Long-Term Safety and Efficacy of Oral Deucrictibant for Treatment of Hereditary Angioedema Attacks: Results of the RAPIDe-2 Extension Study

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Key takeaways

Final Part A results from the RAPIDe-2 extension study are consistent with the Phase 2 RAPIDe-1 study and provide further evidence on the long-term safety and efficacy of deucrictibant immediate-release (IR) capsule for treatment of repeat hereditary angioedema (HAE) attacks.

Safety

Deucrictibant was generally well tolerated with no treatment-related TEAEs

Efficacy

1.1 Hours
Median time to onset of symptom relief with 97.8% of attacks achieving this milestone by 12 hours

89%
of attacks that achieved attack resolution were treated with a single dose of deucrictibant

10.6 Hours
Median time to complete attack resolution

TEAE, treatment-emergent adverse event.

Background

- **HAE:** a bradykinin-mediated condition with painful swelling attacks affecting multiple locations in the body.[1]
- **Unmet need:** guidelines recommend that HAE attacks be treated as early as possible.[2-4] Parenteral administration often leads to on-demand treatment of HAE attacks being delayed or forgone.[5-8]
- **Deucrictibant:** a selective, investigational, orally administered, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of HAE attacks.[9-16]

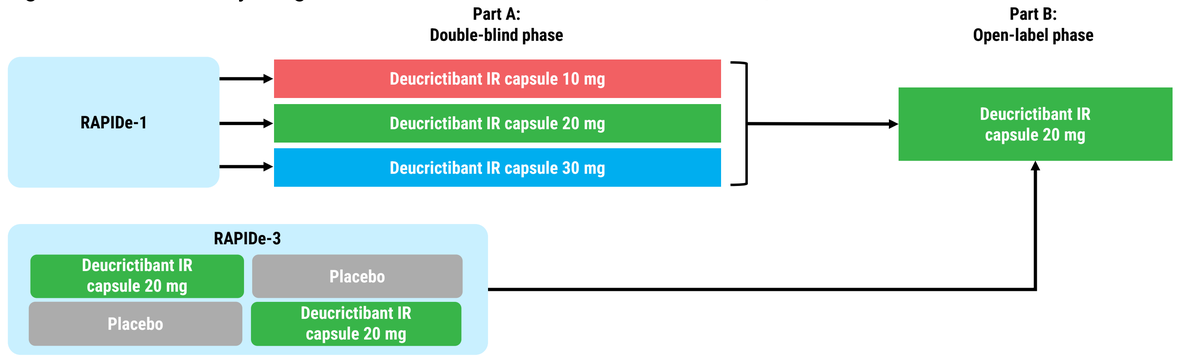
Objective

To evaluate the long-term safety and efficacy of deucrictibant immediate-release (IR) capsule for on-demand treatment of repeat HAE attacks in the RAPIDe-2 extension study.

Methods

- **RAPIDe-2 (NCT05396105)*:** a two-part, Phase 2/3 long-term extension study.[11]
- **Part A eligible participants:** adults who completed RAPIDe-1 (NCT04618211).[9]
- **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.

- **Primary endpoint:** safety including treatment-emergent adverse events (TEAEs), clinical laboratory tests, vital signs, and electrocardiogram (ECG) findings.
- **Secondary endpoints:** efficacy endpoints 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

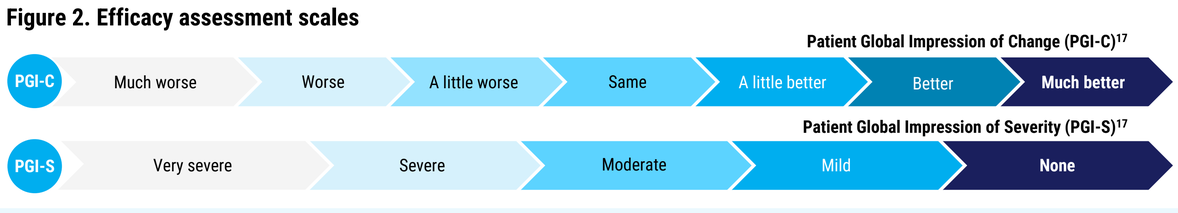


Table 1. Efficacy endpoints

Key efficacy endpoints	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[a]
Complete attack resolution	PGI-S rating of "none" at 24 hours[b]

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.

Results

Data:

- RAPIDe-2 Part A included 465 attacks experienced by 19 participants. Combined dose-blinded group data shown.

