BMT CTN 1903 (AMC-109)
NCT#: 04975698
STATISTICAL ANALYSIS PLAN

Version 1.0

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VERSION HISTORY

Version numbers will always be whole numbers and any changes to the document require up-versioning.

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1.0	10MAY2022	Brent Logan	21JUN2022	Initial document

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LIST OF ABBREVIATIONS

Abbreviations	Description of abbreviations
AE	Adverse Event
BMT CTN	Blood and Marrow Transplant Clinical Trials Network
CBC	Complete Blood Count
CI	Confidence Interval
CMV	Cytomegalovirus
CTCAE	Common Terminology Criteria for Adverse Events
DSMB	Data and Safety Monitoring Board
GVHD	Graft-Versus-Host Disease
HCT	Hematopoietic Cell Transplantation
MOP	Manual of Procedures
NHLBI	National Heart, Lung, and Blood Institute
NIH	National Institutes of Health
TRM	Treatment-Related Mortality
OS	Overall Survival
DFS	Disease-Free Survival
SAE	Serious Adverse Events
SAP	Statistical Analysis Plan
SOC	System Organ Class

PROTOCOL SYNOPSIS

Administration of HIV-specific T cells to HIV+ Patients Receiving High Dose Chemotherapy Followed by Autologous Stem Cell Rescue - Auto-RESIST

Study Chairpersons: Dr. Richard Ambinder and Dr. Kieron Dunleavy

Protocol Officer: Dr. Steven Devine

Primary Objective: The primary objective is to determine 1.) the proportion of participants who can be treated with **HIV antigen-specific T-cells Targeting Conserved Epitopes** (HST-NEETs) within 1 week of autologous hematopoietic stem cell transplantation (ASCT) in a cooperative multi-institutional setting and 2.) the efficacy of HST-NEETs in reducing the HIV intact proviral reservoir at 6 months after ASCT.

Secondary Objectives: Participants will be assessed for the following endpoints:

1. Progression-free survival at 6 months and 1 year post-ASCT;
2. The incidence and severity of acute infusion related toxicities;
3. Impact of therapy on the HIV intact proviral reservoir at 1 year post-ASCT.

Exploratory Objectives: Participants will be assessed for the following:

1. CR and CR+PR rates at Day 100 post-ASCT;
2. Overall survival at 6 months and 1 year post-ASCT;
3. Time to hematopoietic recovery;
4. Incidence of infections at 1 year post-ASCT;
5. Non-relapse mortality at 6 months and 1 year post-ASCT;
6. Toxicities through 1 year post-ASCT;
7. Assessment of plasma DNA in blood (clonal Ig DNA) as a tumor marker at Day 100, 6 months and 1 year post-ASCT;
8. Impact of therapy on the HIV intact proviral reservoir at Day 100 post-ASCT;
9. HIV RNA in plasma at Day 100, 6 months, and 1 year post-ASCT;
10. Impact of therapy on the total proviral HIV DNA at Day 100, 6 months, and 1 year post-ASCT.
11. HST-NEETs persistence and expansion *in vivo.*

Study Design: This is a Phase II multi-center trial single arm trial of autologous transplantation (ASCT) followed by administration of HST-NEETs for treatment of HIV associated lymphoma.

Accrual Objective: The trial will enroll 12 participants.

Accrual Period: The estimated accrual period is four years.

Eligibility Criteria: Eligible participants are HIV positive and plan to be treated by high dose chemotherapy followed by an autologous stem cell transplant (ASCT). Participants are a minimum of 15 years of age with Karnofsky performance status greater than or equal to 70% that have primary refractory or recurrent diffuse large B-cell, immunoblastic, plasmablastic, high grade, Burkitt, primary effusion lymphoma, or classical Hodgkin lymphoma. Participants must have received 2 or 3 prior treatment regimens, including an induction chemotherapy and 1 or 2 salvage regimens. Monoclonal antibody therapy and local radiation will not be counted as prior therapies. Participants must have chemo sensitive disease as demonstrated by complete or partial response to induction or most recent salvage chemotherapy. Participants cannot have had prior autologous, allogeneic HCT, or CART-cell therapy. Participants must initiate conditioning therapy within 3 months of stem cell mobilization or bone marrow harvest. Blood cell mobilization or bone marrow harvest will be carried out per institutional guidelines. Participants may not have HIV refractory to pharmacologic therapy. Patients must not have an uncontrolled infection. Participants must not have received previous cellular therapy.

Treatment Description: Participants will have 100-120 mL of peripheral blood drawn and sent to Children's National Hospital for manufacturing of HST-NEETs 6 weeks prior to ASCT. Participants will receive Carmustine (BCNU) 300 mg/m^2 Day -6, Etoposide (VP-16) 100 mg/m^2 BID Days -5 to -2, Cytarabine (Ara-C) 100 mg/m^2 BID Days -5 to -2, and Melphalan 140 mg/m^2 Day -1 followed by ASCT on Day 0 and will receive one dose of HST-NEETs (2 x10^7 cells) between Days +3 to +7.

Study Duration: Participants will be followed on study for one year post-ASCT.

Interim Analysis: No interim analyses for efficacy or futility are planned.

Stopping Guidelines: Two key safety endpoints (Day 30 treatment related mortality and Grade 3 or higher infusion-related toxicities lasting greater than 24 hours) will be monitored. Any treatment related mortality within 30 days of transplantation will trigger a safety review prior to treatment of subsequent study participants. Three or more infusion events for

will trigger consultation with the Data and Safety Monitoring Board (DSMB). Monitoring Board (DSMB). In the event of graft failure, the protocol will be temporarily halted and reviewed by the NHLBI DSMB. Graft failure will be defined as a failure to achieve three consecutive labs of greater than or equal to 500 neutrophils/μL by Day 100**.**

Correlative Studies: Blood will be collected for monitoring the persistence/expansion of the infused T cells by ELIspot, multimer analysis, intracellular cytokine staining and TCR sequencing. We will also assess intact proviral DNA in peripheral blood mononuclear cells as a measure of the HIV reservoir, and clonal immunoglobulin DNA in plasma as an indicator of minimal residual disease/early relapse.

1 INTRODUCTION

This Statistical Analysis Plan (SAP) elaborates upon the analysis strategy introduced in the study protocol and includes detailed procedures for completing the statistical analysis of study endpoints. The content herein is based on BMT CTN Protocol 1903 version 1.0. If required, revisions to the approved SAP may be made prior to the database hard lock. Revisions will be version controlled.

Any changes to the analyses described in the SAP will be detailed and justified in the final analysis report.

2 STUDY SCHEMA AND ASSESSMENT SCHEDULE

2.1 STUDY SCHEMA

Table 2.1 Study Schema

6 Weeks Pre-ASCT	• 100-120mL Blood Drawn for HST-NEETs Manufacturing[1] • 70 mL Blood Drawn for Intact Proviral DNA Assay (IPDA)[2] • 5 mL Blood Drawn for Single Copy HIV-1 RNA Assay[3] • Disease Assessment
Day -6 to -1	BEAM Conditioning Regimen
Day 0	Autologous Stem Cell Transplant
Day +3 to Day +7	HST-NEETs (2x 10^7 cells/m^2) Administered[4]
Day 100 Post-ASCT	• 70 mL Blood Drawn for IPDA** • 5 mL Blood Drawn for Single Copy HIV-1 RNA Assay[3] • Disease Assessment
6 Months Post-ASCT	• 70 mL Blood Drawn for IPDA** • 5 mL Blood Drawn for Single Copy HIV-1 RNA Assay[3] • Disease Assessment
12 Months Post-ASCT	• 70 mL Blood Drawn for IPDA** • 5 mL Blood Drawn for Single Copy HIV-1 RNA Assay[3] • Disease Assessment

[1]Sample should be shipped at ambient temperature to Children's National Hospital. The standard manufacturing process takes 3 to 6 weeks.

[2] Sample should be shipped to Children's National Hospital.

[3] Sample should be shipped to University of Pittsburgh School of Medicine.

[4]HST-NEETs will be shipped to site. Study staff will thaw and administer cells. If the ideal window of 3-7 days post-transplant is missed, the cells may still be administered up to day 30 and the participant will continue study follow-up.

2.2 SCHEDULE OF ASSESSMENTS

Table 2.2: Follow-Up Schedule

Study Visit	Target Day (Day 0 is ASCT)
Baseline	6 weeks prior to transplant
Pre-Conditioning	Within 1 week prior to conditioning*
Transplant	Day 0
HST-NEETs Infusion	Day +3 to +7
Week 2	Day 14 **± 3** days
Week 3	Day 21 **± 3** days
Week 4	Day 28 **± 3** days
Week 5	Day 35 **± 3** days
Week 8 **	Day 56 **± 3** days**
Day 100	Day 100 **± 14** days
Month 6	Day 180 **± 28** days
Month 12	Day 365 **± 28** days

*Can occur locally, does not require a transplant center visit.

**This study visit is only required for participants receiving HST-NEETs outside of the +3 to+7 day window.

Table 2.3: Study Evaluations

					Post-ASCT								
Study Assessments Testing	**Pre-Enrollment**	**6 weeks before conditioning**	**Pre-Conditioning**	**Day 0 - ASCT**	**Day 3 to 7**	**Day 14**	**Day 21**	**Day 28**	**Day 35**	**Day 56[10]**	**Day 100**	**Day 180**	**Day 365**
History and Physical Exam[4]	X					X	X	X	X	X	X	X	X
Karnofsky Performance Score	X		X										
CBC[6] and Chemistries[7]	X	X	X		X[7]	X[7]	X[7]	X[7]			X	X	X
Hepatitis Panel (HBsAb HBsAg, HBcAb, HCV Ab) [1]	X												
EKG	X												
CT or PET-CT	X		X[5]								X	X	X
DLCO, FEV1, FVC	X												
Creatinine Clearance[2]	X		X										
Bone marrow biopsy for pathology[13]	X												
HIV RNA, CD4 Count	X										X	X	X
Serology Testing [3]	X												
Ejection Fraction	X												
Pregnancy Test[11]	X												

Study Assessments Testing	Pre-Enrollment	6 weeks before conditioning	Pre-Conditioning		Day 3 to 7	Day 14	Day 21	Day 28	Day 35	Day 56[10]	Day 100	Day 180	Day 365
Diagnostic Lymphoma pathology[9]	X												
Plasma DNA Tumor Monitoring (Ig)			X								X	X	X
Blood Collection for HST-NEETs Manufacturing[8]		X											
IPDA[6,14] & HST-NEETs persistence and expansion		X									X	X	X
Single-Copy HIV-1 RNA Assay[12]		X									X	X	X
HST-NEETs Administration					X								
Toxicity Assessment								X	X	X	X	X	X
HIV Titer by standard assay											X	X	X

Footnotes:

[1]If the Hep B Core AB is positive then HepB DNA PCR; if Hep C serology is positive, HCV PCR, or NAT Testing, per institutional standards.

[2]Calculated creatinine clearance is permitted per institutional guidelines.

[3]Serology testing will include CMV IgG, HSV-1 and HSV-2 IgG, RPR or VDRL, toxoplasma IgG, VZV IgG, and HTLV-1 antibody, performed per institutional standards.

[4]To include:

a. Lumbar puncture(s) for determination of presence of CNS disease for non-Hodgkin's lymphoma participants only.

b. Duration of AIDS diagnosis, history of prior opportunistic illnesses.

c. Presence or absence of “B”- symptoms (unexplained fevers, night sweats, involuntary weight loss greater than 10% normal body weight).

d. Medication list to include all antiviral, antibiotics and opportunistic prophylaxis.

This includes Height and Weight, body surface area, neurologic examination, careful measurement of all palpable peripheral lymph nodes and measurement of other sites of disease present on physical.

[5]CT scans of neck, chest, abdomen and pelvis. Neck CT only required if previous site of disease.

[6]It is critical that a clinical CBC be collected at the same time as IPDA research sample, as indicated in the table above.

[7]CBC with differential, Platelet Count, Creatinine, Bilirubin, Alkaline Phosphatase, AST, ALT, LDH. To be performed at least twice weekly from Day 0 until ANC greater than 500/mm3 for 3 days after nadir reached. Thereafter, once weekly until Day 28 (or 4 weeks), then at Day 100, 180 and 365 post-ASCT.

[8]100-120 mL whole blood shipped to CNH at ambient temperature.

[9]Diagnostic lymphoma pathology local report should be available prior to enrollment. Optional pathology specimens (paraffin block(s) or 10 unstained slides cut at 5 um thickness and placed on charged glass slide) collected pre-enrollment should be sent to the Ambinder Laboratory within 3 weeks of transplant.

