BMT CTN #0601 Statistical Analysis Plan (SAP)

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Finalized after the protocol team call on 5/22/15

Protocol:

BMTCTN #0601 Sickle Cell

Protocol Synopsis:

The BMT CTN protocol #0601 titled "Unrelated Donor Reduced Intensity Bone Marrow Transplant for Children with Severe Sickle Cell Disease" is a Phase II, single arm, multi-center trial. The primary objective is to determine event-free survival (EFS) at 1 year after unrelated donor (URD) hematopoietic stem cell transplantation (HCT) using bone marrow (BM) in participants with sickle cell disease (SCD). Secondary objectives include determining the effect of HCT on clinical and laboratory manifestations of severe sickle cell disease including stroke and determining the incidence of other transplant-related outcomes. The target sample size (after the last protocol amendment) is 30 BM participants, and participants will be followed for two years post-transplant.

Study Status and Publication Plan:

Recall the study was originally designed to determine the EFS after URD HCT using bone marrow or umbilical cord blood with the target sample size of 45. The cord blood arm of the trial was closed in June 2010 because of an excess graft rejection rate and the study results of the cord blood participants have been published (Kamani, et al 2012). This analysis will exclude the participants who received a cord blood transplant.

The study opened to accrual in April 2008 and closed accrual in April 2014. By the time of accrual closure, 30 patients were enrolled to the study in the BM cohort. All patients have completed 1-year follow up by May 1, 2015. Twenty-four patients have completed the follow-up per protocol and six are still being followed for the 2-year assessments post transplant. Among the six patients who have only 1-year follow-up as of now, three of them will reach 2-year follow-up during August to December 2015 and another three will reach 2-year follow up during January to March 2016. The Endpoint Review Committee (ERC) has reviewed the primary endpoint and some secondary endpoints including graft rejection and GVHD for all the study patients with the available data and it is expected that ERC process including data QC will be completed by the end of May 2015. Data lock is planned on June 1, 2015 to generate the data analysis report to facilitate the writing team. Analysis report will be updated in late 2015 to include the longer follow up of

the study patients for the ASH presentation and manuscript. The analysis report will be provided to the team within 2 weeks of the data lock. The writing team will prepare an ASH abstract (submission deadline is August 4, 2015) and also work on the manuscript for a simultaneous publication of ASH presentation and manuscript.

Primary Endpoint:

The primary objective is to determine event-free survival (EFS) at 1 year after URD HCT using BM in patients with sickle cell disease (SCD). Per protocol, death, disease recurrence or graft rejection by 1 year will be considered events for this endpoint. Disease recurrence is defined as the return of sickle erythropoiesis (Hb S level > 70%) with or without recurrence of clinical complications of sickle cell disease such as stroke, acute chest syndrome, and veno-occlusive crisis (VOC). Primary graft rejection is defined as the presence of < 20% donor cells assessed by bone marrow or peripheral blood chimerism assays on Day 42. Infusion of a second stem cell product on or prior to Day 42 will be considered primary graft rejection. The presence of < 20% donor derived hematopoietic cells in peripheral blood or bone marrow after Day 42 in a patient with prior evidence of > 20% donor cells will be considered late graft rejection. Infusion of a second stem cell product beyond Day 42 will be considered late graft rejection. The Study Chair(s) should be contacted prior to any decisions regarding infusion of additional donor cells/second transplant.

Note/concern: This is the definition of primary endpoint in the protocol. Will keep this as is in this SAP to ensure the definition to be consistent as the protocol.

Patients to Include:

The study enrolled a total of 30 BM patients and all of them received a transplant per study. The BMT CTN Data and Safety Monitoring Board (DSMB panel #1) has recommended to exclude one in-eligible patient that was inadvertently enrolled to the study from the final publication in previous DSMB review. The study outcomes for all the patients including this ineligible case have been reviewed by the Endpoint Review Committee of the study. This case and all other patients who will not be included in the final analysis along with the rationale will be eventually determined by the ERC and confirmed by the statistician and NHLBI.

Note/concern: The protocol team agrees to follow the DSMB recommendation to exclude this patient in the final analysis. This patient had 6/8 HLA match and already completed the 2-year follow-up per protocol. The rationale of excluding this and the follow up status of this patient will be briefly described in the manuscript for completeness.

