WARRIOR-SCD: Whole-person Assessment of Response and Risk after transformative therapies:

Investigating Outcomes and Resilience in Sickle Cell Disease

A Cure Sickle Cell Initiative Long Term Follow-Up Study

Study Summary

The purpose of this Study is to assess the long-term outcomes of individuals with sickle cell disease (SCD) who received gene therapy (GT) or hematopoietic cell transplantation (HCT) on clinical trials or as standard-of-care.

Study Design

Study Overview

This is an observational study of selected individuals with SCD who have received GT or HCT on an NHLBI supported clinical trial or as standard-of-care therapy. The study will follow these individuals to understand the long-term safety and efficacy of these therapies.

Collection of data and specimens will be collected under 3 separate protocols approved by the institutional review board (IRB). Clinical data will be collected under the CIBMTR Research Database Protocol. Patient-reported data will be collected under the CIBMTR Protocol for the Collection of Patient-Reported Outcomes (PRO) Data. Specimens will be collected under the Blood and Marrow Transplant Clinical Trials Network (BMT CTN) Protocol 2402 (Hematopoietic Cell Transplant and Gene Therapy for Non-Malignant Blood Disorders Biobank Resource -the *HOPE Resource*) at centers who activate that protocol. Clinical data and PRO data from this study will be linked with biospecimens for patients who consent to the BMT CTN 2402 protocol.

To participate in the PRO protocol, patients must opt in to be contacted for future research when they sign the Research Database Protocol. CIBMTR staff will then manage all consent and data collection activities. It is recommended, but not required, that centers participate in the BMT CTN 2402 HOPE Resource protocol to participate in the data collection part of this study.

Hypothesis

Individuals who receive either GT or HCT will have preserved organ function compared to baseline and a mortality rate and quality of life comparable to 1) US residents in general and 2) superior to individuals with SCD who do not receive these therapies.

Specific Objectives

The primary objective of this study is to collect long-term follow-up data from individuals with SCD who have received GT or HCT. The study will focus on the following clinical outcomes of interest, collecting specific details pertaining to each outcome.

- Acute and chronic pain
- End-organ function, including brain, lung, heart, kidney, and endocrine

- Other specific complications of SCD (e.g., retinopathy, priapism)
- Complications of conditioning and the GT and HCT procedure, e.g., graft-versus-host disease, graft persistence, and others
- Development of malignancy, including myelodysplastic syndrome (MDS), leukemia, and solid tumors
- Reproductive health
- Quality of life
- Death

Participants

Eligibility Criteria

- Individuals who receive gene therapy or HCT for SCD on a NHLBI funded clinical trial in 2017 or later, or
- Individuals who received or are scheduled to receive gene therapy or HCT for SCD in 2023 or later, either as standard-of-care or on an investigational protocol at participating centers
- Individuals who signed (or legal guardian signed) the CIBMTR Research Database Protocol consent and assent as age appropriate

Exclusion Criteria

- Recipient did not provide consent to the CIBMTR Research Database Protocol

Recruitment

Accrual

The study aims to accrue 309 patients. Accrual will continue for 4 years or until 309 patients are accrued, whichever occurs first. It is expected that 30-40% of patients will be gene therapy recipients.

Participating Centers

Participating centers will recruit patients and obtain consent for research. CIBMTR will compile a Center List, identifying centers that were involved in an NIH-sponsored clinical trial of GT or HCT for SCD or who, after discussion with NHLBI, are deemed to have a population of interest.

Center-facing informational and training materials are available for hematologists and other health care providers, both at the centers where patients receive their therapies and to other centers where patients may receive ongoing care. Center Participation Materials will describe project requirements, patient selection, data collection processes, center training, and center reimbursement.

Strategies for Patient and Provider Engagement

- **Infrastructure**: CIBMTR data collection infrastructure will allow centers to initiate CIBMTR database registration at the time an infusion is planned.
- **Materials for Patients**: CIBMTR will provide the center: 1) patient engagement materials developed in a variety of media, including flyers and webinars and 2) project information to support patient enrollment.
- **Materials for Providers**: CIBMTR will develop and distribute provider engagement materials for distribution to staff and faculty in the institution's sickle cell center and GT/HCT center and materials for distribution to the center's referring providers. Ongoing outreach activities will be coordinated by a single point of contact within CIBMTR, for both the transplant provider and the SCD care provider. The study will support varied strategies for interactions with hematologists and other health care providers, both at the centers where patients receive their therapies and at other centers where they may receive ongoing care.
- **Outreach to SCD Advocacy Groups**: CIBMTR will collaborate with the American Society of Hematology Community Advisory Boards and others. CIBMTR will solicit input from these groups on educational material content, frequently asked questions (FAQs), and engagement opportunities. Subsequently, all materials will be provided to advocacy groups for distribution. This is intended as an ongoing conversation throughout the life of the study.
- **Patient-Reported Outcomes (PRO) Survey Incentive**: Patients will receive a $50 gift card for completing their first PRO survey and a $25 gift card for each subsequently completed survey until project completion, subject to available funding. Gift cards will be sent to the parent/guardian of pediatric patients.

Data Collection

The clinical data forms, PRO measures, and corresponding data collection timepoints are outlined below. To minimize the burden associated with entering complex clinical information, select reports and test results will be submitted via document upload rather than manual data entry.

