Sickle Cell Disease: Exploring treatment options and psychosocial care

Jennifer Krajewski, MD
Tim Olson, MD, PhD
YoungJae Lee, MSW, LCSW

Jointly planned by The National Marrow Donor Program® /Be The Match® and Sickle Cell Transplant Advocacy & Research Alliance (STAR)
Learning objectives

• Describe treatment advances in BMT and emerging gene therapy for sickle cell disease, including patient eligibility, risks, benefits, and outcomes

• Engage patients and families in clinical trial discussions to advocate for and identify options that reduce participation barriers

• Apply strategies to proactively identify and address psychosocial and financial concerns with treatment choices

• Provide information to address the resource needs of patients and their family
The planners and speakers have the following financial disclosures.

<table>
<thead>
<tr>
<th>Name</th>
<th>Role</th>
<th>Disclosure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jennifer Krajewski, MD</td>
<td>Speaker</td>
<td>None</td>
</tr>
<tr>
<td>Tim Olson, MD, PhD</td>
<td>Speaker</td>
<td>Miltenyi, Honorarium; Bluebird Bio, Consultant Fee; Merck/Novartis, Consultant Fee</td>
</tr>
<tr>
<td>YoungJae Lee, MSW, LCSW</td>
<td>Speaker</td>
<td>None</td>
</tr>
<tr>
<td>Amber Ruffin, MPH</td>
<td>Moderator</td>
<td>None</td>
</tr>
<tr>
<td>Jackie Foster, MPH, RN, OCN</td>
<td>Planner</td>
<td>Stock ownership - Pfizer</td>
</tr>
<tr>
<td>Katie Schoepnner, MSW, LICSW</td>
<td>Planner</td>
<td>None</td>
</tr>
<tr>
<td>Ellyce Hayes</td>
<td>Planner</td>
<td>None</td>
</tr>
<tr>
<td>Nicole Heino</td>
<td>Planner</td>
<td>None</td>
</tr>
<tr>
<td>Lauren Marks</td>
<td>Planner</td>
<td>None</td>
</tr>
</tbody>
</table>
Jennifer Krajewski, MD  
Clinical Assistant Professor, HMH School of Medicine  
Attending, Pediatric Stem Cell Transplantation  
Hackensack University Medical Center  
STAR Alliance Education Committee CO-Chair
Tim Olson, MD, PhD
Pediatric Hematologist-Oncologist
Children’s Hospital of Philadelphia
YoungJae Lee, MSW, LCSW
Licensed Clinical Social Worker
Children’s Cancer Institute,
Hackensack Meridian Health
DEFINITION of Sickle Cell Disease

- A group of genetic disorders characterized by the inheritance of sickle hemoglobin (Hgb S) from both parents or Hgb S from one parent and an abnormal hemoglobin or thalassemia from another parent
  - These disorders include
    - Sickle cell anemia: Hgb SS, Hgb SC
    - Sickle beta thalassemia: SbºThal, Sb+Thal
Who has Sickle Cell Disease in the U.S.?

- It is the most common genetic disease in this country.

<table>
<thead>
<tr>
<th></th>
<th>Sickle cell TRAIT</th>
<th>Sickle cell DISEASE</th>
</tr>
</thead>
<tbody>
<tr>
<td>African Americans</td>
<td>1 out of 12</td>
<td>1 out of 500</td>
</tr>
<tr>
<td>Hispanics</td>
<td>1 out of 100</td>
<td>1 out of 1,400</td>
</tr>
<tr>
<td>Total</td>
<td>~ 2 million people</td>
<td>~100,000 people</td>
</tr>
</tbody>
</table>
## Bone Marrow Transplantation (BMT) for Sickle Cell Disease: The Past

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>N =</th>
<th>Overall Survival (OS)</th>
<th>Event-Free Survival (EFS)</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st US clinical trial Walters, et al. NEJM 1996; 335: 369–376</td>
<td>Children &lt; 16 years old with matched sibling donors, myeloablative regimen</td>
<td>22</td>
<td>91%</td>
<td>73%</td>
<td>16 had stable donor engraftment</td>
</tr>
<tr>
<td>Gluckman, et al. Blood 2017 129: 1548-1556.</td>
<td>All matched sibling BMTs for SCD done worldwide 1986 -2013</td>
<td>1,000</td>
<td>5 years: 91%</td>
<td>5 years: 93%</td>
<td>5 year GVHD-free survival: - 86% &lt; 16 yrs - 77% &gt; 16 yrs</td>
</tr>
<tr>
<td>King, et al. Am J Hematol. 2015; 90: 1093-1098</td>
<td>Reduced intensity conditioning (RIC) for pediatric patients with matched sibling donors. Alemtuzumab (start day -22), melphalan and fludarabine</td>
<td>52; 43 with SCD</td>
<td>94%</td>
<td>92%</td>
<td>- aGVHD: 23% - Extensive cGVHD: 13% - 81% off immune suppression at 1 year</td>
</tr>
</tbody>
</table>
## BMT for Sickle Cell Disease: The Past

