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

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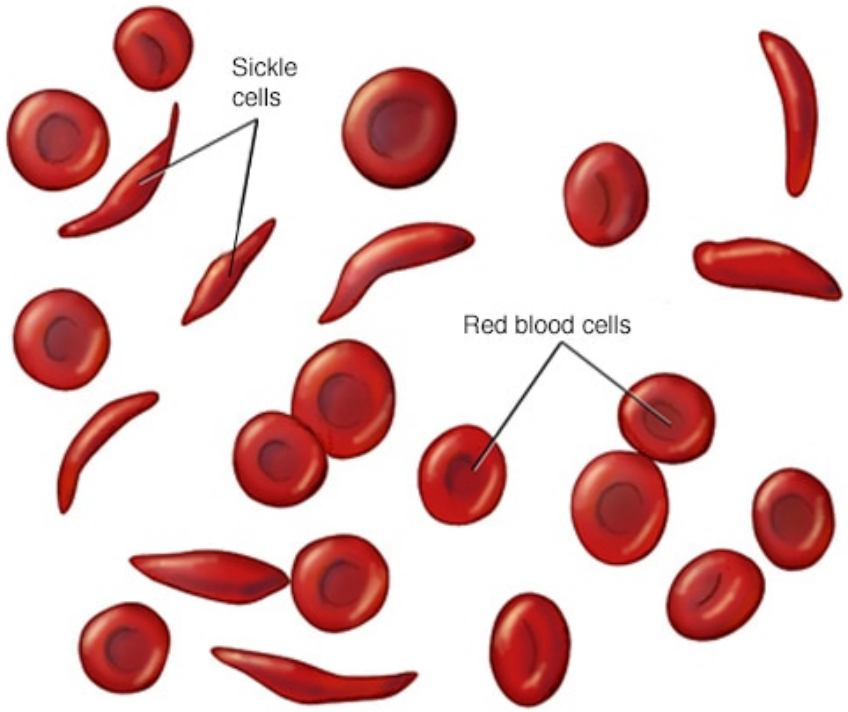
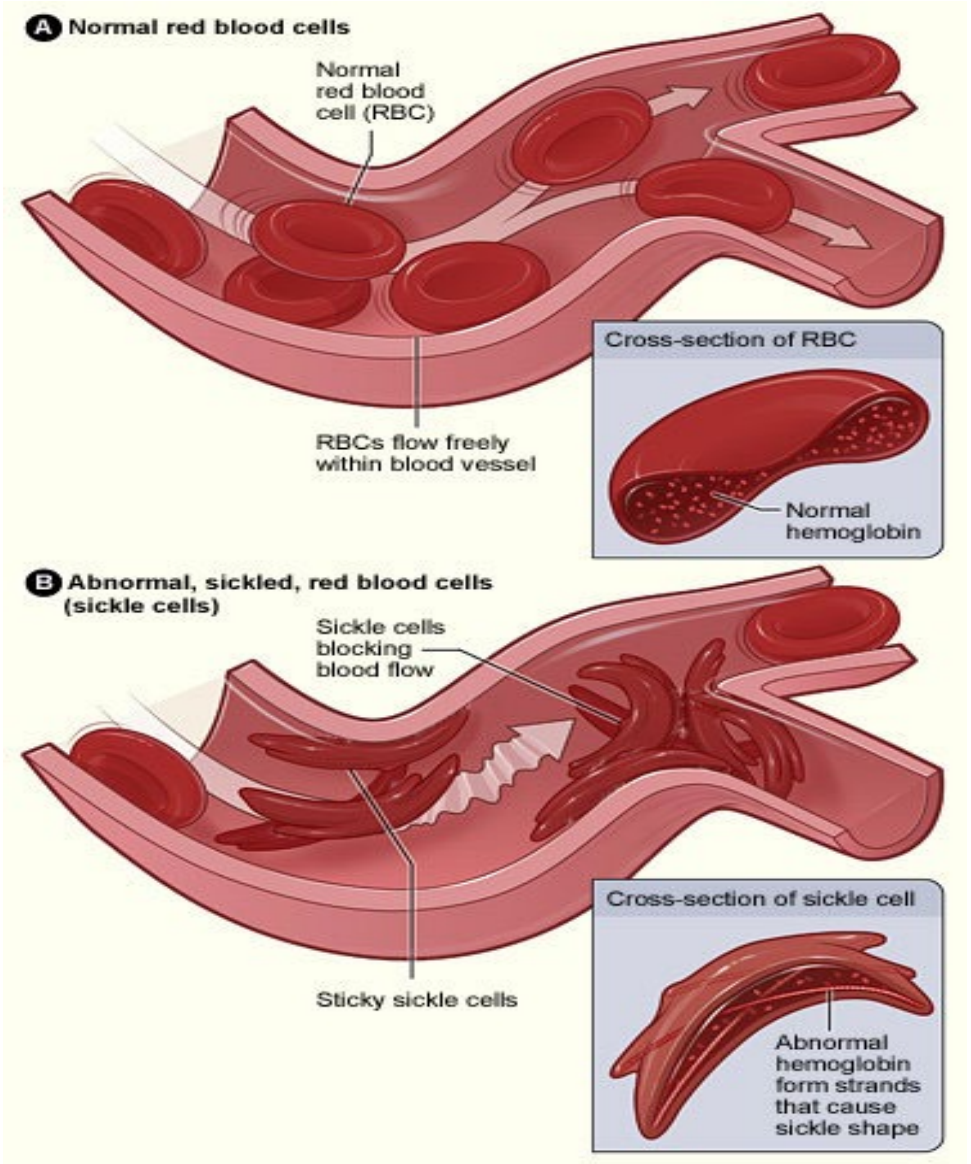
SICKLE CELL DISEASE

