Prophylactic Treatment With Oral Deucrictibant Improves Health-Related Quality of Life in Patients With Hereditary Angioedema

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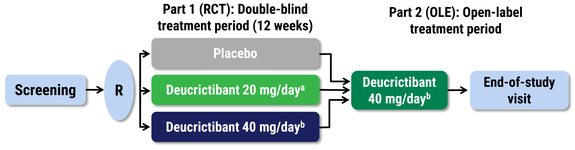
Rationale

- International hereditary angioedema (HAE) guidelines recommend that the goals of treatment are to achieve total disease control and to normalize patients' lives.[1]
- HAE negatively impacts functional and psychological domains of health-related quality of life (HRQoL).[2-6]
- Patients with well-controlled disease report lower disease burden, lower burden on daily activities, and greater HRQoL than patients with poorly-controlled disease.[7]
- Despite the availability of approved therapies for HAE, an unmet need remains for additional prophylactic treatments combining injectable-like efficacy, a well-tolerated profile, and ease of administration.[8-11]
- Deucrictibant is a selective, orally-administered bradykinin B2 receptor antagonist under development for prophylactic and on-demand treatment of HAE attacks.[12-17]

Methods

- CHAPTER-1 (NCT05047185)[17]* is a two-part, Phase 2 study evaluating the efficacy, safety, and tolerability of deucrictibant for long-term prophylaxis against angioedema attacks in HAE-1/2.
- Eligible participants were ≥18 and ≤75 years of age, diagnosed with HAE-1/2, were not receiving other prophylactic treatments at the time of screening, and had experienced ≥3 attacks within the past 3 consecutive months prior to screening or ≥2 attacks during screening (up to 8 weeks).
- In placebo-controlled part 1, participants were randomized to receive 1 of 2 doses of double-blinded deucrictibant (20 mg/day or 40 mg/day) or placebo for 12 weeks of treatment (**Figure 1**).

Figure 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.

- Deucrictibant immediate-release (IR) capsule was dosed twice per day as a proof-of-concept for the once-daily deucrictibant extended-release tablet, which is the intended formulation of deucrictibant for prophylactic HAE treatment.[18]
- Patient-reported outcomes (PROs) were assessed using pre-defined endpoints (**Table 1**).

Table 1. PRO endpoints

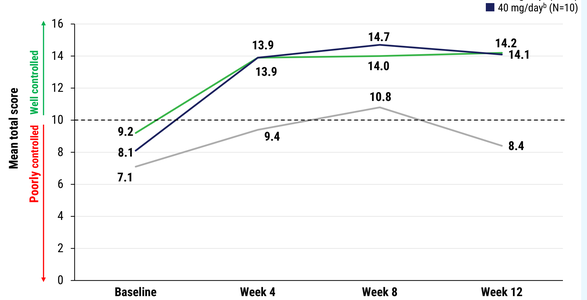
Disease control, HRQoL, and treatment satisfaction were assessed using pre-defined endpoints:	
Disease control	• Angioedema Control Test (AECT): 4-week recall version[19,20]
Health-related quality of life	• Angioedema QoL Questionnaire (AE-QoL)[21,22] • Patient Global Assessment of Change (PGA-Change)
Treatment satisfaction	• Treatment Satisfaction Questionnaire for Medication (TSQM) Version II[23]

HRQoL, health-related quality of life; PRO, patient-reported outcome.

Results

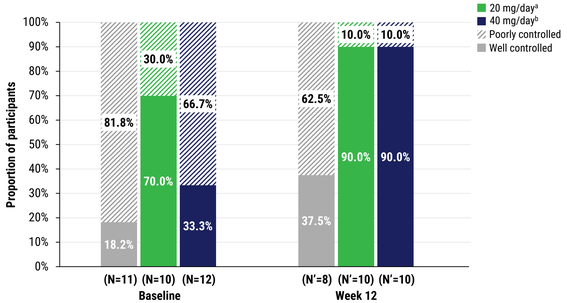
- Results from the CHAPTER-1 randomized controlled trial (RCT) are reported here.
- 34 participants were enrolled and randomized at sites in Canada, Europe, the United Kingdom, and the United States.
- Treatment with deucrictibant resulted in well-controlled HAE by week 4 and throughout treatment (**Figure 2**).
- A total of 90% of participants on deucrictibant showed well-controlled HAE at week 12 (**Figure 3**).