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>N</th>
<th>OS</th>
<th>EFS</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kamani NR, et al. BMT. 2012; 18(8):1265-72</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- cGVHD 62%, 38% extensive</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Unrelated cord blood: very high rates of graft failure. 3/8 patients who engrafted, 38% EFS</td>
</tr>
<tr>
<td>Bolanos-Meade, et al. Blood. 2012; 120(22): 4285-91</td>
<td>Haploidentical donors. RIC (cyclophosphamide, fludarabine, ATG, low-dose total body irradiation) and post-BMT Cy as GVHD prophylaxis</td>
<td>17</td>
<td>100%</td>
<td>65%</td>
<td>- 11 patients had durable engraftment, but only 6 patients off immunosuppression at time of report</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Low EFS due graft rejection</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- 1 patient had aGVHD, resolved</td>
</tr>
<tr>
<td>Hsieh MM, et al. JAMA. 2014; 312(1):48-56.</td>
<td>- Non myeloablative regimen (proximal alemtuzumab &amp; low dose TBI) - Sirolimus as GVHD prophylaxis</td>
<td>30</td>
<td></td>
<td></td>
<td>- 87% engrafted to reverse SCD phenotype</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Graft failure related to non-adherence to sirolimus</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- 1 death: SCD came back &amp; patient suffered a stroke</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- No aGVHD or cGVHD</td>
</tr>
</tbody>
</table>
BMT for Sickle Cell Disease: The Present

How do I find current trials for BMT as a cure for sickle cell disease?

- [clinicaltrials.gov](http://clinicaltrials.gov)
- [curesicklenow.org](http://curesicklenow.org): STAR website
- [BMTCTN.org](http://BMTCTN.org): Blood and Marrow Transplant Clinical Trials Network
- [JCCTP.org/sickle-cell](http://JCCTP.org/sickle-cell): Jason Carter Clinical Trials Program
Sickle transplant Using a Nonmyeloablative approach (SUN Study): NCT03587272

- Uses the same non-myeloablative regimen as in the NIH adult study
- SUN eligibility: Age 2-24 years with an HLA-identical sibling donor

<table>
<thead>
<tr>
<th>Hb SS / Sβ⁰</th>
<th>Hb SC / Sβ⁺ / other SCD</th>
</tr>
</thead>
<tbody>
<tr>
<td>abnormal TCD, infarct on brain MRI</td>
<td>overt stroke</td>
</tr>
<tr>
<td>ACS x 2 (lifetime)</td>
<td>ACS x 2 in previous 2 years</td>
</tr>
<tr>
<td>pain event x 3 (lifetime)</td>
<td>pain event x 3 in previous year</td>
</tr>
<tr>
<td>hospitalization for ACS or pain</td>
<td>hospitalization for ACS or pain</td>
</tr>
<tr>
<td>while on hydroxyurea</td>
<td>while on hydroxyurea</td>
</tr>
<tr>
<td>priapism x 2</td>
<td>priapism x 2</td>
</tr>
<tr>
<td>chronic transfusion</td>
<td>chronic transfusion</td>
</tr>
<tr>
<td>splenic sequestration x 2, or</td>
<td>splenic sequestration x 2, or</td>
</tr>
<tr>
<td>splenectomy after x 1</td>
<td>splenectomy after x 1</td>
</tr>
</tbody>
</table>

- Participating STAR sites
  - Children’s National (DC), Alberta Children’s (Calgary), SickKids (Toronto), Lurie Children’s (Chicago), Nationwide Children’s (Columbus), Levine Children’s (Charlotte NC), Montefiore (NYC), Columbia (NYC)
Early HLA Matched Sibling Hematopoietic Stem Cell Transplantation for Children with Sickle Cell Disease: A STAR Trial: NCT04018937

• Based on:
  1. SCD deprives nearly all patients of a full life (both quality and quantity), even those with relatively mild courses during childhood.
  2. Limiting BMT to children at low risk for GVHD, the risk for transplant related mortality and morbidity can be minimized.
  3. Using the reduced intensity preparative regimen should hopefully reduce the risk for conditioning regimen-related gonadal toxicity.

