

COUNCIL MEETING*Sharing Our Passion for Life*

Increasing Access to BMT for Patients with Sickle Cell Disease

Council Meeting 2016

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Constance Benson; BMT Recipient for SCD



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Disclosures

The following faculty and planning committee staff have no financial disclosures:

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Sonja L. Banks, MPA, MBA	SCDA
Lensa Idossa, MPH	NMDP/Be The Match
Constance Benson	N/A



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Learning objectives

At the conclusion of this session, attendees will be able to:

- Describe advances in BMT for SCD
- Describe a recipient's perspective on BMT
- Discuss initiatives of the NMDP & Sickle Cell Disease Association of America (SCDAA) to address barriers to access and care



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COUNCIL MEETING

Sharing Our Passion for Life

Advances in BMT for SCD

Linda J. Burns, MD, PhD

Vice President and Medical Director
NMDP/Be The Match



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Sickle cell disease: Prevalence

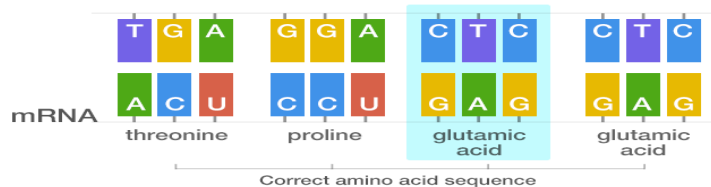
An inherited hemoglobin disorder (Hemoglobin S)

- Autosomal recessive disorder
- More than 300,000 newborns worldwide have SCD
- Affects 100,000 African Americans or Hispanic-Americans
- Occurs in 1 of every 365 African American and 16,300 Hispanic-American births in the United States

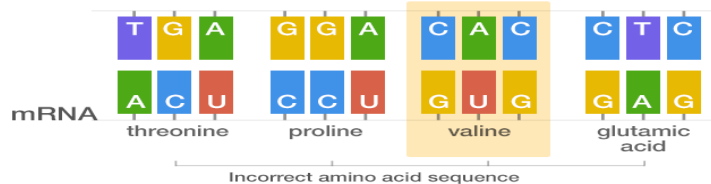
Centers for Disease Control and Prevention; WHO; Piel et al. Lancet 381:142-51.

Single gene mutation causes sickle cell disease

Normal DNA sequence (HbA)

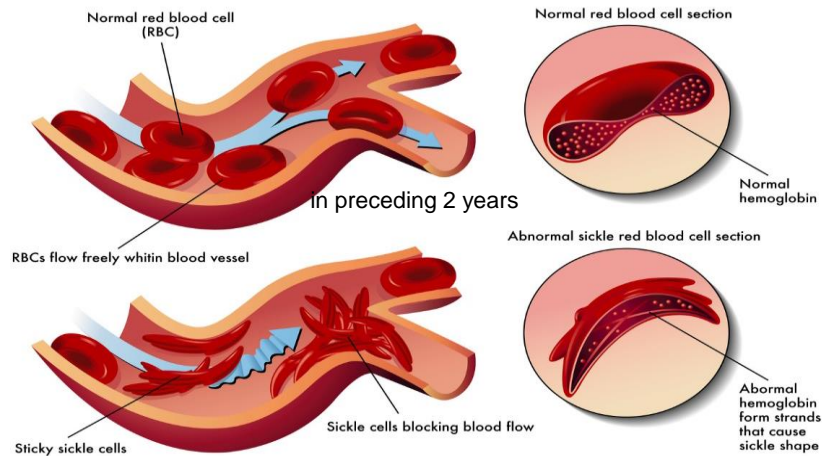


Mutated DNA sequence (HbS)



