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

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

Conflicts of interest disclosure

M.A.R.: Astria, BioCryst, BioMarin, Celldex, CSL Behring, Cycle Pharma, Grifols, Intellia, Ionis, KalVista, Novartis, Pharming, Pharvaris, Sanofi-Regeneron, Takeda; **J.A.:** Astria, BioCryst, CSL Behring, Ionis, KalVista, Pharming, Pharvaris, Takeda; **M.C.:** BioCryst, CSL Behring, KalVista, Menarini, MSD, Novartis, Otsuka, Pharming, Pharvaris, Sobi, Takeda, UCB; **S.K-A.:**BioCryst, Biotest, CSL Behring, Ionis, KalVista, Otsuka, Pharvaris, Takeda; **M.M.:** Astria, BioCryst, CSL Behring, Intellia, KalVista, Novartis, Octapharma, Otsuka, Pharvaris, Takeda; **M.E.M.:** Astria, AstraZeneca, BioCryst, Blueprint, CSL Behring, Celldex, Cogent, GSK, Ionis, Intellia, KalVista, Merck, Novartis, Pharming, Pharvaris, Regeneron, Takeda, Teva; **R.C.:** employee of RC Consultancy and consultant to Pharvaris, holds stocks in Pharvaris; **J.L., U.K.:** employees of Pharvaris, hold stocks in Pharvaris; **E.A-P.:** Astria, BioCryst, BioMarin, CSL Behring, Intellia, Kalvista, Otsuka, Pharming, Pharvaris, Takeda;

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CHAPTER-1 is a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: NCT05047185

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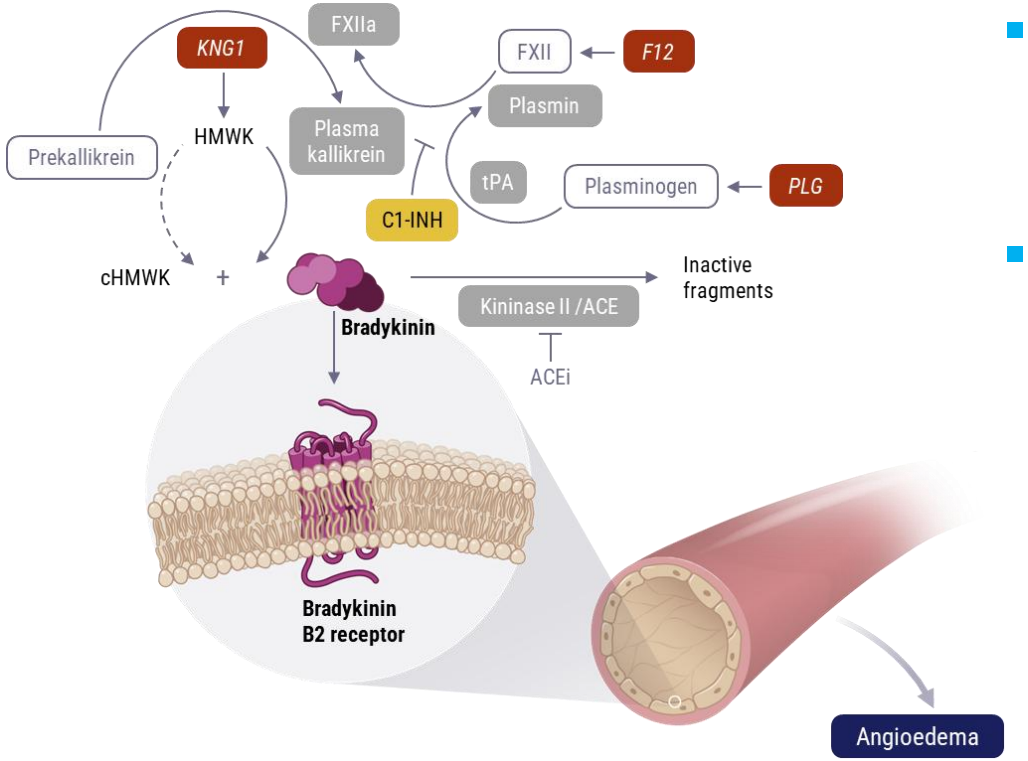
Hereditary angioedema (HAE) is a bradykinin-mediated condition with unmet medical needs



