Long-Term Prophylactic Treatment with Oral Deucrictibant Improves Health-Related Quality of Life of Patients With Hereditary Angioedema: CHAPTER-1 Open-Label Extension Study

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Key takeaways

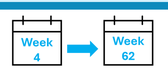
The ongoing Phase 2 CHAPTER-1 open-label extension (OLE) provides additional evidence on the effects of long-term prophylactic treatment with oral deucrictibant on health-related quality of life (HRQoL) for patients with hereditary angioedema (HAE).

PGA-Change

100%

of participants who received deucrictibant 40 mg/day reported improved HRQoL at weeks 12 and 62

AE-QoL



Clinically meaningful improvement in HRQoL at week 4 and effects sustained through week 62

Domains with greatest HRQoL improvements at weeks 12 and 62:

Functioning
Fear / Shame

AE-QoL, Angioedema Quality of Life Questionnaire; HRQoL, health-related quality of life; PGA-Change, Patient Global Assessment of Change.

Background

- **Hereditary angioedema (HAE):** a bradykinin-mediated condition with painful swelling attacks affecting multiple locations in the body and negatively impacting HRQoL.[1-6]
- **Unmet need:** prophylactic treatments combining injectable-like efficacy, a well-tolerated profile, and ease of administration.[7-10]
- **Oral deucrictibant:** a selective, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of HAE attacks.[10-21]

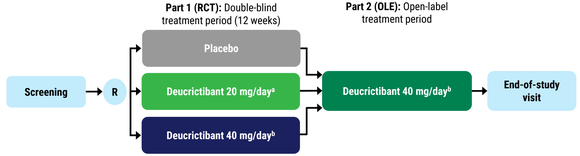
Objective

Evaluate the impact of deucrictibant treatment on HRQoL through 62 weeks in adult participants with HAE in the CHAPTER-1 OLE study.[17]

Methods

- **CHAPTER-1 (NCT05047185)*:** a two-part, Phase 2 study.[17]
  - 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

Deucrictibant

- **Immediate-release (IR) capsule:** dosed twice per day as a proof-of-concept for the extended-release tablet, which is the intended formulation for prophylaxis in HAE.[19-22]

Patient-reported outcome measures:

1. 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 better | A little better | No change | A little worse | Much worse

2. Angioedema Quality of Life Questionnaire (AE-QoL)[24-26]:

A tool validated for HAE where the total score (0–100) is calculated from responses on a five-point scale to 17 questions on HRQoL across four domains:

(1) functioning
(2) fatigue/mood
(3) fear/shame
(4) nutrition

Never | Rarely | Sometimes | Often | Very often

Results

Data

- Data snapshot from OLE (10 June 2024).

Participants in the OLE

- All 30 participants who completed Part 1 RCT enrolled in Part 2 OLE.
- For further information, please see the CHAPTER-1 OLE poster: "Long-Term Safety and Efficacy of Oral Deucrictibant for Prophylaxis in Hereditary Angioedema" Riedl M, et al.
- At data cutoff: 5 participants had discontinued. 25 were ongoing, of which 14 had reached week 62. Mean (SD) exposure to deucrictibant 40 mg/day for 30 participants in the OLE: 12.8 (5.0) months. Maximum exposure to deucrictibant: 20.8 months in the OLE. 23.7 months in the entire study.

Table 1. Demographics and baseline characteristics of participants in the OLE

	Placebo to 40 mg/day[b] (N=9)	20 mg/day[a] to 40 mg/day[b] (N=11)	40 mg/day[b] to 40 mg/day[b] (N=10)	Total (N=30)
Age, years — mean (SD)	**37.1 (12.2)**	**38.4 (17.2)**	**41.8 (14.3)**	**39.1 (14.5)**
Sex — n (%)				
Male	**2 (22.8)**	**6 (54.5)**	**4 (40.0)**	**12 (40.0)**
Female	**7 (77.8)**	**5 (45.5)**	**6 (60.0)**	**18 (60.0)**
Race: White — n (%)	**9 (100)**	**11 (100)**	**10 (100)**	**30 (100)**
BMI, kg/m² — mean (SD)	**26.9 (6.8)**	**29.5 (5.7)**	**25.7 (3.3)**	**27.4 (5.5)**
HAE type — n (%)				
Type 1	**8 (88.9)**	**9 (81.8)**	**10 (100)**	**27 (90.0)**
Type 2	**1 (11.1)**	**2 (18.2)**	**0**	**3 (10.0)**
Baseline HAE attack rate[c]				
Mean (SD)	**1.9 (0.9)**	**2.2 (1.3)**	**2.4 (1.8)**	**2.2 (1.3)**
Median (min, max)	**1.7 (0.7, 3.7)**	**1.7 (1.0, 5.3)**	**1.7 (1.0, 3.3)**	**1.7 (0.7, 6.7)**