[10] This study visit is only required for participants receiving HST-NEETs outside of the Day +3 to Day +7 window.

[11]Pregnancy test is required for females of child-bearing potential and may be performed per institutional practices.

[12] Blood for this plasma assay must be centrifuged and plasma frozen within 3 hours of blood draw.

[13] Bone marrow biopsies for pathology will be collected per institutional standards.

[14]Assessment of the Total Proviral HIV DNA will be included in the IPDA sample. A separate blood draw is not required.

3 STUDY OBJECTIVES AND DESIGN

3.1 STUDY OBJECTIVE

Eligible participants will have 100-120 mL of peripheral blood collected and shipped to Children's National Hospital at ambient temperature. The peripheral blood will be used to manufacture the HST-NEET product. The autologous peripheral blood stem cell graft suitable for rescue following conditioning will be obtained either before or after the collection of blood to generate HST-NEETs. Pre-transplant conditioning will consist of BEAM; BCNU 300 mg/m2 on Day -6, Etoposide 100 mg/m2 BID and Ara-C 100 mg/m2 BID on Days -5, -4, -3 and -2 and Melphalan 140 mg/m2 on Day -1. ASCT on Day 0. If the mobilized graft contains greater than 5.0 x 106 CD34+ cells per kg, any additional cells should be cryopreserved as a "back-up" graft in the event of graft failure related to the HST-NEETs. Participants will receive one dose (2 x 107 cells/m2) of HST-NEETs between Days +3 to +7 based on the clinical condition of the participant (as outlined in Section 2.6). If this window is missed, the HST-NEETs may be administered up to Day +30 post-ASCT. Participants will be followed for at least one year after ASCT.

3.2 HYPOTHESIS AND SPECIFIC OBJECTIVES

3.2.1 PRIMARY HYPOTHESIS

Following high dose chemotherapy and ASCT for participants with HIV-associated lymphoma, infusion of T cells targeting multiple HIV antigens (HST-NEETs) within 1 week will be feasible and these cells will persist and deplete the intact HIV proviral reservoir.

3.2.2 PRIMARY OBJECITVE

The primary objective is to determine both the proportion of participants receiving ASCT who were able to be treated with HST-NEETs within 1 week of ASCT in a cooperative multi-institutional setting and the efficacy of infused HST-NEETs in reducing the HIV intact proviral reservoir at 6 months after ASCT.

3.2.3 SECONDARY OBJECTIVE

Secondary objectives of the study are to assess the following:

1. Progression-free survival at 6 months and 1 year post-ASCT;
2. The incidence and severity of acute infusion-related toxicities;
3. The impact of therapy on the HIV intact proviral reservoir at 1 year post-ASCT.

3.2.4 EXPLORATORY OBJECTIVES

The exploratory objectives are to assess:

1. CR and CR+PR rates at Day 100 post-ASCT;
2. Overall survival at 6 months and 1 year post-ASCT;
3. Time to hematopoietic recovery;
4. Incidence of infections through 1 year post-ASCT;
5. Non-relapse mortality at 6 months and 1 year post-ASCT;
6. Toxicities through 1 year post-ASCT;

7. Assessment of plasma DNA in blood (clonal Ig DNA) as a tumor marker at Day 100, 6 months and 1 year post-ASCT;
8. Impact of therapy on the HIV intact proviral reservoir at Day 100 post-ASCT;
9. HIV RNA in plasma at Day 100, 6 months, and 1 year post-ASCT;
10. Impact of therapy on the total proviral HIV DNA at Day 100, 6 months, and 1 year post-ASCT;
11. HST-NEETs persistence and expansion in vivo.

4 SAMPLE SIZE AND POWER CONSIDERATIONS

4.1 SAMPLE SIZE CALCULATIONS

Since this is a feasibility pilot study, the sample size of 12 participants is based on the anticipated enrollment over a 4 year accrual period. If a participant is lost to follow-up or withdraws before their first blood draw, the participant will be replaced. Based on enrolling 12 participants, we provide the possible confidence intervals for the HST-NEET infusion proportion (Table 4.1) and the statistical power (Table 4.2) for the IPDA outcome.

HST-NEET infusion proportion:

Table 4.1 presents the exact 90% confidence intervals corresponding to zero to 12 infusions of HST-NEETs.

Table 4.1 Exact 90% confidence intervals for the possible HST-NEET infusion proportions in the 12 participants

Number of HST-NEET Infusions	Infusion Proportion (%)	Exact (Clopper-Pearson) 90% Confidence Interval	Number of HST-NEET Infusions	Infusion Proportion (%)	Exact (Clopper-Pearson) 90% Confidence Interval
0	0.00	(0.00, 22.09)	7	58.33	(31.52, 81.90)
1	8.33	(0.43, 33.87)	8	66.67	(39.09, 87.71)
2	16.67	(3.05, 43.81)	9	75.00	(47.27, 92.81)
3	25.00	(7.19, 52.73)	10	83.33	(56.19, 96.95)
4	33.33	(12.29, 60.91)	11	91.67	(66.13, 99.57)
5	41.67	(18.10, 68.48)	12	100	(78.91, 100)
6	50.00	(24.53, 75.47)			

Intact Provirus reduction in participants who were transfused:

Pilot estimates for the baseline distribution of the natural logarithm of IPDA indicate a standard deviation of 1.46. We assume the correlation between baseline and post-intervention log(IPDA) measurements is 0.5. Using a paired t-test with a two-sided significance level of 10%, we estimate that 12 infused participants will have 84.8% statistical power to detect a mean difference of -1.2040 between the baseline and post-intervention log(IPDA). The mean baseline and post-intervention log(IPDA) difference of -1.2040 corresponds to a reduction of 70% (100%[1 - exp(-1.2040)]) in IPDA on the original scale. Participants who were not infused will not be included in this analysis.

Table 4.2 Power Analysis to Detect the Reduction of Intact Proviruses on the Original Scale

		No. of Infused Participants			
	Mean Percent Reduction of IPDA	6	8	10	12
Statistical Power (%)	75%	63.9	77.9	86.9	92.4
	70%	53.8	67.5	77.6	84.8
	60%	37.8	48.3	57.5	65.3
	40%	19.2	23.2	27.1	30.9
	20%	11.8	12.6	13.4	14.2

5 ANALYSIS POPULATIONS

5.1 FEASIBILITY POPULATIONS

All participants who have blood drawn for HST-NEETs manufacturing.

5.2 TRANSPLANT POPULATION

All participants enrolled on the study who proceed to transplant.

5.3 INFUSION POPULATION

All participants who are enrolled on the study that received both a transplant and HST-NEETs infusion anytime up to 30 days.

6 STUDY OUTCOMES

6.1 DEFINITION OF DISEASE STATUS

Tests used for evaluation of disease status include physical examination, laboratory testing, bone marrow biopsy and aspirate, PET scans, and CT scans of neck, chest, abdomen and pelvis as indicated.

Imaging will be assessed at baseline prior to transplant and prospectively. The Lugano Classification will be used to assess response after baseline in comparison to the baseline imaging. As outlined in Appendix B of the protocol, lymphoma response is defined as any participant who does not progress on this study, including participants with active disease who achieve Complete Metabolic Response (CMR)/Complete Radiologic Response (CR), Partial Metabolic Response (PMR)/ Partial Remission (PR), or No Metabolic Response(NMR)/Stable Disease (SD) by PET/CT. Because the natural history of these high risk relapsed and refractory participants is progression (and often mortality), any response or even stable disease is an improvement over expected outcomes.

CT responses will be based on anatomical measurements of target/evaluable/new lesions.

The possible response outcomes are complete radiologic response (CR), partial remission (PR), stable disease (SD) or progressive disease (PD) as defined in Appendix B of the protocol.

6.2 PRIMARY ENDPOINTS

6.2.1 FEASIBILITY

Feasibility is defined as a participant receiving HST-NEETs within 1 week post-ASCT. All eligible and enrolled participants will be considered part of the feasibility assessment.

6.2.2 EFFICACY

Efficacy will be measured by the reduction in intact proviral reservoir. This will be evaluated using the change in intact proviral DNA assay (IPDA) at enrollment through 6 months post-ASCT among participants.

6.3 SECONDARY ENDPOINT

6.3.1 PROGRESSION-FREE SURVIVAL

Participants are considered a failure for this endpoint if they die or if they relapse/progress or receive anti-lymphoma therapy, other than post-transplant consolidative localized radiation (maximum 3 sites) to sites of prior bulk disease pre-transplant (greater than 3cm). The time to this event is the time from transplant until death, relapse/progression, receipt of anti-lymphoma therapy, or last follow up, whichever comes first. This will be assessed at 6 months and 1 year post-ASCT.

6.3.2 ACUTE INFUSION RELATED TOXICITY

Acute infusion related toxicities are defined as toxicities related to the infusion of HST-NEETs that occur within 24 hours of the infusion. Toxicities will be graded per CTCAE criteria v5.0.

6.3.3 INTACT PROVIRAL RESERVOIR

Impact on intact proviral reservoir will be assessed using the IPDA at 4-8 weeks prior to transplant and 12 months following ASCT.

6.4 EXPLORATORY OBJECTIVES

6.4.1 CR AND CR+PR RATE AT DAY 100 POST-ASCT

CR or PR will be assessed according to the LYRIC criteria at Day 100 post-ASCT (see Appendix B of the protocol).

6.4.2 OVERALL SURVIVAL

Overall survival is defined as death from any cause within 6 months and within 1 year post-ASCT. Surviving participants will be censored at the date of last follow-up. Surviving participants will be censored at 1-year if the last follow-up is beyond one year post-ASCT.

6.4.3 ACUTE GVHD RESPONSE TO AAT/PTM

Time to neutrophil recovery will be the first of three consecutive labs of greater than or equal to 500 neutrophils/μL following the expected nadir. Time to platelet engraftment will be the date platelet count is greater than or equal to 20,000/μL for the first of three consecutive labs with no platelet transfusions 7 days prior.

6.4.4 INCIDENCE OF INFECTIONS

The incidence of viral, fungal and bacterial infections will be tabulated. All Grade 2 and Grade 3 infections will be reported according to the BMT CTN Technical MOP from Day 0 up to 1 year post-transplant. Infections of interest will be captured and described. The incidence rate of infections is defined by the number of infections divided by the total person-time accumulated over the duration of the study.

6.4.5 NON-RELAPSE MORTALITY

Non-Relapse Mortality (NRM) is defined as death occurring in a participant without relapse progression and will be measured at 6 months and at 1 year.

6.4.6 TOXICITIES

Toxicities related to the BEAM conditioning regimen and HST-NEETs infusion beyond the 24 hour acute toxicity monitoring period will be defined by using the version 5.0 CTCAE criteria. All grades of toxicity related to HST-NEETs will be collected. Only grade 3 or higher conditioning regimen related toxicities will be collected.

6.4.7 IG DNA IN BLOOD

Blood specimens will be collected prior to the initiation of conditioning, and at Days 100, 6 months and 1 year post-ASCT. The presence of clonal Ig DNA in plasma will be assessed at each of these time points.

6.4.8 INTACT PROVIRAL RESERVOIR AT DAY 100

Impact on intact proviral reservoir assessed using the IPDA Day 100 post-ASCT as compared to baseline at 4-8 weeks prior to transplant.

6.4.9 HIV RNA IN BLOOD

HIV RNA in plasma will be measured by a sensitive investigational single copy assay (SCA, detection limit 0.38 copy/ml). Blood specimens will be collected, and plasma HIV RNA measured, at study visits corresponding to those associated with IPDA testing: 4-8 weeks prior to transplant, and at Days 100, 6 months and 1 year post-ASCT.

6.4.10 TOTAL PROVIRAL HIV DNA

This assay will be measured at study visits corresponding to those associated with IPDA testing: 4-8 weeks prior to transplant, and at Days 100, 6 months and 1 year post-ASCT. This assay will provide information about the proviral reservoir in patients where the IPDA fails due to sequence variation.

6.4.11 HST-NEETS PERSISTENCE AND EXPANSION IN VIVO

Persistence of HST-NEETs will be measured by frequency of HIV-1 antigen-specific (gag, pol, nef) CD8+ T-cells by ELIspot at baseline and post-infusion at timepoints at Days 100, 6 months, and 1 year post transplant. Change in T cell responses from baseline to post-infusion, measured by frequency of cells secreting IFN-γ by multimer analysis and/or intracellular cytokine staining and/or ELIspot and/or TCR sequencing will be done depending on PBMC cell numbers available and reagent availability.

