An international learning collaborative Phase II trial for haploidentical bone marrow transplant in sickle cell disease

A multi-center Phase II prospective clinical trial led by Vanderbilt University

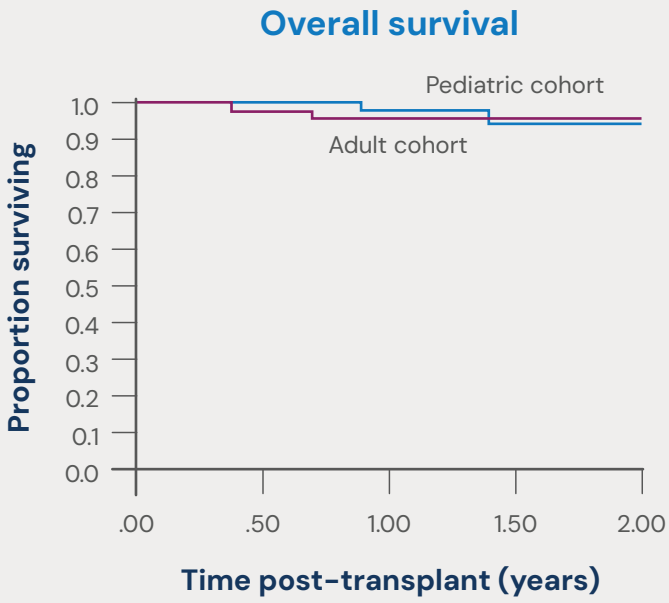
Study details:

This Phase II clinical trial (NCT01850108) evaluated the efficacy and safety of haploidentical (partially matched related donor) bone marrow transplant (BMT) with non-myeloablative conditioning (non-MAC) and a conditioning regimen including thiotepa and post-transplant cyclophosphamide in patients with sickle cell disease (SCD). The study aimed to achieve a 2-year event-free survival (EFS) rate of at least 80%. The study enrolled 70 evaluable patients aged 1-70 years, lacking an HLA-matched sibling donor but with a suitable haploidentical donor, across 8 international sites. The primary outcomes measured were 2-year EFS, overall survival (OS) and graft failure rates.

Results at a glance:

- **2-year EFS** was 82.6%, meeting the study's primary endpoint.
- **2-year OS** was 94.1%, with no significant difference between age groups.
- **Graft failure** occurred in 11.4% of patients, all under 18 years old.
- Among those with **successful engraftment**, 96.6% were off immunosuppression by 1-year post-transplant.
- Severe acute graft-versus-host disease (**GVHD**) occurred in 10.0% of participants. Moderate-severe chronic GVHD was also 10.0%, with a higher incidence in pediatric patients.
- Five participants (7.1%) died due to **infectious complications**.

Figure: OS between adult and pediatric cohorts post-HCT.



Clinical impact:

This trial demonstrates that haploidentical BMT with non-MAC regimens is a viable curative option for SCD patients, especially adults, with an EFS over 80% and OS exceeding 90%. However, the approach may be less effective in pediatric patients, who showed higher rates of graft failure and chronic GVHD. The results support the broader adoption of this protocol, particularly in middle and high-income countries, potentially expanding access to curative treatment for patients with SCD without a matched sibling donor.

Read the published abstract in Blood (DOI: 10.1182/blood.2023023301).

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