SPONSOR:

Magenta

PROTOCOL NUMBER:

IMD-001

STATISTICAL ANALYSIS PLAN

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[redacted]	[redacted]

1 Cover and signature pages

Sponsor:	Magenta
Protocol Number:	IMD-001
Study Title:	A Phase 2, Single-arm, Open-label Study to Evaluate the Safety and Efficacy of MGTA-456 in Patients with Inherited Metabolic Disorders (IMD) Undergoing Hematopoietic Stem Cell (HSC) Transplantation (HSCT)
Document Version No	Final 4.0

We, the undersigned, confirm that we have read, understood and agree to the content of this document and hereby authorise its approval.

Statistician

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Client Representative

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	[redacted]		[redacted]

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2 List of Abbreviations and Definition of Terms

ABC	Adaptive Behavior Composite
AE	Adverse Event
aGVHD	Acute graft versus host disease
ANC	Absolute neutrophil count
ALC	Absolute lymphocyte count
ASR	Annual Safety Report
ATC	Anatomical Therapeutic Chemical
ATG	Antithymocyte globulin
AUCinf	Area under the plasma concentration-time curve from time zero to Infinity
AUClast	Area under the plasma concentration-time curve from time zero to time of last measurable concentration
BU	Busulfan
cALD	Cerebral adrenoleukodystrophy
CBU	Cord blood unit
cGVHD	Chronic graft versus host disease
CRF	Case Report Form
CSF	Cerebrospinal fluid
CTCAE	Common Terminology Criteria for Adverse Events
CY	Cyclophosphamide
DLCO	Diffusing capacity of lung for carbon monoxide
DMC	Data Monitoring Committee
ECG	Electrocardiogram
ECHO	Echocardiogram
eCRF	Electronic Case Report Form
EFS	Event free survival
FAS	Full analysis set
FEV_1	Forced expiratory volume
FLU	Fludarabine
FVC	Forced vital capacity

G-CSF	Granulocyte-colony stimulating factor
GCP	Good clinical practice
GLD	Globoid cell leukodystrophy
GVHD	Graft versus host disease
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HLA	Human leukocyte antigen
HSC	Hematopoietic Stem Cell
HSCT	Hematopoietic Stem Cell Transplantation
ICF	Informed consent form
ICH	International Conference for Harmonisation
IV	Intravenous
IMD	Inherited Metabolic Disorders
IND	Investigational New Drug
LLOQ	Lower limit of quantification
LVEF	Left ventricular ejection fraction
LVSF	Left ventricular shortening fraction
MAC	Myeloablative conditioning
Magenta	Magenta Therapeutics, Inc.
MedDRA	Medical Dictionary for Regulatory Activities
MFI	Mean fluorescence intensity
MLD	Metachromatic leukodystrophy
MRI	Magnetic resonance imaging
MPS-HAQ	Mucopolysaccharidosis-Health Assessment Questionnaire
NFS	Cerebral ALD Neurologic Function Scale Score
OS	Overall survival
PD	Pharmacodynamic
PDCF	Protocol deviation criteria form
PDvs	Protocol deviations
PK	Pharmacokinetic
PT	Preferred Term
SAE	Serious adverse event

SAP	Statistical analysis plan
SEM	Standard error mean
SI	Système International
SOC	System Organ Class
TEAE	Treatment-emergent adverse event
TFL(s)	Table(s), figure(s), listing(s)
TNC	Total nucleated cell
TRM	Transplant-related mortality
UCB	Umbilical cord blood
UCBT	Umbilical cord blood transplant
VLCFA	Very-long-chain fatty acid
WAIS	Wechsler Adult Intelligence Scale
WHODDE	World Health Organization drug dictionary
WISC	Wechsler Intelligence Score for Children
WPPSI	Wechsler Preschool and Primary Scale of Intelligence

3 Introduction

The purpose of this document is to describe the statistical methods, data derivations and data summaries to be employed in the analysis of study IMD-001 for Magenta in MGTA-456 treatment in patients with selected inherited metabolic disorders (IMD) undergoing hematopoietic stem cell (HSC) transplantation (HSCT).

The preparation of this statistical analysis plan (SAP) has been based on International Conference on Harmonisation (ICH) E3 and E9 Guidelines and in reference to Protocol IMD-001 Version 8.0 (10 January 2020).

4 Study Objectives

PRIMARY OBJECTIVES

To evaluate the effect of MGTA-456 on the rate and incidence of neutrophil recovery in patients with IMD undergoing HSCT.

SECONDARY OBJECTIVES

- To evaluate the safety of MGTA-456 in patients with IMD undergoing HSCT;
- To characterize engraftment following transplantation with MGTA-456 and to evaluate the effect of MGTA-456 on chimerism in the CD3 and CD33/66 (or CD15) hematopoietic compartments;
- To assess the incidence of acute and chronic graft versus host disease (GVHD);
- To assess transplant-related mortality (the incidence of TRM).

EXPLORATORY OBJECTIVES

- To assess disease-specific enzyme activity/protein level;
- To investigate plasma and cerebrospinal fluid (CSF) biomarkers for their potential predictive value for clinical outcome in IMD;
- To investigate immune reconstitution and immunoglobulin levels after transplantation with MGTA-456;
- To assess resource utilization;
- To assess the exposure to the manufacturing reagent LHD221 co-infused with the stem cells in this population;
- To assess neurodevelopment outcome;
- To assess peripheral neuropathy over time on patients with metachromatic leukodystrophy (MLD) and globoid cell leukodystrophy (GLD).

5 Study Design

5.1 STUDY DESIGN AND POPULATION

This is a Phase 2, open-label, single-arm study in which patients with IMDs will receive MGTA-456 as a stand-alone HSC graft after myeloablative conditioning (MAC). Approximately 12 patients will be enrolled into 1 of 2 sequential cohorts, with the option to include up to approximately 15 additional patients in an expansion cohort following dosing of Cohort 2.

The study population is children age < 2.5 years with Hurler syndrome, age 2-17 (inclusive) years with cerebral adrenoleukodystrophy (cALD), age <16 years with metachromatic leukodystrophy (MLD) and age ≤ 10 years with globoid cell leukodystrophy (GLD) (also referred to as Krabbe). Age ranges refer to time of consent. In addition:

- children (aged >6 months and <16 years) with IMD (Hurler syndrome, cALD, MLD or GLD) were eligible to enroll prior to Protocol Amendment 8
- children ≤6 months of age were eligible to enroll prior to Protocol Amendment 6

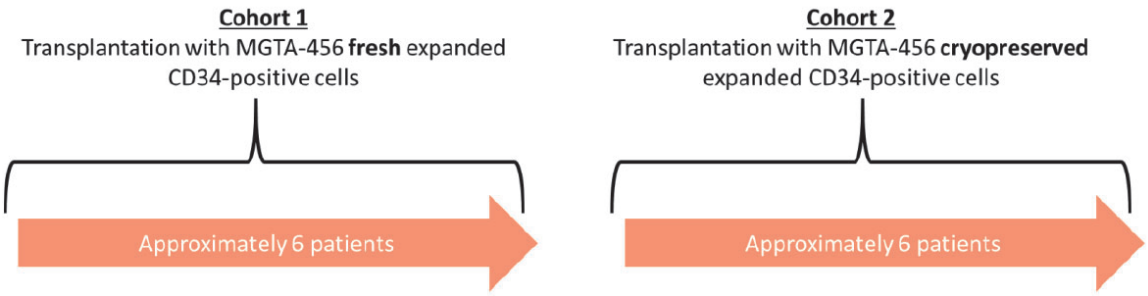
and those patients will continue to be followed in the study.

