NURSING CONSIDERATIONS FOR PATIENTS WITH SICKLE CELL DISEASE IN THE ERA OF GENE THERAPY

Bethann Worster MSN, CRNP
*Nurse Practitioner, Cell Therapy and Transplant Section*

Claire White MSN, RN
*Access Services Manager, Cell Therapy and Transplant Section*
SICKLE CELL DISEASE

• Most common genetic disease in this country

• It is estimated that:
  • SCD affects approximately 100,000 Americans.
  • SCD occurs among about 1 out of every 365 African-American births.
  • SCD occurs among about 1 out of every 16,300 Hispanic-American births.
  • About 1 in 13 African-American babies is born with sickle cell trait (SCT).
SICKLE CELL DISEASE

http://www.nhlbi.nih.gov/health/health-topics/topics/sca/
### SICKLE CELL DISEASE

<table>
<thead>
<tr>
<th></th>
<th>Acute Complications</th>
<th>Chronic Complications</th>
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<tbody>
<tr>
<td>CNS</td>
<td>Stroke, TIA</td>
<td>Cognitive delay, Behavioral issues</td>
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<tr>
<td>Pain</td>
<td>Acute vaso-occlusive episode</td>
<td>Chronic Pain</td>
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<tr>
<td>Pulmonary</td>
<td>Acute Chest Syndrome</td>
<td>Pulmonary Hypertension</td>
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<tr>
<td>Skeletal</td>
<td>Dactylitis, Osteomyelitis</td>
<td>Avascular Necrosis</td>
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<tr>
<td>Spleen</td>
<td>Splenic Sequestration</td>
<td>Functional Asplenia/Asplenia</td>
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<tr>
<td>GU</td>
<td>Priapism</td>
<td>Delayed puberty, erectile dysfunction</td>
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CURRENT MANAGEMENT

• Infection Prevention
  • PCN VK
  • Immunizations
• Pain Management
• Blood Transfusions
• Stroke Monitoring and Prevention
• Hydroxyurea
• Bone Marrow Transplant
CURRENT MANAGEMENT: HYDROXYUREA

- General features:
  - Single-agent, inexpensive, orally administered, once-daily dosing
- Laboratory efficacy:
  - Increases Hgb F and total Hgb, reduces WBC and reticulocytes, and lowers LDH
- Clinical efficacy:
  - Improves anemia, leads to fewer vaso occlusive events and hospitalizations, decreases hemolysis
- Side effects:
  - Few short-term toxicities that might limit adherence, wide therapeutic index
- Compliance issues

CURRENT MANAGEMENT: BONE MARROW TRANSPLANT

• Current indications for BMT include:
  • Vaso-occlusive complications not well controlled with current standard of care therapy
• Only about 20% of patients with SCD have a matched sibling donor
  • Associated with greatest survival and reduced transplant morbidities
• If a matched sib is unavailable, it is difficult to find a full HLA match in unrelated donor registries this limits transplant as an option for many patients
  • Alternative donor options are being pursued via clinical trials
    • Cord blood
    • Haploidentical
    • T cell depleted unrelated donor options
Crizanlizumab for the Prevention of Pain Crises in Sickle Cell Disease

A Phase 3 Randomized Trial of Voxelotor in Sickle Cell Disease

Elliott Vichinsky, M.D., Carolyn C. Hoppe, M.D., Kenneth I. Ataga, M.D., Russell E. Ware, M.D., Ph.D., Videlis Nduba, M.B., Ch.B., M.P.H., Amal El-Beshlawy, M.D., Hoda Hassab, M.D., Maureen M. Achebe, M.D., M.P.H., Salam Alkindi, M.B., B.Ch., R. Clark Brown, M.D., Ph.D., David L. Diuguid, M.D., Paul Telfer, M.D., Dimitris A. Tsitsikas, M.D., Ashraf Elghandour, M.D., Victor R. Gordeuk, M.D., Julie Kanter, M.D., Miguel R. Abboud, M.D., Joshua Lehrer-Graiwer, M.D., Margaret Tonda, Pharm.D., Allison Intondi, Ph.D., Barbara Tong, Ph.D., and Jo Howard, M.D., for the HOPE Trial Investigators
### GENE THERAPY TREATMENT