• Eligibility
  • At least 2 years of age and less than 10 years of age
  • Sickle hemoglobinopathy
  • HLA identical sibling who is less than 10 years of age
  • Donor may carry a hemoglobinopathy trait
  • Meet criteria for symptomatic SCD

• Participating STAR sites
  Columbia University Med Center (NYC), Children’s National Med Center (DC), Med Univ. of S. Carolina (Charleston, SC), Methodist Children’s Hospital (Memphis TN), Hackensack Univ. of Med Center (NJ), Children’s Hospital of Philadelphia (Philadelphia), University of N. Carolina at Chapel Hill (Chapel Hill), Yale University (New Haven, CT), University of Mississippi Medical Center (Jackson, MS), Ann & Robert Lurie Children’s Hospital of (Chicago)
Abatacept for Graft Versus Host Disease Prophylaxis after BMT for Pediatric Sickle Cell Disease: a STAR Trial: NCT02867800

Treatment Description:
- All patients will receive reduced intensity conditioning
- For GVHD prophylaxis, all patients will receive a calcineurin inhibitor, methotrexate, and abatacept

- Eligibility:
  - Age 3 - 20 years with Hgb SS or SB0 thalassemia receiving HLA matched related or unrelated donor BMT who are at increased risk for GVHD
    - All patients getting unrelated donor transplants will be considered be at increased risk for GVHD
    - Patients receiving related donor transplants meeting at least one of the following two criteria will also be considered to be at increased risk for GVHD:
      1) the patient is at least 10 years old
      2) the donor is at least 10 years old

- Participating STAR sites
  - Columbia University Med Center (NYC), Children’s National Med Center (DC), Children’s Hospital of Atlanta (GA), Hackensack Univ. Med Center (NJ), Ann & Robert Lurie Children’s Hospital (Chicago), Nationwide Children’s Hospital (OH), Phoenix Children’s Hospital (AZ)
Acute GVHD Suppression using Costimulation Blockade to Expand Non-malignant Transplant (ASCENT) Trial:
NCT03924401

Multi-center, single arm phase II trial
• Pediatric patients with hemoglobinopathy or acquired or inherited bone marrow failure (two separate strata)
• 7/8 unrelated adult donor
• Abatacept x 8 doses added to standard GVHD prophylaxis regimen

• Eligibility
  • All patients with severe sickle cell

• Participating STAR sites –
  • Hackensack Univ. of Med Center (NJ), Ann & Robert Lurie Children’s Hospital (Chicago), Children’s Hospital of Atlanta (GA), University of Alabama Birmingham (AL), Nemour’s Dupont Children’s Hospital (DE)
Project Sickle Cure (PSC)

Repository for clinical data, image bank, MRI images and blood samples for All STAR centers and all children and adolescents who undergo BMT for SCD

Study Design:

- Prospective, multi-center observational study
- 3 key primary outcomes in children/young adults with sickle cell disease who undergo BMT
  - Neurologic
  - Vascular/endothelial disease
  - Health related quality of life/pain
- Several secondary outcomes
- Planned for fall 2019
Other national trials – currently enrolling

- **BMT CTN 1503**
  - Phase 2 multicenter trial comparing BMT to supportive care in severe sickle cell patients ages 15-41 (NCT02766465)

- **BMT CTN 1507**
  - Phase 2 multicenter trial investigating the use of haploidentical BMT in severe sickle cell patients ages 5-45 (NCT03263559)
BMT for Sickle Cell Disease: The Future

- Further reduction in conditioning for patients with matched sibling donors
- Use of alternative donors
- Gene therapy
Lecture Objectives

• Describe treatment advances in BMT and emerging gene therapy* for sickle cell disease, including patient eligibility, risks, benefits, and outcomes

• Engage patients and families in clinical trial discussions to advocate for and identify options that reduce participation barriers

Outline

1. What is gene therapy for SCD?
2. How does it compare to allogeneic SCT?
3. What are the current outcomes data?
4. New trials
5. Challenges and future directions

* No gene therapy approach for sickle cell disease has been approved by the FDA to date. Clinical trials only.
Sickle Cell Disease: Exploring treatment options and psychosocial care

Gene Therapy for Sickle Cell Disease

Tim Olson MD PhD

Medical Director, Pediatric Blood and Marrow Transplant Program
Cell Therapy and Transplant Section, Division of Oncology
Children’s Hospital of Philadelphia
University of Pennsylvania
Therapy Options for Severe Sickle Cell Disease (Traditional)

- Hydroxyurea (HU)
- Chronic Red Blood Cell (RBC) Transfusions
- Matched Sibling Donor (MSD)-BMT*

*Only an option for 18% of patients with SCD (Mentzer et al. AM J Pediatr Hematol Oncol, 1994)
Therapy Options for Severe SCD in 2019!