Cohort 1 will comprise ~6 patients who will receive MGTA-456 fresh expanded CD34+ cells and Cohort 2 will comprise ~6 patients who will receive MGTA-456 cryopreserved expanded CD34+ cells. The first 6 evaluable patients with IMD will be enrolled in Cohort 1, while the next approximately 6 patients with IMD will be enrolled in Cohort 2. For the study to proceed from Cohort 1 to Cohort 2, none of the stopping rules regarding excessive graft failure, TRM, or Grade 3 to 4 acute GVHD (aGVHD) should be met (see Section 6.4 of the study protocol). Up to approximately 15 additional patients may be included in an expansion cohort following dosing of the initial 6 patients in Cohort 2, based on the recommendation of the Data Monitoring Committee (DMC). These patients will receive cryopreserved MGTA-456 product.

All patients will be followed up to the end of study visit at 1 year after post-transplant.

An overview of the study design is presented in Figure 1 below.

Figure 1. Study Design



Note: Up to approximately 15 additional patients may be included in the study following dosing of Cohort 2 and will receive cryopreserved MGTA-456 product.

After completing the study (end of study visit at 1 year after post-transplant), patients may be transferred to a separate long-term follow-up study, if eligible and willing (after signature of the specific study informed consent form (ICF)). The long-term follow-up study will be covered by a separate protocol and SAP.

5.2 STUDY TREATMENTS AND ASSESSMENTS

Each patient will undergo an approximate 50-day screening period (Day -60 to Day -10). The patient must meet all eligibility criteria before the expansion culture will be initiated. Following MGTA-456 manufacturing, patients will be admitted to begin the transplant conditioning regimen (Day -9 to Day -1).

The schedule of assessments to be performed during the study is detailed in the schedule of assessments table of the study protocol (see Appendix A).

MGTA-456 will be administrated only once during the study period. The day of MGTA-456 administration will be considered Day 0 and will consist of the infusion of the expanded CD34+ fraction followed by the infusion of the CD34-depleted fraction of the cord blood unit (CBU). Infusional toxicity will be assessed within 48 hours after transplant. Each patient will remain hospitalized until neutrophil recovery is achieved. The patient will be monitored with protocol-specific procedures for 1 year following transplant to assess engraftment, graft failure, and late hematological graft failure and other study endpoints.

All eligible patients will have one of the two formulations of MGTA-456 administered, depending on the cohort to which they are enrolled to:

- **Cohort 1 – Fresh MGTA-456 Cell Therapy Product**: Patients with IMD will receive MGTA-456 fresh expanded CD34+ cells.
- **Cohort 2 – Cryopreserved MGTA-456 Cell Therapy Product**: Patients with IMD will

receive cryopreserved MGTA-456 in a single umbilical cord blood transplant (UCBT) setting.

- **Expansion cohort – Cryopreserved MGTA-456 Cell Therapy Product**: Patients with IMD will receive cryopreserved MGTA-456 in a single umbilical cord blood transplant (UCBT) setting. This cohort is optional and has been added in Protocol Amendment 6.

For all cohorts, starting on Day 0 of the study, 2 therapeutic cell preparations will be infused sequentially in the following order:

1. A minimal dose of 10×10^6 CD34+ cells per kg body weight within a range of 20×10^6 to 270×10^6 total nucleated cell (TNC) per kg body weight will be administered.
2. The remaining and entire CD34-depleted fraction derived from the same UCB unit as the ex vivo expanded CD34+ cells (the CD34-depleted fraction). All available CD34-negative cells will be administered.

5.3 RANDOMIZATION AND BLINDING

Randomization will not be used in this study. Patients will be allocated to receive study treatment sequentially into 1 of the 2 cohorts, and potentially in the expansion cohort (with same treatment as patients from cohort 2). As this is an open-label study, blinding procedures are not applicable.

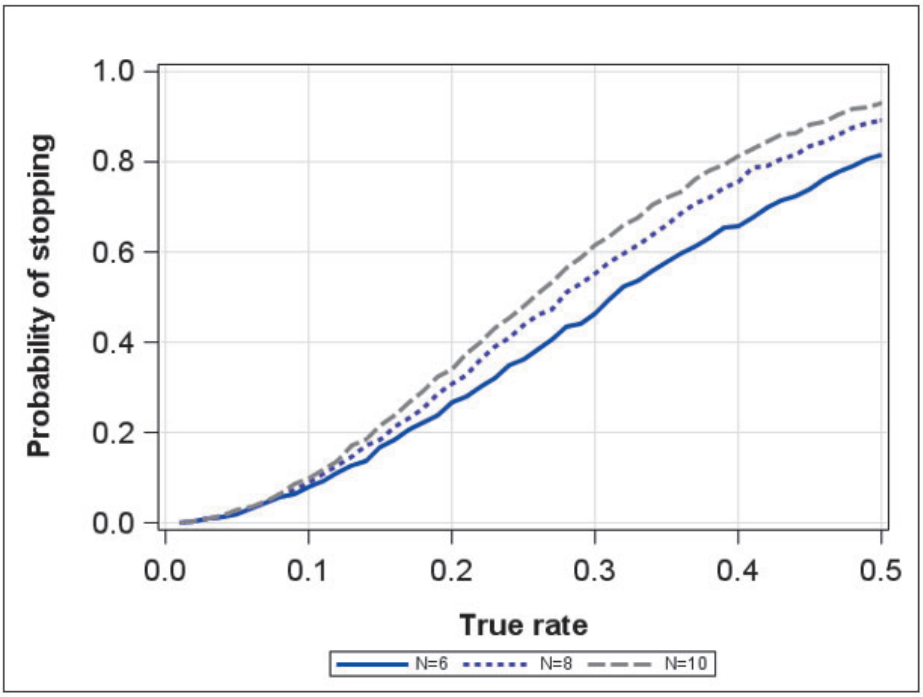
5.4 SAMPLE SIZE JUSTIFICATION

The study will consist of 2 cohorts each of approximately 6 patients, leading to a total sample size of ~12. The sample size is based on practical considerations considering the orphan patient population and expected rates of events leading to study cessation.

The option to include up to approximately 15 additional patients in an expansion cohort following dosing of Cohort 2 was included in Protocol Amendment 6. However, this expansion cohort was not considered at study design stage, thus sample size calculation and corresponding stopping probability is based on the initial planned cohort 1 and cohort 2 patients.

Figure 2 shows the probability of stopping for possible true event rates and for different sample sizes.

Figure 2. Probability of Study Stopping Rules with Various Sample Sizes



6 Statistical Considerations

The SAS system version 9.3 (or higher), will be used for all analysis, unless otherwise specified.

6.1 MISSING DATA HANDLING

No other imputation for missing data will be carried out other than to complete partial dates using standard imputation techniques as described below in section 6.2.

For the time to event variables censoring rules will apply as defined in section 8.7, so there should be no missing data for these endpoints during the analyses.

6.2 PARTIAL DATE IMPUTATION

The following rules should be used when modifying partial or missing dates for reporting purposes such as defining on treatment flags.

A permanent new date variable should be created if there is a requirement to be used in determining flags, sort orders and other derived variables needed for a table, listing or figure. Imputed date variable names will be defined in the derived dataset specifications.

Original (raw) date variables must not be overwritten. Imputed dates will not be displayed in the listings.

General rules

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6.3 BASELINE

Baseline is defined as the last non-missing value/result where assessment date is less than or equal to the date of first conditioning regimen, unless otherwise specified for individual assessments. Baseline will be determined based on all assessments, including additional assessments.

If patient was not treated, then baseline assessment is considered as the last assessment result from screening.

Change from baseline is defined as the difference between the post-baseline assessment value and the baseline value.

