Patient-Reported Outcomes in the Open-Label Extension of the CHAPTER-1 Study Assessing Long-Term Prophylactic Treatment With Oral Deucrictibant in Participants With Hereditary Angioedema

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Key takeaways

Final data from the completed open-label extension (OLE) of the Phase 2 CHAPTER-1 study provide further evidence on the sustained effects of long-term prophylactic treatment with the orally administered bradykinin B2 receptor antagonist deucrictibant on health-related quality of life (HRQoL), disease control, and treatment satisfaction for participants with hereditary angioedema (HAE).

PGA-Change

100%

of participants who received deucrictibant 40 mg/day at weeks 12 and 134 reported improved HRQoL

AE-QoL

Week 4 → Week 134

Clinically meaningful improvement in HRQoL at week 4 and effects sustained through week 134

AECT

>96%

of participants at weeks 18–134 in the OLE reported well-controlled HAE[a]

TSQM

Week 12 → Week 134

Greater overall participant satisfaction vs placebo at week 12 remained high through week 134

AECT, Angioedema Control Test; AE-QoL, Angioedema Quality of Life Questionnaire; HAE, hereditary angioedema; HRQoL, health-related quality of life; OLE, open-label extension; PGA-Change, Patient Global Assessment of Change; TSQM, Treatment Satisfaction Questionnaire for Medication. [a]Well-controlled HAE defined as AECT score ≥10.

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

Background

- **Hereditary angioedema (HAE):** a bradykinin-mediated condition with painful swelling attacks affecting multiple locations in the body and negatively impacting health-related quality of life (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 attacks of bradykinin-mediated angioedema, including HAE.[11-22]

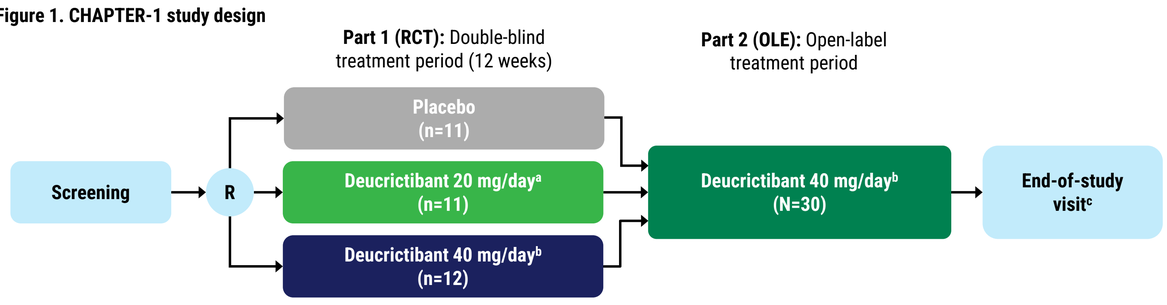
Objective

To evaluate the long-term impact of orally administered deucrictibant prophylactic treatment on HRQoL, disease control, and treatment satisfaction in adults with HAE in the open-label extension (OLE) of the CHAPTER-1 study.[19]

Methods

- **CHAPTER-1 (NCT05047185)*:** a two-part, Phase 2 study.[19]
  - Part 1 randomized controlled trial (RCT) and part 2 OLE were completed.
- **Eligible participants:** adults diagnosed with HAE-1/2, not receiving other prophylactic treatments at screening, and with a pre-specified minimum number of attacks in the 3 months prior to screening.

Figure 1. CHAPTER-1 study design



IR, immediate-release; OLE, open-label extension; R, randomization; RCT, randomized controlled trial. n = number of participants randomized in each treatment group in the RCT. N = number of participants. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily. [c]Twenty-one participants rolled over to the CHAPTER-4 open-label study (NCT06679881)[18] in which deucrictibant extended-release tablet is administered.