Table 2. Participant characteristics

Participant characteristics	Deucrictibant IR capsule (combined dose group[a]) (N=19)
Age in years, mean (SD)	44.4 (17.6)
Sex: male/female, n (%)	7 (36.8) / 12 (63.2)
Race: White/other, n	18 / 1
BMI, mean (SD)	26.8 (4.0)
Years since HAE diagnosis, mean (SD)	23.3 (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]All participants who received any dose of deucrictibant in the study. Study baseline refers to results at the screening or enrollment visit of RAPIDe-2 Part A. For parameters whose values remained constant over time, baseline values from RAPIDe-1 were used. For parameters without results at the screening or enrollment 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. Data for combined dose group shown (deucrictibant 10 mg, 20 mg, and 30 mg).

Results

Safety analysis (Part A)

- Included all participants who received ≥1 dose of deucrictibant IR capsule in the study.
- No treatment-related TEAEs.
- No treatment-related serious or severe TEAEs, no treatment-related TEAEs in laboratory parameters, vital signs, or ECG findings.
- No TEAEs leading to treatment discontinuation, study withdrawal, or death.

Table 3. TEAEs within 3 days of study drug administration

Adverse events	Deucrictibant IR capsule (combined dose group) (N=19; A=465)
Attacks with any TEAE, n (%)	12 (2.6)
Treatment-related TEAEs, n	0
Serious TEAEs, n	1[a]
Treatment-related serious TEAEs, n	0
TEAEs leading to study drug discontinuation, study withdrawal, or death, n	0

A, # of treated attacks; ECG, electrocardiogram; IR, immediate-release; N, # of participants; TEAE, treatment-emergent adverse event, defined as adverse event occurring from first study drug administration. [a]Tooth caries unrelated to treatment. Data for combined dose group shown (deucrictibant 10 mg, 20 mg, and 30 mg).

Efficacy analysis (Part A)

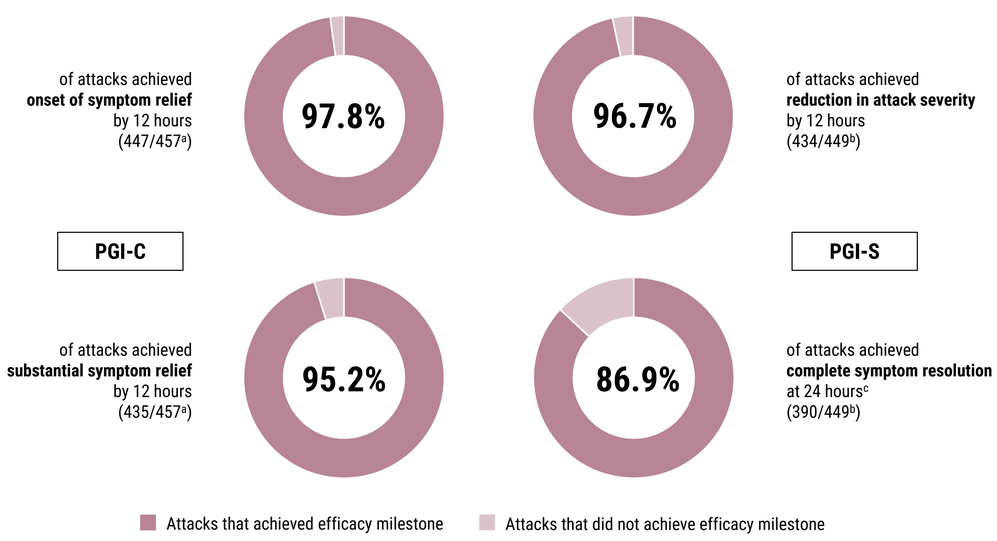
- Modified intention-to-treat analysis set: participants who treated ≥1 attack with deucrictibant IR capsule and non-missing PGI-C results from ≥1 post-treatment timepoint.

Figure 3. Median time to achieving key efficacy endpoints

Median time to: (95% CIs)	Onset of symptom relief	Substantial symptom relief	Reduction in attack severity	Complete attack resolution
	1.1 hours (1.0, 1.1)[a,b]	2.5 hours (2.1, 2.9)[b,c]	2.8 hours (2.3, 2.9)[b,d]	10.6 hours (8.5, 11.5)[b,e]

