Protocol Title: A Study to Compare Bone Marrow Transplantation to Standard Care in Adolescents and Young Adults with Severe Sickle Cell Disease (BMT CTN #1503)

Target Population: Severe Sickle Cell Disease

Summary: This is a prospective phase II multi-center clinical that will compare survival and sickle related outcomes in adolescents and young adults with severe Sickle Cell Disease after hematopoietic stem cell transplantation or standard of care based on availability of HLA-matched related or unrelated donor. HLA typing and donor search is initiated upon confirmation of clinical eligibility for the study.

Key Inclusion Criteria:
- Age 15.00 - 40.99 Years.
- Severe Sickle Cell Disease [Hemoglobin SS (HbSS), Hemoglobin SC (HbSC) or Hemoglobin S Beta Thalassemia (HbSB) genotype] with at least 1 of the following manifestations:
  - Clinically significant neurologic event (stroke) or any neurological deficit lasting > 24 Hours
  - History of ≥ 2 episodes of acute chest syndrome (ACS) in the 2-year period preceding enrollment
  - ≥ 3 pain crises per year in the 2-year period preceding referral
  - Administration of regular RBC transfusion therapy, defined as receiving ≥ 8 transfusions per year for ≥ 1 Year to prevent vaso-occlusive clinical complications
  - Echocardiographic finding of tricuspid valve regurgitant jet (TRJ) velocity ≥ 2.7 m/sec
- LVEF > 40% or LV shortening fraction > 26% by cardiac echocardiogram or by MUGA.

Key Exclusion Criteria:
- HLA typing prior to referral (consultation with HCT physician).
  - However, if a subject has had HLA typing with documentation that relatives were not HLA typed and that a search of the unrelated donor registry was not performed the subject will be considered eligible.
- Uncontrolled bacterial, viral or fungal infection in the 6 Weeks before enrollment.
- Seropositivity for HIV.
- Previous HCT.
- Participation in a clinical trial in which the patient received an investigational drug or device must be discontinued at enrollment.
- History of substance abuse.
- Demonstrated lack of compliance with prior medical care (determined by referring physician).
- Pregnant or breast-feeding females.
- Inability to receive HCT due to alloimmunization, defined as the inability to receive pRBC transfusion therapy.

Additional Eligibility Criteria for Transplant after Biologic Assignment to the Donor Arm:
- Participants who are receiving ≥ 8 pRBC transfusions for ≥ 1 Year or have received ≥ 20 pRBC transfusions (cumulative) will undergo liver MRI for estimation of hepatic iron content.
- Cerebral MRI/MRA within 30 Days prior to initiation of transplant conditioning.
- Absence of donor specific HLA antibodies.
- HLA-matched donor must be medically fit to donate and willing to donate bone marrow.

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For additional information: https://clinicaltrials.gov/ct2/show/NCT02766465