

Oral Deucricitbant for On-Demand Treatment of Hereditary Angioedema Attacks: End of Progression Results from RAPiDe-3

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Key takeaways

The Phase 3 RAPiDe-3 trial for treatment of attacks in multiple types of hereditary angioedema (HAE) demonstrated that attacks treated with the bradykinin B2 receptor antagonist deucricitbant immediate-release (IR) capsule, were shown to achieve End of Progression™ (EoP) of attack manifestations faster than those treated with placebo.

EoP of attack manifestations

was measured in the RAPiDe-3 trial for the first time as a pre-specified endpoint in an HAE on-demand trial

17.47 minutes

Median time to EoP of attack manifestations in participants taking deucricitbant IR

>90%

of participants taking deucricitbant were shown to achieve EoP of attack manifestations in 12 hours

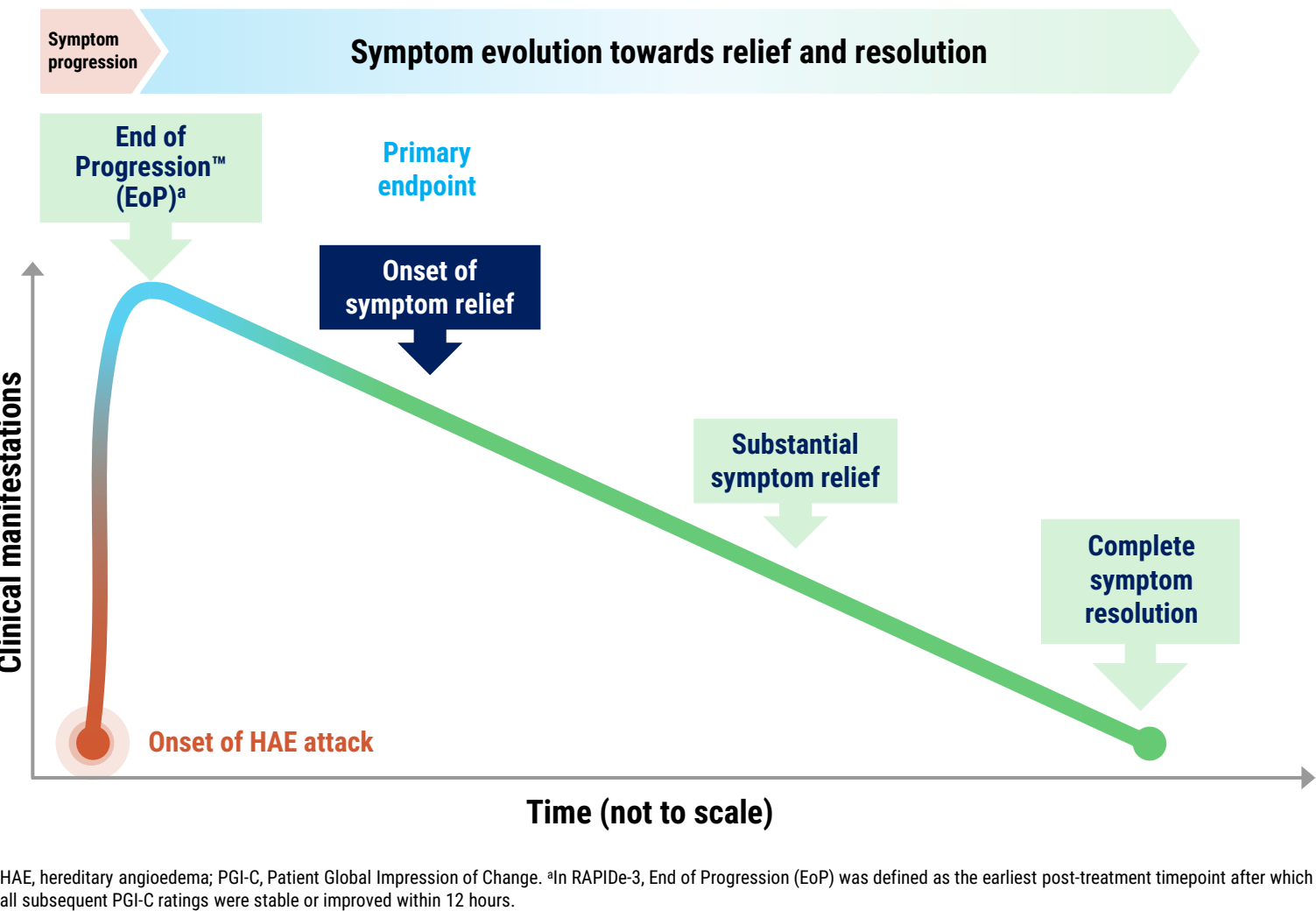
For complete information on the efficacy and safety of deucricitbant IR in the RAPiDe-3 trial, please see poster by Hide et al.

