Poster #22

Long-Term Safety and Efficacy of Oral Deucrictibant for Prophylaxis in Hereditary Angioedema: Data Snapshot Results of the CHAPTER-1 Open-Label Extension Study

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Key takeaways

The ongoing Phase 2 CHAPTER-1 open-label extension (OLE) study provides further evidence on the long-term safety and efficacy of oral deucrictibant for the prevention of hereditary angioedema (HAE) attacks.

Safety

Deucrictibant was generally well tolerated with one treatment-related TEAE of tooth discoloration

Efficacy

1.5 YEARS
Attack rate reduced by week 1 in the RCT and remained low ≥1.5 years in the OLE

~80% of participants achieved **≥90%** reduction in attack rate in the OLE

Use of bradykinin B2 receptor antagonism for both LTP and ODT did not alter ODT response

LTP, long-term prophylaxis; ODT, on-demand treatment; OLE, open-label extension; RCT, randomized controlled trial; TEAE, treatment-emergent adverse event.

Background

- **Hereditary angioedema (HAE):** a bradykinin-mediated condition with painful swelling attacks affecting multiple locations in the body.[1]
- **Unmet need:** additional prophylactic treatments offering injectable-like efficacy, a well-tolerated profile, and ease of administration.[2-5]
- **Oral deucrictibant:** a selective, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of HAE attacks.[5-15]

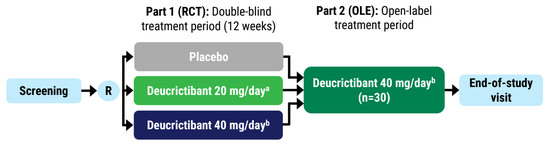
Objective

To evaluate the safety and efficacy of deucrictibant for long-term prophylaxis of HAE attacks in adults in the CHAPTER-1 open-label extension study.[12]

Methods

- **CHAPTER-1 (NCT05047185)*:** a two-part, Phase 2 study.[12]
  - 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.

- All 30 participants who completed the RCT enrolled into the ongoing OLE.
  - In the RCT, these 30 participants were randomized to deucrictibant 20 mg/day (N=11) or 40 mg/day (N=10), or placebo (N=9).
- **Post-hoc analysis:** duration of attacks was not a pre-specified CHAPTER-1 measure and calculated post-hoc based on available data for attacks that used icatibant once only as on-demand treatment (ODT).

Results

Participants in the OLE

- At data cutoff (10 June 2024), 30 participants in the OLE had received deucrictibant 40 mg/day for a mean (SD) treatment duration of 12.8 (5.0) months.
  - Maximum exposure to deucrictibant: 20.8 months in the OLE; 23.7 months in the entire study.

Safety analysis

- Deucrictibant was generally well tolerated.
  - One treatment-related treatment-emergent adverse event (TEAE) of tooth discoloration reported.

Table 1. Adverse events in the OLE

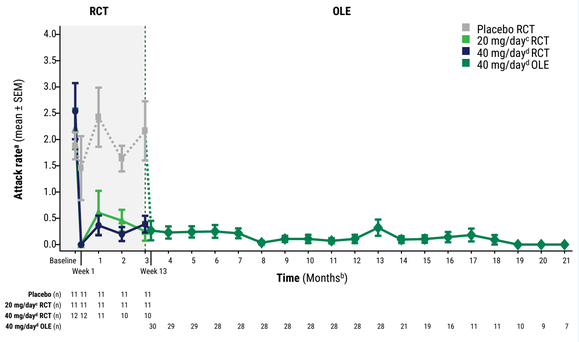
	Placebo to 40 mg/day[a] (N=9)		20 mg/day[b] to 40 mg/day[a] (N=11)		40 mg/day[a] to 40 mg/day[a] (N=10)		Total (N=30)	
	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n
TEAEs	**5 (55.6)**	**25**	**7 (63.6)**	**31**	**6 (60.0)**	**16**	**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	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. TEAE defined as adverse events that start or pre-existing adverse events that have worsened during the period between the first study dose in OLE and 4 weeks after the last dose in OLE or the End of Study Visit, whichever is later. N = number of participants who received ≥1 dose of study treatment in the OLE by the cutoff date of 10 June 2024. [a]Deucrictibant IR capsule, 20 mg twice daily. [b]Deucrictibant IR capsule, 10 mg twice daily.

Efficacy analysis

- RCT: Deucrictibant reduced the attack rate by week 1.
- OLE: Low attack rate sustained through ≥1.5 years.

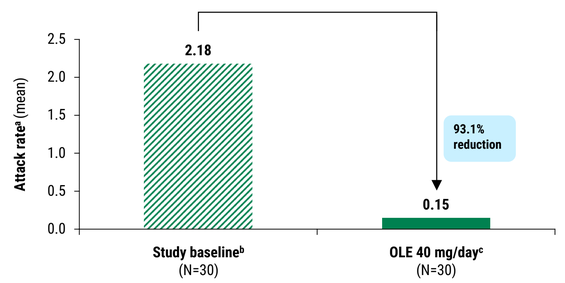
Figure 2. Attack rate reduced by week 1 in the RCT remained low through ≥1.5 years in the OLE



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.

