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

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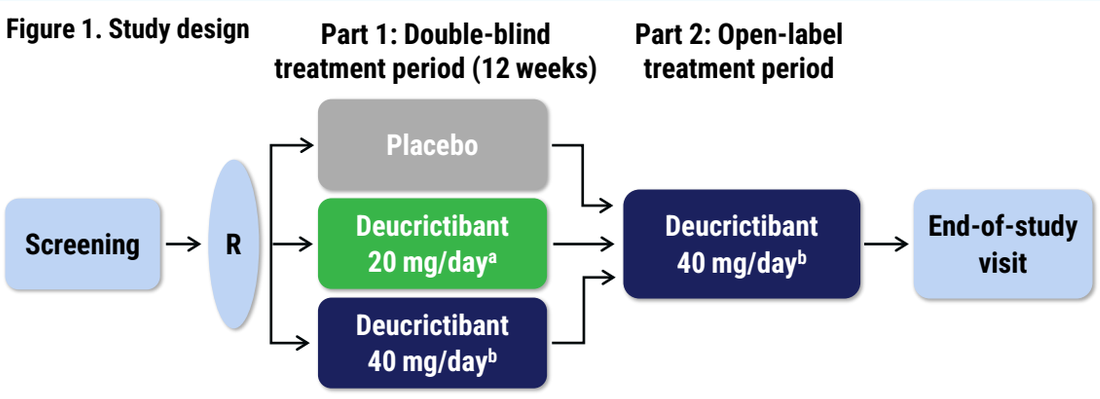
Rationale

- Excess bradykinin is the main mediator of the clinical manifestations of hereditary angioedema (HAE) attacks.[1]
- In people with HAE, health-related quality of life (HRQoL) is negatively impacted, including functional and psychological impairment.[2]
- Despite the availability of approved therapies, an unmet need remains for additional prophylactic treatments combining injectable-like efficacy, a well-tolerated profile, and ease of administration.[3-6]
- Deucrictibant is an orally administered, highly potent, specific antagonist of the bradykinin B2 receptor under development for on-demand and prophylactic treatment of HAE attacks.[4,7-11]

Methods

- CHAPTER-1 (NCT05047185)[11,†] 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; R, randomization. [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.[12]
- Two HRQoL patient-reported outcomes were assessed using pre-defined endpoints:
  - **Patient Global Assessment of Change (PGA-Change) questionnaire:** measures change in participants' HRQoL since starting study treatment on a 5-point response scale from "much worse" to "much better".
  - **Angioedema QoL questionnaire (AE-QoL):** a tool developed for recurrent angioedema and validated in HAE that consists of 17 questions using a 5-point response scale ranging from 1 (never) to 5 (very often) across 4 domains—"nutrition", "fatigue/mood", "fear/shame", and "functioning". The total scores for each domain and across all domains are transformed into a linear scale (0–100); higher scores indicate greater impairment.[13,14]

Results

- Thirty-four participants were enrolled and randomized at sites in Canada, Europe, the United Kingdom, and the United States.
- Participant mean age was 40.2 years and over half were female (21/34, 61.8%) (**Table 1**).

Table 1. Baseline characteristics

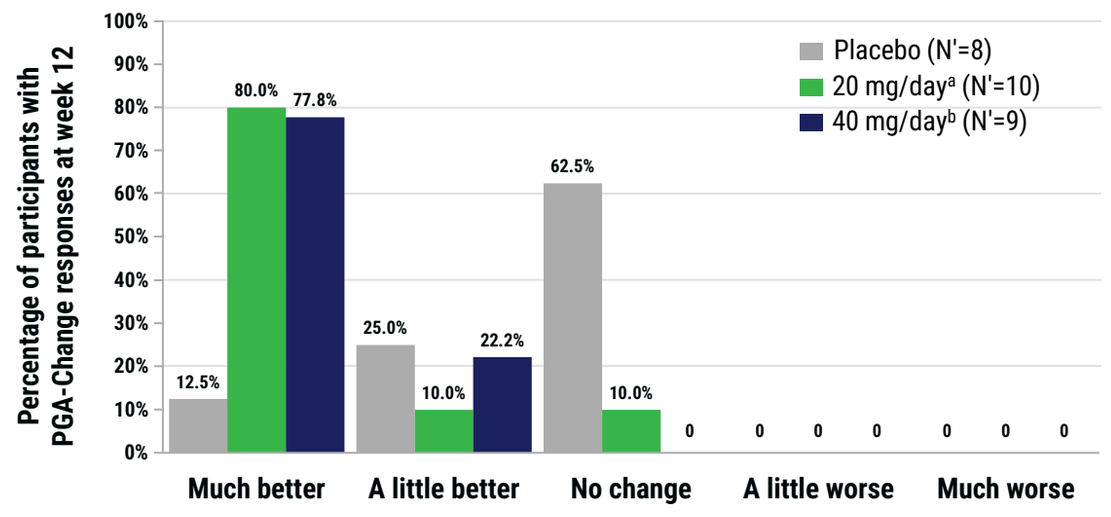
	Placebo (N=11)	Deucrictibant IR capsule 20 mg/day[a] (N=11)	Deucrictibant IR capsule 40 mg/day[b] (N=12)	All (N=34)
Age (years), mean (SD)	41.4 (14.5)	38.4 (17.2)	40.8 (15.2)	40.2 (15.2)
Female, n (%)	8 (72.7)	5 (45.5)	8 (66.7)	21 (61.8)
White, n (%)	11 (100)	11 (100)	12 (100)	34 (100)
HAE type, n (%)				
Type 1	10 (90.9)	9 (81.8)	12 (100)	31 (91.2)
Type 2	1 (9.1)	2 (18.2)	0 (0)	3 (8.8)
Baseline monthly[c] HAE attack rate, mean	1.9	2.1	2.5	2.2