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

Background

- Hereditary angioedema (HAE):** a condition characterized by excess bradykinin, which activates bradykinin B2 receptors, causing increased fluid migration from the blood vessels to the surrounding tissues. HAE causes recurrent and unpredictable episodes of painful angioedema attacks affecting multiple locations in the body with varying degrees of severity.¹
- Unmet need:** an unmet need remains for additional orally administered treatments combining ease of administration, rapid and sustained effects, and a well-tolerated safety profile.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
 - EoP may serve as a clinically meaningful indicator of attacks starting to evolve to relief and resolution.²
 - Achieving EoP can also offer psychological reassurance by reducing the uncertainty associated with HAE attack escalation.
- Time to EoP as an outcome to measure treatment efficacy:** was recommended for inclusion by the Acute Treatment Outcomes in Hereditary Angioedema (AURORA) consensus project.
 - The AURORA project brought together patients, clinicians, researchers, industry representatives, and regulatory stakeholders to develop a set of core outcomes recommended for inclusion in clinical trials of on-demand treatments for HAE attacks²:
 - 95% of participants agreed that time to EoP should be included as one of the five core outcomes, as it represented the earliest sign of treatment effects.²
- Oral deucricitbant:** a selective bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of bradykinin-mediated angioedema attacks.⁵⁻¹²

Figure 1. Evolution of an HAE attack



Objective

To evaluate the time to EoP of attack manifestations as a pre-specified outcome aimed to document initial or earliest clinical evidence of acute attack manifestations ceasing worsening and starting to evolve towards relief and resolution following on-demand treatment with deucricitbant IR vs placebo in adolescents and adults with HAE.

Methods

- RAPiDe-3 (NCT06343779)*:** a global, Phase 3, randomized, double-blind, placebo-controlled, crossover trial.
- Participants:** adolescents (aged ≥12 to <18 years) and adults (aged ≥18 to ≤75 years) with hereditary angioedema type 1 or 2 (HAE-C1INH), or HAE with normal C1 inhibitor (HAE-nC1INH). Participants on long-term HAE prophylaxis were also enrolled.
- Study drugs:** participants self-administered deucricitbant 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

