Protocol 145-ADS-202

A Phase II Study Evaluating the Safety and Efficacy of MGTA-145 in Combination with Plerixafor for the Mobilization and Transplantation of HLA-Matched Donor Hematopoietic Stem Cells in Recipients with Hematological Malignancies

Resource for Clinical Investigation in Blood and Marrow Transplantation and Magenta Therapeutics, Inc.

Statistical Analysis Plan (SAP)

Version 1.0

April 15, 2022

Sponsored by the Magenta Therapeutics and National Marrow Donor Program® (NMDP)

VERSION HISTORY

Version #	Creation/Revision Date	Reason for Change
1.0	April 15, 2022	Initial Document, Early termination of trial

PROTOCOL SYNOPSIS

Protocol Title (Full)	A Phase II Study Evaluating the Safety and Efficacy of MGTA-145 in Combination with Plerixafor for the Mobilization and Transplantation of HLA-Matched Donor Hematopoietic Stem Cells in Recipients with Hematological Malignancies
Protocol Title (Short)	MGTA-145 in Combination with Plerixafor for the Mobilization and Transplantation of HLA-Matched Donor Hematopoietic Stem Cells in Recipients with Hematological Malignancies
Study Objective(s)	**Primary Hypothesis:** Human leukocyte antigen (HLA) matched donors receiving injections of plerixafor at 240 µg/kg combined with MGTA-145 0.015 mg/kg will safely mobilize sufficient CD34+ cells (at least 2.0 x 10^6 CD34+ cells/kg actual recipient weight at baseline) following one day of leukapheresis to support hematopoietic stem cell transplantation (HSCT). The hematopoietic cells mobilized by MGTA-145 + plerixafor will be functional and will result in prompt and durable hematopoietic recovery following transplantation into HLA-matched siblings and matched unrelated recipients with hematological malignancies. **Primary Objectives:** To determine the proportion of donors whose cells can be successfully mobilized and collected with a sufficient CD34+ cell dose using same-day, single-dose MGTA-145 + plerixafor as the mobilizing agents. Donor mobilization following MGTA-145 + plerixafor will be considered successful if ≥ 2.0 x 10^6 CD34+ cells/kg actual recipient weight are collected in one leukapheresis collection. All donors receiving MGTA-145 + plerixafor will be included in the analysis of the primary objective. **Secondary Objectives:** *Donor related* 1. To determine the proportion of donors whose cells can be successfully mobilized and collected with a target CD34+ cell dose of at least 4.0 x 10^6 $CD34^+$ cells/kg actual recipient weight in one apheresis collection 2. To ascertain the incidence and severity of acute adverse events (AEs) before and during apheresis experienced by donors receiving MGTA-145 + plerixafor 3. To characterize the adverse effects experienced by donors receiving MGTA-145 + plerixafor *Recipient Related* 1. To determine the incidence of and kinetics of neutrophil and platelet recovery after transplantation of hematopoietic cells mobilized with MGTA-145 + plerixafor 2. To determine the incidence of primary and secondary graft failure after transplantation of hematopoietic cells mobilized with MGTA-145 + plerixafor

	3. To determine the incidence and severity of acute and chronic graft versus host disease (GVHD) after transplantation of hematopoietic cells mobilized with MGTA-145 + plerixafor 4. To determine the incidence of treatment-related mortality and disease relapse/progression after transplantation of hematopoietic cells mobilized with MGTA-145 + plerixafor 5. To determine the probability of progression-free and overall survival after transplantation of hematopoietic cells mobilized with MGTA-145 + plerixafor 6. To characterize the adverse effects experienced by recipients receiving grafts mobilized by MGTA-145 + plerixafor
Study Population	The donor population for the study includes those subjects undergoing peripheral blood mobilization and collection of grafts for allogeneic HSCT. The recipient population for the study includes those subjects with acute myelogenous leukemia (AML), acute lymphoblastic leukemia (ALL) or myelodysplastic syndrome (MDS) receiving a hematopoietic stem cell transplant using the product obtained from a donor who underwent mobilization using MGTA-145 in combination with plerixafor.
Study Design/Phase	This is a Phase II, open-label, multicenter, prospective study of MGTA-145 + plerixafor mobilized HLA-matched sibling and matched unrelated donor allografts for myeloablative HSCT in recipients with hematological malignancies. Donors will undergo 1 or 2 days of mobilization and apheresis. The target collection is at least 4.0 x 10^6 CD34+ cells/kg actual recipient weight. Donors who achieve this target in one day will not undergo a second day of mobilization and apheresis. Donors who collect < 4.0 x 10^6 CD34+ cells/kg actual recipient weight will undergo a second day of mobilization and apheresis. AEs will be reported using event terms and grading for severity per the Common Terminology Criteria for Adverse Events (CTCAE) version 5. Donors will be contacted at Week 1, Month 1, and Month 6 to assess the donor's medical condition. Donors will have blood work at Month 1. The design utilizes established Center for International Blood and Marrow Transplant Research (CIBMTR) transplant recipient follow up procedures to capture transplant outcome data. NMDP will implement the study within its clinical investigation group and with Resource for Clinical Investigation in Blood and Marrow Transplantation (RCI BMT) Data Safety Monitoring Board (DSMB) oversight.
Treatment Description	*Donor:* Eligible donors will receive subcutaneous plerixafor at 240 µg/kg actual donor weight followed by MGTA-145 infusion (0.015 mg/kg) approximately 2 hours later and commence apheresis as soon as feasible thereafter. Some donors will require a second dose of MGTA-145 + plerixafor and apheresis the day after the first collection to reach the target CD34+ cell collection goal. The target CD34+ cell dose is ≥ 4.0 x 10^6/kg actual recipient weight with a minimum of ≥ 2.0 x 10^6/kg actual recipient weight.

	Recipient: Eligible recipients will undergo conditioning using a myeloablative regimen after an adequate allograft has been collected from the donor. Allograft will be cryopreserved and stored until transplant Day 0. GVHD prophylaxis may include post-transplant cyclophosphamide or a calcineurin phosphatase inhibitor in combination with methotrexate, mycophenolate mofetil, or sirolimus in accordance with local institutional guidelines. Recipients will receive G-CSF 5 µg/kg/day starting day +7 until absolute neutrophil count (ANC) > 1.5 x 10^9/L for two consecutive days.
Planned Number of Subjects	Approximately 28 donors. With a 5% drop out prior to transplant, it is anticipated that this will lead to 28 donors evaluable for mobilization endpoints and 26-27 recipients available for transplant follow up. The study employs a two-stage Simon minimax design in which 13 donors are enrolled in stage 1 and 15 donors are enrolled in stage 2.
Planned Number of Sites	Up to 10
Method of Assigning Patients to Treatment	Single arm, non-randomized
Follow-up Schedule	Donors will be followed from Day 1 (Baseline, MGTA-145 infusion) through 6-months post-mobilization. Donors will also complete survey assessments from prior to mobilization through 1-month post-mobilization. Recipients will be followed from Day 0 (Day of Transplant) through 1-year post-transplant. Recipients will be asked to co-enroll on the CIBMTR Outcomes Database Protocol.
Study Duration	2.5 years (1.5 years enrollment + up to 1-year follow-up)
Participation Duration	6 months for donors 1 year for recipients
Key Inclusion Criteria	<u>Donor Inclusion Criteria:</u> 1. Donor medical suitability and eligibility will be determined following Institution or NMDP/Be The Match standards 2. Age 18-65 years old at the time of signing informed consent 3. 8/8 (HLA- A, B, C, and DRB1) HLA-matched sibling or volunteer unrelated donor 4. Fulfill Institution or NMDP/Be The Match criteria to serve as a mobilized blood cell donor 5. Serum creatinine < 1.5 x institution upper limit of normal (ULN) or estimated creatinine clearance (CRCL) > 50 mL/min using the Modification of Diet in Renal Disease Study (MDRD) equation or similar method

