Long-Term Treatment of Hereditary Angioedema Attacks With Oral Deucrictibant: RAPIDe-2 Extension Study Results

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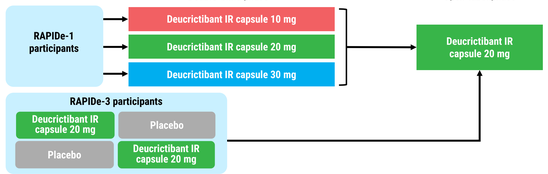
Rationale

- International guidelines recommend that hereditary angioedema (HAE) attacks are treated as early as possible.[1-3]
- The burden associated with parenteral administration of currently approved on-demand medications[4-8] often leads to treatment of HAE attacks being delayed or forgone.[9-13]
- An unmet need exists for on-demand oral therapies that are effective and well-tolerated and may reduce the treatment burden, thus enabling prompt administration.[13]
- Deucrictibant is a selective, orally administered bradykinin B2 receptor antagonist under development for prophylactic and on-demand treatment of HAE attacks.[14-19]
- In the RAPIDe-1 Phase 2 trial (NCT04618211),[14] deucrictibant immediate-release (IR) capsule reduced time to onset of symptom relief and to resolution of HAE attacks vs placebo and was well tolerated.[15]

Methods

- RAPIDe-2 (NCT05396105)[16†] is an ongoing two-part Phase 2/3 extension study evaluating long-term safety and efficacy of orally administered deucrictibant IR capsule for the treatment of HAE attacks.
- Part A enrolls adult (≥18 years) participants who completed RAPIDe-1. Participants continue self-administering the same double-blinded dose of deucrictibant IR capsule (10 mg, 20 mg, or 30 mg) received in RAPIDe-1 to treat qualifying non-laryngeal attacks (≥1 symptom with Visual Analogue Scale score ≥30), and laryngeal attacks presenting without breathing difficulties (**Figure 1**).

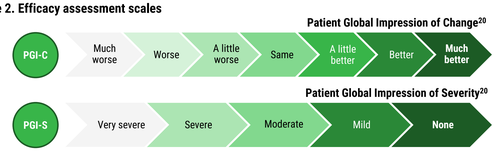
Figure 1. RAPIDe-2 study design



IR, immediate-release.

- The primary endpoint assesses safety, including treatment-emergent adverse events (TEAEs), clinical laboratory tests, vital signs, and electrocardiogram (ECG) findings.
- Patient-reported outcome (PRO) tools are used to assess efficacy (**Figure 2**), with data collection pre-specified at pre-treatment, every hour up to 6 hours, and then at 8, 12, 24, and 48 hours, from administration of deucrictibant IR capsule.
- Key efficacy endpoints (**Figure 2**) include:
  - Time to onset of symptom relief, defined as Patient Global Impression of Change (PGI-C) rating of at least "a little better" for 2 consecutive timepoints by 12 hours post-treatment.
  - Time to substantial symptom relief, defined as PGI-C rating of at least "better" for 2 consecutive timepoints by 12 hours post-treatment.
  - Time to reduction in attack severity, defined as achieving ≥1-level reduction in the Patient Global Impression of Severity (PGI-S) from pre-treatment for 2 consecutive timepoints by 12 hours post-treatment.
  - Proportion of attacks achieving complete attack resolution, defined as achieving PGI-S rating of "none" at 24 hours post-treatment.

Figure 2. Efficacy assessment scales



Results

- Data from the RAPIDe-2 Part A combined-dose group at the date of cutoff are reported here.
- A total of 265 attacks from 17 participants were included in the modified intention-to-treat efficacy analysis set (data cutoff: 1 March 2024), defined as all participants who had ≥1 attack treated with deucrictibant IR capsule and non-missing PGI-C results from ≥1 post-treatment timepoint.
- A total of 337 attacks from 19 participants were included in the safety analysis set (data cutoff: 10 June 2024), defined as all participants who received any dose of deucrictibant IR capsule in the study.
  - 7 of 337 attacks were laryngeal.
- Baseline characteristics were consistent with the RAPIDe-1 Phase 2 trial (**Table 1**).

Table 1. Baseline characteristics

	Deucrictibant IR capsule (combined dose group)
Number of attacks treated[a]	337
Number of participants[a]	19
Age in years, mean (SD)	42.7 (17.6)
Sex: Male/female, n (%)	7 (36.8) / 12 (63.2)
Race: White/other	18 / 1
BMI, mean (SD)	27.0 (3.8)
Years since HAE diagnosis, mean (SD)	21.7 (15.2)
HAE type, n (%)	
HAE-1	17 (89.5)
HAE-2	2 (10.5)

BMI, body mass index; HAE, hereditary angioedema; IR, immediate-release; SD, standard deviation. [a]Number by the cutoff date of 10 June 2024.

Safety

- Deucrictibant IR capsule was well-tolerated across all doses, with no treatment-related TEAEs (**Table 2**).
- No treatment-related serious or severe TEAEs, no treatment-related TEAEs in laboratory parameters, vital signs, or ECG findings, and no TEAEs leading to treatment discontinuation, study withdrawal, or death were reported.