Patient-reported outcome instruments

Patient Global Assessment of Change (PGA-Change)[23]: a tool that uses a five-point Likert response scale to assess the change in the impact of HAE on patients' 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 composed of a 17-item questionnaire with a five-point response scale used across four domains, "functioning", "fatigue/mood", "fear/shame", and "nutrition":

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 measure disease control and aid management decisions in patients with recurrent angioedema (AECT-4wk — 4-week recall used):

0 → 1 → 2 → 3 → 4

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

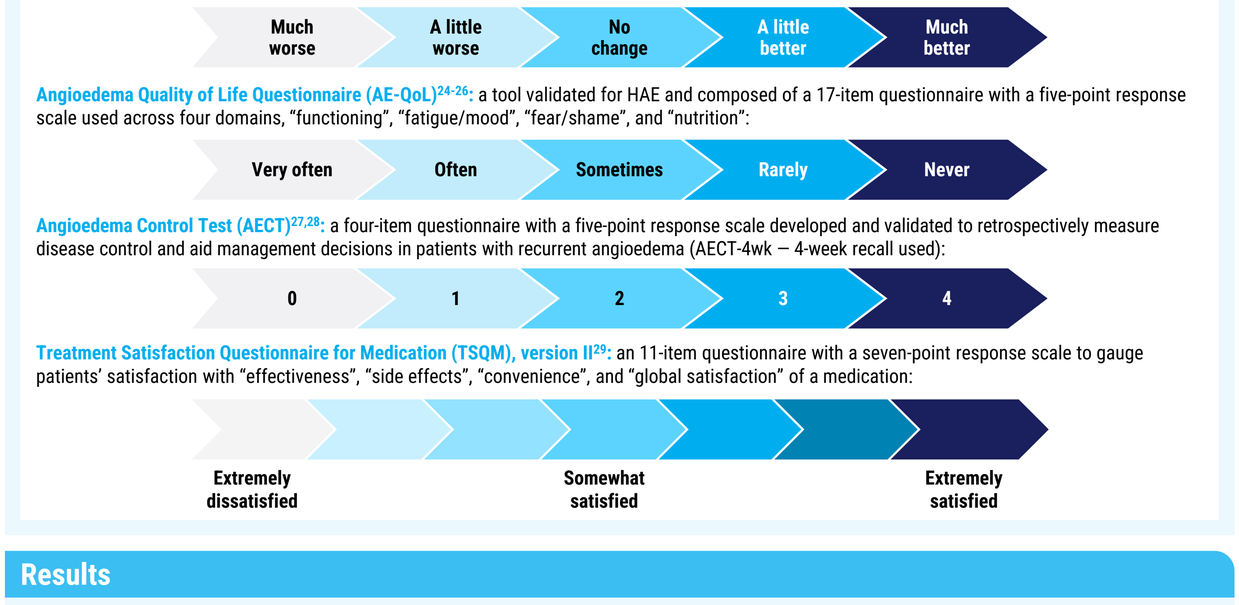
Extremely dissatisfied → Somewhat satisfied → Extremely satisfied

Results

- This analysis included all 30 participants who completed the Part 1 RCT and enrolled into the Part 2 OLE. Twenty-one participants were on study at the time of CHAPTER-1 study end, and all continued into the ongoing CHAPTER-4 open-label study (NCT06679881)[18] in which deucrictibant extended-release (XR) tablet once daily is self-administered. None of the nine discontinuations in the CHAPTER-1 OLE were reported as treatment-related or associated with an adverse event.
  - Mean (SD) treatment duration in the OLE was 22.2 (8.1) months.
  - Maximum deucrictibant exposure during the entire study was 33.8 months.

Health-related quality of life using PGA-Change

Figure 2. PGA-Change: HRQoL improved at week 12 and through week 134 compared with study baseline

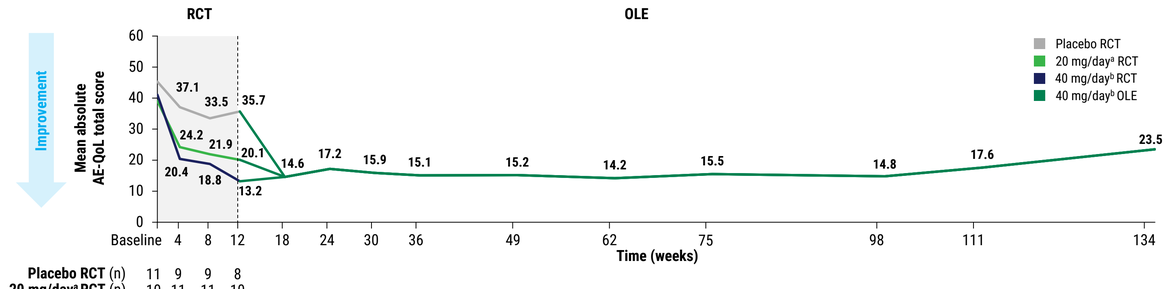


HRQoL, health-related quality of life; IR, immediate-release; OLE, open-label extension; PGA-Change, Patient Global Assessment of Change; RCT, randomized controlled trial. n = number of participants with PGA-Change results at the given week. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant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

