Long-Term Safety and Efficacy of Oral Deucrictibant for Hereditary Angioedema Prophylaxis

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Notes: Use QR code overleaf to view full author details.

These data were presented at the Bradykinin Symposium in September 2024.

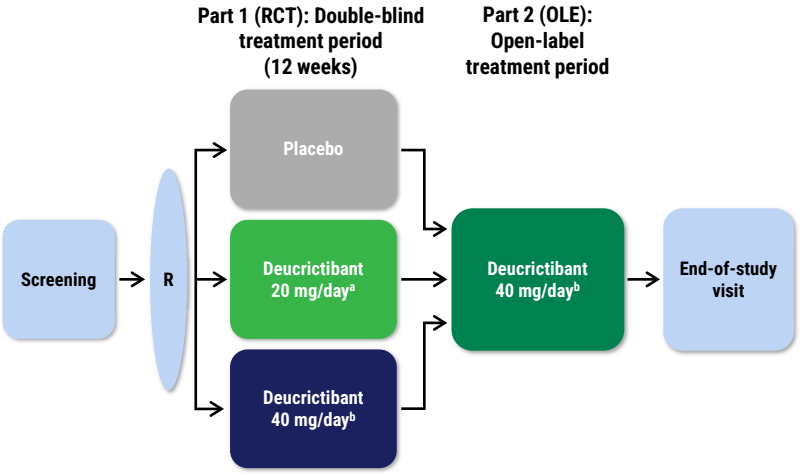
Results from the ongoing CHAPTER-1 open-label extension (OLE) study provide further evidence on the long-term safety and efficacy of deucrictibant for the prevention of hereditary angioedema (HAE) attacks and support further development of oral deucrictibant as a potential prophylactic therapy for HAE.

- All 30 participants who completed the randomized controlled trial (RCT) enrolled into the ongoing OLE.
- In the OLE, deucrictibant continued to be well tolerated with no safety signals observed.
- Deucrictibant treatment resulted in early-onset reduction in attack rate, which remained low through >1.5 years of treatment.
- The rate of "moderate and severe" attacks and attacks treated with on-demand medication also remained low in the OLE.

Methods

- CHAPTER-1 (NCT05047185) is a two-part, Phase 2 study, in which a total of 30 participants completed the double-blind, placebo-controlled RCT (part 1) and enrolled into the OLE (part 2).
- In the ongoing OLE, participants receive open-label treatment with deucrictibant 40 mg/day to evaluate the safety and efficacy of deucrictibant when administered for long-term prophylaxis against HAE attacks.
- Eligible participants were (a) aged ≥18 and ≤75 years, (b) diagnosed with HAE-1/2, (c) not receiving other prophylactic treatments at screening, and (d) experienced ≥3 attacks within 3 months prior to screening or ≥2 attacks during screening up to 8 weeks.
- Deucrictibant immediate-release (IR) capsule was dosed twice per day as a proof-of-concept for the once-daily deucrictibant extended-release (XR) tablet, which is the intended formulation of deucrictibant for prophylactic HAE treatment.

Figure 1. CHAPTER-1 study design



IR, immediate-release; OLE, open-label extension; R, randomization; RCT, randomized controlled trial. [a]Deucrictibant IR capsules, 10 mg twice daily. [b]Deucrictibant IR capsules, 20 mg twice daily.

Results

Table 1. Adverse events in the OLE

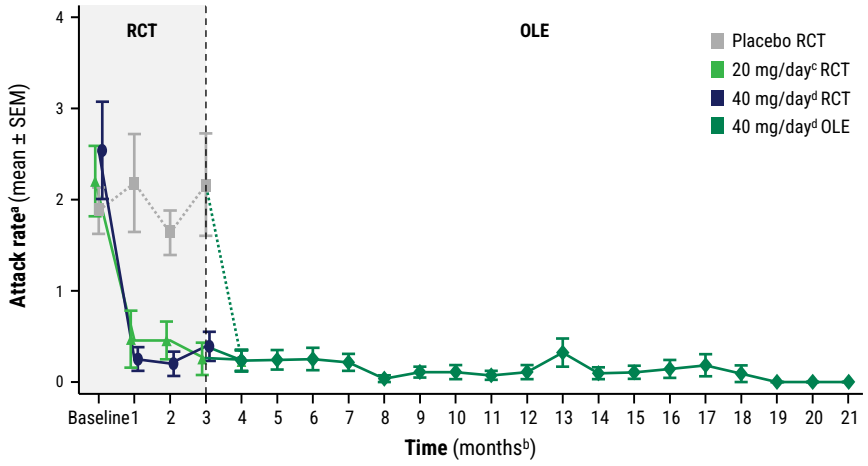
Adverse events	Placebo to 40 mg/day[a] (N=9)		20 mg/day[b] to 40 mg/day[a] (N=11)		40 mg/day[a] to 40 mg/day[a] (N=10)		Total (N=30)	
	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n
TEAEs	**5 (55.6)**	**25**	**7 (63.6)**	**31**	**6 (60.0)**	**16**	**18 (60.0)**	**72**
Treatment-related TEAEs	**1 (11.1)**	**1**	**0**	**0**	**0**	**0**	**1 (3.3)**	**1**
Tooth discoloration	1 (11.1)	1	0	0	0	0	1 (3.3)	1
Serious TEAEs	**0**	**0**	**1 (9.1)**	**1**	**1 (10.0)**	**1**	**2 (6.7)**	**2**
Tendon injury	0	0	0	0	1 (10.0)	1	1 (3.3)	1
Hip arthroplasty (arthritis)	0	0	1 (9.1)	1	0		1 (3.3)	1
Treatment-related serious TEAEs	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
TEAEs leading to study drug discontinuation, study withdrawal, or death	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**

IR, immediate release; OLE, open-label extension; TEAE, treatment emergent adverse event. N = number of participants who received at least one dose of blinded study treatment (data cutoff in the OLE: 10 June 2024). [a]Deucrictibant IR capsule, 20 mg twice daily. [b]Deucrictibant IR capsule, 10 mg twice daily.