- Hydroxyurea
- Chronic RBC Transfusions
- Anti-Sickling Agents
- Zinc finger γ globin activator
- Demethylating agents, HDAC inhibitors
- E- or P-Selectin Inhibition
- NO pathway Vasodilators
- Haplo-BMT with post-transplant Cyclophosphamide (CY)
- Unrelated Donor BMT w/wo T cell depletion
- MSD-BMT
- Lentivirus-based Gene Rx
- HSC Gene editing
Gene Rx for SCD: What is it?

- Genetic manipulation of autologous hematopoietic stem cells (HSC) to enhance production of normal hemoglobin

- Therapeutic goal: depends on disease

  - **Thalassemia Major**
    - Increase total hemoglobin to reduce or eliminate transfusion needs

  - **Sickle Cell Disease**
    - Reduce HbS% and RBC sickling to decrease disease complications
    - (increase in total hemoglobin a secondary benefit?)
Discussing Gene Therapy Trials with Families (Key Points)

- These therapies are experimental
  - Safety: thus far data suggest low risk of mortality/short-term toxicity
  - Efficacy: unknown (and a moving target)

- Comparison with allogeneic (allo)-BMT
  - Allo-BMT approaches for SCD other than MSD-BMT are also experimental
  - Failed attempt at gene therapy may preclude future eligibility for allo-BMT clinical trials (and vice versa)

- Late effects
  - Fertility: likely high risk (but no actual data for single agent conditioning)
  - Malignancy risk: from genetic manipulation or from conditioning
Lentivirus Based Gene Therapy for Hemoglobin Disorders

Collect stem cells from patient with genetic defect in beta globin → GMP* Ex vivo lentiviral transduction → production of gene of interest → Infusion of genetically modified HSC back into patient

Condition Patient with Stem Cell-Directed Chemotherapy

Options for Gene Addition

1. $\beta$-globin: increases HbA (NCT02140554)
2. $\gamma$-globin: increases HbF (NCT02186418)
3. Short hairpin(sh)RNA (miR) targeting BCL11A enhancer: increases HbF (NCT03282656 )

*GMP → Good Manufacturing Practice regulations per Code of Federal Regulations (CFR)
Gene Editing for Hemoglobin Disorders

Collect stem cells from patient with genetic defect in beta globin

Nuclease-guided strand breaks at gene of interest → gene correction or disruption

Infusion of genetically corrected HSC back into patient

Goals of gene editing

1. Gene correction: difficult, needs homologous recombination (inefficient, no current trials)

2. Gene disruption by error-prone non-homologous end joining (NHEJ) creation of insertions/deletions (efficient, currently in trials)

HbF induction by disrupting BCL11a enhancer

Condition Patient with Stem Cell-Directed Chemotherapy

This is not embryonic gene editing!!
Timeline of Gene Therapy

Stage 1: Screening and Eligibility

Stage 2: Stem Cell Collection and Product Manufacture

Stage 3: Conditioning, Stem Cell Infusion, and Supportive Care Pre-Engraftment

Stage 4: Long-term Follow-up

Added Step vs. Allo-BMT!
Patient (not donor) needs to go through collection

Potentially longer follow-up mandated vs. Allo-BMT
Stage 1: Screening and Eligibility

- Mostly similar to Criteria Used for allo-BMT with some differences
- **Genotype:** Hb SS, SB⁰, SB⁺ (studies to date do not include Hb SC)
- **Disease features:** Evidence of recurrent vaso-occlusion episodes (VOE)
  - **Example:** 4 episodes in preceding two years of VOE such as:
    - pain requiring IV pain medication administration
    - acute chest syndrome (ACS)
    - priapism
    - hepatic or splenic sequestration
- Inclusion of patients with prior stroke remains controversial!
- **Age:** lower limit of 18 y/o or 12 y/o typical in early phases of studies
- **Failure of medical therapy (HU) often an inclusion requirement**
- **Typically need 2 years of prior treatment records** (often a problem with outside referral patients)
- **Bone marrow (BM) aspirate/biopsy part of pre-treatment assessments**
- **Exclusions:** prior BMT and available MSD
Stage 2: Stem Cell Collection and Product Manufacture