6.4 REPORTING GUDELINES

The following guidelines will be followed:

- **Page Orientation:** Landscape.
- **Post-text tables and listings**: will be generated in .lst and converted to rtf.
- **Post-text figures**: will be generated directly in .rtf.
- No in-text outputs are planned.
- **Font**: Courier New font with minimum of 8 point font size.
- **Margins**: Left: 3.8 cm, Right: 2 cm, Top: 3 cm, Bottom 2 cm on A4 paper.
- Columns header will be left aligned.
- **Treatment labels** will be the following and displayed in the following order, unless otherwise stated:
    - Cohort 1
    - Cohort 2
    - Expansion cohort**
    - Overall
    - Screening only*
    - Conditioning only*

  * In some cases, also a screening only column (including patients that discontinued or withdrawn before the conditioning regimen) and conditioning only column (including patients that discontinued or withdrawn between conditioning regimen and MGTA-456 infusion) will be considered.

  **To be displayed only if the expansion cohort will be included in the study.

- **Visit labels**: the visit labels displayed in Table 1 will be used as required.

Table 1: Visit Labels

Study Phase	CRF Visit	Tables, Figures and Listings Label
Screening	Screening	Screening
Conditioning	Conditioning Phase Day -9	COND Day -9
	Conditioning Phase Day -8	COND Day -8
	Conditioning Phase Day -7	COND Day -7
	Conditioning Phase Day -6	COND Day -6
	Conditioning Phase Day -5	COND Day -5
	Conditioning Phase Day -4	COND Day -4
	Conditioning Phase Day -3	COND Day -3
	Conditioning Phase Day -2	COND Day -2
	Conditioning Phase Day -1	COND Day -1
Transplant	Transplant Day 0	Day 0
Follow-up	Day 7	Day 7
	Day 14	Day 14
	Day 21	Day 21
	Day 28	Day 28
	Day 35	Day 35
	Day 42	Day 42
	Day 60	Day 60
	Day 84	Day 84
	Day 100	Day 100
	Day 180	Day 180
	End of Study	Day 360/EOS

- **Unscheduled visit / repeat assessments**: Data obtained at unscheduled or repeat assessments will be included in time to event analyses and baseline determination. All other data from unscheduled or repeat assessment will not be included in summaries but only be presented in data listings, if not otherwise specified. For all unscheduled visits (Unsch.) is concatenated to the name of the corresponding visit, when presenting in listings. For all repeat assessments (R) is concatenated to the name of the corresponding visit, when presenting in listings.

- **N:** The number of patients in the specified population and cohort.
- **Continuous data** will be summarized using number of patients (n), mean, standard deviation (SD), median, minimum value, maximum value and number of missing data (if there are any). For time to event summaries, median, quartiles (Q1 and Q3) and corresponding 95% confidence interval (CI) for the median will be presented. For PK summaries, geometric mean, coefficient of variation (arithmetic and geometric) will also be presented in addition to the arithmetic mean, SD, median, minimum value and maximum value.
- **Categorical data** will be summarized using n and percentage based on number of non-missing data.
    - All categories will be presented, even if no patients are counted in a particular category.
    - In case 1 or more patients have missing data for the summary, the number of missing data will be presented as a separate category, labeled accordingly as 'Missing', if not otherwise stated.
    - Counts of zero in any category will be presented without percentage.
    - All summaries percentages will be calculated using the number of patients with an assessment, unless otherwise stated.
    - For AEs, medical history, prior and concomitant medications the counts are based on single counts of patients with multiple events/treatments under same category, while the percentages are calculated using N.
- **Precision of summary statistics:**
    - Integer – Sample size (n, N) and number of missing data (if displayed);
    - One additional decimal place than reported/collected – mean, median, other percentile, confidence interval;
    - Two additional decimal places than reported/collected – standard deviation, standard error mean (SEM);
    - Same number of decimal places as reported/collected – minimum, maximum;
    - Percentages – one decimal place.
- **Study day, as displayed in TFLs:** Will be calculated with reference to MGTA-456 infusion start date as Day 0 for consistency with the protocol. This will be derived as: (assessment date – start date of MGTA-456 infusion). This will be the study day as presented in the TFLs.
- **Study day, for inclusion in CDISC compliant datasets:** Will be calculated with reference to MGTA-456 infusion start date as Day 1. It will be included in CDISC compliant datasets only and will not be displayed in TFLs. This will be calculated as (assessment date – start

date of MGTA-456 infusion)+1 if it's on or after start of MGTA-456 infusion, or (assessment date – start date of MGTA-456 infusion) if it is prior to start of MGTA-456 infusion.

- Data will be presented in listings by cohort and patient diagnosis. The order will be subject ID, visit, assessment date/time and assessment type/parameters (in order collected on eCRF, unless otherwise specified). In case of clinical laboratory results, the listings will be presented in order of cohort, diagnosis, subject ID, parameter, assessment date/time, visit.
- Dates will be presented in format YYYY-MM-DD.
- Version 4.03 of the NCI-CTC grading criteria (CTCAE v4) will be used for relevant tables.
- Latest version of the Medical Dictionary for Regulatory Activities (MedDRA) will be used for relevant tables. The version will be documented in the footnote of the corresponding TFLs.
- Latest version of the WHO Drug Global dictionary will be used for prior and concomitant medication coding. The version will be documented in the footnote of the corresponding TFLs.
- File naming: Each TFL output file will be named with a t, l or f to denote the output type and then according to its table numbering in the following way: Table 14.2-1.1 would be t14_2_1_1, Table 14.2-11 would be t14_2_11, Listing 16.2.7-1.1 would be l16_2_7_1_1, and Figure 14.2-2.1 would be f14_2_2_1.

7 Analysis Sets

7.1 ANALYSIS SETS

Non-evaluable patients are defined as subjects that have major protocol deviations. Therefore, the non-evaluable patients will not be included in the analysis sets that require patients with no major protocol deviations as per their definitions from below.

The following analysis sets are defined for this study:

All patients

"All patients" population consists of all patients who were enrolled regardless of whether they received MGTA-456 or not.

Full analysis set (FAS)

The full analysis set will include all patients that received MGTA-456. This analysis set will be used for all assessments of efficacy and safety.

Pharmacokinetic (PK) analysis set

The PK analysis set will include all patients that received MGTA-456, with available PK data and no major protocol deviations with relevant impact on PK data.

Pharmacodynamic (PD) analysis set

The PD analysis set will include all patients that received MGTA-456, with available PD data and no major protocol deviations with relevant impact on PD data.

According to protocol, PD data is referring to efficacy data. Therefore, the PD analysis set is equivalent to the standard Per-protocol analysis set.

To note, in case two analysis sets are identical (same patients in both analysis sets) and TFLs are planned to be produced for both analysis sets (one being repeat of the other, the only difference being the analysis set) then only the TFLs planned for one of the two analysis sets will be produced. For example, if FAS and PD analysis set contains same patients, then only the outputs planned for FAS will be produced.

7.2 PROTOCOL DEVIATIONS

The full list of types of protocol deviations (PDvs) and their relation to the analysis sets, along with the method of identification of each protocol deviation, are detailed in the protocol deviation criteria form (PDCF) which is separate to this SAP. This will be used as a basis for identifying patients with protocol deviations throughout the study.

Protocol deviations noted during the trial by the Clinical Research Associates (CRAs), Medical Monitors or Data managers will be tracked throughout the study. In addition, some PDvs will be identified programmatically in SAS® using data from the clinical database. All PDvs will be read into SAS® prior to reporting.

At the PDvs review meetings, a consolidated list of PDvs will be reviewed by the team. Prior to database lock, during a final review classification meeting, PDvs will be reviewed and agreement of the final analysis populations will be made.

Major protocol deviations will be summarized by deviation category and corresponding protocol deviation coded terms. Also, minor protocol deviations will be presented in the summary table by

deviation category and corresponding protocol deviation coded terms. A listing of all protocol deviations by patient will also be provided.

