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ReachMD

www.reachmd.com

info@reachmd.com

(866) 423-7849

Considering the Promise of New and Emerging Treatments for Hemophilia: Managing Thrombotic Risks

Announcer:

Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. McDaniel:

This is CME for ReachMD. I'm Dr. Jenny McDaniel, and I'm joined today by Dr. Stephanie Ambrose. Today, we will be discussing managing thrombotic risks with rebalancing therapies. Dr. Ambrose, can you start us off?

Dr. Ambrose:

Absolutely. So rebalancing therapies are a novel therapy that we've not had access to previously. These rebalancing therapies can be used in patients with hemophilia A or hemophilia B, with or without inhibitors, offering a novel approach for patients who may have very limited options. Dr. McDaniel?

Dr. McDaniel:

Thank you. So these rebalancing therapies are really exciting for the reasons you highlighted, but they do bring some challenges. One of the challenges is the limitation on ability to test. So our traditional coagulation tests, like our PTT and PT and our factor levels are not going to reflect these rebalancing therapies. And of course, historically, we have always been able to utilize a factor level or something to help guide us with treatment. So this is a territory where we're entering treatment without having a wonderful test to guide us, so we're having to evaluate with more of a clinical response rather than laboratory values.

There are some global coagulation assays that could be potential options to think about, such as the thrombin generation assay, which may provide some insights into the global hemostasis for patients on treatments like rebalancing agents. But at this time, they are not universally available and also lack standardization and clear target ranges.

We know that rebalancing therapies reduce the natural anticoagulants in the body,

so we are pushing towards that more growth thrombotic state in an effort to achieve better hemostasis for patients with bleeding disorders. But with that could come potential risk for thrombotic events, especially in patients who may have other risk factors for thrombosis, or if we are using rebalancing agents in combination with other procoagulant therapies.

So one thing to think about with this new category of rebalancing agents is, is there a reversal strategy for the agent that could be utilized in the setting of thrombosis or a high risk for thrombosis? There are not currently any reversal strategies for marstacimab or concizumab. Fitusiran does have a reversal strategy available with antithrombin concentrate.

Dr. Ambrose. I'll let you review some of the clinical trial data that we have.

Dr. Ambrose:

Of course. So clinical trials show that rebalancing agents do reduce the annualized bleeding rate. But they don't provide a normal hemostasis profile, so patients may still experience breakthrough bleeding events, and the degree of hemostatic correction varies among individuals. So it's important to note that patients may require factor replacement, but you will need to do this in adjusted doses. Lower initial dosing with titration based on thrombin generation assays may reduce thrombotic risk while maintaining efficacy.

You need to really think through a patient's personal history when determining whether or not they would be an appropriate candidate for one of the rebalancing therapies. So assessing their thrombotic risk profile. What's their personal history? Have they had issues with blood clots previously? Do they have a strong family history of blood clots? And are there other risk factors that would increase their potential for developing blood clots that they possess? All of those are factors that must be taken into consideration when discussing whether or not a patient would be a good candidate.

When you do choose to use a rebalancing agent for patients, it's important that the lowest effective dose is used for that patient, and so it's going to be fairly individualized amongst patients in really trying to navigate this and help patients walk through the idea of this therapy, because it's very different than anything that they've had access to previously. The monitoring does become more difficult, and so patients really need to understand the risk-benefit of using these therapies.

We need to ensure that there is awareness among patients and the care team of the reduced factor dosing for patients on these therapies. Many of our patients are so used to being able to administer factor replacement whenever they have bleeding events. And while they will need to administer factor replacement even on rebalancing therapies, it's important that they understand that the dosing needs to be much less due to the prothrombotic concerns with rebalancing therapies.

As such, it's going to be very important to develop individualized emergency bleed management plans.

Well, this has been a great bite-sized discussion, so please make sure to tune in to the rest of the microlearning activities in this series for more information. Thanks for listening.

Announcer:

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