Figure 2. AECT: Well-controlled HAE by week 4 in deucrictibant-treated participants



AECT, Angioedema Control Test; IR, immediate-release. N = number of participants with AECT data at week 12. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

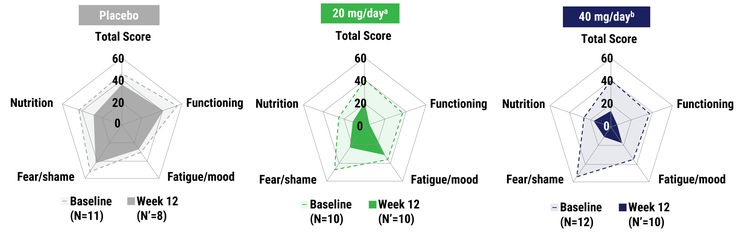
Figure 3. AECT: 90% well-controlled at week 12 in deucrictibant-treated participants



AECT, Angioedema Control Test; HAE, hereditary angioedema; IR, immediate-release; RCT, randomized controlled trial. N = number of participants randomized in each treatment group in the RCT. N' = number of participants with AECT data at week 12. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule; 20 mg twice daily.

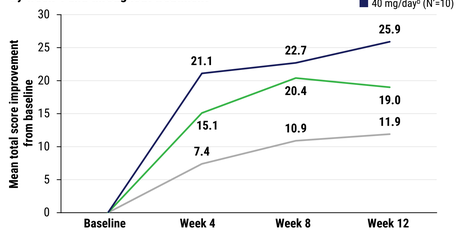
- The mean AE-QoL Total Score improved from baseline to week 12 by 19.0 and 25.9 points in participants receiving deucrictibant 20 mg/day and 40 mg/day, respectively, vs 11.9 points in the placebo group (**Figures 4 and 5**).
- The AE-QoL domains that showed the greatest improvement with deucrictibant treatment were "fear/shame" and "functioning" (**Figure 4**).

Figure 4. AE-QoL: HRQoL improvement across all domains



AE-QoL, Angioedema Quality of Life Questionnaire; HRQoL, health-related quality of life; IR, immediate-release; Q, quartile; SD, standard deviation. N = number of randomized participants with AE-QoL data at baseline. N' = number of participants with AE-QoL data at week 12. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

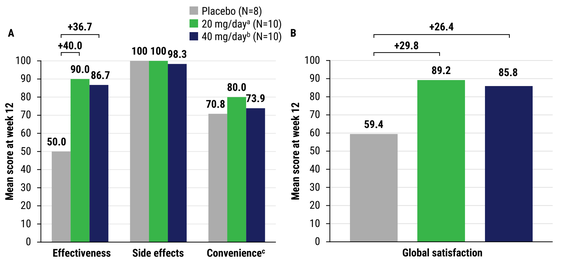
Figure 5. AE-QoL: Total Score improvement from baseline by week 4 and throughout treatment



Results

- Deucrictibant resulted in greater patient satisfaction with treatment effectiveness (**Figure 6A**) and greater overall patient satisfaction (**Figure 6B**) vs placebo.

Figure 6. TSQM: Improvement in patient satisfaction in deucrictibant-treated participants



IR, immediate-release; TSQM, Treatment Satisfaction Questionnaire for Medication. N = number of participants with TSQM results at week 12. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily. [c]Dose frequency was twice daily using IR capsule; once daily tablet is the intended formulation for the Phase 3 trial.

Conclusions

- **The CHAPTER-1 Phase 2 trial provides encouraging results on the effects of prophylactic treatment with oral deucrictibant for 12 weeks on HAE control, HRQoL, and treatment satisfaction in people living with HAE.**
  - **Deucrictibant improved disease control from as early as week 4 vs placebo, with 90% of participants in the deucrictibant groups demonstrating well-controlled HAE at week 12.**
  - **Deucrictibant improved AE-QoL scores, particularly in "functioning" and "fear/shame" domains.**
  - **Participants reported high levels of satisfaction with deucrictibant.**
- **Confirmation of these data in the planned Phase 3 study may provide further evidence on deucrictibant as a potential treatment to address existing unmet needs in HAE disease control and HRQoL.**
- **CHAPTER-1 OLE data showing maintained improvement in disease control and HRQoL through one year of deucrictibant treatment to be presented at upcoming scientific conferences.**

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