6.5 ADVERSE EVENT REPORTING REQUIREMENTS

6.5.1 DEFINITIONS

Safety outcomes of interest include adverse events (AEs), serious adverse events (SAEs), and deaths. SAEs are defined as AEs that resulted in one of the following outcomes: death, a threat to life, requiring or prolonging inpatient hospitalization, causing persistent or significant disability, causing a congenital anomaly or birth defect, or requiring intervention to prevent any of the aforementioned outcomes.

Adverse Event: An Adverse Event (AE) is defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease that is temporally associated with the use of a medical treatment or procedure regardless of whether it is considered related to the medical treatment or procedure.

Expectedness: An adverse event can be Expected or Unexpected

- **Expected adverse events** are those that have been previously identified as resulting from administration of the agent. For the purposes of this study, an adverse event is considered expected when it appears in the current adverse event list, the Investigator's Brochure, the package insert or is included in the informed consent document as a potential risk.

- **Unexpected adverse events** are those that vary in nature, intensity or frequency from information in the current adverse event list, the Investigator's Brochure, the package insert, or when it is not included in the informed consent document as a potential risk.

Serious Adverse Event: A serious adverse event (SAE), as defined by per 21 CFR 312.32, is any adverse event that results in one of the following outcomes, regardless of causality and expectedness:

- **Results in death**

- **Is life-threatening**. Life-threatening means that the person was at immediate risk of death from the reaction as it occurred, i.e., it does not include a reaction which hypothetically might have caused death had it occurred in a more severe form.

- **Requires or prolongs inpatient hospitalization** (i.e., the event required at least a 24-hour hospitalization or prolonged a hospitalization beyond the expected length of stay). Hospitalization admissions and/or surgical operations scheduled to occur during the study period but planned prior to study entry are not considered SAEs if the illness or disease existed before the person was enrolled in the trial, provided that it did not deteriorate in an unexpected manner during the trial (e.g., surgery performed earlier than planned).

- **Results in persistent or significant disability/incapacity**. Disability is defined as a substantial disruption of a person's ability to conduct normal life functions.

- **Is a congenital anomaly or birth defect;** or

- **Is an important medical event** when, based upon appropriate medical judgment, it may jeopardize the participant and require medical or surgical intervention to prevent one of the outcomes listed above. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home; blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

Medical and scientific judgment should be exercised in deciding whether expected reporting is also appropriate in situations other than those listed above. For example, important medical events may not be immediately life threatening or result in death or hospitalization but may jeopardize the patient or may require intervention to prevent one of the outcomes listed in the definition above (e.g., suspected transmission of an infectious agent by a medicinal product is considered a Serious Adverse Event). Any event is considered a Serious Adverse Event if it is associated with clinical signs or symptoms judged by the investigator to have a significant clinical impact.

6.5.2 CLASSIFICATION OF ADVERSE EVENTS BY SEVERITY

The severity refers to the intensity of the reported event. The Investigator must categorize the severity of each SAE according to the National Cancer Institute (NCI) CTCAE Version 5.0. CTCAE guidelines can be referenced at the following website: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf. For any term that is not specifically listed in the CTCAE scale, intensity will be assigned a grade of one through five using the following CTCAE guidelines:

- Grade 1: Mild; asymptomatic or mild symptoms, clinical or diagnostic observations only; intervention not indicated
- Grade 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living
- Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living

- Grade 4: Life-threatening consequences; urgent intervention indicated
- Grade 5: Death related to AE.

6.5.3 CLASSIFICATION OF ADVERSE EVENTS BY RELATIONSHIP TO INVESTIGATIONAL PRODUCT

The relationship of each reported event to the study therapy will be assessed by the Investigator; after careful consideration of all relevant factors such as (but not limited to) the underlying study indication, coexisting disease, concomitant medication, relevant history, pattern of the SAE, temporal relationship to any study therapy interventions and dechallenge or rechallenge according to the following guidelines:

- Possibly, Probably, or Definitely Related: there is a reasonable possibility that the study therapy caused the event. A relationship of possibly, probably or definitely related to the investigational product is considered related for the purposes of regulatory authority reporting.
- Unlikely, or Not Related: There is no reasonable possibility that the investigational product caused the event. An unlikely or not related relationship to the investigational product is considered not related for the purposes of regulatory authority reporting.

6.5.4 BMT CTN ADVERSE EVENT REPORTING GUIDELINES

Adverse event reporting will be consistent with BMT CTN procedures (BMT CTN Administrative Manual of Procedures, Chapter 6). It is BMT CTN policy that AEs must be reported even if the investigator is unsure whether a relationship exists between the adverse event and the use of study treatment.

Unexpected, serious adverse events (SAEs) will be reported through an expedited AE reporting system via Advantage eClinical. Unexpected, life-threatening and fatal SAEs must be reported within 24 hours of knowledge of the event. All other unexpected SAEs must be reported within three business days of knowledge of the event. Events entered in Advantage eClinical will be reported using NCI's Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0.

Expected AEs will be reported using NCI's Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 at regular intervals as defined on the Form Submission Schedule, including calendar-driven case report forms (e.g., Toxicity and GVHD) or event-driven case report forms (e.g., Relapse/Progression, Infection, and Death). Any expected life-threatening SAE not collected on another study form must be reported through the expedited AE reporting system via Advantage eClinical.

The Data and Safety Monitoring Board will receive summary reports of all unexpected SAEs on a semi-annual basis.

6.5.5 ADVERSE EVENTS OF SPECIAL INTEREST

Adverse events of special interest (AESIs) are required to be reported by the investigator within 24 hours of notification of the event.

Adverse events of special interest for this study are as follows:

- Infusion related reaction including allergic reactions and anaphylaxis occurring during or post HST-NEETs infusion.

6.5.6 PROCEDURE IN CASE OF PREGNANCY

If a female participant becomes pregnant during the study dosing period or within 90 days from the HST-NEETs infusion, the investigator should report within 24 hours through an expedited AE reporting system via Advantage eClinical®. The expected date of delivery or expected date of the end of the pregnancy, last menstruation, estimated conception date, pregnancy result, neonatal data and other related information will be requested.

The investigator will follow the medical status of the mother, as well as the fetus, as if the pregnancy is an SAE and will report the outcome. Additional information regarding the outcome of a pregnancy (which is categorized as an SAE) is mentioned below.

“Spontaneous abortion” includes miscarriage, abortion and missed abortion

Death of an infant within 1 month after birth should be reported as an SAE regardless of its relationship with the study drug

If an infant dies more than 1 month after the birth, it should be reported if a relationship between the death and intrauterine exposure to the study drug is judged as “possible” by the investigator

In the case of a delivery of a living newborn, the “normality” of the infant is evaluated at the birth

Unless a congenital anomaly is identified prior to spontaneous abortion or miscarriage, the embryo or fetus should be assessed for congenital defects by visual examination

Information will be collected at the time of delivery/birth and 6 months and 12 months after birth. If the participant completes the final study follow-up prior to 12 months after birth, a final status should be reported following the final study visit.

7 STATISTICAL METHODOLOGY

7.1 GENERAL GUIDELINES

Counts and percentages will be used to describe categorical variables, while the number of subjects (N), median, mean, standard deviation, and range will be used to summarize continuous variables.

All statistical analyses including primary and secondary outcomes will use the infusion or transplant population as appropriate. All hypothesis tests will be two-sided with a type I error rate of 10% unless stated otherwise.

All data processing, summarization, and analyses will be performed using SAS Version 9.4 or higher, or R version 4.0 or higher. Specifications for the table, figure, and data listing formats can be found in the templates created for this SAP in Appendix B.

7.2 DEMOGRAPHICS AND DISPOSITION

7.2.1 DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Demographic and baseline characteristics will be summarized using descriptive statistics Demographics and baseline characteristics will be summarized for all participants using descriptive statistics. Characteristics to be examined are: age, gender, race/ethnicity, performance status, disease stage, genotype, HIV viral load, CD4+ counts, and number of prior chemotherapy regimens as treatment of primary malignancy and number of prior HIV regimens.

7.2.2 PARTICIPANT DISPOSITION

The number and percentage of patients experiencing the following on study:

- Enrollment (100%)
- Transplanted
- Number and percent of patients died on study
- Number and percent withdrawn from study
- Number and percent loss to follow up
- Number and percent who are alive up to 12 months post-transplant and completed planned study follow-up

In addition, the reasons for patients withdrawing from the study will be tabulated.

7.2.3 PROTOCOL DEVIATIONS

The number and percentage of patients in the study with any protocol deviation will be tabulated by the deviation category. A listing of all protocol deviations will be provided.

7.3 STATISTICAL ANALYSIS

7.3.1 PRIMARY ENDPOINT

7.3.1.1 Primary Analysis

HST-NEET infusion proportion:

We will report the proportion of HST-NEET infusion. Additionally, a 90% Clopper-Pearson confidence interval approach for that rate will be computed. This analysis will include all 12 participants.

Intact provirus reduction in participants who were transfused:

The logarithm of intact proviral DNA assay (IPDA) will be collected within 1 week prior to the initiation of conditioning, and at Day 100, 6 months, and 1 year post-transplant. The presence IPDA will be assessed at each time point and will be summarized using descriptive statistics with plots of the outcome vs time (in days). We will model the IPDA

using a mixed model with time as a covariate. We will consider using a nonparametric counterpart to the mixed model if our outcome is not normal.

7.3.2 SECONDARY ENDPOINTS

7.3.2.1 Progression-Free Survival (PFS)

The event is relapse/progression or death or receive anti-lymphoma therapy, other than post-transplant consolidative localized radiation (maximum 3 sites) to sites of prior bulk disease pre-transplant (greater than 3cm). The time to this event is the time from transplant until death, relapse/progression, receipt of anti-lymphoma therapy, or last follow up, whichever comes first. Progression-free survival (PFS) will be estimated using the Kaplan-Meier product limit estimator and Kaplan-Meier plots with 90% confidence intervals (Fay, Brittain, and Proschan 2013) along with corresponding life-table survival estimates. The PFS probability and 90% confidence interval will be calculated at 6 months and one year post-transplant. Actual data points will be listed in tabular form. This analysis will be done on the transplant population.

7.3.2.2 Acute Infusion Related Toxicities

Toxicities that occur over the course of time will be tabulated using the version 5.0 CTCAE criteria. The clinical safety monitoring period for HST-NEETs will be 28 days following infusion. The proportion of participants developing toxicity will be described by type of toxicity, grade, and time period. The 90% Clopper-Pearson confidence interval will be used. This analysis will be done on the infusion population.

7.3.3 ANALYSIS OF EXPLORATORY ENDPOINTS

7.3.3.1 CR and CR+PR Rat at Day 100 after ASCT

The frequencies and proportions of participants who have a CR (or PR) will be described with 90% Clopper-Pearson confidence intervals at Day 100 after ASCT. This analysis will be done on the transplant population.

7.3.3.2 Overall Survival

The event is death by any cause. The time to this event is from transplant. Participants are censored at the time of last follow-up. We will estimate the Kaplan Meier curve at 6-month and 1-year overall survival (OS) probability based on the Kaplan-Meier product limit estimator with corresponding 90% confidence intervals (Fay, Brittain, and Proschan 2013). Actual data points will be listed in tabular form. This analysis will be done on the transplant population.

7.3.3.3 Time to Hematopoietic Recovery

Hematologic function will be defined by ANC greater than 500, Hemoglobin greater than 10g/dL without transfusion support, and platelets greater than 100,000 and measured at Day 100 and 1 year. Use of growth factors will be noted. Time to neutrophil recovery and platelet engraftment from transplant will be estimated using cumulative incidence function

with corresponding 95% confidence interval with death prior to engraftment as the competing risk. Estimates of the cumulative incidence function will be summarized. Actual data points will be listed in tabular form. This analysis will be done on the transplant population.

7.3.3.4 Incidence of Infections

The incidence rate of infections is defined by the number of infections divided by the total person-time accumulated over the duration of the study. All Grade 2 and higher infections will be reported according to the BMT CTN Technical MOP from Day 0 up to 1 year post-transplant. The incidence rate of infections will be computed based on the Poisson distribution. This analysis will be done on the transplant population.

7.3.3.5 Non-Relapse Mortality

Non-Relapse Mortality (NRM) is defined as death occurring in a participant without relapse or progression. Progression is a competing risk event. A cumulative incidence curve will be computed along with a 90% confidence interval at 6 months and at 1 year post-transplant. Estimates of the cumulative incidence function will be summarized. Actual data points will be listed in tabular form. This analysis will be done on the transplant population.

7.3.3.6 Toxicity

Toxicities related to the BEAM conditioning regimen and HST-NEETs infusion beyond the 24 hour acute toxicity monitoring period will be defined by using the version 5.0 CTCAE criteria. The data will be collected up to day 365 starting at Day 28. All grade of toxicity related to HST-NEETs will be collected. Only grade 3 or higher conditioning regimen related toxicities will be collected. The frequencies and proportions of participants with toxicities will be described with 90% Clopper-Pearson confidence intervals. This analysis will be done on the infusion population.

