CURE
SICKLE
CELL.

CURRENT & ONGOING GENETIC THERAPY CLINICAL TRIALS IN SICKLE CELL DISEASE

It's time to rewrite the story of sickle cell.

Clinical trials are medical studies aimed at finding safe and effective ways to prevent, detect, or treat diseases. Some clinical trials are testing ways of treating disease by changing a patient's genetic material. These are called genetic therapies, and most often they work by adding a healthy copy of a defective gene into the patient's cells. In the future, these techniques may allow doctors to treat a disorder by inserting a gene into a patient's cells instead of using drugs or surgery. Researchers are testing other approaches in addition to replacing the mutated gene with a healthy copy. They are inactivating, or "knocking out," a mutated gene that is functioning improperly. They also are introducing a new gene into the body to help fight a disease. Although genetic therapy is a promising new treatment option for many rare diseases, the technique is still being studied to ensure that it is safe and effective.

How can you help rewrite the story of sickle cell disease? Clinical trial participation is one of the most important ways we can move towards a future without sickle cell disease. We encourage adults, as well as children, healthy volunteers, those living with sickle cell disease, and people from diverse ethnic and racial backgrounds to consider participating in clinical trials.

Researchers are currently studying a number of potential new treatment options and also working towards cures. This document includes genetic therapy trials only. For information on other sickle cell disease trials, please visit: *https://clinicaltrials.gov*.

Have questions and want to learn more about clinical trials? Go to www.nih.gov/health-information/nih-clinical-research-trials-you.

National Heart, Lung, and Blood Institute

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INTERVENTIONAL

▸ Pilot and Feasibility Study of Hematopoietic Stem Cell Gene Transfer for Sickle Cell Disease: *Phase 1* *

ACTIVE / NOT RECRUITING

Age Range	**3–40 Years**
Trial Time Frame	**2/2018–12/2024**
Ref. No.	**NCT03282656**

This is an open-label, non-randomized, single center, pilot and feasibility, single-arm cohort study involving a single infusion of autologous bone marrow derived CD34+ HSC cells transduced with the lentiviral vector containing a short-hairpin RNA targeting BCL11a.

https://ClinicalTrials.gov/show/NCT03282656

▸ Clinical Research Study of Autologous Stem Cell Transplantation for Sickle Cell Disease: *Phase 1 / 2*

ACTIVE / NOT RECRUITING

Age Range	**18 Years and Older**
Trial Time Frame	**12/2014–12/2025**
Ref. No.	**NCT02247843**

This Phase I clinical trial will assess the safety and efficacy of an autologous transplant of lentiviral vector modified peripheral blood for adults with severe sickle cell disease.

https://ClinicalTrials.gov/show/NCT02247843

▸ Safety of Blood Stem Cell Mobilization With Plerixafor in Patients With Sickle Cell Disease: *Phase 1*

RECRUITING

Age Range	**18–40 Years**
Trial Time Frame	**9/2018–9/2024**
Ref. No.	**NCT03664830**

This study will investigate whether up to two injections of plerixafor represent a safe and effective strategy for mobilizing adequate numbers of CD34+ hematopoietic stem progenitor cells (HSPC) for autologous hematopoietic cell transplantation (HCT).

https://ClinicalTrials.gov/show/NCT03664830

▸ Safety Trial of Escalation of Plerixafor for Mobilization of Cells and Evaluation of Gene Transfer: *Phase 1*

RECRUITING

Age Range	**18–65 Years**
Trial Time Frame	**9/2014–7/2025**
Ref. No.	**NCT02193191**

This study will look at the safety and efficacy of a drug called Plerixafor. Plerixafor is approved by the U.S. Food and Drug Administration (FDA) for use in increasing blood stem cell counts before collection in cancer patients.

https://ClinicalTrials.gov/show/NCT02193191

▸ A Safety and Efficacy Study Evaluating CTX001 in Subjects With Severe Sickle Cell Disease: *Phase 1 / 2 / 3*

ACTIVE / NOT RECRUITING

Age Range	**12–35 Years**
Trial Time Frame	**11/2018–10/2024**
Ref. No.	**NCT03745287**