- 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).

cdc.gov

SICKLE CELL DISEASE





http://www.nhlbi.nih.gov/health/health-topics/topics/sca/

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SICKLE CELL DISEASE

	Acute Complications	Chronic Complications
CNS	Stroke, TIA	Cognitive delay, Behavioral issues
Pain	Acute vaso-occlusive episode	Chronic Pain
Pulmonary	Acute Chest Syndrome	Pulmonary Hypertension
Skeletal	Dactylitis, Osteomyelitis	Avascular Necrosis
Spleen	Splenic Sequestration	Functional Asplenia/Asplenia
GU	Priapism	Delayed puberty, erectile dysfunction

CURRENT MANAGEMENT

- Infection Prevention
  - PCN VK
  - Immunizations
- Pain Management
- Blood Transfusions
- Stroke Monitoring and Prevention
- Hydroxyurea
- Bone Marrow Transplant

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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

- Agrawal, R. K., Patel, R. K., Shah, V., Nainiwal, L., & Trivedi, B. (2014). Hydroxyurea in sickle cell disease: drug review. *Indian journal of hematology & blood transfusion : an official journal of Indian Society of Hematology and Blood Transfusion*, *30*(2), 91–96. https://doi.org/10.1007/s12288-013-0261-4

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 pursed via clinical trials
    - Cord blood
    - Haploidentical
    - T cell depleted unrelated donor options

EMERGING THERAPIES

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Crizanlizumab for the Prevention of Pain Crises in Sickle Cell Disease

K.I. Ataga, A. Kutlar, J. Kanter, D. Liles, R. Cancado, J. Friedrisch, T.H. Guthrie, J. Knight-Madden, O.A. Alvarez, V.R. Gordeuk, S. Gualandro, M.P. Colella, W.R. Smith, S.A. Rollins, J.W. Stocker, and R.P. Rother

EMERGING THERAPIES

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 8, 2019 VOL. 381 NO. 6

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

Gene Addition	Gene Editing	Gene Silencing
- Involves the introduction of a new gene	- Involves changing the primary DNA sequence of an existing gene	- Uses genetic techniques to reduce the expression level of a gene