Table 2. TEAEs within 5 days after administration of study drug

Adverse events	Deucrictibant IR capsule (combined dose group)
Number of attacks treated[a]	337
Number of participants[a]	19
Attacks with any TEAE, n (%)	13 (3.9)
Treatment-related TEAEs, n	0
Serious TEAEs, n	1[b]
Treatment-related serious TEAEs, n	0
TEAEs leading to study drug discontinuation, study withdrawal, or death, n	0

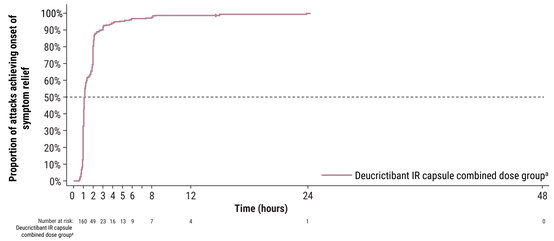
IR, immediate-release; TEAE, treatment-emergent adverse event (defined as adverse event occurring during time window from first study drug administration). [a]Number in the safety analysis set (data cutoff: 10 June 2024). [b]Tooth caries unrelated to treatment.

Results

Efficacy

- The median time to onset of symptom relief was 1.1 hours (95% CI, 1.0, 1.2) (**Figure 3, Table 3**).
- By 12 hours, 98.5% (261/265) of attacks achieved onset of symptom relief (**Table 3, Figure 4**).

Figure 3. Kaplan-Meier plot of time to onset of symptom relief



IR, immediate-release. [a]Includes 10 mg, 20 mg, and 30 mg dose groups.

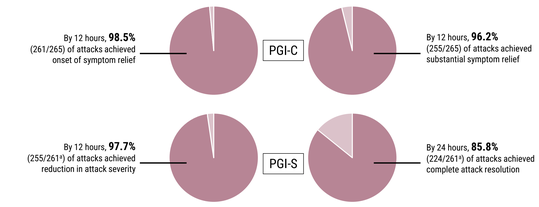
Table 3. Median time to achieving key efficacy endpoints

	Deucrictibant IR capsule (combined dose group)
Number of attacks treated[a]	265
Number of participants with treated attacks[a]	17
Median time to onset of symptom relief using PGI-C, hours (95% CI)	1.1 (1.0, 1.2)
Median time to substantial symptom relief using PGI-C, hours (95% CI)	2.7 (2.1, 2.9)
Median time to reduction in attack severity using PGI-S,[b] hours (95% CI)	2.6 (2.0, 2.9)
Median time to complete attack resolution using PGI-S,[b] hours (95% CI)	11.5 (11.0, 13.0)

CI, confidence interval; IR, immediate-release; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]Number in the modified intention-to-treat efficacy analysis set (data cutoff: 01 March 2024). [b]261 attacks have non-missing pre-treatment PGI-S.

- By 24 hours, 85.8% (224/261) of attacks achieved complete attack resolution (**Figure 4**).
  - 90.2% (202/224) of attacks achieved this milestone with a single dose of deucrictibant IR capsule (**Figure 5**).

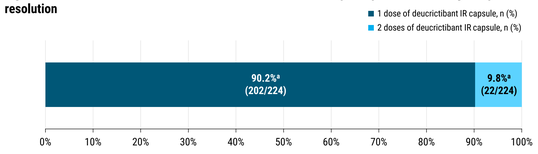
Figure 4. Proportion of attacks achieving key efficacy endpoints



PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]261 attacks have non-missing pre-treatment PGI-S.

Results

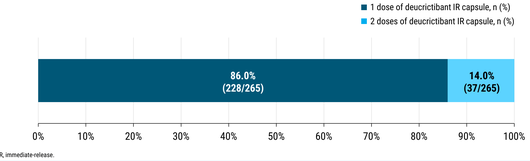
Figure 5. Attacks treated with 1 or 2 doses of deucrictibant IR capsule prior to achieving complete attack resolution



IR, immediate-release; PGI-S, Patient Global Impression of Severity. *Percentage of 224 attacks achieving complete attack resolution using PGI-S by 24 hours.

- A total of 86.0% (228/265) of all attacks were treated with a single dose of deucrictibant IR capsule (**Figure 6**).

Figure 6. Attacks treated with 1 or 2 doses of deucrictibant IR capsule



IR, immediate-release.

Conclusions

- **In the current analysis of the ongoing RAPIDe-2 Phase 2/3 extension study, deucrictibant IR capsule was well-tolerated for all studied doses with no safety signals observed.**
- **Efficacy analysis showed:**
  - **1.1 hours median time to onset of symptom relief using PGI-C – by 12 hours: 98.5% of attacks.**
  - **2.7 hours median time to substantial symptom relief using PGI-C – by 12 hours: 96.2% of attacks.**
  - **2.6 hours median time to reduction in attack severity using PGI-S – by 12 hours: 97.7% of attacks.**
  - **11.5 hours median time to complete attack resolution using PGI-S – by 24 hours: 85.8% of attacks.**
  - **86.0% of attacks were treated with a single dose of deucrictibant IR capsule.**
- **Results from the ongoing RAPIDe-2 extension are consistent with the Phase 2 RAPIDe-1 study and provide evidence on the long-term safety and efficacy of deucrictibant IR capsule for repeat treatment of HAE attacks.**

References

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

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