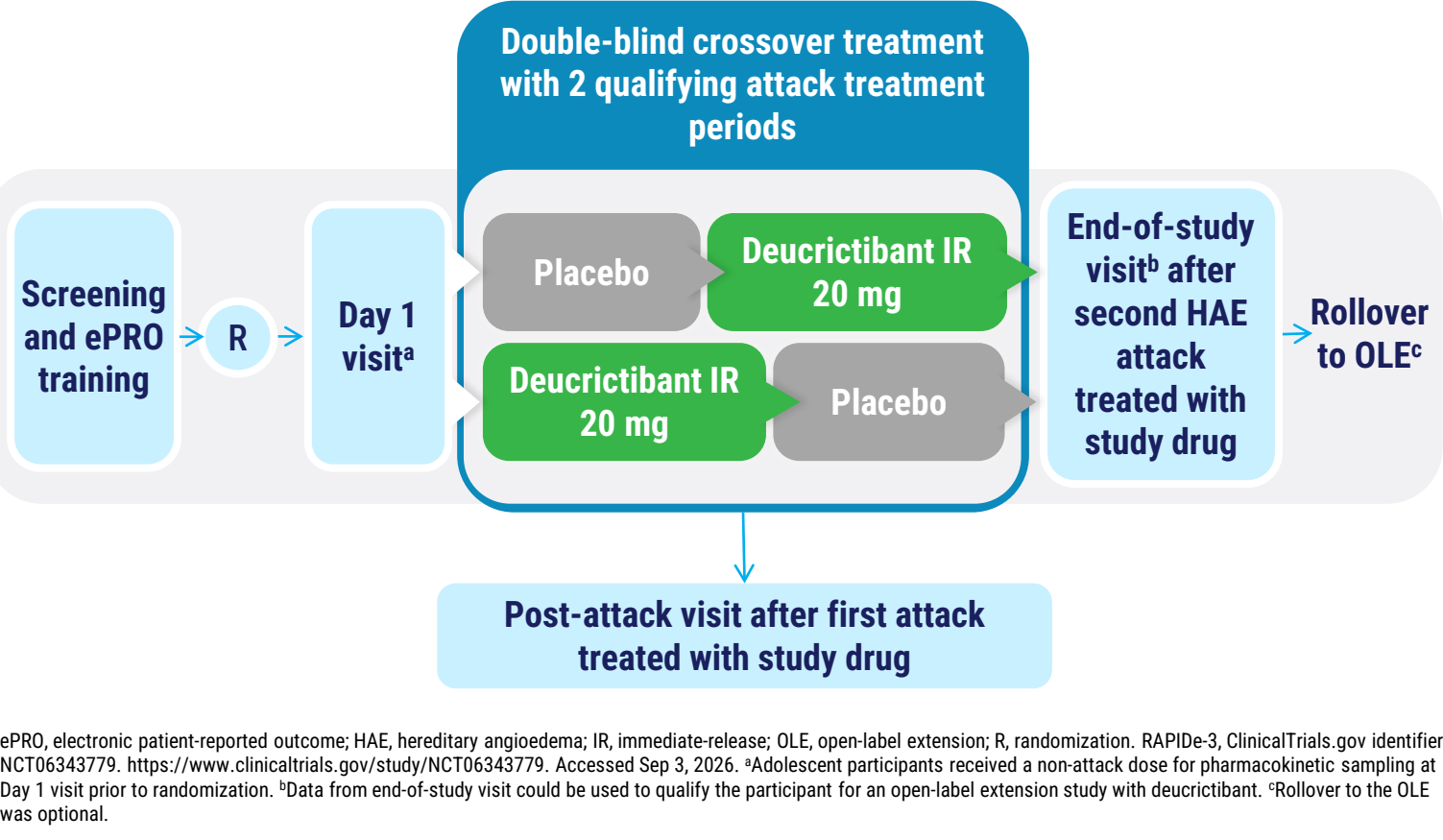


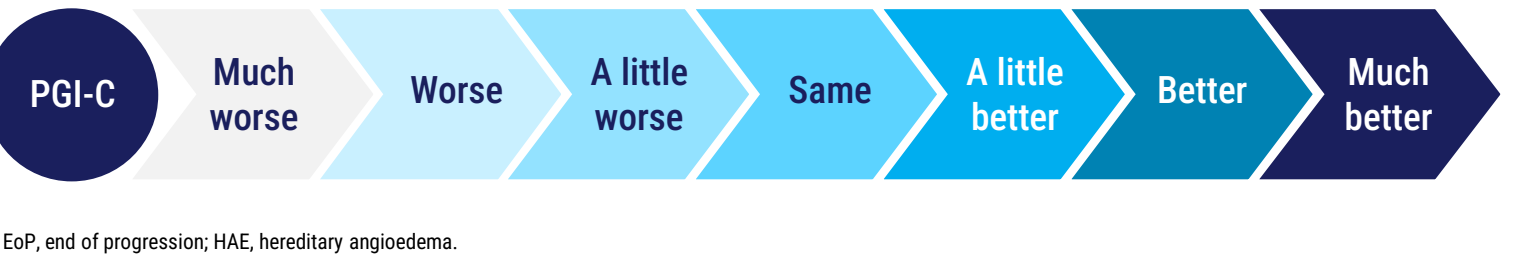
Table 1. Assessment of time to EoP of HAE attack manifestations

Parameter	Details
Time to EoP of attack manifestations	The time to the earliest post-treatment timepoint after which all subsequent Patient Global Impression of Change (PGI-C) scale ratings were stable or improved within 12 hours
Instrument	PGI-C
Type of analysis	Pre-specified secondary endpoint (5th in the hierarchical testing order) ⁷
Window for endpoint assessment	Baseline to 12 (+1) hours

EoP, end of progression; HAE, hereditary angioedema.

Figure 3. Scale used to assess time to EoP of HAE attack manifestations

Patient Global Impression of Change (PGI-C)¹³: a tool that uses a seven-point Likert response scale to assess the change in HAE attack manifestations since starting study treatment compared with pre-treatment.