This is a single-arm, open-label, multi-site, single-dose study to evaluate the safety and efficacy of autologous CRISPR-Cas9 Modified CD34+ Human Hematopoietic Stem and Progenitor Cells (hHSPCs) using CTX001.

https://ClinicalTrials.gov/show/NCT03745287

▸ A Study Evaluating Gene Therapy With BB305 Lentiviral Vector in Sickle Cell Disease: *Phase 3*

RECRUITING

Age Range	**2–50 Years**
Trial Time Frame	**2/2020–5/2027**
Ref. No.	**NCT04293185**

This is a non-randomized, open-label, multi-site, single-dose study in approximately 35 adults and pediatric subjects with sickle cell disease. The study will evaluate hematopoietic stem cell (HSC) transplantation (HSCT) with LentiGlobin BB305 Drug Product for SCD.

https://clinicaltrials.gov/ct2/show/NCT04293185

▸ Study of Safety and Efficacy of Genome-edited Hematopoietic Stem and Progenitor Cells in Sickle Cell Disease: *Phase 1 / 2*

ACTIVE / NOT RECRUITING

Age Range	**2–40 Years**
Trial Time Frame	**8/2020–8/2025**
Ref. No.	**NCT04443907**

This study will evaluate two genome-edited, autologous, hematopoietic stem and progenitor cell (HSPC) products - OTQ923 and HIX763 - each reducing the biologic activity of BCL11A, increasing fetal hemoglobin (HbF) and reducing complications of sickle cell disease.

https://clinicaltrials.gov/ct2/show/NCT04443907

* *Funded by the Cure Sickle Cell Initiative*

INTERVENTIONAL CONTINUED

▸ Study to Evaluate the Safety and Efficacy of EDIT-301 for Autologous HSCT in Subjects With Severe Sickle Cell Disease: *Phase 1 / 2*

RECRUITING

Age Range	**12–50 Years**
Trial Time Frame	**5/2021–8/2025**
Ref. No.	**NCT04853576**

The purpose of this study is to evaluate the efficacy, safety and tolerability of treatment with EDIT-301 in adult subjects with severe sickle cell disease (SCD).

https://clinicaltrials.gov/ct2/show/NCT04853576

▸ Transplantation of CRISPRCas9 Corrected Hematopoietic Stem Cells (CRISPR_SCD001) in Patients With Severe Sickle Cell Disease: *Phase 1 / 2* *

NOT YET RECRUITING

Age Range	**12–35 Years**
Trial Time Frame	**6/2024–6/2025**
Ref. No.	**NCT04774536**

This is an open label, non-randomized, 2-center, phase 1/2 trial of a single infusion of sickle allele modified cluster of differentiation (CD34+) hematopoietic stem progenitor cells (HSPCs) in subjects with in subjects ≥12 years old to 35 years old severe Sickle Cell Disease (SCD). The study will evaluate the hematopoietic stem cell transplantation (HSCT) using CRISPR/Cas9 edited red blood cells (known as CRISPR_SCD001 Drug Product).

https://clinicaltrials.gov/ct2/show/NCT04774536

▸ Evaluation of Safety and Efficacy of CTX001 in Pediatric Participants With Severe Sickle Cell Disease: *Phase 3*

RECRUITING

Age Range	**2-11 Years**
Trial Time Frame	**5/2022–5/2026**
Ref. No.	**NCT05329649**

This is a single-dose, open-label study in pediatric participants with severe SCD and hydroxyurea (HU) failure or intolerance. The study will evaluate the safety and efficacy of autologous CRISPR-Cas9 modified CD34+ human hematopoietic stem and progenitor cells (hHSPCs) (CTX001).

https://clinicaltrials.gov/ct2/show/NCT05329649

▸ A Gene Transfer Study Inducing Fetal Hemoglobin in Sickle Cell Disease (GRASP, BMT CTN 2001): *Phase 2* *

RECRUITING

Age Range	**13–40 Years**
Trial Time Frame	**7/2022–5/2026**
Ref. No.	**NCT05353647**

This is an open-label, non-randomized, multi-center, phase 2 study involving a single infusion of autologous bone marrow derived CD34+ HSC cells transduced with the lentiviral vector containing a short-hairpin RNA targeting BCL11a. 25 patients ages 13 to 40 will be enrolled at sites across the US. The main goal of this study is to determine whether the treatment will lead to a complete absence of severe vaso-occlusive events (VOEs) in patients with severe SCD.

