CHAPTER-1 Open-Label Extension Study: Long-Term Prophylactic Treatment with Oral Deucrictibant Improved Health-Related Quality of Life 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

100%

of participants at weeks 62–134 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, investigational, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of attacks of bradykinin-mediated angioedema, including HAE.[11-23]

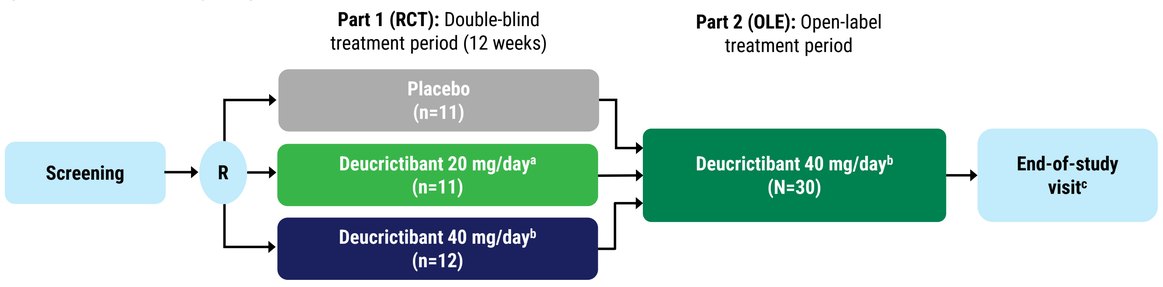
Objective

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.[18]

Methods

- **CHAPTER-1 (NCT05047185)*:** a two-part, Phase 2 study.[18,21]
  - 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[20] (NCT06679881) OLE in which deucrictibant extended-release tablet is administered.

Patient-reported outcome instruments

Patient Global Assessment of Change (PGA-Change)[24]: a tool that uses a five-point Likert response scale to assess 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)[25-27]: 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)[28,29]: 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 — 4-week recall used):

0 | 1 | 2 | 3 | 4

Treatment Satisfaction Questionnaire for Medication (TSQM), version II[30]: 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:

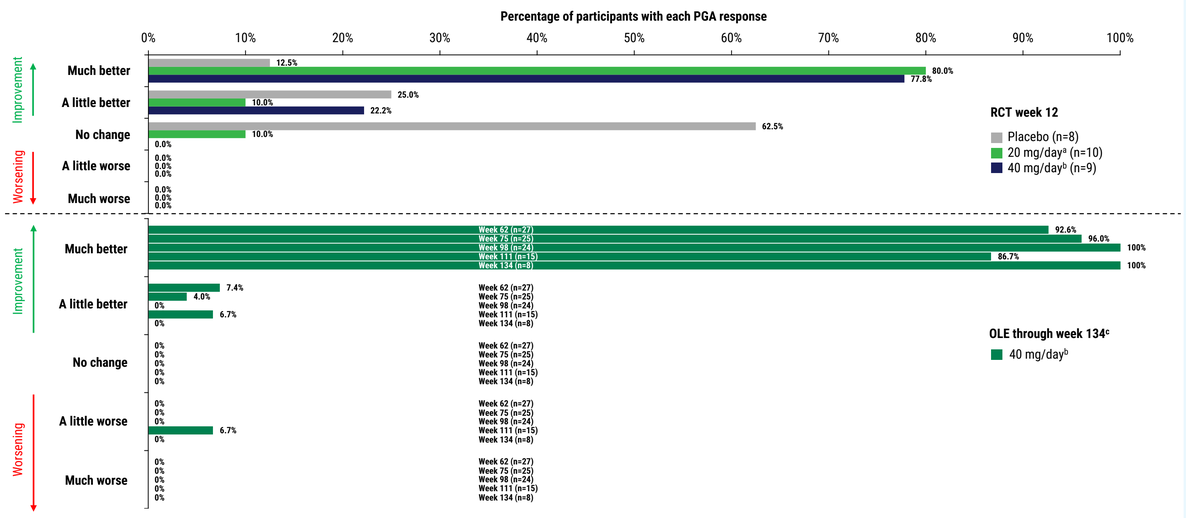
Extremely dissatisfied | Somewhat satisfied | Extremely satisfied

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 OLE (NCT06679881)[20] in which deucrictibant extended-release (XR) tablet is self-administered. None of the 9 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