CIBMTR clinical data collection forms and timepoints

HCT Cohort

Number	Name	Pre Transplant (baseline)	Day 100	Day 180	Annually	Event-driven
2804	CIBMTR Research ID Assignment	•				
N/A	Consent Tool	•				
2814	Indication	•				
2820	Recipient Contact Information	•				
2807	Race, Ethnicity and Ancestry	•				
2400	Pre-Transplant Essential Data	•				
2402	Disease Classification	•				
2000	Recipient Baseline Data	•				

Number	Name	Pre Transplant (baseline)	Day 100	Day 180	Annually	Event-driven
2006	Hematopoietic Cellular Transplant (HCT) Infusion	•				
2030	Sickle Cell Disease Pre-Infusion Data	•				
2559	WARRIOR-SCD Pre-Infusion Supplemental Data	•				
2100	Post-Infusion Follow-Up		•	•	•	
3504	Organ Function / Late Effects		•	•	•	
2130	Sickle Cell Disease Post-Infusion Data		•	•	•	
3505	Transfusion		•	•	•	
2560	WARRIOR-SCD Post-Infusion Supplemental Data		•	•	•	
2900	Recipient Death Data					•
3500	Subsequent Neoplasms					•
3501	Pregnancy					•

Gene Therapy Cohort

Number	Name	At Cell Collection	Pre Infusion (baseline)	Day 100	Day 180	Annually	Event-driven
2804	CIBMTR Research ID Assignment	•					
N/A	Consent Tool	•					
2814	Indication	•	•				
2820	Recipient Contact Information	•					
2807	Race, Ethnicity and Ancestry	•					
2400	Pre-Transplant Essential Data		•				
2402	Disease Classification		•				
2000	Recipient Baseline Data		•				
2003	Gene Therapy Product		•				
2030	Sickle Cell Disease Pre-Infusion Data		•				
2559	WARRIOR-SCD Pre-Infusion Supplemental Data		•				
2100	Post-Infusion Follow-Up			•	•	•	
3504	Organ Function / Late Effects			•	•	•	
2103	Gene Therapy Persistence			•	•	•	
2130	Sickle Cell Disease Post-Infusion Data			•	•	•	
3505	Transfusion			•	•	•	
2560	WARRIOR-SCD Post-Infusion Supplemental Data			•	•	•	
2900	Recipient Death Data						•
3500	Subsequent Neoplasms						•
3501	Pregnancy						•
3502	Laboratory Studies						•
3506	Marrow Surveillance						•

Schedule of PRO and Sociodemographic Data Collection

Domain	Measure	
	Pediatrics	**Adults**
Global health	PROMIS global health	PROMIS global health
Physical function	PROMIS mobility PROMIS upper extremity	PROMIS physical function
Anxiety	PROMIS anxiety	PROMIS anxiety
Depression	PROMIS depressive symptoms	PROMIS depression
Fatigue	PROMIS fatigue	PROMIS fatigue
Sleep	PROMIS sleep disturbance	PROMIS sleep disturbance
Pain	**PROMIS pain interference** [a]	**PROMIS pain interference**[a]
	ASCQ-ME pain episodes	ASCQ-ME pain episodes
	PROMIS pain behavior	PROMIS pain behavior
	PROMIS pain quality - sensory	PROMIS pain - neuropathic
	(captured in pain quality – sensory)	PROMIS pain - nociceptive
	Chronic pain questions	Chronic pain questions
Social relationships	PROMIS peer relationships	PROMIS ability to participate in social roles and activities
Family relationships	PROMIS family relationships	Not assessed
Sexual function	Not assessed	PROMIS sexual function
Financial toxicity (pre-TX, Day 180, annually)	COST-FACIT version 2[b]	COST-FACIT version 2
Sociodemographic (pre-TX, Y1, every other year)	Standard questions[b]	Standard questions
Reproductive health questions (pre-TX)	Sperm banking or oocytes pre-conditioning, other questions as indicated. *Questions to be determined*	Sperm banking or oocytes pre-conditioning, other questions as indicated. *Questions to be determined*
(Pre-TX)	Not assessed	Biological children conceived pre-treatment
(Pre-TX, annually)	Not assessed	Pregnancy status, result of pregnancy, source of pregnancy (e.g., result of sperm or oocyte banking), difficulty conceiving post treatment
(Pre-TX, annually)	Not applicable	Females, age ≥ 11: Have you been diagnosed with premature menopause or put on hormone replacement therapy?
(Pre-TX, annually)	Not applicable	Males, age ≥ 11: Have you had a semen analysis in the past 12 months?
(Pre-TX, annually)	Not applicable	Males, age ≥ 11: If yes, were results normal or abnormal?

Note: PROs assessments include pre-TX, Day 100, Day 180, Day 365, annually thereafter, unless noted in table.

Abbreviations: ASCQ-ME, Adult Sickle Cell Quality of Life Measurement Information System; COST-FACIT: Comprehensive Score for Financial Toxicity–Functional Assessment of Chronic Illness Therapy; PROMIS: Patient-Reported Outcomes Measurement Information Systems; TX, treatment.

[a] Primary outcome variable; see statistical power calculation in Section 4.

[b] All measures are self-reported by the patient unless designated with "b" and are therefore completed by parent/guardian.