Long-Term Safety and Efficacy of Oral Deucrictibant for Prophylaxis in Hereditary Angioedema: Results of the CHAPTER-1 Open-Label Extension Study

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Key takeaways

The ongoing Phase 2 CHAPTER-1 open-label extension (OLE) study provides further evidence on the long-term safety and efficacy of oral deucrictibant for prevention of hereditary angioedema (HAE) attacks.

Safety

Deucrictibant was well tolerated with no safety signals

Efficacy

1.5 YEARS
Reduced attack rate in the RCT remained low ≥1.5 years in the OLE

~80% of participants achieved ≥90% reduction in attack rate

0
Median proportion of days with symptoms reduced in the RCT and was zero in the OLE

OLE, open-label extension; RCT, randomized controlled trial.

Background

- **Hereditary angioedema (HAE):** a bradykinin-mediated condition with painful swelling attacks affecting multiple locations in the body.[1]
- **Unmet need:** prophylactic treatments combining injectable-like efficacy, a well-tolerated profile, and ease of administration.[2-5]
- **Oral deucrictibant:** a selective, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of HAE attacks.[5-15]

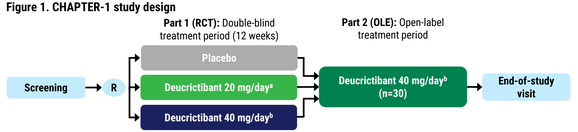
Objective

Evaluate the safety and efficacy of deucrictibant for long-term prophylaxis of HAE attacks in adults in the CHAPTER-1 open-label extension study.[12]

Methods

- **CHAPTER-1 (NCT05047185)*:** a two-part, Phase 2 study.[12]
  - Part 1 randomized placebo-controlled trial (RCT) is complete.
  - Part 2 OLE is ongoing.
- **Eligible participants:** adults diagnosed with HAE-1/2, not receiving other prophylactic treatments at screening, and with a pre-specified minimum number of attacks.

Figure 1. CHAPTER-1 study design



IR, immediate-release; OLE, open-label extension; R, randomization; RCT, randomized controlled trial. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

- All 30 participants who completed the RCT enrolled into the ongoing OLE.
  - In the RCT, these 30 participants were randomized to deucrictibant 20 mg/day (N=11) or 40 mg/day (N=10), or placebo (N=9).

Results

Participants in the OLE

- At data cutoff (10 June 2024), 30 participants in the OLE had received deucrictibant 40 mg/day for a mean (SD) treatment duration of 12.83 (5.03) months.

Safety analysis

- Deucrictibant was generally well tolerated.
  - One treatment-related treatment-emergent adverse event (TEAE) of tooth discoloration reported.

Table 1. Adverse events in the OLE

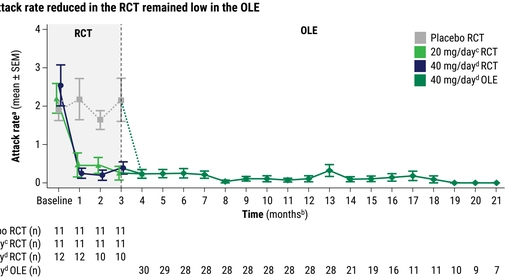
	Placebo to 40 mg/day[a] (N=9)		20 mg/day[b] to 40 mg/day[a] (N=11)		40 mg/day[a] to 40 mg/day[a] (N=10)		Total (N=30)	
	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n
TEAEs	**5 (55.6)**	**25**	**7 (63.6)**	**31**	**6 (60.0)**	**16**	**18 (60.0)**	**72**
Treatment-related TEAEs	**1 (11.1)**	**1**	**0**	**0**	**0**	**0**	**1 (3.3)**	**1**
Tooth discoloration	1 (11.1)	1	0	0	0	0	1 (3.3)	1
Serious TEAEs	**0**	**0**	**1 (9.1)**	**1**	**1 (10.0)**	**1**	**2 (6.7)**	**2**
Tendon injury	0	0	0	0	1 (10.0)	1	1 (3.3)	1
Hip arthroplasty (arthritis)	0	0	1 (9.1)	1	0	0	1 (3.3)	1
Treatment-related serious TEAEs	**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**

IR, immediate release; OLE, open-label extension; TEAE, treatment-emergent adverse event. TEAE defined as adverse event occurring during time window from first study drug administration.
N = number of participants who received ≥1 dose of study treatment in the OLE by the cutoff date of 10 June 2024. [a]Deucrictibant IR capsule, 20 mg twice daily. [b]Deucrictibant IR capsule, 10 mg twice daily.