7.3.3.7 IG DNA in Blood

Blood specimens will be collected within 1 week prior to the initiation of conditioning, and at Day 100, 6 months, and 1 year post-transplant. The presence of clonal Ig DNA in plasma will be assessed at each time point and will be summarized using descriptive statistics with plots of the outcome vs time (in days). We will model the Ig DNA in blood using a mixed model with time as a covariate. We will consider using a nonparametric counterpart to the mixed model if our outcome is not normal. This analysis will be done on the infusion population.

7.3.3.8 HIV RNA in Blood

HIV RNA will be collected within 1 week prior to the initiation of conditioning, and at Day 100, 6 months, and 1 year post-transplant. The presence of HIV RNA will be assessed at each time point and will be summarized using descriptive statistics with plots of the outcome vs time (in days). We will model the HIV RNA in blood using a mixed model with time as a covariate. We will consider using a nonparametric counterpart to the mixed model if our outcome is not normal. This analysis will be done on the infusion population.

7.3.3.9 Total Proviral HIV DNA (TPDNA)

Impact on total proviral HIV DNA will be assessed using the TPDNA at 6 months following autologous HCT. The difference in log(TPDNA) measured pre-transplant and at 6 months post-transplant will be compared using a paired t-test. The difference in means will be computed with 90% confidence interval based on the t-distribution along the corresponding p-value. This analysis will be done on the infusion population.

7.3.3.10 Persistence and Expansion of HST-NEETs in VIVO

Persistence and expansion of HST-NEETs will be measured within 1 week prior to the initiation of conditioning, and at Day 100, 6 months, and 1 year post-transplant. The persistence and expansion of HST-NEETs will be assessed at each time point and will be summarized using descriptive statistics with plots of the outcome vs time (in days). We will model the outcome using a mixed model with time as a covariate. We will consider using a nonparametric counterpart to the mixed model if our outcome is not normal. This analysis will be done on the infusion population.

7.3.3.11 Relapse/Progression of Primary Disease

The time from randomization until relapse/progression of the primary disease will be described in the ITT population graphically for each treatment arm using the Aalen-Johansen estimator, with relapse/progression of the primary disease treated as a competing risk. Estimates of the cumulative incidence of relapse/progression will be provided at 6 and 12 months post-randomization along with 95% CIs computed using the complementary log-log transformation. Gray's test will be used to compare the cumulative incidence of relapse/progression within 12 months of randomization between arms.

A Cox proportional hazards model with mixed effects will be used to compare the cause-specific hazards of relapse/progression between treatment arms while adjusting for an MN risk fixed effect and center-group lognormal frailties. The Cox regression model will be used to evaluate the adjusted hazard ratio of treatment (AAT vs. PTM) using a point estimate and a 95% CI.

7.4 MISSING DATA AND SENSITIVITY ANALYSIS

Minimal missing data (< 5%) is expected. If more than 5% of the primary endpoint data are missing, an appropriate imputation method will be applied, and corresponding sensitivity analyses will be conducted provided there is sufficient data.

For time-to-event outcomes such as TRM, OS, DFS, and relapse/progression, patients that withdraw or are lost to follow-up are assumed to be censored at random. For other endpoints, the occurrence of missing data, whether due to the patient's missing assessment(s) or withdrawal from the study, is assumed to be missing at random (MAR).

7.5 SAFETY ANALYSIS

Monitoring of safety will be conducted by reviewing treatment-related mortality (TRM) within 30 days of transplantation and infusion-related toxicities. Any treatment-related mortality event observed within 30 days of transplantation will undergo a thorough safety review by the NHLBI DSMB prior

to treatment of subsequent participants. Policies and composition of the DSMB are described in the BMT CTN's Manual of Procedures. As there is underlying risk of TRM associated with auto-transplantation, Table 7.5.1 shows the probability of observing 1 or more, 2 or more, and 3 or more events as a function of the underlying TRM rate to help guide decision making during the safety review. The probability of observing three or more events is 0.02 and 0.75 if the TRM rate is 5% and 30%, respectively. If the TRM rate is 5%, the probability of observing one or more events, two or more events and three or more events is 0.46, 0.12 and 0.02, respectively.

Table 7.1 Probabilities of Observing Events Based on Underlying Day 30 TRM Rates

Day 30 TRM Rate	5%	10%	20%	25%	30%
Probability of 1 or more events	0.46	0.72	0.93	0.97	0.99
Probability of 2 or more events	0.12	0.34	0.73	0.84	0.91
Probability of 3 or more events	0.02	0.11	0.44	0.61	0.75

The frequency of Grade 3 or higher infusion-related toxicities with a duration of 24 hours or more will also be monitored. If three or more of these events are observed, the NHLBI will be notified and the DSMB will be consulted regarding continuation of the study. This stopping guideline serves as a trigger for consultation with the DSMB for additional review and is not a formal stopping rule that would mandate closure of study enrollment.

In the event of graft failure, the protocol will be temporarily halted and reviewed by the NHLBI DSMB. Graft failure will be defined as a failure to achieve three consecutive labs of greater than or equal to 500 neutrophils/μL by Day 100.

7.6 INTERIM ANALYSIS

There will be no interim analyses for efficacy or futility.

8 CHANGES TO PROTOCOL-SPECIFIED ANALYSIS

The current SAP elaborates on the protocol-specified analysis and makes no deviation from it. Any future changes made to the protocol-specified analysis, and the justification for these changes, will be documented in the amendment to this SAP.

9 REFERENCES

Aalen, O. O. and S. Johansen (1978). An empirical transition matrix for non-homogeneous Markov chains based on censored observations. *Scand J* Stat 141-150.

Clopper, C. J., and E. S. Pearson. (1934). The Use of Confidence or Fiducial Limits Illustrated in the Case of the Binomial. *Biometrika* 26: 404-413.

Fay, M.P., Brittain, E.H. and Proschan, M.A. (2013). Pointwise confidence intervals for a survival distribution with small samples or heavy censoring. *Biostatistics*, 14(4), pp.723-736.

APPENDIX A:
STATISTICAL ANALYSIS PLAN APPROVAL SIGNATURE PAGE

BMT CTN 1903 (AMC-109) Statistical Analysis Plan Prepared and Accepted by:

Protocol Chairperson/Officer:

Signature: Steve Devine, MD I am approving this document. Date: 21/Jun/2022 08:50 PM EDT

Print Name: Steve Devine, MD DDMMMYYYY

Title: Protocol Chairperson/Officer

Medical College of Wisconsin BMT CTN 1903 Protocol Statistician:

Signature: Brent Logan, PhD I am approving this document. Date: 22/Jun/2022 05:18 PM EDT

Print Name: Brent Logan, PhD DDMMMYYYY

Title: BMT CTN 1903 Statistician

Emmes BMT CTN 1903 Statistician:

Signature: Maggie Wu I am approving this document. Date: 22/Jun/2022 09:07 AM EDT

Print Name: Maggie Wu DDMMMYYYY

Title: Emmes BMT CTN 1903 Statistician

APPENDIX B: TABLES, LISTINGS, AND FIGURES

List of Tables:

List of Figures:

Table 1: Study Enrollment Over Time

Center	Year					Total
	2021	2022	2022	2023	2024	
Center 1	**XX**	**XX**	**XX**	**XX**	**XX**	**XX**
Center 2	**XX**	**XX**	**XX**	**XX**	**XX**	**XX**
Center K	**XX**	**XX**	**XX**	**XX**	**XX**	**XX**
All Centers	**XX**	**XX**	**XX**	**XX**	**XX**	**XX**

Table 2: Actual vs. Projected Enrolment

Months After Study Initiation	Projected	Cumulative Projected	Actual	Cumulative Actual
0 – 3	XX	XX	XX	XX
4 – 6	XX	XX	XX	XX
7 – 9	XX	XX	XX	XX
10 – 12	XX	XX	XX	XX
13 – 15	XX	XX	XX	XX
16 – 18	XX	XX	XX	XX
19 – 21	XX	XX	XX	XX
22 – 24	XX	XX	XX	XX
25 – 27	XX	XX	XX	XX
28 – 30	XX	XX	XX	XX
31 – 33	XX	XX	XX	XX
34 – 36	XX	XX	XX	XX
37-39	XX	XX	XX	XX
40-42	XX	XX	XX	XX
43-45	XX	XX	XX	XX
46-48	XX	XX	XX	XX

Figure 1: Actual vs. Projected Enrolment

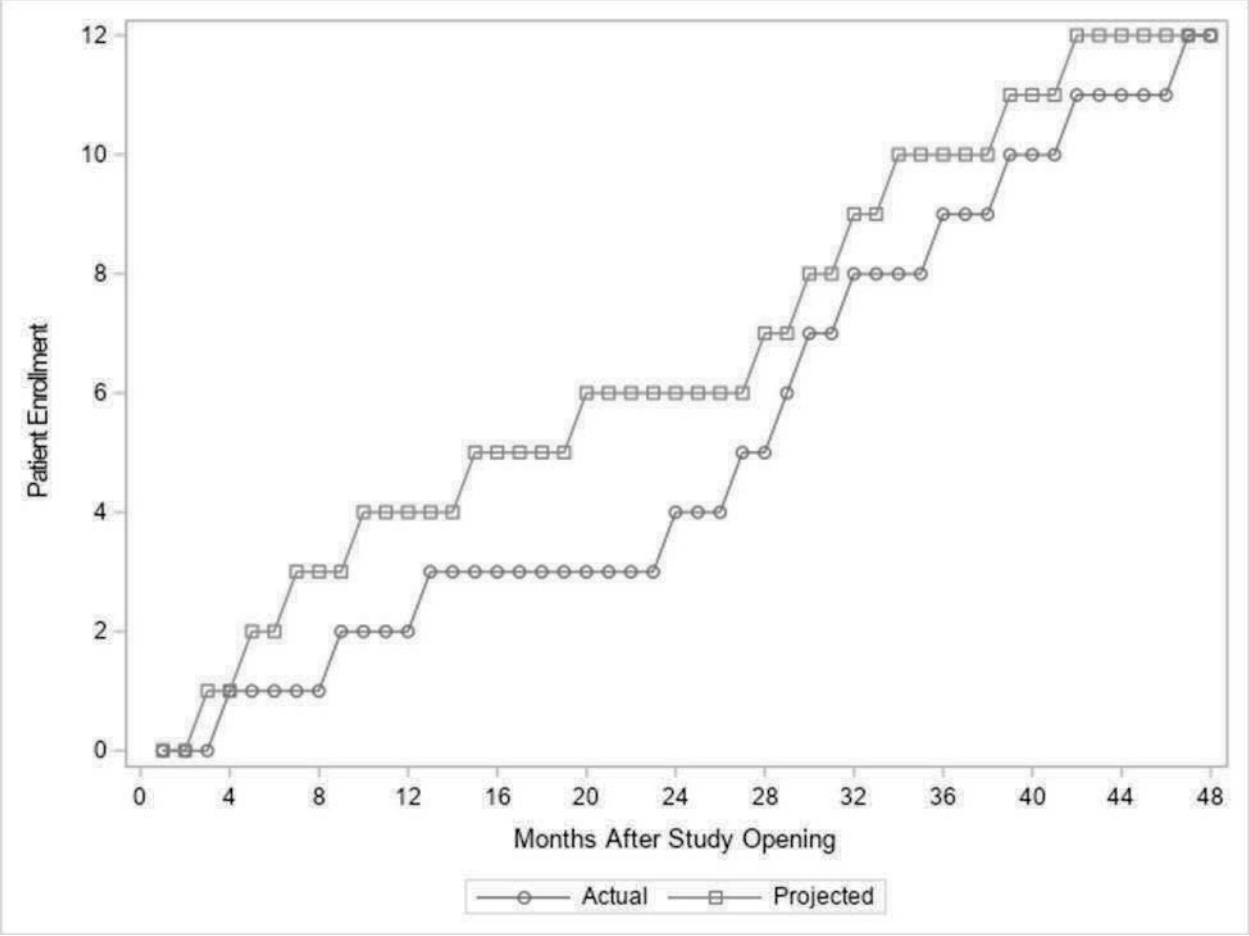

Table 3: Analysis Populations

Analysis Set	N	Description
Feasibility	XX	All participants who have blood drawn for HST-NEETs manufacturing.
Transplant	XX	All participants enrolled on the study who proceed to transplant.
Infusion	XX	All participants who are enrolled on the study that received both a transplant and HST-NEETs.

