Early and Sustained Effects of Deucrictibant Immediate-Release Capsule for On-Demand Treatment of Hereditary Angioedema Attacks

John Anderson[1], William R. Lumry[2], H. Henry Li[3], Raffi Tachdjian[4], Daniel F. Soteres[5], Timothy J. Craig[6,7], Joshua S. Jacobs[8], Michael E. Manning[9], Peng Lu[10], Marc A. Riedl[11]

[1]AllerVie Health, Birmingham, AL, USA; [2]AARA Research Center, Dallas, TX, USA; [3]Institute for Asthma and Allergy, Chevy Chase, MD, USA; [4]University of California at Los Angeles, Los Angeles, CA, USA; [5]Asthma & Allergy Associates and Research Center, P.C., Colorado Springs, CO, USA, University of Colorado Health Sciences Center, Aurora, CO, USA; [6]Penn State University, Hershey, PA, USA; [7]Vinmec-VinUni Institute of Immunology, Vinmec Hospital, Times City, Vietnam, and Vin University, Hanoi, Vietnam; [8]Allergy and Asthma Clinical Research, Walnut Creek, CA, USA; [9]Allergy, Asthma and Immunology Associates, Ltd., Scottsdale, AZ, USA; [10]Pharvaris Inc., Lexington, MA, USA; [11]University of California San Diego, La Jolla, CA, USA.

Key takeaways

The Phase 3 RAPIDe-3 trial for the treatment of attacks in multiple types of hereditary angioedema (HAE) demonstrated that attacks treated with the bradykinin B2 receptor antagonist, deucrictibant immediate-release (IR) capsule, achieved rapid end of progression (EoP) of attack manifestations, sustained symptom relief, and complete symptom resolution.

17.47 minutes
Median time to EoP of HAE attack manifestations in participants taking deucrictibant IR

>96%
of deucrictibant-treated HAE attacks that met the predefined endpoints achieved sustained responses[a]

>80%
of deucrictibant-treated HAE attacks that met the predefined endpoints with a sustained response, achieved it with a single capsule[b]

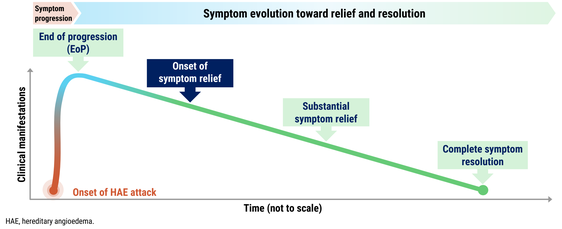
[a]Calculated based on the total number of attacks that achieved the pre-specified endpoint; [b]Calculated based on the total number of attacks that achieved the pre-specified endpoint with a sustained response.

This presentation includes data for an investigational product not yet approved by regulatory authorities.

Background

- **Hereditary angioedema (HAE):** a bradykinin-mediated condition with painful swelling attacks affecting multiple locations in the body.[1]
- **Unmet need:** an unmet need remains for additional orally administered treatments combining ease of administration with rapid and sustained effects.[2-4]
- **End of progression (EoP):** defined as the earliest post-treatment timepoint after which attack manifestations stop worsening further, which marks the earliest evidence of treatment effects.[2]
  - It can serve as a clinically meaningful indicator of attacks starting to evolve toward relief and resolution.[2]
  - Achieving EoP can also offer psychological reassurance by reducing the uncertainty associated with HAE attack escalation.
- **The AURORA project:** a consensus study developed a set of core outcomes recommended for inclusion in clinical trials of on-demand treatments for HAE attacks.[2]
  - **Early treatment response:** captured by time to EoP.[2]
  - **Sustained response:** no symptoms worsening after they start improving; sustained relief after initial improvement reduces the uncertainty and anticipatory anxiety associated with future attacks, enabling patients to return more confidently to normal life.[2]
- **Oral deucrictibant:** a selective bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of bradykinin-mediated angioedema attacks.[5-12]

Figure 1. Schematic representation of the evolution of an HAE attack



HAE, hereditary angioedema.

