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Shh…Gene-Silencing Therapies for ATTRv-PN

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

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Dr. Waddington-Cruz:
So this is CME on ReachMD, and I'm Dr. Márcia Waddington-Cruz. Here with me today is Dr. Sami Khella.

So, Sami, can you tell us about the safety and efficacy data of currently available disease-modifying treatments for ATTRv polyneuropathy?

Dr. Khella:
Thank you, Márcia. So the benefits of treatment are now undisputable, or indisputable. These therapies that have been FDA-approved have been approved for both a cardiomyopathy as well as a polyneuropathy in the United States. And to take a couple of points about the cardiomyopathy treatments, tafamidis is the approved drug for cardiomyopathy, and this is a TTR stabilizer. These stabilize the TTR tetramer and prevent it from disaggregating and depositing as a toxic protein in the tissues. It is effective and especially effective when it's used early in the disease.

Patisiran, inotersen, vutrisiran, and eplontersen are the drugs that have been FDA-approved as silencers of TTR. These reduce the amount of TTR in the bloodstream and reduce its toxic side effects in causing a peripheral neuropathy. Patisiran is given as an infusion every 3 weeks. Inotersen was given as a subcutaneous injection but is now being phased out in favor of eplontersen, which is going to be an infusion that's once a month. Vutrisiran is given every 3 months.

So the 3 drugs that will be available to patients are patisiran, vutrisiran, and eplontersen. These work well and have had no serious side effects to date. Of course, the effectiveness of these drugs cannot be compared head-to-head because there are no clinical trials that have compared them head-to-head. But we do know that these drugs work well in patients with stage 1 and stage 2 polyneuropathy. So they are effective for preventing the polyneuropathy from getting worse and perhaps even improving the neuropathy to some extent if they have started early.

There are depleters that are in clinical trials at this time, and these depleting agents are not yet FDA-approved, but they are on the horizon being tested to see if we can diminish the amount of toxic protein that's in the tissues causing the symptoms of neuropathy or cardiomyopathy.

Dr. Waddington-Cruz:
So as Sami said, it's a very, very nice moment we're living because we have choice to treat the patients. We are now getting access to the second generation of siRNAs [small interfering ribonucleic acid]. Patients are getting stable, both for stage 1 and stage 2 polyneuropathy. And the side effects are much more tolerable. We don't have to worry about flu-like symptoms or about stopping the drug due to platelets or to renal function. The patients are really living their lives; they are stable or improving. But it's like this, we are

very lucky to be able to witness this moment, have choice, have individual treatment. And as Sami said, maybe in the near future, combined therapies to achieve the best treatment for the patient.

Announcer:
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