	Recipient Inclusion Criteria: 1. At least 18 years old at the time of signing informed consent 2. Has an available 8/8 (HLA- A, B, C, and DRB1) HLA-matched sibling or volunteer unrelated donor willing to donate peripheral blood stem cells (PBSC) for transplant 3. Fulfill additional individual Transplant Center Criteria for transplant beyond NMDP/Be The Match criteria 4. One of the following diagnoses: • Acute myelogenous leukemia (AML) in 1st remission or beyond with ≤ 5% marrow blasts and no circulating blasts. Documentation of bone marrow assessment will be accepted within 45 days prior to the date of consent. • Acute lymphoblastic leukemia (ALL) in 1st remission or beyond with ≤ 5% marrow blasts and no circulating blasts. Documentation of bone marrow assessment will be accepted within 45 days prior to the date of consent. • Patients with myelodysplasia (MDS) with no circulating blasts and with less than 10% blasts in the bone marrow (higher blast percentage allowed in MDS due to lack of differences in outcomes with < 5% or 5-10% blasts in MDS). Documentation of bone marrow assessment will be accepted within 45 days prior to the date of consent. 5. Cardiac function: Left ventricular ejection fraction at least 45% based on most recent echocardiogram or MUGA results obtained via standard of care 6. Estimated creatinine clearance acceptable per local institutional guidelines 7. Pulmonary function: diffusing capacity of the lungs for carbon monoxide (DLCO) corrected for hemoglobin at least 50% and forced expiratory volume in first second (FEV1) predicted at least 50% based on most recent DLCO results obtained via standard of care 8. Liver function acceptable per local institutional guidelines 9. Karnofsky performance status (KPS) of 70% or greater 10. Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI) score of 4 or less
Key Exclusion Criteria	Donor Exclusion Criteria: 1. Donor unwilling or unable to give informed consent, or unable to comply with the protocol including required follow-up and testing 2. Donor already enrolled on another investigational agent study 3. Pregnant or breastfeeding females, sexually active female and male donors not willing or able to use adequate contraception, or males who do not agree to refrain from donating sperm, from the time of consent through 3 months after treatment with MGTA-145 + plerixafor

	Recipient Exclusion Criteria: 1. Subject unwilling or unable to give informed consent, or unable to comply with the protocol including required follow-up and testing 2. Subject whose donor does not meet the eligibility criteria and is a screen fail 3. Subjects with a prior allogeneic transplant 4. Subjects with active, uncontrolled infection at the time of the transplant preparative regimen 5. Pregnant or breastfeeding females, sexually active female or male subjects not willing or able to use adequate contraception, or males who do not agree to refrain from donating sperm, from the time of consent through 3 months after PBSC infusion 6. Subjects with clinical evidence of active Central Nervous System (CNS) tumor involvement as evidenced by documented disease on examination of spinal fluid or MRI within 45 days of start of conditioning 7. A condition, which, in the opinion of the clinical investigator, would interfere with the evaluation of primary and secondary endpoints 8. Planned treatment with a new investigational agent from the time of transplant through 30 days post-transplant
Statistical Method	
Primary Statistical Analysis Plan	The primary endpoint of this study is the collection of a clinically adequate allograft in one apheresis session. A donor is considered successful for this endpoint if ≥ 2.0 x 10^6 CD34+ cells/kg actual recipient weight are collected in one leukapheresis collection using MGTA-145 + plerixafor. The proportion of donors who mobilize ≥ 2.0 x 10^6 CD34+ cells/kg actual recipient weight in one leukapheresis collection will be estimated along with a 90% confidence interval for consistency with the one-sided type I error rate of 5%. A 95% confidence interval will also be provided. The primary analysis will use the Donor Treated Population, where donors who do not undergo apheresis will be considered a failure for this endpoint.
Sample Size Justification	The sample size for this study is 28 donors receiving at least one dose of the combination regimen of MGTA-145 + plerixafor. It is expected that 90% of donors treated with MGTA-145 + plerixafor will mobilize ≥ 2.0 x 10^6 CD34+ cells/kg within one leukapheresis collection. MGTA-145 + plerixafor is considered an unacceptable mobilizing agent if fewer than 70% of donors achieve this cell-dose threshold within one leukapheresis collection. Using a two-stage Simon minimax design, assuming the true successful collection probability of 90%, 28 donors provide 85% power to reject the probability of successful collection of 70% or lower using a one-sided Type I error α=0.05. This is equivalent to testing the null hypothesis H0: $p \leq 0.70$ against the alternative hypothesis H1: $p > 0.70$ with 85% power to contrast a successful collection probability of 90% vs. 70%.

Table of Contents

List of Abbreviations

Abbreviations	Description of abbreviations
ADA	Anti-drug antibody
AE	Adverse event
AESI	Adverse event of special interest
aGVHD	Acute graft-versus-host disease
ALL	Acute lymphoblastic leukemia
AML	Acute myelogenous leukemia
ANC	Absolute neutrophil count
BPI	Brief pain inventory
CBC	Complete blood count
cGVHD	Chronic graft-versus-host disease
CI	Confidence interval
CIBMTR	Center for International Blood and Marrow Transplant Research
CMV	Cytomegalovirus
CNS	Central nervous system
CR	Complete remission
CRCL	Creatinine clearance
CTCAE	Common Terminology Criteria for Adverse Events
DLCO	Diffusing capacity of the lungs for carbon monoxide
DSMB	Data and Safety Monitoring Board
ECG	Echocardiogram
EDC	Electronic data capture
FDA	U.S. Food and Drug Administration
FEV1	Forced expiratory volume in first second
GVHD	Graft-versus-host disease
HCT-CI	Hematopoietic cell transplantation-comorbidity index
HLA	Human leukocyte antigen
HRU	Healthcare resource use
HSCT	Hematopoietic stem cell transplantation
IV	Intravenous
KG	Kilogram
KPS	Karnofsky performance status
LA	Leukapheresis
MAGIC	Mount Sinai Acute GVHD International Consortium
MDRD	Modification of diet in real disease
MDS	Myelodysplastic syndrome
MeDRA	Medical Dictionary for Regulatory Activities
MG	Milligram
MUGA	Multigated acquisition
NMDP	National Marrow Donor Program

OS	Overall survival
PBSC	Peripheral blood stem cell
PCR	Polymerase chain reaction
PK	Pharmacokinetic
PROMIS	Patient-Reported Outcomes Measurement Information System
PT	Prothrombin time
PTT	Partial thromboplastin time
RCI BMT	Resource for Clinical Investigation in Blood and Marrow Transplantation
SAE	Serious adverse events
SAP	Statistical analysis plan
SOC	System organ class
SRG	Survey research group
TRM	Treatment-related mortality
ULN	Upper limit of normal
UP	Unanticipated problems
WPAI	Work productivity and activity impairment

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 efficacy and safety endpoints.

The content herein is based on Protocol 145-ADS-202 Version 2.0 (dated 23 Sep 2020) but may be amended based on future protocol amendments. In order to prevent bias from arising in the analysis, Version 1.0 of the SAP will be finalized and signed before the first analysis of study data. 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. Assessment Schedule

Assessment schedules for the donor subjects and recipient subjects are found in Table 1 and Table 2, respectively. These schedules review the reporting periods for the subjects for specific study visit data.