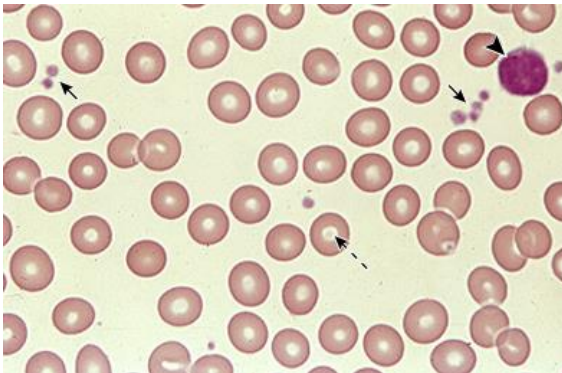
Hemoglobin S = Sticky red blood cells

Sickle-Cell Anemia

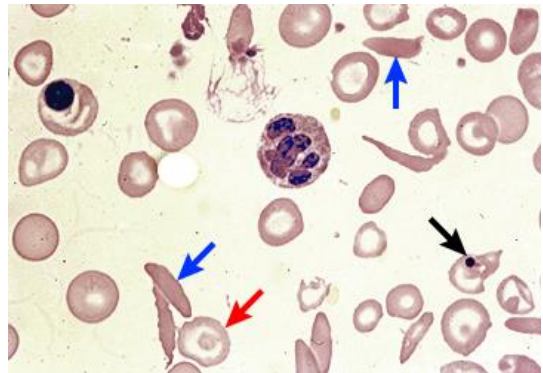


Findings on peripheral blood smears

Normal



Sickle cell disease



Complications of SCD

Severity varies among patients

- Infections
- Severe anemia from breakdown of red blood cells within 10-20 days (compared with 120 days)
- Stroke
- Vaso-occlusive crises (severe pain)
- Acute chest syndrome (lungs)
- Infarctions (heart, kidneys, bone)

Treatment of SCD: Preventive care

- Prevent infections: vaccinations and penicillin prophylaxis
- Transfusion therapy (red blood cells)
- Hydroxyurea
 - Increases amount of fetal hemoglobin
 - FDA approved for patients with severe disease

BMT in SCD is evolving

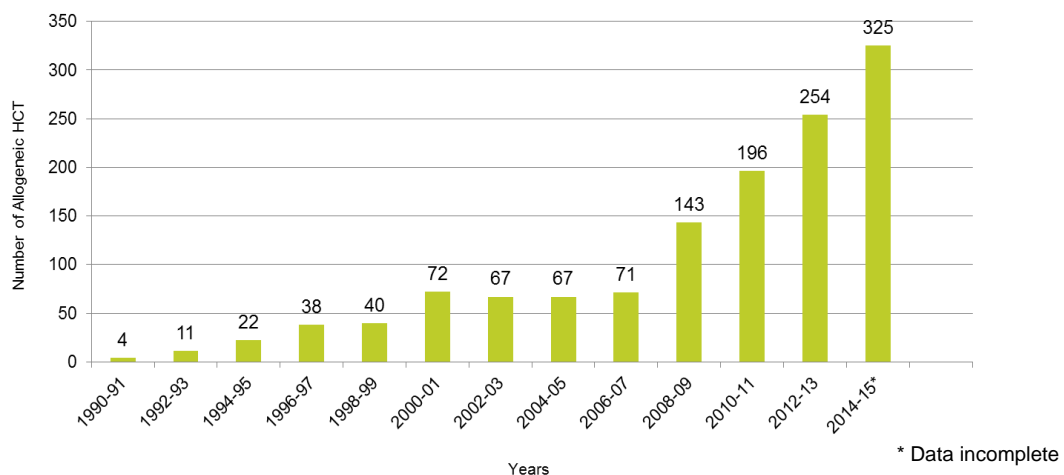
- Potentially curative therapy
- First report in 1984 in patient with both AML and SCD (HLA-matched sibling BMT cured both diseases)
- Excellent results in HLA matched sibling transplantation
 - Event free survival **>90%**
 - Acceptable rates of graft rejection and graft-versus-host disease (GVHD)
 - Only **18%** of patients with SCD have an HLA-matched sibling donor in the United States



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Increasing number of patients who received a first allogeneic HCT for SCD: 1990-2015

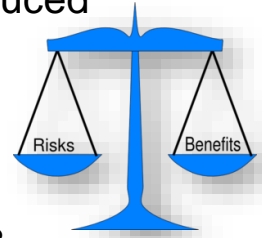


The data presented here are preliminary and were obtained from the Statistical Center of the Center for International Blood and Marrow Transplant Research (CIBMTR). The analysis has not been reviewed or approved by the Advisory or Scientific Committee of the CIBMTR.