Table of Contents

DATA SUMMARY:

Brief summary for the report being provided. Descriptions for each exhibit are shown below in order.

EXHIBIT 0601-1: DEMOGRAPHICS AND BASELINE CHARACTERISTICS

These will be described in a table as below. Frequencies and percents for categorical covariates. Median and range for continuous covariates.

Table 1

	N (%)
Total Transplanted and Eligible	
Gender	
Female	
Male	
Ethnicity	
Hispanic or Latino	
Not Hispanic or Latino	
Unknown	
Not Answered	
Race	
American Indian/Alaskan Native	
Asian	
Hawaiian/Pacific Islander	
Black or African American	
White	
More than One Race	
Other, Specify	
Unknown	
Not Answered	
Age, yrs	
Mean (Std. Dev.)	
Median (range)	
3-10	
11-15	
16-20	

Table 1 (cont'd)

	N (%)
Total Transplanted and Eligible	
Lansky Performance Score	
100	
90	
80	
70	
Sickle Cell Disease Genotype	
Hb SS	
Sβo thalassemia	
Hb SC	
Hb Sβ+ thalassemia	
HLA Match Score	
8/8	
Direct Bilirubin	
Mean	
Std. Dev.	
Median	
Creatinine	
Mean	
Std. Dev.	
Median	
Pulmonary Function Tests Performed	
Yes	
No	
DLCO	
Mean (Std. Dev.)	
Median (range)	
Ferritin Level (ng/ml)	
Mean (Std. Dev.)	
Median (range)	

Table 1 (cont'd)

	N (%)
Total Transplanted and Eligible	
Disease symptoms (categories not mutually exclusive)	
Stroke	
Neurological Deficit	
Acute Chest Syndrome	
Severe pain	
Hemoglobin electrophoresis HbS (%)	
Mean (Std. Dev.)	
Median (range)	
Donor Gender	
Female	
Male	
Donor Ethnicity	
Hispanic or Latino	
Not Hispanic or Latino	
Unknown	
Not Answered	
Donor Age, yrs	
Mean (Std. Dev.)	
Median (range)	
18-29	
30-39	
40-49	
50-65	

Note/concern: Donor age, gender, ethnicity, sickle cell trait, CD34+ and TNC data needs to be retrieved from CIBMTR data system and can be listed under donor characteristics. Cardiac function, splenic function, cerebral MRI, QOL, neurocognitive function, liver biopsy at baseline will also be included if data available.

EXHIBIT 0601-2: EVENT-FREE SURVIVAL

The primary analysis will consist of estimating 1 year EFS probability based on the Kaplan-Meier product limit estimator. The 1 year EFS probability and confidence interval will be calculated. In addition, the frequencies of each component of the composite endpoint (death, primary graft failure and secondary graft failure) will be described.

Note/concern: The protocol team agreed that even though the protocol defined disease recurrence as one part of the primary endpoints. However, the frequency of disease recurrence will not be computed. Instead it will be described for the cases with sufficient data. This does not impact the EFS as a composite primary endpoint.

Results for this endpoint will be summarized in the below table, besides the EFS curve.

Time point	EFS Estimate	95% Confidence Interval
1 year post transplant		
2 years post transplant		

EXHIBIT 0601-3: OVERALL SURVIVAL

Overall survival is defined as time from transplant to death or last follow-up, whichever comes first.

Results for this endpoint will be summarized in the below table, besides the OS curve.

Time point	OS Estimate	95% Confidence Interval
1 year post transplant		
2 years post transplant		

EXHIBIT 0601-4: PRIMARY CAUSE OF DEATH

Table listing the primary causes of death (COD). The ERC adjudicated COD will be used instead of the center-reported COD. Results will be shown as below:

COD	**N**	**(%)**
Disease Recurrence		
Graft Rejection		
Acute GVHD		
Chronic GVHD		
Infection		
Organ Failure		
Other		
Total		

EXHIBIT 0601-5: NEUTROPHIL RECOVERY

Time to ANC engraftment is defined as the first of three measurements on different days that the patient has an absolute neutrophil count of $\geq$ 500/μL following conditioning regimen induced nadir. To assess the incidence of engraftment from day of transplant, the cumulative incidence rate will be computed along with a 95% confidence interval at 28 days post-transplant. Death prior to neutrophil engraftment will be considered as a competing risk. Results for this endpoint will also include a cumulative incidence curve.