- Excess bradykinin is the main mediator of the clinical manifestations of bradykinin-mediated angioedema attacks, including HAE.[1]
- An unmet need remains for additional prophylactic therapies combining[2-5]:
  - Injectable-like efficacy
  - A well-tolerated profile
  - Ease of administration

ACE, angiotensin converting enzyme; ACEi, ACE inhibitor; C1-INH, C1 inhibitor; cHMWK, cleaved HMWK; *F12*, gene encoding FXII; FXII, factor XII; FXIIa, factor XIIa; HAE, hereditary angioedema; HMWK, high-molecular-weight kininogen, *KNG1*, gene encoding HMWK; *PLG*, gene encoding plasminogen; tPA, tissue plasminogen activator.
1. Busse PJ, et al. *N Engl J Med.* 2020;382:1136–48. **2.** Bouillet L, et al. *Allergy Asthma Proc*. 2022;43:406–12. **3.** Betschel SD, et al. *J Allergy Clin Immunol Pract*. 2023;11:2315–25. **4.** CBER. The voice of the patient – hereditary angioedema. May 2018. https://www.fda.gov/media/113509/download. **5.** Covella B, et al. *Future Pharmacol*. 2024;4:41–53.

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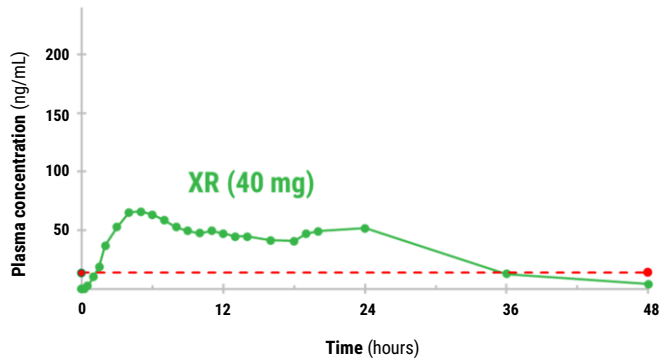
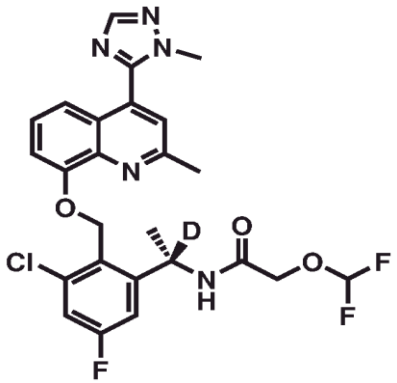
Deucrictibant is an investigational oral therapy for the prophylactic and on-demand treatment of bradykinin-mediated attacks

DEUCRICTIBANT extended-release (XR) tablet

sustained absorption[1]



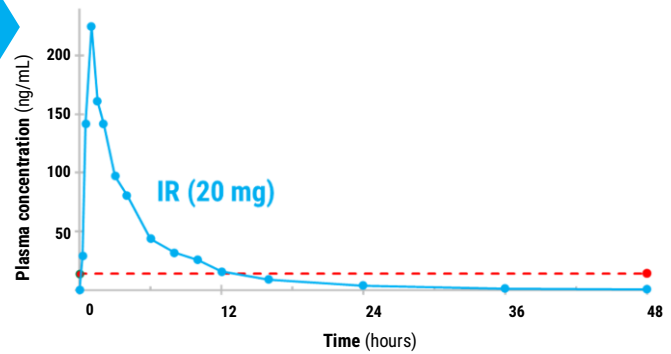
In studies, deucrictibant maintained sustained therapeutic exposure over 24 hours[1] from day one, allowing for once-daily oral prevention HAE attacks[2]



deucrictibant

DEUCRICTIBANT immediate-release (IR) capsule

rapid absorption[3]



