STATISTICAL ANALYSIS PLAN TITLE PAGE

Type of Document:	☒ Statistical Analysis Plan ☐ SAP Amendment ☐ Interim SAP
Protocol Title	Islet Transplantation in Type 1 Diabetic Patients Using the UIC Protocol, Phase 3
Protocol Number:	UIH-002
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STATISTICAL ANALYSIS PLAN SIGNATURE PAGE

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ABBREVIATIONS

AE	Adverse event
AIR	Acute insulin response
BUN	Blood urea nitrogen
CGL	Complete graft loss
CIC	Chicago Islet Consortium
CRF	Case report form
CSR	Clinical study report
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
ECG	Electrocardiogram
HepB	Hepatitis B
HepC	Hepatitis C
HIV	Human Immunodeficiency Virus
HYPO	Hypoglycemic
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
ITT	Intent-to-treat
IVGTT	Intravenous glucose tolerance test
LLN	Lower limit of normal
MedDRA	Medical Dictionary for Regulatory Activities
OGTT	Oral glucose tolerance test
PCS	Potentially clinically significant
PRA	Panel reactive antibody
PT	MedDRA preferred term
QA	Quality assurance
RBC	Red blood cells
SAE	Serious adverse event
SAP	Statistical analysis plan
SBP	Systolic blood pressure
SHE	Severe hypoglycemic events
SOC	MedDRA system organ class
T1D	Type I diabetes
TEAE	Treatment-emergent adverse event
TCAE	Terminology Criteria for Adverse Events in Trials of Adult Pancreatic Islet Transplantation
ULN	Upper limit of normal
WBC	White blood cell count
WHO	World Health Organization

1. INTRODUCTION

This statistical analysis plan (SAP) is being developed after review of Islet Transplantation at the University of Illinois at Chicago protocol version 0031 (August 7, 2014) and the corresponding case report form (CRF), but before any analyses of the data. The SAP contains detailed information to aid in the performance of the statistical analysis and reporting of the study data for use in the final Clinical Study Report (CSR). This SAP is being written with due consideration of the recommendations outlined in the most recent International Conference on Harmonization (ICH) E9 Guideline entitled Guidance for Industry: Statistical Principles for Clinical Trials[1] and the most recent ICH E3 Guideline entitled Guidance for Industry: Structure and Content of Clinical Study Reports[2].

This SAP describes the populations that will be analyzed and the patient characteristics, safety, and efficacy parameters that will be evaluated. This SAP provides details of the specific statistical methods that will be used. If additional analyses are required to supplement the planned analyses described in this SAP, they may be completed as *post-hoc* and will be described in detail in the CSR.

2. PROTOCOL SUMMARY

2.1. Objectives

The primary objective of this study is to demonstrate the safety and efficacy of allogeneic islet transplantation in Type 1 diabetic patients performed at the University of Illinois, Hospital and Health Sciences System (UI Health; AKA University of Illinois at Chicago [UIC])

The purpose is to demonstrate that islet transplantation achieves better glycemic control than state-of-the-art insulin treatment in the management of Type 1 diabetic patients with brittle control and a history of severe hypoglycemic episodes with hypoglycemia unawareness. The series of transplants performed with the protocol described herein will provide the basis for a biological license application (BLA) in islet transplantation.

2.2. Design and Methodology

The herein presented protocol is a Phase 3 study. It is a single-center, single-arm, open label trial in which 1-3 allogeneic pancreatic islet transplants per patient will be applied to a total of at least 50 study participants at the University of Illinois at Chicago.

This protocol is designed as a limited series of islet transplants for at least 50 Type 1 diabetic adult patients considered to have brittle diabetes for which glycemic control using insulin is problematic if not impossible.

2.3. Planned Number of Patients

The study plans to perform islet transplants for 50 or more patients. Please see Section 2.8 for sample size and power considerations.

2.4. Main Criteria for Inclusion

Enrolling patients must have Type 1 diabetes mellitus for more than 5 years, complicated by the following situations that persist despite intensive insulin management efforts:

a. At least one episode of severe hypoglycemia in the past 3 years defined as an event with symptoms compatible with hypoglycemia in which the patient required the assistance of another person, and which was associated with either a blood glucose level < 50 mg/dL (2.8 mmol/L) or prompt recovery after oral carbohydrate, intravenous glucose, or glucagon administration.
b. Reduced awareness of hypoglycemia, as defined by the absence of adequate autonomic symptoms at capillary glucose levels of < 54 mg/dL (3 mmol/L as reported by the patient).

Please see IND BB-11807 Section 6.4.2 for recipient exclusion criteria.

2.5. Treatment Regimens

2.5.1 Islet Dosing and Administration

Allogeneic human islets of Langerhans are a cellular therapy product with systemic effect derived from the pancreas of a cadaveric donor. Islets will be isolated from human pancreases procured from deceased multi-organ donors. A minimum amount of islets of about 10,000 IE/kg recipient body weight is required for engraftment and confirmed C-peptide expression based on the Edmonton series.

This form of procedure may require multiple transplants in order to reach this desired minimum number of islets, as previous clinical studies were unable to reliably reach insulin independence with a single transplant. Eligibility criteria for subsequent islet transplant(s) are described in Section 6.5.1 of IND BB-11807.

The islets of Langerhans mixture will be delivered either: 1) slowly into the portal vein via a syringe attached to a catheter hub or using an infusion bag or 2) by transvenous access to the right jugular vein via an ultrasound guided Microstik. A guiding sheath is advanced through the right atrium and into the right hepatic vein. Position is confirmed with injection of contrast medium.

Further details of the islet transplant procedure can be found in Section 6.5.1 of IND BB-11807.

2.5.2 Immunosuppression Regimens

Participants in the trial will receive immunosuppression using agents approved by the FDA for organ transplantation and evaluated for use in human islet transplantation under IND to prevent allotransplant rejection. Beginning with the initial transplant, a steroid free immunosuppressive regimen will be administered to all patients. Patients will receive initial doses of basiliximab, sirolimus, low dose tacrolimus, and etanercept. Patients presenting with preformed antibodies against human leukocyte antigens will receive a more intense induction protocol with the addition of a polyclonal anti-T-cell antibody preparation (Thymoglobulin) instead of basiliximab for the initial transplant. Sirolimus and tacrolimus will be given according to the Edmonton protocol. In addition, participants will receive etanercept. Mycophenolate mofetil may be used for patients who do not tolerate the adverse effects of sirolimus or tacrolimus. Other immunosuppressant medications may be used for patients who do not tolerate the adverse effects of sirolimus, tacrolimus, or mycophenolate mofetil. If azathioprine is planned, the patient may be tested for the presence of thiopurine methyltransferase (TPMT).

Please see Section 6.5.2 of IND BB-11807 for the detailed schedule of immunosuppression medications.

2.5.3. Other Medications

Exenatide will be administered at a dose of 5 mcg subcutaneously given with 1 hour pre-transplant and post-transplant bid for 1 week at any time within a 60 minute period before or after the morning and evening meals. After 1 week of therapy, if tolerated well, the dose will be increased to 10 mcg bid. Exenatide will be given for a total of 6 months after the last islet transplant and may be extended if necessary

In addition to prolonged immunosuppression, transplant patients routinely need other medications. These include the use of prophylactic anti-infective drugs used in patients receiving prolonged immunosuppression. Anti-infective drugs used under this protocol include trimethoprim / sulfamethoxazole for a minimum period of six months, and valganciclovir (Valcyte®) for 3 months post-transplant. With the use of prophylactic anti-infective drugs, total WBC counts and kidney function will be monitored at routine visits. If total WBC counts fall below 3,000, or if other conditions warrant a change in prophylaxis, sulfamethoxazole will be discontinued and substituted with pentamidine 300 mg by inhalation each month for a minimum of six months.

During the transplant procedures, additional medications, local anesthetics, and contrast media are also used. Heparin is used during the transplant to reduce coagulation risks that may lead to liver thrombosis. And for 1 week following the transplant, subcutaneous longer acting, low molecular weight heparin (enoxaparin, Lovenox®) is used. Study patients will be monitored for hemorrhage and bruising while receiving these anticoagulants.

Other medications may be required according to medical conditions presenting during the study period, and will be given according to best medical practice.

2.6. Duration of Treatment

The study duration will be approximately 10 years. The study will consist of a Screening/Baseline Phase, a Treatment Phase, and a Follow-up Phase. The Screening/Baseline Phase will consist of clinical and laboratory evaluations done at the first screening and repeated every 3 months (or 6 months for some, if needed) during the period awaiting the first transplant. The Treatment Phase will consist of Immediate Pre-Transplant Work-up, Transplant Period and Early Post-Transplant Period, all of which span from the moment a patient is admitted to the transplant unit up to when he/she is discharged after transplant, per protocol. Patients will remain in-clinic for a minimum of 24 hours post-transplant until the protocol-defined discharge criteria are met during the Treatment Phase. The Follow-up Phase includes continuous in-home monitoring of glucose levels and scheduled clinic visits that occur on an outpatient basis and will consist of efficacy and safety assessments for a period of 52 weeks post-transplant, followed by additional follow-up for up to 10 years (see Section 17.1 Schedule of Assessments for details). Individual patients will receive one or more transplants as needed as pre-determined by protocol and will be evaluated for efficacy and monitored for safety for up to 10 years following the last transplant.

2.7. Criteria for Evaluation

2.7.1 Safety:

Safety assessments will be performed during the Screening/Baseline Phase, prior to and following the islet cell transplant during the Treatment Phase (at specified times), and during the Follow-up Phase.

Safety of islet cell transplantation in Type 1 diabetes depends primarily on determining the incidence of serious and unexpected complications or adverse events. The surgical implantation procedure has associated risk and complications of the islet cell infusion will be followed closely. The post-transplant immunosuppression regimen also has expected toxicities, both acute and chronic. Laboratory measures and signs and symptoms will be followed at specified intervals. Some of these measures are often more subjective and

variable in nature, but should provide a clear indication of relative safety for patients enrolled in this study.

All study participants who receive an islet cell transplant will be followed for safety up to 1 year following the last transplantation or up to the data cut-off date, 13 April 2015. The safety of the islet transplantation and associated immunosuppressive therapies will be evaluated by analysis of adverse experiences, clinical laboratory tests, and physical examination. Safety events will be analyzed by their incidence, severity, and relationship to islet cell transplantation. In particular, the following parameters are of primary interest in assessing the clinical safety of islet cell transplantation:

One year after first and the last islet transplants we will evaluate:

a. Procedure Related Events

The incidence and severity of adverse events related to the islet infusion procedure including:

- Bleeding (> 2 g/dl decrease in hemoglobin concentration)
- Portal vein thrombosis, branch or main
- Biliary puncture
- Wound complication (infection or subsequent hernia)
- Increased transaminase levels (> 5 times upper level of normal)

b. Immunosuppression Related Events

The incidence and severity of adverse events related to immunosuppression including allergy:

- Reduction in GFR (> 25% reduction in estimated GFR from baseline by Cockroft and Gault formula)
- Increase in urinary albumin excretion
  - New onset microalbuminuria (albumin > 30 mg/day confirmed by 24 hour urine collection) in patients who were previously within normal limits
  - For those patients with baseline microalbuminuria (30-300 mg/day), new onset overt albuminuria (greater than 300 mg/day confirmed by 24 hour urine collection)
- Panel Reactive Antibody (PRA, please see Section 2.9 Changes from the Planned Protocol Analysis)
- Addition or intensification of antihypertensive therapy
- Oral ulcers
- Lower extremity edema
- Gastrointestinal toxicity (diarrhea)
- Neutropenia (neutrophils < 1.3 thous/μL)
- Anemia (hemoglobin men < 12.1, women < 11.7 g/dL)
- Thrombocytopenia (platelets < 150 thous/μL)
- Infections (viral, bacterial, or fungal)

- Neoplasms, benign or malignant

Severity will be graded according to Collaborative Islet Transplant Consortium *Terminology Criteria for Adverse Events (TCAE) In Trials of Adult Pancreatic Islet Transplantation, Version5.0 (03 August 2011)*

2.7.2 Efficacy:

a. **Primary Efficacy Endpoint**:

The proportion of patients with an HbA1c ≤ 6.5% and free of severe hypoglycemic events at 1 year after the first and 1 year after the last islet cell infusion, respectively (for the addition of time point see Section 2.9 Changes from the Planned Protocol Analysis).

Standard insulin treatment can rarely improve glycemic control in brittle Type 1 diabetic patients who are already on state-of-the-art insulin therapy. The rate of aforementioned favorable outcome achieved under standard insulin treatment over-a-year from a population-based diabetes registry database is as low as 0.3% (Tiwari et al., 2012). In general these patients require insulin reduction to reduce hypoglycemic episodes, which would likely lead to higher HbA1c. In contrast, islet transplantation can reduce hypoglycemic episodes without increasing HbA1c.