Table 4: Participant Disposition

	N	%
Enrolled	XX	100.0
Died on Study	XX	XX.X
Withdrew from Study	XX	XX.X
Completed Planned Study Follow-up	XX	XX.X

Table 5: Demographic and Baseline Characteristics

Variable	Total (N=XX) N (100%)
Gender	
Male	XX (XX.X)
Female	XX (XX.X)
Ethnicity	
Hispanic or Latino	XX (XX.X)
Not Hispanic or Latino	XX (XX.X)
Unknown	
Not Answered	
Race	
American Indian/Alaska Native	XX (XX.X)
Asian	XX (XX.X)
Hawaiian/Pacific Islander	XX (XX.X)
Black or African American	XX (XX.X)
White	XX (XX.X)
More than One Race	XX (XX.X)
Other, Specify	XX (XX.X)
Unknown	XX (XX.X)
Not Answered	XX (XX.X)
Age (years)	
Median (range)	XX.X (XX.X, XX.X)
Mean (SD)	XX.X (XX.X)
18-65	XX (XX.X)
65 or Older	XX (XX.X)
Karnofsky / Lansky Performance Score	
At least 90	XX (XX.X)
Less Than 90	XX (XX.X)
Primary Disease	
Follicular Lymphoma	XX (XX.X)
Diffuse Large B-Cell Lymphoma	XX (XX.X)

Variable	Total (N=XX) N (100%)
Mantle Cell Lymphoma	XX (XX.X)
Marginal B-cell Cell Lymphoma	XX (XX.X)
Classical Hodgkin's Lymphoma	XX (XX.X)
Lymphoproliferative Disease	XX (XX.X)
Time from Disease Diagnosis to Transplant	
Median (range)	XX.X (XX.X, XX.X)
Mean (SD)	XX.X (XX.X)
HIV Viral Load	
Median (range)	XX.X (XX.X, XX.X)
Mean (SD)	XX.X (XX.X)
CD4+ Count	
Median (range)	XX.X (XX.X, XX.X)
Mean (SD)	XX.X (XX.X)
Number of Prior Chemotherapy Regimens	
2+	XX (XX.X)
Number of Prior HIV Regimens	
0	XX (XX.X)
1	XX (XX.X)
2+	XX (XX.X)
HIV Genotype	
Group M	XX (XX.X)
…	XX (XX.X)
Group P	XX (XX.X)
Disease Risk Index	
Low	XX (XX.X)
IM	XX (XX.X)
High/ Very High	XX (XX.X)
HCT-CI	
0	XX (XX.X)
1	XX (XX.X)
2	XX (XX.X)
3	XX (XX.X)
4+	XX (XX.X)
Planned Post-Transplant Maintenance Therapy	
No	XX (XX.X)
Yes	XX (XX.X)

Table 6: HST-NEET Infusion Proportion

HST-NEET infusion	N	Percent	90% CI	
Yes (within 7 days)	XX	XX.X%	XX.X	XX.X
Yes (within 30 days)	XX	XX.X%	XX.X	XX.X

Table 7: Descriptive Summary Statistics of Intact Proviral Reservoir DNA Assay

Assessment	N	Mean	Median	Std. Dev.	Min.	Max.
Baseline	XX	XX.X	XX.X	XX.X	XX.X	XX.X
Day 100	XX	XX.X	XX.X	XX.X	XX.X	XX.X
6 Months	XX	XX.X	XX.X	XX.X	XX.X	XX.X
12 Months	XX	XX.X	XX.X	XX.X	XX.X	XX.X

Figure 2: Mean IPDA vs Time

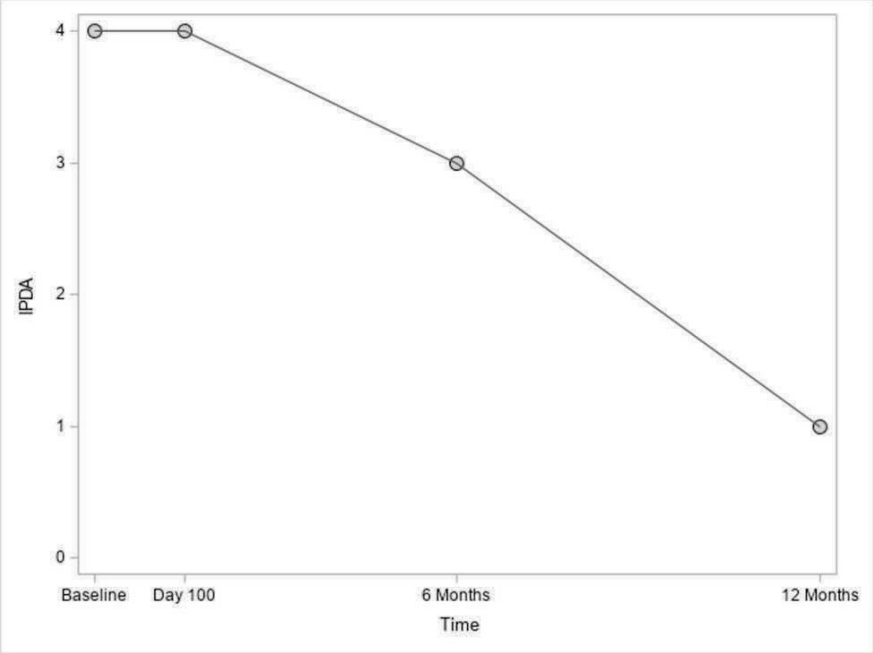

Figure 3: Spaghetti Plot of IPDA

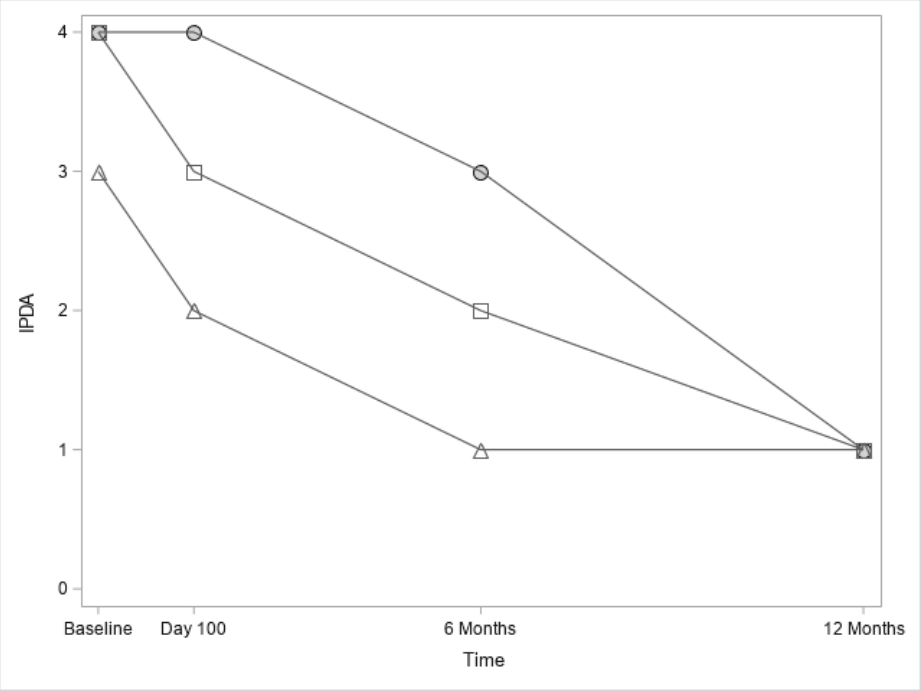

Table 8: Repeated Measures Analysis of IPDA

Covariate	Level	N	Estimate	Std. Err.	90% CI	
Time	**Baseline**	XX	0.0			
	Day 100	XX	XX.X	XX.X	XX.X	XX.X
	6 Months	XX	XX.X	XX.X	XX.X	XX.X
	12 Months	XX	XX.X	XX.X	XX.X	XX.X

Table 9: Compound Symmetry Covariance Matrix (IPDA)

Covariance Parameter	Estimate	Std. Err.	Z-value	P-value
Diagonal Elements	XX.X	XX.X	XX.X	0.XXX
Off Diagonal Elements	XX.X	XX.X	XX.X	0.XXX

Table 10: Total Proviral HIV DNA at 6-Months

		Difference: A-B							
N	**DF**	**Mean**	**Std. Dev.**	**Std. Err.**	**Min.**	**Max.**	**90% CI**	**t-Stat**	**p-value**
XX	XX	XX.X	XX.X	XX.X	XX.X	XX.X	[XX.X, XX.X]	XX.X	0.XXX