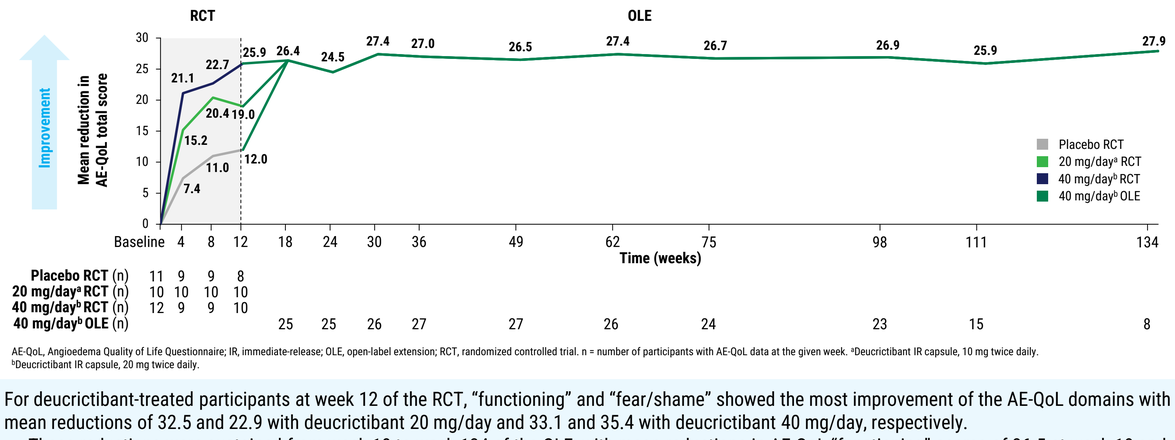


HRQoL, health-related quality of life; IR, immediate-release; OLE, open-label extension; PGA-Change, Patient Global Assessment of Change; RCT, randomized controlled trial. n = number of participants with PGA-Change results at the given week. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant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

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



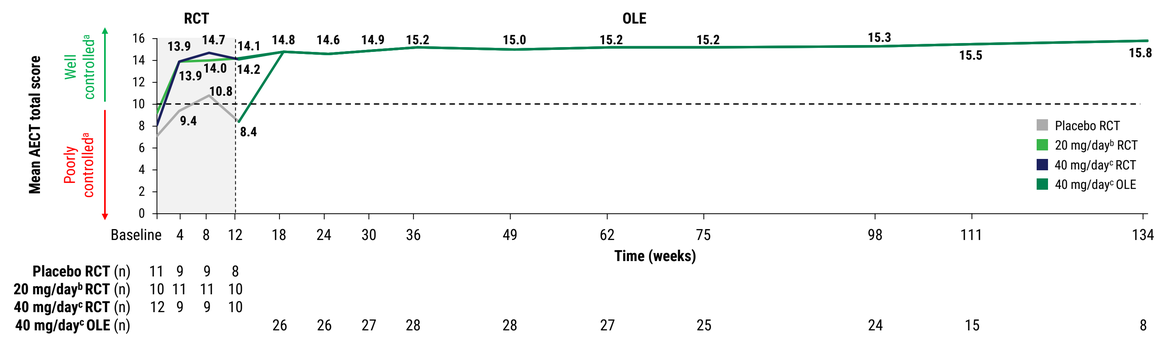
AE-QoL, Angioedema Quality of Life Questionnaire; IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial. n = number of participants with AE-QoL data at the given week. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

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 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 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.