8 Methods of Analyses and Presentations

8.1 SUBJECT DISPOSITION

The subject disposition summaries will be presented on the all patients population by cohort and overall. Overall will include all patients, including screen failures. Summaries for patients who underwent screening only and conditioning only will also be presented.

The number and percentages of patients in each analysis population will be summarized.

The summary of subject disposition will be showing the number and percentages of patients belonging to the following categories:

- Patients included in the study (i.e. signed informed consent);
- Patients started conditioning;
- Patients discontinued during conditioning;
- Patients completed conditioning;
- Patients completed conditioning but not continued with MGTA-456 infusion, along with the reasons for not continuing with MGTA-456 infusion;
- Patients completed MGTA-456 infusion but discontinued during follow-up, along with the reasons for discontinuation;
- Patients completed the study.

Information on analysis populations, study completion and discontinuation will also be displayed in subject listings.

8.2 DEMOGRAPHIC AND BASELINE CHARACTERISTICS

The following demographic and baseline characteristics will be summarized on the FAS and on the PD analysis set, by cohort and overall:

- Age, derived in years, with the tens place for decimal included, as the difference between the date of birth to MGTA-456 infusion start date: (MGTA-456 infusion start date – date of birth)/(12*30.4375). In case the patient discontinued or withdrawn before MGTA-456 infusion then the age as collected on demographic CRF page will be reported.
- Gender;
- Child bearing status;
- Race;
- Ethnicity;
- Height;
- Weight;
- Lansky performance status at study entry.

Separately the disease history of the corresponding IMD will be summarized on the FAS, by cohort and overall:

- Patients with the IMD included in the study;
- Time between diagnosis and parental consent, derived as number of months between the diagnosis date to parental consent date: (date of parental consent – date of diagnosis)/30.4375.

In addition, listings of the above data will be produced for all patients.

Furthermore, disease history details for each of the corresponding IMD will be presented for all patients in listings.

8.3 MEDICAL HISTORY

Medical histories and concomitant diseases will be coded using MedDRA. The version of the dictionary will be provided in the medical histories and concomitant diseases TFLs footnotes. Summaries of patient medical histories and concomitant diseases will be produced on the FAS, by cohort and overall, by system organ class (SOC) and preferred term (PT).

Listing of medical history will be produced for all patients.

8.4 PRIOR AND CONCOMITANT MEDICATION

Medications other than the conditioning treatment and MGTA-456 infusion will be coded using the WHO Drug Global dictionary. The version of the dictionary will be provided in the corresponding TFLs footnotes.

To note, transfusions are collected on a separate CRF page, following PA6.

Medications (including transfusions) will be defined as follows:

- Prior Medication: Any medication whose end date is before the MGTA-456 infusion date.
- Concomitant Medication: Any medication whose start or end date is either the same as or after the MGTA-456 infusion date.

Any medication (including transfusions) with a missing medication end date will be assumed to be concomitant medication. Also, ongoing medications are considered as concomitant medications.

Summaries of concomitant medications (including transfusions) will be produced on the FAS by cohort and overall, by Anatomical Therapeutic Chemical (ATC) class (level 1) and preferred term. An additional summary of concomitant medications will be produced by preferred term.

In addition, a listing of prior and concomitant medications will be presented for all patients.

A separate listing will be presented for all patients for the transfusions collected on the separate CRF page, following PA6.

8.5 CONDITIONING TREATMENT

A listing of conditioning treatment administration with Antithymocyte globulin (ATG), Fludarabine (FLU), Busulfan (BU) and Cyclophosphamide (CY) will be presented.

To note, patients enrolled in the study before PA6 had the following conditioning treatment given: ATG given daily between Day -9 to Day -6; FLU and BU given daily between Day -5 to Day -2. The conditioning treatment changed in PA6, therefore all patients enrolled in the study following PA6 had the following conditioning treatment given: BU given daily between Day -9 to Day -6; CY and ATG given daily between Day -5 to Day -2. Details are found in the study protocol and corresponding amendments.

8.6 STUDY DRUG EXPOSURE AND/OR COMPLIANCE

Exposure to conditioning treatment (ATG, FLU, BU and CY) is assessed through duration of treatment which is defined in days as follows:

Duration of conditioning ATG treatment (days) = [Date of last conditioning ATG treatment – Date of first conditioning ATG treatment] + 1;

Duration of conditioning FLU treatment (days) = [Date of last conditioning FLU treatment – Date of first conditioning FLU treatment] + 1;

Duration of conditioning BU treatment (days) = [Date of last conditioning BU treatment – Date of first conditioning BU treatment] + 1.

Duration of conditioning CY treatment (days) = [Date of last conditioning CY treatment – Date of first conditioning CY treatment] + 1.

To note, duration of conditioning CY treatment will be calculated only for patients enrolled in the study following PA6.

All summaries for exposure to conditioning treatments will be presented by cohort on the FAS.

MGTA-456 infusion exposure and compliance will be summarized by cell types (CD34enriched and CD34depleted) and for total TNC dose (=CD34enriched cells + CD34depleted cells) through volume of infusion and percentage of actual volume administered from the labeled volume which will be calculated for each cell type and for total TNC dose as follows:

- Total product volume administered (mL);
- Percentage of the actual volume administered from the labeled volume (%), derived as:

  [(Total product volume administered (mL)/Labeled volume (mL))*100].

The amount of total product volume administered and percentage of the actual volume administered from the labeled volume will be calculated for each cell types (CD34enriched and CD34depleted) and for total TNC dose. For example, if patient has two bags of CD34enriched cell type then the total product volume administered and the corresponding percentages of actual from labeled volume will be considered based on the total amount of volume in both bags.

In addition, actual CD34 dose, actual CD3 dose, actual TNC dose and corresponding percentages

of actual from planned dose will be calculated and summarized accordingly:

- Actual CD34 dose (x10^6/kg) = [(Total product volume administered (mL)/Labeled volume (mL))] * (Planned CD34 dose (x10^6/kg));
- Percentage of the actual CD34 dose from the labeled CD34 dose (%), derived as:

  [(Actual CD34 dose (x10^6/kg)/ CD34 dose on label (x10^6/kg))*100].

Similar calculations will be considered for the actual CD3 dose, percentage of the actual CD3 dose from the labeled CD3 dose, actual TNC dose and percentage of the actual TNC dose from the labeled TNC dose.

To note, similarly as for the volume of product, the calculations for actual CD34 dose, actual CD3 dose, actual TNC dose and corresponding percentages of actual from planned dose will be calculated for each cell types (CD34enriched and CD34depleted) and for total TNC dose. For example, if patient has two bags of CD34enriched cell type then the actual CD34 dose, actual CD3 dose, actual TNC dose and corresponding percentages will be considered based on the total amount of cells in both bags. The calculated actual TNC dose for CD34enriched, CD34depleted and total TNC dose should be converted to x10^7/kg for the summary statistics and for presenting in the corresponding listing.

All summaries for exposure and compliance of MGTA-456 infusion will be presented by cohort on the FAS.

Details of MGTA-456 infusion administration and treatment exposure and compliance will be listed.

8.7 EFFICACY DATA ENDPOINTS AND ANALYSES

All primary efficacy analyses and summaries will be presented by cohort, on the FAS and on the PD analysis set. All secondary and exploratory efficacy analyses and summaries will be presented by cohort, on the FAS, unless otherwise specified.

All efficacy endpoints defined as below will be listed.

8.7.1 Primary Efficacy Endpoint and Analyses

Primary efficacy analysis is based on engraftment with MGTA-456 and the corresponding time to

neutrophil recovery.