Note: A=log(TPDNA) pre-transplant, B=log(TPDNA) 6 months post-transplant

Table 11: Acute Infusion Related Toxicities

	N	Percent	90% CI	
Day 28	XX	XX.X%	XX.X	XX.X

Table 12: Toxicity Proportion

	N	Percent	90% CI	
Day 28	XX	XX.X%	XX.X	XX.X

Table 13: CR and CR+PR Rate at Day-100 after ASCT

	N	Percent	90% CI	
CR	XX	XX.X%	XX.X	XX.X
CR+PR	XX	XX.X%	XX.X	XX.X

Figure 4: Progression-Free Survival

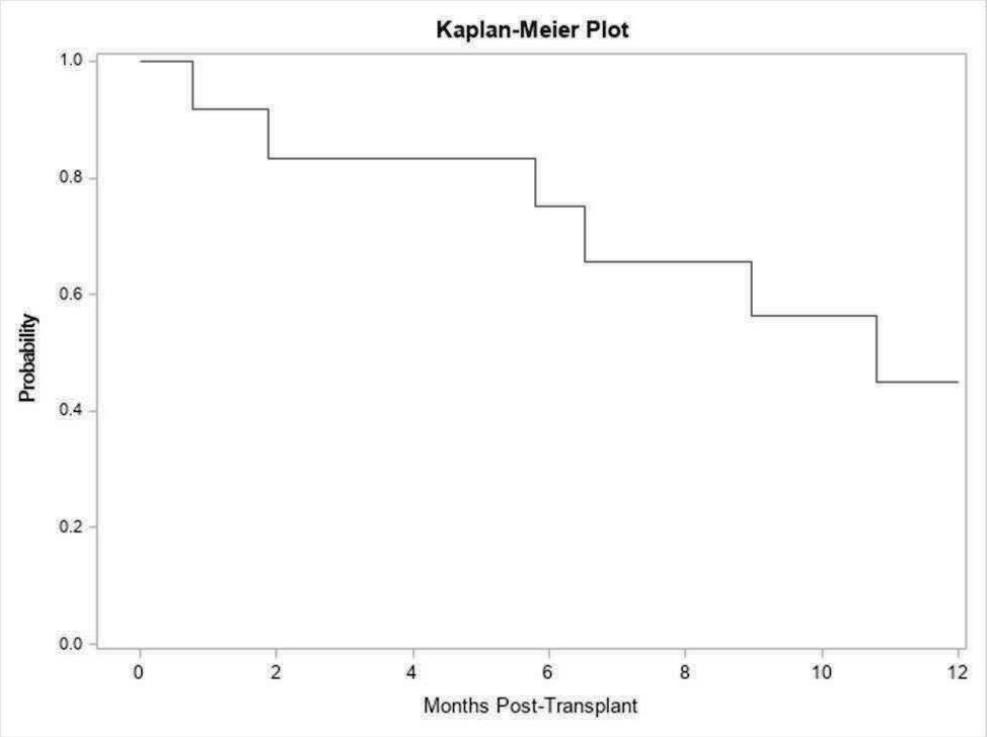

Figure 5: Overall Survival

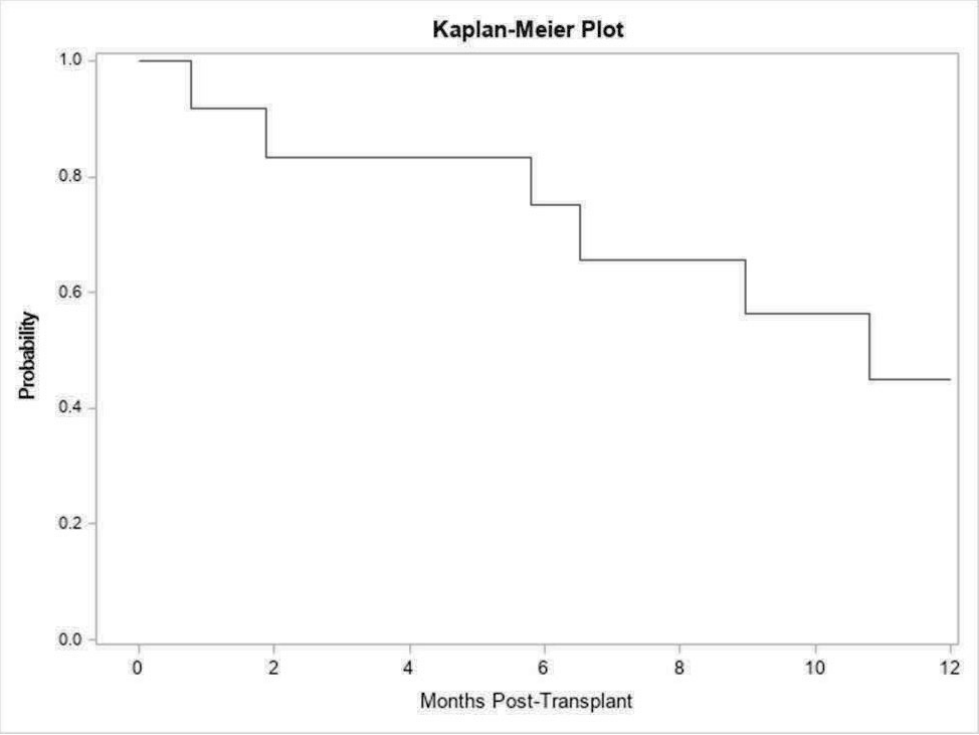

Figure 6: Non-Relapse Mortality

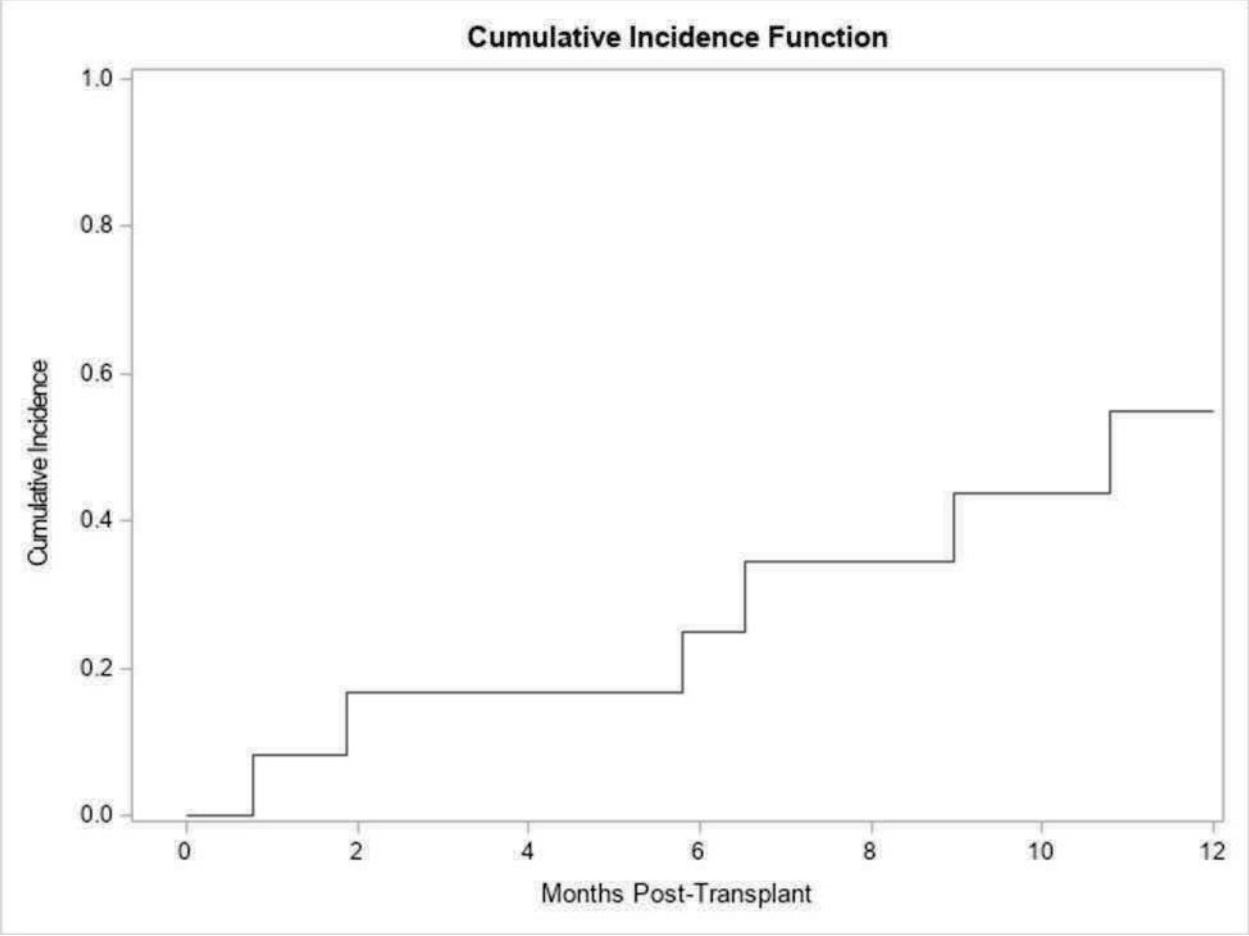

Table 14: Probability Estimates for PFS and OS

	(N=XX)		
Outcomes	**# Events**	**Prob. Estimate**	**90% CI**
PFS			
Day 180	XX	XX.X%	(XX.X%, XX.X%)
12 Months	XX	XX.X%	(XX.X%, XX.X%)
OS			
Day 180	XX	XX.X%	(XX.X%, XX.X%)
12 Months	XX	XX.X%	(XX.X%, XX.X%)

Table 15: Data Listing of Time to Event Outcomes

PID	Time From HCT to Death	Time From HCT to Relapse	Time From HCT to Neutrophil Recovery	Time From HCT to Platelet Recovery	Dead (Yes/No, event date if yes)	PFS (Yes/No, event date if yes)	NRM (Yes/No, event date if yes)
1	XX	XX	XX	XX	XX	XX	XX
2	XX	XX	XX	XX	XX	XX	XX
3	XX	XX	XX	XX	XX	XX	XX
	XX	XX	XX	XX	XX	XX	XX
	XX	XX	XX	XX	XX	XX	XX
	XX	XX	XX	XX	XX	XX	XX
11	XX	XX	XX	XX	XX	XX	XX
12	XX	XX	XX	XX	XX	XX	XX

Table 16: Data Listing of Demographics and Baseline Characteristics

PID	Gender	Ethnicity	Race	Age									Planned Therapy
1	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
2	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
3	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
11	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
12	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX

Table 17: Cumulative Incidence for NRM, Neutrophil and Platelet Recovery

	(N=XX)		
Outcomes	**# Events**	**Prob. Estimate**	**90% CI**
NRM			
Day 180	XX	XX.X%	(XX.X%, XX.X%)
12 Months	XX	XX.X%	(XX.X%, XX.X%)
Neutrophil Recovery			
Day 100	XX	XX.X%	(XX.X%, XX.X%)
12 Months	XX	XX.X%	(XX.X%, XX.X%)
Platelet Engraftment			
Day 100	XX	XX.X%	(XX.X%, XX.X%)
12 Months	XX	XX.X%	(XX.X%, XX.X%)

Figure 7: Cumulative Incidence of Neutrophil Recovery

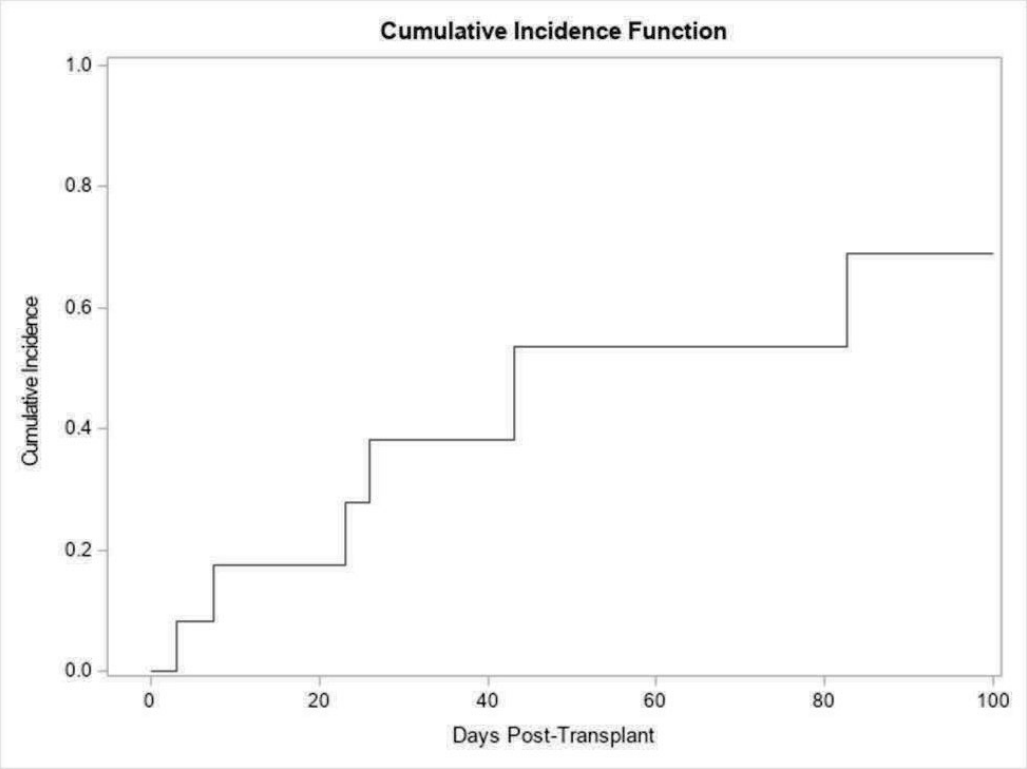

Figure 8: Cumulative Incidence of Platelet Recovery

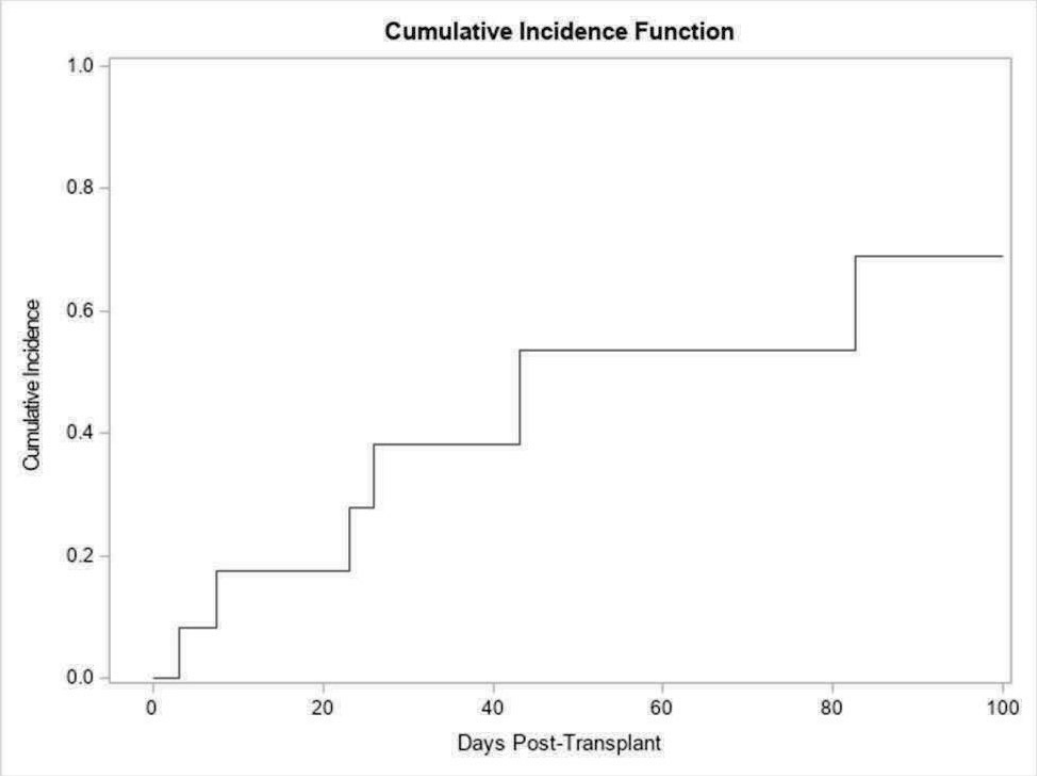

Table 18: Descriptive Summary Statistics of Ig DNA in Blood

Assessment	N	Mean	Median	Std. Dev.	Min.	Max.
Baseline	XX	XX.X	XX.X	XX.X	XX.X	XX.X
Day 100	XX	XX.X	XX.X	XX.X	XX.X	XX.X
6 Months	XX	XX.X	XX.X	XX.X	XX.X	XX.X
12 Months	XX	XX.X	XX.X	XX.X	XX.X	XX.X