Patient criteria for alternative donor BMT is a major question

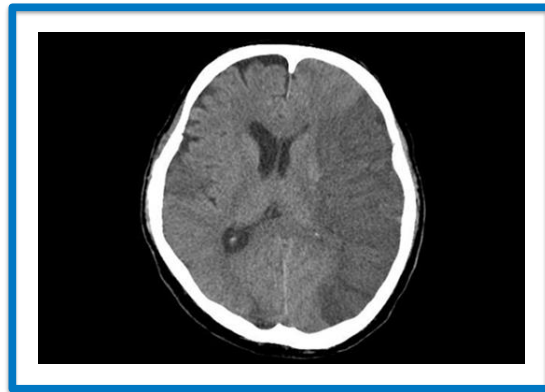
- Need to balance potential cure versus transplantation-related mortality and potential for treatment-induced malignancy

(risks versus benefits)

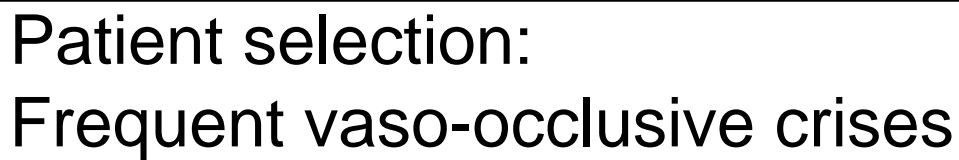


- *Which patients should be considered for BMT?*

Patient selection: Stroke



Trans-cranial Doppler ultrasound testing to predict stroke



Patient selection: Acute chest syndrome

Symptoms:

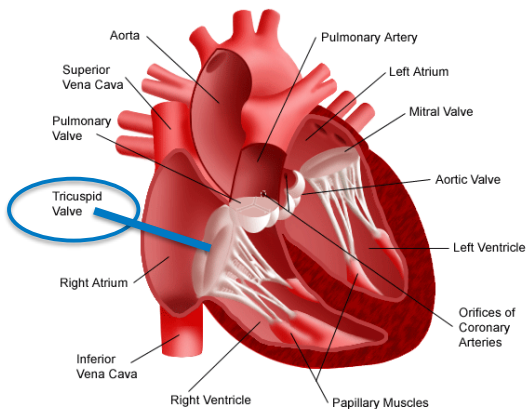
- Fever
- Low oxygen levels
- Shortness of breath
- Chest pain



Patient selection :

Tricuspid valve regurgitant jet (TRJ) ≥ 2.7 m/sec (measure of pulmonary hypertension)

Interior View of the Heart



Transplant trials within BMT CTN

Study	Patient population	Donor	Status
BMT CTN 0601	Children	Unrelated donor	Published 9/2016
BMT CTN 1503 STRIDE	Young adults	Matched sibling or unrelated donor	Just started
BMT CTN 1507	Children	Haploidentical	In development

A BMT CTN phase II Trial of Unrelated Donor Transplantation for Children with Severe SCD

BMT CTN 0601

NCT00745420

Shenoy et al. Blood 2016; pre-published on line September 13, 2016

Trial design

- Multicenter phase II trial, 2008-2014
- Enrolled 30 children, aged 4-19 years
- Reduced intensity conditioning (alemtuzumab, fludarabine, melphalan) with CSA or tacrolimus + MTX + methylpred GVHD prophylaxis

