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Apheresis Collection Challenges for Patients with Hemoglobinopathy

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Case Scenario

An 18-year-old female with sickle cell disease (SCD) and a history of frequent pain crises is being treated with hydroxyurea, crizanlizumab, and voxelotor. She is a candidate for either of the two Food and Drug Administration (FDA)-approved gene therapies. Her blood type is A+ with a positive red cell alloantibody screen for anti-Fy^a and anti-D. She has a history of episodic transfusions with no history of hemolytic transfusion reactions.

Questions and Answers

What medications should be discontinued before mobilization and collection in a patient with SCD?

Medication	Lyfgenia (lovotibeglogene autotemcel)	Casgevy (exagamglogene autotemcel)
Hydroxyurea	Discontinue at least 2 months before mobilization, through mobilization, and all cycles of apheresis collection	Discontinue at least 8 weeks before start of mobilization and conditioning

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Medication	Lyfgenia (lovotibeglogene autotemcel)	Casgevy (exagamglogene autotemcel)
L-glutamine	Discontinue at least 2 months before mobilization because it is unclear how these agents would interact with the mobilization agent	No guidance
Voxelotor and crizanlizumab	Discontinue at least 2 months before mobilization because it is unclear how these agents would interact with the mobilization agent	Discontinue at least 8 weeks before start of mobilization and conditioning
Erythropoietin	Discontinue at least 2 months before mobilization	No guidance
Iron chelators	Discontinue at least 7 days before mobilization	Discontinue at least 7 days before starting myeloablative conditioning. Avoid nonmyelosuppressive iron chelators for at least 3 months. Avoid use of myelosuppressive iron chelators for at least 6 months after Casgevy infusion.
Granulocyte colony-stimulating factor (G-CSF)	Should NOT be administered before mobilization or with the mobilization agent	Should NOT be administered for CD34+ hematopoietic stem cell mobilization
Prophylactic human immunodeficiency virus (HIV) antiretroviral medications	Discontinue at least 1 month before mobilization and throughout all cycles of apheresis	No guidance

How many months of red cell exchange are required before mobilization and collection?

To prepare patients for mobilization and apheresis collection, patients need at least two cycles of red cell transfusions starting at least 60 days before mobilization and through myeloablative conditioning as well. One transfusion should be performed per month. Red cell exchange (RCE) is preferred over simple transfusions. An RCE procedure should be performed within 4 days before mobilization.

What should the target hemoglobin and hemoglobin S percentage be?

The target hemoglobin level for Lyfgenia is 8 to 10 g/dL and not to exceed 12 g/dL. For Casgevy, the target hemoglobin is ≤11g/dL. The hemoglobin S (HbS) target level should be less than 30% for both drugs.

What are some potential collection challenges or problems that may be encountered, and what are some potential solutions?

Challenge	Potential Solution
Insufficient trained personnel	Externally contracted services Part-time/per-diem apheresis instrument operators
Insufficient bed/chair capacity	Extended apheresis unit hours Apheresis unit space expansion
Difficulty in procuring donor Red Blood Cells (RBCs) for RCE because of red cell alloantibodies	Advance planning/notification of blood supplier Exchange with a higher fraction of cells remaining, and have a shorter interval between RCEs Extended phenotype matching to prevent red cell alloimmunization Matching of partial red cell antigens
Delayed HbS quantification results	Target a more conservative HbS level (eg, <20%) Communication with HbS quantification lab to prioritize samples Analyze baseline trend and determine rate of HbS rise
Delayed mobilization/collection	Consider simple transfusion if short delay