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Etranacogene Dezaparvovec for Hemophilia B: Efficacy and Safety Four Years Post-Infusion

Announcer:
You're listening to *Clinician's Roundtable* on ReachMD, and this episode is brought to you by CSL Behring. Here's your host, Dr. Brian McDonough.

Dr. McDonough:
Welcome to *Clinician's Roundtable* on ReachMD. I'm Dr. Brian McDonough, and joining me to discuss data from the phase III HOPE-B study on the treatment option etranacogene dezaparvovec for hemophilia B is Dr. Guy Young. In addition to contributing to this trial, he's also the Director of the Hemostasis and Thrombosis Program at the Children's Hospital of Los Angeles, and a Professor of Pediatrics at the Keck School of Medicine of the University of Southern California. Dr. Young, thanks for being here today.

Dr. Young:
Yes, thank you for having me.

Dr. McDonough:
Let's start off with some background, Dr. Young. Can you tell us about etranacogene dezaparvovec and how it works to treat patients with hemophilia B?

Dr. Young:
Sure. Etranacogene dezaparvovec is a gene therapy treatment. So it is essentially designed to replace or place into the body of patients with hemophilia B a functional copy of the factor IX gene. So if you have hemophilia B, you have a mutation in the factor IX gene, resulting in decreased production of factor IX, which is a critical component of the coagulation system. That results in bleeding symptoms.

So this drug is essentially a viral vector. So it's composed of a viral shell, and inside that viral shell is the factor IX gene. And this viral shell, which is called AAV—or specifically, in this case, AAV5—is designed to go into hepatocytes. Hepatocytes are the natural site of synthesis of factor IX. And so after an infusion of this medication, the viral vector goes into the hepatocytes, drops off the factor IX gene, that goes into the nucleus, and then the patient now has a functional copy of the factor IX gene that they didn't have before to produce the factor IX protein, which will then hopefully result in factor IX levels that prevent bleeding.

Dr. McDonough:
With that background in mind, let's zero in on the HOPE-B study. What was the objective here?

Dr. Young:
The HOPE-B study was designed to assess whether or not etranacogene dezaparvovec was effective at preventing bleeding. Essentially, the design of the study was such that patients would enter the study and continue on their standard of care treatment, which was a factor IX replacement therapy given intravenously once or twice a week. After at least six months of such therapy, they would then get their infusion of etranacogene dezaparvovec, and then the same data collected during this prospective observational phase would be collected after the infusion, particularly collecting data such as the rate of bleeding. How many bleeds happened? Where did they happen? How many infusions, or how much infusion of factor IX was needed? And then other secondary objectives, including quality of life and, of course, safety.

Dr. McDonough:

For those just tuning in, you're listening to *Clinician's Roundtable* on ReachMD. I'm Dr. Brian McDonough, and I'm speaking with Dr. Guy Young about recent data from the phase III HOPE-B study on etranacogene dezaparvovec.

So Dr. Young, if we move on to the findings from this trial, what can you tell us about the efficacy of etranacogene dezaparvovec four years post infusion?

Dr. Young:
Sure. Well, what we found is that the bleeding rates were substantially lower with etranacogene dezaparvovec as opposed to the best previous therapy—the standard of care factor IX replacement that the patients were on in the observational phase. So essentially, in the observational phase, the bleed rates were around 4, and after the infusion of etranacogene dezaparvovec, they were around 2 and even dropped lower to 1.5. Though it should be noted some of that was influenced by the few patients who didn't respond.

A key takeaway is that more than half the patients—in fact, close to two-thirds of the patients—after their single infusion of this medication had no bleeding events, even out to four years. And I think that's really what patients are looking for: a treatment that essentially will allow them to live their life without being concerned about bleeding.

Dr. McDonough:
And were there any adverse events we should know about?

Dr. Young:
The key adverse events in the trial were infusion-related reactions, which occurred during the infusion and were fairly mild and managed with medication or slowing the infusion rate down. These are not different than the infusion-related reactions with other infusible medications.

And then the other was some mild hepatotoxicity with elevations of the ALT and AST, and these were managed with corticosteroids. This is felt to be an immune-related response against the viral vector that is in the hepatocytes—essentially the immune system thinking that there's a viral infection of the liver when we know we actually put these viral vectors in there. That occurred in 16 percent of the patients.

Those are the two key adverse events. I think otherwise, overall, the safety was really good. There were no serious adverse events related to the medication itself.

Dr. McDonough:
As we approach the end of our program, Dr. Young, do you have any key takeaways you'd like to share with our audience?

Dr. Young:
Certainly. I think the key takeaway is that this is a commercially available medication that patients with hemophilia B—who are older than 18, because it is only for adults—have an option to receive. And I think, personally, that the data suggesting that a single infusion—and that's a key point here, that this is just given one time—can result in patients having good factor IX levels, not bleeding overall, and being very safe. I think it's an excellent treatment option that patients should consider and discuss with their physicians.

Dr. McDonough:
With those final insights in mind, I want to thank my guest, Dr. Guy Young, for joining me to share data from the phase 3 HOPE-B study on etranacogene dezaparvovec. Dr. Young, it was great having you on the program.

Dr. Young:
Thank you very much.

Announcer:
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