Patient selection criteria	Number of children
Stroke	12
Trans-cranial Doppler velocity >200 cm/second	2
≥3 vaso-occlusive pain crises/year in preceding 2 years	12
≥2 acute chest syndrome episodes in preceding 2 years	4

Results

- Median follow-up = 26 months
- Engraftment = 90%
- 7 GVHD-related deaths
- 34% incidence of posterior reversible encephalopathy syndrome

Outcome	Number of children
1 and 2 year event free survival	76%; 60%
1 and 2 year overall survival	86%; 79%
Grade II-IV acute GVHD at day 100	28%
1-year incidence chronic GVHD	28%

Author's conclusions

- Children with SCD engrafted unrelated donor marrow after reduced intensity conditioning
- Significant improvements in perception of general health and quality of life
- A high incidence of GVHD and associated mortality compromised safety of the trial
- Although the reduced intensity conditioning provided successful engraftment, *the regimen cannot be considered safe for widespread adaptation*
- Future trials should focus on strategies to minimize risks of GVHD



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Shenoy et al. Blood 2016; pre-published on line September 13, 2016

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Hematopoietic Cell Transplantation for Young Adults with Severe Sickle Cell Disease (STRIDE)

BMT CTN 1503

NCT01565616



Eligibility criteria

- Age 15 – 40 years
- Stroke or neurologic deficit lasting >24 hours
- ≥ 2 episodes of acute chest syndrome in preceding 2 years
- ≥ 3 episodes of vaso-occlusive crisis in preceding 2 years
- ≥ 8 transfusions per year for ≥ 1 year to prevent SCD-related complications
- Tricuspid valve regurgitant jet (TRJ) ≥ 2.7 m/sec

Study design and enrollment plan

- Designed as a biologic assignment trial of donor versus no donor
- Donor may be an HLA-matched sibling or unrelated donor
- Accrue 200 patients over 3 years
- Anticipated enrollment: Now – June 2019
- Follow-up: Two-years from biologic assignment

Primary endpoint

- Difference in the proportion of patients surviving at 2 years
- The difference between the donor and no donor arms should not exceed 15% at 2 years (if it does, unlikely BMT will offer better survival compared to standard of care long-term)

Secondary endpoints

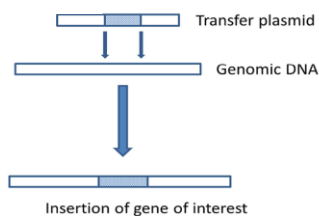
- Measure the benefit of BMT on:
 - Sickle-related events
 - Organ function (pulmonary, renal)
 - Quality of life
 - Pain assessments (via e-diary)

Autologous BMT and gene therapy

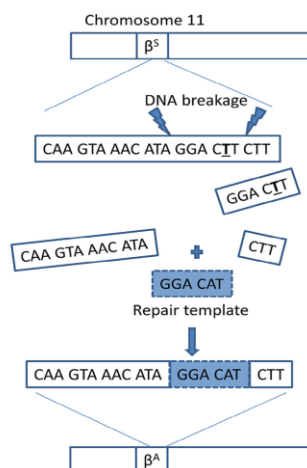
- Novel approach to potentially cure SCD
- Reverses the gene mutation underlying SCD
- Results in production of red blood cells that make normal hemoglobin

Autologous BMT and gene therapy

Gene addition



Gene editing



Summary

- BMT in SCD is potentially curative
- Excellent results in HLA matched sibling transplantation
- Need to balance benefits versus risks in alternative donor BMT
- Gene therapy holds promise
- There are many issues to work out, so





Giving New Voice An SCDAA Overview.....

Working Together to Change Lives

Sonja L. Banks, MPA, MBA
President & COO
Sickle Cell Disease Association of America, Inc.



The Sickle Cell Disease Association of America, Inc. (SCDAA) serves as the nation's only volunteer organization working full time on a national level to resolve issues surrounding sickle cell disease.



