Frequently Asked Questions

Q: Is diphenhydramine a good choice for treating anaphylaxis in a patient who has an allergic reaction to inhibitor therapy?

A: No, diphenhydramine will not protect against the massive histamine release that occurs during anaphylaxis. New research presented by Weiss-Tessbach and colleagues at the American Society of Hematology 2023 Annual Meeting indicates a role for recombinant human diamine oxidase against histamine-induced shock.

Q: How do you fit efanesoctocog alfa and emicizumab into the current treatment armamentarium?

A: There is still much discussion on how to approach treatment with these new agents. At this time, efanesoctocog alfa and emicizumab are primarily being used in patients who have been previously treated with factor VIII therapy. According to Glaivy Batsuli, MD, who is a pediatric provider, patients who wish to switch or prioritize prophylaxis are active adolescents, many of whom play sports and want better protection from the risk of joint bleeds. At the same time, there are individuals who prefer using factor VIII therapy because factor levels can be measured and the level of protection is quantifiable.

Q: How do you present and discuss all the various types of treatments available, including gene therapy, with an adult patient with hemophilia A?

A: Regimens for prophylaxis are much more individualized today than they were 20 years ago, when these regimens were fairly standard. This is because we engage in shared decision-making by sitting down with patients and their families to discuss their activity levels, hobbies, goals, and aspirations, as well as all the treatment options that are available. Some patients who have heard of new products and understand the mechanisms of those agents are interested in switching to a new treatment regimen. The pros and cons of gene therapy are discussed with each patient. Many patients are

interested to hear about the research around gene therapy, although there are not many who want to immediately undergo gene therapy. These are the types of discussion we will be having as even more agents are approved.

Q: Given the liver function abnormalities observed with fitusiran therapy, how many patients underwent liver biopsy?

A: None of the patients with elevated liver enzyme levels underwent liver biopsy in the ATLAS clinical trial program. Many of the liver enzyme elevations experienced by patients were mild (ie, 1-3 times the upper limit of normal [ULN]), although there were some patients who experienced elevations of more than 3-times the ULN. Currently, it is unknown why these elevations are occurring other than fitusiran contains a conjugate directing it to the liver where it acts to reduce antithrombin production. There are also no current insights into the reason behind the observed side effects of cholecystitis and cholelithiasis. A new protocol is being put into place, which adjusts the dosing paradigm such that antithrombin levels remain higher after treatment than with previous protocols to address all safety issues, including the observation of thrombosis. These data will be released soon.

Q: In clinical trials, how long do you wait before using another "new" agent in patients who have had a severe adverse event to a previous agent?

A: There are switching studies underway for these agents to determine this. It is incumbent upon treating physicians to learn about all the properties of these agents to individualize care safely and effectively.

One of the advantages of having a wide array of treatment options is that they have different side effects. For example, an older patient with a risk of thrombosis may not be a good candidate for a rebalancing agent. A patient with that type of risk profile may be better off using one of the types of factor therapy or could be a good candidate for gene therapy.

While having a variety of agents with different mechanisms of action, modes of administration, frequencies of administration, and side-effect profiles benefits patients by allowing them to individualize therapy, it makes treatment more complicated for the physician. It is especially important for providers to understand how to switch to different products safely. The mechanism of action and half-life of the agent must be taken into account to minimize any adverse effects from using multiple agents back-to-back.