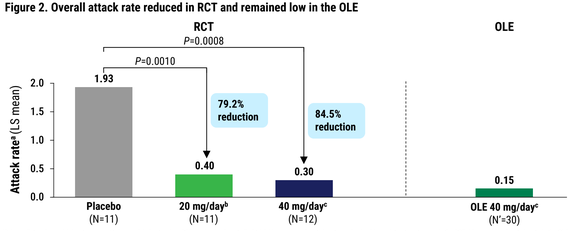
BMI, body mass index; HAE, hereditary angioedema; IR, immediate-release; max, maximum; min, minimum; OLE, open-label extension; SD, standard deviation. N = number of participants in the OLE. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily. [c]Based on time normalized number of attacks per 4 weeks.

Results

Attack rate in the OLE

- The attack rate was significantly reduced with deucrictibant at week 12 and remained low in the OLE.

Figure 2. Overall attack rate reduced in RCT and remained low in the OLE

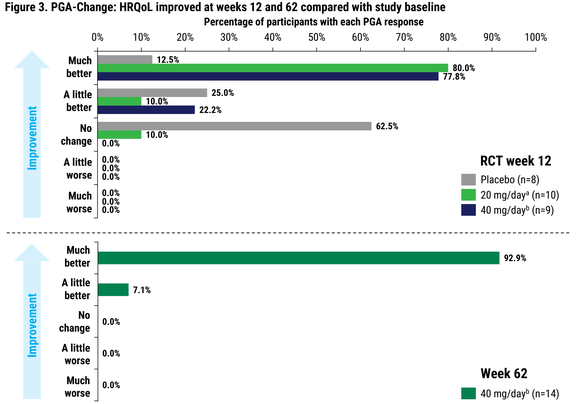


IR, immediate release; LS, least squares; OLE, open-label extension; RCT, randomized controlled trial. N = number of participants randomized in each treatment group in the RCT. N' = number of participants in the OLE. LS mean estimates of attack rate are based on Poisson regression models adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied. [a]Based on time normalized number of attacks per 4 weeks. [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily.

Participants at week 62:

- At data cutoff: 14 participants had reached at least the week 62 visit.
  - Mean (SD) exposure to deucrictibant 40 mg/day for 14 participants in the OLE: 16.9 (3.0) months.

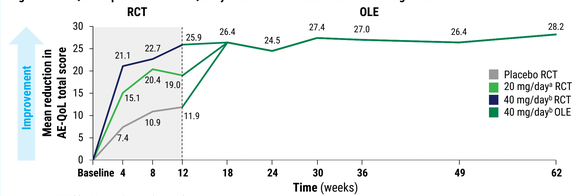
Figure 3. PGA-Change: HRQoL improved at weeks 12 and 62 compared with study baseline



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

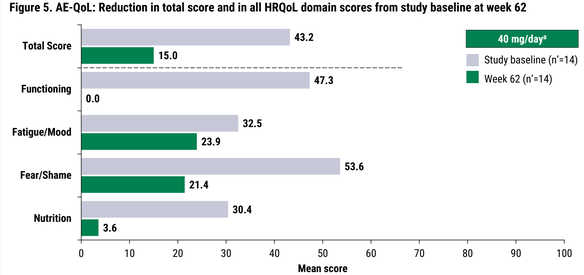
Figure 4. AE-QoL: Improvement in HRQoL by week 4 and effects sustained through week 62



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	26	14

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 5. AE-QoL: Reduction in total score and in all HRQoL domain scores from study baseline at week 62



AE-QoL, Angioedema Quality of Life Questionnaire; HRQoL, health-related quality of life; IR, immediate-release. n' = number of participants who reached week 62 at time of data cutoff. [a]Deucrictibant IR capsule, 20 mg twice daily.

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

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