Oral Deucrictibant Immediate-Release Capsule for On-Demand Treatment of Hereditary Angioedema Attacks: Phase 3 RAPIDe-3 Trial Results

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Key takeaways

Results from the pivotal RAPIDe-3 trial for treatment of attacks in multiple types of hereditary angioedema provide further evidence on the rapid and sustained efficacy, safety, and tolerability of the orally administered bradykinin B2 receptor antagonist deucrictibant immediate-release (IR) capsule. This trial met the primary and all 11 secondary efficacy endpoints.

- **1.28 hours** — Median time to onset of symptom relief (primary endpoint)
- **17.47 minutes** — Median time to end of progression of attack symptoms
- **11.95 hours** — Median time to complete symptom resolution
- Deucrictibant was generally well tolerated with no severe or serious treatment-related TEAEs

TEAE, treatment-emergent adverse event.

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

Background

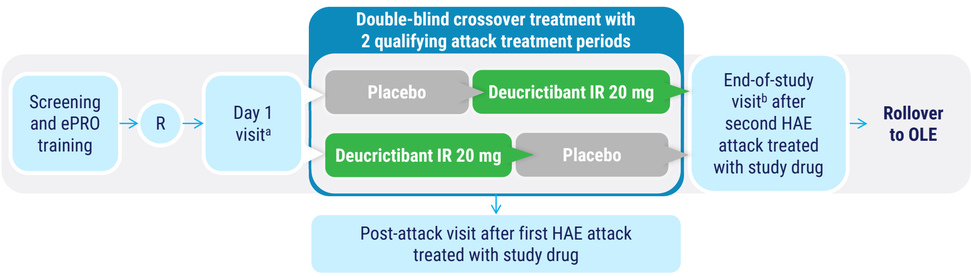
- **Hereditary angioedema (HAE):** a bradykinin-mediated condition with painful swelling attacks affecting multiple locations in the body.[1]
- **Unmet need:** an unmet need remains for additional orally administered treatments combining ease of administration, rapid and sustained effects, and a well-tolerated safety profile.[2,3]
- **Oral deucrictibant:** a selective bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of bradykinin-mediated angioedema attacks.[4-12]

Objective

- To assess the efficacy, safety, and tolerability of oral deucrictibant immediate-release (IR) capsule for on-demand treatment of attacks in adolescents and adults with HAE, including participants with HAE with normal C1 inhibitor (HAE-nC1INH).

Methods

Figure 1. RAPIDe-3 study design



ePRO, electronic patient-reported outcome; HAE, hereditary angioedema; IR, immediate-release; OLE, open-label extension; R, randomization. RAPIDe-3, ClinicalTrials.gov identifier: NCT06343779. Accessed March 3, 2026. https://www.clinicaltrials.gov/study/NCT06343779. [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 open-label extension study with deucrictibant.

- **RAPIDe-3 (NCT06343779)*:** a global, Phase 3, randomized, double-blind, placebo-controlled trial.
- **Participants:** adolescents (aged ≥12 to <18 years) and adults (aged ≥18 to ≤75 years) with HAE-C1INH type 1 or 2, or 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 non-laryngeal or non-severe laryngeal attacks without breathing difficulties or stridor, and with at least one symptom item score of ≥20 on the Angioedema syMptom Rating scAle (AMRA) assessment.
- **Analysis sets:** Primary efficacy analysis included all randomized participants who treated the two attacks with study drug (one per period) in the 2×2 crossover design. Safety analysis included all participants who received ≥1 dose of study drug.

Table 1. Selected efficacy[a] and safety 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		
Proportion of attacks achieving onset of symptom relief	PGI-C	Proportion of study-drug treated attacks achieving a PGI-C rating of at least "a little better" at 4 hours post-treatment
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
Time to reduction in attack severity	PGI-S	Time to a ≥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
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
Use of conventional on-demand treatment as rescue medication	–	Proportion of study-drug treated attacks using conventional on-demand treatment as rescue medication to treat an attack within 24 hours post-treatment
Safety endpoint		
TEAEs and serious TEAEs	–	TEAE defined as an adverse event from the first study drug administration through the end-of-study visit

PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity; TEAE, treatment-emergent adverse event. [a]The primary and first 6 of 11 hierarchical order-ranked secondary endpoints.