Results

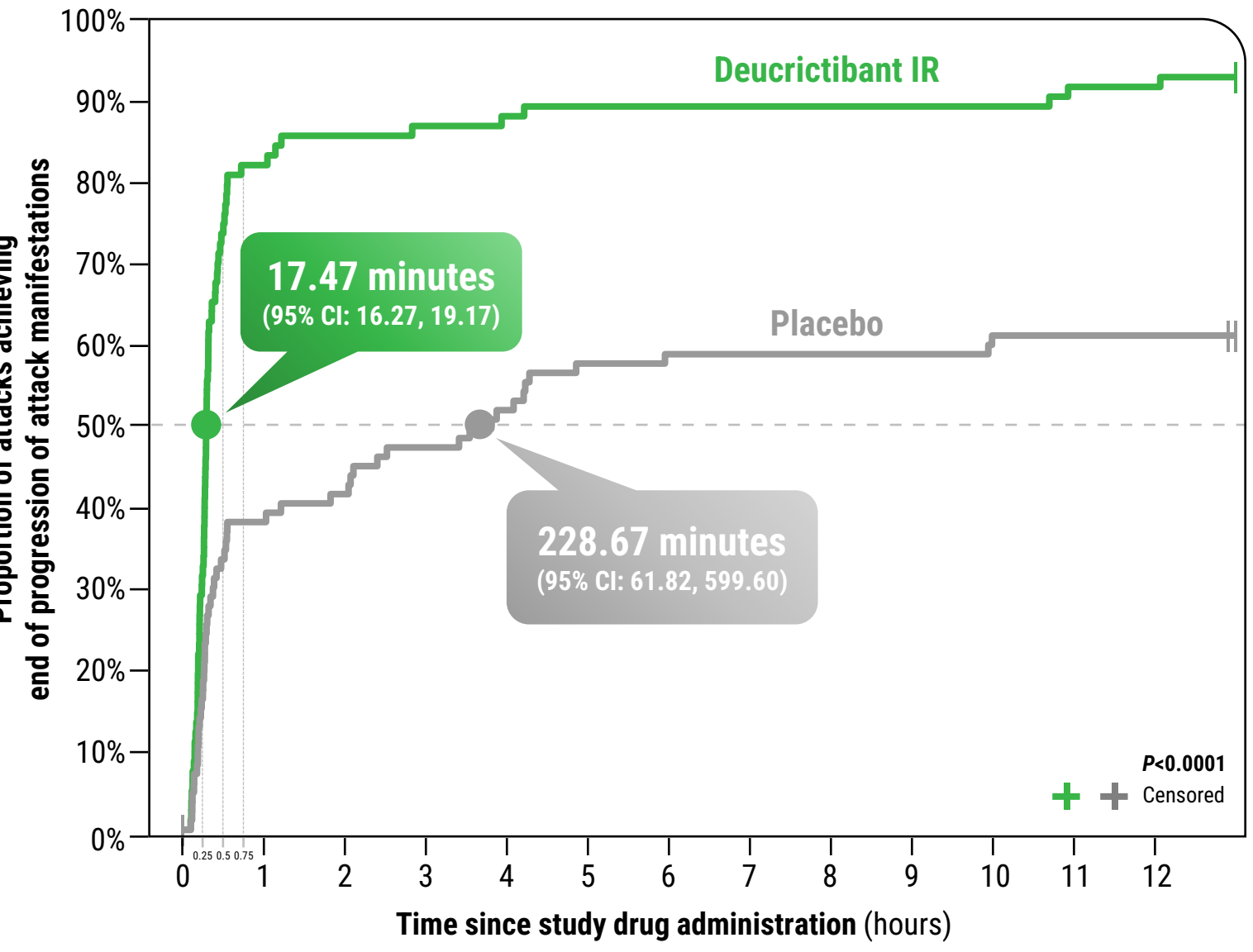
Table 2. Participant baseline demographics and disease characteristics

Participant characteristics	All randomized participants (N=134)
Age in years, mean (SD)	39.0 (14.7)
Sex: Female, n (%)	76 (56.7)
Years since HAE diagnosis, mean (SD)	17.7 (13.0)
Number of attacks within 3 months before screening, mean (SD)	4.4 (3.3)
HAE type, n (%)	
HAE-C1INH-type 1	118 (88.1)
HAE-C1INH-type 2	10 (7.5)
Unspecified type 1 or 2	2 (1.5)
HAE-nC1INH ^a	4 (3.0)
Current long-term prophylaxis use, n (%) ^b	31 (23.1)

HAE-C1INH-type 1, hereditary angioedema type 1; HAE-C1INH-type 2, hereditary angioedema type 2; HAE-nC1INH, hereditary angioedema with normal C1 inhibitor; SD, standard deviation. ^aIncluded participants with HAE-nC1INH associated with a documented genetic variant. ^bLong-term prophylaxis medication included lanadelumab (13 [9.7%]), berotralstat (6 [6.0%]), C1 esterase inhibitor (6 [4.5%]), and other (4 [3.0%]).