- **SCD-specific challenge**: patients cannot receive G-CSF for peripheral stem cell mobilization

- **Early Studies**: CD34+ stem cell collection via bone marrow harvest
  - Limited CD34+ cell quantity
  - Qualitative limitations in CD34+ cells → suboptimal manufacture

- **Breakthrough**: Plerixafor only mobilization (PMID’s: 29472357, 29419425)
  - Enables safe, effective peripheral stem cell harvest by apheresis
  - Requires apheresis catheter and pre-collection transfusion regimen

- **Challenges remain**:
  - Yield, optimal timing of plerixafor, multiple collections
  - Inflammatory state impact on collection quality?
## Stage 3: Conditioning, Stem Cell Infusion, and Supportive Care Pre-Engraftment

- Most studies to date have used myeloablative busulfan (PK-targeted 4 day)
  - Risk of hepatic veno-occlusive disease (VOD) (particularly for chronically transfused)
  - Risk of pulmonary fibrosis
  - 1 study currently using melphalan (NCT02186418): low risk of VOD
- No serotherapy or post-transplant immune suppression
  - Antiviral prophylaxis similar to autologous BMT and not allogeneic BMT
- Due to intensive transfusion requirements, admission through engraftment is standard

### Conditioning/Supportive Care Comparison to Allogeneic BMT (RIC)

#### PROS
- No risk of GVHD
- Lower infection risk (CMV)
- Less nephrotoxicity
- Fewer medications

#### CONS
- Myeloablation/VOD risk
- Slower platelet engraftment
- Takes longer to determine preliminary efficacy
Stage 4: Long-term Follow-up

Many follow-up needs are similar to allogeneic BMT....

- Endocrine/Fertility (preservation methods recommended)
- Screening for secondary non-hematologic malignancies
- Pulmonary function screening
- Management of prior SCD sequelae (chronic pain, vasculopathy)

....however some are unique!

- Monitoring of transgene persistence
  - Biomarker monitoring
- Long-term clinical monitoring of independence from SCD-related complications
- Hematology malignancy screening
  - related to genetic construct
  - related to single agent alkylator conditioning
Outcomes to date: Lentiglobin gene therapy for severe SCD
(bluebird bio, Inc. sponsored studies, phase 1/2)

Gene Addition of anti-sickling (T87Q) \(\beta\)-globin

**Hgb-205** (NCT02151526)
- **Collection:** BM harvest
- **Manufacturing Process:** original
- **Number of SCD patients:** 1 reported
- **Follow-up:** 15 months (time of report)
- **Hematologic outcomes:** Hgb\(^{T87Q}\) 5.5 g/dL, total Hgb 11.8 g/dL, Hb \%S 49%
- **Clinical outcome:** resolution of SCD symptoms (Sx)

**Hgb-206 Group A** (NCT02140554)
- **Collection:** BM harvest
- **Manufacturing Process:** original
- **Number of SCD patients:** 7
- **Follow-up (median):** 24 months
- **Hematologic outcomes (median):** Hgb\(^{T87Q}\) 0.8 g/dL, total Hgb 8.9 g/dL
- **Clinical outcome:** Reduction in SCD Sx

**Hgb-206 Group B** (NCT02140554)
- **Collection:** BM harvest
- **Manufacturing Process:** Refined (plus increased busulfan target and pre-harvest transfusions)
- **Number of SCD patients:** 2
- **Follow-up:** 8 and 14 months
- **Hematologic outcomes (median):** Hgb\(^{T87Q}\) 3.2-7.2 g/dL, total Hgb 11-12.8 g/dL
- **Clinical outcome:** Reduction in SCD Sx

Ribeil et al., NEJM 2017 PMID: 28249145  Kanter et al., 2018 ASH Annual Meeting
Outcomes to date: Lentiglobin gene therapy for severe SCD (bluebird bio, Inc. sponsored studies, phase 1/2)

**Hgb-206 Group C** (NCT02140554)

**Collection:** Plerixafor mobilization of peripheral stem cells

**Manufacturing Process:** Refined

**Number of SCD patients:** 25 enrolled, **13 infused** (as of March, 2019)

**Follow-up (median):** 9 months (1-15.2)

**Apheresis, manufacture, infusion outcomes (n=19 patients, n=35 cycles):**
- only 7 grade ≥ 3 events, all resolved (VOE and other pain complaints most common)
- CD34 cells (x 10⁶) collected per cycle: 10.1 (3.9-20)
- CD34 cells (x 10⁶) infused: 4.5 (3-8)  VCN 3.8 (2.8-5.6)

