Poster #23

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 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

Over 98%
of attacks that achieved symptom relief or resolution with a single dose of deucrictibant had a durable response without symptom reoccurrence

TEAE, treatment-related adverse event.

Background

- **HAE:** a bradykinin-mediated condition with painful swelling attacks affecting multiple locations in the body.[1]
- **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.[5-8]
- **Oral deucrictibant:** a selective, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of HAE attacks.[9-16]

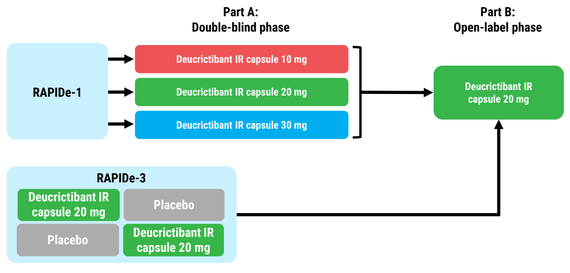
Objective

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

Methods

- **RAPIDe-2 (NCT05396105)*:** a two-part, double-blind, Phase 2/3 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.

Methods

- **Primary endpoint:** safety including treatment-emergent adverse events (TEAEs), clinical laboratory tests, vital signs, and electrocardiogram 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

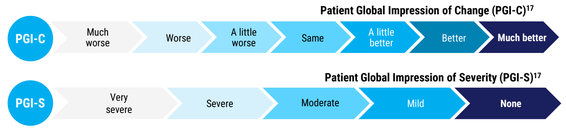


Table 1. Efficacy endpoints

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.

Post-hoc analyses

- **Durability of treatment response:** the achievement and maintenance of serial milestones of symptom relief and resolution without reoccurrence of symptoms following a single-dose of deucrictibant only.
  - **Symptom reoccurrence:** following the achievement of each efficacy milestone, symptom reoccurrence was evaluated as any instance where the milestone was no longer being met within 24 hours.
- **Upper airway attacks:** confirmed by investigators and defined as swelling of the lips/tongue or any sensation of lump in the throat, difficulty swallowing, or voice change (assessed with AMRA-5).

Results

Data:

- RAPIDe-2 Part A included 465 attacks from 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 remain 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

- 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

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

Efficacy analysis

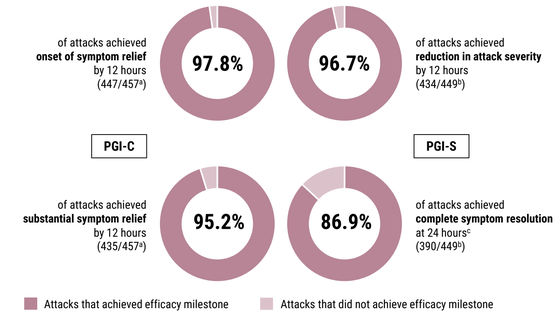
- Modified intention-to-treat analysis set: participants who treated ≥1 attack with deucrictibant IR capsule and non-missing PGI-C results from ≥1 post-treatment timepoint.

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 point 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.

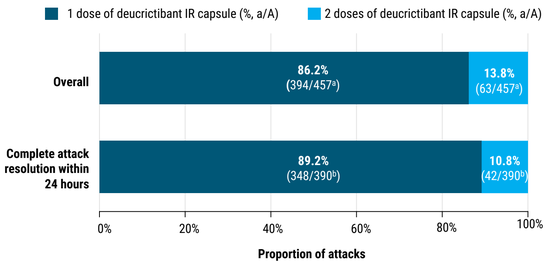
Figure 4. Majority of attacks achieved key efficacy endpoints



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 at least 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.

Results

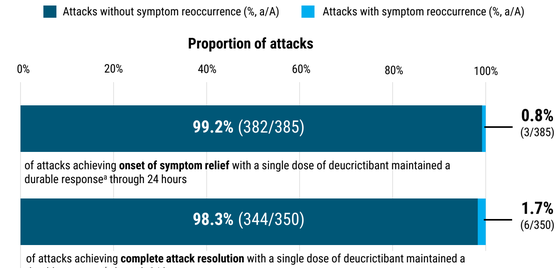
Figure 5. Majority of attacks treated with a single dose of deucrictibant and without rescue medication



IR, immediate-release. A = number of attacks. 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.

Durability of response to treatment

Figure 6. Over 98% of attacks that achieved symptom relief or resolution with a single dose of deucrictibant had a durable response without symptom reoccurrence



PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. A = number of study-drug treated attacks that achieved the efficacy milestone with a single dose of deucrictibant. [a]Defined as PGI-C rating remaining "same" or better within 24 hours after reaching "a little better" for 2 consecutive timepoints within 12 hours post-treatment. [b]Defined as PGI-S rating better than "none" within 24 hours after reaching "none" within 24 hours post-treatment. Combined dose group data shown (deucrictibant 10 mg, 20 mg, and 30 mg).

Treatment outcomes of upper airway attacks

- Of 465 attacks, 14 were upper airway, including laryngeal, attacks without breathing difficulties.
- Similar times to symptom relief and resolution were observed for upper airway attacks and other attacks.

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

References

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COI: M.A.R.: Astria, BioCryst, BioMarin, Celldex, CSL Behring, Cycle Pharma, Grifols, Intellia, Ionis, KalVista, Novartis, Pharming, Pharvaris, Sanofi-Regeneron, Takeda; **J.A.:** Astria, BioCryst, CSL Behring, Ionis, KalVista, Pharming, Pharvaris, Takeda; **E.A-P.:** Astria, BioCryst, BioMarin, CSL Behring, Intellia, KalVista, Pharming, Pharvaris, Takeda; **L.B.:** BioCryst, Blueprint, CSL Behring, GSK, KalVista, Novartis, Pharvaris, 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.:** BioCryst, CSL Behring, Pharming, Takeda; **R.H.:** BioCryst, CSL Behring, KalVista, Pharming, Pharvaris, Takeda; **J.S.J.:** BioCryst, CSL Behring, Cycle Pharma, Intellia, Ionis, KalVista, Pharming, Pharvaris, Takeda; **R.L.:** BioCryst, CSL Behring, Ionis, KalVista, Novartis, Pharming, Pharvaris, Takeda; **M.E.M.:** Astria, AstraZeneca, BioCryst, Blueprint, Celldex, Cogent, CSL Behring, GSK, Ionis, Intellia, KalVista, Merck, Novartis, Pharming, Pharvaris, Regeneron, Takeda, Teva; **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, Pharvaris, Takeda; **G.G., Y.L., P.L., J.S., M.Y.:** employees of Pharvaris, hold stocks in Pharvaris; **A.V.:** AstraZeneca, Berlin-Chemie/Menarini Group, CSL Behring, KalVista, Novartis, Pharming, Pharvaris, Sobi, Takeda.
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