Table 1: Assessments for Donors

Study Visit	Screening[1]	Day 1 (Baseline)[2]	Day 1 (Plerixafor Dosing)[2]	Day 1 (MGTA-145 Dosing)[2]	Post-LA, Day 1	Day 3-4[3]	Week 1[4]	Month 1[4]	Month 6[4] End of Study
Study Day	**-30 - 1**	**1**	**1**	**1**	**1**	**3-4**	**7 (±2 days)**	**28 (±7 days)**	**180 (±14 days)**
Informed Consent	X								
Medical History and Medications	X	X							
Physical Exam, Height and Weight	X[5]	X[6]							
Vital Signs[7]	X		X[8]	X[9]	X				
KPS	X								
ECG	X								
CBC with differential and platelet count	X	X[6]			X			X	
Serum Creatinine & PT/PTT	X								
Serum Pregnancy Test[10]	X	X[10]							
Urinalysis	X								
Infectious disease markers[11]	X								
ABO/Rh Typing	X								
Chimerism	X								
Donor Survey Assessments[12]		X[12]			X	X		X	
ADA Sample		X[6]						X	
Flow cytometric analysis for CD34+ cells		X[6]		X[13]	X[14]				
Plerixafor Dosing			X[15]						
PK				X[16]					
MGTA-145 Infusion				X[17]					
Leukapheresis (LA)				X[18]					
Colony Forming Unit					X[14]				
Graft Immunophenotyping					X[14]				
Medical assessment (Virtual visit)							X	X	X
AEs/SAEs[19]	X								

1 Screening occurs up to 30 days prior to the start of stem cell mobilization; screening and determination of eligibility of unrelated donors is managed by Be The Match Donor Services.
2 If donor undergoes a second day of mobilization and apheresis, all Day 1 assessments must be repeated and donors will follow the same schedule (i.e., Day 7 will remain Day 7)
3 Donor survey visit only. CIBMTR SRG will contact donors.
4 Study site staff will contact donors at Week 1, Month 1, and Month 6 for virtual visits to assess donor medical condition. Donors will have blood work at Month 1.
5 Height only required at Screening
6 To be obtained prior to dosing
7 Vital signs include blood pressure, pulse, respiration rate and temperature
8 Vital signs and AEs monitored prior to plerixafor dosing; and 30 minutes (±10 minutes) and 60 minutes (±10 minutes)) following injection; and per local institutional guidelines
9 Vital signs and AEs monitored prior to MGTA-145 dosing; during infusion; and 30 minutes (±10 minutes), 60 minutes (±10 minutes, 120 minutes (±20 minutes), and 240 minutes (±20 minutes) following start of infusion
10 For females of childbearing potential. Day 1 test can be performed up to 48 hours prior to dosing
11 Infectious disease markers collected as required by FDA
12 CIBMTR SRG will contact donors to complete survey assessments. Baseline donor survey assessment to be administered up to 14 days prior to Day 1. See Table 9.7
13 To be collected after MGTA-145 infusion but prior to apheresis
14 Sample will come from the apheresis product
15 Plerixafor will be administered subcutaneously at 240 µg/kg/actual donor weight approximately 2 hours prior to planned leukapheresis
16 PK samples to be collected prior to MGTA-145 infusion (within 60 minutes of the start of the infusion) and 15-30 minutes after start of infusion
17 MGTA-145 administered at dose of 0.015 mg/kg via IV infusion over 3 minutes approximately 2 hours after plerixafor; the infusion time may range from 1 to 10 minutes if clinically indicated
18 As soon as feasible after MGTA-145 infusion (approximately 30 minutes post infusion), begin apheresis to process at least 4 times blood volume, but no more than the institutional limit.
19 SAEs to be reported from informed consent through 6 months post mobilization. AEs to be collected from informed consent through 72 hours post mobilization. See Table 9.8 of the protocol.

Table 2: Assessments for Recipients

Study Visit	Screening[1]	Day 0	Days 1-21[2]	Day 28 ± 3 days	Day 56 ± 7 days	Day 100 ± 7 days	Day 180 ± 14 days	Day 365 ± 14 days
Informed Consent	X							
Medical History and Medications[3]	X							
Physical Exam and Vital Signs[4]	X	X[5]	X	X	X	X	X	X
Height and Weight	X							
KPS	X						X	X
CBC with differential and platelet count	X	X[5]	X[6]	X[7]	X[8]	X[8]	X	X
Serum creatinine/AST/ALT/LDH/Total bilirubin	X	X[5]	X[9]	X	X	X	X	X
Serum Pregnancy Test	X[10]							
Urinalysis	X							
Infectious disease markers[11]	X[12]							
ABO/Rh Typing	X[12]							
Chimerism	X[12]			X		X	X	X
Disease specific staging and assessment	X							X
Assessment of HCT-CI score	X							
Bone marrow assessment	X[13]							X[14]
Allograft Infusion		X						
GVHD Assessment [15]			X	X	X	X	X	X
Immune Reconstitution				X		X	X	X
AEs/SAEs[16]	X							

1 Screening occurs up to 45 days prior to the start of the conditioning regimen
2 Visits to occur Day +1 through neutrophil recovery or Day +21 (whichever is first)
3 Includes most recent echocardiogram or MUGA and DLCO results obtained via standard of care
4 Vital signs include blood pressure, pulse, respiration rate, and temperature
5 To be obtained prior to receiving allograft
6 CBC with differential and platelet counts to be performed daily until neutrophil recovery occurs; in the event that neutrophil recovery occurs but not platelet recovery, a CBC should continue to be obtained daily until platelet count recovery or Day +21 (whichever is first)
7 If platelet and/or neutrophil recovery has not occurred at this time, CBC to be performed 3 times per week until recovery
8 If platelet and/or neutrophil recovery has not occurred at this time, CBC to be performed 2 times per week until recovery
9 Blood chemistries performed 2 times per week
10 For females of childbearing potential
11 Infectious disease markers collected as required by FDA
12 May be performed earlier than 45 days prior to the start of the conditioning regimen
13 Documentation of bone marrow assessment will be accepted within 45 days prior to the date of consent
14 Bone marrow aspirate and biopsy required if leukocyte count is outside of the normal laboratory range at the transplant center and/or platelet count is < 100 x 10^9/L
15 Recipients will be assessed for or the development of acute GVHD weekly at Days 1-100 and for chronic GVHD at Days 100, 180, and 365 and more frequently as clinically indicated
16 SAEs to be reported from Day 0 through 1-year post-transplant; Related AEs to be collected from Day 0 through 1-year post-transplant

3. Study Objectives and Design

3.1 Study Objectives

This study is a Phase II, open-label, multicenter prospective study of MGTA 145 + plerixafor mobilized HLA-matched sibling and matched unrelated donor allografts for myeloablative HSCT in recipients with hematological malignancies. The primary endpoint is the proportion of donors for whom a clinically adequate allograft (≥ 2.0 x 10^6 CD34+ cells/kg actual recipient weight) can be obtained within one apheresis collection.

3.1.1 Primary Objective

To determine the proportion of donors whose cells can be successfully mobilized and collected with a sufficient CD34+ cell dose using same-day, single-dose MGTA-145 + plerixafor as the mobilizing agents. Donor mobilization following MGTA-145 + plerixafor will be considered successful if ≥ 2.0 x 10^6 CD34+ cells/kg actual recipient weight are collected in one leukapheresis collection. All donors receiving MGTA 145 + plerixafor will be included in the analysis of the primary objective.