Engraftment with MGTA-456 is defined as achieving an absolute neutrophil count (ANC) ≥0.5 × 10^9/L for 3 consecutive days.

Incidence of engraftment with MGTA-456 will be presented by cohort. The associated two-sided 95% Clopper-Pearson confidence intervals (Cis) and one-sided 95% Clopper-Pearson Cis will also be presented.

Time to neutrophil recovery is defined as time from MGTA-456 infusion until the first day of 3 consecutive days with an ANC ≥0.5 × 10^9/L.

Time to neutrophil recovery (days) = (Date of first day of 3 consecutive days with an ANC ≥0.5 × 10^9/L – Date of MGTA-456 infusion) + 1

Patients who reach the time point of analysis without an engraftment with MGTA-456 will have the time to neutrophil recovery censored at the date of last laboratory assessment with a ANC result.

Time to neutrophil recovery (days) = (Date of last laboratory assessment with ANC result – Date of MGTA-456 infusion) + 1

Patients discontinued the study and who are lost to follow-up will be censored at the date of last available assessment.

Time to neutrophil recovery (days) = (Date of last available assessment – Date of MGTA-456 infusion) + 1

Estimates of the survival function for time to neutrophil recovery (median [95% CI], Q1 and Q3) will be obtained using the Kaplan-Meier method. The CI for the median will be calculated using the Brookmeyer and Crowley method. Time to neutrophil recovery will also be presented graphically showing the number of patients at risk at relevant timepoints (day 30, day 42, day 60, day 100, day 180 etc as applicable). Time to neutrophil recovery summaries and graphical presentation will be presented by cohort.

8.7.1.1 Supportive Analysis 1

Duration (total # of days) of neutropenia (ANC<0.5 × 10^9/L) within 15, 28 and 42 days following MGTA-456 infusion will be determined for each patient.

In addition, duration (total # of days) of neutropenia (ANC <0.5 × 10^9/L) from time of MGTA-456 infusion to day of neutrophil recovery will be calculated for each patient.

The duration (total # of days) of neutropenia within 15, 28 and 42 days will be summarized by cohort.

Summary statistics for the duration (total # of days) of neutropenia from time of MGTA-456 infusion to day of neutrophil recovery will be presented on the FAS by cohort.

Duration (total # of days) of neutropenia (ANC<0.5 × 10^9/L) within 15, 28 and 42 days following MGTA-456 infusion and duration (total # of days) of neutropenia (ANC <0.5 × 10^9/L) from time of MGTA-456 infusion to day of neutrophil recovery will be presented in a separate efficacy listing, for all subjects included in FAS.

8.7.1.2 Supportive Analysis 2

Daily ANC values from day of MGTA-456 infusion (day 0) to day 15 following MGTA-456 infusion will be summarized by each study day for each cohort, on the FAS. The SEM will be also presented for the summary statistics. A graph of mean (+/-SEM) will be presented by cohort and overall, on the FAS.

8.7.2 Secondary Efficacy Endpoints and Analyses

8.7.2.1 Late Hematological Graft Failure

Late hematological graft failure is defined as meeting 1 of the following 3 criteria:

1) <5% donor whole blood or myeloid chimerism in peripheral blood or bone marrow beyond Day 42 post-transplant in patients with prior hematopoietic recovery with ≥5% donor cells by Day 42 post-transplant;
2) Sustained decline in the ANC to <500/mm^3 for 3 consecutive measurements on different days, unresponsive to growth factor therapy after initial hematopoietic recovery by Day 42;
3) Subsequent bone marrow aplasia identified after initial hematopoietic recovery by Day

Late hematological graft failure data will be analysed and presented as collected in the database.

Incidence of late hematological graft failure will be presented by cohort. The associated two-sided 95% Clopper-Pearson Cis and one-sided 95% Clopper-Pearson Cis will also be presented.

8.7.2.2 Myeloid and Lymphoid Engraftment

Contribution of MGTA-456 to myeloid and lymphoid engraftment as determined by percent chimerism in CD33/66 (or CD15), CD3, CD19 and CD56 cells will be summarized at relevant visits (Screening, Day 7, Day 14, Day 21, Day 28, Day 60, Day 84, Day 100, Day 180 and Day 360) by cohort. To note, following Protocol Amendment 6, chimerism is collected also at Day 84.

All chimerism data (CD33/66, CD19+, CD3+, CD56+ and CD33/15 for both donor and recipient) will be presented in a separate listing.

8.7.2.3 Platelet Recovery

Platelet recovery is defined in 2 ways:

[1] Platelet count ≥20 × 10^9/L for 3 consecutive laboratory measurements on different days without transfusion in the prior 7 days.
[2] Platelet count ≥50 × 10^9/L for 3 consecutive laboratory measurements on different days without transfusion in the prior 7 days.

For the platelet recovery analyses, the date of platelet recovery will be derived accordingly based on the corresponding data.

To note, transfusions are collected on a separate CRF page, following PA6. All transfusions captured on both prior and concomitant medications and transfusion CRF pages will be considered for the derivation of the platelet recovery endpoints.

Incidence of platelet recovery will be presented separately for platelet recovery definitions [1] and [2], by cohort. The associated two-sided 95% Clopper-Pearson Cis and one-sided 95% Clopper-Pearson Cis will also be presented.

Time to platelet recovery is defined considering the two definitions of platelet recovery, as follows.

Separate analyses will be considered for each time to platelet recovery, based on the definitions [1] and [2].

To note, all patients that have an event of platelet recovery based on definition [2] are fulfilling also definition [1] for platelet recovery, therefore will be included in both analyses accordingly.

[1] Time to platelet recovery defined as platelet count ≥20 x 10^9/L for 3 consecutive laboratory measurements on different days without transfusion in the prior 7 days

Time to platelet recovery is defined as time from MGTA-456 infusion until the first day of 3 consecutive laboratory measurements on different days with a platelet count ≥20 x 10^9/L without transfusion in the prior 7 days.

Time to platelet recovery [1] (days) = (Date of first day of 3 consecutive laboratory measurements on different days with a platelet count ≥20 x 10^9/L without transfusion in the prior 7 days – Date of MGTA-456 infusion) + 1

Patients who reach the time point of analysis without having a date of platelet recovery as defined above, will have the time to platelet recovery censored at the date of last laboratory assessment with a platelet count result.

Time to platelet recovery [1] (days) = (Date of last laboratory assessment with platelet count result – Date of MGTA-456 infusion) + 1

Patients discontinued the study and who are lost to follow-up will be censored at the date of last available assessment.

Time to platelet recovery [1] (days) = (Date of last available assessment – Date of MGTA-456 infusion) + 1

[2] Time to platelet recovery defined as platelet count ≥50 x 10^9/L for 3 consecutive laboratory measurements on different days without transfusion in the prior 7 days

Time to platelet recovery is defined as time from MGTA-456 infusion until the first day of 3 consecutive laboratory measurements on different days with a platelet count ≥50 x 10^9/L without transfusion in the prior 7 days.

Time to platelet recovery [2] (days) = (Date of first day of 3 consecutive laboratory measurements on different days with a platelet count ≥50 x 10^9/L without transfusion in the prior 7 days – Date of MGTA-456 infusion) + 1

Patients who reach the time point of analysis without having a date of platelet recovery as defined above, will have the time to platelet recovery censored at the date of last laboratory assessment with a platelet count result.

Time to platelet recovery [2] (days) = (Date of last laboratory assessment with platelet count result – Date of MGTA-456 infusion) + 1

Patients discontinued the study and who are lost to follow-up will be censored at the date of last available assessment.

Time to platelet recovery [2] (days) = (Date of last available assessment – Date of MGTA-456 infusion) + 1

Estimates for the survival function for time to platelet recovery will be summarized and presented graphically, similarly as the time to neutrophil recovery.