In studies, deucrictibant rapidly reached therapeutic exposure within 15-30 minutes[3], supporting on-demand oral treatment of HAE attacks[4]

HAE, hereditary angioedema; IR, immediate-release; XR, extended-release. **1.** Zhang et al. Presented at C1INH Workshop; May 29-June 1, 2025. **2.** CHAPTER-3. ClinicalTrials.gov identifier: NCT06669754. Accessed September 19, 2025. https://clinicaltrials.gov/study/NCT06669754. **3.** Maurer M, et al. Presented at AAAAI; Feb 24-27, 2023; San Antonio, TX, USA. **4.** RAPIDe-3. ClinicalTrials.gov identifier: NCT06343779. Accessed September 19, 2025. https://www.clinicaltrials.gov/study/NCT06343779.

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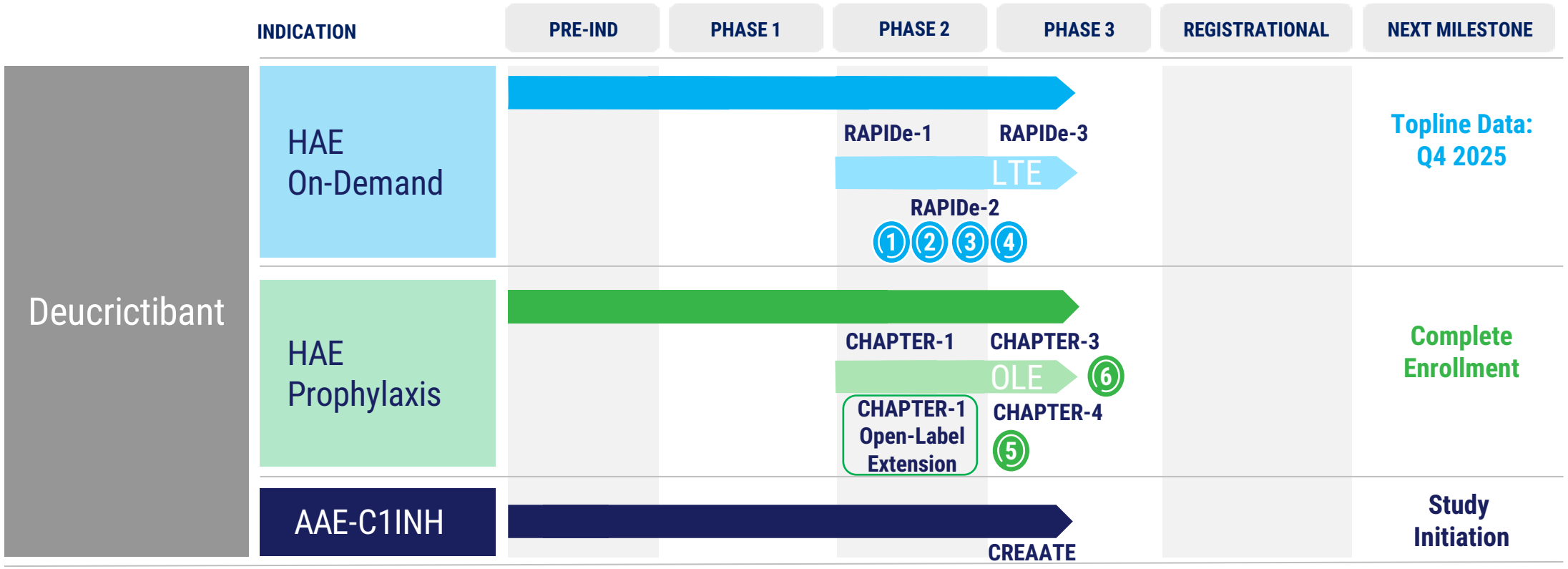
Deucrictibant development program in bradykinin-mediated angioedema