**Hematologic outcomes:**
- At last visit: **Hgb₈₇Q** (range) **4.5-8.8 g/dL.**  total Hgb (range) 10.2-15 g/dL
- 9 months post-SCT: **HbS% (median): 49%**
- Near resolution of hemolysis parameters

**Clinical outcomes:**
- **100% overall survival, marked reduction in VOE events**
- Typical busulfan related adverse events (AE), no VOD, and no clonal dominance

Kanter et al., 2019 EHA Annual Meeting
### Gene Addition (3 additional trials)

<table>
<thead>
<tr>
<th>Product</th>
<th>ARU-1801 (NCT02186418)</th>
<th>Aruvant Sciences GmbH</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Approach</strong></td>
<td>Gene addition of γ-globin, melphalan conditioning</td>
<td></td>
</tr>
<tr>
<td><strong>Status</strong></td>
<td>Recruiting at 1 U.S. site</td>
<td></td>
</tr>
<tr>
<td><strong>Target enrollment</strong></td>
<td>10 pts, age 3-35 y/o eligible</td>
<td></td>
</tr>
<tr>
<td><strong>Results reported to date</strong></td>
<td>2 pts, HbF ~20% at Day 180, ↓ SCD complications (Malik et al., 2018 ASH)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Product</th>
<th>BCH_BB-LCRshRNA(miR) (NCT03282656)</th>
<th>Boston Childrens Hospital (Williams)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Approach</strong></td>
<td>Gene addition of shRNA targeting BCL11A enhancer (↑HbF)</td>
<td></td>
</tr>
<tr>
<td><strong>Status</strong></td>
<td>Recruiting at 1 U.S. site</td>
<td></td>
</tr>
<tr>
<td><strong>Target enrollment</strong></td>
<td>7 pts, age 3-40 y/o eligible</td>
<td></td>
</tr>
<tr>
<td><strong>Results reported to date</strong></td>
<td>3 pts presented, HbF &gt;20% in 2 patients &gt; Day 60, ↓ SCD complications (Esrick et al., 2018 ASH)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Product</th>
<th>βAS3-globin (NCT02247843)</th>
<th>University of California, Los Angeles (Kohn)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Approach</strong></td>
<td>gene addition of modified, anti-sickling β-globin</td>
<td></td>
</tr>
<tr>
<td><strong>Status</strong></td>
<td>Recruiting at 1 U.S. site</td>
<td></td>
</tr>
<tr>
<td><strong>Target enrollment</strong></td>
<td>6 pts, Age ≥ 18 y/o</td>
<td></td>
</tr>
<tr>
<td><strong>Results reported to date</strong></td>
<td>none</td>
<td></td>
</tr>
</tbody>
</table>

### Gene Editing (2 trials)

<table>
<thead>
<tr>
<th>Product</th>
<th>CTX001 (NCT03745287)</th>
<th>CRISPR Therapeutics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Approach</strong></td>
<td>CRISPR/CAS9-based gene-editing of BCL11A (↑HbF)</td>
<td></td>
</tr>
<tr>
<td><strong>Status</strong></td>
<td>Recruiting at ≥ 5 U.S. sites</td>
<td></td>
</tr>
<tr>
<td><strong>Target enrollment</strong></td>
<td>up to 45 pts, age 18-35 y/o eligible initially (pediatric subgroup anticipated)</td>
<td></td>
</tr>
<tr>
<td><strong>Results reported to date</strong></td>
<td>none</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Product</th>
<th>BIVV003 (NCT03653247)</th>
<th>Bioverativ (Sanofi)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Approach</strong></td>
<td>Zinc finger nuclease-based gene-editing of BCL11A (↑HbF)</td>
<td></td>
</tr>
<tr>
<td><strong>Status</strong></td>
<td>Recruiting at 3 U.S. sites</td>
<td></td>
</tr>
<tr>
<td><strong>Target enrollment</strong></td>
<td>up to 8 pts, age 18-35 y/o</td>
<td></td>
</tr>
<tr>
<td><strong>Results reported to date</strong></td>
<td>none</td>
<td></td>
</tr>
</tbody>
</table>

Visit [JCCTP.org/sickle-cell](http://JCCTP.org/sickle-cell) – patient friendly trial information
Challenges and Future Directions

❖ Availability
  ❖ **Current:** limited trial slots
  ❖ **Future:** limited manufacturing capacity?