Neutrophil Recovery	
Day 28 incidence rate (95% CI)	
Median time to Neutrophil Recovery	

EXHIBIT 0601-6: PLATELET RECOVERY

Platelet engraftment will be defined as the first day of a minimum of three measurements on different days that the patient has achieved a platelet count > 50,000/mL AND is platelet transfusion independent for a minimum of seven days following conditioning regimen induced nadir. The first of the three days will be designated the day of platelet engraftment. Subjects must not have had platelet transfusions during the preceding 7 days. This endpoint will be evaluated through 100 days. Incidence of platelet recovery will be estimated using cumulative incidence function, treating death as a competing risk. Incidence rate will be provided with the 95% confidence interval for each criterion. Curve for cumulative incidence of platelet recovery will be displayed.

Results for this endpoint will be summarized in the below table, besides the cumulative incidence curve.

Platelet Recovery	
Platelet recovery to >50k Day 100 incidence rate (95% CI)	
Median time to Platelet recovery to >50k	

EXHIBIT 0601-7: GRAFT REJECTION

This endpoint includes primary graft rejection and secondary graft rejection. Primary graft rejection is defined as the presence of < 20% donor cells assessed by bone marrow or peripheral blood chimerism assays on Day 42. Infusion of a second stem cell product on or prior to Day 42 will be considered primary graft rejection. The presence of < 20% donor derived hematopoietic cells in peripheral blood or bone marrow after Day 42 in a patient with prior evidence of > 20% donor cells will be considered late graft rejection. Infusion of a second stem cell product beyond Day 42 will be considered late graft rejection. Events will be summarized in the table as below.

Graft Rejection	**N**	**(%)**
Primary graft rejection		
Secondary graft rejection		
Total		

EXHIBIT 0601-8: ACUTE GVHD

Table to summarize the maximum acute GVHD post transplant. Plots of cumulative incidence of acute GVHD grade II-IV (Panel A) and acute GVHD grade III-IV (Panel B) from the time of transplant. Provide estimates of cumulative incidence of acute GVHD grade II-IV or III-IV at day 100 (as well as Day 180) post transplant, with 95% confidence intervals. Death prior to occurrence of acute GVHD will be considered as a competing risk.
Results for this endpoint will be summarized in the below tables, besides the cumulative incidence curves.

Maximum Acute GVHD Grade	Total	
	N	(%)
Grade 0, No aGVHD		
Grade I		
Grade II		
Grade III		
Grade IV		
Total Transplanted		

Secondary Endpoint: Acute GVHD	Rate (95% CI)
Day 100 Incidence of Grade II-IV acute GVHD	
Day 100 Incidence of Grade III-IV acute GVHD	
Day 180 Incidence of Grade II-IV acute GVHD	
Day 180 Incidence of Grade III-IV acute GVHD	

EXHIBIT 0601-9: CHRONIC GVHD

Table to summarize the maximum grade and overall maximum severity of chronic GVHD . Cumulative incidence of chronic GVHD post transplant will be plotted. Provide incidence rate of chronic GVHD at 1-year and 2-year post transplant, with 95% confidence intervals. Death prior to occurrence of chronic GVHD will be considered as a competing risk.
Results for this endpoint will be summarized in the below tables, besides the cumulative incidence curves.

Secondary Endpoint: Chronic GVHD	Rate (95% CI)
1-year Incidence of chronic GVHD	
2-year Incidence of chronic GVHD	
Maximum Grade of chronic GVHD Limited Extensive	
Maximum Severity of chronic GVHD Mild Moderate Severe	

EXHIBIT 0601-10: UNEXPECTED GRADES 3-5 ADVERSE EVENTS

Table listing the unexpected grades 3-5 adverse events (AEs) including onset date, severity, relationship to protocol and medical monitor assessment.

Patient ID	Center	AE Onset Date	Days Since Transplant	Adverse Event Description [Medical Monitor Description]	Event Severity	Relationship to Protocol	Effect on Therapy/ Intervention	DCC Expected ?

EXHIBIT 0601-11: CORE AND PROTOCOL-SPECIFIC TOXICITY (GRADE > 2)

Use bar graphs to show the toxicity frequency within 1 year post transplant for each assessment period and overall from transplant through 1 year. Assessment time points include Day 0, Day 28, Day 56, Day 100, Day 180 and Day 365. Also use a summary table to show frequency with maximum toxicity of patients experiencing grades 3-5 toxicities.