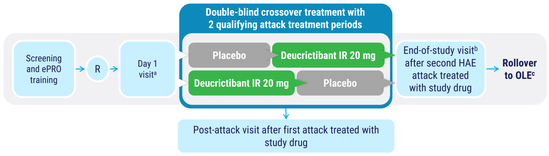
Objective

- To further evaluate the rapidity and durability of treatment response with orally administered deucrictibant immediate-release (IR) for on-demand treatment of HAE attacks in RAPIDe-3

Methods

- **RAPIDe-3 (NCT06343779)*:** a global, Phase 3, randomized, double-blind, placebo-controlled, crossover trial of the efficacy, safety, and tolerability of oral deucrictibant IR for on-demand treatment of HAE attacks.[7]
- **Participants:** adolescents (aged ≥12 to <18 years) and adults (aged ≥18 to ≤75 years) with HAE-C1INH type 1 or type 2, or HAE with normal C1 inhibitor (HAE-nC1INH). Participants on long-term HAE prophylaxis were also enrolled.
- **Study drugs:** participants self-administered deucrictibant IR capsule 20 mg or placebo to treat two qualifying attacks in a crossover design. Qualifying attacks were defined as either a non-laryngeal attack with at least one symptom item score of ≥20 on the Angioedema syMptom Rating scAle (AMRA) assessment, or a non-severe laryngeal attack without breathing difficulties or stridor.
- **Analysis set:** primary efficacy analysis included all randomized participants who had two attacks treated with study drug in accordance with the crossover design.

Figure 2. RAPIDe-3 trial design



ePRO, electronic patient-reported outcome; HAE, hereditary angioedema; IR, immediate-release; OLE, open-label extension; R, randomization. [a]Adolescent participants received a non-attack dose for pharmacokinetic sampling at day 1 visit prior to randomization. [b]Data from end-of-study visit could be used to qualify the participant for an OLE study with deucrictibant. [c]Rollover to the OLE was optional.

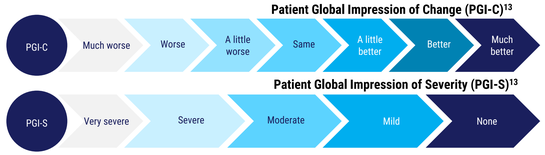
Table 1. Selected efficacy[a] endpoints

Endpoint	Instrument	Definition
Primary endpoint		
Time to onset of symptom relief	PGI-C	Time to a PGI-C rating of at least "a little better" for 2 consecutive timepoints within 12 hours post-treatment
Secondary endpoints		
Time to end of progression in attack symptoms	PGI-C	Time to the earliest post-treatment timepoint after which all subsequent PGI-C ratings are stable or improved within 12 hours
Time to substantial symptom relief	PGI-C	Time to a PGI-C rating of at least "better" for 2 consecutive timepoints within 12 hours post-treatment
Reduction in attack severity	PGI-S	Time to ≥1-level reduction in PGI-S score from pre-treatment for 2 consecutive timepoints within 12 hours post-treatment
Time to complete symptom resolution	PGI-S	Time to PGI-S rating of "none" within 48 hours post-treatment

PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]The primary and 4 of 11 secondary endpoints are not listed in the same order as in the hierarchical testing procedure.

- **Study outcomes:** time to onset of sustained symptom relief, time to sustained substantial symptom relief, sustained reduction in attack severity, and sustained complete symptom resolution, where a sustained response was defined as achieving and maintaining the efficacy endpoint across all remaining timepoints within the assessment duration.