Results

- 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, and 113 participants had ≥1 attack treated with study drug.
- Demographics and baseline characteristics were generally balanced across treatment groups.

Table 2. Participant demographics and baseline disease characteristics

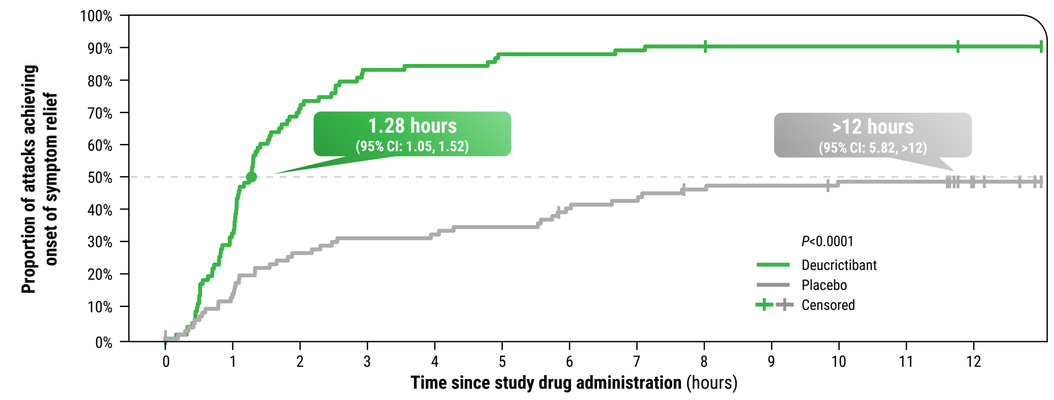
Participant characteristics	All randomized participants (N=134)
Age in years, mean (SD)	39.0 (14.7)
≥12 to <18, n (%)	10 (7.5)
≥18 to <65, n (%)	116 (86.6)
≥65, n (%)	8 (6.0)
Sex: Female, n (%)	76 (56.7)
BMI, mean (SD)	26.5 (5.9)
Race, n (%)	
White	93 (69.4)
Asian	19 (14.2)
Black or African American	10 (7.5)
American Indian or Alaska Native	1 (0.7)
Other	7 (5.2)
Not reported	4 (3.0)
Region, n (%)[a]	
Europe	56 (41.8)
Rest of world	40 (29.9)
North America	38 (28.4)
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 HAE-C1INH Type 1 or 2	2 (1.5)
HAE-nC1INH[b]	4 (3.0)
Current LTP use, n (%)[c]	31 (23.1)

BMI, body mass index; C1INH, C1 inhibitor; HAE, hereditary angioedema; LTP, long-term prophylaxis; SD, standard deviation. [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]Participants with HAE-nC1INH were required to have either a documented associated genetic mutation or, in case of no documented mutation, had to meet a pre-defined clinical evaluation. [c]LTP medication included lanadelumab (13 [9.7%]), berotralstat (8 [6.0%]), complement c1 esterase inhibitor (6 [4.5%]), and other (4 [3.0%]).