The protocol definition of severe hypoglycemic event: An event with symptoms compatible with hypoglycemia in which the patient required the assistance of another person and which was associated with either a blood glucose level < 50 mg/dl (2.8 mmol/L) or prompt recovery after oral carbohydrate, intravenous glucose, or glucagon administration.

A broader clinical definition of severe hypoglycemic event that will apply to some of the exploratory endpoints as described later: receiving any of thrid-party assistance to treat a hypoglycemic reaction would sufficiently determine the occurrence of a SHE, regardless of blood glucose levels which may or may not be available.

b. **Secondary Efficacy Endpoint**:

The secondary efficacy endpoints will focus on more detailed analysis of glycemic control, and will include the following:

1) **Insulin independence**: We will evaluate the proportion of patients presenting with insulin independence while fulfilling the primary endpoint at 1 year after the first and 1 year after the last islet cell infusion, respectively.

   Definition of insulin-independence:
   - Absence of exogenous insulin injection

- Fasting capillary glucose level should not exceed 140 mg/dL (7.8 mmol/L) more than three times in the past week based on measuring capillary glucose levels a minimum of 7 times in a seven day period.
- Fasting plasma glucose level ≤ 126 mg/dL (7.0 mmol/L); if the fasting plasma glucose level is > 126 mg/dL (7.0 mmol/L), it must be confirmed in an additional one out of two measurements.
- 2-hour postprandial capillary glucose should not exceed 180 mg/dl (10.0 mmol/L) more than one out of every seven times in the past week based on measuring capillary glucose levels a minimum of 7 times in a seven day period (for the modification see Section 2.9 Changes from the Planned Protocol Analysis).
- Evidence of endogenous insulin production defined as fasting or stimulated C-peptide levels ≥ 0.5 ng/mL (0.16 nmol/L)

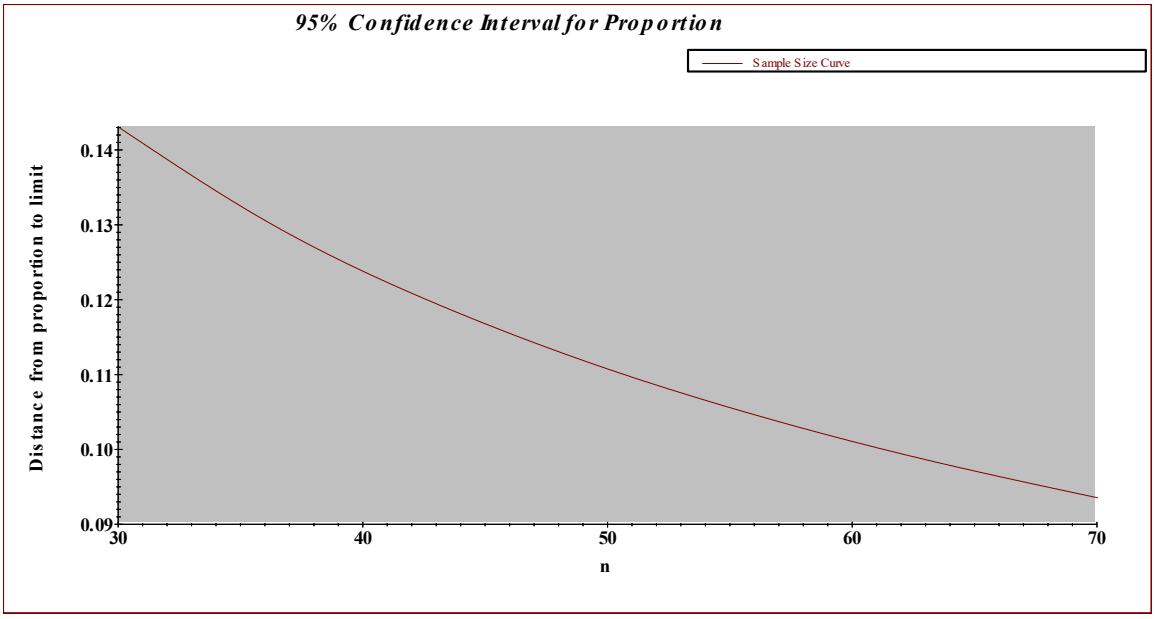
2) **Hypoglycemic episodes** will be measured by the number and severity of hypoglycemic episodes quantified by the Ryan HYPO Score, and the percent reduction will be reported.
3) **Glucose variability and hypoglycemia duration will be measured by continuous glucose monitoring system (CGMS)** for a 3-day period at three different time points: 1) at screening, 2) one year after first islet transplant, and 3) one year after last islet transplant. The following measurements and analysis will be reported:
    - Mean glucose concentration
    - Percent of time in the following ranges:

< 60 mg/dl
60-140 mg/dl
141-200 mg/dl
> 200 mg/dl

2.8. Sample Size and Power Considerations

For the primary endpoint (composite HbA1c ≤ 6.5% and absence of severe hypoglycemic events), we expect 80% of the transplant population to achieve this endpoint. Therefore, assuming a sample size of 50, a two-sided 95.0% confidence interval for a single proportion will extend ± 0.111 from the observed proportion. When the sample size is 40, a two-sided 95.0% confidence interval for a single proportion will extend ± 0.124 from the observed proportion (Figure 1). Proportion and surrounding confidence interval will be reported.

Figure 1. Sample Size Curve for 95% Confidence Interval for Proportion



From recent CITR report, the population rate of favorable outcome under standard insulin treatment for T1D patients indicated as eligible for islet transplant is below 1% (Tiwari et al., 2012). Historical data on islet transplants performed at multiple sites in North America show that the observed favorable outcome rate is at least 70% across all centers. An increase of 50% in the rate of favorable outcome is considered the minimal difference needed to show clinically meaningful benefit. The power of a single-arm trial at a one-sided significance level 0.05 with varying sample sizes and varying observed favorable outcome rates is shown in Table 1.

Table 1. Power of a single-arm trial at a one-sided significance level 0.05

	Sample Size			
	15	20	30	50
Observed Favorable Outcome Rate (%)	Power for the true improvement of the favorable outcome rate to be at least 50% (%)			
65	32	39	51	70
70	50	60	75	91.5
75	71	81	93	99.1
80	88	95	99.2	>99.9

We had planned to enroll at least 50 patients. However, with as few as 15 patients and an observed favorable outcome rate at 80%, we will have 88% of power to show the true treatment effect that at least 50% more of T1D patients than those under standard insulin treatment will attain the favorable outcome through the UIC islet transplantation treatment.

2.9. Changes from the Planned Protocol Analysis

A second definition of SHE was added in addition to the protocol definition for exploratory analysis. The protocol definition tends to exclude some clinically valid SHEs with a more limiting blood glucose parameter. The purpose of using the second definition is to compare the SHE outcomes by this broader clinical definition with that by the protocol definition, and to demonstrate that the efficacy evaluation is not biased by the differential definitions of SHE.

Evaluation of PRA was omitted in the protocol and is added back as a critical safety endpoint based on its clinical significance.

The original protocol-planned evaluation of primary and secondary endpoints was scheduled at 1 year following the first transplant. The evaluation and analyses are also planned for the time point at 1 year after last transplant in order to take into consideration that patients can have more than one transplant, and thus the 1-year-post-last-transplant evaluation is important in providing adequate efficacy assessment.

For the secondary endpoint based on patient self-monitored post-prandial capillary glucose levels, the evaluation minimum requirement is reduced from three out of 21 times a week to a proportionally one out of every seven times measured. The change is based on the consideration that this piece of information relies totally on patient reported diary data, and frequent and random missing of data is expected. The reduction of minimum data requirement here is an attempt to unbiased efforts in maximizing the reportable results.

3. GENERAL CONSIDERATIONS FOR DATA ANALYSIS AND REPORTING

This section discusses general policies to be employed in the analysis of the data from the study. Departures from these general policies may be given in the specific detailed sections of this SAP. When this situation occurs, the rules set forth in the specific section take precedence over the general policies.

3.1. Data Analysis

All individual data entered into the clinical database will be presented in listings. In general, the listings will present the patients sorted by transplant number, collection day, and collection time.

Demographic, baseline characteristics, safety and efficacy variables will be summarized across the ITT population at designated time points of collection. Continuous variables (e.g., age) will be summarized using the number of observations, mean, standard deviation, median, minimum, and maximum values. Categorical variables (e.g., race) will be summarized using the number and percentage of patients in each category.

Missing data will stay missing unless an imputation rule is defined otherwise. Partially missing date/time variables will only be imputed when a derivation involving the date/time value is needed in the analysis. The imputation will be done as follows (when applicable): when the month/day is missing, July 1st will be imputed; when only the day is missing, the 15th of the month will be imputed; when time of day is the only missing element, 12:00 (out of 24 hours) will be imputed.

3.2. Format

The following formatting conventions will apply as specified for the data displays:

- All tables, listings, and figures will be presented in landscape orientation.
- All tables and listings will be produced using the Courier New font, with font size 10 or larger for tables and font size 9 for listings.
- Legends will be used for all figures with more than one variable or item displayed.
- Figures will be in black and white (no color).
- Specialized text styles, such as bolding, italics, shading, superscripted and subscripted text, will not be used in tables, figures, and listings.
- Only standard keyboard characters will be used in tables and listings. Special characters, such as non-printable control characters, printer specific, or font specific characters, will not be used on a table, figure, or listing. Hexadecimal derived characters may be used if they are appropriate to help display math symbols (e.g., μ).
- Mixed case will be used for all titles, footnotes, column headers, and programmer-supplied formats.

3.3. Headers

All tables, listings, and figures will have a header section that precedes the body of the display. The header will include:

- The protocol name, UIH002, and the population used in the data display (ITT, Safety, etc.) identified in the upper left corner.
- The number of pages, formatted as Page X of N located in the upper right corner.

- The title of the display centered on the page. The first title line will be the number of the table, figure, or data listing. Subsequent title lines will be the title (description) of the table, figure, or data listing.

3.4. Body of the Data Display

The following conventions will be used within the body of the data display:

- Missing values for both numeric and character variables will be presented as blanks in a table or listing.
- All percentages will be rounded to the nearest whole number. The number and percentage of responses will always be presented in the form XX (XX) where the percentage is in parentheses.
- All summaries for categorical variables will include all categories, even if none of the patients had a response in a particular category. Additionally a "missing" category will be added to enumerate missing observations for each variable. This ensures completeness.
- All means and medians will be to one more significant digit than the measured value. Standard errors will be to two more significant digits than the measured value. The minimum and maximum will be the same as reported.
- All summary listings and CRF patient data listings will be sorted for presentation by patient and then by transplant number within patient.
- All date values will be presented as DDMMMYYYY (e.g. 21AUG2014) format. A 4-digit year is required for all dates.
- All observed time values will be presented using a 24-hour clock HH:MM:SS format (e.g., 01:35:45, or 11:26). Seconds will only be reported if they were measured as part of the study.
- The sample size (n) shown as a summary statistic will be the number of patients with non-missing values. Additionally, the total number of patients will always be displayed.

3.5. Footers

All tables, listings, and figures will have a footer section that follows the body of the data display. The footer will conform to the following conventions:

- All footnotes will be left justified and listed under the respective table, listing, or figure.
- Footnotes will be present on all pages where appropriate.
- Footnotes will be used sparingly and must add value to the table, figure, or data listing. If more than 4 footnote lines are planned then a cover page may be used if needed to display footnotes.

- The last line of the footer section will be a standard source line that indicates the name of the program used to produce the data display and the date and time of production of the data display.

4. ANALYSIS POPULATIONS

ITT population: Any patient in whom protocol-directed therapy (e.g., pre-transplant immunosuppression) is initiated will be included in the Intent-to-treat (ITT) population. All efficacy analyses will be on this ITT population regardless whether transplantation occurs or not.

Safety Population: Any patient in whom protocol-directed therapy is initiated will be included in the Safety population, which is the same as the ITT population. Patients in this population might not receive an islet transplant. All safety analyses will be on this Safety population.

5. PATIENT ACCOUNTABILITY

The disposition of patients will be summarized for all patients entered in the clinical database. The following disposition information will be summarized:

- The number and percent of patients who completed the study and the number and percent of patients who were withdrawn;
- The number and percent of patients withdrawing by reason for withdrawal;
- The number and percent of patients not reaching 1 year post first transplant henceforth determined ongoing as of April 13, 2015 and
- The number and percentage of patients included in the Intent-to-treat populations.

All percentages will use the number of patients entered into the database as the denominator. In addition, a data listing of patients withdrawn will be provided and will include for each patient: demographics (age and race), day of withdrawal relative to day of study medication, concomitant medications taken, and reason for withdrawal.

6. PROTOCOL DEVIATIONS

Protocol deviations will be evaluated for all patients entered in the database. All patients having a protocol deviation will be identified in patient data listing to be included in the Appendix of the CSR. The listing will include relevant information regarding the type of protocol deviation. Protocol deviations will include the following:

- Inclusion/exclusion criteria that were not met as reported on the Inclusion/Exclusion page of the CRF or the Study Continuation Record page of the CRF;
- Consent violations;
- Administration of prohibited medications;
- Altered protocol-specified study therapy;

7. TREATMENT COMPLIANCE

A patient data listing for all patients for whom there was non-compliance to the transplant and/or drug administration rules, if any, will be include in the Appendix of the CSR.

8. DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Patient demographics and other baseline characteristics will be collected during the waiting period for islet transplant, and will be summarized descriptively using the ITT population. No inferential tests will be performed.

8.1. Baseline Data

Baseline data consist of demographic information and medical/physical assessments collected during the screening/waiting period. These data will be grouped into the following categories:

Demographic variables

- Age
- Sex
- Race (Caucasian, Black, Native American, Oriental, Other)
- Ethnicity (Hispanic, non-Hispanic)

Body habitus variables

- Weight (kg)
- Height (cm)
- BMI (kg/m^2)

Diabetes control variables

- Insulin requirement (units/kg/day)
- HbA1c
- Reduced awareness of hypoglycemia

- Frequency of severe hypoglycemic events (SHE)
- Ryan hypoglycemia severity (HYPO) score
- Fasting plasma glucose and C-peptide
- Glucose and C-peptide 90 minutes post glucose challenge (Mixed Meal Test)

Health conditions

- Clinically significant medical histories
- Clinically significant current medical conditions
- Abnormal physical examination findings at screening
- Prior/Concomitant medication use at baseline

8.2. Analysis of Baseline Data

8.2.1 Analysis of demographic variables

Age will be reported in years and calculated using the formula Age = (date of the islet transplant – the date of birth) /365.25 and will be rounded to one decimal place. In the case when no transplant is done, the age at enrollment (calculated using the date of Informed Consent instead) will be used for baseline. The distribution of age at baseline will be displayed as mean, standard deviation, median, minimum and maximum.

Sex, race and ethnicity will be tabulated and counts and percents will be displayed.

8.2.2 Analysis of body habitus variables

Weight, height and BMI will be summarized using mean, standard deviation, median, minimum and maximum. Weight at the immediate pre-transplant visit (see Section 17.1 Schedule of Assessments) or the last available measurement before transplant in the case when no transplant is done will be used for baseline analysis. Height is only measured at the first screening visit and will be used throughout the study. BMI is computed using the formula BMI = weight/(square of height) (kg/m^2) and will be rounded to one decimal place.

8.2.3 Analysis of baseline diabetes control variables

The diabetes control variables are all continuous scale variables and will be summarized as mean, standard deviation, median, minimum and maximum.

Insulin requirement will be taken from self-reported insulin regimen on the current medication list at the point of immediate pre-transplant assessment. If a range instead of an exact dose schedule is given, the average value of the range will be used. Insulin dosing will be summarized in total units per kg per day by administration routes. If the insulin doses are

reported as units per day, the value will be divided by the patient weight (in kg) measured at the corresponding visit to derive the requirement in units/kg/day.

Reduced awareness of hypoglycemia is reported qualitatively at enrollment. The proportion of patients having reduced awareness of hypoglycemia at baseline will be summarized.

Baseline SHE frequencies will be based on records available during the time period between study enrollment and the first islet transplant. A SHE is identified as a hypoglycemic event in which the patient required assistance, including help from someone else to recognize or treat the reaction, injection of Glucagon, or use of hospital/ambulance. Additionally, either a blood glucose (BG) level under 50 mg/dL (when recorded) or recovery with juice/food/glucagon is concomitant of a SHE.

The frequency of SHE is calculated by dividing the total number of SHE by the total number of days during which the events were recorded and then multiplied by 30 to produce incidence per month. Note that the duration of time between enrollment and the first transplant may vary by patient. The frequencies of SHE will be summarized at baseline.

Baseline hypoglycemia severity will be quantified by the HYPO Score (Ryan EA, et al., 2004). The HYPO score is a scalar quantity based on patient recording of blood glucose readings and hypoglycemic events throughout the screening period prior to the first islet transplant. A hypoglycemic event occurs when a blood sugar reading is less than 54 mg/dL and a series of self-reported questionnaire items determine the severity. Points are awarded for each occurrence of documented hypoglycemia and extra points are given depending on the neuroglycopenic symptoms experienced or lack thereof. No points are awarded if there are autonomic symptoms, even if some neuroglycopenic symptoms are also present. Additional points are given for the need of outside help to either recognize or treat the event. A patient's baseline HYPO score is computed for the complete year by dividing the total score, the sum of points awarded to each hypoglycemic event reported, by the total number of days between enrollment and initial islet infusion (up to 365 days prior to the initial infusion), and then multiplying with 365. A larger HYPO score indicates greater severity. The analysis of the raw HYPO score adopts the methods for continuous scale variable.

Baseline lab test results for all the other variables will be taken from the CRF at the immediate pre-transplant assessment, if available. If a test was not scheduled for the immediate pre-transplant work-up, then the last available lab result from the screening visit prior to the first transplant will be used to represent baseline value.

For baseline Mixed Meal Test results, the proportions of patients' fasting and 90-minute C-peptide levels not exceeding the lowest detectable limit, 0.1 ng/mL, will be evaluated. C-

peptide levels reported as less than 0.1 ng/mL will be given the value 0 for any planned analyses that involve calculations based on C-peptide measures.

8.2.4 Analysis of baseline health conditions

To assess the overall health of the study patients, the following patient characteristics at baseline will be summarized using number and percentage of patients in each category:

- Clinically significant medical histories by body system;
- Clinically significant current medical conditions by body system;
- Abnormal physical examination findings by body system; and
- Prior/Concomitant medication use at baseline.

"Clinically significant" conditions are whichever conditions that by *a priori* decision of the P.I. may affect the outcome of the islet transplant, including autoimmune diseases, pre-existing CVD, any indications of being at-risk for kidney diseases, and pre-existing mild kidney problems. Current medical conditions will include those conditions reported on the Medical History page of the CRF as current up to the date/time of islet transplant. The remaining conditions reported on the Medical History page of the CRF will be counted in the medical history summary. For the medical history summary, the current medical condition summary and the concomitant medication summary, the percent of patients will be based on the total number of patients in the Safety population. For the physical examination summary, the percent of patients will be based on the number of patients for which the specific body system was assessed. This will include all patients for whom the Normal/Abnormal response is not missing or the response is not reported as 'Not Done'. The results of physical examination throughout the screening phase up to the immediate pre-transplant work-up will be counted accumulatively. However, more than one abnormality identified for a single patient under the same body system will be counted only once.

For the prior/concomitant medication summary, all medications will be coded to preferred drug names and therapeutic drug class using the World Health Organization (WHO) Drug Dictionary Enhanced. Use of prior/concomitant medications will be summarized for each therapeutic drug class and each preferred drug name. Prior/concomitant medications will include medications that are not part of the treatment regimens (see Section 2.5.) reported on the Current/Prior Medications page of the CRF with a start date/time prior to the date/time of initial islet transplant but indicated as ongoing at the last scheduled visit before the first transplant.

9. EFFICACY EVALUATIONS

9.1. Analysis of Primary Endpoints

The primary endpoint is the proportion of patients with 1) an HbA1c ≤ 6.5% at Day 365, AND 2) free of severe hypoglycemic events (for definition see Section 2.7.2a) from Day 28 to Day 365, inclusive, following the first and the last islet transplant, respectively, with the day of corresponding transplant designated Day 0.

9.1.1. Analysis of Primary Endpoints

The primary analysis is to estimate the true rate of this composite favorable outcome at one year in patients in the ITT population. The proportion of favorable outcomes will be used as the point estimate. An exact (Clopper-Pearson) two-sided 95% confidence interval will be constructed assuming an underlying binomial distribution for the ITT population via SAS:

```
proc freq data=dataset order=freq;

   tables binary_outcome / binomial(exact) alpha=.05;

run;
```

Failure to achieve the favorable outcome will be summarized in two sub-groups: the rate of patients having an HbA1c > 6.5% at Day 365, and the rate of patients who experienced any SHE from Day 28 to Day 365.

The primary endpoint will be assessed for all treated patients from first transplant (including patients with >1 transplant within 1 year of first exposure) and from last transplant. A patient's HbA1c results may be reported on visit days that do not fall on the exact Day 365. In this case the records from the date that is the closest to and within 4 weeks (28 days) before or after Day 365 will be used.

9.1.2. Treatment of Missing Data

The primary endpoint should be evaluable for all patients in the ITT population. However missing data can occur due to death, if the patient withdraws consent to be followed, or if immunosuppression is begun but the patient never receives a transplant. In these cases the endpoint will be classified as failure to achieve a favorable outcome. Should the endpoint not be evaluated for a patient for other reasons, a failure will be imputed unless data available at a time longer than one year after transplant indicates otherwise, in which case, that later value will be imputed.

All imputations will be reported in a patient data listing along with the reasons for imputation. The rates and the exact 95% confidence intervals for complete data and imputed data will be compared to ascertain the sensitivity of the imputation.

9.2. Analysis of Secondary Endpoints

Except for the primary analyses there are no explicit or implied hypotheses in the protocol. Changes in the secondary outcomes are of interest as they will relate to efficacy as measured by the primary outcome variable. All the secondary endpoints will be evaluated at 1 year after the first and 1 year after the last transplant, respectively, with the day of corresponding transplant always designated Day 0.

We will evaluate the proportions of patients presenting with insulin independence among all patients and among the patients who fulfilled the primary endpoint, respectively. **Insulin independence** while fulfilling the primary endpoint will be further evaluated by the following parameters:

- Absence of exogenous insulin injection reported at Day 365.
- Fasting capillary glucose level not exceeding 140 mg/dL (7.8 mmol/L) more than three times in a week (based on measuring capillary glucose levels a minimum of 7 times in a seven day period) at Day 365 ± 28 days.
- Fasting plasma glucose level ≤ 126 mg/dL (7.0 mmol/L) at Day 365 ± 28 days (if the fasting plasma glucose level is > 126 mg/dL [7.0 mmol/L], it must be confirmed in an additional one out of two measurements).
- 2-hour postprandial capillary glucose not exceeding 180 mg/dl (10.0 mmol/L) more than one out of every seven times in a week (based on measuring capillary glucose levels a minimum of 7 times in a seven day period) at Day 365 ± 28 days.
- Evidence of endogenous insulin production defined as fasting or stimulated C-peptide levels ≥ 0.5 ng/mL (0.16 nmol/L) at Day 365 ± 28 days.

Number and percent (over the total number of patients attaining primary endpoint) of patients attaining each outcome listed above will be summarized.

Hypoglycemic episodes will be measured by the Ryan HYPO Score (Ryan et al., 2004) derived from the number and severity of hypoglycemic episodes recorded throughout the follow-up phase from Day 28 to Day 365. Additionally the percent reduction from baseline will be reported.

Glucose variability and hypoglycemia duration will be measured by continuous glucose monitoring system (CGMS) for a 3-day period at three different time points: 1) at screening, 2) one year after first islet transplant, and 3) one year after last islet transplant. The following measurements and analysis will be reported:

- Mean glucose concentration
- Percent of time in the following ranges:
  < 60 mg/dl
  60-140 mg/dl
  141-200 mg/dl
  > 200 mg/dl

As with the primary endpoint, the secondary endpoints should be available for all transplanted patients and the analyses will be conducted for the ITT population. If a categorical endpoint is not available for a patient, then it will be treated with the same missing data rules as used for the primary endpoint. If a scalar endpoint is not available for a patient within the designated time window around Day 365, a later value will be imputed if an evaluation is done at a time longer than one year after the final transplant, otherwise the patient will stay missing for the endpoint. If for any endpoints more than 50% of patients do not report data, the endpoints will then not be summarized.

All imputations and missing data will be reported in a patient data listing along with the reasons for imputation and/or missing data.

10. SAFETY EVALUATIONS

Safety analyses will be conducted for the Safety Population. Summaries will be prepared for the targeted safety endpoints listed below and for all observed adverse events (AE). All patients in the Safety population will be analyzed for safety endpoints for1 year after the first and the last transplantation (if applicable) or up to the data cut-off date, 13 April 2015.

10.1. Adverse Events

An adverse event is any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome, or disease that either occurs during the study, having been absent at baseline, or if present at baseline, appears to worsen.

10.1.1. Definitions

The following definitions will be applied consistently to the safety analysis:

Baseline (Clinical Labs, Physical Examinations)	The baseline value will be the result collected at the immediate pre-transplant work-up visit, if scheduled, or the most recent screening visit prior to the islet transplant where the lab/examination was scheduled.
Baseline (Vital Signs)	The baseline value will be the result collected at the immediate pre-transplant work-up visit. If this assessment was not obtained, then the most recent value obtained for

	the specific parameter prior to the islet infusion will be used as the baseline value.
Baseline (ECG parameters)	The baseline value will be the most recent pre-transplant value obtained.
Change from baseline	Value at the time point – value at baseline
Treatment-emergent	Any safety assessment that occurred at the onset of or after start of the first islet infusion, up to the end of 1-year follow-up after the last infusion.