3.2 Secondary Objectives

3.2.1 Donor Related

3.2.1.1 To determine the proportion of donors whose cells can be successfully mobilized and collected with a target CD34+ cell dose of at least 4.0 x 10^6 CD34+ cells/kg actual recipient weight in one apheresis collection

3.2.1.2 To ascertain the incidence and severity of acute adverse events (AEs) before and during apheresis experienced by donors receiving MGTA-145 + plerixafor

3.2.1.3 To characterize the adverse effects experienced by donors receiving MGTA-145 + plerixafor

3.2.2 Recipient Related

3.2.2.1 To determine the incidence of and kinetics of neutrophil and platelet recovery after transplantation of hematopoietic cells mobilized with MGTA-145 + plerixafor

3.2.2.2 To determine the incidence of primary and secondary graft failure after transplantation of hematopoietic cells mobilized with MGTA-145 + plerixafor

3.2.2.3 To determine the incidence and severity of acute and chronic graft versus host disease (GVHD) after transplantation of hematopoietic cells mobilized with MGTA-145 + plerixafor

3.2.2.4 To determine the incidence of treatment-related mortality and disease relapse/progression after transplantation of hematopoietic cells mobilized with MGTA-145 + plerixafor

3.2.2.5 To determine the probability of progression-free and overall survival after transplantation of hematopoietic cells mobilized with MGTA 145 + plerixafor

3.2.2.6 To characterize the adverse effects experienced by recipients receiving grafts mobilized by MGTA-145 + plerixafor

3.3 Exploratory Objectives

3.3.1 Graft Related

3.3.1.1 To describe the cellular composition of allografts mobilized with MGTA-145 + plerixafor (stem/progenitor cells, T/B/NK-cells, colony forming units)

3.3.2 Recipient Related

3.3.2.1 To describe T-cell (CD3+) and myeloid chimerism after transplantation of hematopoietic cells mobilized with MGTA-145 + plerixafor

3.3.2.2 To assess the rate and quality of immune reconstitution as evidenced by peripheral blood immunophenotype after transplantation of hematopoietic cells mobilized with MGTA-145 + plerixafor

3.3.2.3 To determine the incidence of CMV reactivation after transplantation of hematopoietic cells mobilized with MGTA-145 + plerixafor in cytomegalovirus (CMV) seropositive recipients

3.3.3 Donor Related

3.3.3.1 To characterize the PK of MGTA-145

3.3.3.2 To assess treatment related Anti-drug Antibody (ADA)

3.3.3.3 To describe donation experience of PBSC donors mobilized with MGTA-145 + plerixafor

3.4 Study Design

This is a Phase II, open-label, multicenter, prospective study of MGTA-145 + plerixafor-mobilized HLA-matched sibling and matched unrelated donor allografts for myeloablative HSCT in recipients with hematological malignancies. This study will establish the safety and efficacy of the combination of MGTA-145 infusion and subcutaneous plerixafor for HSC mobilization. Donor-recipient pairs will be recruited for this study. Collection and transplant outcomes will be assessed. AEs will be reported using event terms and grading for severity per the Common Terminology Criteria for Adverse Events (CTCAE) version 5. This study is designed as a Simon minimax two-stage trial. The target enrollment is 28 donors receiving at least one dose of the combination regimen of MGTA-145 + plerixafor. The number of recipients may vary if the mobilization is unsuccessful in some donors. It is estimated that 18 months of accrual will be necessary to enroll the targeted sample size. The trial will remain open until the last recipient enrolled has been followed for one year. The primary endpoint of this study is the collection of sufficient CD34+ cells using MGTA-145 + plerixafor as the mobilizing agent. A donor is considered successful for this endpoint if ≥ 2.0×10^6 CD34+ cells/kg recipient weight are collected in one leukapheresis collection using MGTA-145 + plerixafor. One interim analysis for futility will be conducted after 13 donors are evaluable for the primary endpoint, based on the Simon two-stage design. There will be no interim analyses for efficacy. Safety monitoring rules related to donor and recipient AEs are in place as described further below.

3.5 Randomization

There will be no randomization in this study. At enrollment, each center will declare whether or not a recipient is intended to receive a myeloablative regimen.

4. Sample Size and Power Considerations

4.1 Sample Size and Power

The sample size for this study is 28 donors receiving at least one dose of the combination regimen of MGTA-145 + plerixafor. It is expected that 90% of donors treated with MGTA-145 + plerixafor will mobilize ≥ 2.0 x 10^6 CD34+ cells/kg within one leukapheresis collection. MGTA-145 + plerixafor is considered an unacceptable mobilizing agent if fewer than 70% of donors achieve this cell-dose threshold within one leukapheresis collection.

Using a two-stage Simon minimax design, assuming the true successful collection probability of 90%, 28 donors provide 85% power to reject the probability of successful collection of 70% or lower using a one-sided Type I error α=0.05. This is equivalent to testing the null hypothesis H_0: $p \leq 0.70$ against the alternative hypothesis H_1: $p > 0.70$ with 85% power to contrast a successful collection probability of 90% vs. 70%.

In this design, 13 donors are accrued in the first stage. If 9 or fewer donors mobilize sufficient CD34+ cells (at least 2.0 x 10^6 CD34+ cells/kg actual recipient weight at baseline) within one leukapheresis collection, the study will be terminated due to inadequate response. Otherwise, accrue 15 additional donors in stage 2. At the end of this stage, if at least 24 out of 28 donors successfully mobilize ≥ 2.0 x 10^6 CD34+ cells/kg within one leukapheresis collections, it will be concluded that MGTA-145 + plerixafor is effective and can be recommended for further investigation.

Table 3 shows the power to reject successful collection probability of 70% or lower for other plausible true probability of successful collection using the same design.

Table 3: Power and Operating Characteristics for Plausible values of Primary Endpoint

True probability of successful collection (p1)	Power
0.85	58%
0.90	85%
0.95	99%

4.2 Interim Analysis and Stopping Guidelines

There will be no interim analysis for efficacy. Interim analyses for futility will be induced by the two-stage design as described in section 3.4. Safety monitoring is described below.

Monitoring of Donor safety: Donors will be monitored closely for AEs up to 72 hours following infusion. If a CTCAE grade 3 or greater AE believed to be at least possibly related to plerixafor or MGTA-145 is observed in any of the donors, the AE must be entered in Medidata Rave® EDC application within 24 hours of learning of the event. This will notify the CIBMTR Medical Monitor who will consult with Magenta, the NMDP Protocol Chair and the DSMB Study Chairperson. At that time, a decision will be made as to whether the DSMB needs to meet to review the AE further and whether the study enrollment should be suspended, at least temporarily until the DSMB meeting. Refer to Section 9.8 of the protocol for Adverse Event Reporting Requirements.

Monitoring of Recipient safety: Three safety monitoring rules will be utilized to monitor recipient safety. The CIBMTR Medical Monitor will review the relevant data on a weekly basis to assess whether any stopping rules have been met. If a stopping rule as described below is triggered, the DSMB will be notified, and enrollment will be paused while the DSMB conducts a review of the safety data. The safety monitoring rules serve as a trigger for consultation with the DSMB for additional review and would not mandate automatic closure of study enrollment. Since all events being monitored are expected to occur with some frequency in the general transplant population, a sequential hypothesis testing framework will be utilized to identify whether the event rate is exceeding what is expected. The following safety endpoints and null hypothesis values will be used for sequential testing. The monitoring thresholds are calibrated so that the overall type 1 error rate is no more than 5% across all three of the sequential tests.

