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; 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.[11-21]

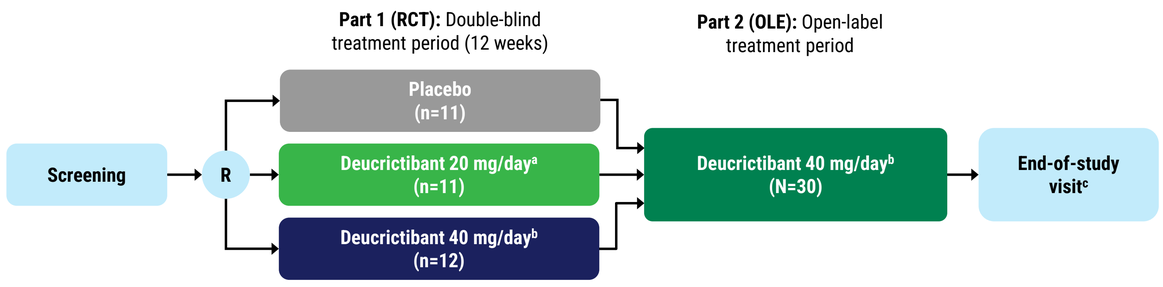
Objective

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)[22]: 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)[23-25]: 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)[26,27]: 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[28]: 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:

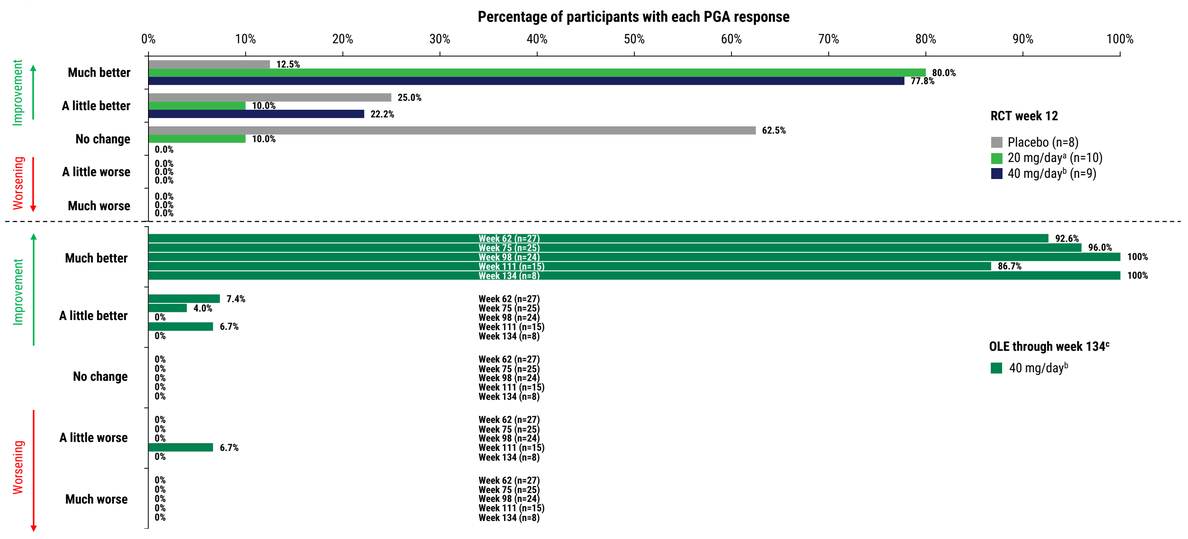
Extremely dissatisfied | Somewhat satisfied | Extremely satisfied

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 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