Figure 9: Mean Ig DNA vs Time

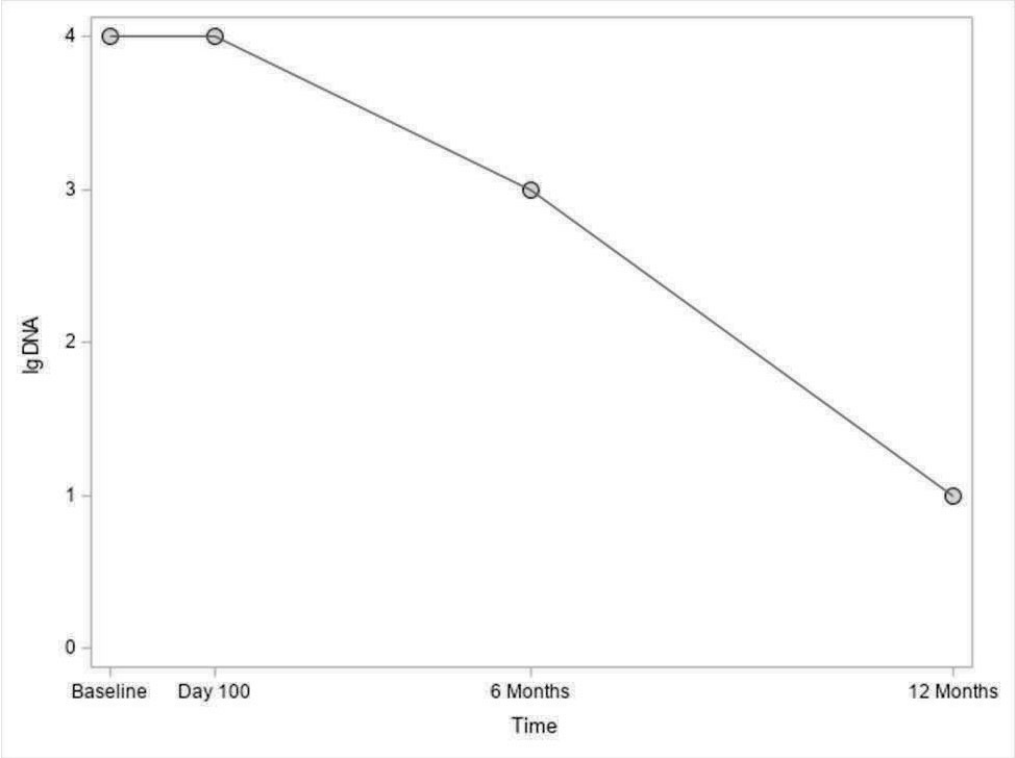

Figure 10: Spaghetti Plot of Ig DNA

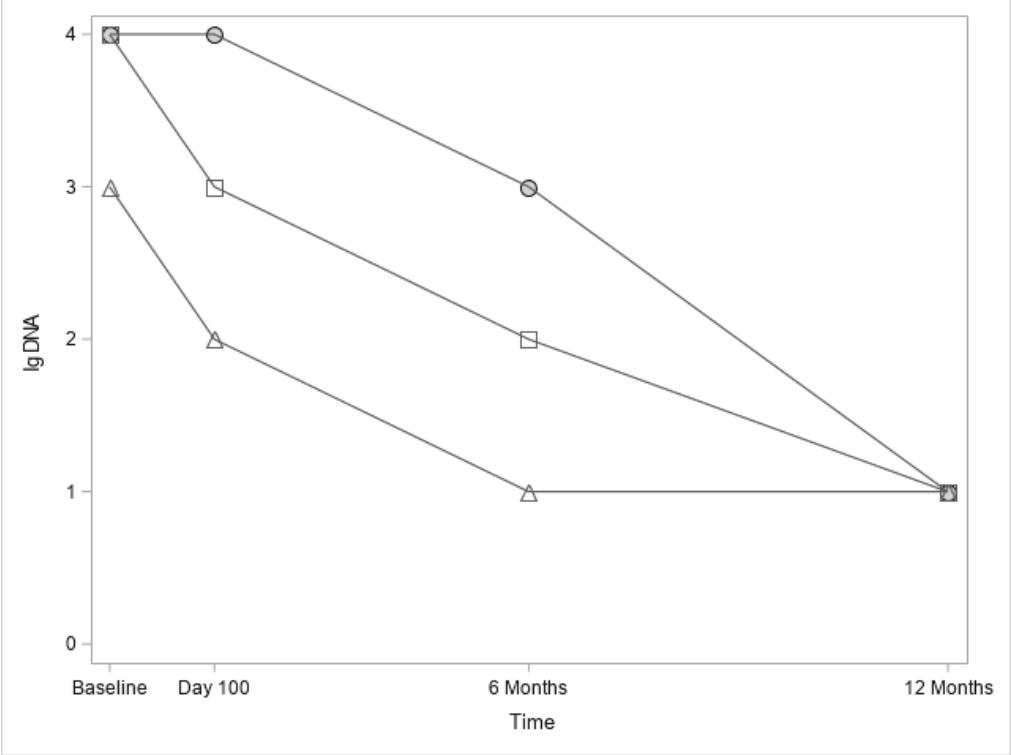

Table 19: Repeated Measures Analysis of Ig DNA in Blood

Covariate	Level	N	Estimate	Std. Err.	90% CI	
Time	**Baseline**	XX	0.0			
	Day 100	XX	XX.X	XX.X	XX.X	XX.X
	6 Months	XX	XX.X	XX.X	XX.X	XX.X
	12 Months	XX	XX.X	XX.X	XX.X	XX.X

Table 20: Compound Symmetry Covariance Matrix (Ig DNA)

Covariance Parameter	Estimate	Std. Err.	Z-value	P-value
Diagonal Elements	XX.X	XX.X	XX.X	0.XXX
Off Diagonal Elements	XX.X	XX.X	XX.X	0.XXX

Table 21: Descriptive Summary Statistics of HIV RNA in Blood

Assessment	N	Mean	Median	Std. Dev.	Min.	Max.
Baseline	XX	XX.X	XX.X	XX.X	XX.X	XX.X
Day 100	XX	XX.X	XX.X	XX.X	XX.X	XX.X
6 Months	XX	XX.X	XX.X	XX.X	XX.X	XX.X
12 Months	XX	XX.X	XX.X	XX.X	XX.X	XX.X

Figure 11: Mean HIV RNA vs Time

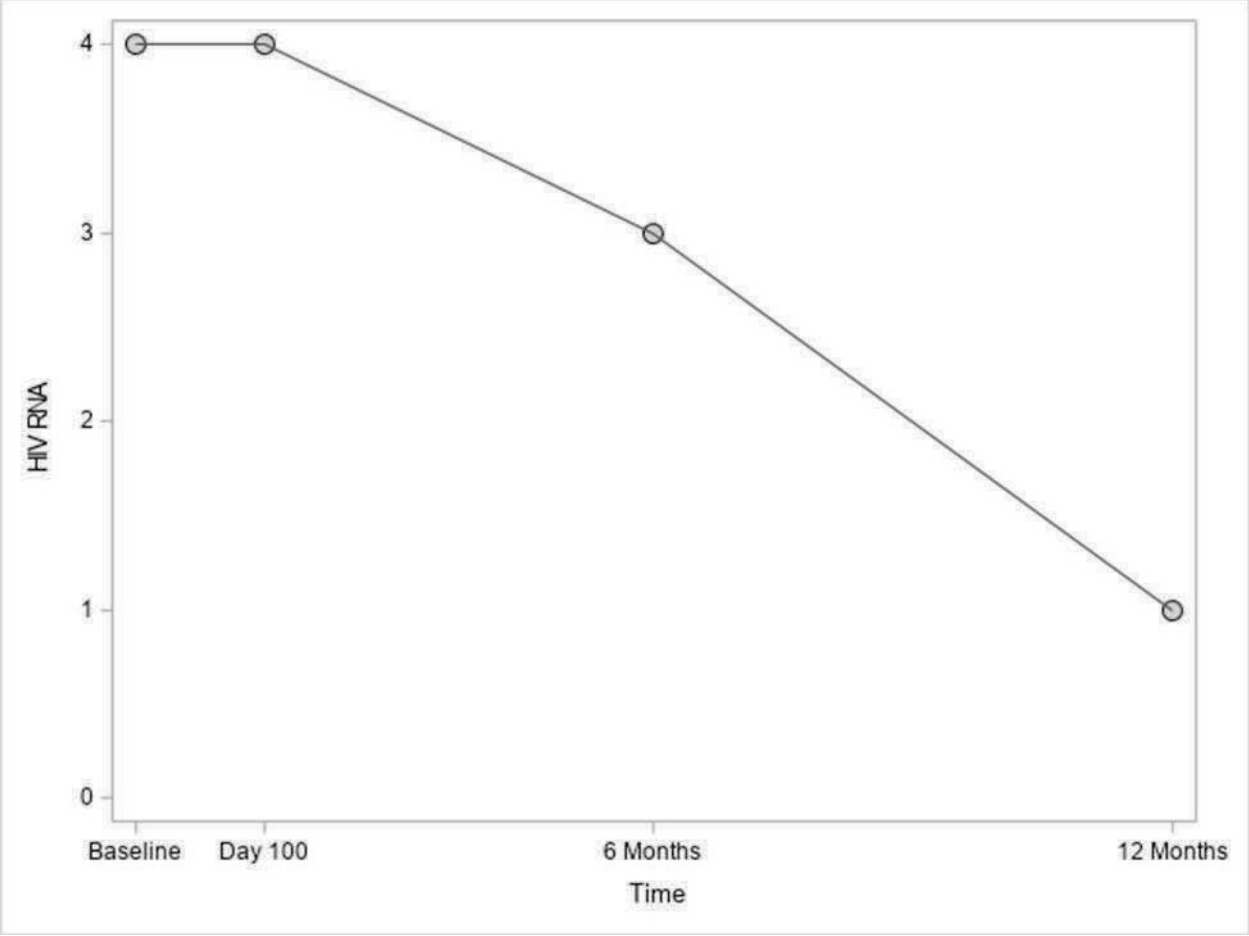

Figure 12: Spaghetti Plot of HIV RNA

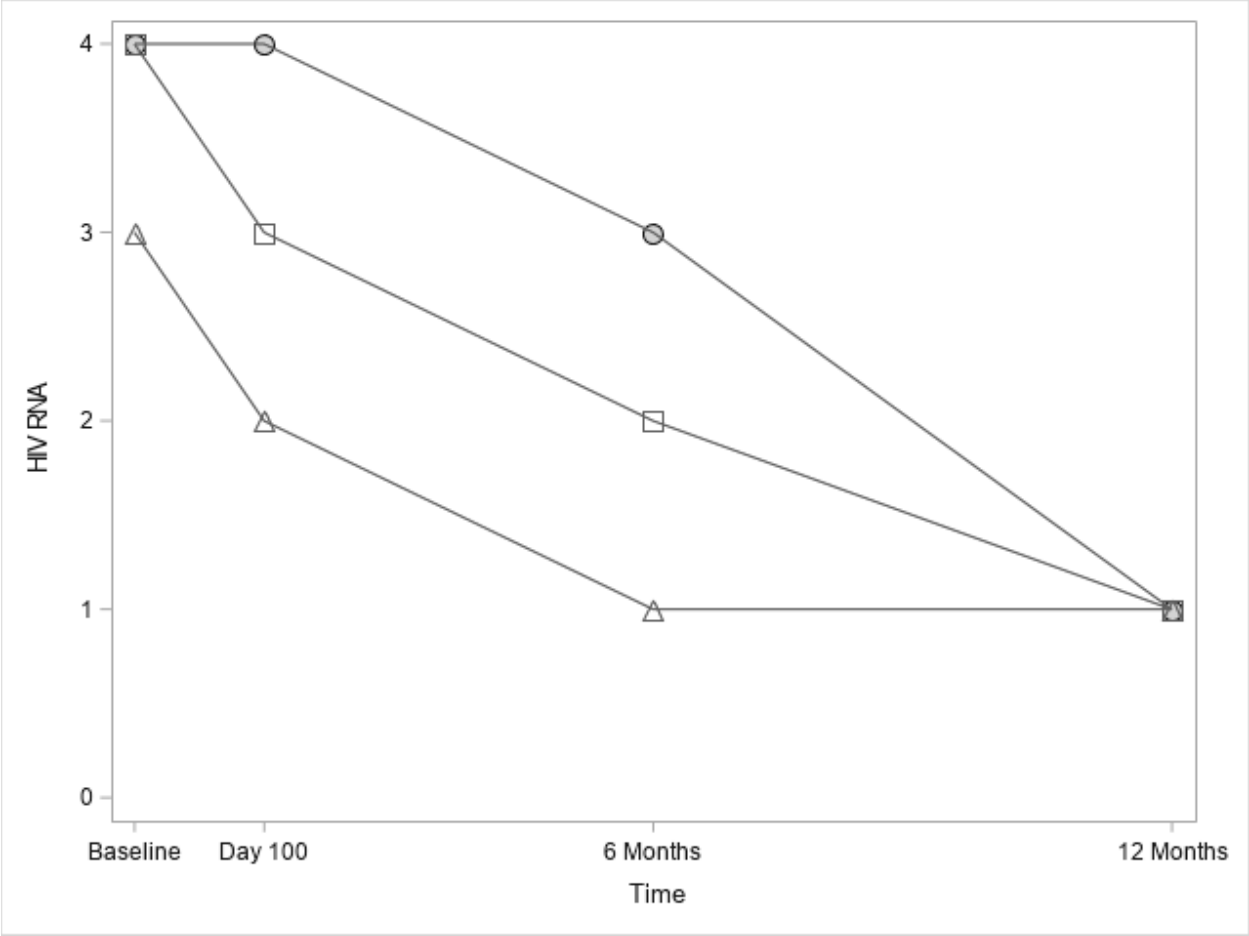

Table 22: Repeated Measures Analysis of HIV RNA in Blood

Covariate	Level	N	Estimate	Std. Err.	90% CI	
Time	**Baseline**	XX	0.0			
	Day 100	XX	XX.X	XX.X	XX.X	XX.X
	6 Months	XX	XX.X	XX.X	XX.X	XX.X
	12 Months	XX	XX.X	XX.X	XX.X	XX.X