https://clinicaltrials.gov/ct2/show/NCT05353647

▸ Haploidentical Hematopoietic Stem Cell Transplantation (HSCT) for Patients With Severe Sickle Cell Disease

RECRUITING

Age Range	**2–25 Years**
Trial Time Frame	**04/2020–11/2027**
Ref. No.	**NCT04207320**

The purpose of this study is to develop a safe and curative stem cell transplant approach to treating sickle cell disease by assessing the safety of haploidentical hematopoietic stem cell transplantation using aβ+ T-cell depletion for children and adolescents with severe sickle cell disease (SCD).

https://clinicaltrials.gov/ct2/show/NCT04207320

▸ A Study Evaluating the Safety and Efficacy of BEAM-101 in Patients With Severe Sickle Cell Disease (BEACON): *Phase 1/2*

RECRUITING

Age Range	**18–35 Years**
Trial Time Frame	**8/2022–2/2025**
Ref. No.	**NCT05456880**

This is an open-label, single-arm, multicenter, Phase 1/2 study evaluating the safety and efficacy of the administration of autologous base edited CD34+ HSPCs (BEAM-101) in patients with severe SCD.

https://clinicaltrials.gov/ct2/show/NCT05456880

INTERVENTIONAL CONTINUED

▸ Evaluation of Efficacy and Safety of a Single Dose of CTX001 in Participants With Transfusion-Dependent β-Thalassemia and Severe Sickle Cell Disease: *Phase 3*

RECRUITING

Age Range	**12–25 Years**
Trial Time Frame	**8/2022–2/2025**
Ref. No.	**NCT05477563**

This is a single-dose, open-label study in participants with transfusion-dependent β-thalassemia (TDT) or severe SCD. The study will evaluate the safety and efficacy of autologous CRISPR-Cas9 modified CD34+ human hematopoietic stem and progenitor cells (hHSPCs) using CTX001.

https://clinicaltrials.gov/ct2/show/NCT05477563

▸ Non-myeloablative Haploidentical HCT Study for Patients With Sickle Cell Disease, Including Compromised Organ Function: *Phase 1/2*

RECRUITING

Age Range	**4–100 Years**
Trial Time Frame	**12/2023–3/2033**
Ref. No.	**NCT06145282**

Haploidentical hematopoietic cell transplantation offers a widely available curative option for individuals with sickle cell disease. The goal is to reverse SCD while avoiding unacceptable graft rejection, graft-versus-host disease, infectious complications, and hyperinflammatory responses. We hypothesize that a moderate amount of immunosuppression will maximize efficacy while avoiding unacceptable toxicity.

https://clinicaltrials.gov/ct2/show/NCT06145282

▸ St. Jude Autologous Genome Edited Stem Cells For Sickle Cell Disease-1 (SAGES1): *Phase 1*

NOT YET RECRUITING

Age Range	**18–24 Years**
Trial Time Frame	**9/2024–12/2028**
Ref. No.	**NCT06506461**

This study is being done to test the safety of a new treatment called gene editing in Sickle Cell Disease (SCD) patients and to see if a single dose of this genetically modified cellular product will increase the amount of a certain hemoglobin called fetal hemoglobin (HbF) and help reduce the symptoms of SCD.

https://clinicaltrials.gov/ct2/show/NCT06506461

▸ Gene Correction in Autologous CD34+ Hematopoietic Stem Cells (HbS to HbA) to Treat Severe Sickle Cell Disease (Restore): *Phase 1/2*

RECRUITING

Age Range	**12-40 Years**
Trial Time Frame	**11/2021–7/2027**
Ref. No.	**NCT04819841**

This study is a first-in-human, single-arm, open-label Phase I/II study of nula-cel in approximately 15 participants, diagnosed with severe Sickle Cell Disease. The primary objective is to evaluate safety of the treatment in this patient population, as well as preliminary efficacy and pharmacodynamic data.