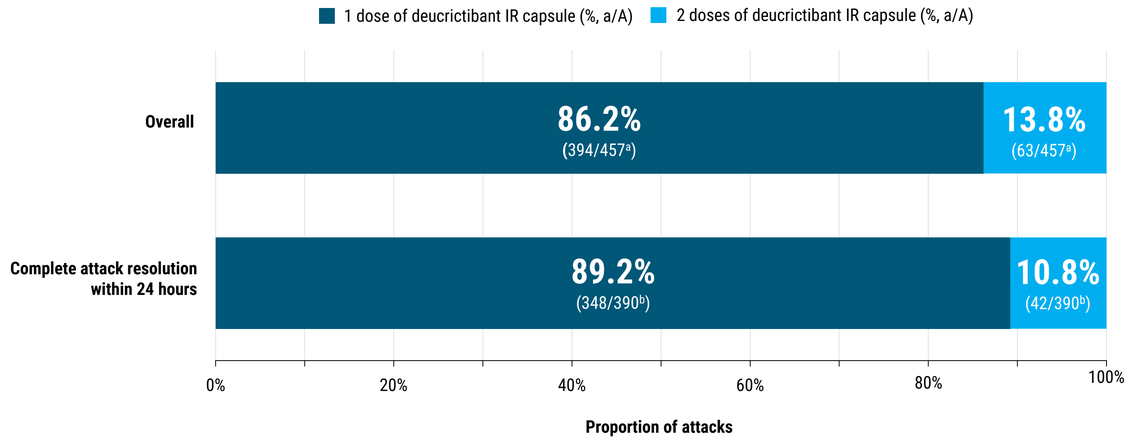
CI, confidence interval; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]PGI-C rating of at least "a little better" for 2 consecutive timepoints by 12 hours post-treatment regardless of any missing intervening assessments and without rescue medication use. [b]Within-participant correlation was not accounted for in all Kaplan-Meier estimates. [c]PGI-C rating of at least "better" for 2 consecutive timepoints by 12 hours post-treatment regardless of any missing intervening assessments and without rescue medication use. [d]≥1-level reduction in PGI-S from pre-treatment for 2 consecutive timepoints by 12 hours post-treatment and without rescue medication use. [e]PGI-S rating of "none" within 48 hours post-treatment and without rescue medication use.

Figure 4. Majority of attacks achieved key efficacy endpoints



PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]457 attacks have at least 1 post-treatment PGI-C result. [b]449 attacks have non-missing pre-treatment PGI-S and ≥1 post-treatment PGI-S. [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 5. Majority of attacks treated with a single dose of deucrictibant and without rescue medication



A, # of attacks; IR, immediate-release. Data for combined dose group shown (deucrictibant 10 mg, 20 mg, and 30 mg). [a]Proportion of attacks that were not treated with rescue medication within 24 hours post-treatment; 8 attacks used rescue medication within 24 hours post-treatment. [b]Proportion of attacks achieving complete attack resolution, 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.

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

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COI: A.V.: AstraZeneca, Berlin-Chemie/Menarini Group, CSL Behring, KalVista, Novartis, Pharming, Pharvaris, Sobi, Takeda; **J.A.:** BioCryst, BioMarin, CSL Behring, Cycle Pharma, KalVista, Pharming, Pharvaris, Takeda; **E.A-P.:** Astria, BioCryst, CSL Behring, Intellia, Kalvista, Otsuka, Pharvaris, Takeda; **L.B.:** BioCryst, Blueprint, CSL Behring, Novartis, Takeda; **H.C.:** AstraZeneca (Alexion), CSL Behring, KalVista, Merck, Novartis, Pharming, Pharvaris, Roche, Sanofi, Sobi, Takeda; **H.F.:** BioCryst, CSL Behring, Intellia, KalVista, ONO Pharmaceutical, Pharming, Pharvaris, Takeda; **D.G.:** Pharming, Takeda; **R.H.:** BioCryst, CSL Behring, KalVista, Pharming, Pharvaris, Takeda; **J.S.J.:** BioCryst, CSL Behring, Cycle Pharma, Oasis, Pharming, Pharvaris, Takeda; **R.L.:** BioCryst, CSL Behring, Ionis, KalVista, Novartis, Pharming, Pharvaris, Takeda; **M.E.M.:** Allakos, Amgen, AstraZeneca, BioCryst, Blueprint, CSL Behring, Cycle Pharma, Genentech, GSK, KalVista, Merck, Novartis, Pharming, Pharvaris, Sanofi/Regeneron, Takeda; **A.R.:** BioCryst, CSL Behring, Pharming, Pharvaris, Stallergens, Takeda, Teva; **G.S.:** Pharvaris, Takeda; **M.Sta.:** no conflicts of interests to disclose relative to this work; **M.Sto.:** BioCryst, CSL Behring, KalVista, Pharming, Takeda; **G.G., Y.L., P.L., J.S., M.Y.:** employees of Pharvaris, hold stocks in Pharvaris; **M.A.R.:** Astria, BioCryst, BioMarin, Celldex, CSL Behring, Cycle Pharma, Grifols, Intellia, Ionis, KalVista, Novartis, Pharming, Pharvaris, Sanofi-Regeneron, Takeda.
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