Our Mission

"To advocate for and enhance our membership's ability to improve the quality of health, life and services for individuals, families and communities affected by sickle cell disease and related conditions, while promoting the search for a cure for all people in the world with sickle cell disease."



Our Members

"MO's are the foundation to both SCDA and the SCD community."

- ▶ Community based organizations designed to serve individuals and families in their respective communities by offering program and outreach services.
- ▶ Assist clients with finding quality healthcare
- ▶ Maintain databases of individuals and families that have been served over the years
- ▶ Community Outreach
- ▶ Educate local communities



Giving New Voice

SCDAA Current Initiatives

2016 – 2017 Key Focus Areas

- ▶ **CBO CAPACITY BUILDING**
- ▶ **LEGISLATIVE ADVOCACY**
- ▶ **AWARENESS & OUTREACH**
- ▶ **TREATMENT & RESEARCH**

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Community – Based Capacity Building

- ▶ **Launch SCDA Leadership & Training Academy**
 - Professional Training
 - Organizational Capacity Training
 - Program Training
- ▶ **Launched the National SCD Community Health Worker (CHW) training program**

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Legislative Advocacy

- ▶ **Re-introduced Re-Authorization of Sickle Cell Treatment Act - Bill H.R. 1807 in the House**
Treatment Centers, Surveillance, Clinical Research and Transition programs
- ▶ **Recently Testified before Energy and Commerce Health Subcommittee**
- ▶ **Established Access to Inpatient Drug Therapy Congressional language**

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Awareness & Outreach

- ▶ **Clinical Trial Awareness Initiatives**
- ▶ **Bone Marrow Donation and Donor Education**
- ▶ **National Blood Drive Campaign**
- ▶ **Hydroxyurea Education**
- ▶ **National Public Awareness Campaign**

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Research & Programs

- **Strengthen Research Portfolio**
 - Expand Post Doctoral Fellowship Program
 - Clinical Trial Education Navigator Program
- **HRSA Newborn Screening Coordinating Center**
 - CHW Outreach and Medical Home Assistance
- **Get Connected Patient Powered Registry**

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Purpose of “Get Connected”....

- Establish a network of children, adults and families living with sickle cell disease, SCDA member organizations, health care providers and other community-based organizations to distribute information related to clinical care, research, health services, health policy and health care advocacy
- Establish a registry for children and adults living with sickle cell disease to store medical information related to diagnosis, treatment and potential cure
- Establish a network of providers that are educated about the unique health care and psychosocial needs of children and adults living with sickle cell disease
- Connect children and adults with sickle cell disease to high quality resources for information on health care including behavioral health, clinical research and ancillary health care resources
- Establish a network to support clinical research through community-based research navigators

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*“Coming together is a
beginning.
Keeping together is progress.
Working together is success.”*

Henry Ford

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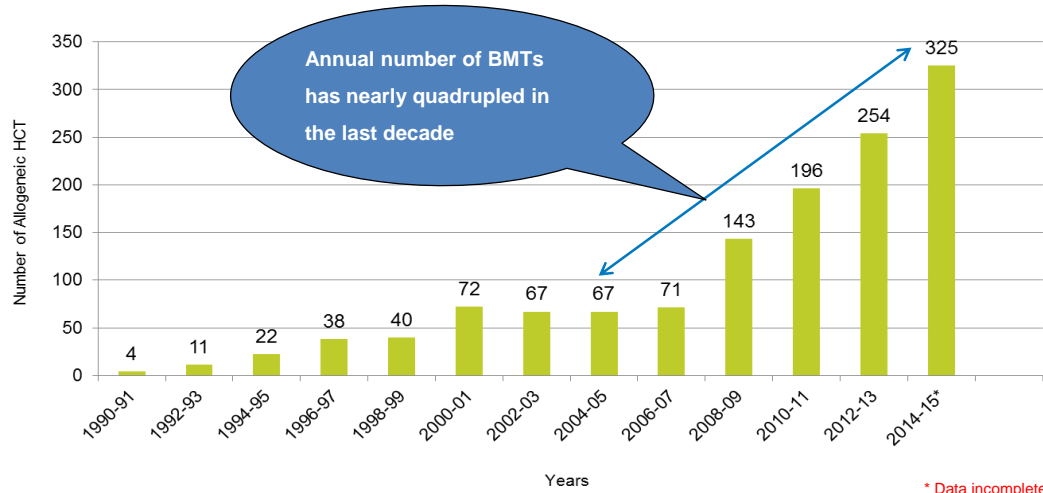
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NMDP/Be The Match Initiatives to Address Barriers to Access and Care