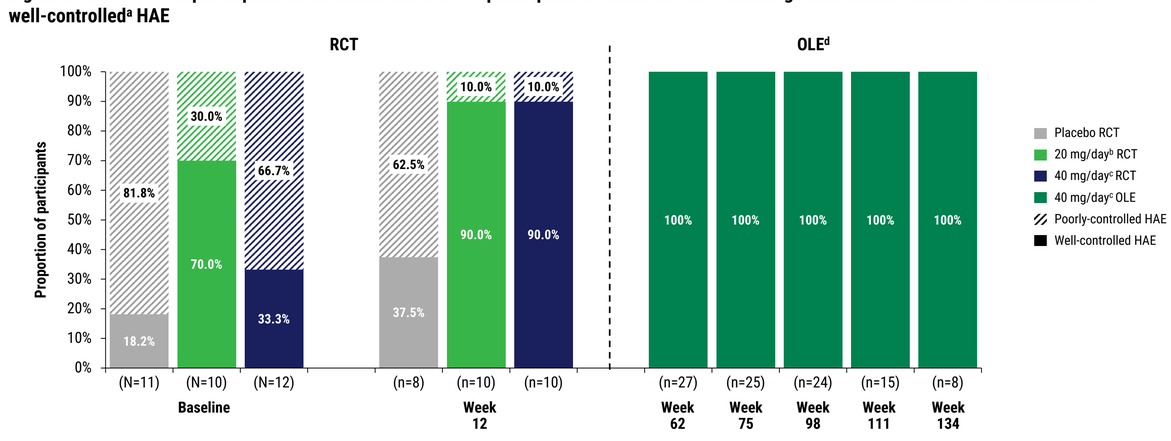
Disease control

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



AECT, Angioedema Control Test; 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.[28,29] [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily.

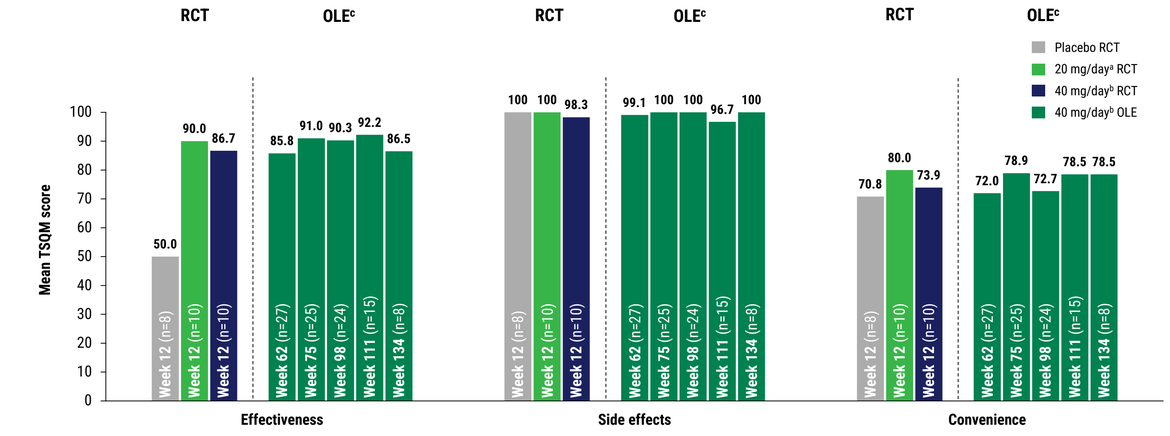
Figure 5. AECT: 90% of participants at 12 weeks and 100% of participants at weeks 62–134 receiving deucrictibant achieved the definition of well-controlled[a] HAE



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 with AECT data. n = number of participants with AECT results at the given week. [a]Well-controlled HAE defined as AECT score ≥10.[28,29] [b]Deucrictibant IR capsule,10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily. [d]Data are shown for the final five visits during the OLE.