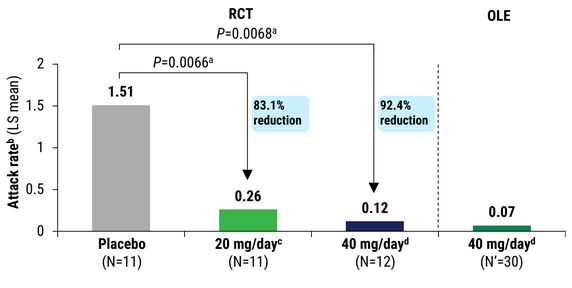
Results

Figure 3. Attack rate reduced in the OLE compared with study baseline



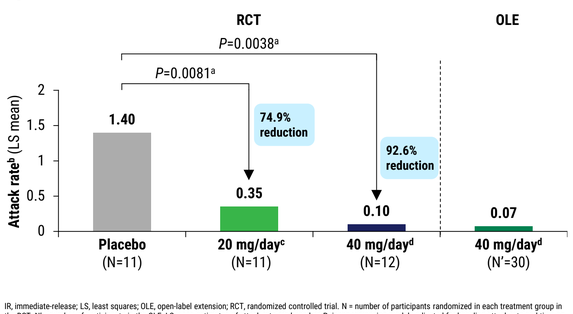
IR, immediate-release; LS, least squares; OLE, open-label extension. N = number of participants in the OLE. [a]Based on time normalized number of attacks per 4 weeks. [b]Baseline attack rate is raw (unadjusted) mean. OLE attack rate is LS mean. No multiplicity adjustment was applied. [c]Deucrictibant IR capsule, 20 mg twice daily.

Figure 4. "Moderate and severe" attack rate reduced in the 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]The *P*-values in this figure are nominal. [b]Based on time normalized number of attacks per 4 weeks. [c]Deucrictibant IR capsule, 10 mg twice daily. [d]Deucrictibant IR capsule, 20 mg twice daily.

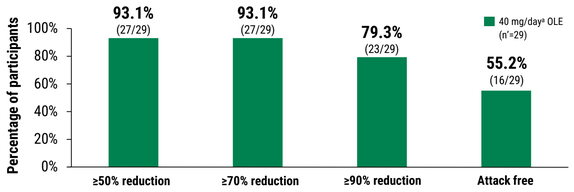
Figure 5. On-demand–treated attack rate reduced in the RCT and remained low in the OLE



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]The *P*-values in this figure are nominal. [b]Based on time normalized number of attacks per 4 weeks. [c]Deucrictibant IR capsule, 10 mg twice daily. [d]Deucrictibant IR capsule, 20 mg twice daily.

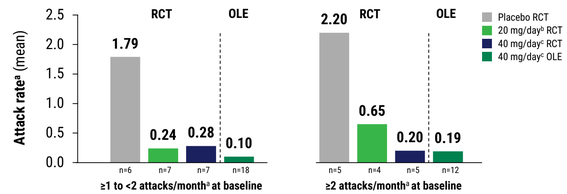
Results

Figure 6. Attack rate reduced relative to RCT study baseline with over half of participants attack free during the OLE



IR, immediate-release; OLE, open-label extension, RCT, randomized controlled trial. [a]Participants with ≥4 weeks of treatment in the OLE receiving 40 mg/day (deucrictibant IR capsule, 20 mg twice daily).

Figure 7. Attack rate decreased in the RCT and remained low in the OLE regardless of baseline attack rate



IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial. n = number of participants in each treatment group. [a]Attack rate is raw unadjusted mean number of attacks per 4 weeks. [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily.

Post-hoc analysis

- Use of bradykinin B2 receptor antagonism for both long-term prophylaxis (LTP) and ODT did not alter ODT response.

Table 2. Mean attack duration for participants who used icatibant once as ODT

	Icatibant as ODT in placebo group (RCT)		Icatibant as ODT in deucrictibant group (RCT & OLE)	
Attack severity	Number of participants (n) and attacks (a)	Mean (SD) duration[a] of attack, days	Number of participants (n) and attacks (a)	Mean (SD) duration[a] of attack, days
Mild	n=3, a=4	**2.11** (1.32)	n=1, a=2	**2.58** (2.00)
Moderate	n=4, a=13	**1.03** (1.15)	n=6, a=11	**1.03** (0.79)
Severe	n=4, a=8	**0.76** (0.32)	n=2, a=7	**0.64** (0.54)
Total	n=5, a=25	**1.12** (1.06)	n=8, a=20	**1.05** (0.98)

ODT, on-demand treatment; OLE open-label extension; RCT, randomized controlled trial; SD, standard deviation. [a]Duration of attack calculated as the time between the reported time of onset of attack symptoms and the reported time of resolution of attack symptoms.

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

References

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