- The first monitoring rule is based on primary graft failure, where the null hypothesis is an incidence of graft failure no higher than 3% of recipients by Day 28.
- The second monitoring rule is based on treatment-related mortality (TRM), where the null hypothesis is an incidence of TRM no higher than 15% of recipients by Day 100.
- The third monitoring rule is based on grades 3-4 acute GVHD (aGVHD), where the null hypothesis is an incidence of grade 3-4 aGVHD no higher than 10% of recipients by Day 100.

Monitoring rules for recipients and their operating characteristics were obtained using the R package ‘clinfun’, using a 5% one-sided type I error rate across the sequential tests for each event. These are described in Table 4.

Table 4: Monitoring Guidelines among Recipients Receiving Allografts Successfully Mobilized by MGTA-145 + Plerixafor

Graft Failure at day 28						
Number of recipients (n)	2-9	10-23	24-28			
Stopping boundary (x)	2	3	4			
TRM by day 100						
Number of recipients (n)	4-8	9-11	12-15	16-19	20-24	25-28
Stopping boundary (x)	4	5	6	7	8	9
aGVHD grade 3-4						
Number of recipients (n)	3-6	7-11	12-17	18-22	23-28	
Stopping boundary (x)	3	4	5	6	7	

*Stopping guideline is triggered if ≥ x recipients out of n experience events described

The graft failure pausing rule has a 5% chance of being triggered if the true graft failure rate is 3%, and an 85% chance of being triggered if the true graft failure rate is 18%. If the true graft failure rate is 18%, the stopping rule will be triggered on average after approximately 13 subjects are evaluable for the graft failure endpoint. Similarly, the TRM pausing rule has a 5% chance of being triggered if the true TRM rate is 15%, and an 89% chance of being triggered if the true TRM rate is 40%. If the true TRM rate is 40%, the stopping rule will be triggered on average after approximately 14 subjects are evaluable for the TRM endpoint. Finally, the grade 3-4 aGVHD pausing rule has a 5% chance of being triggered if the true rate is 10%, and an 83% chance of being triggered if the true rate is 30%. If the true grade 3-4 aGVHD rate is 30%, the stopping rule will be triggered on average after approximately 15 subjects are evaluable for the grade 3-4 aGVHD endpoint.

Triggering a safety monitoring rule does not mean discontinuation from the study for subjects currently enrolled, and remaining study procedures should be completed as indicated by the study protocol, especially for efficacy and safety endpoints, namely, to capture AE, SAE, and unanticipated problems (UPs). Refer to Appendix G and Appendix H of the protocol for more information. If a clinically significant finding is identified after enrollment, the investigator or qualified designee will determine if any change in subject management is needed.

5. Analysis Populations

A subject is defined as completing the study based on these criteria:

- A donor subject who receives treatment and completes the 6-month follow-up visit or contact
- A recipient subject who receives treatment and completes the Day 100 follow-up visit or contact

5.1 Donor treated Population:

Includes all donors receiving any exposure to both parts of the combination regimen of MGTA-145 + plerixafor. This population will be used for the primary donor efficacy analysis and for safety analyses of the donor.

5.2 Plerixafor-only Population:

Includes all donors receiving exposure to plerixafor who did not receive any MGTA-145. This population will be followed for safety purposes.

5.3 Recipient Analysis Population:

Includes all enrolled subjects receiving a MGTA-145 + plerixafor-mobilized allograft. This will be used for the primary analysis of the recipient outcomes

6. Outcomes

6.1 Primary Endpoint

The primary endpoint is defined as achieving a clinically adequate allograft (a graft that contains ≥ 2.0 x 10^6 CD34+ cells/kg recipient weight collected) within one apheresis collection.

6.2 Secondary Endpoints

6.2.1 Clinically desirable allograft in one apheresis collection

This secondary endpoint is defined as achieving a graft that contains ≥ 4.0 x 10^6 CD34+ cells/kg recipient weight collected in one apheresis session.

6.2.2 Clinically adequate allograft overall

This secondary endpoint is defined as achieving a graft that contains ≥ 2.0 x 10^6 CD34+ cells/kg recipient weight collected across all apheresis sessions.

6.2.3 Assessment of AEs in Donors

Assessment of AEs in donors will be done during the infusion and 30 minutes (±10 minutes), 60 minutes (±10 minutes) after the administration of plerixafor and 30 minutes (±10 minutes), 60 minutes (±10 minutes, 120 minutes (±20 minutes), and 240 minutes (±20 minutes) following start of MGTA-145 infusion. In addition to monitoring the donor on the days of collection, donors will be contacted at Week 1, Month 1, and Month 6 to assess the donor's medical condition.

Back pain is an AE of special interest, and information on the date and time of onset, date and time of resolution, concomitant medications and supportive care used to treat the back pain, action taken with study drug, peak severity of the pain on a 0-10 numeric rating scale, and relationship to study drug will be assessed and documented in Medidata Rave® EDC application.

6.2.4 Assessment of AEs related to Allograft

Assessment of AEs related to the allograft will include measurement of the recipient's blood pressure, pulse, respiration rate and temperature one hour prior to the allograft infusion and then approximately 15 minutes, 30 minutes, 1 hour, 2 hours, and 4 hours post infusion.

6.2.5 Neutrophil Recovery

Time to neutrophil recovery is measured by determining the first of 3 consecutive daily measurements of neutrophil count ≥ 0.5 $x10^9$/L following conditioning regimen induced nadir. Although unlikely, recipients who do not experience a drop in the neutrophil count < 0.5 $x10^9$/L will not be evaluable for neutrophil recovery but will be evaluable for graft failure based on the degree of donor cell chimerism at Day +28.

6.2.6 Platelet Recovery

Platelet recovery is defined as the first day when the platelet count is ≥ 20 × 10^9/L measured by at least 3 consecutive laboratory values that show that level was achieved and maintained. The recipient should not have any platelet transfusions in the 7 days prior to the date selected for achieving ≥20 × 10^9/L and the date should be the first of 3 consecutive lab values tested on different days.

6.2.7 Graft Failure

Primary graft failure is defined as failure to experience neutrophil recovery by Day +28 following a conditioning regimen induced neutrophil nadir < 0.5 $x10^9$/L. For recipients not experiencing a fall in the neutrophil count to < 0.5 $x10^9$/L following conditioning, graft failure will be defined as < 5% donor cell chimerism in the myeloid and CD3+ cell compartments by Day +28. Secondary graft failure will be defined as a fall in the neutrophil count after primary engraftment to < 0.5 $x10^9$/L sustained for more than three days that cannot be attributed to other causes such as drugs, infection, GVHD, etc., is not responsive to G-CSF or GM-CSF and is associated with a fall in donor chimerism to < 5%. Fall in donor chimerism to less than 5% following primary engraftment will also be considered secondary graft failure even in the absence of a fall in the peripheral blood counts.

6.2.8 Acute GVHD

Mount Sinai Acute GVHD International Consortium (MAGIC) clinical criteria (see Appendix C of the protocol) and histological grading of skin, liver or gastrointestinal pathology and confidence levels where possible will be used to establish and grade acute GVHD. In the first 100 days after transplantation recipients will be assessed by a transplant physician or designee (e.g., mid-level provider) for the development of acute GVHD approximately weekly.