❖ Exportability
  ❖ Conditioning/infusion straightforward
  ❖ Collection requires specialized expertise

❖ Long Term Follow-up
  ❖ Coordinating network of centers likely needed

❖ In the future...
  ❖ Head to head comparisons with Allo-BMT
  ❖ Elimination of alkylating agent conditioning?
Questions?

olsont@email.chop.edu
Identifying and Addressing Psychosocial and Financial Concerns

YoungJae Lee, MSW, LCSW
SICKLE CELL DISEASE VS. CANCER

- Genetic disease
- Chronic illness
- More common in certain ethnic groups
  - People of African, Central and South American, Middle Eastern, Asian, Indian and Mediterranean descent
CULTURE: “customary beliefs, social forms, and material traits of a racial, religious, or social group” Merriam-Webster Dictionary

CULTURE IS:
- Diverse
- Variable
- Multifaceted

CULTURE IS NOT:
- Homogeneous
- Invariable
- Uniform
Culture is inseparable from these conditions:

- Social
- Economical
- Political
- Religious
- Psychological
- Physiological
STIGMATIZATION:

“the process of identifying an attribute of a person or group and associating the attribute with a stereotype that negatively labels or brands another in a way that is perceived as disgraceful by society”

Dr. Coretta M. Jenerette

Journal of the National Medical Association, 2010
ASSESSMENT:

What are the family’s past experiences and baseline functioning?
HOW DO WE ADDRESS THESE ISSUES?

Explanatory model approach:
how the social world affects their illness and is affected by their illness
1. Communication
   - Listen first, then speak
   - Ask questions

2. Hear their story
   - Learn about their journey
   - Learn what they know/don’t know
   - Learn about their concerns

3. Educate
   - Offer information
   - Debunk myths
   - Address their concerns
“There ain't no need to watch where I'm going, I just need to know where I've been.”

- **Tow Mater**,  
  **Cars**
ADDRESSING FERTILITY

- Fertility Preservation Team
  - Physician
  - Nurse Practitioner
  - RN Case Manager
  - Social Worker

**FERTILITY PRESERVATION**

**MALE FERTILITY**

**TESTICULAR TISSUE FREEZING - EXPERIMENTAL (TESTICULAR TISSUE CRYOPRESERVATION)**

**Process**
This is a procedure for boys who have not gone through puberty, while under anesthesia. A small incision is made to the scrotum. A slice of testicular tissue is removed. The tissue is sent to pathology approximately 23% of the tissue is saved and frozen for the patient's use at a later date and 23% of the tissue is used for research.

- University of Pittsburgh
- No fee is done from testicular tissue cryopreservation

**Dr. David Shin**
Adult Urologist
TESTICULAR BIOPSY

1525 Inwood Rd
350 Essex Street
Hackensack, New Jersey

**SPERM BANKING**

**SPERM CRYOPRESERVATION**

**Process**
This process saves sperm for future use. The semen is collected and checked under a microscope to count the sperm cells and see how healthy they are. The sperm cells are then frozen and stored.

- For post-potential notes
- Patients and family can contact Sperm and Embryo Bank of New Jersey for consultation

**Sperm and Embryo Bank of New Jersey**

SPERM BANKING

908-436-8944
800 N. Little Lane
Mountain Lakes, New Jersey

**THINGS TO CONSIDER**

**Testicular Tissue Freezing**
- How much time is needed for this process?
- What are the risks to my son?
- What are the costs?
- Is insurance accepted?
- Is there a genetic concern?
- What is the fertility success rate?
- How long is the procedure?

**Sperm Banking**
- Can I wait to start this process?
- How and where is the semen collected?
- What are the maintenance storage and long term costs?
- What happens if I or my son no longer want the sperm to be stored?

**CONTACT INFORMATION**

Youngsoo Lee, MSW, LOSTA
30 Prospect Avenue
Hackensack, NJ 07606
954-966-0109
THINGS TO CONSIDER

Egg Freezing
- How much time is needed for this process?
- What do we need to do before the procedure?
- How long is the procedure?
- Where are eggs stored?
- Is insurance accepted? What is the out of pocket cost?
- What are the storage and long term costs?

Ovarian Suppression
- How does it work?
- What is the fertility success rate?
- Is there a genetic concern?
- How soon can it be done?