Efficacy analysis

- RCT: Deucrictibant reduced the attack rate, with effects observed within the first month.
- OLE: Low attack rate maintained through ≥1.5 years.

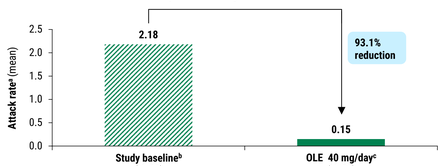
Figure 2. Attack rate reduced in the RCT remained low in the OLE



IR, immediate release; OLE, open-label extension; RCT, randomized controlled trial; SEM, standard error of the mean. n = number of patients analyzed at each timepoint. [a]Based on time normalized number of attacks per 4 weeks. [b]1 month = 4 weeks. [c]Deucrictibant IR capsule, 10 mg twice daily. [d]Deucrictibant IR capsule, 20 mg twice daily.

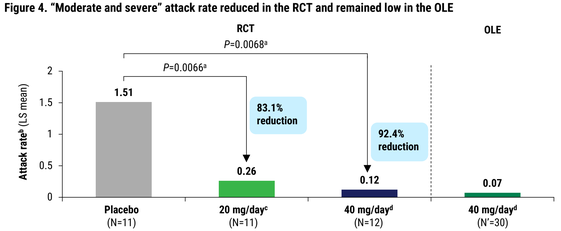
Results

Figure 3. Attack rate reduced in the OLE compared to study baseline



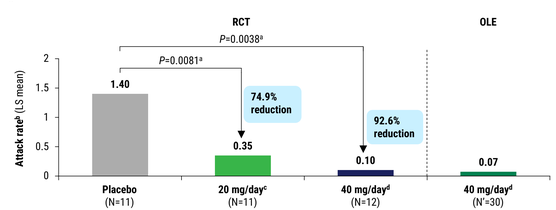
IR, immediate release; LS, least squares; OLE, open-label extension. N = number of participants in the OLE. [a]Based on time normalized number of attacks per 4 weeks. [b]Baseline attack rate is raw (unadjusted) mean. OLE attack rate is LS mean. LS mean estimate of attack rate is based on Poisson regression models adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied. [c]Deucrictibant IR capsule, 20 mg twice daily.

Figure 4. "Moderate and severe" attack rate reduced in the RCT and remained low in the OLE



IR, immediate release; LS, least squares; OLE, open-label extension; RCT, randomized controlled trial. N = number of participants randomized in each treatment group in the RCT. N' = number of participants in the OLE. LS mean estimates of attack rate are based on Poisson regression models adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied. *The *P*-values in this figure are nominal. [a]Based on time normalized number of attacks per 4 weeks. [c]Deucrictibant IR capsule, 10 mg twice daily. [d]Deucrictibant IR capsule, 20 mg twice daily.

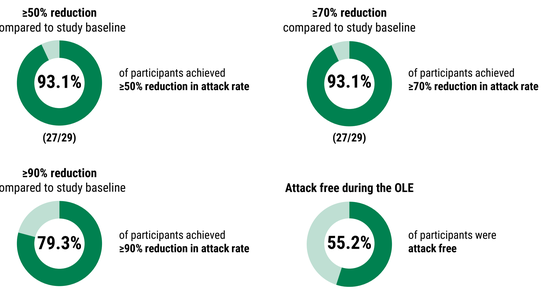
Figure 5. On-demand–treated attack rate reduced in the RCT and remained low in the OLE



IR, immediate release; LS, least squares; OLE, open-label extension; RCT, randomized controlled trial. N = number of participants randomized in each treatment group in the RCT. N' = number of participants in the OLE. LS mean estimates of attack rate are based on Poisson regression models adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied. *The *P*-values in this figure are nominal. [a]Based on time normalized number of attacks per 4 weeks. [c]Deucrictibant IR capsule, 10 mg twice daily. [d]Deucrictibant IR capsule, 20 mg twice daily.

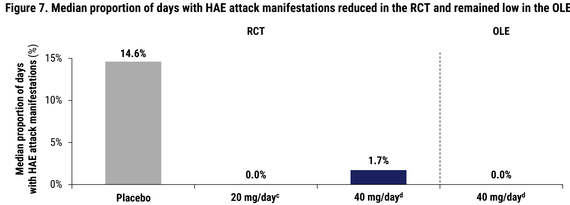
Results

Figure 6. Attack rate reduced relative to study baseline and over half of participants attack-free during the OLE



IR, immediate-release; OLE, open-label extension, RCT, randomized controlled trial. Participants with ≥4 weeks of treatment in the OLE receiving 40 mg/day (deucrictibant IR capsule, 20 mg twice daily).