10.1.2. Serious Adverse Event (SAE)

A serious adverse event (experience) is defined as any adverse experience that suggests a significant hazard, contraindication, side effect, or untoward medical occurrence that:

1. Results in death
2. Is life-threatening
3. Requires or prolongs hospitalization, including emergency room care
4. Causes persistent or significant disability or incapacity
5. Results in congenital anomaly
6. Requires intervention to prevent permanent impairment or damage or in the judgment of the investigator represents significant hazard to the study participant.

10.1.3. Assessment of Causality

The relationship or attribution of a medical event or toxicity, or a serious adverse event (being possibly related or not) to an investigational product or therapy represents the best estimate of the principal investigator or sub-investigator at the time of reporting the causal relationship.

The investigator's determination of treatment-relatedness (attribution) for each medical event or toxicity is recorded in the source documentation. For this protocol, the attribution will be dichotomized into the "possibly related" or "not possibly related" categories.

10.1.4. Severity of Adverse Event

AEs will be graded on a scale from 1 to 5 using Collaborative Islet Transplant Consortium *Terminology Criteria for Adverse Events (TCAE) In Trials of Adult Pancreatic Islet Transplantation, Version5.0 (03 August 2011)*:

Grade 1 = Mild adverse event
Grade 2 = Moderate adverse event
Grade 3 = Severe and undesirable adverse event
Grade 4 = Life-threatening or disabling adverse event

Grade 5 = Death.

Adverse events *not* included in the TCAE listing will be recorded and graded 1 to 5 according to the *General Grade Definitions* provided below (see Table 2).

Table 2. General Grade Definitions for Items Not in TCAE Listing

Grade	Descriptor	Definition
1	Mild	Transient or mild discomforts (< 48 hours), no or minimal medical intervention/therapy required, hospitalization not necessary (non-prescription or single-use prescription therapy may be employed to relieve symptoms, e.g., aspirin for simple headache, acetaminophen for post-surgical pain)
2	Moderate	Mild to moderate limitation in activity; some assistance may be needed; no or minimal intervention/therapy required, hospitalization possible
3	Severe	Marked limitation in activity, some assistance usually required; medical intervention/therapy required, hospitalization possible
4	Life-Threatening or Disabling	Extreme limitation in activity, significant assistance required; significant medical/therapy intervention required, hospitalization or hospice care probable
5	Death	Death

10.1.5. Analyses of Adverse Events

Adverse events will be coded to the Medical Dictionary for Regulatory Activities (MedDRA) preferred terms (PT) and system organ classes (SOC) using version 17.0 or higher. All tabular AE summaries will be for treatment-emergent adverse events (TEAE). For all percentages, the number of patients in the ITT population will comprise the denominator.

An overall summary table will be developed to report, across the total safety population and by number of transplants received, starting from the day of first islet cells infusion to the end of 1-year follow-up after the last transplant, the total number of events and the number and percent of patients having at least one event and those related to treatment in the following categories:

a. Procedure Related Events
   The incidence and severity of adverse events related to the islet infusion procedure including:

   - Bleeding (> 2 g/dl decrease in hemoglobin concentration) identified within 24 hours post transplant.

- Portal vein thrombosis, branch or main, detected by ultrasound by the end of Day 7 (or on the first visit post-transplant if it does not fall on Day 7 exactly).
- Biliary puncture identified within 24 hours post transplant.
- Wound complication (infection or subsequent hernia) identified by the end of Day 7 (or on the first post-transplant visit if it does not fall on Day 7 exactly).
- Increased transaminase levels (> 5 times upper level of normal) identified by the end of Day 30 (or on the post-transplant visit that is closest to Day 30 if it does not fall on Day 30 exactly).

b. Immunosuppression/study drug Related Events

The incidence and severity of adverse events related to immunosuppression and/or the study drug (islets), including:

- Allergy
- Reduction in GFR (> 25% reduction in estimated GFR from baseline by Cockroft and Gault formula:

$$eC_{Cr} = \frac{(140-Age)\times(Weight\ in\ kilograms)\times[0.85\ if\ Female]}{72\times(Serum\ Creatinie\ in\ mg/dL)})$$

- Increase in urinary albumin excretion
- New onset microalbuminuria (albumin > 30 mg/day confirmed by 24 hour urine collection) in patients who were previously within normal limits
- For those patients with baseline microalbuminuria (30-300 mg/day), new onset overt albuminuria (greater than 300 mg/day confirmed by 24 hour urine collection)
- Sensitization evidenced by increase in PRA by at least 20% relative to baseline
- Addition or intensification of antihypertensive therapy
- Oral ulcers
- Lower extremity edema
- Gastrointestinal toxicity (diarrhea)
- Neutropenia (neutrophils < 1.3 thous/µL)
- Anemia (hemoglobin men < 12.1, women < 11.7 g/dL)
- Thrombocytopenia (platelets < 150 thous/µL)
- Infections (viral, bacterial, or fungal)
- Neoplasms, benign or malignant

c. All other TEAEs

The incidence and severity of adverse events reported outside the two aforementioned categories.

The overall summaries will also be done for the following types of AE's:

- SAEs
- TEAEs that lead to discontinuation of the study
- TEAEs resulting in death
- TEAEs graded at least 3 (severe) on the severity scale

In addition to an overall 1-year summary of AEs under each aforementioned category, a summary (number of events and the number and percent of patients having at least one event in the category) by windows of time will be provided for a respective group of AEs after the first transplant: events within the first week (by Day 7), first month (by Day 30), the first three months (by Day 90), the first six months (by Day 180), and the first year (by Day 365). The total number of patients being followed within the specific time window will be used as denominator for calculating the proportion in that time window.

In addition, summaries by SOC and PT will be developed for the following types of AE's:

- TEAEs
- TEAEs reported as related to islet transplantation
- TEAEs reported as having a severe or beyond intensity

The summaries of all TEAEs will present the number of AEs and the number and percent of patients having an AE by SOC and by specific PT. The summary of treatment-related TEAEs and the summary of severe-or-beyond (graded 3-5) AEs will only report the number and percent of patients for each SOC and PT. For the summary of AEs reported as possibly related to islet transplant, missing relationships to the treatment will be counted as possibly related to islet transplant. Likewise, if the maximum severity of an AE is not reported, then the maximum severity of the AE will be imputed.

In addition to these summary tables, patients with treatment-emergent SAEs and patients who discontinued prematurely due to a TEAE will be presented in separate patient listings. The listings will provide all of the information reported for that AE and will include the length of time from study drug administration to the occurrence of the AE. If there are any deaths in the study, a similar listing of all TEAEs for patients who died will be provided.

10.2. Concomitant Medications

All medications used in line with islet transplantation as described in the protocol will be summarized and reported as study concomitant medications. Concomitant medications during the study will include immunosuppressants and other medications that are part of the protocol directed treatment (see Section 2.5, Treatment Regimens) and are reported on the

Current/Prior Medications page of the CRF with a start date/time on or after the date/time when the protocol-directed therapy is initiated.

For the in-study concomitant medications summary, all medications will be coded to preferred drug names and therapeutic drug class using the World Health Organization (WHO) Drug Dictionary Enhanced. Use of concomitant medications across all patients will be summarized for each therapeutic drug class and each preferred drug name.

Patients with treatment-emergent SAEs, patients who discontinued prematurely due to a TEAE and patients who died during the safety evaluation period will be presented in separate patient listings which provide all of the information on prior/concomitant medications administration, include the dosing and schedule of medications, and trough level of immunosuppressants before each dosing change up to the occurrence of the AE/death.

10.3. Clinical Laboratory Tests

All treatment-emergent abnormal values as determined based upon the normal values provided by the central laboratory will be listed with relevant patient information. In addition, for those tests that have potentially clinically significant (PCS) criteria, all PCS treatment-emergent values will be identified. The following PCS criteria will be used:

Clinical Chemistry Variable	**PCS Criteria**
Albumin	<2 g/dL
Alkaline phosphatase	> 5.0 – 20.0 x ULN*
Amylase	>2.0 – 5.0 x ULN
Calcium	<7.0 – 6.0 or >12.5 – 13.5 mg/dL
Carbon dioxide	<11 – 8 mmol/L
Cholesterol (total)	>400 – 500 mg/dL
Creatinine	>1.5 x ULN
Potassium	<3.0 - 2.5 or >6.0 - 7.0 mmol/L
PRA	> 20%**
Serum aspartate aminotransferase [SGOT (AST)]	>5.0 – 20.0 x ULN
Serum alanine aminotransferase [SGPT (ALT)]	>5.0 – 20.0 x ULN
Sodium	<130 - 120 or >155 - 160 mmol/L
Total bilirubin	>3.0 – 10.0 x ULN
Hemoglobin (urine)	Present
Albumin (urine)	>30 or 300 mg/24 hrs depending on baseline level***
Total protein (urine)	1.0 – 3.0 g/24 hrs

Clinical Chemistry Variable	PCS Criteria
Hemoglobin	< 8.0 – 6.5 g/dL
WBC Neutrophils/granulocytes	<1.0 – 0.5 x 10^9 /L
Platelets	<50 – 25 x 10^9/L

*LLN=Lower Limit of Normal; ULN=Upper Limit of Normal

**Post allogeneic transplant

***See safety endpoints in Section 2.7.1b.

For hematology and clinical chemistry laboratory parameters, actual values at Baseline and each follow-up visit will be summarized. The change from baseline values will be summarized at each visit. If repeated samples are performed for any scheduled time point, the first non-missing assessment for that time point will be used in these analyses.

10.4. Vital Signs and Other Observations Related to Safety

10.4.1. Vital Signs

The vital sign parameters will include heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), respiration rate, and temperature. All PCS treatment-emergent vital sign values will be listed with relevant patient information. The PCS values will be identified based on the following criteria:

Vital Sign Variable	PCS Criteria
Systolic Blood Pressure	>150 mmHg or an increase of ≥20 mmHg
	<90 mmHg or a decrease of ≥20 mmHg
Diastolic Blood Pressure	>100 mmHg or an increase of ≥20 mmHg
	<50 mmHg or a decrease of ≥15 mmHg
Heart Rate	>120 bpm and an increase of ≥15 beats/min
	<50 bpm and a decrease of ≥15 beats/min

The actual vital sign values and the change from baseline values will be summarized at each scheduled time point post-transplant during the treatment and follow-up.

10.4.2. Electrocardiogram (12-Lead)

At each scheduled time point during the Treatment and Follow-up Phases up to the last assessment that is closest to Day 365 ± 28 days with Day 0 being the day of last islet transplantation, the qualitative interpretation of the ECG results (normal, abnormal) will be analyzed by presenting the number and percentage of patients who worsened at that time

point. Worsening will be defined as a change from a rating of normal/abnormal not clinically significant on both of the pre-transplant assessments to abnormal clinically significant at the time of evaluation. All treatment-emergent worsening in ECG results will be listed with relevant patient information.

11. SEQUENCE OF PLANNED ANALYSES

11.1. Interim Analyses

No interim analysis is planned for this study.

11.2. Final Analyses and Reporting

Final analyses and reporting will be completed after all SAS® programming has been validated and the database has been locked and passed a quality assurance (QA) assessment.

12. LIST OF PLANNED TABLE, FIGURES, AND GRAPHS

This section lists the tables, figures, and graphs that are planned for inclusion in Section 14 of the CSR. Each table, figure, or graph is assigned a number and categorized based upon the structure of the CSR-Section 14. A shell for each unique type of table and figure is provided in Section 14 of this SAP. Each table shell provides sufficient detail on the population to be summarized, the statistics required for the summary, and any programming (or computation) notes that are required to support development of the table.