https://clinicaltrials.gov/ct2/show/NCT04819841

▸ Evaluation of Efficacy and Safety of a Single Dose of Exa-cel in Participants With Severe Sickle Cell Disease, βS/βC Genotype: *Phase 3*

NOT YET RECRUITING

Age Range	**12-35 Years**
Trial Time Frame	**04/2024–12/2029**
Ref. No.	**NCT05951205**

The purpose of the study is to evaluate the efficacy and safety of CTX001 (exa-cel) in adolescent and adult participants with severe sickle cell disease (SCD), βS/βC genotype (HbSC).

https://clinicaltrials.gov/ct2/show/NCT05951205

OBSERVATIONAL

▸ Long-term Follow-up of Subjects With Sickle Cell Disease Treated With Ex Vivo Gene Therapy

RECRUITING BY INVITATION ONLY

Age Range	**2–53 Years**
Trial Time Frame	**10/2020–5/2038**
Ref. No.	**NCT04628585**

This is a multi-center, long-term safety and efficacy follow-up study for subjects who have been treated with ex vivo gene therapy drug product in bluebird bio-sponsored clinical studies. After completing the parent clinical study (approximately 2 years), eligible subjects will be followed for an additional 13 years for a total of 15 years post-drug product infusion.

https://ClinicalTrials.gov/show/NCT04628585

▸ Long-term Follow-up Study in Subjects Who Received CTX001

RECRUITING BY INVITATION ONLY

Age Range	**18 Years and Older**
Trial Time Frame	**1/2021–9/2039**
Ref. No.	**NCT04208529**

This is a multi-site, observational study to evaluate the long-term safety and efficacy of CTX001 in subjects who received CTX001 in Study CTX001-111 (NCT03655678) or Study CTX001-121 (NCT03745287).

https://ClinicalTrials.gov/show/NCT04208529

▸ Cooperative Assessment of Late Effects for SCD Curative Therapies (COALESCE)

RECRUITING

Age Range	**4–65 Years**
Trial Time Frame	**7/2022–12/2025**
Ref. No.	**NCT05153967**

The primary goal of this study is to determine whether curative therapies for individuals with SCD will result in improved or worsening heart, lung, and kidney damage when compared to individuals with SCD receiving standard therapy. The investigators will also explore whether certain genes are associated with a good or bad outcome after curative therapy for SCD.

https://ClinicalTrials.gov/show/NCT05153967

▸ Discarded Bone Marrow for Hematology Research

RECRUITING

Age Range	**Child, Adult, Older Adult**
Trial Time Frame	**7/2022–1/2035**
Ref. No.	**NCT04671212**

The primary objective of this study is to establish a mechanism to obtain discarded bone marrow-containing bone samples from hemoglobinopathy, as well as non-hemoglobinopathy individuals. The processing of samples will help to understand how best to manipulate HSPC's from hemoglobinopathy patients with gene therapy and gene technologies in the laboratory environment. It will also allow us to establish a reservoir of samples that can be studied in the future to assess cellular function and fitness for transplant.

https://ClinicalTrials.gov/show/NCT04671212

▸ Long-term Follow-up (LTFU) of Patients Treated With Genome-edited Autologous Hematopoietic Stem and Progenitor Cells (HSPC)

RECRUITING

Age Range	**18 Years and Older**
Trial Time Frame	**4/2024–01/2039**
Ref. No.	**NCT06155500**

This study is monitoring patients treated with OTQ923, an investigational drug product of ex vivo genome-edited autologous hematopoietic stem and progenitor cells (HSPCs) that induces fetal hemoglobin (HbF) production, for a total of 15 years following infusion to monitor long-term safety and efficacy.

https://www.clinicaltrials.gov/study/NCT06155500

▸ A Long-Term Follow-Up Study of Participants With Sickle Cell Disease or Transfusion Dependent β-Thalassemia Who Received EDIT-301

NOT YET RECRUITING

Age Range	**12-50 Years**
Trial Time Frame	**6/2024–08/2040**
Ref. No.	**NCT06363760**

The purpose of this study is to evaluate the long-term safety and efficacy of EDIT-301 in participants with severe sickle cell disease (SCD) or transfusion-dependent β-thalassemia (TDT) who have received EDIT-301.

https://www.clinicaltrials.gov/study/NCT06363760