Figure 7. Median proportion of days with HAE attack manifestations reduced in the RCT and remained low in the OLE



HAE, hereditary angioedema; IR, immediate release; OLE, open-label extension; RCT, randomized controlled trial. N = Number of participants with ≥4 weeks of treatment in the RCT. N' = Number of participants with ≥4 weeks of treatment in the OLE. [c]Deucrictibant IR capsule, 10 mg twice daily. [d]Deucrictibant IR capsule, 20 mg twice daily.

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

COI: M.A.R.: Astria, BioCryst, BioMarin, Celldex, CSL Behring, Cycle Pharma, Grifols, Intellia, Ionis, KalVista, Novartis, Pharming, Pharvaris, Sanofi-Regeneron, Takeda. **J.A.:** BioCryst, BioMarin, CSL Behring, Cycle Pharma, KalVista, Pharming, Pharvaris, Takeda; **F.A.:** CSL Behring, Takeda; **M.C.:** BioCryst, CSL Behring, KalVista, Menarini, MSD, Novartis, Pharming, Pharvaris, Sobi, Takeda, UCB; **H.C.:** AstraZeneca (Alexion), CSL Behring, KalVista, Merck, Novartis, Pharming, Pharvaris, Roche, Sanofi, Sobi, Takeda; **N.C.:** Novartis, Takeda; **E.E.:** Biocryst, Dr. Falk Pharma, Novartis, Pharming, Pharvaris; **M.G.:** BioCryst, CSL Behring, Novartis; **S.G.:** Baxter, CSL Behring, Dyax, Grifols, Pharming/Swedish Orphan, Takeda, Viropharma; **M.D.G.:** CSL Behring; **P.G.:** BioCryst, CSL Behring, KalVista, Pharming, Takeda; **T.K.:** BioCryst, CSL Behring, KalVista, Novartis, Pharvaris, Sanofi/Regeneron, Takeda; **M.M.:** BioCryst, CSL Behring, Intellia, KalVista, Novartis, Octapharma, 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; **M.S.:** BioCryst, CSL Behring, KalVista, Pharming, Takeda; **M.D.T.:** none; **A.V.:** AstraZeneca, Berlin-Chemie/Menarini Group, CSL Behring, KalVista, Novartis, Pharming, Pharvaris, Sobi, Takeda; **H.J.W.:** BioCryst, BioMarin, CSL Behring, Genentech, GSK, Takeda; **W.H.Y.:** Aimmune, ALK, Amgen, AnaptysBio, Astan Therapeutics, AstraZeneca, BioCryst, Celgene, CSL Behring, DBV Technologies, Dermira, Eli Lilly, Galderma, Genentech/Roche, Glenmark, GSK, Haleon, Incyte Biosciences, Ionis, Merck, Novartis, Novavax, Pharming, Pharvaris, Providence, Regeneron, Sanofi Genzyme, Takeda, VBI; medical advisor (volunteer) for Hereditary Angioedema Canada, a patient organization; member of Angioedema Centers of Reference and Excellence; **A.Z.:** BioCryst, CSL Behring, KalVista, Pharming, Takeda; **R.C.:** Employee of RC Consultancy and consultant to Pharvaris, holds stocks in Pharvaris; **S.M.:** Employee of Mulders Clinical Consulting and consultant to Pharvaris, holds stocks in Pharvaris; **J.L.:** Employee of Pharvaris, holds stocks in Pharvaris; **U.F.:** Employee of Pharvaris, holds stocks in Pharvaris; **U.K.:** Employee of Pharvaris, holds stocks in Pharvaris; **J.K.:** Employee of JCK Consult and consultant to Pharvaris, holds stocks/stock options in Pharvaris; **A.L.:** Employee of GrayMatters Consulting and consultant to Pharvaris, holds stocks/stock options in Pharvaris; advisor to Kosa Pharma; **P.L.:** Employee of Pharvaris, holds stocks/stock options in Pharvaris; **E.A-P.:** Astria, BioCryst, BioMarin, CSL Behring, Intellia, KalVista, Pharming, Pharvaris, Takeda.

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