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

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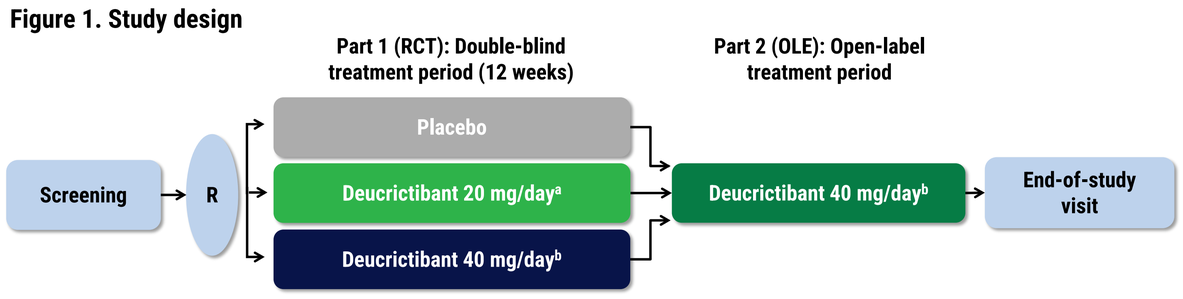
Rationale

- 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.[18,19]
- Patient-reported outcomes (PROs) were assessed using pre-defined endpoints (**Table 1**).

Table 1. PRO endpoints

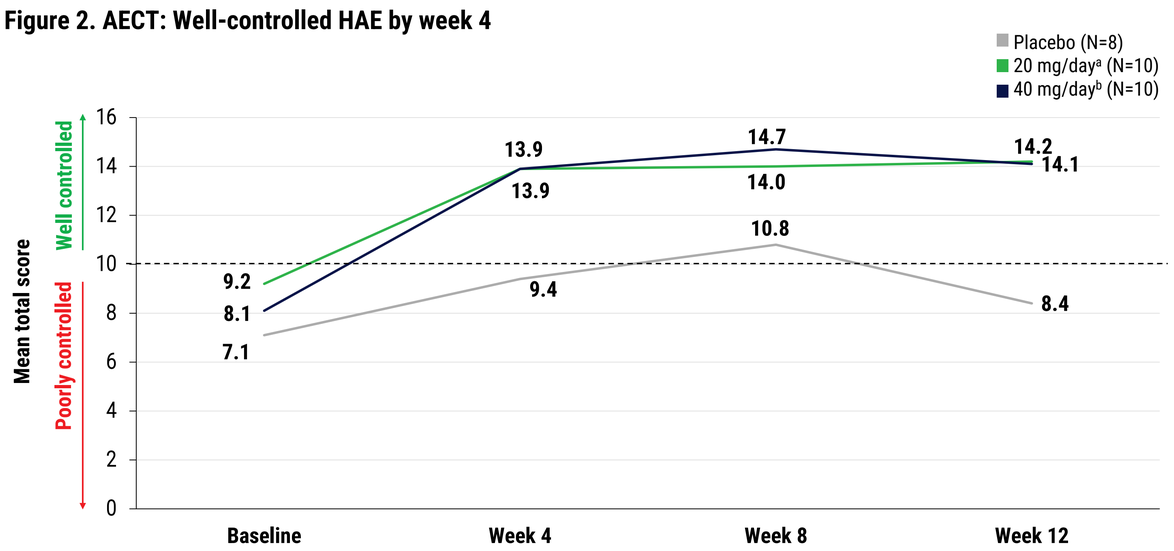
Disease control, HRQoL, and treatment satisfaction were assessed using pre-defined endpoints:	
Disease control	• Angioedema Control Test (AECT): 4-week recall version[20,21]
Health-related quality of life	• Angioedema QoL Questionnaire (AE-QoL)[22,23] • Patient Global Assessment of Change (PGA-Change)
Treatment satisfaction	• Treatment Satisfaction Questionnaire for Medication (TSQM) Version II[24]

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

Results

- Thirty-four participants were enrolled and randomized at sites in Canada, Europe, the United Kingdom, and the United States.
- Results from the CHAPTER-1 randomized controlled trial (RCT) are reported here.
- Treatment with deucrictibant resulted in well-controlled HAE by week 4 and throughout treatment (**Figure 2**).