Results for this endpoint will be summarized in the below tables, besides the bar graphs.

Toxicities within 1 Year	**Maximum Grade (N)**			**Total (N %)**
	3	4	5	
RPLS/PRES				
Thrombocytopenia				
Pulmonary Hypertension				
CNS Cerebrovascular Ischemia				
Hypertension				
Hemorrhage CNS				
Seizures				
Needs Dialysis				
Vascular Leak				
HUS-TTP-DIC				
Hemorrhage				
Dyspnea				
Hypoxia				
Left Ventricular Systolic Dysfunction				
Cardiac Arrhythmia				
Hypotension				
Hemorrhagic Cystitis				
Mucositis Stomatitis				
Somnolence				
Abnormal Liver Symptoms				
Overall, Total # Patients with Any Toxicities				
Total # Transplanted				

EXHIBIT 0601-12: TRANSPLANT-RELATED COMPLICATION

Transplant-related complications include: Idiopathic pneumonia syndrome (IPS); Veno-occlusive disease; CNS toxicity; Infection. CNS toxicity will be defined as patient experiencing seizures, CNS hemorrhage, or RPLS. Infection is defined as CMV reactivation with/without clinical disease, adenovirus infection, EBV, and invasive fungal infections.

The frequency of transplant-related complications, both overall and by type of complication, will be described using proportions in below table.

	# Patient with Complication **N (%)**
Hepatic veno-occlusive disease (VOD)	
Idiopathic pneumonia syndrome (IPS)	
Seizures Grade 2 Grade 3 Grade 4	
CNS hemorrhage	
Reversible posterior leukoencephalopathy syndrome (RPLS) or Posterior reversible encephalopathy syndrome (PRES)	
Infections CMV Adenovirus EBV IFI (proven/probable fungal infection)	
Overall, Total Number of Patients with any complications	
Total # Transplanted	

EXHIBIT 0601-13: REVERSE POSTERIOR LEUKOENCEPHALOPATHY SYNDROME OR POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (RPLS/PRES)

A cumulative incidence curve will be plotted to show the RPLS/PRES occurring within 1 year post transplantation for the study patients.

Secondary Endpoint: RPLS/PRES	Rate (95% CI)
1-year Incidence of RPLS/PRES	

EXHIBIT 0601-14: INFECTION SUMMARY

Table to summarize the site-reported infections. Number of infections per patient and maximum severity of infections per patient will be tabulated on a per patient basis. Total number of infections by type of organism will also be tabulated. Results will be summarized in the below table.

	N %
# Patients Transplanted	
# Patients with Infections	
# Patients with Infection Reports =1 =2 =3 =4 =5 >=6	
Total Infection Events	
Maximum Severity by Patient	

None Moderate Severe Life Threatening/Fatal	
Infection by Type (# of patients) Bacterial Viral Fungal Protozoal Other	

Note/concern: This table will use the site-reported infection data. The protocol team will only use as reference to see if any further exploration will be needed to look into the infection outcomes.

EXHIBIT 0601-15: DISEASE-RELATED COMPLICATION - STROKE

Per protocol, an overt stroke is defined as a focal neurologic event and neurologic deficit lasting more than 24 hours with neuroimaging changes. Children with new MRI lesions and ongoing neurologic injury to the brain that does not result in focal motor impairment are referred to as having silent cerebral infarcts. These lesions are defined as a MRI signal abnormality measuring at least 3 mm visible on two views on T-2 weighted images. Both forms of neurologic injury that develop as a new event post-transplant will be considered a disease related complication.

Frequency and proportion will be computed.

Note/concern: This is the definition of stroke in the protocol. The MRI results will first be collected and reviewed by investigators. Due to the timeline, will not be available for the abstract but will be included for the manuscript.

EXHIBIT 0601-16: IMMUNE RECONSTITUTION

Lymphocyte subpopulations (absolute number of CD3, CD4, CD8, CD 16+56 and CD19 cells) will be measured by flow cytometry. Immunoglobulin levels (IgG, A and M) will also be quantified. Descriptive statistics will be computed for all the immune reconstitution assays, as tabulated in the below table. Figures will be shown to display the immune reconstitution over time on patient level in Box plot for each assay.