Figure 3. Scales used to assess study endpoints



Results

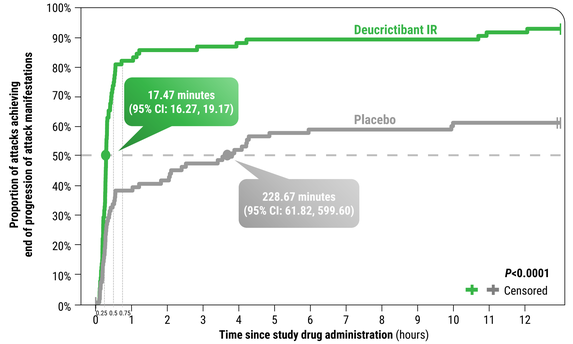
- The primary efficacy analysis set included 88 participants who had one deucrictibant-treated attack and one placebo-treated attack, for a total of 176 attacks.

Table 2. Participant baseline demographics and disease characteristics

Participant characteristics	Primary efficacy analysis group (N=88[b])
Age in years, mean (SD)	38.7 (13.6)
≥12 to <18, n (%)	5 (5.7)
≥18 to <65, n (%)	80 (90.9)
≥65, n (%)	3 (3.4)
Sex: Female, n (%)	47 (53.4)
BMI, mean (SD)	26.2 (5.6)
Race, n (%)	
White	60 (68.2)
Asian	16 (18.2)
Black or African American	4 (4.5)
American Indian or Alaska Native	1 (1.1)
Other	3 (3.4)
Not reported	4 (4.5)
Region, n (%)[a]	
North America	19 (21.6)
Europe	38 (43.2)
Rest of world	31 (35.2)
Years since HAE diagnosis, mean (SD)	17.3 (12.24)
Number of attacks within 3 months before screening, mean (SD)	5.0[b] (3.75)
HAE type, n (%)	
HAE-C1INH type 1	79 (89.8)
HAE-C1INH type 2	8 (9.1)
Unspecified HAE-C1INH type 1 or 2[c]	1 (1.1)
Current LTP use, n (%)[d]	18 (20.5)

BMI, body-mass index; HAE, hereditary angioedema; HAE-C1INH type 1, hereditary angioedema type 1; HAE-C1INH type 2, hereditary angioedema type 2; SD, standard deviation; LTP, long-term prophylaxis. [a]Geographic region of North America included Canada, Puerto Rico, United States of America; Europe included Austria, Bulgaria, Czech Republic, France, Germany, Hungary, Italy, Netherlands, Poland, Spain, Sweden, United Kingdom; Rest of world included Argentina, Australia, Brazil, Hong Kong, Japan, Saudi Arabia, South Africa, South Korea, Turkey. [b]N=86. [c]Not specified HAE type 1 or 2 and not normal C1 by participant at baseline. [d]LTP medication included lanadelumab (7 [38.9%]), berotralstat (5 [27.8%]), complement C1 esterase inhibitor (4 [22.2%]), and other (danazol, 2 [11.1%]). Adapted from "Oral deucrictibant for on-demand treatment of hereditary angioedema attacks: a phase 3, multicentre, randomised, double-blind, placebo-controlled crossover trial" by Marc A Riedl, Philip H Li, Adil Adatia, et al., 2026, *The Lancet*, published online October 8, 2026, doi: 10.1016/S0140-6736(26)01296-1, licensed under CC BY 4.0.

Figure 4. EoP of HAE attack manifestations was achieved faster with deucrictibant IR than with placebo

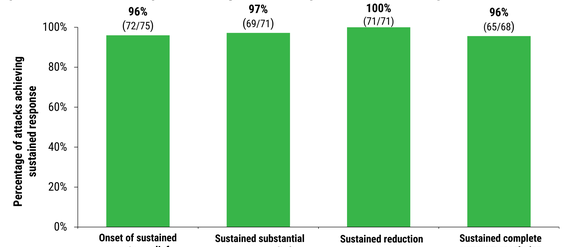


CI, confidence interval; EoP, end of progression; HAE, hereditary angioedema; IR, immediate-release; PGI-C, Patient Global Impression of Change. [a]If the event of interest was not achieved within the pre-specified timeframe, the attack was right censored at the last observation before the upper end of the data entry window. For attacks with rescue medication use, they were treated as right censored at the upper end of the data entry window. [b]Time to EoP of attack manifestations was the earliest post-treatment timepoint after which all subsequent PGI-C ratings were stable or improved. Adapted from "Oral deucrictibant for on-demand treatment of hereditary angioedema attacks: a phase 3, multicentre, randomised, double-blind, placebo-controlled crossover trial" by Marc A Riedl, Philip H Li, Adil Adatia, et al., 2026, *The Lancet*, published online October 8, 2026, doi: 10.1016/S0140-6736(26)01296-1, licensed under CC BY 4.0.