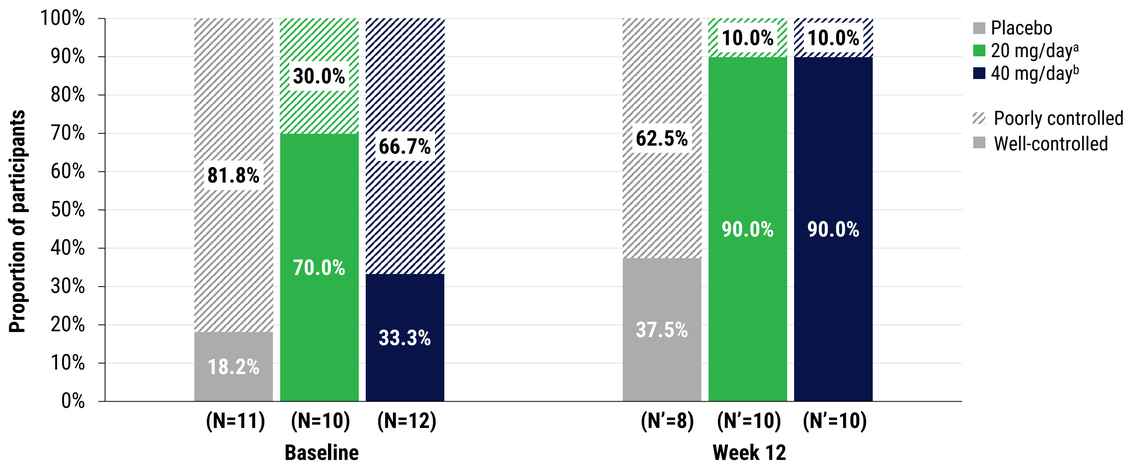
Figure 2. AECT: Well-controlled HAE by week 4



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.

- A total of 90% of participants on deucrictibant showed well-controlled HAE at week 12 (**Figure 3**).

Figure 3. AECT: 90% well-controlled at week 12



AECT, Angioedema Control Test; 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.

Results

- 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 4, Table 2**).
- 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

