

Oral Deucrictribant Immediate-Release Capsule for On-Demand Treatment of Hereditary Angioedema Attacks: Regional Subgroup Analysis From the Phase 3 RAPIDe-3 Trial

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Conflicts of interest disclosure

I declare the following, real or perceived, conflicts of interest:

- **Receipt of grants/research support:** Astria, BioCryst, CSL Behring, Ionis Pharmaceuticals, KalVista, Octapharma, Pharvaris, and Takeda.
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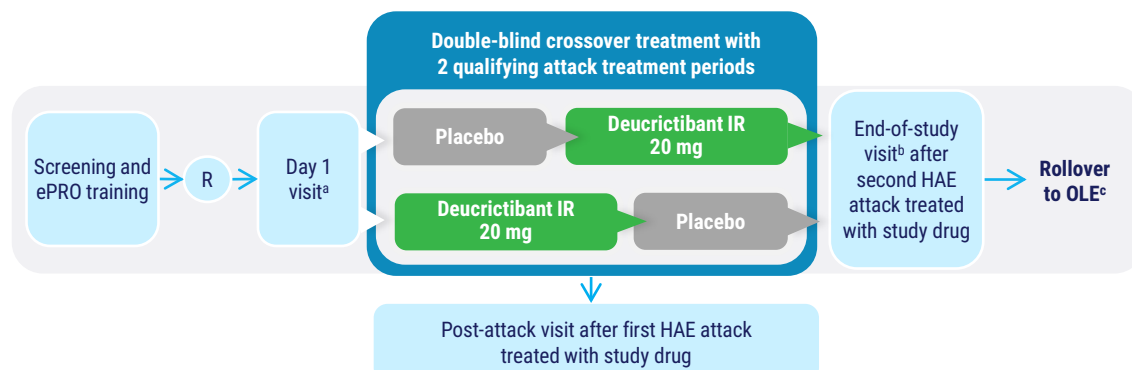
COIs for coauthors are included in the accompanying poster.

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Methods

RAPIDe-3 study design



ePRO, electronic patient-reported outcome; HAE, hereditary angioedema; IR, immediate-release; OLE, open-label extension; R, randomization. ^aAdolescent participants received a non-attack dose for pharmacokinetic sampling at Day 1 visit prior to randomization. ^bData from end-of-study visit could be used to qualify the participant for an OLE study with deucricitibant. ^cRollover to the OLE was optional. Riedl MA, et al. *Lancet*. 2026; doi: 10.1016/S0140-6736(26)01296-1.

- Participants:** adolescents (aged ≥ 12 to < 18 years) and adults (aged ≥ 18 to ≤ 75 years) with HAE-C1INH type 1 or 2, or HAE-nC1INH, including those on long-term HAE prophylaxis.
- Study drugs:** participants self-administered deucricitibant IR capsule 20 mg or placebo to treat two qualifying attacks in a crossover design.
- Qualifying attacks:** defined as either a non-laryngeal attack with at least one symptom item score of ≥ 20 on the Angioedema syMptom Rating sAle (AMRA) assessment, or a non-severe laryngeal attack without breathing difficulties or stridor.