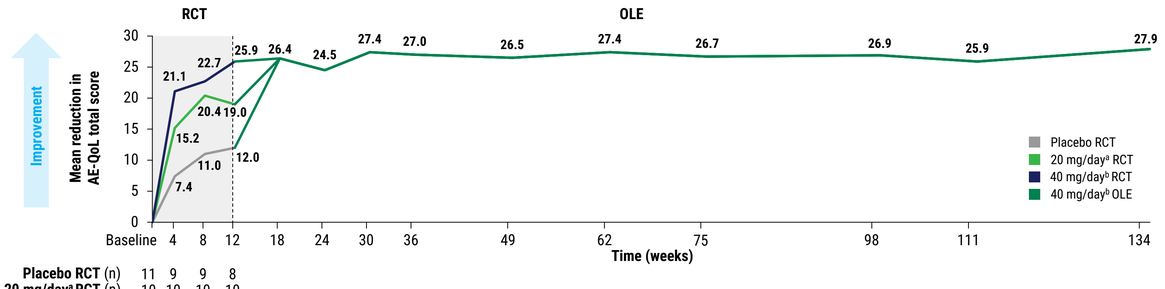


HRQoL, health-related quality of life; IR, immediate-release; OLE, open-label extension; PGA-Change, Patient Global Assessment of Change; RCT, randomized controlled trial. n = number of participants with PGA-Change results at the given week. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant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



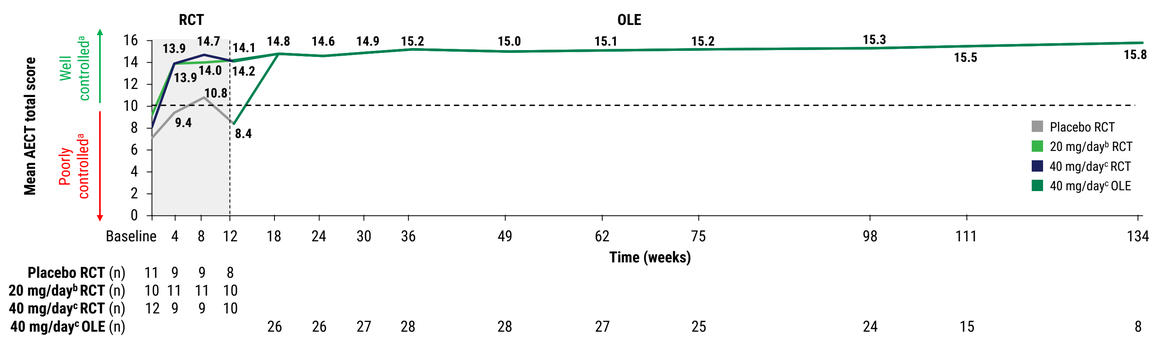
Baseline	4	8	12	18	24	30	36	49	62	75	98	111	134
Placebo RCT (n)	11	9	9	8										
20 mg/day[a] RCT (n)	10	10	10	10										
40 mg/day[b] RCT (n)	12	9	9	10										
40 mg/day[b] OLE (n)					25	25	26	27	27	26	24	23	15	8

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 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

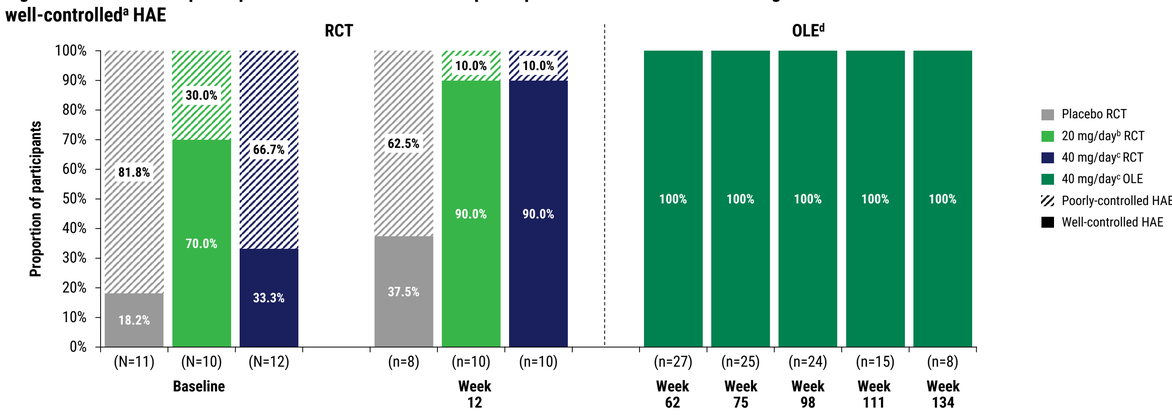
Figure 4. AECT: Improvement in disease control by week 4 and effects sustained through week 134