12.1. Demographic Data

Table	Title	Population
14.1.1	Patient Disposition and Reason for Early Discontinuation	Safety
14.1.2	Demographics and Patient Characteristics	Safety
14.1.3	Baseline Diabetes Control	Safety
14.1.4	Medical History	Safety
14.1.5	Current Medical Conditions	Safety
14.1.6	Screening Physical Examination Results	Safety
14.1.7	Prior/Concomitant Medication Use at Baseline	Safety
14.1.8	Listing of Islet Infusions by Patients	Safety

12.2. Efficacy Data

Table	Title	Population
14.2.1	Summary of Primary Efficacy Endpoint	ITT

14.2.2.a	Summary of Patients Attaining Insulin Independence at 1 Year after First and Last Transplant	ITT
14.2.2.b	Summary of Patients' HYPO score at 1 Year after First and Last Transplant	ITT
14.2.2.c	Summary of Patients' Glucose Variability and Hypoglycemia Duration at 1 Year after First and Last Transplant	ITT

Figure	**Title**	**Population**
14.2.1	Cumulative Percent of Patients Attaining HbA1c Reduction from Baseline at 1 Year after Last Transplant	ITT

12.3. Safety Data

Table	**Title**	**Population**
14.3.1	Overall Summary of Treatment-Emergent Adverse Events	Safety
14.3.2	Summary of Treatment-Emergent Adverse Events by Time after First Transplant	Safety
14.3.3	Incidence of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term	Safety
14.3.4	Incidence of Treatment-Emergent Islet Transplant Related Adverse Events by System Organ Class and Preferred Term	Safety
14.3.5	Incidence of Severe-or-Beyond Treatment-Emergent Adverse Events	Safety
14.3.6	Listing of Serious Adverse Events	Safety
14.3.7	Listing of Adverse Events Leading to Premature Discontinuation	Safety
14.3.8	Concomitant Medications from Initial Transplant to 1 Year after Last Transplant	Safety
14.3.9	Listing of Concomitant Medication Use of Patients with Serious Adverse Events, Adverse	Safety

Table	Title	Population
	Events Leading to Premature Discontinuation, and Death	
14.3.10	Hematology– Actual and Change from Baseline Results	Safety
14.3.11	Hematology – Leukocytes and Differential – Actual and Change from Baseline Results	Safety
14.3.12	Clinical Chemistry – Liver Function – Actual and Change from Baseline Results	Safety
14.3.13	Clinical Chemistry – Electrolytes/Renal Function – Actual and Change from Baseline Results	Safety
14.3.14	Clinical Chemistry – Lipid Panel - Actual and Change from Baseline Results	Safety
14.3.15	Clinical Chemistry – Other - Actual and Change from Baseline Results	Safety
14.3.16	Immunology – PRA – Actual and Change from Baseline Results	Safety
14.3.17	24-Hour Urine – Shifts from Normal at Baseline to Abnormal after Transplants	Safety
14.3.18	Listing of Treatment-Emergent Laboratory Abnormalities and PCS Results	Safety
14.3.19	Vital Signs – Systolic Blood Pressure (mmHg) – Actual, and Change from Baseline Results	Safety
14.3.20	Vital Signs – Diastolic Blood Pressure (mmHg) – Actual and Change from Baseline Results	Safety
14.3.21	Vital Signs – Heart Rate (beats/min) – Actual and Change from Baseline Results	Safety
14.3.22	Vital Signs – Temperature – Actual and Change from Baseline Results	Safety
14.3.23	Listing of Vital Signs for Patients with PCS Treatment-Emergent Results	Safety
14.3.24	Electrocardiogram - Worsening from Baseline to 1 Year Post Last Transplant	Safety
14.3.25	Listing of Patients with Treatment-Emergent ECG Abnormalities	Safety

13. LIST OF PLANNED PATIENT DATA LISTINGS

This section indicates the patient data listings that are planned for inclusion in the CSR, Appendix-Section 16.2. Each table, figure, or graph is assigned a number and categorized based upon the structure of the CSR, Appendix -Section 16.2.

13.1. Discontinued Patients

Listing	Title
16.2.1a	Discontinued Patients
16.2.1b	Disposition

13.2. Protocol Deviations

Listing	Title
16.2.2a	Protocol Deviations
16.2.2b	Informed Consent and Inclusion/Exclusion Criteria
16.2.2c	Study Continuation Record

13.3. Patients Excluded from the Efficacy Analysis

16.2.3	Patients Excluded from the Efficacy Analysis

13.4. Demographic Data

Listing	Title
16.2.4a	Demographics
16.2.4b	Medical History
16.2.4c	Concomitant Medications

13.5. Compliance and Immunosuppressant Data (if available)

Listing	Title
16.2.5	Treatment Non-Compliance

13.6. Individual Efficacy Response Data

16.2.6a	Individual level of HbA1c and Hypoglycemic Events at 1 Year after First Transplant
16.2.6b	Individual Insulin Independence at 1 Year after First Transplant
16.2.6c	Individual HYPO Score and Percent Reduction from Baseline at 1 Year after First Transplant

16.2.6d	Individual Graft Failure at 1 Year after First and Last Transplant
16.2.6e	Individual Imputed Value and Reason for Imputation in Efficacy Evaluation

13.7. Adverse Event Listings (each patient)

Listing	Title
16.2.7a	Adverse Events
16.2.7b	Mapping of AE Verbatim Terms to Preferred Terms and Body Systems

13.8. Listing of Individual Laboratory Measurements by Patient When Required by Regulatory Authorities

Listing	Title
16.2.8a	Laboratory Assessments– Hematology
16.2.8b	Laboratory Assessments– Clinical Chemistry
16.2.8c	Laboratory Assessments– Urinalysis
16.2.8d	Laboratory Assessments– Other

13.9. Listing of Vital Signs and Other Observations Related to Safety

Listing	Title
16.2.9a	Vital Signs
16.2.9b	Electrocardiogram – Diagnosis
16.2.9c	Investigator Comments

14. TABLE SHELLS

Protocol: UIH-002 Page x of N
Population: All Enrolled

TABLE 14.1.1
Patient Disposition and Reason for Early Discontinuation

		Reason for Early Discontinuation					
Disposition [1]	Total n (%)	Death n (%)	Adverse Event n (%)	Consent Withdrawn n (%)	Non-compliance n (%)	Lost to follow-up n (%)	Other n (%)
Completed	XX (XX)						
Early Discont.	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)
Ongoing	XX (XX)						
Safety Pop.	XX (XX)						

Note: The denominator for all percentages is the corresponding population N.
[1] Disposition as of 1 year after last transplant or April 13th, 2015, whichever occurred first.

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Population: Safety

TABLE 14.1.2
Demographics and Patient Characteristics

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Safety population (N=X)	n	Mean	SD	Median	Minimum	Maximum
Age (years)	X	XX	XX	XX	XX	XX
Weight (kg)	X	XX	XX	XX	XX	XX
Height (cm)	X	XX	XX	XX	XX	XX
BMI (kg/m^2)	X	XX	XX	XX	XX	XX

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	Race				
	Caucasian n (%)	Black n (%)	Oriental n (%)	Native American n (%)	Other n (%)
Safety population (N=X)	XX (XX)	XX (XX)	XX (XX)	XX (XX)	XX (XX)

	Ethnicity	
	Hispanic n (%)	Non-Hispanic n (%)
Safety population (N=X)	XX (XX)	XX (XX)

	Gender	
	Male n (%)	Female n (%)
Safety population (N=X)	XX (XX)	XX (XX)

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Population: Safety

TABLE 14.1.3
Baseline Diabetes Control

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Safety population (N=X)							
Variable	n	Mean	SD	Median	Minimum	Maximum	Missing n (%)
Insulin Requirement (unit/kg/day)	X	XX	XX	XX	XX	XX	XX (XX)
HbA1c (%)	X	XX	XX	XX	XX	XX	XX (XX)
Frequency of SHE (episodes/month)	X	XX	XX	XX	XX	XX	XX (XX)
HYPO Score	X	XX	XX	XX	XX	XX	XX (XX)
Mixed Meal Test: Fasting Plasma Glucose (mg/mL)	X	XX	XX	XX	XX	XX	XX (XX)
90-min Glucose post glucose challenge (mg/dL)	X	XX	XX	XX	XX	XX	XX (XX)

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Safety population (N=X)	n (%) of Patients	Missing n (%)
Reduced awareness of hypoglycemia [1]	X (XX)	X (XX)
Mixed Meal Test:		
Fasting C-peptide < 0.1 ng/mL [2]	X (XX)	X (XX)
90-min C-peptide post glucose challenge < 0.1 ng/mL	X (XX)	X (XX)

[1] Reported qualitatively only at enrollment.
[2] 0.1 ng/ml is the undetectable lower limit for C-peptide.

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TABLE 14.1.4
Medical History

Number (%) of Patients with Clinically Significant Medical History Conditions

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Safety population (N=X)	Body System				
	Allergy n (%)	Immunology n (%)	Renal/Genitourinary n (%)	Cardio-vascular n (%)	Missing n (%)
	X (XX)	X (XX)	X (XX)	X (XX)	X (XX)

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TABLE 14.1.5
Current Medical Conditions

Number (%) of Patients with Clinically Significant Current Medical Conditions

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Safety population (N=X)	Body System				
	Allergy n (%)	Immunology n (%)	Renal/Genitourinary n (%)	Cardio-vascular n (%)	Missing n (%)
	X (XX)	X (XX)	X (XX)	X (XX)	X (XX)

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TABLE 14.1.6
Screening Physical Examination Results

	Body System Number (%) of Patients with an Abnormality					
	Eyes	ENT	Respiratory	Gastro-intestinal	Genitourinary	Extremities
Safety population (N=X)	X/X (XX)	X/X (XX)	X/X (XX)	X/X (XX)	X/X (XX)	X/X (XX)

	Nervous System	Dermatologic	Lymph Nodes	Endocrine/ Metabolic
	X/X (XX)	X/X (XX)	X/X (XX)	X/X (XX)

Note: The denominator is the number of patients that had the body system evaluated during the physical exam.

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Population: Safety

TABLE 14.1.7
Prior/Concomitant Medication Use at Baseline

Drug Class/ Preferred Drug Name	Islet Transplantation (N=X) n (%)
Subj. taking a prior/con. med.	X (XX)
Drug Class 1	
Preferred Name 1.1	X (XX)
Preferred Name 1.2	X (XX)
Preferred Name 1.3	X (XX)
etc.	
Missing	X (XX)

Note: Medications were coded using WHO Therapeutic drug classes and preferred names.

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Table 14.1.8
Listing of Islet Infusions by Patients

Total # of Tx Received	Subj. No.	Seq. of Islet Infusion	Date of Islet Infusion
1 Tx	XXX	1	DDMMMYYYY
	XXX	1	DDMMMYYYY
	etc.		
2 Tx's	XXX	1	DDMMMYYYY
		2	DDMMMYYYY
	etc.		
3 Tx's	XXX	1	DDMMMYYYY
		2	DDMMMYYYY
		3	DDMMMYYYY
	etc.		

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TABLE 14.2.1
Summary of Primary Efficacy Endpoint

ITT population (N=X)	Time of Evaluation Number (%) of Patients			
	1 Year after First Tx	(95% C.I.)	1 Year after Last Tx	(95% C.I.)
Success (HbA1c ≤ 6.5% + Free of SHE [1])	X (XX)	(XX, XX)	X (XX)	(XX, XX)
Failure Total	X (XX)		X (XX)	
HbA1c > 6.5%	X (XX)		X (XX)	
Any SHE [1]	X (XX)		X (XX)	
Missing [2]	X (XX)		X (XX)	

[1] SHE occurring between Day 28 and Day 365 (Day 0 being the day of corresponding transplant).
[2] Missing endpoints are imputed as failure.

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TABLE 14.2.2a
Summary of Secondary Efficacy Endpoints:
Patients Attaining Insulin Independence at 1 Year after First and Last Transplant

ITT population (N=X)	Number (%) of Patients			
	First Tx Day 365	Missing	Last Tx Day 365	Missing
Absence of exogenous insulin	X (XX)	X (XX)	X (XX)	X (XX)
Among patients fulfilling the primary efficacy outcome (N=X):				
Absence of exogenous insulin	X (XX)	X (XX)	X (XX)	X (XX)
Fasting capillary glucose in a week:				
Not exceeding 140 mg/dL more than 3X	X (XX)	X (XX)	X (XX)	X (XX)
Fasting plasma glucose ≤ 126 mg/dL	X (XX)	X (XX)	X (XX)	X (XX)
Postprandial capillary glucose in a week:				
Not exceeding 180 mg/dl more than 1X/7X	X (XX)	X (XX)	X (XX)	X (XX)
C-peptide (fasting or stimulated) ≥ 0.5 ng/mL	X (XX)	X (XX)	X (XX)	X (XX)

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TABLE 14.2.2b
Summary of Secondary Efficacy Endpoints:
Patients' HYPO Score at 1 Year after First and Last Transplant

	ITT population (N=X)	n	Mean	SD	Median	Minimum	Maximum	Missing n (%)
HYPO	Baseline (pre-Tx):	X	XX	XX	XX	XX	XX	X (XX)
	First Tx Day 365	X	XX	XX	XX	XX	XX	X (XX)
	% Reduction from baseline	X	XX	XX	XX	XX	XX	X (XX)
	Last Tx Day 365	X	XX	XX	XX	XX	XX	X (XX)
	% Reduction from baseline	X	XX	XX	XX	XX	XX	X (XX)

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TABLE 14.2.2c
Summary of Secondary Efficacy Endpoints:
Patients' Glucose Variability and Hypoglycemia Duration at 1 Year after First and Last Transplant

ITT population (N=X)		n	Mean	SD	Median	Minimum	Maximum	Missing n (%)
Baseline	Mean Glucose	X	XX	XX	XX	XX	XX	X (XX)
	Percent time in range:							
	< 60 mg/dl	X	XX	XX	XX	XX	XX	X (XX)
	60-140 mg/dl	X	XX	XX	XX	XX	XX	X (XX)
	141-200 mg/dl	X	XX	XX	XX	XX	XX	X (XX)
	> 200 mg/dl	X	XX	XX	XX	XX	XX	X (XX)
First Tx								
Day 365	Mean Glucose	X	XX	XX	XX	XX	XX	X (XX)
	Percent time in range:							
	< 60 mg/dl	X	XX	XX	XX	XX	XX	X (XX)
	60-140 mg/dl	X	XX	XX	XX	XX	XX	X (XX)
	141-200 mg/dl	X	XX	XX	XX	XX	XX	X (XX)
	> 200 mg/dl	X	XX	XX	XX	XX	XX	X (XX)
Last Tx								
Day 365	Mean Glucose	X	XX	XX	XX	XX	XX	X (XX)
	Percent time in range:							
	< 60 mg/dl	X	XX	XX	XX	XX	XX	X (XX)
	60-140 mg/dl	X	XX	XX	XX	XX	XX	X (XX)
	141-200 mg/dl	X	XX	XX	XX	XX	XX	X (XX)
	> 200 mg/dl	X	XX	XX	XX	XX	XX	X (XX)

Note: Baseline levels were measured prior to the initial transplant.