GENE THERAPY TREATMENT

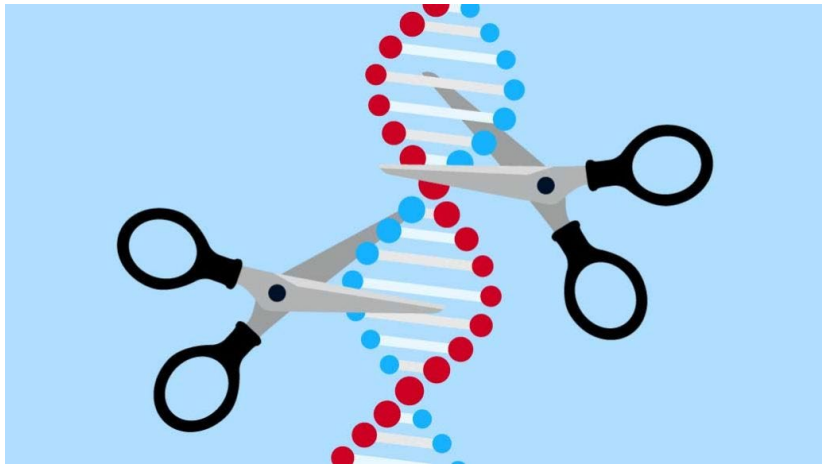
Step 1: Screening and Eligibility

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



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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

SCD GENE THERAPY OUTCOMES DATA

"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"

American Society of Hematology Annual Meeting
Dec. 05, 2020

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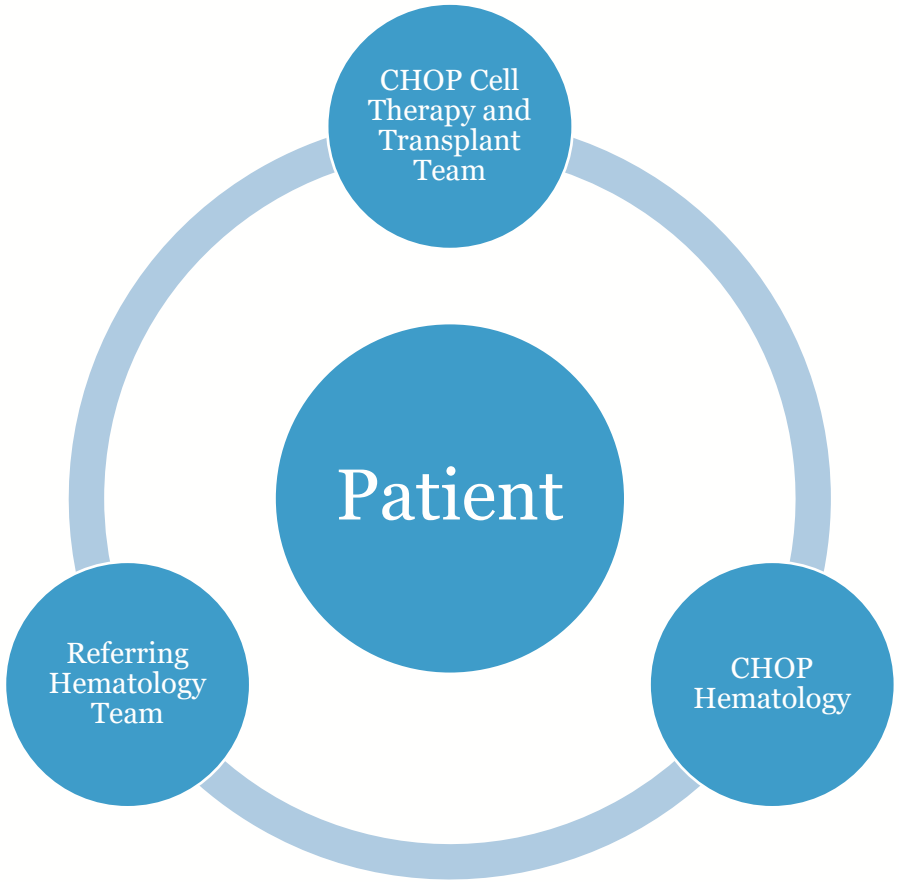
SCD GENE THERAPY OUTCOMES DATA

"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



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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