Results

Health-related quality of life using AE-QoL

Figure 3. AE-QoL: Improvement in total score by week 4 and effects sustained through week 134



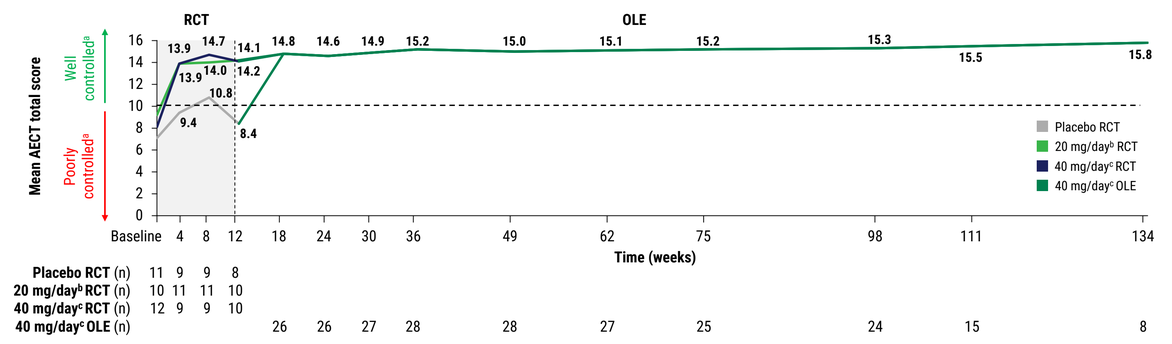
	Baseline	4	8	12	18	24	30	36	49	62	75	98	111	134
Placebo RCT (n)	11	9	9	8										
20 mg/day[a] RCT (n)	10	11	11	10										
40 mg/day[b] RCT (n)	12	9	9	10										
40 mg/day[b] OLE (n)					26	26	27	28	28	27	25	24	15	8

AE-QoL, Angioedema Quality of Life Questionnaire; 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.

- For deucrictibant-treated participants at week 12 of the RCT, "functioning" and "fear/shame" showed the most improvement of the AE-QoL domains with mean reductions from study baseline of 32.5 and 22.9 with deucrictibant 20 mg/day and 33.1 and 35.4 with deucrictibant 40 mg/day, respectively.
  - These reductions from study baseline were sustained from week 18 to week 134 of the OLE, with mean reductions in AE-QoL "functioning" scores of 36.5 at week 18 and 50.8 at week 134, and mean reductions in AE-QoL "fear/shame" scores of 34.0 at week 18 and 30.7 at week 134.

Disease control

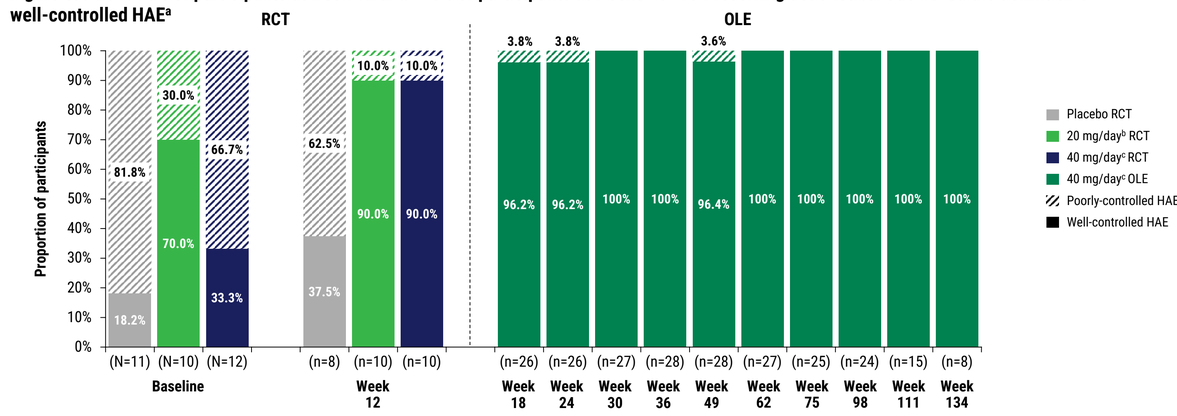
Figure 4. AECT: Improvement in disease control by week 4 and effects sustained through week 134