OVARIAN SUPPRESSION

Process
LUPRON IS A MEDICATION THAT STOPS OR LOWERS THE AMOUNT OF ESTROGEN MADE BY THE OVARIAN. THIS IS GIVEN AS AN INJECTION EITHER EVERY 2 WEEKS OR AS A ONE TIME INJECTION, DEPENDING ON YOUR DAUGHTER’S DIAGNOSIS.

OVARIAN TISSUE PRESERVATION

Process
THIS PROCESS IS FOR PRE-PUBLERTAL FEMALES. PATIENT GOES TO CORNELL, REMOVE ONE OVARY, CUT INTO SLICES, THEN FREEZE AND RE-IMPLANT SLICES ONCE READY TO CONEVE (LAST 3-5 YEARS ONCE IMPLANTED)

Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine
1616 York Avenue 8th floor
New York, NY 10021
ADDRESSING FINANCIAL BARRIERS

- Financial planning
- Insurance education
- Preparation for household responsibilities
  - Work
  - Childcare
  - Transportation
ADDRESSING FINANCIAL BARRIERS

- Governmental assistance
  - SSI, SSDI, Medicaid, Catastrophic Illness in Children Relief Fund Commission

- Community resources
  - Julia’s Butterfly Foundation
  - Tackle Sickle Cell Embrace Kids Foundation
Resources

• Access Link (NJ)
• National Marrow Donor Program/Be The Match
• Bone Marrow & Cancer Foundation Lifeline Fund
• Governmental Assistance
  • Supplemental Security Income
  • Social Security Disability Income
  • Medicaid
  • Catastrophic Illness in Children Relief Fund (NJ)
• Local Community Organizations
  • Julia’s Butterfly Foundation
  • Tackle Sickle Cell Embrace Kids Foundation

• NeedyMeds
• Sickle Cell Disease Association of America, Inc.
• Resources for Children
  • Hole in the Wall Gang
  • Double H Ranch
  • Camp AmeriKids
  • Camp Dream Street
References


Programs and resources for you and your patients

Amber Ruffin, MPH
Program Analyst Diverse and Medically Underserved Populations Patient Advocacy and Navigation
National Marrow Donor Program /Be The Match
Be The Match Patient Support Center

Our services include:

• Patient and caregiver navigation services provided by certified oncology patient navigators
• Confidential telephone counseling and one-on-one support for your patients and families
• Support groups and webinars
• Financial grants for patients
• Information and support in many languages
• Educational books, DVDs, newsletters and fact sheets

Order, view or download: BeTheMatch.org/one-on-one

Bilan, MSW
BMT Patient Navigator
Phone: 1 (888) 999-6743
Email: patientinfo@nmdp.org
SCD Peer Connect Program

• We can help when your patients or caregivers want to talk to someone who’s been through transplant
• Trained Peer Connect volunteers are available to:
  – connect with your patients and caregivers
  – share their experiences
  – provide support and answer questions
• Request a connection - BeTheMatch.org/peerconnect

We’ll listen, laugh and cry with them. We’ve been there—and we get it”
- Ted, transplant recipient and Peer Connect volunteer
Jason Carter Clinical Trials Program
To help your patients with blood cancers, blood disorders, and immune systems diseases find and join clinical trials

- **One-on-one support** for patients & families to help answer questions and guide their clinical trials search

- **Online search tool:** JCCTP.org/sickle-cell

- **Easy-to-understand resources** to learn about cancer treatments and clinical trials

Contact: Anna DeSalvo, MS, CGC
Clinical Trial Patient Education Specialist
Phone: 1 (888) 814-8610
Email: clinicaltrials@jcctp.org
Quick Reference Guidelines for Transplant Consultation and Post-Transplant Care

• Referral Guidelines – 2019 update
  – NMDP/Be The Match & ASBMT: Recommended Timing for Transplant Consultation
  – Up-to-date referral for HCT consultation timing for more than 20 diseases

• Long-Term Survival Guidelines
  – Part I: Long-term screening
  – Part II: Vaccinations
  – Part III: Screening for chronic GVHD

Available in mobile app, print and online:
BeTheMatchClinical.org/guidelines
COMING SOON!

• SC3, STAR and NMDP/BTM have collaborated to develop a handbook to answer common questions about BMT

- History of BMT
- Is BMT for Me
- Benefits of BMT
- Risks of BMT
- BMT Basics
- Finding a donor
- Transplant timeline
- Being a donor
- Resources