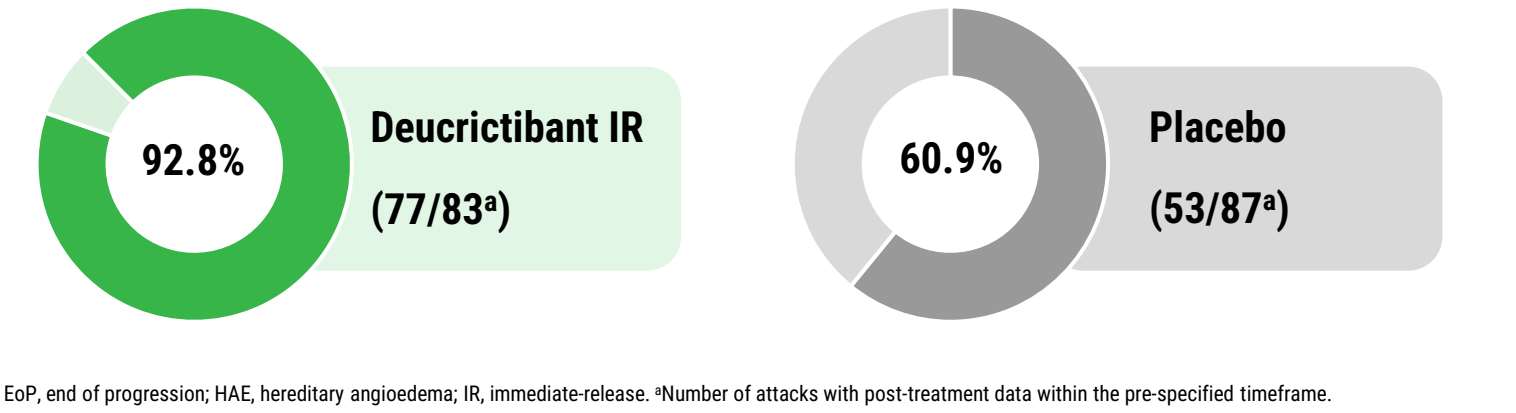
- A total of 134 eligible participants (10 [7.5%] adolescents, 4 [3.0%] with HAE-nC1INH) were enrolled and randomized at 59 sites across 24 countries on 6 continents.
- The primary efficacy analysis set included 88 participants with paired attacks; 113 participants had ≥1 attack treated with study drug.

Figure 4. EoP of HAE attack manifestations was shown to be achieved significantly faster with deucricitbant IR than with placebo^{a,b}



CI, confidence interval; EoP, end of progression; HAE, hereditary angioedema; IR, immediate-release; PGI-C, Patient Global Impression of Change. ^aIf the event of interest was not achieved within the prespecified timeframe or rescue medication was used, the attack was right censored at the last observation before the upper end of the data entry window. ^bTime to EoP of attack manifestations was the earliest post-treatment timepoint after which all subsequent PGI-C ratings were stable or improved.

Figure 5. Proportion of attacks shown to achieve EoP of HAE attack manifestations by 12 hours



EoP, end of progression; HAE, hereditary angioedema; IR, immediate-release. ^aNumber of attacks with post-treatment data within the pre-specified timeframe.

References

- Busse PJ, et al. *N Engl J Med*. 2020;382:1136-48.
- Petersen RS, et al. *J Allergy Clin Immunol Pract*. 2024;12(6):1614-21.
- Betschel SD, et al. *Allergy Asthma Clin Immunol*. 2025;21:25.
- Valerieva A, et al. *Clin Transl Allergy*. 2024;14:e12391.
- Maurer M, et al. *Lancet Haematol*. 2026;13(4):e200-14.
- RAPiDe-2. <https://clinicaltrials.gov/study/NCT05396105>. Accessed August 24, 2026.
- Riedl MA, et al. *Lancet*. 2026; In press.
- Aygören-Pürsün E, et al. *Lancet Haematol*. 2026;13(4):e215-26.
- CHAPTER-3. <https://clinicaltrials.gov/study/NCT06667954>. Accessed August 24, 2026.
- CHAPTER-4. <https://clinicaltrials.gov/study/NCT06679881>. Accessed August 24, 2026.
- CREAATE. <https://clinicaltrials.gov/study/NCT07266805>. Accessed August 24, 2026.
- Covella B, et al. *Future Pharmacol*. 2024;4(1):41-53.
- Cohn DM, et al. *Clin Transl Allergy* 2023;13(9):e12288.