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 100% of participants at weeks 62–134 receiving deucrictibant achieved the definition of well-controlled[a] HAE

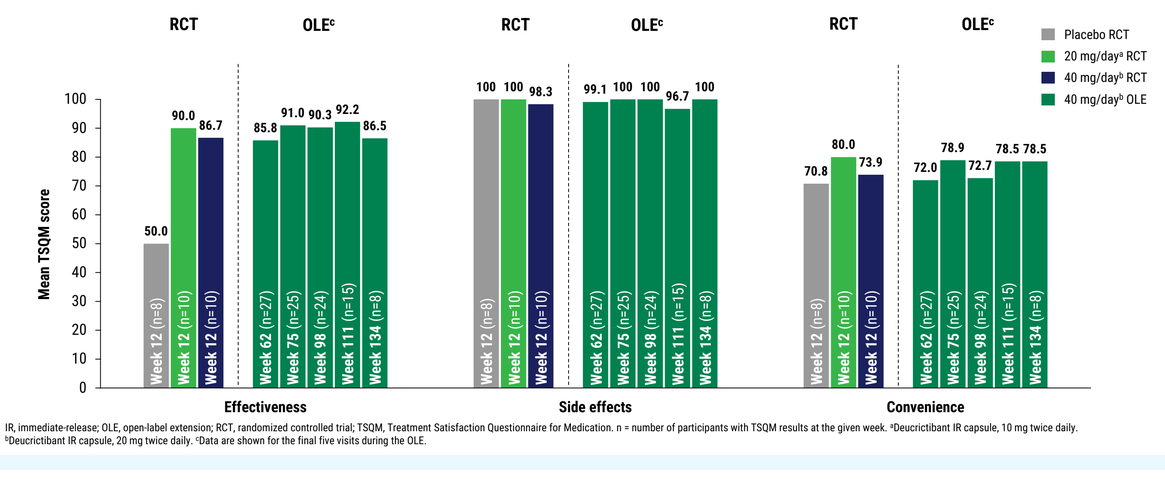


AECT, Angioedema Control Test; HAE, hereditary angioedema; IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial. N = number of participants randomized to each treatment group in the RCT with AECT data. n = number of participants with AECT results at the given week. [a]Well-controlled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

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

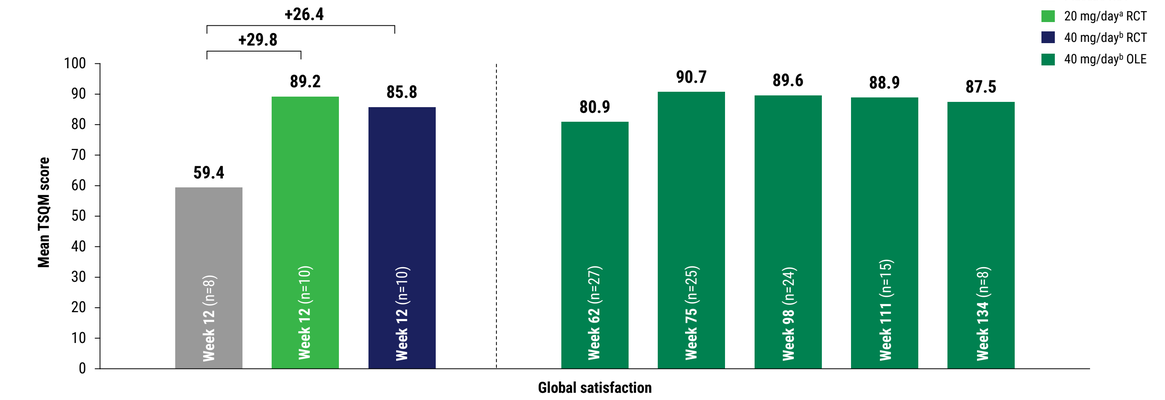
Treatment satisfaction

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. [c]Data are shown for the final five visits during the OLE.

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. [c]Data are shown for the final five visits during the OLE.

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