8.7.2.4 Acute and Chronic GVHD

GVHD will be collected weekly for all patients that underwent the MGTA-456 infusion, starting at Day 7 until hospital discharge, and then at every scheduled visit except Day 84. aGVHD will be collected until Day 100 and cGVHD will be collected at Day 100, Day 180 and Day 360/EOS.

Incidence of grade II–IV aGVHD by visit and incidence of cGVHD by visit will be presented by cohort. The associated two-sided 95% Clopper-Pearson CIs will also be presented.

All data collected for GVHD, including aGVHD and cGVHD will be listed in a separate listing.

8.7.2.5 Overall Survival

Overall survival (OS) is defined as the period from the date of MGTA-456 infusion up to the date of death, regardless of cause of death.

OS (days)= (Date of death – Date of MGTA-456 infusion) + 1

Patients alive at the time of the analysis will have the OS censored at the date of last assessment

when the patient was known alive.

OS (days) = (Date of last assessment patient is known alive – Date of MGTA-456 infusion) + 1

Patients with no post-infusion assessments, will be censored at day 1.

OS (days) = (Date of MGTA-456 infusion – Date of MGTA-456 infusion) + 1 (i.e. Day 1)

Estimates for the survival function for OS will be summarized by cohort and presented graphically, similarly as the time to neutrophil recovery (section 8.7.1).

8.7.2.6 Event Free Survival

Event free survival (EFS) is defined as the period from the date of MGTA-456 infusion up to the date of graft failure (primary or late) or death (regardless of cause of death), whichever occurs first.

To note, primary graft failure is defined as lack of engraftment with MGTA-456 by Day 42. Late graft failure is defined as late hematological graft failure in Section 8.7.2.1.

EFS (days) = [Min (Date of primary graft failure, Date of late graft failure, Date of death) – Date of MGTA-456 infusion] + 1

Patients that had engraftment with MGTA-456 by Day 42 and had no late graft failure and are alive at the time of the analysis will have the EFS censored at the date of last assessment or date of last contact, whichever occurs last.

EFS (days)= [Max (Date of last assessment patient is known alive, Date of last contact) – Date of MGTA-456 infusion] + 1

Patients with no post-infusion data, will be censored at day 1.

EFS (days)= (Date of MGTA-456 infusion – Date of MGTA-456 infusion) + 1 (i.e. Day 1)

Estimates for the survival function for EFS will be summarized by cohort and presented graphically, similarly as the time to neutrophil recovery (section 8.7.1).

8.7.3 Exploratory Efficacy Endpoints and Analyses

8.7.3.1 Blood Enzyme Levels and ABCD1 Protein Level

[redacted]

8.7.3.2 Plasma and CSF Biomarkers

[redacted]

8.7.3.3 Immune Reconstitution and Immunoglobulin Levels

[redacted]

[redacted]

8.7.3.4 Resource utilization

Resource utilization is evaluated through the duration of hospitalization after MGTA-456 infusion,

[redacted]

[redacted]

8.7.3.5 Neurodevelopment and peripheral neuropathy

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

8.7.4 Subgroup Analysis

Not applicable.

8.8 PHARMACOKINETIC ENDPOINTS AND ANALYSES

All PK analyses and summaries will be presented by cohort, on the PK analysis set.

[redacted]

PK concentrations will be plotted over time by cohort. Plots will also be produced for the mean PK concentrations over time by cohort with error bars to illustrate the standard deviation. If the data are sparse, this plot may not be presented.

All PK concentration and corresponding sample details will be presented in a listing.

If possible, the following PK parameters will be determined, by the PK vendor, using the actual recorded sampling times and non-compartmental method(s) with WinNonlin Pro (Version 5.2 or higher): Cmax, AUCinf, AUClast and others if available from the plasma concentration-time data. The PK parameters results will not be presented in a listing.

In addition, ATG PK is evaluation following administration of ATG at scheduled timepoints as described in section 8.7. All ATG PK details are presented in a listing.

8.9 PHARMACODYNAMIC ENDPOINTS AND ANALYSES

[redacted]

8.10 QUALITY OF LIFE OR PHARMACOECONOMIC ENDPOINTS AND ANALYSES

[redacted]

8.11 SAFETY DATA ENDPOINTS AND ANALYSES

8.11.1 Adverse Events (Aes)

Serious adverse events (SAE) will be collected from time conditioning that is initiated at Day -9. Adverse events will be collected from day of transplant Day 0.

Adverse events will be coded using the MedDRA coding system. The version of the dictionary will be provided in the adverse events TFLs footnotes.

Treatment-emergent adverse event (TEAE) is defined as any AE that occurs during or after MGTA-456 infusion, or any event that is present at baseline and continues after the MGTA-456 infusion but increases in severity category.

Any AE that is present at baseline but increases in severity category should be entered into the eCRF as different AE record with the differing grade recorded.

The number and percentage of patients experiencing the following categories of Aes will be summarized by SOC and PT. Patients will be counted only once within each SOC and PT. SOCs will be presented by descending overall frequency, while PTs will be presented by descending overall frequency within each SOC. The following summaries will be presented:

- All Aes (*)
- All TEAEs
- TEAEs related to MGTA-456 infusion
- TEAEs related to MGTA-456 infusion that limit MGTA-456 administration
- Serious treatment-emergent adverse events
- All serious Aes (*)
- TEAEs from transplant to 48 hours after transplant
- TEAEs from day 3 to day 100
- TEAEs following day 100 to the end of the study

(*) All Aes and all serious Aes will be summarized on all patients population, by cohort and overall. Overall will include screening only and conditioning only patients.

To note, in the TEAEs from transplant to 48 hours after transplant summary all TEAEs that occurred following MGTA-45 infusion to 2 days inclusive after MGTA-45 infusion are summarized. Similarly, in the TEAEs from day 3 to day 100 summary all TEAEs that occurred after 3 days and up to 100 days following MGTA-456 infusion are summarized.

An overview of TEAE incidence rates by SOC, PT and maximum severity (as determined by the NCI CTCAE toxicity grading (CTCAE v4)) will be provided. Patients will be counted only once within each SOC, PT and severity.

All summaries will be presented on the full analysis set, by cohort and overall, if not otherwise specified.

All information on Aes will be listed. Separate listings of TEAEs related to MGTA-456 infusion that limit MGTA-456 administration, TEAEs (regardless of causality) from transplant to 48 hours after transplant and SAEs will be provided, on the FAS.

8.11.2 Transplant-Related Mortality (TRM)

All patients who died, having a TRM in the opinion of the investigator, and the associated primary cause of death will be presented in the death listing.

8.11.3 Clinical Laboratory Evaluations

Blood samples for hematology and blood chemistry will be collected at each visit as outlined in the schedule of assessments (see Appendix A and study protocol).

All laboratory parameters results will be converted to SI units in order to standardize the results. The summaries as mentioned below will be based on the standardized values.

Also, clinical laboratory results will be assessed against the NCI-CTCAE v4.03 criteria (CTCAE v4).

Shift tables to show the worst post-baseline NCI-CTCAE grade compared to baseline will be produced for each hematological parameter, by cohort on the FAS. In case of a Hypo/Hyper criteria consider both Hypo and Hyper shift tables for the corresponding parameter. All laboratory results (including results from unscheduled visit/repeat assessments) will be considered to determine the worst post-baseline NCI-CTCAE grade compared to baseline.

Laboratory results will be listed in separate listings for all hematology and blood chemistry parameters, on all patients population. All results below/above the normal range will be flagged in accordingly.

In addition, the following laboratory evaluations will be assessed:

- Viral testing
- Infection surveillance
- Human leukocyte antigen (HLA) typing
- Anti-HLA antibodies
- Urine substrate excretion (*)

(*) Urine substrate excretion assessment is performed only for Hurler and MLD diagnosed patients.