6.2.9 Chronic GVHD

Chronic GVHD will be diagnosed and graded according to the NIH consensus criteria (Appendix D of the protocol) and treated with standard or experimental immunosuppressive therapy as deemed appropriate by the transplant center. Recipient

development of chronic GVHD will be reported at Days 100, 180, and 365, and more frequently if clinically indicated.

6.2.10 Treatment-Related Mortality (TRM)

TRM is defined as death in recipients without relapse or progression of their disease.

6.2.11 Overall Survival

Survival will be measured by assessing if the recipient remains alive by visual observation or telephone call.

6.2.12 Determination of Relapse or Disease Progression

Disease relapse occurs in subjects who entered HSCT in complete remission (CR); progression occurs in those with existing disease at transplant who meet criteria for progressive disease post-HSCT. A recipient will be considered relapsed when there is a recurrence of the original malignant disease after transplantation. This will be determined locally by tests and procedures in place at each participating institution. Date of relapse/progression is defined as the date at which the first observation of hematologic, radiographic, or cytogenetic changes which herald progression/relapse is made. See Appendix E of the protocol for definitions.

6.2.13 Progression-Free Survival

Death or relapse/disease progression will be an event, and the time to the event will be determined as the time from transplant to the first event. Subjects alive and relapse/progression-free will be censored at last contact.

6.3 Exploratory Endpoints

6.3.1 Graft composition

Graft composition will be defined phenotypically by molecular cell markers to stratify leukocyte subsets.

6.3.2 Colony Formation Assay

Colony formation assay is defined as number of functional progenitor cells that form colonies in methylcellulose.

6.3.3 Chimerism

Chimerism is defined as leukocyte subset percentages that are donor vs. recipient over time.

6.3.4 Immune Reconstitution

Immune reconstitution is defined as counts of leukocyte subsets over time, with respect to normal ranges.

6.3.5 CMV Reactivation

CMV reactivation will be defined as a positive test for CMV viremia as determined by an antigenemia assay or quantitative PCR (whichever is in use at each individual institution) that results in the administration of antiviral treatment directed against CMV.

6.3.6 MGTA-145 PK

A validated assay will be used to determine MGTA-145 plasma concentrations. The exact date and time (hours and minutes) of the sampling time and infusion start and end times will be recorded.

6.3.7 Immunogenicity

A validated assay to determine the formation of ADA will be used.

6.3.8 Donor Experience

Donor survey assessments include the Brief Pain Inventory, six PROMIS domains (Fatigue, Gastrointestinal (Diarrhea), Sleep disturbance, Physical function, Anxiety and Depression), EQ-5D, Work Productivity and Activity Impairment (WPAI), a Healthcare Resource Use (HRU) questionnaire, and a Donor Experience questionnaire. These will be collected according to the following schedule.

Table 5: Schedule of Donor Survey Assessments

Survey[1]	Items	Minutes to complete	Baseline Day -14 to Day 0	Post-treatment Day 1[2, 3]	Day 3-4[4]	Month 1 Day 28 (+/-7)
Brief Pain Inventory	15	5	X	X	X	X
PROMIS Fatigue	8	1-2	X	X	X	X
PROMIS (Gastrointestinal, Diarrhea)	6	1-2	X	X	X	X
PROMIS Phys. Function	10	1-2	X	X	X	X
PROMIS Anxiety	4	1-2	X	X		X
PROMIS Depression	4	1-2	X	X		X
PROMIS Sleep disturbance	4	1-2	X	X	X	X
EQ-5D	5	1	X	X	X	X
Work Productivity and Activity Impairment	6	1			X	
Healthcare Resource Use (HRU) utilization	6	1-2			X	
Donor Experience	6	1-2				X
Total items			*46-86*	*46-86*	*50-74*	*52-92*
Total minutes			*12-18*	*12-18*	*13-17*	*14-21*

1- To be completed in the order listed
2- Repeat if 2 days of mobilization and donation
3- To be completed from 60 minutes after apheresis is completed until the end of that day (e.g., midnight)
4- 72-96 hours after last donation

7. Statistical Methodology

7.1 General Guidelines

Due to limited sample size from early termination of the study, all analyses will be summarized using data listings.

The study day for most donor assessments will be computed in reference to the first day of mobilization (Day 1), which is also the day the subject is scheduled to receive both plerixafor and MGTA-145. The study day for recipient assessments will be computed in reference to the infusion of the allograft product (Day 0). Baseline values are defined as the last available measurements before these two study days, respectively.

All data listings that include an event date will contain a relative study day. For the purpose of this analysis, relative study day is defined as:

- Donor relative Day 1: first day of plerixafor and MGTA-145 dosing
- Recipient relative Day 0: first day of HSCT

All data processing, summarization, and analyses will be performed using SAS Version 9.4 or higher and 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.

7.2 Handling of Missing and Incomplete Data

Data imputation will not be performed since this is a small phase II trial.

7.3 Multiple Comparisons

No formal multiplicity adjustment is being used as this is a single arm phase II trial.

7.4 Demographics and Disposition

7.4.1 Demographic and Baseline Characteristics

Demographic and baseline characteristics will be summarized for all donors and recipients using data listings. Donor characteristics to be examined using the Donor Treated Population are: age, gender, weight, race/ethnicity, CMV status. Recipient characteristics to be examined using the Recipient Analysis Population are: age, gender, weight, race/ethnicity, KPS, disease status at transplant, time from diagnosis to transplantation, cytogenetics at diagnosis, conditioning regimen, GVHD prophylaxis, graft source and recipient CMV status.

7.4.2 Participant Disposition

The data listings of subject disposition for the donor populations will include:

- Donors in the Donor Treated population

- Donors in the Plerixafor-only Population
- Donor Treated population withdrawn from study after initiating study drug
- Donor Treated population who completed planned study follow-up
- Reasons for donors withdrawing from the study.

The data listings of subject disposition for the recipient populations will include:

- Recipients in the Recipient Analysis population
- Recipient Analysis population withdrawn from study after receiving a MGTA-145+ plerixafor mobilized allograft
- Recipient Analysis population who completed planned study follow-up
- Reasons for recipients withdrawing from the study.

7.4.3 Protocol Deviations

7.4.3.1 Important Protocol Deviations

A listing of all important protocol deviations will be provided according to ICH E3: Guideline for Industry Structure and Content of Clinical Study Reports.

7.5 Primary Endpoint Analysis

The primary endpoint of this study is the collection of a clinically adequate allograft in one apheresis session. A donor is considered successful for this endpoint if ≥ 2.0 x 10^6 CD34+ cells/kg actual recipient weight are collected in one leukapheresis collection using MGTA-145 + plerixafor.

A data listing of CD34+ cell counts will be provided.

7.5.1 Secondary Endpoints

SAFETY ENDPOINTS

Incidence of Donor AEs

Adverse Events will be provided in a listing.

Incidence of AEs related to the Allograft

Type and severity of AEs experienced by the recipient related to the allograft will be listed in the recipient analysis population. Safety data will be coded using Medical Dictionary for Regulatory Activities (MeDRA) Coding Version 23.1 or above.

EFFICACY ENDPOINTS

Clinically desirable allograft in one apheresis collection

A data listing of this endpoint will be provided.

Clinically adequate allograft overall

A data listing of this endpoint will be provided.

Neutrophil Recovery Status and Time to Neutrophil Recovery

A data listing of these endpoints will be provided.

Platelet Recovery and Time to Platelet Recovery

A data listing of these endpoints will be provided.