Goal: Reduce the percentage of sickled cells circulating to decrease disease complications

<table>
<thead>
<tr>
<th>Gene Addition</th>
<th>Gene Editing</th>
<th>Gene Silencing</th>
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<tbody>
<tr>
<td>- Involves the introduction of a new gene</td>
<td>- Involves changing the primary DNA sequence of an existing gene</td>
<td>- Uses genetic techniques to reduce the expression level of a gene</td>
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GENE THERAPY TREATMENT

Step 1: Screening and Eligibility

Step 2: Stem Cell Mobilization, Apheresis and Cell Manufacturing

Step 3: Inpatient Stay: Busulfan Conditioning, Stem Cell Infusion

Step 4: Inpatient Stay: Awaiting Engraftment

Step 5: Long Term Outpatient Follow up
WHICH THERAPY IS RIGHT FOR MY CHILD?

Gene Therapy Pros:
- No risk of GVH or graft rejection
  - No immunosuppression
  - Less infection risk
  - Less medicines post PSCT

Gene Therapy Cons:
- Hgb S isn’t completely eliminated
  - Clinical Trial Availability
  - Waiting period to see success
“Sickle cell disease: All three patients were free of vaso-occlusive crises with 3 to 15 months of follow-up after CTX001 infusion

Nineteen patients have been dosed with CTX001 across both programs”
SCD GENE THERAPY OUTCOMES DATA

“No severe vaso-occlusive events (VOEs) reported through 24 months of follow-up in patients who had a history of at least four severe VOEs and at least six months of follow-up (n=19)

At up to 30 months follow-up and 32 patients treated, Group C patients continue to produce consistent levels of gene therapy-derived anti-sickling hemoglobin (HbAT87Q), reducing levels of abnormal sickle hemoglobin (HbS) that cause symptoms of SCD

Positive patient-reported quality of life outcomes assessed with validated PROMIS-57 demonstrate clinically meaningful reductions in pain intensity at Month 12 post-LentiGlobin for SCD treatment”
CELLULAR GENE THERAPY INTAKE PROCESS

Patient

CHOP Cell Therapy and Transplant Team

Referring Hematology Team

CHOP Hematology
TEAM STRUCTURE

Gene Therapy Social Worker
Gene Therapy Transplant Coordinator
Gene Therapy Research Coordinator
Hematology Physician
Nurse Navigator
Gene Therapy Transplant Physician
Insurance Specialist
Fertility Preservation Team
Gene Therapy Transplant Nurse Practitioner
Psychology Team
Apheresis Team
WHAT ARE WE LOOKING FOR

- Disease Characteristics and Severity
- Organ Function
- Social Support
- Current Treatment Regimen
WHAT ARE WE LOOKING FOR

βS/βS or βS/β0 genotype

Disease Characteristics and Severity

Splenic Sequestration Occurrence

Priapism Occurrence

Acute Pain Events

Acute Chest Syndrome
WHAT ARE WE LOOKING FOR

- Pulmonary Function
- Liver Function
- Clinical Picture
- Cardiac Function
- Vascular Access
- Neurologic and Cerebrovascular Function
- Active Infections
WHAT ARE WE LOOKING FOR

Current Treatment Regimen

Hydroxyurea

Pain Management and Hydration Plan

Red Blood Cell Transfusions

Crizanlizumab
WHAT ARE WE LOOKING FOR

- Committed Caregiver
- Informed Consent
- Individual Patient Needs
Contact Information:

Bethann Worster: WORSTER@chop.edu
Claire White: WHITEC3@chop.edu
REFERENCES


