

Transcript Details

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The Future of ATTR-CM Care: A Look at What's Next

Announcer:

This is *Heart Matters* on ReachMD. On this episode, Dr. Sumeet Mitter will share insights on the future of transthyretin amyloid cardiomyopathy, or ATTR-CM, management. Dr. Mitter is the Director of Inova Schar Heart and Vascular Research and the Infiltrative and Restrictive Cardiomyopathy Center at Inova Health in Virginia. Let's hear from him now.

Dr. Mitter:

There are a number of trials right now that are going to be looking at removal or depletion of deposited transthyretin amyloid. These are using humanized monoclonal antibodies to try to create an immune cascade that could, through an immune reaction, remove some of the deposited TTR. And if, in preliminary data—some look at biomarkers, some look at imaging—we see some improvements, will that lead to a true reversal in the disease state? Meaning not only better imaging and better lab biomarkers, but actually better event rates, meaning improved survival, and less hospitalization—will the heart actually start looking better, and is that marrying to a reduction in clinical events? But the question after that is, is that a permanent therapy? Or how long do people have to be on a reversal agent? And would we then look into combination therapy, either a stabilizer or silencer class of medication along with a depleter if this were shown to be effective? That's actually what's really exciting to see. Can we get to reversal? But then there's still the nidus for this to keep going, so we keep someone on some type of therapy to silence or stabilize production.

There's also a permanent gene editing trial going on called Magnitude using CRISPR-Cas9 technology to permanently alter the TTR gene sequence to basically make it a non-coding portion of the hepatic DNA, so you can't make a foreign protein. The silencing class of medications is technically reversible because that goes through an RNA process. But with gene editing technology, that could potentially be irreversible. So that trial's been reactivated recently, but that's also another frontier that we're looking into within the landscape of amyloid therapies. Can we just do a one-and-done treatment? It might be a long treatment, but then patients won't have to continuously be redosed. So we're looking at antibody studies for reversal of disease and permanent gene editing.

At the end of the day, we know from all these studies that patients have the best outcomes if they're diagnosed the earliest because they have the longest window for treatment exposure and treatment benefit. We want to be able to diagnose early so people don't have a clinical cascade of unfortunate events.

Evuzamitide is a PET tracer that can actually detect the presence of an amyloid protein in various organs throughout the body much earlier than we would otherwise detect it in other forms of directed imaging or tissue biopsy, which sometimes can be of low yield depending on the tissue. And so that's really exciting because that helps us potentially diagnose earlier, target therapies, and understand also the natural history of the disease state in organs that are afflicted by transthyretin amyloid that we don't often necessarily track because the therapeutic pipeline wasn't developed beyond the heart or the nervous system. So we may start learning more about the kidneys or the lungs. That's really exciting to me.

Announcer:

That was Dr. Sumeet Mitter discussing the future of ATTR-CM care. To access this and other episodes in our series, visit *Heart Matters* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!