CURE SICKLE CELL.

CureSCi CDE Project
Monitoring Side Effects Working Group Summary

The goal of the Monitoring Side Effects Working Group (WG) has developed recommendations for data collection in genetic studies with curative intent in sickle cell disease (SCD). The standard data form recommendations are to facilitate harmonized data collection that will reduce study start-up time, reduce trial costs, and improve data quality and data sharing. The Cure Sickle Cell Initiative (CureSCi) library of recommendations or common data elements (CDE) will facilitate the preparation of data collection tools and present the current state of science through a hierarchical presentation of data elements to collect along with any guidelines for clinical research genetic studies in sickle cell disease.

The Monitoring Side Effects WG defines the following time periods in regards to side effects:

- **Acute** as being first 100 days after infusion (gene therapy/gene editing)
- **Mid** being 100 days to 2 years post-infusion; and,
- **Late** as being 2-15 years.

After some deliberation, the WG defined their scope (see **Table A**) with understanding that there would be some overlap with Physical Examination/Medical History and Genetics/Assays working groups. In addition, side effects were identified when possible to fit into three categories: SCD related (disease-related); conditioning-related; or therapy-related.

Table A

Timeline	Acute			Mid			Late		
Cause	Therapy Related	Conditioning Related	Disease Related	Therapy Related	Conditioning Related	Disease Related	Therapy Related	Conditioning Related	Disease Related
Infections	X	X	X	X	X	X	X	X	X
Liver toxicity	X	X	X	X	X	X	X	X	X
Mucositis	X	X	X	X	X	X	X	X	X
Transfusion support duration	X	X	X	X	X	X	X	X	X
Genotoxicity (off-target effects and insertional mutagenesis, conditioning related clonal proliferation)	X	X	NA	X	X	NA	X	X	NA
Presence and Durability of gene modified HSC graft	X	X	NA	X	X	NA	X	X	NA
Endocrine insufficiency, infertility, growth	X	X	X	X	X	X	X	X	X

CURE SICKLE CELL.

Timeline	Acute			Mid			Late		
Cause	Therapy Related	Conditioning Related	Disease Related	Therapy Related	Conditioning Related	Disease Related	Therapy Related	Conditioning Related	Disease Related
delay and osteoporosis/avascular necrosis									
Neurological side effects (e.g., seizures, stroke, hemorrhage)	X	X	X	X	X	X	X	X	X
Neuropsychological effects	X	X	X	X	X	X	X	X	X
Iron Overload	X	X	X	X	X	X	X	X	X
Secondary malignancy	X	X	NA	X	X	NA	X	X	NA
Immune function and/or responses	X	X	X	X	X	X	X	X	X
Pulmonary Function	X	X	X	X	X	X	X	X	X
Infusional toxicity (acute)	X	NA	NA	NA	NA	NA	NA	NA	NA
Cytopenia (duration of neutropenia, thrombocytopenia)	X	X	X	X	X	X	X	X	X
Serious AEs – Hospitalization (duration)	X	X	X	X	X	X	X	X	X
Organ specific toxicities (supplemental) – liver, lung, kidney, heart, brain, GI	X	X	X	X	X	X	X	X	X
Mortality and survival	X	X	X	X	X	X	X	X	X

CURE SICKLE CELL.

Summary Table:

Domain/Subdomain	CRF	Classification	Notes
Safety Data	Genotoxicity Module	TBD	Related to Genetically Modified HSC Infusion. This module was reviewed also by the Genetics/Assays WG.
Safety Data	Infusional Toxicity	Supplemental-Highly Recommended	For genetically modified cells – required elements
Treatment and Intervention Data	Genetic Persistence	TBD	Baseline and Post therapy monitoring. This module was reviewed also by the Genetics/Assays WG.
Treatment and Intervention Data	HCT Infusion	Supplemental	Form used for autologous back up
Safety Data	Cytopenia Module	Supplemental	Form modified from CIBMTR
Safety Data	Immune function and/or responses Module	Supplemental	CIBMTR Form 2031 revision 2 June 2009
Safety Data	Infections Module	Supplemental	Modified from BMT CTN Infection Form. This module was reviewed also by the Physical Examination/Medical History WG.

CURE SICKLE CELL.

Domain/Subdomain	CRF	Classification	Notes
Safety Data	Iron Overload Module	Core and Supplemental	
Safety Data	Spleen Toxicities	Supplemental	
Safety Data	Toxicity Form	Supplemental	BMT CNT form
Safety Data	Malignant Neoplasm Module	Supplemental	Secondary/new malignancy form was drafted new by WG members.
Treatment and Intervention Data	Cellular Therapy Essential Data Follow-Up Form	Supplemental	
Assessments and Examinations / Chronic Conditions	Endocrine, Fertility and Bone	Core and Supplemental	Core elements on Avascular necrosis and fertility preservation questions. This was also presented in the Physical Examination/Medical History WG public review files.
Safety Data	Mortality and survival Module (Death Form)	Supplemental	
Safety Data	Serious Adverse Events	Core and Supplemental Elements	Standard form adopted from National Institute of Neurological Disorders and Stroke CDEs