HOT TOPIC: Matched Related Donor Hematopoietic Stem Cell Transplant for Children with Sickle Cell Disease

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Stem cells are collected from donor’s bone marrow or blood (harvest).

Bone marrow or blood is taken to processing laboratory where stem cells are concentrated and prepared for freezing process.

Bone marrow or blood is preserved by freezing to keep stem cells alive until they are infused into patient’s bloodstream.

High dose chemotherapy and/or radiation therapy is given to the patient (conditioning regimen).

Thawed stem cells are infused into the patient.

Matched related donor stem cell transplant

Matched related donors

- Donors are sibling with same parents
- Most common form of transplant for children with SCD

Treatment option for children with (severe?) sickle cell disease and matched sibling donor\(^1\)

- Overall survival ~95%
- Disease-free survival ~92%
- <1 in 10 children have complications, such as graft-versus-host disease

\(^1\) Roberts I and Fuente J. Sickle cell disease: the price of cure. Blood 2016;128:2486-2488; doi: https://doi.org/10.1182/blood-2016-10-740969
91% survival for sibling donor (Center for International Blood and Marrow Transplant Research)

95% survival for sibling donor (European Blood and Marrow Transplant)

Hot Topic: Guidelines Conflict on Transplant

2014 NHLBI Expert Panel Report: More information needed\(^1\)

- “Although clinical trials have provided promising results, and cure appears to be possible in a large proportion of patients receiving HSCT, additional research is still needed that addresses the potential risks of this therapy (e.g., failure of engraftment and chronic graft-versus-host disease) before HSCT can become a widely used therapy.”

2014 EBMT Inborn Error and EBMT Paediatric Working Parties\(^2\)

- Young patients with *symptomatic* SCD who have an HLA-identical sibling donor should be transplanted as early as possible, preferably at pre-school age.
- Unmanipulated BM or UCB (whenever available) from HLA-identical sibling donors are the recommended stem cell source.


## Indications for transplant

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<tr>
<th>Children</th>
<th>Adults (15-40 years)</th>
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<tr>
<td>• Children with HbSS or HbSβ⁰-thalassemia &lt; 16 years of age</td>
<td>• Clinically significant neurological event (stroke) or and neurological deficit lasting &gt; 24 hours</td>
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<td>• Stroke or CNS event lasting &gt; 24 hours</td>
<td>• ≥ 2 episodes of acute chest syndrome in 2 years despite supportive care measures (asthma therapy and/or hydroxyurea)</td>
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<td>• Impaired neuropsychological function with abnormal cerebral MRI/MRA</td>
<td>• ≥ 3 episodes of severe pain crises/year in 2 years despite supportive care measures (pain management and/or hydroxyurea)</td>
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<td>• Recurrent acute chest syndrome</td>
<td>• ≥ 8 transfusions/year for ≥ 1 year to prevent vaso-occlusive complications (pain, stroke and ACS)</td>
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<td>• Stage I or II sickle lung disease</td>
<td>• Pulmonary hypertension (tricuspid valve regurgitant jet ≥ 2.7 m/s on Echocardiogram)</td>
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<td>• Recurrent vao-occlusive painful episodes or priapism</td>
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<td>• Sickle nephropathy (glomerular filtration rate 30-50% of predicted normal)</td>
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Barriers to transplant

To date, << 1% of SCD in the United States has received transplant

Barriers include

• Unclear if transplant has higher mortality and morbidity than if managed with supportive care, such as hydroxyurea
• Donors: Only ~18% of individuals with SCD have a HLA-identical sibling donor
• Infertility risk
• Graft-versus-host disease occurs ~10% of patients and may cause chronic debilitating disorder
• Unknown late effects

Establish Benefit/Harms for HSCT

Evaluate impact on gonadal function

Optimize transplant conditioning regimens
  • Prevent chronic graft-versus-host disease
  • Unrelated donors

Perform prospective comparison to standard care (on-going, STRIDE)

Impact of transplant on quality of life

Other resources