Results

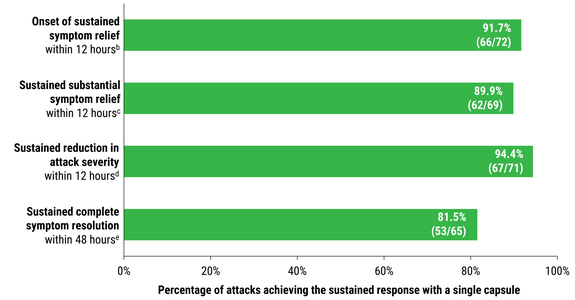
- Seventy-five of the 77 (97.4%) deucrictibant-treated attacks that achieved EoP within 12 hours were treated with a single capsule.

Figure 5. More than 95% of deucrictibant-treated attacks maintained achievement of the predefined clinical endpoints throughout the respective assessment periods[a]



PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity [a]Percentage was calculated based on the total number of attacks that met the predefined endpoints. [b]PGI-C rating of at least "a little better" sustained at each timepoint through 12 hours post-treatment. [c]PGI-C rating of at least "better" sustained at each timepoint through 12 hours post-treatment. [d]A ≥1-level reduction in PGI-S from pre-treatment sustained at each timepoint through 12 hours post-treatment. [e]A PGI-S rating of "none" sustained at each timepoint through 48 hours post-treatment.

Figure 6. Most deucrictibant-treated HAE attacks that met the predefined endpoints with a sustained response achieved it with a single capsule[a]



HAE, hereditary angioedema; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]Percentage was calculated based on the total number of attacks that met the predefined endpoints with a sustained response. [b]PGI-C rating of at least "a little better" sustained at each timepoint through 12 hours post-treatment. [c]PGI-C rating of at least "better" sustained at each timepoint through 12 hours post-treatment. [d]A ≥1-level reduction in PGI-S from pre-treatment sustained at each timepoint through 12 hours post-treatment. [e]A PGI-S rating of "none" sustained at each timepoint through 48 hours post-treatment.

References

1. Busse PJ, et al. *N Engl J Med*. 2020;382:1136-48. **2.** Petersen RS, et al. *J Allergy Clin Immunol Pract*. 2024;12(6):1614-21. **3.** Betschel SD, et al. *Allergy Asthma Clin Immunol*. 2025;21:25. **4.** Valerieva A, et al. *Clin Transl Allergy*. 2024;14:e12391. **5.** Maurer M, et al. *Lancet Haematol*. 2026;13(4):e200-14. **6.** RAPIDe-2. https://clinicaltrials.gov/study/NCT05396105. Accessed September 28, 2026. **7.** Riedl MA, et al. *Lancet*. 2026. doi: 10.1016/S0140-6736(26)01296-1. **8.** Aygören-Pürsün E, et al. *Lancet Haematol*. 2026;13(4):e215-26. **9.** CHAPTER-3. https://clinicaltrials.gov/study/ NCT06669754. Accessed September 28, 2026. **10.** CHAPTER-4. https://clinicaltrials.gov/study/NCT06679881. Accessed September 28, 2026. **11.** CREAATE. https://clinicaltrials.gov/study/NCT07266805. Accessed September 28, 2026. **12.** Covella B, et al. *Future Pharmacol*. 2024;4(1):41-53. **13.** Cohn DM, et al. *Clin Transl Allergy*. 2023;13(9):e12288.

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