ASH 2016 Highlights
Innovations In Sickle Cell Disease

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The path to achieving a cure for SCD?

**Stem Cell Transplantation**

- Data from 1000 children with SCD from Europe, Brazil, United States, Africa and the Middle East who underwent stem cell transplants from matched, sibling donors

**Gene Therapy**

- Patient serves as own donor
- Engineered viral vector used to insert normal copy of single gene that is defective in SCD

**Graphs**

- **Overall Survival**
  - BM
  - PB
  - CB
  - 94% Overall Survival @3Y

- **Hemoglobin Concentration (g/dL)**
  - Total Hb 11.7 g/dL
  - HbA (transfused)
  - HbS 49%
  - HbA^{T87Q} 47%
  - HbF 2%

*Months Post Drug Product Infusion*
Druggable Targets in SCD?

- Polymerization of sickle hemoglobin
- Alterations in RBC membrane
- Reduced nitric oxide bioavailability
- Endothelial dysfunction
- Platelet activation
- Pro-inflammatory cytokine production
- Activation of adhesion molecules on leukocytes, endothelial cells and platelets

Microcirculation 2004;11(2):179-93
The Biopharmaceutical Development Process


~$2.6B over 10 years to bring therapy to market


SCD Therapeutics by Clinical Pipeline Phase

- Phase II 41%
- Phase III 19%
- Pre-Clinical 18%
- Phase I 18%
- Phase IV 4%
What this Means in Practice

There are going to be many more SCD-related clinical trials in the foreseeable future.

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They will all need patients from the same limited population.
Exacerbating Existing Barriers

1. **Finding appropriate investigators and sites**
   - Knowledgeable about the disease area
   - Capacity for conducting clinical research

2. **Finding eligible cohorts**
   - Sponsor’s perspective: It is difficult to identify and recruit eligible patients
   - Patient’s perspective: It is difficult to identify trials for which I am eligible

3. **Evaluating effectiveness**
   - Therapeutic outcome measures do not exist for many disease areas
Moving Into An Era Of Novel Therapies for Sickle Cell Disease: Are We There Yet?

- Have we optimized use of existing treatment?
- How will the concomitant use of hydroxyurea affect the efficacy of new agents?
- Are we closer to having more therapeutic options for patients with sickle cell?