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STEM CELL TRANSPLANTATION AS TREATMENT OF SICKLE CELL DISEASE

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Hematopoietic Stem Cell Transplantation (HSCT) is a treatment for some types of cancers and blood disorders. This article discusses the use of HSCT in sickle cell disease (SCD).

Bone marrow is the soft, spongy tissue inside bones. It contains cells called hematopoietic stem cells. These cells can turn into several other types of cells including red and white blood cells. In the past, stem cells could only be collected from the bone marrow, so patients who needed a stem cell transplant received a “bone marrow transplant.” Today, stem cells are usually collected from the blood, instead of the bone marrow. For this reason, they are now more commonly called stem cell transplants. The infusion of hematopoietic stem cells from a healthy donor into a patient with SCD is a potentially curative treatment in that the SCD patient can now potentially make new healthy red blood cells. However, before stem cells can be infused in the patient, the patient must first be treated with a preparative regimen consisting of agents design.1 /TT0 B1 (an bee(p)9 imen consis)9.f cells includ/pm4 (s8sA)0 (tit3(p)gtr)19..1 2(a)10 (bl. a)ϕ nee
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been performed which comprised a total of 40 adult patients with SCD who received a non-myeloablative preparative regimen prior to HSCT. The transplant was successful in 90% of the patients and no patients experienced acute or chronic GVHD. Despite these encouraging results, non-myeloablative preparatory regimens remain experimental for SCD patients.

Alternative Donors: Another source of stem cells is the cord blood collected at the time of birth. Successful engraftment using cord blood transplant from matched sibling donors in patients with SCD have been reported. Eleven such patients were reported to the Eurocord Registry. There were no transplant-related deaths and one graft failure. The estimated disease free survival 2 years after transplant was 90 percent.

The role of unrelated cord blood transplants in patients with SCD remains uncertain. In one report, seven patients underwent transplant from unrelated, incompletely matched umbilical cord blood. Only three were successful.

The use of stem cell donors who only match half of the recipient HLA proteins (i.e., haploidentical donors mostly a parent) has been proposed as a means of increasing the size of the HSCT donor pool for patients with SCD, but remains experimental. In an observational study, 17 patients with severe SCD underwent haploidentical transplantation. This therapy was well tolerated and was successful in 65% of patients. Further studies are needed to determine the risk-benefit ratio of this approach outside of a clinical trial.

Conclusion / Recommendation: Hematopoietic stem cell transplantation (HSCT) is a potentially curative option in patients with sickle cell disease (SCD).

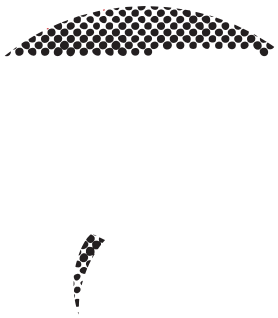
- In several series of patients who have undergone HSCT for SCD, five-year survival rates were 90 to 97 percent, and transplant-related deaths were 7 to 10 percent. SCD recurred in some patients, resulting in a SCD-free survival of 80 to 90 percent.
- Experts recommend HSCT for patients with severe symptoms of SCD that are unresponsive to treatment with transfusions and hydroxyurea if an HLA-matched sibling is available as a donor.
- Early HSCT in young children with SCD has been explored as a possible means of reducing SCD complications and transplant associated side e ects and deaths. However, because accurate predictors that can prospectively define the severity of SCD in infants and children have not been identified, the role of this approach has yet to be defined.
- The use of alternative donors (e.g. umbilical cord blood, mismatched related donors, or matched unrelated donors) remains uncertain in patients with SCD.
- Non-myeloablative preparative regimens have been proposed to reduce regimen-related toxicity, but further data are needed to determine the long-term success.

GBT440: A Pnsdmsh`k Ndv Dhrd`rd-Mnchexhmf

A primary function of hemoglobin, the protein inside red blood cells (RBCs), is to carry oxygen from the lungs for delivery to the tissue (i.e., brain, skin, bone, etc). In sickle cell disease, hemoglobin undergoes a process called polymerization after it releases oxygen to the tissues. This polymerization process results in RBC sickling, RBC destruction and blockage of blood flow to vital organs, which causes organ damage.

In comparison to normal hemoglobin (hemoglobin A), sickle hemoglobin (hemoglobin S) does not bind oxygen as tightly. This observation has led scientists to investigate compounds that can make hemoglobin S bind oxygen to an extent that parallels that of hemoglobin A. If that is accomplished, the process of sickling, in theory, can be prevented.

At the American Society of Hematology meeting held in December 2015, Global Blood Therapeutics presented promising data from multiple preclinical studies on the compound, GBT440. In patients with sickle cell disease, GBT440 was found



THE 2016 ANNUAL SICKLE CELL CONFERENCE

Practical Issues in Sickle Cell Disease XV: More Is Not Always Better!

On Saturday, April 30, the USA Comprehensive Sickle Cell Center will host its 15th Annual Regional Sickle Cell Conference. National and local experts will present up-to-date information on treating patients with sickle cell disease.

A central theme of this year's conference will be red blood cell transfusions — indications and therapeutic targets as well as transfusion complications. Additionally, experts will focus on addressing sickle cell pain crisis as a diagnosis of exclusion.

The conference targets physicians, physician assistants, nurse practitioners, nurses and allied health professionals. It is supported by the Dr. Cecil L. Parker, Jr., Lectureship Endowment, which was created to address the educational needs of the clients and health care providers of the Gulf Coast community.

The conference will be held from 8 a.m. to 4 p.m. in the University of South Alabama's Health Sciences Building, College of Nursing Auditorium, Room 1013; 5721 USA Drive North; Mobile, AL 36688.

Register early for a chance to win complimentary admission to the 2017 Annual Regional Sickle Cell Conference. The early bird registration deadline is April 15, 2016. For additional conference information visit http://www.usahealthsystem.com/sicklecellcenter or call 251-470-5893.