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Released: 08/11/2025
Valid until: 08/11/2026
Time needed to complete: 1h 00m

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Emerging Therapies for Acute HAE: New Target, New Therapies

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Hello, everyone. This is CME on ReachMD, and I'm Dr. Anna Valerieva. For today, I'm going to be speaking in this brief lecture on emerging therapies for treatment of acute HAE. We're going to be reviewing new targets and new therapies under development.

So we know very well that HAE is an unpredictable disease. It has a great impact on the quality of life of patients, and it can be life-threatening when there is angioedema affecting the airways. Also, the suffering comes from abdominal HAE attacks, and there is specific burden with all angioedema manifestations per se.

Currently, we have traditional therapies, being injectable therapies like C1 inhibitors and bradykinin receptor antagonists, and a kallikrein-kinin inhibitor, which is subcutaneous. But they have certain limitations, being injectable therapies. Thus, they can cause delayed application and a variable response towards the delayed administration of the therapy.

So these unmet needs are pushing medicine to delivering faster-acting, more convenient medications for treatment of acute HAE, while potentially improving quality of life of patients and reducing the burden of the treatment of HAE drugs.

So treatment of acute HAE is looking into grabbing this window of opportunity once having an acute angioedema manifestation. So today, I'm going to be reviewing those two key investigational therapies with a brief overview. We're going to be looking into sebetralstat, being an oral kallikrein-kinin inhibitor already published its phase 3 data and awaiting for authorities' approval. And we're going to be reviewing deucrictibant, an oral B2 receptor antagonist currently in an ongoing phase 3 trial.

So the mechanism of action of sebetralstat is already mentioned as being an orally available, upstream regulator of the kallikrein-kinin system, selectively inhibiting plasma kallikrein. And we know that the current trials have demonstrated that more than 90% inhibition of the plasma kallikrein has been achieved as little as 15 minutes after administration, and it has already published its phase 2 and phase 3 data quality journals, suggesting for around 1.6 hours improvement of symptom relief, so beginning of symptom relief. And this was compared to 9 hours compared to placebo. The safety was also tolerable, so it was demonstrated with no safety signals.

So the latest announced data was from the KONFIDENT-S real-world study, which is currently ongoing. And it allows treatment of all angioedema attacks without qualification and regardless of severity. We see here, for the first time, something that's very interesting. We see that patients are treating acute angioedema as early as recognized. You can see, overall median time to treatment was reported 10

minutes, and abdominal attacks within 20 minutes, and laryngeal attacks in about 11.5 minutes. There were no safety signals from this current report of more than 1,700 attacks that were reported as of the date of September 2024.

They also announced data on the patients who were treated with sebetralstat, on top of ongoing long-term prophylaxis. This is a good discussion whether we can give a kallikrein inhibitor on top of other kallikrein inhibitors. And as you can see, the median time to beginning of symptom relief was as the one reported in the other trials, or even a little bit better. You can see, 1.3 hours after treatment of the attack. Same was also demonstrated for berotralstat, being another oral kallikrein inhibitor for longer-term prophylaxis.

A big question always remains, whether we can treat laryngeal attacks with an oral agent. And, as you can see here, the data from this KONFIDENT-S trial is supporting this approach with having improvement of laryngeal attacks. As you can see in other attacks, in 1.3 hours median time to beginning of symptom relief. And there were no reports of difficulty swallowing.

Moving forward to the deucrictibant. Deucrictibant is an orally available immediate release capsule in current investigation for acute treatment of HAE. But it has also another program for long-term prophylaxis of HAE. In this immediate release capsule, you can see that the studies have demonstrated therapeutic exposure within 15 to 30 minutes, supporting it being a good possible treatment for acute HAE attacks.

I'm going to be reviewing data for the RAPIDe-1 and RAPIDe-2 part A; the double-blind phased open-label extension. So this is the phase 2 data. So in this current phase 2 data, we see no safety signals. The agent is generally well-tolerated, and the efficacy major milestones are very promising. As you can see, onset of symptom relief within 1.1 hours, substantial symptom relief within 2.7 hours, complete attack resolution in 11.5 hours, which is quite, quite very, very promising data.

Complete attack resolution, as you can see, also was demonstrated with one dose of deucrictibant in 90.2% of the attacks that have been treated. And if we are going to look into upper airway angioedema, here the data comes from less nber of attacks. Only 7 attacks were treated for acute angioedema affecting the airways. But as you can see from those attacks nearly 86% of them, they have been improved with a single dose deucrictibant. And the same percent of nearly 86% did not require any rescue medication within 48 hours after this treatment.

So with this, I'm going to be speaking some final words about the influence on current treatment possibilities with these novel agents that potentially, will improve easier administration for acute HAE. Thus, earlier intervention can lead to optimized management and guidelines adherence, and of course, potentially improving quality of life. At least enhance patient adherence and satisfaction can lead to change in the current paradigm of treatment of acute HAE. And as a lot of us like to say, less is more. Like, here, we have less attack as being untreated or forgone, less time impaired due to HAE, and potentially, less limitations for our patients due to their disease.

And with this, I'm wishing you a great day. Thank you.

Announcer:

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