All the above laboratory evaluations details will be presented in listings, on all patients population.

Clinically relevant deviations of laboratory test results will be evaluated for criteria defining an AE by the investigator. In the case these events fulfil the criteria of Aes, these will be collected as Aes on the corresponding eCRF and will be presented and summarized as defined in section 8.11.1.

In addition, pregnancy test results will be presented in a listing, on all patients population.

8.11.4 Physical Examination

A complete physical examination will be assessed during screening and include the examination of general appearance, skin, neck (including thyroid), eyes, ears, nose, throat, lungs, chest, heart, abdomen, back, lymph nodes, extremities, vascular and nervous system.

Physical examination details will be listed, on the all patients population.

Any significant findings that are present prior to MGTA-456 infusion may be recorded as medical history, and will be presented and summarized as defined in section 8.3. Significant findings observed after MGTA-456 administration which meet the definition of an AE will be appropriately recorded on the corresponding AE eCRF, and will be presented and summarized as defined in section 8.11.1.

8.11.5 Vital Signs

Height, head circumference, weight, temperature, oxygen saturation, systolic and diastolic blood pressure, pulse and respiratory rate will be assessed during vital signs assessment, at each visit as outlined in the schedule of assessments (see Appendix A and study protocol). Head circumference will be measured for patients with Hurler syndrome only. Oxygen saturation can be assessed separately on the corresponding eCRF page, but will be presented as part of vital signs data. On day of transplant/infusion (Day 0), vital signs will be assessed as follows:

- Before PA8: at pre-infusion (-1 hour), at time of MGTA-456 infusion, and 0.25, 0.5, 0.75, 1, 2, 4, and 8 hours post-infusion after the complete dose of expanded product is given, except for weight which will be collected at pre-infusion only. For subsequent infusions of CD34-depleted fractions, vital signs should be collected prior to infusion, 0.25 hours during infusion and 0.25 and 1 hour post last infusion.
- From PA8 onwards: at pre-infusion (-1 hour), at time of 15 minutes after the infusion, of the first bag begins, prior to the infusion of the second bag and 15 minutes after the completion of the second bag, except for weight which will be collected at pre-infusion only. For subsequent infusions of CD34-depleted fractions, vital signs should be collected prior to infusion, 15 minutes after the infusion of the first bag begins, prior to the infusion

of the second bag and 15 minutes after the completion of the second bag.

Vital sign parameters will be summarized for the first 8 hours post MGTA-456 infusion (including the pre-infusion assessment), on the FAS by cohort. All vital sign results assessed post MGTA-456 infusion will be summarized by the corresponding timepoint as collected.

All vital signs measurements (including all Day 0 timepoints measurements, as per timepoint labels as collected in the corresponding CRF pages) will be listed, on all patients population. All values below/above the normal range will be flagged as Low (L)/High (H) results, as per criteria defined in Table 3.

Table 3: Vital Sign Parameters Normal Ranges

Vital Sign Parameter	Age category	Lower range	Upper range
Pulse	16+ years	43	104
	12-15 years	47	108
	6-11 years	52	123
	3-5 years	65	136
	1-2 years	82	156
	0-1 years	93	181
Respiratory rate	16+ years	11	22
	12-15 years	12	23
	6-11 years	14	27
	3-5 years	17	33
	1-2 years	19	53
	0-1 years	22	66
Systolic Blood Pressure	16+ years	111	147
	12-15 years	101	142
	10-11 years	97	130
	6-9 years	91	129
	3-5 years	86	123
	1-2 years	80	117
	0-1 years	50	70
Diastolic Blood Pressure	16+ years	63	97
	12-15 years	59	93
	10-11 years	58	90

Vital Sign Parameter	Age category	Lower range	Upper range
	6-9 years	53	89
	3-5 years	44	82
	1-2 years	34	71
	0-1 years	33	47

8.11.6 Echocardiogram (ECHO) and Electrocardiogram (ECG)

ECHO and ECG assessments will be performed during screening, on Day 100 and 180 (only for Hurler syndrome patients) and at Day 360/EOS. The heart rate, PR, RR, QT intervals, QRS duration, and an overall interpretation will be collected during the ECG assessment, while the left ventricular ejection fraction (LVEF) and left ventricular shortening fraction (LVSF) will be measured during the ECHO assessment.

All ECHO and ECG assessment measurements will be listed, on the all patients population.

Any clinically significant abnormalities will be evaluated for criteria defining an AE by the investigators. In the case these events fulfil the criteria of AEs, these will be collected as AEs on the corresponding eCRF and will be presented and summarized as defined in section 8.11.1.

8.11.7 Pulmonary Function Test (PFT)

PFT assessment will be performed (if patient is capable) during screening and at Day 360/EOS. In case the patient is not capable to perform the PFT assessment, only the oxygen saturation collected during vital sign assessment will be collected. The forced expiratory volume (FEV_1), forced vital capacity (FVC) and diffusing capacity of lung for carbon monoxide (DLCO) (as % of predicted value) will be collected during the PFT assessment.

All PFT assessment measurements will be listed, on all patients population.

8.11.8 Magnetic resonance imaging (MRI) and Chest X-ray

MRI of the brain will be performed during screening and at Day 360/EOS for all patients, while cALD, MLD, or GLD patients will have a MRI assessment performed also at Days 28, 60, 100 and 180. A chest X-ray will be performed at screening and at Day 360/EOS.

All MRI and chest X-ray assessment details will be listed, on the all patients population.

9 Interim Analyses and DMCs

No interim analyses are planned.

A subset of the TFLs may be produced for publication purposes at agreed times with Magenta.

In addition, there will be a review of safety data by an independent Data Monitoring Committee (DMC) at defined timepoints. Details regarding DMCs are contained in the DMC Charter. The DMC TFLs shells are flagged in accordingly in the TFL Shells document.

10 Annual safety report

Annual safety report (ASR) will include safety data. ASR is intended to serve as an annual report to regulatory authorities for US only studies as per US Investigational New Drug (IND) number at the IND birthdate. ASR requirements and corresponding outputs will be covered by a separate document.