Primary and Secondary Graft Failure

A data listing of this endpoint will be provided.

Acute Graft versus Host Disease of Grades 2-4 and 3-4

A data listing of this endpoint will be provided.

Chronic Graft versus Host Disease

A data listing of this endpoint will be provided.

Relapse/Progression

A data listing of relapse/progression status will be provided.

Time to Relapse/Progression

The event is relapse/progression or death. The time to this event is the time from transplant to relapse/progression, death, lost to follow-up (censored), or end of study (censored) whichever comes first, where the clock starts at Day 0. A data listing of this endpoint will be provided.

Overall Survival and Time to Death

The event is death from any cause. The time to this event is the time from transplant to death, lost to follow-up (censored), or end of study (censored) whichever comes first, where the clock starts at Day 0. A data listing of this endpoint will be provided.

7.5.2 Exploratory Endpoints

Donor Chimerism

Donor and host cells will be measured at Day 28, 100, 180 and at one-year post-transplant. The degree of donor chimerism will be provided for each donor at each time point in a table listing.

Colony Formation

Number of functional progenitor cells that form in methylcellulose (defined as total CFU-GM, CFU-GEMM, CFU-E, and BFU-E) will be measured. Data will be shown for each donor in a data listing.

Immunologic Reconstitution

Immune reconstitution assays which will include a quantitation of absolute numbers of CD3+, CD3+CD4+, CD3+CD8+, CD19+ and CD3-CD56+ cells in recipients on Day 28, 100, 180 and at one-year post-transplant. These data will be shown for each donor at each time point in a data listing.

Incidence of CMV Reactivation

A data listing of this endpoint will be provided

Cellular Composition of Allografts

The proportions of CD34+, CD3+, CD3+CD8+, CD3+CD4+, CD19+, CD34+C90+CD45RA- and CD3-CD56+ cells in the allografts collected will be shown for each donor using a data listing.

PK Analysis

Individual Concentration-time parameters will be listed for each donor.

Immunogenicity

A data listing of the number and percentage of positive ADAs will be provided for each donor.

Donor Survey Assessments

Donor survey assessments (WPAI, HRU, Donor experience surveys, PROMIS and EQ-5D) will be described using data listings.

8. Changes to Protocol-specified Analysis

The trial was stopped early due to sponsor decision to terminate the study with only 4 donors and 3 recipients enrolled. The pre-specified analysis in the original version of the SAP will not be performed. The analysis will be performed in accordance with this updated SAP version.

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.

Kalbfleisch, J. D. and Prentice, R. L. (1980). The Statistical Analysis of Failure Time Data. New York: John Wiley & Sons.

ICH Harmonised Tripartite Guideline: Structure and Content of Clinical Study Reports E3. FDA, United States - Implemented; Date: 1 July 1996; Reference: Vol. 61, p. 37320

APPENDIX A – TABLES AND FIGURES

Tables:

Figures:

No table of figures entries found.

Table 1: Subject Disposition

Subject ID discontinued	Reason for discontinuing
XXXXXX	XXXXXX
XXXXXX	XXXXXX
XXXXXX	XXXXXX
XXXXXX	XXXXXX
XXXXXX	XXXXXX

Table 2: Listing of Demographic and Baseline Characteristics of Donors

Variable	M145-1-D	M145-2-D	M145-3-D	M145-4-D
Gender	XX	XX	XX	XX
Ethnicity	XX	XX	XX	XX
Race	XX	XX	XX	XX
Age (years)	XX.XX	XX.XX	XX.XX	XX.XX
Weight (kg)	XX.XX	XX.XX	XX.XX	XX.XX
CMV Status	XX	XX	XX	XX

Table 3: Listing of Demographic and Baseline Characteristics of Recipients

Variable	M145-1-R	M145-2-R	M145-3-R
Gender	XX	XX	XX
Ethnicity	XX	XX	XX
Race	XX	XX	XX
Age (years)	XX.XX	XX.XX	XX.XX
Weight (kg)	XX.XX	XX.XX	XX.XX
Karnofsky Performance Score	XX	XX	XX
Primary Disease	XX	XX	XX
Primary Disease Status at Transplant	XX	XX	XX
Time from Disease Diagnosis to Transplant	XX	XX	XX
Cytogenetics at Dx	XX	XX	XX
Disease Risk Index	XX	XX	XX
HCT-CI	XX	XX	XX
Donor Type	XX	XX	XX
Recipient CMV Status	XX	XX	XX
GVHD Prophylaxis	XX	XX	XX
Graft Source	XX	XX	XX
Conditioning Regimen	XX	XX	XX

Table 4: Listing of Primary and Secondary Endpoints: Cell Counts of Allograft

	M145-1-D	M145-2-D	M145-3-D	M145-4-D
Cells collected in apheresis session 1 (cells)	XX	XX	XX	XX

	M145-1-D	M145-2-D	M145-3-D	M145-4-D
Quality of cell dose apheresis session 1	Clinically desirable/ Clinically adequate/ Clinically undesirable	Clinically desirable/ Clinically adequate/ Clinically undesirable	Clinically desirable/ Clinically adequate/ Clinically undesirable	Clinically desirable/ Clinically adequate/ Clinically undesirable
Cells collected in all apheresis sessions (cells)	XX	XX	XX	XX
Quality of cell dose for all apheresis sessions	Clinically desirable/ Clinically adequate/ Clinically undesirable	Clinically desirable/ Clinically adequate/ Clinically undesirable	Clinically desirable/ Clinically adequate/ Clinically undesirable	Clinically desirable/ Clinically adequate/ Clinically undesirable

Table 5: Adverse Event Listing Following Mobilization in Donor Treated Population

ID	System Organ Class /Preferred Term /Verbatim Term	CTCAE Grade	AE Outcome	AE Action Taken	TEAE	SAE	AESI	Related AE	AE Start Date/ AE End Date
M145-X-D	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy
	…	…	…	…	…	…	…	…	…
	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy
…	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy
	…	…	…	…	…	…	…	…	…
	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy
M145-X-D	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy
	…	…	…	…	…	…	…	…	…
	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy

Table 6: Adverse Event Listing Following Mobilization in Plerixafor Only Population

ID	System Organ Class /Preferred Term /Verbatim Term	CTCAE Grade	AE Outcome	AE Action Taken	TEAE	SAE	AESI	Related AE	AE Start Date/ AE End Date
M145-X-D	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy
	…	…	…	…	…	…	…	…	…
	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy
…	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy
	…	…	…	…	…	…	…	…	…
	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy
M145-X-D	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy
	…	…	…	…	…	…	…	…	…
	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy

Table 7: Listing of Recipient Adverse Events Reported Through 1 Year Post Infusion

ID	System Organ Class /Preferred Term /Verbatim Term	CTCAE Grade	AE Outcome	AE Action Taken	TEAE	SAE	AESI	Related AE	AE Start Date/ AE End Date	Withdrawal due to AEs/SAEs
M145-X-R	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy	Yes/No
	…	…	…	…	…	…	…	…	…	…
	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy	Yes/No
…	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy	Yes/No
	…	…	…	…	…	…	…	…	…	…
	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy	Yes/No
M145-X-R	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy	Yes/No
	…	…	…	…	…	…	…	…	…	…
	SOC X /Category X /XXXX	X	XXXXXXX	XXXXXX	Yes/No	Yes/No	Yes/No	Yes/No	ddmmmyyyy/ ddmmmyyyy	Yes/No