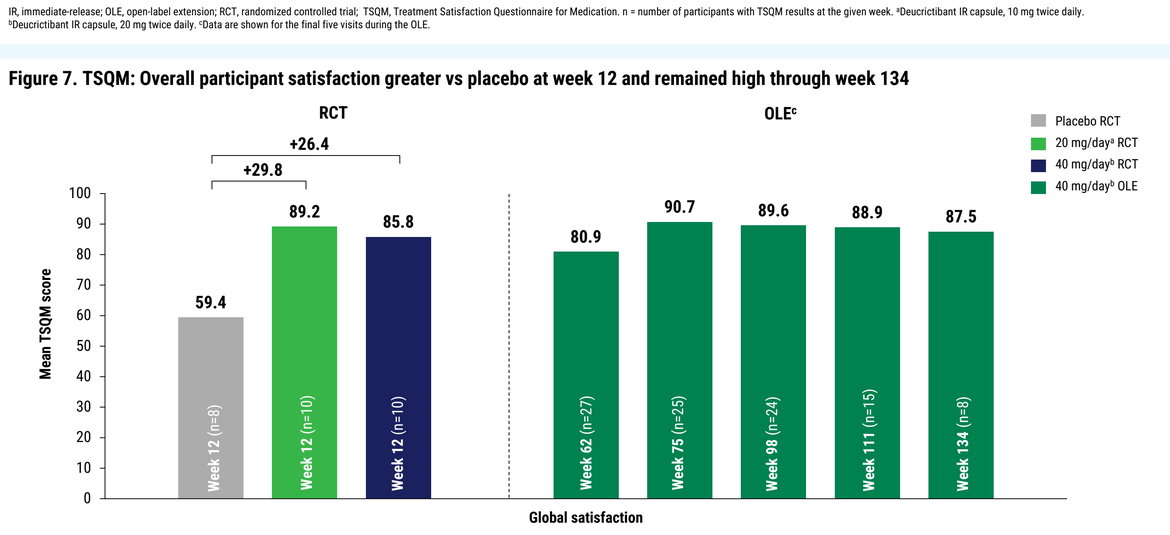
Treatment satisfaction

Figure 6. TSQM: Participant satisfaction with effectiveness 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. [c]Data are shown for the final five visits during the OLE.

Figure 7. TSQM: Overall participant satisfaction 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. [c]Data are shown for the final five visits during the OLE.

References

1. Busse PJ, et al. *N Engl J Med*. 2020;382:1136-48. **2**. Maurer M, et al. *Allergy*. 2022;77:1961-90. **3**. Bork K, et al. *Allergy Asthma Clin Immunol*. 2021;17:40. **4**. Bygum A, et al. *Front Med*. 2017;4:212. **5**. Mendivil J, et al. *Orphanet J Rare Dis*. 2021;16:94. **6**. Chong-Neto HJ. *World Allergy Organ J*. 2023;16:100758. **7**. Lumry WR, et al. *Allergy Asthma Proc*. 2010;31(5):407-14. **8**. Bouillet L, et al. *Allergy Asthma Proc*. 2022;43:406-12. **9**. Covella B, et al. *Future Pharmacol*. 2024;4:41-53. **10**. Center for Biologics Evaluation and Research. The voice of the patient – hereditary angioedema. US Food and Drug Administration; May 2018. https://www.fda.gov/media/113509/download. Accessed February 25, 2026. **11**. Betschel SD, et al. *J Allergy Clin Immunol Pract*. 2023;11:2315-25. **12**. Lesage A, et al. *Front Pharmacol*. 2020;11:916. **13**. Lesage A, et al. *Int Immunopharmacol*. 2022;105:108523. **14**. RAPIDe-1. https://clinicaltrials.gov/study/NCT04618211. Accessed February 25, 2026. **15**. RAPIDe-2. https://www.clinicaltrials.gov/study/NCT05396105. Accessed February 25, 2026. **16**. RAPIDe-3. https://clinicaltrials.gov/study/NCT06343779. Accessed February 25, 2026.**17**. Maurer M, et al. *Lancet Haem*. 2026; In press. **18**. CHAPTER-1. https://www.clinicaltrials.gov/study/NCT05047185. Accessed February 25, 2026. **19**. CHAPTER-3. https://clinicaltrials.gov/study/NCT06669754. Accessed February 25, 2026. **20**. CHAPTER-4. https://clinicaltrials.gov/study/NCT06679881. Accessed February 25, 2026. **21**. Aygören-Pürsün E, et al. *Lancet Haem*. 2026; In press. **22**. CREAATE. https://clinicaltrials.gov/study/NCT07266805. Accessed February 25, 2026. **23**. Zanichelli A, et al. Presented at: 14th C1-Inhibitor Deficiency and Angioedema Workshop 2025. May 29–June 1, 2025; Budapest, Hungary. **24**. US Dept of Health, Education, and Welfare, Guy W. (Ed). ECDEU Assessment Manual for Psychopharmacology, 1976. **25**. Weller K, et al. *Allergy*. 2012;67:1289-98. **26**. Weller K, et al. *Allergy*. 2016;71:1203-9. **27**. Vanya M, et al. *J Patient Rep Outcomes*. 2023;7:33. **28**. Weller K, et al. *Allergy*. 2020;75:1165-77. **29**. Weller K, et al. *J Allergy Clin Immunol Pract*. 2020;8:2050-7. **30**. Atkinson MJ, et al. *Value Health*. 2005;8(s1):S9-S24.

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Acknowledgments: Medical writing support was provided by Jonny Turner, PhD, of Envision Spark, an Envision Medical Communications agency, a part of Envision Pharma Group, and funded by Pharvaris.

***CHAPTER-1 was a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: NCT05047185.**