Lensa Idossa, MPH; Program Analyst, NMDP/Be The Match

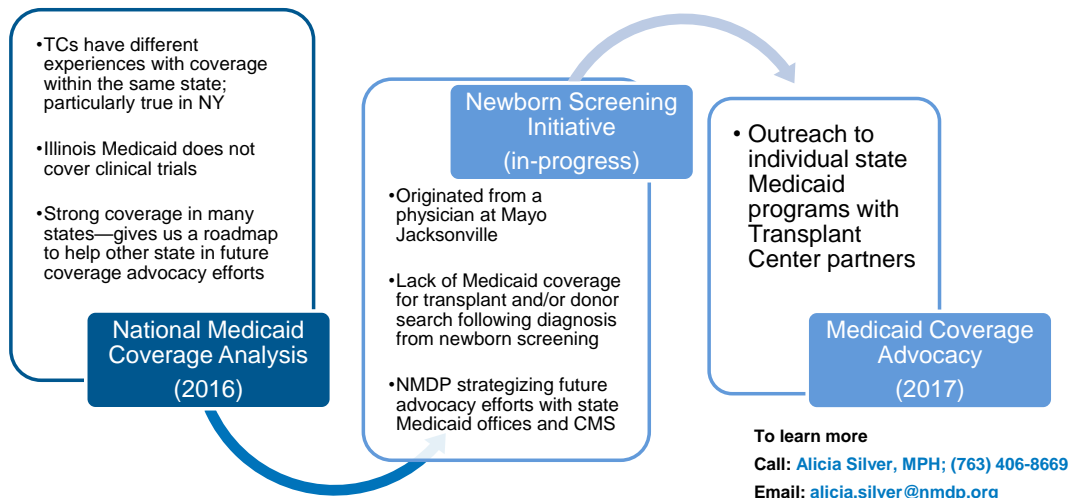
Number of patients who received a first allogeneic BMT for SCD: Reported to CIBMTR 1990-2015



