages will be reported to 1 decimal place.

Zero counts will be displayed as 0 and corresponding percentages will be displayed as 0. Dashes ("-") and "NA" will be used to denote cells that are not applicable or cells displaying values that are structurally zero (i.e., values that will always be zero). "NE" (meaning Not Estimable) will be used for any summaries or statistics that could not be estimated or are undefined (e.g., due to dividing by zero).

Missing values will be displayed as null/empty cells in patient listings.

3.1.3 Analysis Software and Other Technical Details

SAS version 9.4 or above will be used to generate all tables, figures, and listings.

3.2 Analysis Populations

Transplanted Patients

Any patient enrolled and received an omidubicel transplantation regardless of subsequent withdrawal from the study.

All Patients

Any patient enrolled regardless of whether they received an omidubicel transplantation or subsequent withdrawal from the study.

3.3 Subgroups, Interactions, and Covariates

The protocol does not define any formal subgroup analyses, and the study is not adequately powered to perform subgroup analyses.

3.4 Handling of Missing Data

No imputation will be done for missing data.

4 SUMMARY OF STUDY CONDUCT AND PATIENTS

4.1 Disposition of Patients

Patient disposition will be described in tables. A CONSORT diagram will describe the patient disposition for all consented patients and loss to follow-up through the course of the study. A summary of the length of follow-up for transplanted patients from the date of transplant will be presented.

4.2 Demographic and Other Baseline Characteristics

Demographics (e.g. age, sex, race, ethnicity) and relevant baseline information (e.g. primary diagnosis, HLA match /6, and /8) will be presented and summarized with appropriate descriptive statistics. These summaries will be based on transplanted patients.

Descriptive statistics will be provided for cell doses.

4.3 Prior and Concomitant Medications

Concomitant medications will not be presented.

4.4 Study Treatments

All patients are to receive a single omidubicel transplantation. The occurrence and timing of the transplantation will be recorded.

4.5 Protocol Deviations

Patient listings and summary tables will be presented for protocol deviations recorded in the study.

5 EFFICACY EVALUATION

5.1 Analysis of Primary Efficacy Endpoints

The primary objective of the Phase IIIb trial is to assess the time from transplant to neutrophil engraftment.

Neutrophil engraftment is defined as achieving an absolute neutrophil count (ANC) greater than or equal to 0.5 x 10^9/L on 3 consecutive measurements by Day 42 post-transplant inclusive. The first day of the three measurements will be designated the day of neutrophil engraftment.

Primary graft failure is defined as failure to achieve neutrophil engraftment by Day 42 post-transplant as described above. Infusion of a second stem cell product on or prior to Day 42 post-transplant will be considered primary graft failure, with the following exception:

- Infusion of an additional stem cell product after documented neutrophil engraftment will be considered secondary graft failure, even if it occurs on or prior to Day 42 post-transplant.

5.1.1 Cumulative Incidence

The number of patients who achieved neutrophil engraftment will be summarized and a by-patient listing will be presented. The minimum, median, and maximum time to neutrophil engraftment will be presented. The estimated cumulative incidence will be presented. The graphics will be based on a calculation of the cumulative incidence with death, second transplant, and relapse as competing risks at the time they occur if they occur prior to neutrophil engraftment, and no transplant as a competing risk at Day 0. If the patient fails to achieve neutrophil engraftment, they will be considered to have a competing risk at Day 43. If there is not neutrophil engraftment and if the competing risk scenarios are not met, the patient will be censored as Day 101 post transplantation or on the day of loss to follow-up when this occurs before Day 101 post transplantation.

5.1.2 Sensitivity Analyses

No sensitivity analysis is planned for this study.

5.2 Analysis of Secondary Efficacy Endpoints

5.2.1 Time to Platelet Engraftment

5.2.1.1 Days to Platelet Engraftment of 20K

The number of days to the first day of a minimum of 3 consecutive measurements on different days in which the platelet count is 20,000 cells/ul or higher with no platelet transfusion within the previous 7 days (count day of engraftment as one of the preceding 7 days) will be calculated. The first day of the three measurements will be designated the day of platelet engraftment. The proportion of patients with platelet count of at least 20,000 cells/ul will be estimated from the cumulative incidence curve, with death, relapse, and second transplant as competing events. The minimum, median, and maximum time to platelet engraftment > 20K will be presented.