HAE, hereditary angioedema; IR, immediate-release; SD, standard deviation. N = number of randomized participants. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily. [c]1 month = 4 weeks.

Results (continued)

- Ninety percent (9/10) of participants receiving deucrictibant 20 mg/day and 100% (9/9) of those receiving deucrictibant 40 mg/day reported improvement in PGA-Change at week 12 compared to baseline; 80.0% (8/10) and 77.8% (7/9) of participants reported feeling "much better" in the deucrictibant 20 mg/day and 40 mg/day groups, respectively (**Figure 2**).
- The majority of participants in the placebo group (62.5%, 5/8) experienced "no change" at week 12 compared to baseline; 12.5% (1/8) of participants in the placebo group reported feeling "much better" (**Figure 2**).

Figure 2. PGA-Change results at week 12



IR, immediate-release; PGA-Change, Patient Global Assessment of Change questionnaire. N' = number of participants with PGA-Change results 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 (**Figure 3**).
- The AE-QoL domains that showed the greatest improvement with deucrictibant treatment were "fear/shame" and "functioning" (**Figure 3**).

Figure 3. Change in AE-QoL total score from baseline to week 12

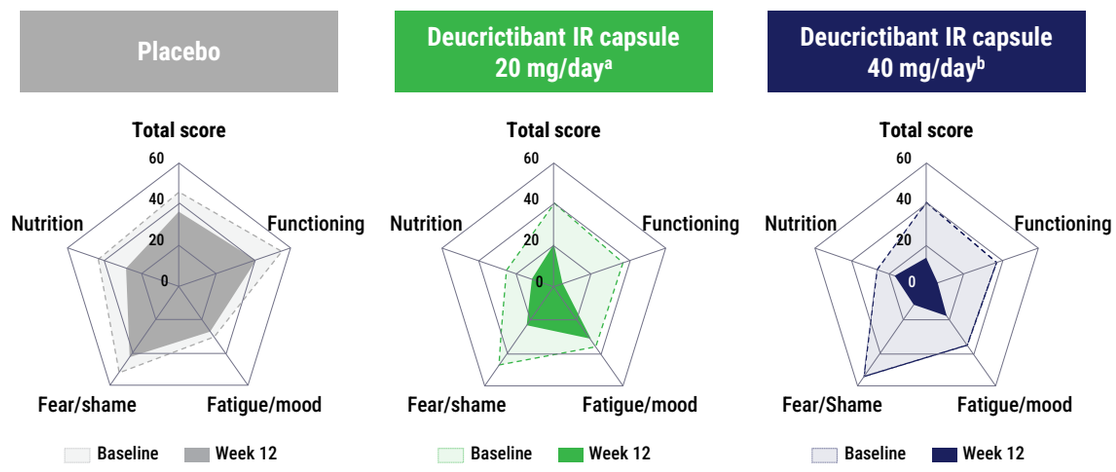


Table 2. Change in AE-QoL total score from baseline to week 12

AE-QoL total score	Placebo	Deucrictibant IR capsule 20 mg/day[a]	Deucrictibant IR capsule 40 mg/day[b]
Baseline	**N=11**	**N=10**	**N=12**
Mean (SD)	45.3 (18.5)	39.1 (22.0)	41.1 (15.5)
Median (Q1, Q3)	42.6 (29.4, 57.4)	37.5 (16.2, 55.9)	40.4 (31.6, 49.3)
Week 12	**N'=8**	**N'=10**	**N'=10**
Mean (SD)	35.7 (19.6)	20.2 (15.6)	13.2 (6.9)
Median (Q1, Q3)	37.5 (19.1, 49.3)	18.4 (7.4, 33.8)	12.5 (10.3, 17.7)

AE-QoL, Angioedema Quality of Life questionnaire; 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.

Conclusions

- **Analyses of CHAPTER-1 trial data provide evidence that prophylactic treatment with oral deucrictibant for 12 weeks improved HRQoL for people living with HAE.**
- **These results support further development of deucrictibant as a potential prophylactic therapy for HAE.**

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

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