11 Changes to Planned Analyses

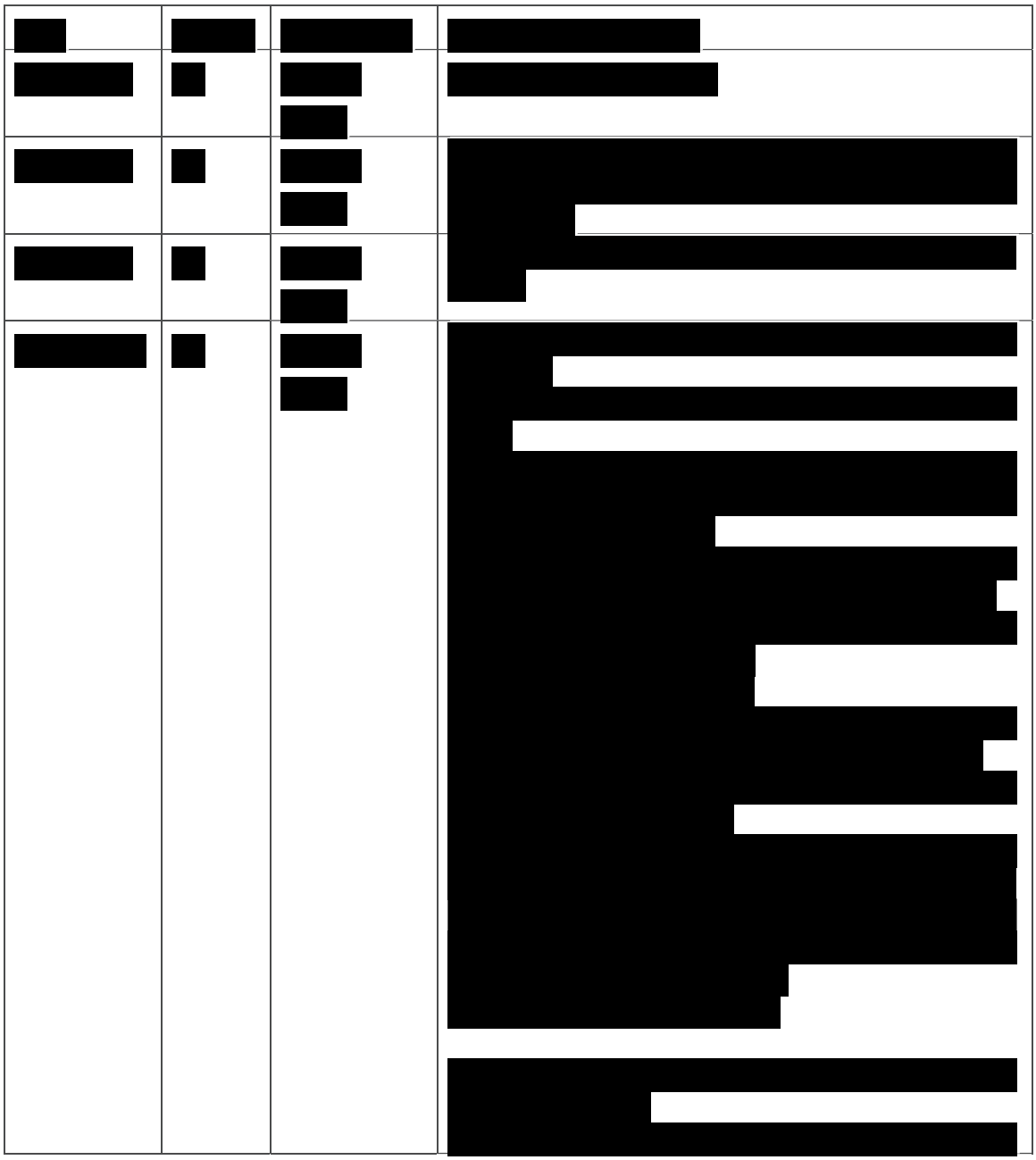
The following are changes to the planned analyses from that stated in the protocol (Amendment 8, 10 Jan 2020):

- An 'All patients' population set has also been defined.
- Defined a screening only and conditioning only group of patients. The screening only patients are patients that discontinued or withdrawn before the conditioning regimen, while the conditioning only patients are patients that discontinued or withdrawn between conditioning regimen and MGTA-456 infusion.
- Only patients receiving MGTA-456 infusion to be included in the PK analysis set and PD analysis set. Definition of PK analysis set and PD analysis set updated accordingly.
- Event free survival (EFS) efficacy endpoint has been also defined.

After the decision to stop recruitment and prior to DBL it was decided that the following data would no longer be reported:

- Plasma biomarker listing
- LHD221 PK parameter listing.

12 Document History



13 References

[1] (CTCAE v4)
http://evs.nci.nih.gov/ftp1/CTCAE/CTCAE_4.03_2010-06-14_QuickReference_5x7.pdf
Brookmeyer, R. and Crowley, J. (1982), "A Confidence Interval for the Median Survival Time," *Biometrics*, 38, 29–41.
Kaplan, E. L. and Meier, P. (1958), “Nonparametric Estimation from Incomplete Observations,” *Journal of the American Statistical Association*, 53, 457–481.

14 Appendices

14.1 APPENDIX A – Study assessments

[redacted]

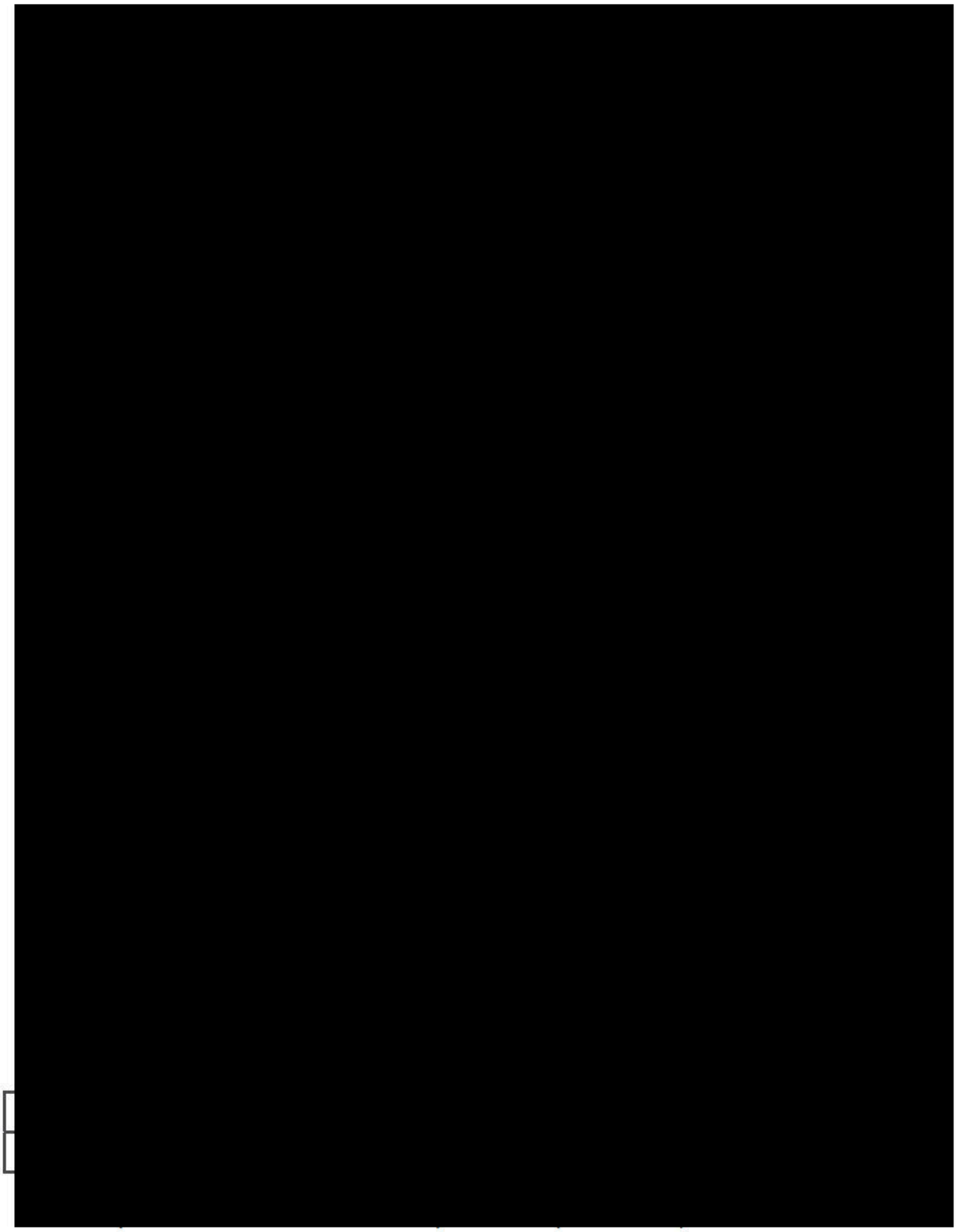
14.2 APPENDIX B – Protocol amendment changes

[redacted]

[redacted]

[redacted]

[redacted]



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14.4 APPENDIX D - Tables, Figures and Listing shells

[redacted]

Certificate Of Completion

[redacted]

[redacted]

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