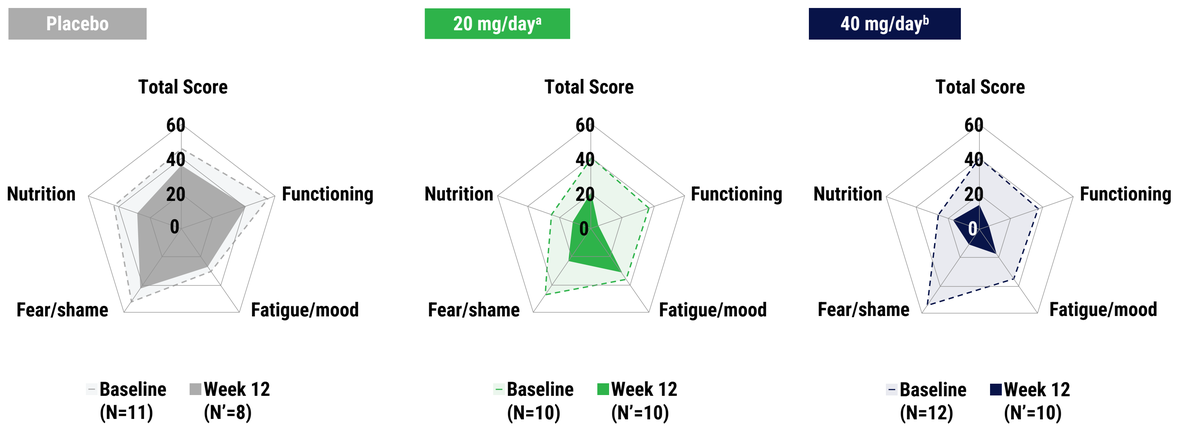


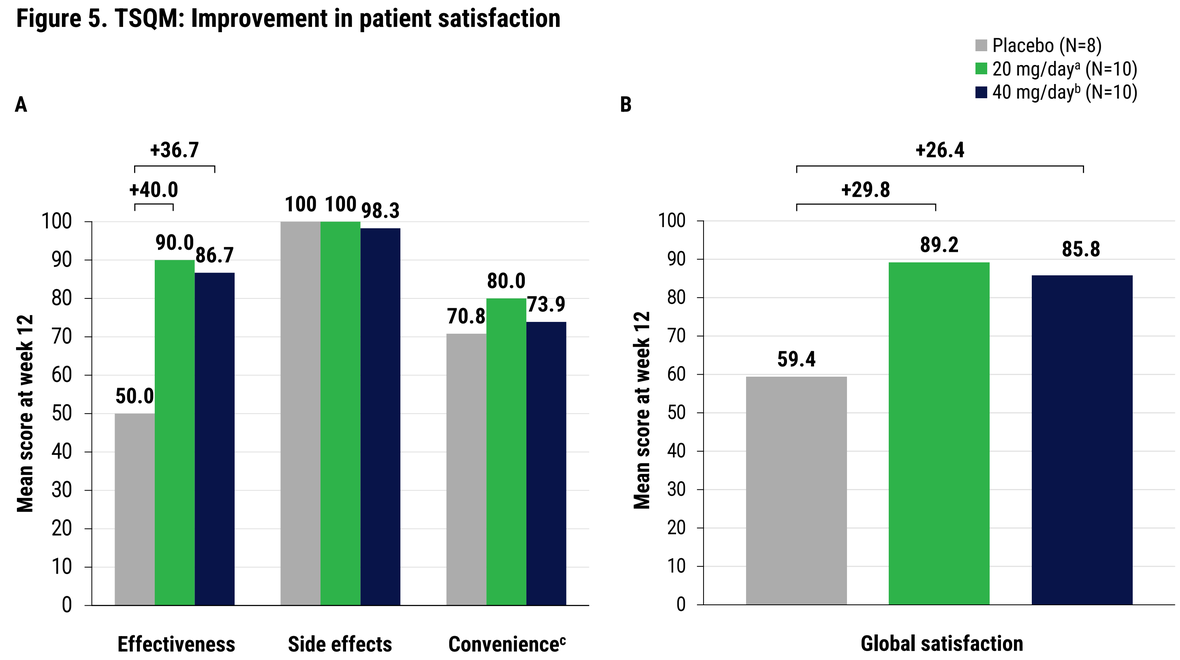
Table 2. AE-QoL: HRQoL Total Score improvement

AE-QoL Total Score	Placebo	Deucrictibant 20 mg/day[a]	Deucrictibant 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; 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.

- Deucrictibant treatment resulted in greater patient satisfaction with effectiveness (**Figure 5A**) and greater overall patient satisfaction (**Figure 5B**) vs placebo.

Figure 5. TSQM: Improvement in patient satisfaction



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.**

References

1. Maurer M, et al. *Allergy*. 2022;77:1961-90. **2.** Bork K, et al. *Allergy Asthma Clin Immunol*. 2021;17:40. **3.** Bygum A, et al. *Front Med*. 2017;4:212. **4.** Mendivil J, et al. *Orphanet J Rare Dis*. 2021;16:94. **5.** Chong-Neto HJ. *World Allergy Organ J*. 2023;16:100758. **6.** Lumry WR, et al. *Allergy Asthma Proc*. 2010;31(5):407-14. **7.** Grumach A, et al. *J Allergy Clin Immunol*. 2024;153(2)(suppl). Abstract AB92. **8.** Betschel SD, et al. *J Allergy Clin Immunol Pract*. 2023;11:2315-25. **9.** Bouillet L, et al. *Allergy Asthma Proc*. 2022;43:406-12. **10.** Center for Biologics Evaluation and Research. The voice of the patient – hereditary angioedema. US Food and Drug Administration; May 2018. Accessed September 16, 2024. https://www.fda.gov/media/113509/download. **11.** Covella B, et al. *Future Pharmacol*. 2024;4:41-53; **12.** https://clinicaltrials.gov/study/NCT04618211. Accessed September 16, 2024. **13.** Maurer M, et al. Presented at: AAAAI; Feb 25-28, 2022; San Antonio, TX, USA. **14.** https://www.clinicaltrials.gov/study/NCT05396105. Accessed September 16, 2024. **15.** https://clinicaltrials.gov/study/NCT06343779. Accessed September 16, 2024. **16.** Riedl MA, et al. Presented at: AAAAI; Feb 23-26, 2024; Washington, DC, USA. **17.** https://www.clinicaltrials.gov/study/NCT05047185. Accessed September 16, 2024. **18.** Groen K, et al. Presented at: ACAAI; Nov 10–14, 2022; Louisville, KY, USA. **19.** Petersen RS et al. Presented at: Bradykinin Symposium 2024; Sep 5–6, 2024; Berlin, Germany. **20.** Weller K, et al. *Allergy*. 2020;75(5):1165-77. **21**. Weller K, et al. *J Allergy Clin Immunol Pract*. 2020b;8(6):2050-57. **22**.Weller K, et al. *Allergy*. 2012;67:1289-98. **23**. Weller K, et al. *Allergy*. 2016;71:1203-9. **24**. Atkinson MJ, et al. *Value Health*. 2005;8(s1):S9-24.

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

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