	Baseline	4	8	12	18	24	30	36	49	62	75	98	111	134
Placebo RCT (n)	11	9	9	8										
20 mg/day[b] RCT (n)	10	11	11	10										
40 mg/day[c] RCT (n)	12	9	9	10										
40 mg/day[c] OLE (n)					26	26	27	28	28	27	25	24	15	8

AECT, Angioedema Control Test; HAE, hereditary angioedema; IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial. n = number of participants with AECT data at the given week. [a]Poorly controlled HAE defined as AECT score <10; well-controlled HAE defined as AECT score ≥10.[26,27] [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily.

Figure 5. AECT: 90% of participants at week 12 and >96% of participants at weeks 18–134 receiving deucrictibant achieved the definition of well-controlled HAE[a]

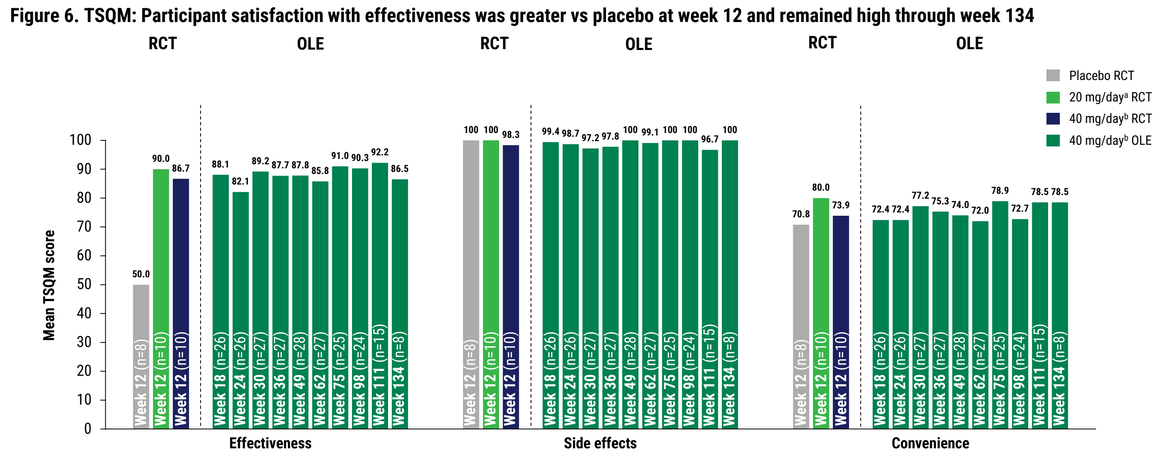


AECT, Angioedema Control Test; HAE, hereditary angioedema; IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial. N = number of participants randomized to each treatment group in the RCT with AECT data. n = number of participants with AECT results at the given week. [a]Well-controlled HAE defined as AECT score ≥10.[26,27] [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily.

- The majority of participants (>60%) had achieved the maximum AECT-4wk score of 16 at weeks 62–134.

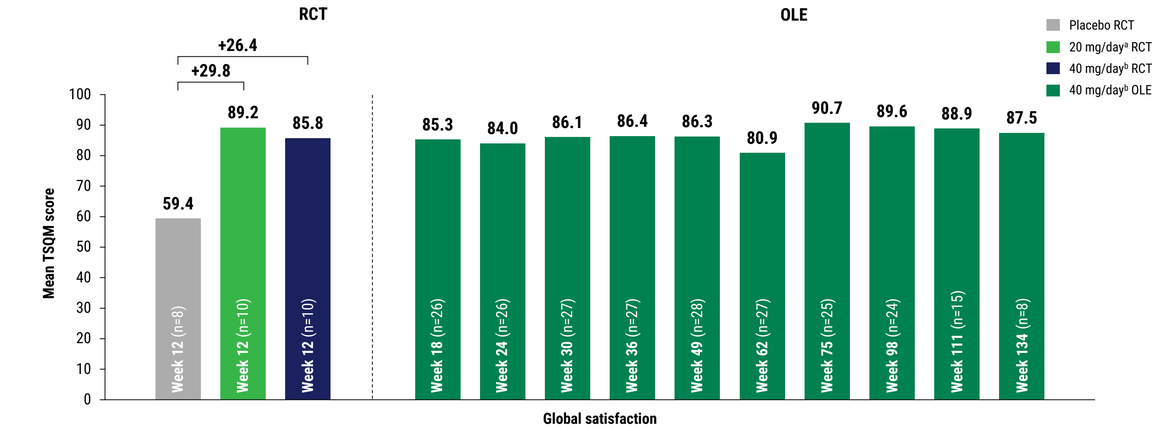
Treatment satisfaction

Figure 6. TSQM: Participant satisfaction with effectiveness was greater vs placebo at week 12 and remained high through week 134