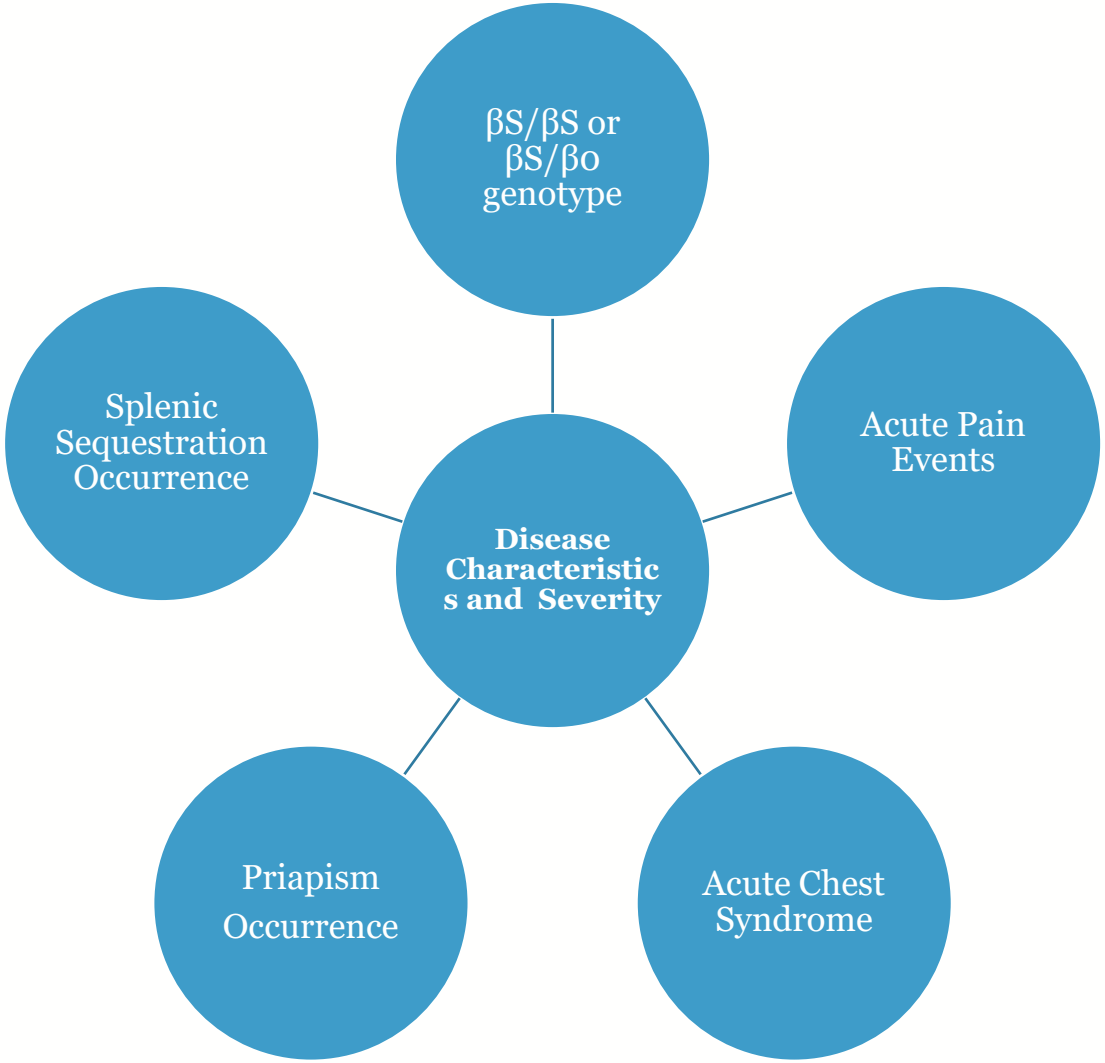
Disease Characteristics and Severity

Organ Function

Social Support

Current Treatment Regimen

