Improving Interprofessional Management of Sickle Cell Disease with Disease-Directed Therapies

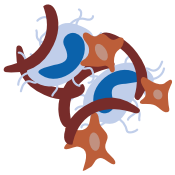
Clinical Fact Sheet Reference Guide

What are Vaso-occlusive Crises (VOCs)

- Normal red blood cells (RBCs) are doughnut shaped and flexible, rolling through the vasculature supplying oxygen and nutrients to the body

- RBCs with sickle cell hemoglobin have different properties and are more likely to stick to the cells (endothelium) on the inside of the blood vessel

- White blood cells and activated endothelial cells can also trigger adhesive interactions with sickled RBCs, other white blood cells, and platelets due to chronic vascular damage



- Blockage of small blood bessels results in vaso-occlusion, which leads to a lack of oxygen to tissues

- Recurrent episodes of vaso-occlusion can lead to severe unpredictable acute pain that may require hospitalization

Factors that may increase the likelihood of pain crises

- Cold temperatures
- Dehydration
- Infection
- Stress

Management of VOCs

- Pain-relieving medications (analgesics, opioids)
- Supplementary oxygen
- Fluids to manage dehydration
- Blood transfusion
- Hydroxyurea
  - Indicated to reduce the frequency of painful crises and to reduce the need for blood transfusions in adult patients with sickle cell anemia with recurrent moderate to severe painful crises
  - Can improve the clinical course of SCD by increasing the production of HgF, thereby reducing frequency and intensity of vaso-occlusive pain crises

Impact of Vasco-Occlusion on Organs

- Pain can affect any part of the body, but most commonly occurs in the back, chest, or extremities
- VOC is the most common cause of hospitalization related to SCD
- Ongoing vaso-occlusion and VOCs are associated with increased risk for organ damage, organ failure, and death
- Damage occurs due to vaso-occlusion (lack of oxygen), blood vessel damage, and secondary complications
- Ongoing inflammatory response, cell activation, and multicellular adhesion contribute to tissue damage
- Vaso-occlusion and VOCs are associated with decreased organ function and can result in life-threatening complications such as:
  - Acute chest syndrome (ACS; blockage of bloodflow to the lungs)
    - Symptoms: chest pain, coughing, difficulty breathing, and fever
  - Pulmonary hypertension
  - Renal failure
  - Stroke

Novel Agents for Prevention of Vaso-Occlusive Crisis and Pain Management

Agent	Mechanism of Action	Administration	Clinnical Trial(s)		Indication(s)
Crizanlizumab	P-selectin blocker humanized IgG2 kappa monoclonal antibody	Intravenous infusion over a period of 30 minutes on Week 0, Week 2, and every 4 weeks thereafter	SUSTAIN	45% reduction in the median annual rate of VOCs vs. placebo (1.63 vs. 2.98)	To reduce the frequency of vasoocclusive crises in adults and pediatric patients aged 16 years and older with sickle cell disease
L-glutamine	Amino acid	Oral, twice daily	NCT01179217	Reduction in the number of sickle cell crises vs. placebo (median 3 vs. 4)	To reduce the acute complications of sickle cell disease in adult and pediatric patients 5 years of age and older
Voxelotor	Hemoglobin S polymerization inhibitor	Oral, once daily	HOPE HOPE-KIDS 1	Significantly increased hemoglobin levels Hb increase >1 g/dL: Ages ≥12: 51% Ages 4-12: 36%	Treatment of sickle cell disease in adults and pediatric patients 4 years of age and older

Provided by: AXIS Medical Education

This activity is supported by an educational grant from Novartis Pharmaceuticals Corporation.

CDC. https://www.cdc.gov/dotw/sickle-cell-disease/. Rees et al. *Lancet* 2010;376(9757):2018-2031. Piel et al. *N Engl J Med.* 2017;376:1561-1573. Zhang et al. *Blood* 2016;127(7):801-809. Habara and Steinberg. *Exp Biol Med.* 2016;241(7):689-696. Belcher et al. *Am J Physiol Heart Circ Physiol.* 2005;288:H2715-H2725. Powars et al. *Medicine (Baltimore).*2005;84(6):363-376. Elmariah et al. *Am J Hematol.* 2014;89(5):530-535. Platt et al. *N Engl J Med.* 1994;330(23):1639-1644. Nath Grande et al. *Am J Pathol.* 2005;166(4):963-972. Tran et al. *Blood* 2017;130(22):2377-2385. Ballas et al. *Blood* 2012;120(18):3647-3656. Piel et al. *N Engl J Med.* 2017;376(16):1561-1573.
Adakveo (crizanlizumab-tmca) [prescribing information]. July 2021. East Hanover, New Jersey: Novartis Pharmaceuticals Corp. https://www.novartis.us/sites/www.novartis.us/files/adakveo.pdf. Oxbryta (voxelotor) [prescribing information]. December 2021. South San Francisco, California: Global Therapeutics, Inc. https://www.oxbryta.com/pdf/prescribing-information.pdf. FDA News Release. July 7, 2017. FDA approved L-glutamine powder for the treatment of sickle cell disease. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approved-l-glutamine-powder-treatment-sickle-cell-disease.

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