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: Overall participant satisfaction was greater vs placebo at week 12 and remained high through week 134



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.

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COI: M.M.: Argo, Astria, BioCryst, CSL Behring, Intellia, KalVista, Octapharma, Otsuka, Pharvaris, Takeda; **J.A.:** Astria, BioCryst, CSL Behring, Intellia, Ionis, KalVista, Pharming, Pharvaris, Takeda; **F.A.:** BioCryst, CSL Behring, KalVista, Otsuka, Takeda; **M.C.:** ADARx, BioCryst, Chiesi, CSL Behring, Gentili, KalVista, Menarini, MSD, NeoPharmed, Novartis, Otsuka, Pharming, Pharvaris, Sobi, Takeda, UCB; **H.C.:** AstraZeneca (Alexion), CSL Behring, KalVista, Merck, Novartis, Pharming, Pharvaris, Roche, Sanofi, Sobi, Takeda; **N.C.:** ALK, BioCryst, CSL Vifor, HSE Dublin and Midlands, Laboratory Reform, GSK, Novartis, Pharming, Pharvaris, Takeda; **E.E.:** Biocryst, Dr. Falk Pharma, Novartis, Pharming, Pharvaris; **M.G.:** none to disclose; **S.G.:** BioCryst, BioCryst/ Neopharmed Gentili, CSL Behring, KalVista, Otsuka, Pharming, Pharvaris, Takeda; **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.:** ADARx, Astria, BioCryst, CSL Behring, KalVista, Otsuka, Pharvaris, Sanofi, Takeda; **M.E.M.:** AstraZeneca, Astria, BioCryst, Blueprint, Celldex, Cogent, CSL Behring, GSK, Intellia, Ionis, KalVista, Merck, Novartis, Pharming, Pharvaris, Regeneron, Takeda, Teva; **M.S.:** BioCryst, CSL Behring, KalVista, Pharming, Pharvaris, Takeda; **M.D.T.:** none to report; **A.V.:** ADARx, AstraZeneca, Astria, Bulgarian Society of Allergology, Chiesi, CSL Behring, EAACI Angioedema Working Group, Ionis, Kalvista Pharmaceuticals, Novartis, Pharming, Pharvaris, Takeda; **H.J.W.:** BioCryst, BioMarin, CSL Behring, Genentech, GSK, Takeda; **W.H.Y.:** Aimmune Therapeutics, ALK Abelló, AnaptysBio, Angioedema Centers of Reference and Excellence, Areteia, Aslan, AstraZeneca, Astria, BioCryst, Blueprint, Bristol Myers Squibb, Celgene, Celldex, CSL Behring, DBV Technologies, Dermira, Eli Lilly, Escient, Galderma, Genentech, Glenmark, GSK, Haleon, Hereditary Angioedema Canada, Incyte, Intellia, Ionis, Merck, Moderna, Novartis, Novavax, Pharming, Pharvaris, Providence, RAPT Therapeutics, Regeneron, Roche, Sanofi, Stallergenes, Takeda, Upstream Bio, VBI; **A.Z.:** Astria, BioCryst, CSL Behring, Intellia, KalVista, Otsuka, 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, P.L.:** 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; consultant to Pharvaris; holds stocks/stock options in Pharvaris; advisor to Kosa Pharma; **E.A-P.:** Astria, BioCryst, BioMarin, CSL Behring, Intellia, KalVista, Otsuka, Pharming, Pharvaris, Takeda; **M.A.R.:** ADARx, Astria, BioCryst, BioMarin, Celldex, CSL Behring, Cycle Pharma, Grifols, Intellia, Ionis, KalVista, Novartis, Pharming, Pharvaris, Sanofi-Regeneron, Takeda, US Hereditary Angioedema Association.

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