WHAT ARE WE LOOKING FOR



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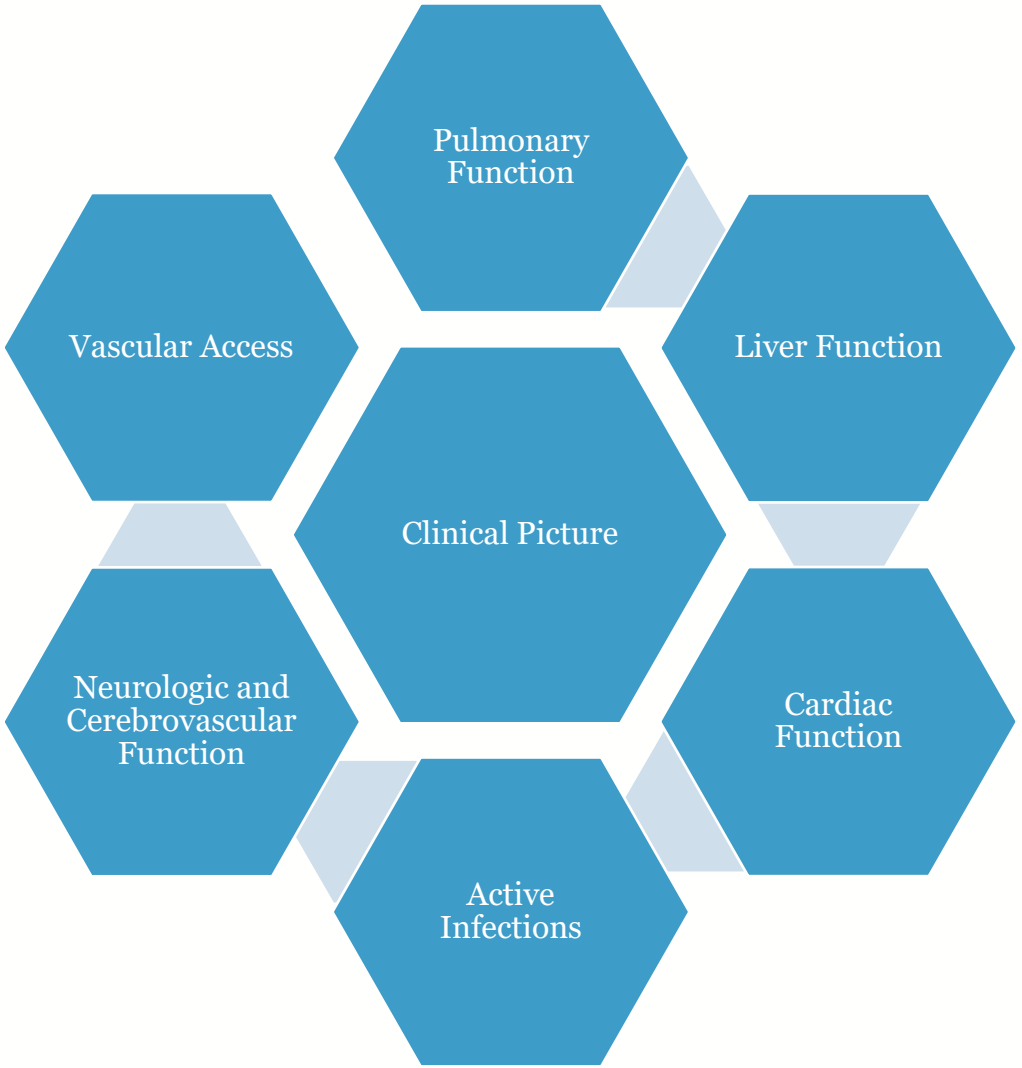