		N	Mean	Std Dev	Median	Min	Max
CD3 (cells/μL)	**Day 180**						
	Day 365						
	Day 730						
CD4 (cells/μL)	**Day 180**						
	Day 365						
	Day 730						
CD8 (cells/μL)	**Day 180**						
	Day 365						
	Day 730						
CD19 (cells/μL)	**Day 180**						
	Day 365						
	Day 730						
CD56+/CD16+ (cells/μL)	**Day 180**						
	Day 365						
	Day 730						
IgG (mg/dL)	**Day 180**						
	Day 365						
	Day 730						
IgA (mg/dL)	**Day 180**						
	Day 365						
	Day 730						
IgM (mg/dL)	**Day 180**						
	Day 365						
	Day 730						

EXHIBIT 0601-17: HEALTH-RELATED QUALITY OF LIFE

Both parent reported and child self-reported health-related QOL was collected for the study patients at baseline, on Day 100, 6 months, 1 year and 2 years of transplant. Mean QOL scores and confidence intervals will be computed at each time point. For both parent and child reported health-related QOL mean scores, a paired student T test will be used to look for differences in mean scores between baseline and 2 years after the HCT. To determine the magnitude of differences, standardized effect sizes (or z-scores) will be calculated. This will be done by taking the difference between the mean domain scores of the baseline score and the follow-up scores and dividing by the standard deviation of the baseline. Domain scores will also be compared between baseline and 2 years post-transplant with a Bonferroni correction for multiple testing. In addition, mixed models for repeated measures data will be used to assess whether QOL is changing significantly over each time point among survivors.

Pearson correlation coefficients will be used to determine the association between child and parent health-related QOL scores. Fisher's z-transformation will be used to test whether this correlation is significantly different from 0 and to construct confidence intervals for the correlation coefficient. A paired t-test will be used to test the difference between the mean CHQ scores of the child and parent at each time point.

Note/Concern: Upon the team discussion, Julie Panepinto would be the leading investigator to analyze the 0601 QOL data. EMMES has collected the data (in CRFs - C50 and C87) but do not have the manual/reference below. It was decided that the raw data will be conveyed to Dr. Panepinto for analysis upon the data lock. 1 year QOL data is important to know so it would be best if this can be included for the abstract.
Manual or documents for 0601 Health-related QOL scoring needed for 0601 final analysis:
ADMINISTERING THE CHILD HEALTH QUESTIONNAIRE
(From Landgraf, Abetz, and Ware, Child Health Questionnaire (CHQ): A User's Manual, 1999)
Reference from the protocol:
[78] Panepinto JA, O'Mahar KM, DeBaun MR, Loberiza FR, Scott JP. Health-related quality of life in children with sickle cell disease: child and parent perception. Br J Haematol. 2005 Aug;130(3):437-44.
[79] Panepinto JA, O'Mahar KM, DeBaun MR, Rennie KM, Scott JP. Validity of the child health questionnaire for use in children with sickle cell disease. J Pediatr Hematol Oncol. 2004 Sep;26(9):574-8.

EXHIBIT 0601-18: NEUROCOGNITIVE EVALUATION

All patients will be assessed with a cognitive battery at study entry and 2-year follow-up. The major indicator of cognitive loss will be decline in general intellectual abilities (IQ) as assessed by the Wechsler Abbreviated Scale of Intelligence (WASI) or Wechsler Preschool and Primary Scale of Intelligence (WIPPSI-III).
Other secondary outcomes, including the Behavior Rating Inventory of Executive Function (BRIEF) Continuous Performance Test Second Edition (CPT-II), VMI, Children's Memory Scale (CMS), and California Verbal Learning Test (CVLTC) will be compared in the same manner by comparing the composite t-score for each age-appropriate cognitive domain test over time.
A paired t-test will be used to assess the change from baseline in WASI IQ and change from baseline in BRIEF and other age-appropriate tests T-Scores over time. In addition to using statistical techniques to evaluate changes in IQ, clinical significance will also be evaluated.
Functional scores and confidence intervals will be computed at each time point in age-appropriate fashion. Mixed models for repeated measures data will be used to assess whether functional scores change significantly after transplant over time.