Table 23: Compound Symmetry Covariance Matrix (HIV RNA)

Covariance Parameter	Estimate	Std. Err.	Z-value	P-value
Diagonal Elements	XX.X	XX.X	XX.X	0.XXX
Off Diagonal Elements	XX.X	XX.X	XX.X	0.XXX

Table 24: Descriptive Summary Statistics of MST-NEETs in Vivo

Assessment	N	Mean	Median	Std. Dev.	Min.	Max.
Baseline	XX	XX.X	XX.X	XX.X	XX.X	XX.X
Day 100	XX	XX.X	XX.X	XX.X	XX.X	XX.X
6 Months	XX	XX.X	XX.X	XX.X	XX.X	XX.X
12 Months	XX	XX.X	XX.X	XX.X	XX.X	XX.X

Figure 13: Mean HST-NEETs vs Time

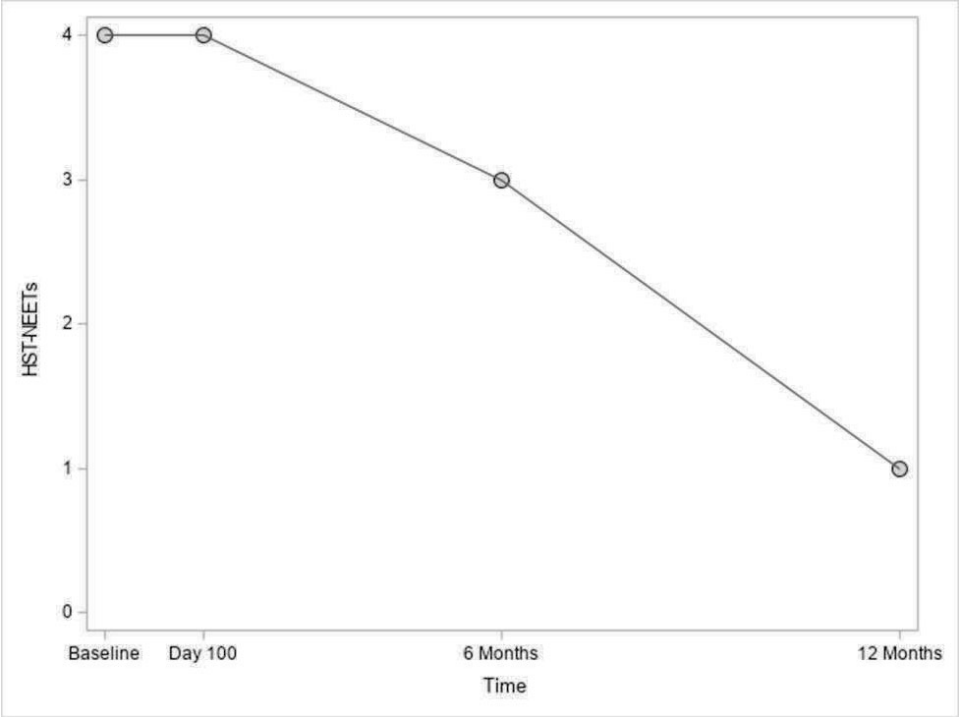

Figure 14: Spaghetti Plot of HST-NEETs

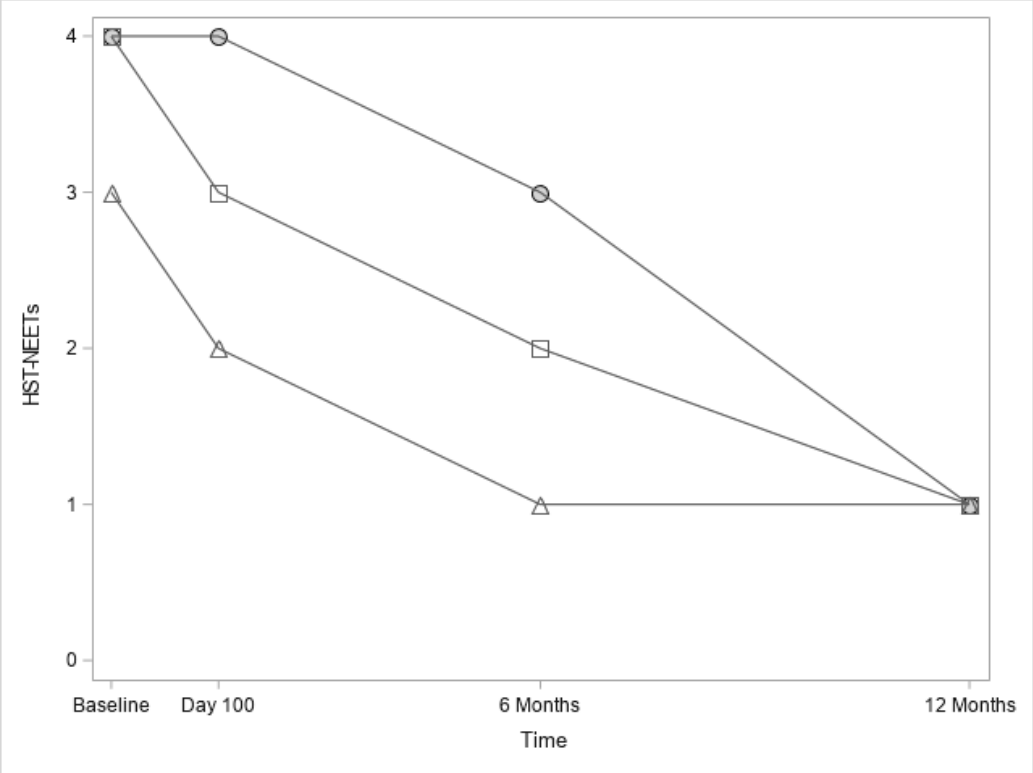

Table 25: Repeated Measures Analysis of HST-NEETs in Vivo

Covariate	Level	N	Estimate	Std. Err.	90% CI	
Time	**Baseline**	XX	0.0			
	Day 100	XX	XX.X	XX.X	XX.X	XX.X
	6 Months	XX	XX.X	XX.X	XX.X	XX.X
	12 Months	XX	XX.X	XX.X	XX.X	XX.X

Table 26: Compound Symmetry Covariance Matrix (HST-NEETs in Vivo)

Covariance Parameter	Estimate	Std. Err.	Z-value	P-value
Diagonal Elements	XX.X	XX.X	XX.X	0.XXX
Off Diagonal Elements	XX.X	XX.X	XX.X	0.XXX

Table 27: AEs Occurring Through 12-Months Post-Transplant by System Organ Class

	N=XX	
	# Events (%)	**# Participants Affected (%)**
System Organ Class[1]		
Class 1	XX (XX.X%)	XX (XX.X%)
Class 2	XX (XX.X%)	XX (XX.X%)
…	XX (XX.X%)	XX (XX.X%)
Class K	XX (XX.X%)	XX (XX.X%)

[1] Classified per MedDRA coding.

Table 28: Adverse Events Occurring Through 12-Months Post-Transplant

N=XX	
# Participants Affected	**% Participants Affected (90% CI)**
XX	XX.X% (XX.X%, XX.X%)

Table 29: Adverse Events Summary Through 12-Month Post-Transplant

Adverse Events – Number of Participants Affected		
	N=XX	
Category	**N**	**%**
Adverse Events (AEs)	XX	XX.X
Severe Adverse Events (SAEs)	XX	XX.X

Table 30: Adverse Events Reports Through 12-Months Post-Transplant

		N=XX		
System Organ Class	**Preferred Term**	**# Events**	**Participants Affected**	**% of participants**
SOC #1	**Category 1**	XX	XX	XX.X
	Category 2	XX	XX	XX.X
	…			
	Category K	XX	XX	XX.X
SOC #2	**Category 1**	XX	XX	XX.X
	Category 2	XX	XX	XX.X
	…			
	Category K	XX	XX	XX.X
…				
Total		XX	XX	XX.X

Table 31: Severe Adverse Events Reported Through 12-Months Post-Transplant

		N=XX		
System Organ Class	**Preferred Term**	**# Events**	**Participants Affected**	**% of participants**
SOC #1	**Category 1**	XX	XX	XX.X
	Category 2	XX	XX	XX.X
	…			
	Category K	XX	XX	XX.X
SOC #2	**Category 1**	XX	XX	XX.X
	Category 2	XX	XX	XX.X
	…			
	Category K	XX	XX	XX.X
…				
Total		XX	XX	XX.X

Table 32: Toxicities Through 12-Month Post-Transplant

	N=XX	
	N	**%**
Maximum Toxicity Grade		
Grade 0 - 2	XX	XX.X
Grade 3	XX	XX.X
Grade 4	XX	XX.X
Grade 5	XX	XX.X
Toxicity Type 1		

	N=XX	
	N	%
Grade 0 – 2	XX	XX.X
Grade 3	XX	XX.X
Grade 4	XX	XX.X
Grade 5	XX	XX.X
Toxicity Type 2		
Grade 0 – 2	XX	XX.X
Grade 3	XX	XX.X
Grade 4	XX	XX.X
Grade 5	XX	XX.X
Toxicity Type K		
Grade 0 – 2	XX	XX.X
Grade 3	XX	XX.X
Grade 4	XX	XX.X
Grade 5	XX	XX.X

[1] Classified per CTCAE version 5.0

Table 33: Infections

	N=XX	
	# Infections (%)	# Participants Affected (%)
Total Number of Infections	XX (100.0%)	XX (100.0%)
Infection Site		
Site 1	XX (XX.X%)	XX (XX.X%)
Site 2	XX (XX.X%)	XX (XX.X%)
…	XX (XX.X%)	XX (XX.X%)
Site K	XX (XX.X%)	XX (XX.X%)
Time of Onset Post-transplant		
000 -100 days	XX (XX.X%)	XX (XX.X%)
101 – 180 days	XX (XX.X%)	XX (XX.X%)
181 – 365 days	XX (XX.X%)	XX (XX.X%)
Infection Severity		
Grade 2	XX (XX.X%)	XX (XX.X%)
Grade 3	XX (XX.X%)	XX (XX.X%)

Table 34: Incidence Rate of Infections

N	Incidence Rate	90% CI	
XX	XX.X	XX.X	XX.X

Table 35: Primary Cause of Death

	(N=XX)	
Cause of Death	**N**	**%**
Cause 1	XX	XX.X
Cause 2	XX	XX.X
Cause K	XX	XX.X
Total	XX	100.0
Total Deaths	XX	XX.X
Total Enrolled	XX	100.0

Table 36: Reasons for Incomplete Study Plan and/or Withdrawal

Reason for Failure to Complete Study Treatment and/or Withdrawal from Study	N	%
Reason 1	X	X
Reason 2	X	X
Reason K	X	X
Total	X	X

Table 37: Significant Protocol Deviations

Center	Patient ID	Treatment Group	Deviation Description