Long-Term Prophylactic Treatment With Oral Deucrictibant Improved Disease Control and Health-Related Quality of Life in Hereditary Angioedema: CHAPTER-1

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Key takeaways

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

OLE
Up to ~34 months
Duration of treatment reached in CHAPTER-1 RCT + OLE

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 who reached the final 5 timepoints in the OLE-reported well-controlled HAE[a]

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; RCT, randomized controlled trial. [a]Well-controlled HAE defined as AECT score ≥10.

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, investigational, orally administered bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of attacks of bradykinin-mediated angioedema, including HAE.[11-22]

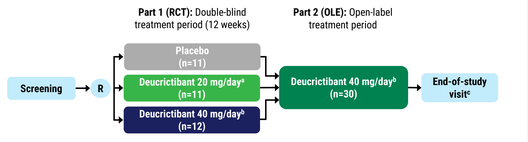
Objective

To evaluate the long-term impact of deucrictibant treatment on health-related quality of life (HRQoL) and disease control in adults with HAE.[18]

Methods

- **CHAPTER-1 (NCT05047185)*:** a two-part, Phase 2 study.[18,19]
  - Part 1 randomized controlled trial (RCT) and Part 2 (OLE) are complete.
- **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



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. [c]Twenty-one participants rolled over to the CHAPTER-4 (NCT05679881) OLE in which deucrictibant extended-release (XR) tablet is administered.

Methods

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 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 comprised 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

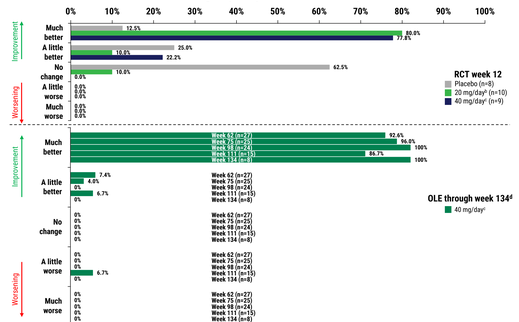
Angioedema Control Test (AECT)[27,28]: a four-item questionnaire with a five-point response scale developed and validated to retrospectively quantify disease control and aid management decisions in patients with recurrent angioedema (AECT-4Wk — 4-week recall used):

0 | 1 | 2 | 3 | 4

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)[21] in which deucrictibant extended-release (XR) tablet is administered. None of the 9 discontinuations in the CHAPTER-1 OLE were reported as treatment-related.
  - Mean (SD) treatment duration in the OLE was 22.2 (8.1) months.[a]
  - Maximum deucrictibant exposure during the entire study was 33.8 months.[a]

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

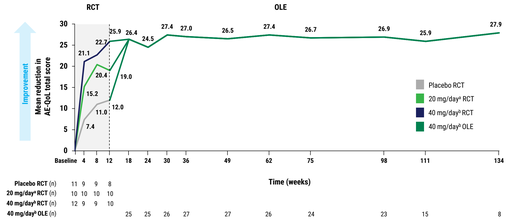


HRQoL, health-related quality of life; IR, immediate release; OLE, open-label extension; PGA-Change, Patient Global Assessment of Change; RCT, randomized controlled trial. n = number of participants with PGA-Change results at the given week. [a]1 month defined as 28 days. [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily. [d]Data shown for the final five visits of the OLE.

Results

Health-related quality of life using AE-QoL

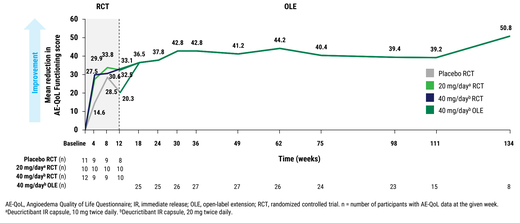
Figure 3. AE-QoL: Improvement in Total Score by week 4 and effects sustained through week 134



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.

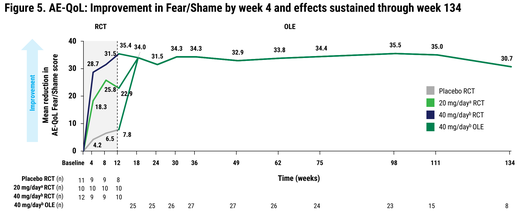
AE-QoL Subdomains "Functioning" and "Fear/Shame"

Figure 4. AE-QoL: Improvement in Functioning 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.

Figure 5. AE-QoL: Improvement in Fear/Shame by week 4 and effects sustained through week 134

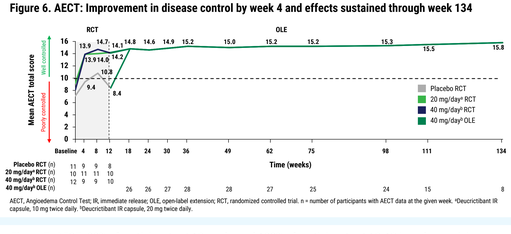


AE-QoL, Angioedema Quality of Life Questionnaire; IR, immediate release; OLE, open-label extension; RCT, randomized controlled trial. n = number of participants with AE-QoL data at the given week. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

Results

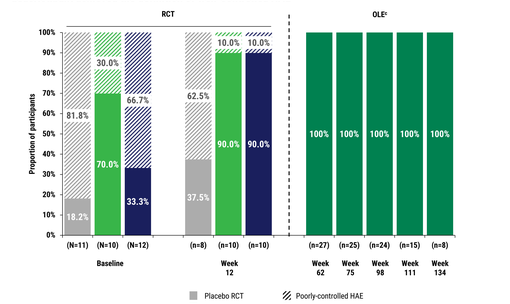
Disease control

Figure 6. 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]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

Figure 7. AECT: 90% of participants at 12 weeks and 100% of participants at 62-134 weeks receiving deucrictibant achieved the definition of 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. [a]Data are shown for the final five visits during the OLE.

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

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