Safety and Efficacy of Oral Deucrictibant for Treatment of Upper Airway and Laryngeal Hereditary Angioedema Attacks: Results from the RAPIDe-2 Extension Study

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Key takeaways

The final data from Part A of the RAPIDe-2 study showed that safety and efficacy outcomes of treatment with deucrictibant immediate-release (IR) capsule were consistent for both hereditary angioedema (HAE) attacks affecting the upper airway, including laryngeal attacks, and HAE attacks occurring in other locations.

Safety

- No treatment-related TEAEs across upper airway and non-upper airway attacks

Efficacy

- **1.4 hours** — Median time to onset of symptom relief for upper airway attacks
- Similar times to symptom relief and resolution for upper airway and other attacks
- **92.9%** of upper airway attacks were treated with a single dose of deucrictibant IR capsule

IR, immediate-release; TEAEs, treatment-emergent adverse events.

Background

- **Hereditary angioedema (HAE):** a bradykinin-mediated condition with painful swelling attacks affecting multiple locations in the body and potentially life-threatening when airways, including the larynx, are involved.[1-4]
- **Current landscape:** guidelines recommend HAE attacks are treated as early as possible.[2-4] Parenteral administration often leads to on-demand treatment of HAE attacks being delayed or forgone.[5-9]
- **Deucrictibant:** a selective, orally bioavailable, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of HAE attacks.[10-17]

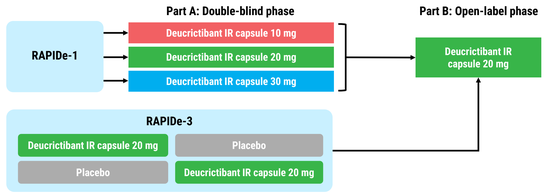
Objective

Evaluate the safety and efficacy of deucrictibant immediate-release (IR) capsule for on-demand treatment of upper airway, including laryngeal, HAE attacks.

Methods

- **RAPIDe-2 (NCT05396105)*:** a two-part, double-blind Phase 2/3 extension study.[12]
- **Part A eligible participants:** adults who completed RAPIDe-1 (NCT04618211).[10]
- **Part A prophylaxis:** no long-term HAE prophylaxis treatment was allowed. Recent use of long-term HAE prophylaxis treatment prior to screening was allowed provided a pre-specified washout period was observed.

Figure 1. RAPIDe-2 study design

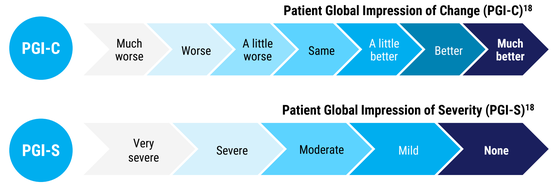


IR, immediate-release.

Methods

- **Primary endpoint:** safety, including treatment-emergent adverse events (TEAEs), clinical laboratory tests, vital signs, and ECG findings.
- **Secondary endpoints:** efficacy endpoints assessed using patient-reported outcome tools.
- **Data collection:** pre-specified at pre-treatment, hourly for 6 hours, and at 8, 12, 24, and 48 hours post-treatment.

Figure 2. Efficacy assessment scales



PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity.

Table 1. Efficacy endpoints

Key efficacy endpoints included	Defined as
Time to and proportion of attacks achieving	
Onset of symptom relief	PGI-C rating of at least "a little better" for 2 consecutive timepoints by 12 hours[a]
Substantial symptom relief	PGI-C rating of at least "better" for 2 consecutive timepoints by 12 hours[a]
Reduction in attack severity	≥1-level reduction in the PGI-S from pre-treatment for 2 consecutive timepoints by 12 hours[b]
Complete attack resolution	PGI-S rating of "none" within 48 hours for time-to-event analysis PGI-S rating of "none" at 24 hours for proportion analysis

PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]If rescue medication used within 14.5 hours post-treatment, time to event was censored at 14.5 hours regardless of whether event occurred within 12 hours post-treatment. [b]Rescue medication use within 33.5 hours post-treatment was regarded as not achieving complete attack resolution at 24 hours.

- **Post-hoc analysis:** safety and efficacy for on-demand treatment of upper airway attacks, including laryngeal attacks without breathing difficulties.
  - Upper airway attacks confirmed by investigators as per protocol definition if the following manifestations of an attack were reported: swelling of the lips/tongue or any sensation of lump in the throat, difficulty swallowing, or voice change.
  - Difficulty swallowing and voice change as manifestations of an attack were assessed prior to treatment using the 5-symptom composite Angioedema syMptom Rating scAle (AMRA-5).
  - AMRA is a numeric rating scale derived from the visual analogue scale (VAS) to assess symptoms of HAE attacks.[19]

Results

Data

- Final combined dose group data from RAPIDe-2 Part A.

Attacks

- 465 attacks were treated by 19 participants.
  - 14 upper airway, including laryngeal, attacks were treated by 7 participants.
  - Difficulty in swallowing and/or voice change were reported as manifestations of 6 attacks prior to treatment.