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TABLE 14.3.1
Overall Summary of Treatment-Emergent Adverse Events

	# of Islet Transplantations Received			
Type of AE	Total [1] (N=X)	1 Tx (N=X)	2 Tx's (N=X)	3 Tx's (N=X)
TEAEs				
Events	X	X	X	X
Patients: n(%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Serious TEAEs				
Events	X	X	X	X
Patients: n(%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
TEAEs leading to discontinuation				
Events	X	X	X	X
Patients: n(%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
TEAEs with an outcome of death				
Events	X	X	X	X
Patients: n(%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
TEAEs related to treatment [2]				
Events	X	X	X	X
Patients: n(%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
TEAEs rated as severe or beyond [3]				
Events	X	X	X	X
Patients: n(%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)

[1] The Total column summarizes all AEs in the corresponding category starting from initial transplant to 1 year after the last transplant.
[2] Events related to procedure, immunosuppression or any study drugs were determined to be related to treatment. Missing relatedness was counted as being related.
[3] Severe-or-beyond events are those graded 3-5 on the TCAE severity grading. Missing severity was counted as being grade 5.

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Population: Safety

TABLE 14.3.2
Summary of Treatment-Emergent Adverse Events by Time after First Transplant

	Islet Transplantation 1					
Type of AE	Total [1] (N=X)	1 week (N=X)	1 month (N=X)	3 months (N=X)	6 months (N=X)	1 year (N=X)
TEAEs						
Events	X	X	X	X	X	X
Patients: n(%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Serious TEAEs						
Events	X	X	X	X	X	X
Patients: n(%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
TEAEs leading to discontinuation						
Events	X	X	X	X	X	X
Patients: n(%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
TEAEs with an outcome of death						
Events	X	X	X	X	X	X
Patients: n(%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
TEAEs related to treatment [2]						
Events	X	X	X	X	X	X
Patients: n(%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
TEAEs rated as severe or beyond [3]						
Events	X	X	X	X	X	X
Patients: n(%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)

[1] The Total column summarizes all AEs in the corresponding category starting from initial transplant to 1 year after the last transplant.
[2] Events related to procedure, immunosuppression or any study drugs were determined to be related to treatment. Missing relatedness was counted as being related.
[3] Severe-or-beyond events are those graded 3-5 on the TCAE severity grading. Missing severity was counted as being grade 5.

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Population: Safety

TABLE 14.3.3
Number and Incidence of Treatment-Emergent Adverse Events
by System Organ Class and Preferred Term

<PAGE 1 FORMAT>

System Organ Class/ Preferred Term	Islet Transplantation			
	Total [1] (N=X)	1 Transplant (N=X)	2 Transplants (N=X)	3 Transplants … (N=X)
	Events Subjs	Events Subjs	Events Subjs	Events Subjs
Patients with at least one TEAE	X (XX%)	X (XX%)	X (XX%)	X (XX%)
System Organ Class 1	X X (XX%)	X X (XX%)	X X (XX%)	X X (XX%)
Preferred Term 1.1	X X (XX%)	X X (XX%)	X X (XX%)	X X (XX%)
Preferred Term 1.2	X X (XX%)	X X (XX%)	X X (XX%)	X X (XX%)
Preferred Term 1.3	X X (XX%)	X X (XX%)	X X (XX%)	X X (XX%)
etc.				

[1] The Total column summarizes all AEs in the corresponding category starting from initial transplant to 1 year after the last transplant.

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Population: Safety

TABLE 14.3.4
Incidence of Islet Transplantation Related Treatment-Emergent Adverse Events
by System Organ Class and Preferred Term

<PAGE 1 FORMAT>

System Organ Class/ Preferred Term	Islet Transplantation			
	Total [1] (N=X)	1 Transplant (N=X)	2 Transplants (N=X)	3 Transplants … (N=X)
	Events Subjs	Events Subjs	Events Subjs	Events Subjs
Patients with at least one TEAE related to islet transplantation [2]	X (XX%)	X (XX%)	X (XX%)	X (XX%)
System Organ Class 1	X X (XX%)	X X (XX%)	X X (XX%)	X X (XX%)
Preferred Term 1.1	X X (XX%)	X X (XX%)	X X (XX%)	X X (XX%)
Preferred Term 1.2	X X (XX%)	X X (XX%)	X X (XX%)	X X (XX%)
Preferred Term 1.3	X X (XX%)	X X (XX%)	X X (XX%)	X X (XX%)
etc.				

[1] The Total column summarizes all AEs in the corresponding category starting from initial transplant to 1 year after the last transplant.
[2] AE related to islet transplantation, including immunosuppression, study drugs and/or procedure. Missing relatedness was counted as being related.

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Population: Safety

TABLE 14.3.5
Incidence of Severe-or-Beyond Treatment-Emergent Adverse Events
by System Organ Class and Preferred Term

<PAGE 1 FORMAT>

System Organ Class/ Preferred Term	Islet Transplantation			
	Total [1] (N=X) n (%)	1 Transplant (N=X) n (%)	2 Transplants (N=X) n (%)	3 Transplants … (N=X) n (%)
Patients with at least one severe-or-beyond TEAE [2]	X (XX%)	X (XX%)	X (XX%)	X (XX%)
System Organ Class 1	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Preferred Term 1.1	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Preferred Term 1.2	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Preferred Term 1.3	X (XX%)	X (XX%)	X (XX%)	X (XX%)
etc.				

[1] The Total column summarizes all AEs in the corresponding category starting from initial transplant to 1 year after the last transplant.
[2] Severe-or-beyond events are those graded 3-5 on the TCAE severity grading. Missing severity was counted as being grade 5.

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Table 14.3.6
Listing of Serious Adverse Events

Total # of Tx Received	Subj. No.	Adverse Event System Organ Class/ Preferred Term	Time of Onset (days) [1]	Dur. of AE (days)	Maximum Intensity/ Rel. to Tx	Action Taken/ Outcome	Discon-tinued because of this AE?
1 Tx	XXX	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXX	XX	XXXX	XXXXXXXXX/ XXXXXXXXX	XXXXXXXXX/ XXXXXXXXX	XXX
	XXX	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXX	XX	XXXX	XXXXXXXXX/ XXXXXXXXX	XXXXXXXXX/ XXXXXXXXX	XXX
	etc.						
2 Tx's	XXX	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXX	XX	XXXX	XXXXXXXXX/ XXXXXXXXX	XXXXXXXXX/ XXXXXXXXX	XXX
	XXX	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXX	XX	XXXX	XXXXXXXXX/ XXXXXXXXX	XXXXXXXXX/ XXXXXXXXX	XXX
	etc.						
3 Tx's	XXX	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXX	XX	XXXX	XXXXXXXXX/ XXXXXXXXX	XXXXXXXXX/ XXXXXXXXX	XXX
	XXX	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXX	XX	XXXX	XXXXXXXXX/ XXXXXXXXX	XXXXXXXXX/ XXXXXXXXX	XXX
	etc.						

[1] Relative to the day of the most recent transplant.

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Population: Safety

Table 14.3.7
Listing of Adverse Events Leading to Premature Discontinuation

Total # of Tx Received	Subj. No.	Adverse Event System Organ Class/ Preferred Term	Time of Onset (days) [1]	Dur. of AE (days)	Maximum Intensity/ Rel. to Tx	Action Taken/ Outcome	SAE?
1 Tx	XXX	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXX	XX	XXXX	XXXXXXXXX/ XXXXXXXXX	XXXXXXXXX/ XXXXXXXXX	XXX
	XXX	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXX	XX	XXXX	XXXXXXXXX/ XXXXXXXXX	XXXXXXXXX/ XXXXXXXXX	XXX
	etc.						
2 Tx's	XXX	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXX	XX	XXXX	XXXXXXXXX/ XXXXXXXXX	XXXXXXXXX/ XXXXXXXXX	XXX
	XXX	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXX	XX	XXXX	XXXXXXXXX/ XXXXXXXXX	XXXXXXXXX/ XXXXXXXXX	XXX
	etc.						
3 Tx's	XXX	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXX	XX	XXXX	XXXXXXXXX/ XXXXXXXXX	XXXXXXXXX/ XXXXXXXXX	XXX
	XXX	XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXX	XX	XXXX	XXXXXXXXX/ XXXXXXXXX	XXXXXXXXX/ XXXXXXXXX	XXX
	etc.						

[1] Relative to the day of the most recent transplant.

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TABLE 14.3.8
Concomitant Medications from Initial Transplant to 1 Year after Last Transplant

Drug Class/ Preferred Drug Name	Islet Transplantation (N=X) n (%)
Subj. taking a con. med.	X (XX)
Drug Class 1	
Preferred Name 1.1	X (XX)
Preferred Name 1.2	X (XX)
Preferred Name 1.3	X (XX)
etc.	
Missing	X (XX)

Note: Medications were coded using WHO Therapeutic drug classes and preferred names.

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Table 14.3.9
Listing of Concomitant Medication Use of Patients with Serious Adverse Events, Adverse Events Leading to Premature Discontinuation, and Death

Total # of Tx	Subj. No.	Adverse Event System Organ Class/ Preferred Term	Study days of onset [1]	Date of onset	Discon-tinued because of this AE?	Drug Class/ Preferred Drug Name	Dosing/ Frequency	Start date/ End date	Trough level [2] before dosing change
1	XXX	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX	XXX	XXX	XXX	XXXXXXXXX/ XXXXXXXXX	XXXXXX/ XXXXXX etc.	XXXXX/ XXXXX	
						XXXXXXXXX/ XXXXXXXXX	XXXXXX/ XXXXXX	XXXXX/ XXXXX	XXX
							XXXXXX/ XXXXXX etc.	XXXXX/ XXXXX	XXX
						etc.			
	etc.								
2	XXX	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX		XXX	XXX	XXXXXXXXX/ XXXXXXXXX etc.	XXXXXX/ XXXXXX	XXXXX/ XXXXX	
	etc.								
etc.									

[1] Relative to the day of the initial transplant.
[2] Only applicable to immunosuppression regimens.

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Population: Safety

TABLE 14.3.10
Hematology – Hemagram - Actual and Change from Baseline Results

<PAGE 1 FORMAT>

Transplant #	Parameter Name (SI Units)	Actual						Change from Baseline					
		n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 1 (N=X)													
Baseline [1]	RBC (units)	X	XX	XX	XX	XX	XX						
	Hematocrit (units)	X	XX	XX	XX	XX	XX						
	Hemoglobin (units)	X	XX	XX	XX	XX	XX						
	Platelet Count (units)	X	XX	XX	XX	XX	XX						
Day 1 [2]	RBC (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Hematocrit (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Hemoglobin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Platelet Count (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 1	RBC (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Hematocrit (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Hemoglobin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Platelet Count (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

[1] Baseline is always the value before the initial transplant.
[2] Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

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Population: Safety

TABLE 14.3.10
Hematology – Hemagram - Actual and Change from Baseline Results

<PAGE 2 FORMAT>

Transplant #	Parameter Name (SI Units)	Actual						Change from Baseline					
		n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 2 (N=X)													
Day 1	RBC (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Hematocrit (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Hemoglobin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Platelet Count (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 1	RBC (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Hematocrit (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Hemoglobin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Platelet Count (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

Note: Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

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Population: Safety

TABLE 14.3.10
Hematology – Hemagram - Actual and Change from Baseline Results

<PAGE 3 FORMAT>

Transplant #	Parameter Name (SI Units)	Actual						Change from Baseline					
		n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 3 (N=X)													
Day 1	RBC (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Hematocrit (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Hemoglobin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Platelet Count (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 1	RBC (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Hematocrit (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Hemoglobin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Platelet Count (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

Note: Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

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Population: Safety

TABLE 14.3.11

Hematology – Leukocytes and Differential- Actual and Change from Baseline Results

<PAGE 1 FORMAT>

	Parameter Name	Actual						Change from Baseline					
Transplant #	(SI Units)	n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 1 (N=XX)													
Baseline[1]	WBC (units)	X	XX	XX	XX	XX	XX						
	Neutrophils (units)	X	XX	XX	XX	XX	XX						
	Lymphocytes (units)	X	XX	XX	XX	XX	XX						
	Monocytes (units)	X	XX	XX	XX	XX	XX						
	Eosinophils (units)	X	XX	XX	XX	XX	XX						
	Basophils (units)	X	XX	XX	XX	XX	XX						
Day 1 [2]	WBC (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Neutrophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Lymphocytes (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Monocytes (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Eosinophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Basophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 1	WBC (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Neutrophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Lymphocytes (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Monocytes (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Eosinophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Basophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

[1] Baseline is always the value before the initial transplant.