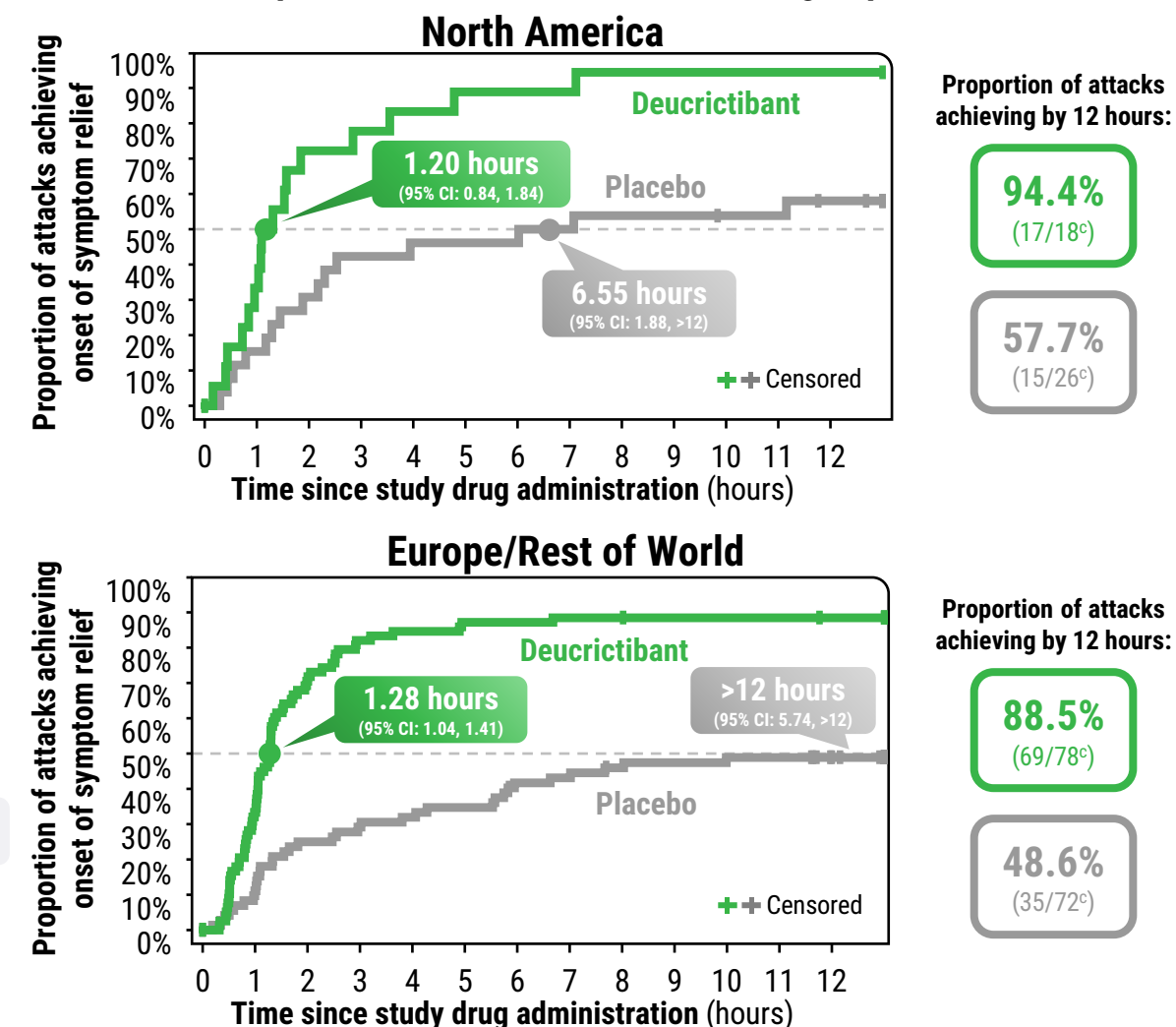
Results

- In total, RAPIDe-3 enrolled 134 participants. The North American and European/Rest of World subgroups included 38 and 96 participants, respectively.
- In this analysis, 113 participants had ≥ 1 attack treated with study drug.

C1INH, C1 inhibitor; HAE, hereditary angioedema; nC1INH, normal C1 inhibitor.

Results

Deucricitibant-treated attacks were shown to achieve onset of symptom relief faster than placebo-treated attacks in both subgroups^{a,b}



CI, confidence interval; PGI-C, Patient Global Impression of Change. ^aIf 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. ^bPGI-C rating of at least "a little better" for 2 consecutive timepoints within 12 hours post-treatment. ^cNumber of attacks with post-treatment data within the pre-specified timeframe.

Results

Efficacy endpoints

Deucrictibant

Placebo

Safety endpoint

Reduction in attack severity^{a,b}

NA

Median time to:
Proportion of attacks achieving by 12 hours:

2.43 hours
(95% CI: 1.03, 5.12)
83.3%
(15/18^c)

>12 hours
(95% CI: 2.65, >12)
48.0%
(12/25^c)

EU/RoW

Median time to:
Proportion of attacks achieving by 12 hours:

2.53 hours
(95% CI: 1.70, 2.98)
82.1%
(64/78^c)

>12 hours
(95% CI: 12.10, >12)
37.7%
(26/69^c)

Complete symptom resolution^{a,d}

NA

Median time to:
Proportion of attacks achieving by 12 hours:

11.61 hours
(95% CI: 2.94, 26.14)
88.9%
(16/18^c)

>48 hours
(95% CI: 17.21, >48)
50.0%
(13/26^c)

EU/RoW

Median time to:
Proportion of attacks achieving by 12 hours:

12.04 hours
(95% CI: 8.64, 21.79)
76.9%
(60/78^c)

>48 hours
(95% CI: >48, >48)
34.7%
(25/72^c)

- The only event reported more than once within 3 days post-treatment was fatigue: a single event was reported by 2 participants, 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, or electrocardiogram parameters.

