Poster #20

Long-Term Prophylactic Treatment with Oral Deucrictibant Improves Disease Control and Health-Related Quality of Life in Participants with Hereditary Angioedema: CHAPTER-1 Open-Label Extension Study

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Key takeaways

The ongoing Phase 2 CHAPTER-1 open-label extension (OLE) provides additional evidence on the sustained effects of long-term prophylactic treatment with oral deucrictibant on disease control, health-related quality of life (HRQoL), and treatment satisfaction for participants with hereditary angioedema (HAE).

PGA-Change	AE-QoL	AECT	TSQM
100% of participants who received deucrictibant 40 mg/day reported improved HRQoL at weeks 12 and 62	Week 4 → Week 62: **Clinically meaningful improvement in HRQoL at week 4 and effects sustained through week 62**	**100%** of participants with a week 62 assessment reported well-controlled HAE	**Treatment satisfaction** High in participants receiving deucrictibant up to week 12 and sustained in the OLE

AECT, Angioedema Control Test; AE-QoL, Angioedema Quality of Life Questionnaire; HRQoL, health-related quality of life; PGA-Change, Patient Global Assessment of Change; TSQM, Treatment Satisfaction Questionnaire for Medication.

Background

- **Hereditary angioedema (HAE):** a bradykinin-mediated condition with painful swelling attacks affecting multiple locations in the body and negatively impacting HRQoL.[1-7]
- **Unmet need:** additional prophylactic treatments offering injectable-like efficacy, a well-tolerated profile, and ease of administration.[8-11]
- **Oral deucrictibant:** a selective, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of HAE attacks.[11-22]

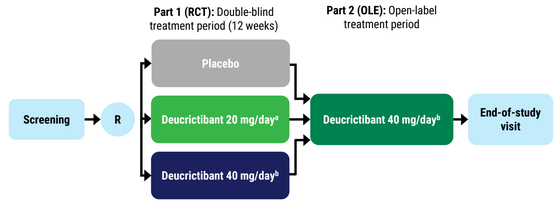
Objective

Evaluate the impact of deucrictibant treatment on disease control, HRQoL, and treatment satisfaction through 62 weeks in adult participants with HAE in the CHAPTER-1 OLE study (data snapshot 10 June 2024).[18]

Methods

- **CHAPTER-1 (NCT05047185)*:** a two-part, Phase 2 study.[18]
  - Part 1 randomized 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.

Methods

- **Patient Global Assessment of Change (PGA-Change)[23]:** a tool to measure the change in the impact of HAE on patient's HRQoL since starting study treatment compared with pre-treatment:

Much worse	A little worse	No change	A little better	Much better

- **Angioedema Quality of Life Questionnaire (AE-QoL)[24-26]:** a tool validated for HAE and comprising a 17-item questionnaire across four domains, "functioning", "fatigue/mood", "fear/shame", and "nutrition", on a five-point response scale:

Very often	Often	Sometimes	Rarely	Never

- **Angioedema Control Test (AECT)[27,28]:** a four-item questionnaire with a five-point response scale developed and validated to retrospectively quantify disease control and aid management decisions in patients with recurrent angioedema (AECT-4Wk — four-week recall used):

0	1	2	3	4

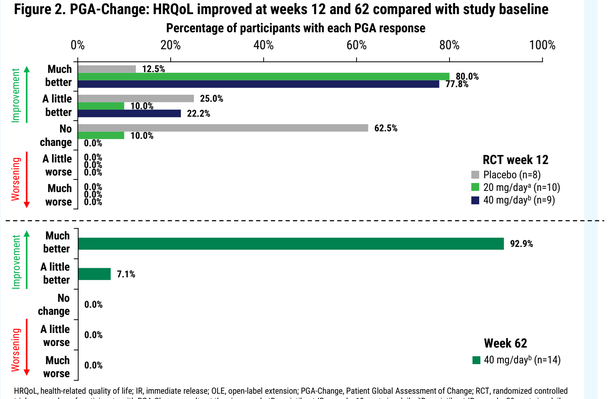
- **Treatment Satisfaction Questionnaire for Medication (TSQM) Version II[29]:** an 11-item questionnaire to gauge patients' satisfaction with "effectiveness", "side effects", "convenience", and "global satisfaction" of a medication:

Extremely dissatisfied	Somewhat satisfied	Extremely satisfied

Results

- All 30 participants who completed the Part 1 RCT enrolled in the Part 2 OLE.
  - At data cutoff: five participants had discontinued. 25 were ongoing, of which 14 had reached at least the week 62 visit.
- This analysis included the 14 participants who had reached at least the week 62 visit.
  - Mean (SD) exposure to deucrictibant 40 mg/day for these 14 participants in the OLE: 16.9 (3.0) months.
  - Min-max exposure in the OLE: 12.4–20.8 months.
  - Maximum exposure to deucrictibant in the entire study: 23.7 months.