[2] Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

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Population: Safety

TABLE 14.3.11

Hematology – Leukocytes and Differential- Actual and Change from Baseline Results

<PAGE 2 FORMAT>

Transplant #	Parameter Name (SI Units)	Actual						Change from Baseline					
		n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 2 (N=XX)													
Day 1	WBC (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Neutrophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Lymphocytes (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Monocytes (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Eosinophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Basophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 1	WBC (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Neutrophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Lymphocytes (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Monocytes (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Eosinophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Basophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

Note: Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

XXXXXXXXXX.sas, DDMMMYYYY:HHMM

Population: Safety

TABLE 14.3.11

Hematology – Leukocytes and Differential- Actual and Change from Baseline Results

<PAGE 3 FORMAT>

Transplant #	Parameter Name (SI Units)	Actual						Change from Baseline					
		n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 3 (N=XX)													
Day 1	WBC (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Neutrophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Lymphocytes (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Monocytes (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Eosinophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Basophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 1	WBC (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Neutrophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Lymphocytes (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Monocytes (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Eosinophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Basophils (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

Note: Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

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Population: Safety

TABLE 14.3.12

Clinical Chemistry – Liver Function - Actual and Change from Baseline Results

<PAGE 1 FORMAT>

		Actual						Change from Baseline					
Tx #	Parameter Name (SI Units)	n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 1 (N=X)													
Baseline[1]	ALT (units)	X	XX	XX	XX	XX	XX						
	AST (units)	X	XX	XX	XX	XX	XX						
	Total Bilirubin (units)	X	XX	XX	XX	XX	XX						
	Alkaline Phosphatase (units)	X	XX	XX	XX	XX	XX						
	Albumin (units)	X	XX	XX	XX	XX	XX						
Day 1[2]	ALT (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	AST (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Total Bilirubin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Alkaline Phosphatase (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Albumin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 1	ALT (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	AST (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Total Bilirubin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Alkaline Phosphatase (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Albumin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

[1] Baseline is always the value before the initial transplant.
[2] Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

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Population: Safety

TABLE 14.3.12

Clinical Chemistry – Liver Function - Actual and Change from Baseline Results

<PAGE 2 FORMAT>

Tx #	Parameter Name (SI Units)	Actual						Change from Baseline					
		n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 2 (N=X)													
Day 1	ALT (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	AST (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Total Bilirubin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Alkaline Phosphatase (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Albumin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 1	ALT (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	AST (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Total Bilirubin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Alkaline Phosphatase (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Albumin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

Note: Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

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Population: Safety

TABLE 14.3.12

Clinical Chemistry – Liver Function - Actual and Change from Baseline Results

<PAGE 3 FORMAT>

	Parameter Name	Actual						Change from Baseline					
Tx #	(SI Units)	n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 3 (N=X)													
Day 1	ALT (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	AST (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Total Bilirubin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Alkaline Phosphatase (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Albumin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 1	ALT (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	AST (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Total Bilirubin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Alkaline Phosphatase (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Albumin (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

Note: Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

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Population: Safety

TABLE 14.3.13

Clinical Chemistry – Electrolytes/Renal Function - Actual and Change from Baseline Results

<PAGE 1 FORMAT>

		Actual						Change from Baseline					
Tx #	Parameter Name (SI Units)	n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 1 (N=X)													
Baseline[1]	Sodium (units)	X	XX	XX	XX	XX	XX						
	Potassium (units)	X	XX	XX	XX	XX	XX						
	Chloride (units)	X	XX	XX	XX	XX	XX						
	BUN (units)	X	XX	XX	XX	XX	XX						
	Creatinine (units)	X	XX	XX	XX	XX	XX						
	eGFR (mL/min)	X	XX	XX	XX	XX	XX						
Day 1 [2]	Sodium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Potassium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Chloride (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	BUN (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Creatinine (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	eGFR (mL/min)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 1	Sodium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Potassium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Chloride (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	BUN (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Creatinine (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	eGFR (mL/min)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

[1] Baseline is always the value before the initial transplant.

[2] Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

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TABLE 14.3.13

Clinical Chemistry – Electrolytes/Renal Function - Actual and Change from Baseline Results

<PAGE 2 FORMAT>

	Parameter Name	Actual						Change from Baseline					
Tx #	(SI Units)	n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 2 (N=X)													
Day 1	Sodium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Potassium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Chloride (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	BUN (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Creatinine (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	eGFR (mL/min)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 1	Sodium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Potassium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Chloride (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	BUN (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Creatinine (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	eGFR (mL/min)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

Note: Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

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TABLE 14.3.13

Clinical Chemistry – Electrolytes/Renal Function - Actual and Change from Baseline Results

<PAGE 3 FORMAT>

		Actual						Change from Baseline					
Tx #	Parameter Name (SI Units)	n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 3 (N=X)													
Day 1	Sodium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Potassium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Chloride (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	BUN (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Creatinine (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	eGFR (mL/min)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 1	Sodium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Potassium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Chloride (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	BUN (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Creatinine (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	eGFR (mL/min)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

Note: Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

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TABLE 14.3.14
Clinical Chemistry – Lipid Panel - Actual and Change from Baseline Results

<PAGE 1 FORMAT>

		Actual						Change from Baseline					
Tx #	Parameter Name (SI Units)	n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 1 (N=X)													
Baseline[1]	Total Cholesterol (units)	X	XX	XX	XX	XX	XX						
	HDL (units)	X	XX	XX	XX	XX	XX						
	LDL (units)	X	XX	XX	XX	XX	XX						
	TGs (units)	X	XX	XX	XX	XX	XX						
Week 4-5	Total Cholesterol (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	HDL (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	LDL (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	TGs (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 8-9	Total Cholesterol (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	HDL (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	LDL (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	TGs (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

[1] Baseline is always the value before the initial transplant.

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Population: Safety

TABLE 14.3.14
Clinical Chemistry – Lipid Panel - Actual and Change from Baseline Results
<PAGE 2 FORMAT>

Tx #	Parameter Name (SI Units)	Actual						Change from Baseline					
		n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 2 (N=X)													
Week 4-5	Total Cholesterol (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	HDL (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	LDL (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	TGs (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 8-9	Total Cholesterol (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	HDL (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	LDL (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	TGs (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

XXXXXXXXXX.sas, DDMMMYYYY:HHMM

Population: Safety

TABLE 14.3.14
Clinical Chemistry – Lipid Panel - Actual and Change from Baseline Results

<PAGE 3 FORMAT>

Tx #	Parameter Name (SI Units)	Actual						Change from Baseline					
		n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 3 (N=X)													
Week 4-5	Total Cholesterol (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	HDL (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	LDL (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	TGs (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 8-9	Total Cholesterol (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	HDL (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	LDL (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	TGs (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

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Population: Safety

TABLE 14.3.15
Clinical Chemistry – Other - Actual and Change from Baseline Results

<PAGE 1 FORMAT>

Tx #	Parameter Name (SI Units)	Actual						Change from Baseline					
		n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 1 (N=X)													
Baseline[1]	Glucose (units)	X	XX	XX	XX	XX	XX						
	Total Protein (units)	X	XX	XX	XX	XX	XX						
	Calcium (units)	X	XX	XX	XX	XX	XX						
	Carbon Dioxide (units)	X	XX	XX	XX	XX	XX						
Day 1[2]	Glucose (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Total Protein (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Calcium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Carbon Dioxide (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 1	Glucose (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Total Protein (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Calcium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Carbon Dioxide (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

[1] Baseline is always the value before the initial transplant.
[2] Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

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Population: Safety

TABLE 14.3.15
Clinical Chemistry – Other - Actual and Change from Baseline Results

<PAGE 2 FORMAT>

Tx #	Parameter Name (SI Units)	Actual						Change from Baseline					
		n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 2 (N=X)													
Day 1	Glucose (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Total Protein (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Calcium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Carbon Dioxide (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 1	Glucose (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Total Protein (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Calcium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Carbon Dioxide (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

Note: Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

XXXXXXXXXX.sas, DDMMMYYYY:HHMM

Population: Safety

TABLE 14.3.15
Clinical Chemistry – Other - Actual and Change from Baseline Results

<PAGE 3 FORMAT>

Tx #	Parameter Name (SI Units)	Actual						Change from Baseline					
		n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 3 (N=X)													
Day 1	Glucose (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Total Protein (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Calcium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Carbon Dioxide (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 1	Glucose (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Total Protein (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Calcium (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Carbon Dioxide (units)	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

Note: Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

XXXXXXXXXX.sas, DDMMMYYYY:HHMM

TABLE 14.3.16
Immunology – PRA - Actual and Change from Baseline Results

		Actual						Change from Baseline					
Tx #	PRA (%)	n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
Tx 1 (N=X)													
Baseline[1]	Class I	X	XX	XX	XX	XX	XX						
	Class II	X	XX	XX	XX	XX	XX						
Week 3	Class I	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Class II	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 12	Class I	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Class II	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													
Tx 2 (N=X)													
Week 3	Class I	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Class II	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 12	Class I	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Class II	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													
Tx 3 (N=X)													
Week 3	Class I	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Class II	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Week 12	Class I	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Class II	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
Etc.													

[1] Baseline is always the last value before the initial transplant.

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Table 14.3.17
Urine Albumin - Shifts from Normal at Baseline to Abnormal after Transplants

Tx Sequence	Baseline [1] Status	Patients at Baseline	Abnormal[2] at Week 8/9 n (%)	Abnormal at Week 20 n (%)	Abnormal at Week 40 n (%)	Abnormal at Week 52 n (%)
Tx 1 (N=X)	Normal	XX	X (X)	X (X)	X (X)	X (X)
	Microalbuminuria (30-300 mg/day)	XX	X (X)	X (X)	X (X)	X (X)
Tx 2 (N=X)	Normal		X (X)	X (X)	X (X)	X (X)
	Microalbuminuria (30-300 mg/day)		X (X)	X (X)	X (X)	X (X)
Tx 3 (N=X)	Normal		X (X)	X (X)	X (X)	X (X)
	Microalbuminuria (30-300 mg/day)		X (X)	X (X)	X (X)	X (X)
Total New Onset Abnormal up to 1 Year after Last Tx			XX (XX)			

Note: All percentages are based upon the number of patients at baseline for the specific baseline status.
[1] Baseline is always the value before the initial transplant.
[2] For patients with normal baseline, new onset of microalbuminuria (>30 mg/day) is counted as “abnormal”; for those with baseline microalbuminuria, new onset of overt albuminuria (> 300 mg/day) is counted as “abnormal”.

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Table 14.3.18
Listing of Treatment-Emergent Laboratory Abnormalities and PCS Results

# of Tx Received	ID	Age (yrs.)	Assessment	Laboratory Parameter	Normal LLN	Normal ULN	Abnormal Result	PCS Criteria (if any)	PCS Result? (Y/N)	Baseline Result
1 Tx	XXX	XX	XXXXXXXX	XXXXXXXXXX	XXX	XXX	XXXXXX	XXXXXXX	X	XXXXXX
				XXXXXXXXXX	XXX	XXX	XXXXXX	XXXX	X	XXXXXX
			XXXXXXXX	XXXXXXXXXX	XXX	XXX	XXXXXXX			XXXXXXX
				XXXXXXXXXX	XXX	XXX	XXXXXX	XXXX	X	XXXXXX
			XXXXXXXX	XXXXXXXXXX	XXX	XXX	XXXXXXXX			XXXXXXXX
				XXXXXXXXXX	XXX	XXX	XXXXXX	XXXX	X	XXXXXX
	XXX	XX	XXXXXXXX	XXXXXXXXXX	XXX	XXX	XXXXXX	XXXX	X	XXXXXX
				XXXXXXXXXX	XXX	XXX	XXXXXX	XXXX	X	XXXXXX
			XXXXXXXX	XXXXXXXXXX	XXX	XXX	XXXXXXXX			XXXXXXXX
				XXXXXXXXXX	XXX	XXX	XXXXXX	XXXX	X	XXXXXX
	Etc.									
2 Tx	XXX	XX	XXXXXXXX	XXXXXXXXXX	XXX	XXX	XXXXXX	XXXXXXX	X	XXXXXX
				XXXXXXXXXX	XXX	XXX	XXXXXX	XXXX	X	XXXXXX
Etc.										

Note: PCS = Potentially Clinically Significant

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TABLE 14.3.19
Vitals Signs – Systolic Blood Pressure (mmHg) – Actual and Change from Baseline Results

# of Tx Received	Assessment Time	Actual						Change from Baseline					
		n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
1 Tx (N=XX)													
	Baseline[1]	X	XX	XX	XX	XX	XX						
	Day 1[2]												
	15 min	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	30 min	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	45 min	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	1 hr												
	etc.	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	Week 1	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	etc.	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
2 Tx's (N=XX)													
Etc.													