Secondary analysis of the secondary outcome will be performed. This secondary analysis will be an adjustment of the secondary study outcome for potential confounding factors (e.g., adjust the secondary study outcome for confounding factors such as gender, age, medical history, co-morbidities, etc.). Since the secondary study outcome is a continuous measure, we will be able to make these adjustments with the use of generalized linear models (e.g., analysis of covariance). Generalized linear models can help to determine whether the apparent effect of one variable (e.g., treatment) on the outcome of interest (e.g., the mean change from baseline of IQ after 2-years of follow-up) is accounted for by differences in other patient characteristics (e.g., treatment compliance, gender, age, medical history, co-morbidities, etc.).

Note/Concern: Similarly as QOL, EMMES has collected the data on Neurocognitive Testing (in CRF - NCT) but do not have sufficient resources to conduct the analysis, will convey the raw data to the leading investigator Dr. Allison King. Also protocol defined the secondary analysis using multivariate models. It makes more sense to conduct HQL analysis after 2-year data is complete. So this part of the data analysis will not be included in the abstract but will be included in the manuscript.

EXHIBIT 0601-19: ACCRUAL OVER TIME

Table showing accrual numbers for each participating center, actual accrual versus projected accrual number.

EXHIBIT 0601-20: SIGNIFICANT PROTOCOL DEVIATIONS

Table listing the cumulative significant protocol deviations occurred during the study, including transplant center, patient ID, description of the protocol deviations.

EXHIBIT 0601-21: SAFETY MONITORING

The key safety endpoints of the study include overall mortality, graft rejection, and GVHD. Safety monitoring has been conducted during the study course and interim analysis presented to the DSMB review. A truncated Sequential Probability Ratio Test (SPRT) for a binomial outcome will be used to monitor each type of toxicity as described below. The SPRT can be represented graphically. At each interim analysis, the total number of patients enrolled is plotted against the total number of patients who have experienced toxicity. The continuation region of the SPRT is defined by two parallel lines. Only the upper boundary will be used for monitoring the study to protect against high incidences of toxicity. An SPRT contrasting 15% versus 30% 100 day mortality results in decision boundaries with a common slope of 0.219 and the intercept of 2.097, with nominal type I and II errors of 14% and 10%, respectively. An SPRT contrasting 20% versus 35% 100 day graft rejection results in decision boundaries with a common slope of 0.271 and the intercept of 2.473, with nominal type I and II errors of 12% and 20%, respectively. The stopping rule and operating characteristics for Day 100 acute GVHD are identical to that for overall mortality. SPRT graph for each safety endpoint will be displayed.

EXHIBIT 0601-22: PATIENT NARRATIVE AND OUTCOME SUMMARY

Just to facilitate the interpretation of study outcomes on a patient level, a brief per patient narrative will be provided to include demographic and baseline information, transplant course, complications post transplant and last follow up etc. A table of data listing will be as below for cases 1-30.

Case #	Patient ID	Enroll Date	Gen-der	Age (yrs) at enroll	Lansky Score at enroll	Trans-plant date	Neutrophil Recovery (Date)	Platelet Recovery to >50k (Date)	PRES/RPLS (Y/N, Date)	Graft Reject (Date)	Disease Recurr-ence (Date)	Death (Date, COD)	Grade 2-4 Acute GVHD (Date, Max Grade)	Chronic GVHD (Date, Max Grade)	Toxicity (Max CTCAE grade)	Lansky Score at 2 years	On/off immuno-supp ressant (Date)	Days of Follow -up Post Trans-plant
1																		
2																		
3																		
4																		
5																		
6																		
7																		
8																		
9																		
10																		
11																		
12																		
13																		
14																		
15																		

Case #	Patient ID	Enroll Date	Gen-der	Age (yrs) at enroll	Lansky Score at enroll	Trans-plant date	Neutrophil Recovery (Date)	Platelet Recovery to >50k (Date)	PRES/RPLS (Y/N, Date)	Graft Reject (Date)	Disease Recurr-ence (Date)	Death (Date, COD)	Grade 2-4 Acute GVHD (Date, Max Grade)	Chronic GVHD (Date, Max Grade)	Toxicity (Max CTCAE grade)	Lansky Score at 2 years	On/off immuno-supp ressant (Date)	Days of Follow -up Post Trans-plant
16																		
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