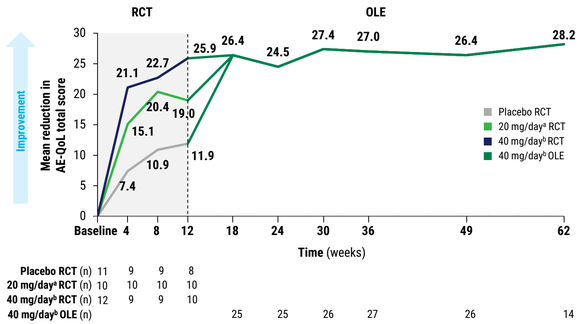
Figure 2. PGA-Change: HRQoL improved at weeks 12 and 62 compared with study baseline



HRQoL, health-related quality of life; IR, immediate release; OLE, open-label extension; PGA-Change, Patient Global Assessment of Change; RCT, randomized controlled trial. n = number of participants with PGA-Change results at the given week. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

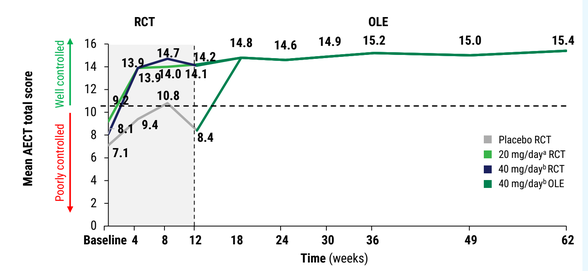
Results

Figure 3. AE-QoL: Improvement in HRQoL by week 4 and effects sustained through week 62



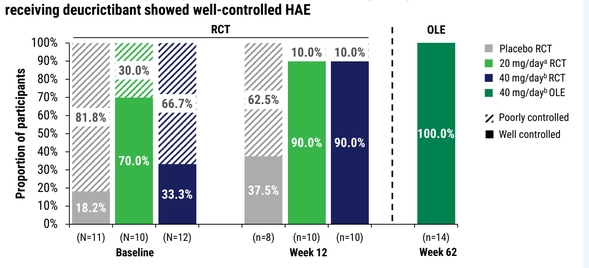
AE-QoL, Angioedema Quality of Life Questionnaire; HRQoL, health-related quality of life; IR, immediate release; OLE, open-label extension; RCT, randomized controlled trial. n = number of participants with AE-QoL data at the given week. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

Figure 4. AECT: Improvement in disease control by week 4 and effects sustained through week 62



AECT, Angioedema Control Test; HAE, hereditary angioedema; IR, immediate release; OLE, open-label extension; RCT, randomized controlled trial. n = number of participants with AECT results at the given week. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

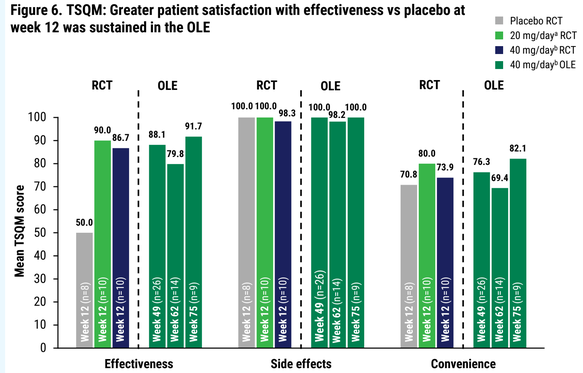
Figure 5. AECT: 90% of participants at 12 weeks and 100% of participants at 62 weeks receiving deucrictibant showed well-controlled HAE



AECT, Angioedema Control Test; HAE, hereditary angioedema; IR, immediate release; OLE, open-label extension; RCT, randomized controlled trial. N = number of participants randomized to each treatment group in the RCT. n = number of participants with AECT results at the given week. [a]Deucrictibant IR capsule,10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

