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### Next-Generation Therapies for Long-Term Prophylactic Treatment of HAE

Announcer:

Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum. Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Cohn:

This is CME on ReachMD. I'm Dr. Danny Cohn, and in this brief lecture I'll review the emerging therapies for long-term prophylactic treatment of hereditary angioedema. As I also recently discussed in episode number 5 with my colleague Thomas Buttgereit, the current treatment options still face some challenges. Some patients may require additional treatments, and there's an unmet need, especially in those patients who lack complete control of their angioedema. And as you may recall, the current treatment guidelines have as an ultimate treatment goal, normalization of patient's life and total control of the disease.

In hereditary angioedema, we know the exact pathophysiology, so we also know the components of the plasma kallikrein-kinin system that can be targeted for novel treatments. There were recently two phase 3 clinical trials that have been successfully completed. The first one is the trial with garadacimab. Garadacimab is a first-in-line monoclonal antibody directed against factor 12A, and in this trial we observed an 87% reduction in angioedema attacks in the treated patients as compared to the patients they were allocated to placebo. Following a loading dose, patients received a single dose every month.

Another recent phase 3 clinical trial that had been completed was the OASIS-HE trial in which donidalorsen was assessed, both the safety and efficacy. Donidalorsen is an antisense oligonucleotide directed against plus messenger-RNA which encodes for plasma prekallikrein, and this decreases the plasma concentrations of plasma prekallikrein. And in this trial, patients who were allocated to a monthly dose of 80 mg of donidalorsen had an average reduction in angioedema attacks of 81% against patients who were allocated to placebo.

And lastly, there's also navenibart, which is a monoclonal antibody directed against plasma kallikrein. And also, this antibody may, because of its very long half-life, be administered as infrequent as once every 6 months. But the phase 3 trial which is currently going on will definitely provide more insight into this question.

But there is more in the pipeline. Several components are now being assessed that require even less frequent administration, including gene editing therapy, which is just a single dose and a small interfering RNA, which is administered probably once every 3 months or maybe once every 6 months.

Even though the current treatment options seem highly effective, some patients still face uncontrolled disease, and other patients face burden with the administration, and therefore, the novel treatment options that are administered less frequently, which also seem highly effective, may therefore help these patients also achieving total control of the disease and normalization of their lives.

Thank you for joining me today and I hope this information will be helpful in your practice.

Announcer:

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