Results

Efficacy

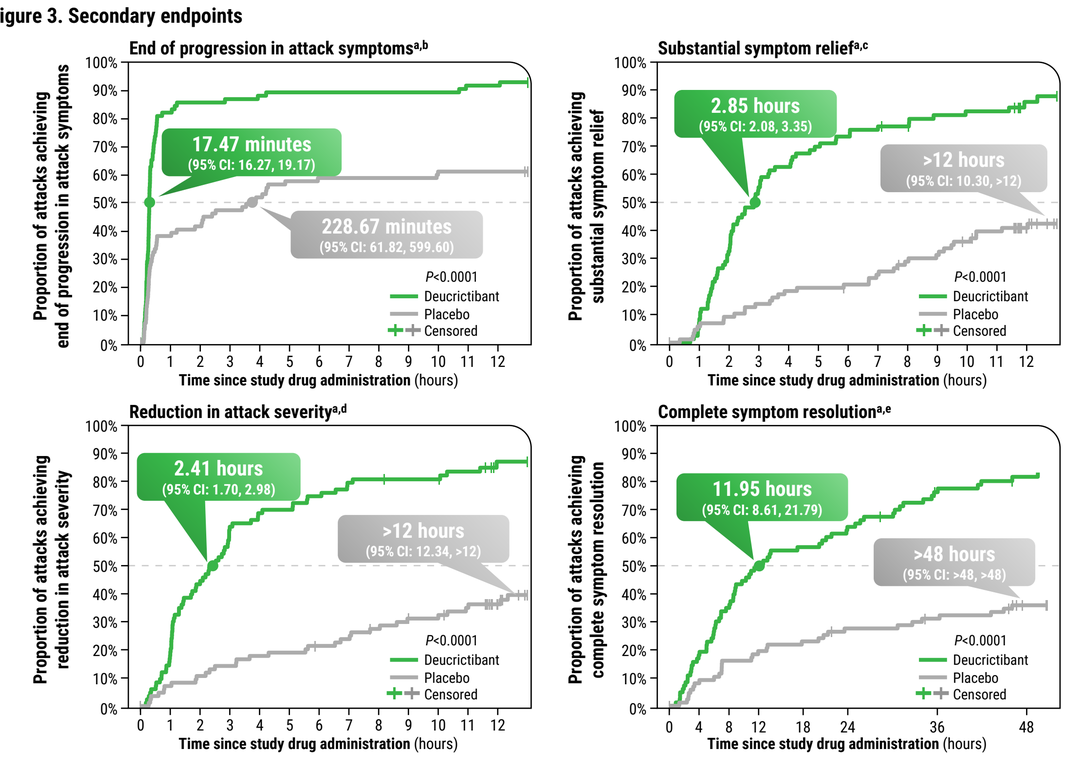
Figure 2. Primary endpoint: Significantly faster onset of symptom relief with deucrictibant compared with placebo[a,b]



CI, confidence interval; 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]PGI-C rating of at least "a little better" for 2 consecutive timepoints within 12 hours post-treatment.

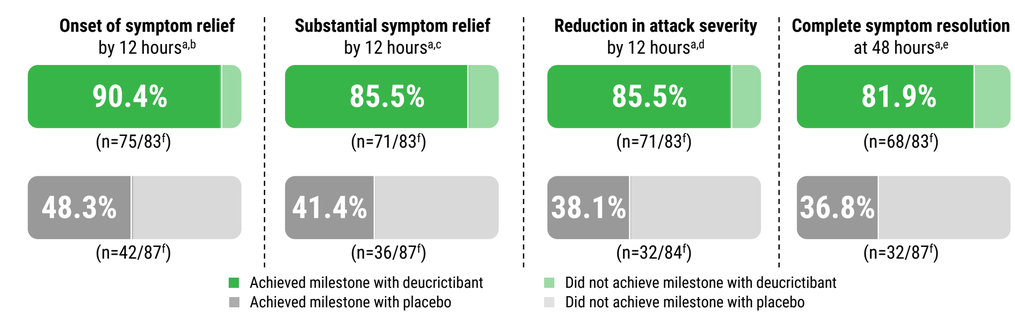
- The proportion of attacks achieving onset of symptom relief at 4 hours was 83.1% for deucrictibant and 27.6% for placebo.