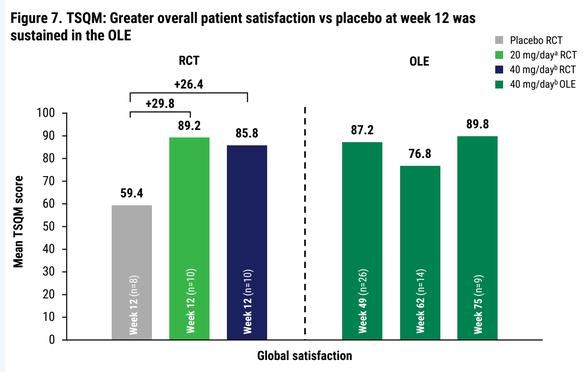
Results

Figure 6. TSQM: Greater patient satisfaction with effectiveness vs placebo at week 12 was sustained in the OLE



IR, immediate release; OLE, open-label extension; RCT, randomized controlled trial; TSQM, Treatment Satisfaction Questionnaire for Medication. n = number of participants with TSQM results at the given week. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

Figure 7. TSQM: Greater overall patient satisfaction vs placebo at week 12 was sustained in the OLE



IR, immediate release; OLE, open-label extension; RCT, randomized controlled trial; TSQM, Treatment Satisfaction Questionnaire for Medication. n = number of participants with TSQM results at the given week. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

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

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COI: M.E.M.: Astria, AstraZeneca, BioCryst, Blueprint, CSL Behring, Celldex, Cogent, GSK, Ionis, Intellia, KalVista, Merck, Novartis, Pharming, Pharvaris, Regeneron, Takeda, Teva; **J.A.:** Astria, BioCryst, CSL Behring, Ionis, KalVista, Pharming, Pharvaris, Takeda; **F.A.:** CSL Behring, Takeda; **E.A-P.:** Astria, BioCryst, BioMarin, CSL Behring, Intellia, Kalvista, Pharming, Pharvaris, Takeda; **M.C.:** BioCryst, CSL Behring, KalVista, Menarini, MSD, Novartis, Otsuka, Pharming, Pharvaris, Sobi, Takeda, UCB; **H.C.:** AstraZeneca (Alexion), CSL Behring, KalVista, Merck, Novartis, Pharming, Pharvaris, Roche, Sanofi, Sobi, Takeda; **N.C.:** BioCryst, CSL Vifor, GSK, Novartis, Pharvaris, Pharming, Takeda; **E.E.:** BioCryst, Dr Falk Pharma, Novartis, Pharming; **M.G.:** BioCryst, CSL Behring, Novartis, member of the immunology clinical reference group; **S.G.:** Baxter, CSL Behring, Dyax, Grifols, Pharming/Swedish Orphan, Takeda, ViroPharma; **M.D.G.:** BioCryst, CSL Behring, Takeda; **P.G.** BioCryst, CSL Behring, KalVista, Pharming, Takeda; **S.K-A.:** BioCryst, Biotest, CSL Behring, Ionis, KalVista, Otsuka, Pharvaris, Takeda; **T.K.:** BioCryst, CSL Behring, KalVista, Otsuka, Pharvaris, Sanofi/Regeneron, Takeda; **M.M.:** Astria, BioCryst, CSL Behring, Intellia, KalVista, Novartis, Octapharma, Otsuka, Pharvaris, Takeda; **M.S.:** BioCryst, CSL Behring, KalVista, Pharming, Pharvaris, Takeda; **M.D.T.:** no conflicts of interests to disclose relative to this work; **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 Therapeutics, ALK Abello, AnaptysBio, Areteia, Aslan, AstraZeneca, Astria, BioCryst, Blueprint, Bristol Myers, Celgene, Celldex, CSL Behring, DBV Technologies, Dermira, Eli Lilly, Escient, Galderma, Genentech, GSK, Glenmark, Haleon, Incyte, Intellia, Ionis, Merck, Moderna, Novartis, Novavax, Pharming, Pharvaris, Providence, RAPT Therapeutics, Regeneron, Roche, Sanofi, Stallergenes, Takeda, Upstream Bio, 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, Pharvaris, 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., U.F., U.K.:** employees of Pharvaris, hold 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 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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