Payer policy initiatives: Medicare

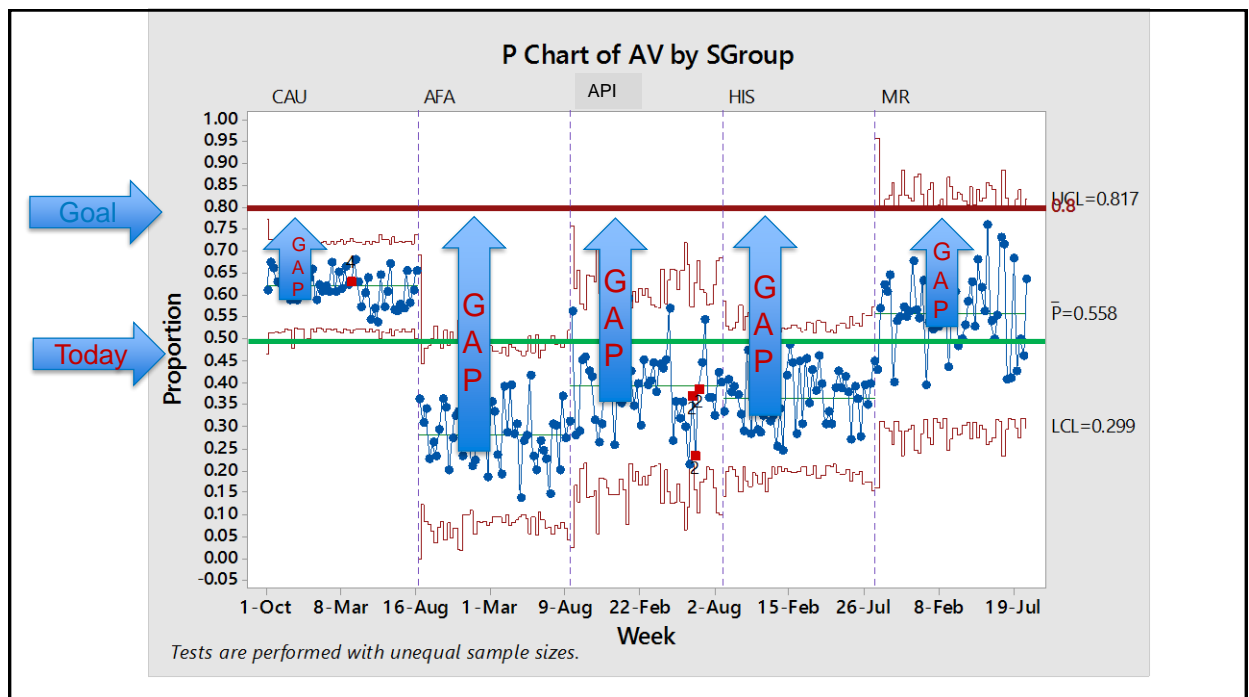
- Be The Match and the American Society for Blood and Marrow Transplantation (ASBMT) petitioned Medicare to cover BMT for SCD
- Medicare issued a positive coverage determination in 2016
 - Requires that patients be enrolled in a Medicare-approved clinical trial (coverage with evidence development)
 - BMT CTN 1503 (STRIDE 2)

Payer policy initiatives: Medicaid



Donor recruitment and availability

- Focus on younger donors
 - 18-24 year old males
- Reach 80% donor availability by 2018
 - Focus on African American and Hispanic donors



Initiatives to increasing donor availability

- Online recruiting
- Member confirmation
 - Bystander management
 - Recommit
- Partnering with recruitment centers to address common challenges

Immunogenetic operations & research initiative

- Proactively typing and contacting all potential 10/10 matches for searching patients
- Activating donors from other countries

Patient assistance programs

2015:
YEAR
AT A
GLANCE



\$3.4 million
in patient
assistance to
2,000 families



Zalika, transplant recipient, with her parents

Partnership with advocacy organizations

- Sickie Cell Disease Association of America
- Foundation for Sickie Cell Disease Research
- ASH Sickie Cell Disease Coalition
- Future:
 - Three additional organizations
 - 10 SCD centers

Educating health professionals

- Host a satellite symposium at the 2016 ASH meeting on *Improving Sickle Cell Disease Outcomes: Treatment decision making, curative therapies, and overcoming barriers to care*
– Friday, Dec. 2nd, 2016 7:00am-11:00am
- The recorded symposium will be offered as an enduring webinar with continuing education credits

Educating patients and families

- We offer many educational resources for patients, caregivers and families
- “Booth in a box” package to reach members of the community with information



BeTheMatch.org/LearnTheBasics

Expanding volunteer base

- *Peer Connect* program
 - Matches patients or caregivers with trained volunteers who are transplant recipients or caregivers
 - Connect with patients and caregivers
 - Share their experiences
 - Provide support and answer questions



(L-R) Lizette, Amanda, Ted and Ed; Peer Connect Volunteers



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2017 priority initiatives

- Increase access to transplant information for patients, caregivers and families
- Increase engagement with health professionals
- Improve donor availability
- Improve donor search
- Advocate for better Medicare & Medicaid coverage



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Thank you!



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