Transcript Details
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Redefining ATTR Treatment: Key Mechanisms and Emerging Data

Announcer:
You're listening to *Heart Matters* on ReachMD. On this episode, Dr. Ahmad Masri will discuss evolving therapeutic approaches to transthyretin amyloidosis, or ATTR. Dr. Masri is an Associate Professor of Medicine in the Division of Cardiovascular Medicine at Oregon Health and Science University. Let's hear from him now.

Dr. Masri:
We have two main mechanisms that we address transthyretin with nowadays. One is stabilizing the protein tetramer itself as it is circulating in the body, and the other one is to silence, knock down, or prevent the production of transthyretin from the liver cells.

Eplontersen is an antisense oligonucleotide, or ASO, that is used as an injection subcutaneously once a month, selectively going to the liver and turning off or turning down the production of transthyretin as a silencing or knockdown agent. And the hope is that you have an offending protein that is accumulating in the heart, for example, and by turning that production down, you are reducing the chances of this protein causing further disease and further worsening.

Eplontersen is approved already for an indication of hereditary transthyretin polyneuropathy, but we are looking forward to a trial called CARDIO-TTRansform. This trial is the largest in transthyretin amyloidosis history, with 1,500 or so patients who were randomized on top of the background therapy—usually tafamidis where and when it's available. That's going to give us primary data on the safety and efficacy of eplontersen in transthyretin cardiomyopathy, but it also will provide us with what we hope is sufficiently powered groups to look into other things like variant transthyretin amyloidosis, women, and patients who were treated with combination therapy of tafamidis plus eplontersen versus tafamidis versus placebo.

So, for coramitug, it's a transthyretin depleter. This is another novel mechanism of action through which you are using a monoclonal antibody that circulates in the body as you give it as an intravenous infusion, and it identifies deposits of amyloid fibrils in the tissue—in this scenario, we hope it's heart tissue—and activates the person's immune system to help in the removal of transthyretin amyloid fibrils.

And so, coramitug just reported its placebo-controlled Phase 2 data at the American Heart Association meeting, showing that you do have a defect on NT-proBNP in this scenario where there is reduction in NT-proBNP, while usually, you think of TTR treatments as stabilizing for NT-proBNP rather than cell reduction. It just delivered on what we would expect around Phase 2 trial—the drug appears to be safe. Patients tolerated it well. The trial was able to enroll and be conducted, and natural progression now is to go to a Phase 3 trial where it can hopefully show that the drug can lead to reduction in heart failure, improvement in symptoms, and improvement in mortality.

Announcer:
That was Dr. Ahmad Masri discussing current and emerging treatment approaches for transthyretin amyloidosis, or ATTR. 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!