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

Results (continued)

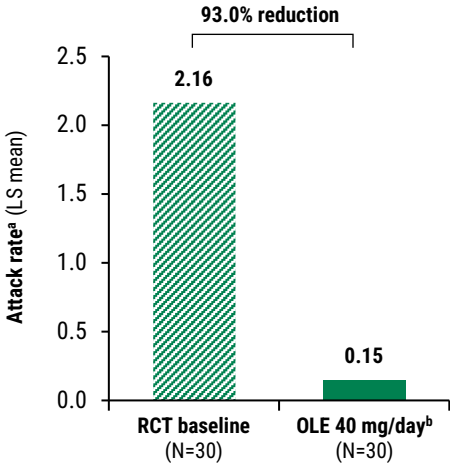
Figure 2. Reduced attack rate in the RCT remained low in the OLE



Placebo RCT (n)	11	11	11	11																	
20 mg/day[c] RCT (n)	11	11	11	11																	
40 mg/day[d] RCT (n)	12	12	10	10																	
40 mg/day[d] OLE (n)					30	29	28	28	28	28	28	28	28	28	21	19	16	11	11	10	9	7

IR, immediate release; OLE, open-label extension; RCT, randomized controlled trial; SEM, standard error of the mean. (n) = number of patients analyzed at each timepoint. [a]Based on time normalized number of attacks per 4 weeks; [b]1 month = 4 weeks; [c]Deucrictibant IR capsule, 10 mg twice daily; [d]Deucrictibant IR capsule, 20 mg twice daily.

Figure 3. Attack rate reduction in the OLE



IR, immediate release; LS, least squares; OLE, open-label extension; RCT, randomized controlled trial. 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, 20 mg twice daily.

Figure 4. Reduced rate of "moderate and severe" attacks in the RCT remained low in the OLE

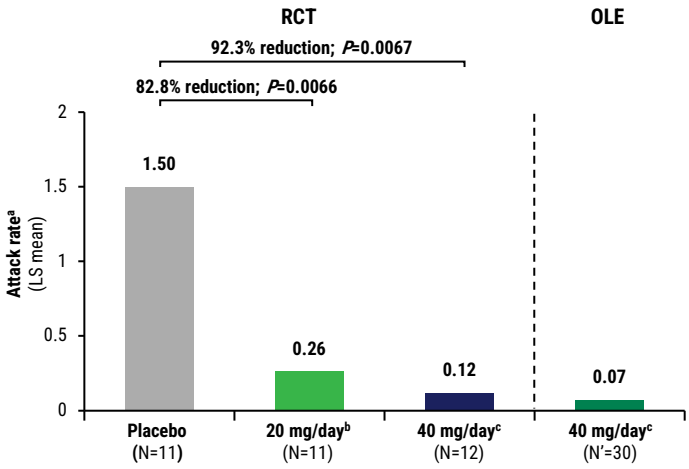
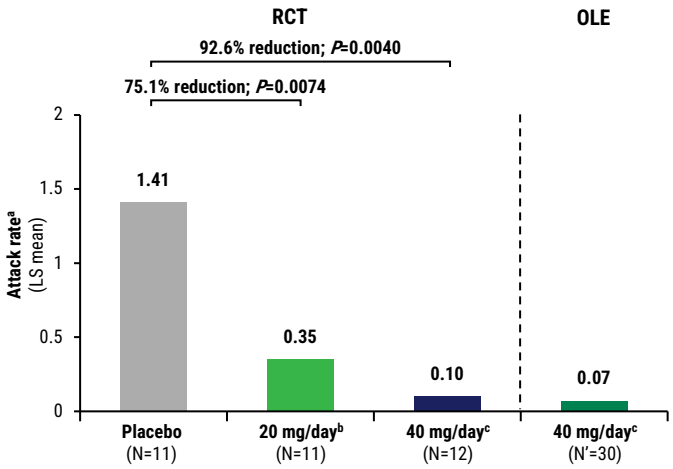


Figure 5. Reduced rate of on-demand–treated attacks in the RCT remained low in the OLE



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. The *P*-values in this figure are nominal. [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.

Conclusions

- **Data from the ongoing Phase 2 CHAPTER-1 open-label extension provide evidence that deucrictibant 40 mg/day continued to be well-tolerated, with no safety signals observed.**
- **Deucrictibant 40mg/day treatment resulted in early-onset reduction in attack rate which remained low through 1.5 years of treatment.**
- **The rates of "moderate and severe" attacks and attacks treated with on-demand medication also reduced in the RCT and remained low in the OLE with deucrictibant treatment.**

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