[1] Baseline is always the value before the initial transplant.
[2] Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

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TABLE 14.3.20

Vitals Signs – Diastolic Blood Pressure (mmHg) – Actual and Change from Baseline Results

# of Tx Received	Assessment Time	Actual						Change from Baseline					
		n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
1 Tx (N=XX)													
	Baseline[1]	X	XX	XX	XX	XX	XX						
	Day 1[2]												
	15 min	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	30 min	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	45 min	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	1 hr	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	etc.												
	Week 1	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	etc.												
2 Tx's (N=XX)													
Etc.													

[1] Baseline is always the value before the initial transplant.
[2] Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

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TABLE 14.3.21
Vitals Signs – Heart Rate (beats/min) – Actual and Change from Baseline Results

# of Tx Received	Assessment Time	Actual						Change from Baseline					
		n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
1 Tx (N=XX)													
	Baseline[1]	X	XX	XX	XX	XX	XX						
	Day 1[2]												
	15 min	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	30 min	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	45 min	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	1 hr	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	etc.												
	Week 1	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	etc.												
2 Tx's (N=XX)													
Etc.													

[1] Baseline is always the value before the initial transplant.
[2] Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

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TABLE 14.3.22
Vitals Signs – Temperature (°F) – Actual and Change from Baseline Results

# of Tx Received	Assessment Time	Actual						Change from Baseline					
		n	Mean	SD	Med	Min	Max	n	Mean	SD	Med	Min	Max
1 Tx (N=XX)													
	Baseline[1]	X	XX	XX	XX	XX	XX						
	Day 1[2]												
	15 min	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	30 min	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	45 min	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	1 hr	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	etc.												
	Week 1	X	XX	XX	XX	XX	XX	X	XX	XX	XX	XX	XX
	etc.												
2 Tx's (N=XX)													
Etc.													

[1] Baseline is always the value before the initial transplant.
[2] Day 1 assessments were obtained during 24 hours post-transplant during the Treatment Phase (in-clinic).

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TABLE 14.3.23
Listing of Vital Signs for Patients with PCS Treatment-Emergent Results

# of Tx Received	Subj. No.	Age (yrs.)	Timepoint	Vital Sign Parameter	PCS? (Y=yes)	Timepoint Value	Baseline Value
1 Tx	XXX	XX	Day 1 30 min	SBP (mmHg)		XX	XX
				SBP (mmHg)		XX	XX
				HR (beats/min)	Y	XX	XX
			etc.				
	XXX	XX	Week 1	SBP (mmHg)		XX	XX
				SBP (mmHg)		XX	XX
				HR (beats/min)	Y	XX	XX
			etc.				
2 Tx	Etc.						

Note: Potentially Clinically Significant (PCS) Criteria:
SBP: >180 mmHg and an increase of >=20 mmHg OR <90 mmHg and a decrease of >=20 mmHg from baseline
DBP: >105 mmHg and an increase of >=15 mmHg OR <50 mmHg and a decrease of >=15 mmHg from baseline
HR: >120 beats/min and an increase of >=15 beats/min OR <50 beats/min and a decrease of >=15 beats/min

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TABLE 14.3.24
Electrocardiogram – Worsening from Baseline to 1 Year Post Last Transplant

Number (%)[1] of Patients Who Worsened [2]

# of Tx Received	Post- Transplant Assessment Time		
	Total	Week 20	Week 52
Total (N=X)			
Worsened	X (XX)		
1 Tx (N=X)			
Worsened	X (XX)	X (XX)	X (XX)
2 Tx (N=X)			
Worsened	X (XX)	X (XX)	X (XX)
3 Tx (N=X)			
Worsened	X (XX)	X (XX)	X (XX)

[1] The denominator is the corresponding number of patients in the leading column.
[2] Worsening is defined as a change from a rating of normal/abnormal not clinically significant on both of the pre-transplant assessments to abnormal clinically significant at the time point.

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TABLE 14.3.25
Listing of Patients with Treatment-Emergent ECG Abnormalities

# of Tx Received	Subj. No.	Age (yrs.)	Timepoint	ECG Abnormality Description
1 Tx	XXX	XX	Week 20	XXXXXXXXXXXXXXXXXXX
			etc.	
2 Tx	XXX	XX	Week 52	XXXXXXXXXXXXXXXXXXX
			etc.	
Total number of patients with at least one event: N = XX				

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15. FIGURE SHELLS

FIGURE 14.2.1
Cumulative Percent of Patients Attaining HbA1c Reduction from Baseline at 1 Year after Last Transplant
(N=XX)

Y-axis: label = " Cumulative Percent”, numbers = 0.0% to 100.0%.

X-axis: label = "HbA1c Change from Baseline", numbers = -3.0 (left) to 0.0 (right) by -0.5.

Figure type: One cumulative percent by value graph for all ITT population will be shown on the graph.

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16. REFERENCES

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17. APPENDIX

17.1. Schedule of Assessments

17.1.1. Schedule of Evaluation for UIC Islet Transplant 1 Year Follow-Up

Visit	A[1]	A[2]	A[3A]	A[3B]	Tx	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Week post transplant	0					1	2	3	4-5	6-7	8-9	10-11	12	16	20	24	28	32	36	40	44	48	52
History, physical exam	X			X	X	3	3	2	2	2	2	2	X	X	X	X	X	X	X	X	X	X	X
Vital signs, weight	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Body mass index	X				X				X				X				X						X
BS-SM 7/day	X	X	X	X	X	X	X																
BS-SM 4/day								X	X	X	X	X	X										
BS-SM 2/day														X	X	X	X	X	X	X	X	X	X
CBC	X			X	X	3	3	2	2	2	2	2	X	X	X	X	X	X	X	X	X	X	X
CMP, direct bilirubin	X		X	X	X	3	3	2	2	2	2	2	X	X	X	X	X	X	X	X	X	X	X
Magnesium					X																		
Phosphorous					X																		
Amylase					X																		
Sirolimus trough level					X	3	3	2	2	2	2	2	X	X	X	X	X	X	X	X	X	X	X
Tacrolimus (FK506) trough level					X	3	3	2	2	2	2	2	X	X	X	X	X	X	X	X	X	X	X
Alternative immunosuppressant**					X	3	3	2	2	2	2	2	X	X	X	X	X	X	X	X	X	X	X
CMV q PCR							X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
EBV q PCR									X		X		X		X		X		X		X		X
Lipid panel	X			X					X		X		X					X				X	
Basal C-peptide	X					3	3	2	2	2	2	2	X	X	X	X	X	X	X	X	X	X	X
HbA1c	X		X	X		X				X			X			X			X			X	X
Fructosamine		X				X				X			X			X			X			X	X
Detailed lipid panel		X																					X
Inflammatory panel		X																					X
Antibodies	X												X			X						X	

Visit	A[1]	A[2]	A[3A]	A[3B]	Tx	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Week post transplant	0					1	2	3	4-5	6-7	8-9	10-11	12	16	20	24	28	32	36	40	44	48	52
IL2 receptor saturation									X		X		X	X	X	X	X	X	X	X	X	X	X
BNP		X				X									X								X
HCG pregnancy (serum)	X			X	X										X								X
Archive research serum		X				X									X								X
Blood type (ABO) (2)	X	X																					
Type, crossmatch					X*																		
PT, PTT, INR	X			X	X																		
QuantiFERON® TB Gold test	X																						
HIV antibody	X			X																			
RPR	X			X																			
Hepatitis panel	X			X																			
EBV panel		X		X*	X*																		
CMV IgG, IgM		X		X*	X*																		
VZVIgG		X		X*																			
PRA	X		X	X			X						X			X			X			X	
Autologous cross match	X																						
HLA		X																					
Donor crossmatch					X																		
Urinalysis		X	X		X								X			X							X
24-hour urine creatinine clearance	X																						
Urine culture, sensitivity					#																		
M/C ratio (random)		X	X	X							X				X					X			X
Sputum culture, sensitivity					#																		
Blood culture, sensitivity					#																		
Glucagon stimulation test	X									X						X							X
Mixed meal test		X														X							X
OGTT										X						X							X

Visit	A[1]	A[2]	A[3A]	A[3B]	Tx	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Week post transplant	0					1	2	3	4-5	6-7	8-9	10-11	12	16	20	24	28	32	36	40	44	48	52
IVGTT										X						X							X
ECG	X			X											X								X
Chest x-ray		X																					X
Abdominal ultrasound, Doppler		X				X																	
Cardiology Consult		X																					
CGMS		X																					X
Primary care	X																						X
Thyroid Ultrasound		X																					X

Visit A: screenings for inclusion

Visits 1 and 2 include 3 evaluations per week; Visit 3 includes 2 evaluations per week; Visits 4 to 7 include 2 evaluations per 2 week period (1 visit per week)

Vital signs: blood pressure, heart rate, respirations, temperature

CMP: comprehensive metabolic profile

CBC: complete blood count

BNP: B-type natriuretic peptide

Antibodies: anti-GAD 65. anti-IA2, anti-islet cell, anti-insulin

IL2 receptor saturation at investigator's discretion

PRA: panel reactive antibodies

Only if hospitalized within the past week

* Only if negative at Screening II

CGMS: continuous glucose monitoring system at Screening A[2], 1 year after first transplant, 1 year after final transplant

** Alternative immunosuppressant trough level only if applicable

17.1.2. Schedule of Evaluation for UIC Islet Transplant 5 Year Follow-Up

Visit	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Months	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60
History, physical exam, vitals	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
BMI	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ECG				X				X				X				X				X
CMP, direct bilirubin	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
CBC	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urinalysis		X		X		X		X		X		X		X		X		X		X
CMV q PCR	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
EBV q PCR		X		X		X		X		X		X		X		X		X		X
M/C ratio		X		X		X		X		X		X		X		X		X		X
IVGTT				X				X				X				X				X
Glucagon stimulation test				X				X				X				X				X
OGTT				X				X				X				X				X
Mixed meal test				X				X				X				X				X
HbA1c and fructosamine	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Basal C-peptide	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
BS-SM twice weekly fasting	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Detailed lipid panel				X				X				X				X				X
Inflammatory panel				X				X				X				X				X
Lipid panel		X				X				X				X				X		
BNP		X				X				X				X				X		
Archive serum		X		X		X		X		X		X		X		X		X		X
Abdominal ultrasound Doppler				X				X				X				X				X
Tacrolimus, Sirolimus	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PRA				X				X				X				X				X
Antibodies				X				X				X				X				X
IL2 receptor saturation	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Primary care screenings, vaccines				X				X				X				X				X
Thyroid Ultrasound				X				X				X				X				X

BMI: body mass index; Vitals: blood pressure, heart rate, temperature, weight; ECG: electrocardiogram; CMP: comprehensive metabolic profile;
CBC: complete blood count; M/C ratio: microalbumin to urine creatinine ratio (random); IVGTT: intravenous glucose tolerance test;
OGTT: oral glucose tolerance test; BNP: B-type natriuretic peptide; PRA: panel reactive antibodies;
Antibodies: anti GAD65, anti IA2, anti islet cell, anti insulin. IL2 receptor saturation at investigator's discretion.

17.1.3. Schedule of Evaluation for UIC Islet Transplant 10 Year Follow-Up

Visit	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Months	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60
History, physical exam, vitals	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
BMI	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
ECG				X				X				X				X				X
CMP, direct bilirubin	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
CBC	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urinalysis		X		X		X		X		X		X		X		X		X		X
CMV q PCR	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
EBV q PCR		X		X		X		X		X		X		X		X		X		X
M/C ratio		X		X		X		X		X		X		X		X		X		X
IVGTT				X				X				X				X				X
Glucagon stimulation test				X				X				X				X				X
OGTT				X				X				X				X				X
Mixed meal test				X				X				X				X				X
HbA1c and fructosamine	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Basal C-peptide	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
BS-SM twice weekly fasting	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Lipid panel		X		X		X		X		X		X		X		X		X		X
BNP		X				X				X				X				X		
Archive serum		X		X		X		X		X		X		X		X		X		X
Abdominal ultrasound Doppler				X				X				X				X				X
Tacrolimus, Sirolimus	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PRA				X				X				X				X				X
Antibodies				X				X				X				X				X
IL2 receptor saturation	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Primary care screenings, vaccines				X				X				X				X				X
Thyroid Ultrasound				X				X				X				X				X

BMI: body mass index; Vitals: blood pressure, heart rate, temperature, weight; ECG: electrocardiogram; CMP: comprehensive metabolic profile;
CBC: complete blood count; M/C ratio: microalbumin to urine creatinine ratio (random); IVGTT: intravenous glucose tolerance test;
OGTT: oral glucose tolerance test; BNP: B-type natriuretic peptide; PRA: panel reactive antibodies;
Antibodies: anti GAD65, anti IA2, anti islet cell, anti insulin. IL2 receptor saturation at investigator's discretion.