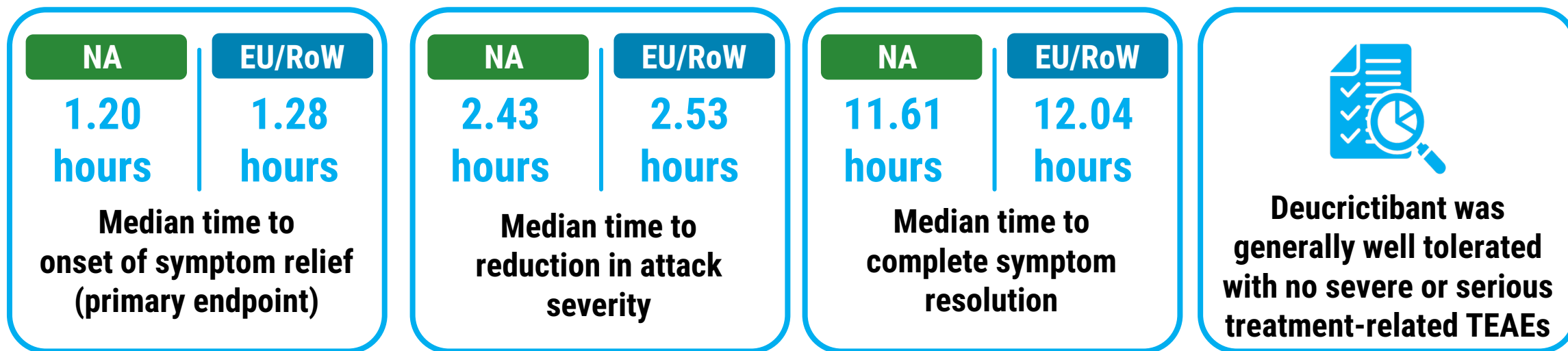
Adverse events occurring within 3 days post-treatment	Non-attack: deucrictibant ^c				Treated attacks: deucrictibant				Treated attacks: placebo			
	NA (N=3)		EU/RoW (N=7)		NA (N=21)		EU/RoW (N=79)		NA (N=26)		EU/RoW (N=75)	
	n	no. of (%) ^d events	n	no. of (%) ^d events	n	no. of (%) ^e events	n	no. of (%) ^e events	n	no. of (%) ^e events	n	no. of (%) ^e events
Any TEAE	0	0	0	0	6 (28.6)	7	9 (11.4)	10	1 (3.8)	1	1 (1.3)	2
Treatment-related TEAEs ^f	0	0	0	0	1 (4.8)	1	4 (5.1)	5	0	0	1 (1.3)	1
Any severe TEAE ^g	0	0	0	0	0	0	0	0	0	0	0	0
Serious TEAEs	0	0	0	0	0	0	0	0	0	0	0	0
TEAEs leading to study drug discontinuation, study withdrawal, or death	0	0	0	0	0	0	0	0	0	0	0	0

CI, confidence interval; EU/RoW, Europe/Rest of World; IR, immediate-release; NA, North America; PGI-S, Patient Global Impression of Severity. ^aIf 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. ^bA ≥1-level reduction in PGI-S score from pre-treatment for 2 consecutive timepoints within 12 hours post-treatment. ^cNumber of attacks with post-treatment data within the pre-specified timeframe. ^dPGI-S rating of "none" within 48 hours post treatment.

EU/RoW, Europe/Rest of World; NA, North America; 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. ^aData based on safety analysis set. ^bTEAE defined as an adverse event from the first study drug administration through the end of study visit. ^cAdolescent participants only. ^dDefined 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. ^eDefined as the number of participants with an adverse event that started within 3 days post-treatment of attack. ^fOne related TEAE of headache in deucrictibant-treated participants in the NA subgroup, and one related TEAE each of dyspepsia, fatigue, lethargy, brain fog, and somnolence in deucrictibant-treated participants, and 1 event of pruritus in placebo-treated participants in the EU/RoW subgroup. ^gAll reported TEAEs were graded 1 (mild) or 2 (moderate) and there were no reported TEAEs graded 4 (life-threatening) or 5 (fatal).

Conclusions

- Results from the pivotal RAPIDe-3 trial for the treatment of attacks in HAE, including HAE-nC1INH, provide further evidence on the efficacy, safety, and tolerability of the orally administered B2R antagonist deucricitbant IR capsule.
- In this regional subgroup analysis, orally administered deucricitbant IR capsule provided faster onset of symptom relief, reduction in attack severity, and complete resolution in both the NA and EU/RoW subgroups compared with placebo.
 - Data were consistent across geographical locations and with the overall study population.



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