Transcript Details
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Current and Emerging Treatments for Transthyretin Amyloid Cardiomyopathy

Announcer:
This is *Heart Matters* on ReachMD. On this episode, we'll hear from Dr. Ahmad Masri, who's an Associate Professor of Medicine in the Division of Cardiovascular Medicine at Oregon Health and Science University. He'll be discussing the latest therapeutic advancements in transthyretin amyloid cardiomyopathy, or ATTR-CM. Here's Dr. Ahmad Masri now.

Dr. Masri:
It is incredible to think back just five or six years ago to how the landscape for TTR cardiomyopathy and polyneuropathy was. Prior to 2017, 2018, there were really no evidence-based approved therapies for these conditions, and now we're looking at slowly inching to having not only multiple medications but also multiple classes. And broadly, we classify these as stabilizers of transthyretin amyloidosis—so these are the drugs that bind to the TTR protein, raising its concentration because they prevent it from breaking down and stabilizing the disease—and then there is the second large group, which what is what we call gene silencers or gene knockdown agents. That's where you use medications to selectively decrease the translation of the availability of the transthyretin protein being secreted from that level, thereby trying to reduce the amount of protein that could be destabilized and could result in disease progression. And these are the approved therapies, and some of them are still investigational, but slowly from there, we're inching toward another class of medication, which is the fibrin depleters. None of these are approved, but they are targeting something different, which is trying to go after the tissue accumulation of the amyloid protein itself, not just the precursor.

And so when we talk about these individual medications, I think we just focus on transthyretin cardiomyopathy-approved therapies. There are three of them right now in the United States. One is tafamidis, which is a TTR stabilizer; one is acoramidis, also a TTR stabilizer; and one is vutrisiran, which is a TTR gene silencer or a knockdown agent. In terms of efficacy, all three have shown in clinical trials to improve outcomes. That includes mortality and heart failure hospitalization. There are some variations in how everything is defined, but the gist is that most of these things have shown somewhat similar results when there are no head-to-head comparisons between them.

When we look at safety profiles of these medications for the trials that were conducted, there are really no large or significant safety signals that are emerging from these. We do mention, for example, with tafamidis, that there are some drug-drug interactions that we have to be aware of. We do mention for acoramidis that there is—which is expected—a slight change in GFR that they have to be aware of, but we don't change our practice because of that. There is some slight reporting of the area but not clinically that significant that we see. And then for vutrisiran we talk about the fact that it's an injectable and some patients can have a site-based reaction for the injection itself and whatnot. But really, truly, none of these medications have a major issue with them that would make us pause and stop before using them.

So looking into the future, I think we will end up in a scenario where we have to think about a few things. One, should we continue to be using monotherapy—only a singular agent for these patients—or is there space for combination therapy? Obviously, we need evidence to go after that. So that's from the perspective of targeting the underlying protein plus combining these agents with an agent that would remove the amyloid from the organ the heart namely itself.

So this is where kind of the future is inching toward for the transthyretin amyloid-targeted therapies. Outside of that, patients are healthier, being diagnosed earlier, and living longer, so we have to also work on understanding the role of traditional heart failure therapies in transthyretin cardiomyopathy as well.

Announcer:
That was Dr. Ahmad Masri talking about the expanding therapeutic landscape for transthyretin amyloid cardiomyopathy. 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!