Table 8: Listing of Efficacy Endpoints of Recipients

Outcome		M145-1-R	M145-2-R	M145-3-R
Neutrophil recovery	**Status**	YES/NO	YES/NO	YES/NO
	Time to recovery in days	XX	XX	XX
Platelet recovery	**Status**	YES/NO	YES/NO	YES/NO
	Time to recovery in days	XX	XX	XX
Chimerism	**Day 28**	Full/Mixed/Graft rejection/Death prior to assessment	Full/Mixed/Graft rejection/Death prior to assessment	Full/Mixed/Graft rejection/Death prior to assessment
	Day 100	Full/Mixed/Graft rejection/Death prior to assessment	Full/Mixed/Graft rejection/Death prior to assessment	Full/Mixed/Graft rejection/Death prior to assessment
	Day 180	Full/Mixed/Graft rejection/Death prior to assessment	Full/Mixed/Graft rejection/Death prior to assessment	Full/Mixed/Graft rejection/Death prior to assessment
	Day 365	Full/Mixed/Graft rejection/Death prior to assessment	Full/Mixed/Graft rejection/Death prior to assessment	Full/Mixed/Graft rejection/Death prior to assessment
Graft failure at day 28	**Status**	Primary/Secondary/No	Primary/Secondary/No	Primary/Secondary/No

Outcome		M145-1-R	M145-2-R	M145-3-R
aGVHD	Maximum grade	Grade II/III/IV	Grade I/III/IV	Grade II/III/IV
	Time to onset in days	XX	XX	XX
cGVHD	Grade	Grade II/III/IV	Grade I/III/IV	Grade II/III/IV
	Time to onset in days	XX	XX	XX
CMV reactivation	Status	YES/NO	YES/NO	YES/NO
	Time to onset in days	XX	XX	XX
Relapse	Status	YES/NO	YES/NO	YES/NO
	Time to relapse in days	XX	XX	XX
Survival	Status	Alive/Dead	Alive/Dead	Alive/Dead
	Time to death of last contact in days	XX	XX	XX

Chimerism: Full (>95% Donor Cells) Mixed (5-95% Donor Cells)/ Graft Rejection (<5% Donor Cells)/ Death Prior To Assessment)

Table 9: Listing of Colony Formation (Donor population)

Measurements	M145-1-D	M145-2-D	M145-3-D	M145-4-D
Total CFU-GM	XX	XX	XX	XX
CFU-GEMM	XX	XX	XX	XX
CFU-E	XX	XX	XX	XX
BFU-E	XX	XX	XX	XX

Table 10: Listing of Immunologic Reconstitution (Recipient population)

Measurement	Assessment Time	Counts		
		M145-1-R	M145-2-R	M145-3-R
CD3+	Day 28	XX	XX	XX
	Day 100	XX	XX	XX
	Day 180	XX	XX	XX
	Day 365	XX	XX	XX
CD3+CD4+	Day 28	XX	XX	XX
	Day 100	XX	XX	XX
	Day 180	XX	XX	XX
	Day 365	XX	XX	XX
CD3+CD8+	Day 28	XX	XX	XX
	Day 100	XX	XX	XX
	Day 180	XX	XX	XX
	Day 365	XX	XX	XX
CD19+	Day 28	XX	XX	XX
	Day 100	XX	XX	XX
	Day 180	XX	XX	XX
	Day 365	XX	XX	XX
CD3-CD56+	Day 28	XX	XX	XX
	Day 100	XX	XX	XX
	Day 180	XX	XX	XX
	Day 365	XX	XX	XX

Table 11: Listing of Cellular Composition of Allografts (Recipient Analysis Population)

Cell subset	Proportion (%)		
	M145-1-R	M145-2-R	M145-3-R
CD34+	XX.XX	XX.XX	XX.XX
CD3+	XX.XX	XX.XX	XX.XX
CD3+CD8+	XX.XX	XX.XX	XX.XX
CD3+CD4+	XX.XX	XX.XX	XX.XX
CD19+	XX.XX	XX.XX	XX.XX
CD34+CD90+CD45RA-	XX.XX	XX.XX	XX.XX
CD3-CD56+	XX.XX	XX.XX	XX.XX

Table 12: Listing of PK Analysis (Donor treated population)

Timepoint	Concentration parameter				
	Parameter	M145-1-D	M145-2-D	M145-3-D	M145-4-D
Prior to MGTA-145 infusion	1	XX.XX	XX.XX	XX.XX	XX.XX
	…	…	…	…	…
	k	XX.XX	XX.XX	XX.XX	XX.XX
After MGTA-145 infusion	1	XX.XX	XX.XX	XX.XX	XX.XX
	…	…	…	…	…
	k	XX.XX	XX.XX	XX.XX	XX.XX

Table 13: Listing of Immunogenicity (Donor Treated Population)

Parameter	Counts			
	M145-1-D	M145-2-D	M145-3-D	M145-4-D
Number of positive ADAs	XX	XX	XX	XX
% of Positive ADAs	XX	XX	XX	XX

Table 14: Donor Survey Assessments

Assessment	Assessment Time	Total Score			
		M145-1-D	M145-2-D	M145-3-D	M145-4-D
BPI	Screening	XX	XX	XX	XX
	Day 1	XX	XX	XX	XX
	Day 2[1]	XX	XX	XX	XX
	Day 3-4	XX	XX	XX	XX
	Day 28	XX	XX	XX	XX
	Screening	XX	XX	XX	XX

Assessment	Assessment Time	Total Score			
		M145-1-D	M145-2-D	M145-3-D	M145-4-D
PROMIS GI symptoms	Day 1	XX	XX	XX	XX
	Day 2[1]	XX	XX	XX	XX
	Day 3-4	XX	XX	XX	XX
	Day 28	XX	XX	XX	XX
PROMIS Fatigue	Screening	XX	XX	XX	XX
	Day 1	XX	XX	XX	XX
	Day 2[1]	XX	XX	XX	XX
	Day 3-4	XX	XX	XX	XX
	Day 28	XX	XX	XX	XX
PROMIS Sleep disturbance	Screening	XX	XX	XX	XX
	Day 1	XX	XX	XX	XX
	Day 2[1]	XX	XX	XX	XX
	Day 3-4	XX	XX	XX	XX
	Day 28	XX	XX	XX	XX
PROMIS Physical function	Screening	XX	XX	XX	XX
	Day 1	XX	XX	XX	XX
	Day 2[1]	XX	XX	XX	XX
	Day 3-4	XX	XX	XX	XX
	Day 28	XX	XX	XX	XX
PROMIS Anxiety	Screening	XX	XX	XX	XX
	Day 1	XX	XX	XX	XX
	Day 2[1]	XX	XX	XX	XX
	Day 28	XX	XX	XX	XX
PROMIS Depression	Screening	XX	XX	XX	XX
	Day 1	XX	XX	XX	XX
	Day 2[1]	XX	XX	XX	XX
	Day 28	XX	XX	XX	XX
EQ-5D	Screening	XX	XX	XX	XX
	Day 1	XX	XX	XX	XX
	Day 2[1]	XX	XX	XX	XX
	Day 3-4	XX	XX	XX	XX
	Day 28	XX	XX	XX	XX
WPAI	Day 3-4	XX	XX	XX	XX
HRU	Day 3-4	XX	XX	XX	XX
Donor experience	Day 28	XX	XX	XX	XX

[1]Only applies to those who had a second day of MGTA-145 dosing and apheresis.

Table 15: Listing of Significant Important Protocol Deviations

Subject ID	Deviation Category	Deviation Timepoint	Deviation Description