5.2.1.2 Days to Platelet Count of 50K

The number of days to the first day of a minimum of 3 consecutive measurements on different days in which the platelet count is 50,000 cells/ul or higher with no platelet transfusion within the previous 7 days (count day of engraftment as one of the preceding 7 days) will be calculated. The first day of the three measurements will be designated the day of platelet engraftment. The proportion of patients with platelet count of at least 50,000 cells/ul will be estimated from the cumulative incidence curve, with death, relapse, and second transplant as competing events. The minimum, median, and maximum time to platelet engraftment > 50K will be presented.

5.2.2 Non-Relapse Mortality

Non-relapse mortality is defined as any death not preceded by relapse.

The estimated cumulative incidence will be presented. The graphics will be based on a calculation of the cumulative incidence with relapse as a competing risk.

5.2.3 Overall Survival

Overall survival is defined as the time from the date of transplantation to death from any cause.

A Kaplan-Meier curve will be computed along with an estimate and a 95% confidence interval at 180, 365 and 730 days post-transplant. , with loss to follow-up as a censoring event.

5.2.4 Disease-Free Survival

Disease-free survival is defined as the survival without disease relapse or death from any cause, whichever comes first.

A Kaplan-Meier curve will be computed along with an estimate and a 95% confidence interval at 365 and 730 days post-transplant. The event time is time from transplant to relapse or death, whichever occurs first, and loss to follow-up as a censoring event.

5.2.5 Donor Chimerism

The chimerism proportions of the host and/or omidubicel will be measured on visits at Days 42, 100, and 730 post-transplant in patients with neutrophil engraftment. Patients who failed to receive a transplant, relapsed, have graft failure, or die before the sample is collected for the Day 42, 100, or 730 visits will be excluded from the analysis for that visit. The proportion as well as cumulative incidence of patients with at least 95% donor chimerism at Day 42, 100 and 730 will be presented.

5.2.6 Secondary Graft Failure

Secondary graft failure is the loss of the graft after initial engraftment. The proportion of graft failure will be calculated using the cumulative incidence curve. Death, relapse, and primary engraftment failure will be considered competing events. Patients with primary graft failure as the first competing risk event will have a competing risk date of Day 43. The cumulative incidence results with be shown in both tabular and graphical form.

5.2.7 Disease Relapse

A cumulative incidence curve will be computed along with an estimate and a 95% confidence interval at 365 and 730 days post-transplant. Death without relapse will be considered as a competing risk.

5.2.8 Graft Versus Host Disease-Free, Relapse-Free Survival (GRFS)

Graft versus host disease-free, relapse-free survival (GRFS) is defined as acute GvHD Grade III-IV, chronic GvHD, relapse, or death by any cause. A Kaplan-Meier curve will be computed along with an estimate and a 95% confidence interval.

5.2.9 Chronic Graft Versus Host Disease-Free, Relapse-Free Survival (CGRFS)

Chronic graft versus host disease-free, relapse-free survival (cGRFS) is defined as chronic GvHD, relapse, or death by any cause. A Kaplan-Meier curve will be computed along with an estimate and a 95% confidence interval.

6 SAFETY EVALUATION

The safety evaluations will be conducted on transplanted patients.

The analysis of adverse events and infections will be descriptive. No formal testing will be done.

6.1 Adverse Events

ICH E6 defines an AE as any untoward medical occurrence in a clinical research participant administered a pharmaceutical product regardless of its causal relationship to the study treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of study product. The occurrence of an AE may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care, or upon review by a study monitor.

Information collected on AEs includes event description, time/date of onset, clinician's assessment of severity, relationship to study product (assessed only by those with the training and authority to make a diagnosis, or his/her designee), time/date of resolution/stabilization of the event.