Figure 3. Secondary endpoints



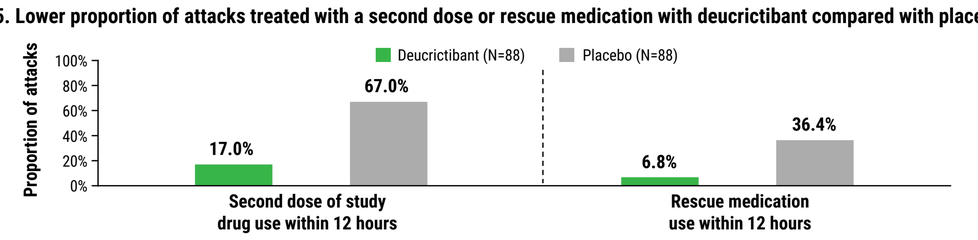
CI, confidence interval; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]If the event of interest was not achieved within the pre-specified timeframe, the attack was right censored at the last observation before the upper end of the data entry window. For attacks with rescue medication use, they were treated as right censored at the upper end of the data entry window. [b]End of progression time is the earliest post-treatment timepoint after which all subsequent PGI-C ratings are stable or improved within 12 hours. [c]PGI-C rating of at least "better" for 2 consecutive timepoints within 12 hours post-treatment. [d]A ≥1-level reduction in PGI-S score from pre-treatment for 2 consecutive timepoints within 12 hours post-treatment. [e]PGI-S rating of "none" within 48 hours post-treatment.

Figure 4. Proportion of attacks achieving efficacy endpoints within pre-specified timeframes



PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [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]PGI-C rating of at least "a little better" for 2 consecutive timepoints within 12 hours post-treatment. [c]PGI-C rating of at least "better" for 2 consecutive timepoints within 12 hours post-treatment. [d]A ≥1-level reduction in PGI-S score from pre-treatment for 2 consecutive timepoints within 12 hours post-treatment. [e]PGI-S rating of "none" within 48 hours post-treatment. [f]Number of participants with post-treatment data within specified timeframe.

Figure 5. Lower proportion of attacks treated with a second dose or rescue medication with deucrictibant compared with placebo



Safety

- One event was reported on more than one occasion within 3 days post-treatment. A single event of fatigue occurred in 2 participants in the deucrictibant group within 3 days of study drug administration, one of which was deemed unrelated to treatment by the investigator.
- No adverse events occurring within 3 days post-treatment were assessed as severe or serious, led to treatment discontinuation, or were associated with changes in clinical laboratory, vital signs, and electrocardiogram parameters.

Table 3. Adverse events occurring within 3 days post-treatment

Adverse events	Non-attack deucrictibant (N=10)[a]		Treated attack deucrictibant (N=100)		Treated attack placebo (N=101)	
	n (%)[b]	no. of events	n (%)[c]	no. of events	n (%)[c]	no. of events
Any TEAE	0	0	15 (15.0)	17	2 (2.0)	3
Treatment-related TEAEs[d]	0	0	5 (5.0)	6	1 (1.0)	1
Any severe TEAE[e]	0	0	0	0	0	0
Serious TEAEs	0	0	0	0	0	0
TEAEs leading to study drug discontinuation, study withdrawal, or death	0	0	0	0	0	0

TEAE, treatment-emergent adverse event. N refers to the total number of participants who received ≥1 dose of study drug. Percentage is calculated based on the N in the header; percentage = 100 x n/N where N is the number of participants. [a]Adolescent participants only. [b]Defined as the number of participants with an adverse event that began within 3 days post-treatment of non-attack period and before the next administration of study drug. [c]Defined as the number of participants with an adverse event that started within 3 days post-treatment of attack. [d]One event each of dyspepsia, fatigue, lethargy, brain fog, headache, and somnolence in deucrictibant-treated participants, and 1 event of pruritus in placebo-treated participants. [e]All reported TEAEs were graded 1 (mild) or 2 (moderate) and there were no reported TEAEs graded 4 (life-threatening), or 5 (fatal).

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