Table 2. Baseline characteristics of participants with and without upper airway attacks

Characteristics	Participants with ≥1 upper airway attacks (n=7)[a]	Participants without upper airway attacks (n=12)[a]
Age in years, mean (SD)	46.0 (19.5)	43.4 (17.2)
Sex: male/female, n (%)	4 (57) / 3 (43)	3 (25) / 9 (75)
Race: White/other, n	7 / 0	11 / 1
BMI, mean (SD)	27.1 (3.8)	26.7 (4.2)
Years since HAE diagnosis, mean (SD)	20.8 (18.9)	24.7 (13.3)
HAE type, n (%)		
HAE-1	6 (85.7)	11 (91.7)
HAE-2	1 (14.3)	1 (8.3)

BMI, body mass index; HAE, hereditary angioedema; SD, standard deviation. n=number of participants. [a]All participants who received any dose of deucrictibant in the study. Study baseline refers to results at the screening or enrolment visit of RAPIDe-2 Part A. For parameters whose values remain constant over time, baseline values from RAPIDe-1 were used. For parameters without results at the screening or enrolment visit of RAPIDe-2 or for parameters not collected at that time, the last available assessment in RAPIDe-1 was used as the baseline values.

Safety analysis

- Deucrictibant was generally well tolerated with no treatment-related treatment-emergent adverse events reported across upper airway and non-upper airway attacks.

Efficacy analysis

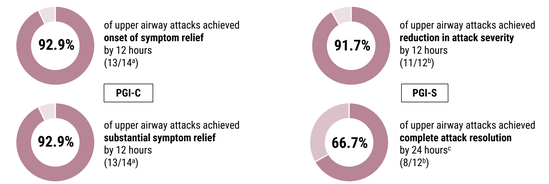
Table 3. Similar times to symptom relief and resolution for upper airway and other attacks

	Upper airway attacks (n=7)	Non-upper airway attacks in participants with upper airway attacks (n=7)	Total non-upper airway attacks (n=19)
Total number of attacks treated[a]	14	177	451
Time to onset of symptom relief[b]			
Number of attacks[c]	14	171	443
Median hours (95% CIs)	**1.4** (0.8, 3.0)	**1.0** (1.0, 1.2)	**1.1** (1.0, 1.1)
Time to substantial symptom relief[b]			
Number of attacks[c]	14	171	443
Median hours (95% CIs)	**3.6** (2.0, 6.1)	**2.7** (2.1, 3.0)	**2.4** (2.1, 2.8)
Time to reduction in attack severity[b]			
Number of attacks[d]	12	169	437
Median hours (95% CIs)	**1.8** (0.9, 3.0)	**2.1** (2.0, 2.8)	**2.8** (2.4, 2.9)
Time to complete attack resolution[b]			
Number of attacks[d]	12	169	437
Median hours (95% CIs)	**8.9** (3.9, 36.3)	**8.0** (7.3, 10.7)	**10.6** (8.5, 11.5)

CI, confidence interval; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]465 attacks treated by 19 participants. [b]Within-participant correlation not accounted for in all Kaplan-Meier estimates. [c]Evaluable attacks include deucrictibant-treated attacks with ≥1 post-treatment PGI-C assessment. [d]Evaluable attacks included deucrictibant-treated attacks with a pre- and ≥1 post-treatment PGI-S assessment.

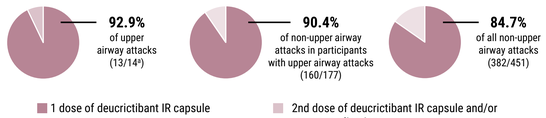
Results

Figure 3. Majority of upper airway attacks achieved key efficacy endpoints



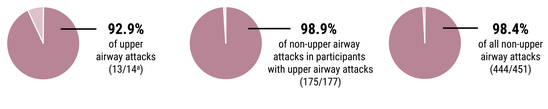
PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]Evaluable attacks include deucrictibant-treated attacks with ≥1 post-treatment PGI-C assessment. [b]Evaluable attacks were study-drug-treated attacks with both a pre- and post-treatment PGI-S result. [c]Defined as achieving PGI-S rating of "none" at the last available timepoint before or at 24 hours post-treatment without use of rescue medication.

Figure 4. Majority of upper airway attacks were treated with a single dose of deucrictibant within 24 hours



IR, immediate-release. . [a]One participant used rescue medication for one upper airway attack and used a single dose of deucrictibant to treat two subsequent upper airway attacks. [b]For non-upper airway attacks, a second dose permitted ≥4 hours after first dose if symptoms persisted or progressed. If symptoms persisted or progressed after the second dose, rescue medication was administered. For upper airway attacks with inadequate response or symptom recurrence ≥4 hours after first dose, only rescue medication was permitted.

Figure 5. Majority of upper airway did not use rescue medication within 24 hours



[a]One participant used rescue medication for one upper airway attack and used a single dose of deucrictibant to treat two subsequent upper airway attacks. [b]For non-upper airway attacks, a second dose permitted ≥4 hours after first dose if symptoms persisted or progressed. If symptoms still persisted or progressed after the second dose, rescue medication was administered. For upper airway attacks with inadequate response or symptom recurrence ≥4 hours after first dose, only rescue medication was permitted.

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

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