An AE or suspected adverse reaction is considered a SAE if, in the view of either the site PI or sponsor, it results in any of the following outcomes:

- Death,
- a life-threatening adverse event,
    - An AE is considered "life-threatening" if, in the view of either the site PI or sponsor, its occurrence places the participant at immediate risk of death. It does not include an AE that, had it occurred in a more severe form, might have caused death.
- inpatient hospitalization or prolongation of existing hospitalization,
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions,
- a congenital anomaly/birth defect, or
- Important medical events that may not result in death, be life-threatening, or require hospitalizations may be considered serious when, based upon appropriate medical judgment they may jeopardize the patient or patient and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

Summary tables will be presented with the number of patients reporting an event within each SOC/PT combination for:

- Treatment-emergent serious adverse events
- Treatment-emergent serious adverse events related to study product
- Grade 3-5 treatment-emergent adverse events related to study product
- Treatment-emergent adverse events

The proportion of grade 2-3 infections, also by subgroups (bacterial, fungal, viral, non-microbiologically defined), and the proportions of patients experiencing these infections will be estimated at 100 and 180 days post transplantation.

Primary cause of death will be tabulated.

6.1.1 Infusion Reactions

Infusion reactions, defined as any event occurring or worsening from start of transplant infusion up through 24 hours following the end of the transplant infusion, regardless of whether the transplant product was determined to cause the event, will be described by nature and severity.

A table will be provided to summarize the maximum severity of infusion reaction reported per patient. The table will show maximum severity levels and the number of patients and the percentage of patients with that maximum severity level. A listing will be provided to show the adverse event description and grade.

6.1.2 Treatment Emergent Adverse Events

A treatment emergent adverse event is defined as an event that emerges during or after transplantation. The proportion of patients with a treatment emergent adverse event will be presented and a listing of those events will be generated.

6.1.3 Maximum Severity of Adverse Events

A table will be provided on a patient level showing the maximum severity of each SOC/PT combination reported for any treatment emergent adverse event. A similar table restricted to serious adverse events will be provided.

6.2 Deaths

Primary cause of death will be summarized. A listing of deaths will be provided with patient ID, cause of death, and death day post transplantation.

6.3 Vital Signs

Vital signs will be tabulated by visit and summarized in patient listings. If multiple measurements of the same vital sign are taken on the same day/time, the available measurements will be averaged for analysis purposes.

6.4 Clinical Laboratory Evaluations

A listing of all laboratory parameters required by the protocol will be provided. Descriptive analyses including value over time, change from baseline over time, and shift tables will be provided for the following parameters: serum creatinine, total bilirubin, alkaline phosphatase, SGOT, SGPT, magnesium, white blood cells, platelet, and hemoglobin. If multiple measurements of the same laboratory parameter are taken on the same day/time, the available measurements will be averaged for analysis purposes. In the case of multiple observations for a study visit, the assessment value that is closest to the planned visit date will be used.

6.5 Acute GvHD

Acute GvHD that is reported without neutrophil engraftment will not be included as an event.

Acute GvHD will be summarized by maximum severity. A patient level listing will be presented.

6.5.1.1 Cumulative Incidence of Acute GvHD Grades II-IV

The time to first occurrence of acute GvHD grade II-IV following transplant will be analyzed and the cumulative incidence curve will be computed. Death, failure to achieve neutrophil engraftment, secondary graft failure, and relapse will be considered competing events. An estimate and a 95% confidence interval will be provided at Day 100 post-transplant.

6.5.1.2 Cumulative Incidence of Acute GvHD Grades III-IV

The analysis will be performed as described in Section 6.5.1.1 except that the time to event will be the first time to acute GvHD grade III-IV instead of grade II-IV.

6.5.2 Chronic GvHD

Chronic GvHD that is reported without neutrophil engraftment will not be included as an event.

Chronic GvHD will be summarized in a patient listing.

6.5.2.1 Cumulative Incidence of Chronic GvHD

The time to first occurrence of chronic GvHD following transplant will be analyzed and the cumulative incidence curve will be computed. Death, failure to achieve neutrophil engraftment, secondary graft failure, and relapse will be considered competing events.

7 INTERIM ANALYSES AND DATA REVIEWS

7.1 Interim Analyses

There is no planned interim analysis.

7.2 Stopping Rules

There are no formal stopping rules.