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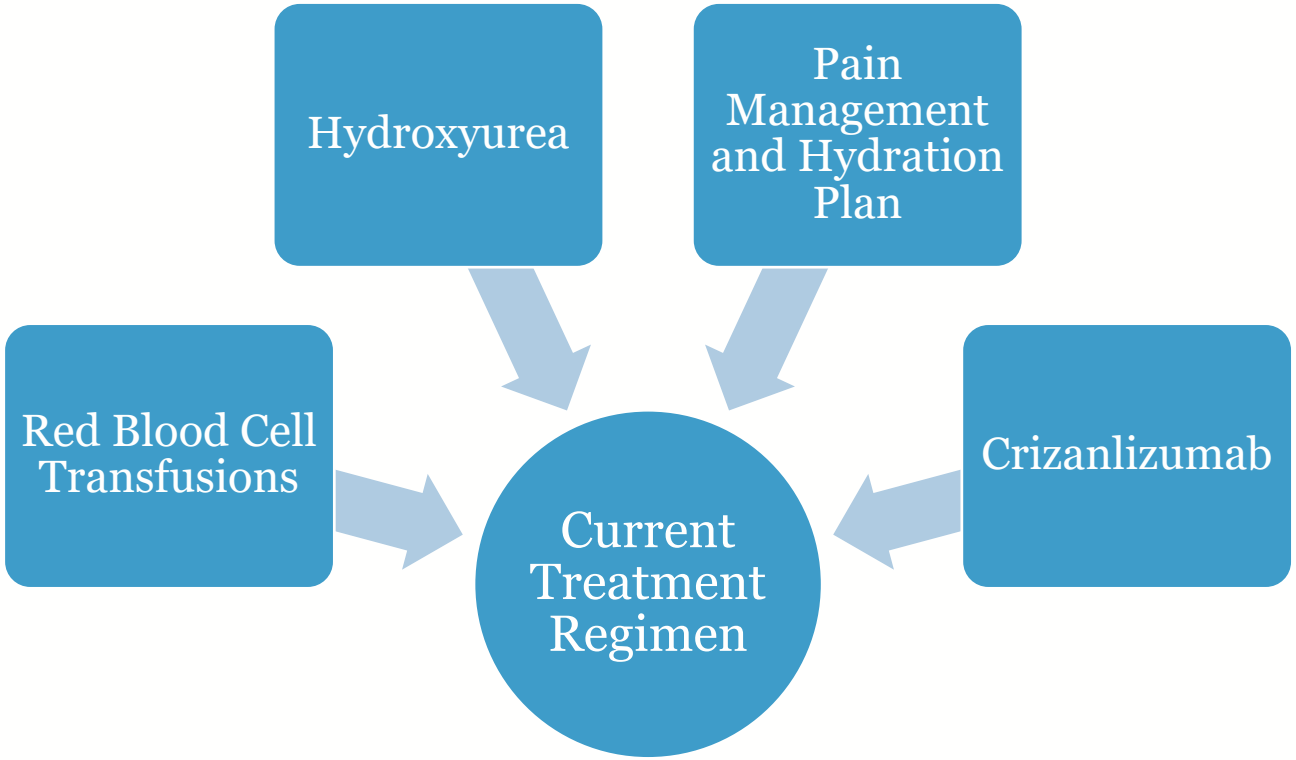

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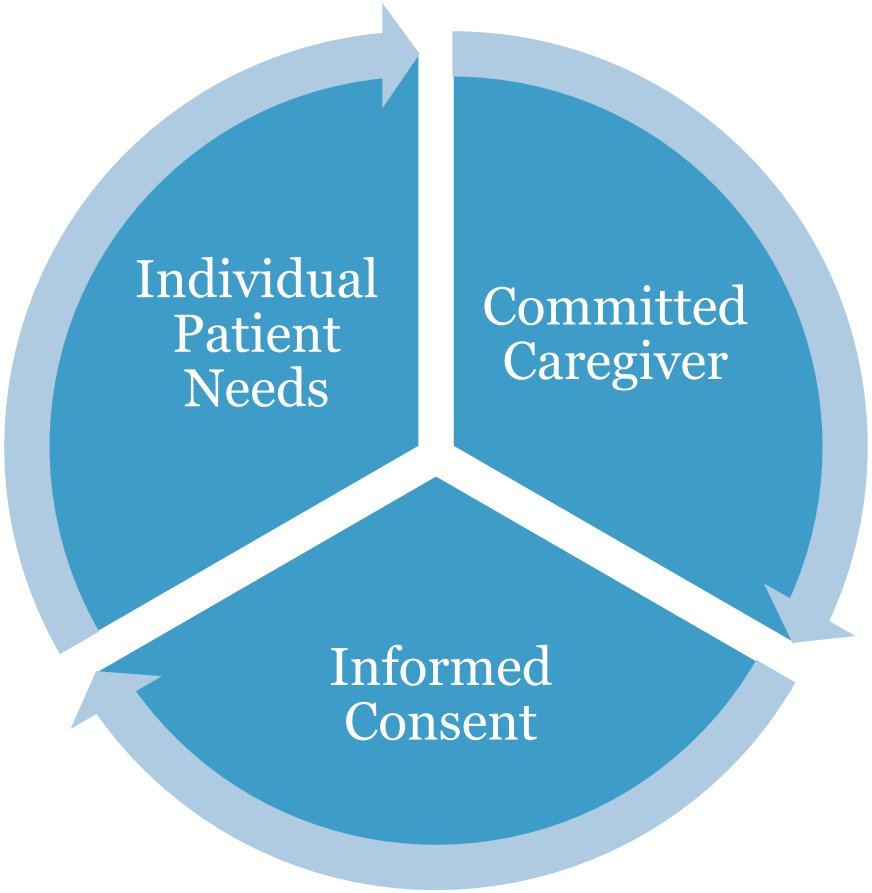

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