Other presentations at ACAAI, 2025

1. Anderson J, et al. RAPIDe-2 Part A Topline
2. Jacobs J.S, et al. RAPIDe-2 durability of treatment response
3. Anderson J, et al. RAPIDe-2 laryngeal attacks
4. Scarupa M.D, et al. Deucrictibant vs. Standard of Care
5. Manning M.E, et al. CHAPTER-1 OLE patient-reported outcomes (final data)
6. Zhang Z-Y, et al. Once-daily XR tablet for prophylaxis

AAE-C1INH, acquired angioedema due to C1-inhibitor deficiency; HAE, hereditary angioedema; LTE, long-term extension; OLE, open-label extension; XR, extended-release. Study, ClinicalTrials.gov identifier: RAPIDe-1, NCT05396105; RAPIDe-2, NCT05396105; RAPIDe-3, NCT06343779; CHAPTER-1, NCT05047185; CHAPTER-3, NCT06669754; CHAPTER-4, NCT06679881.

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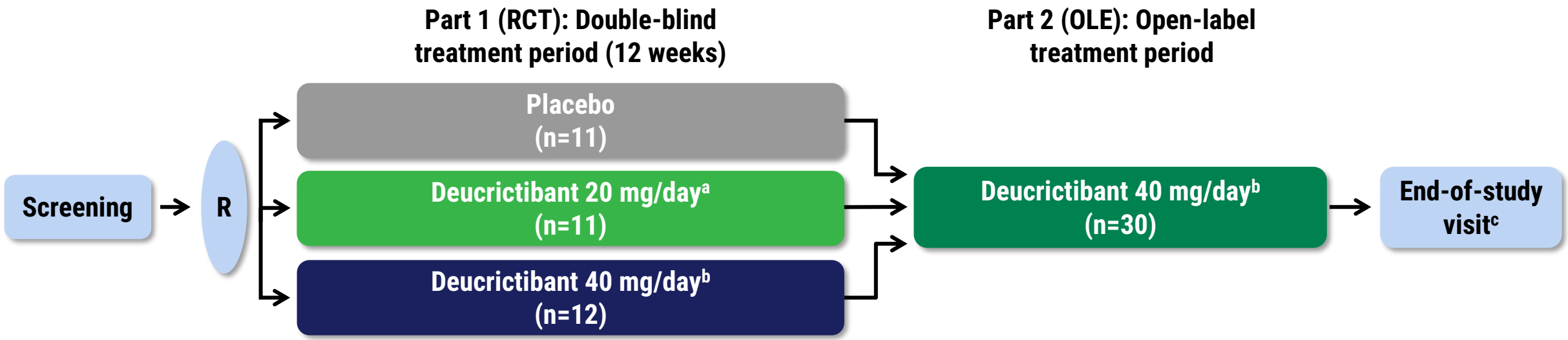
CHAPTER-1: Two-part, Phase 2 study of deucrictibant for long-term prophylaxis of HAE attacks



Part 1 - RCT: Key findings

- Efficacy:
  - Primary endpoint: Monthly attack rate significantly reduced vs placebo
  - Reduction in occurrence of 'moderate and severe' attacks and attacks treated with on-demand medication.
- Safety:
  - Deucrictibant was generally well tolerated with no safety signals.
- All 30 participants who completed the RCT enrolled in the OLE.

Part 2 - OLE: Key objectives

- Evaluate the long-term safety (primary objective) and efficacy of deucrictibant administered for prophylaxis against HAE attacks.

HAE, hereditary angioedema; 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. [C]Twenty-one participants rolled over to the CHAPTER-4 (NCT06679881) OLE in which deucrictibant extended-release (XR) tablet is self-administered. https://clinicaltrials.gov/study/NCT06679881. Accessed September 12, 2025. CHAPTER-1 is a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: NCT05047185. https://www.clinicaltrials.gov/study/NCT05047185. Accessed September 12, 2025.

Deucrictibant was well tolerated with no safety signals in the OLE

- Deucrictibant was generally well tolerated with one treatment-related TEAE reported: asymptomatic increased gamma-glutamyltransferase (<2 ULN), which started during the RCT, resolved temporarily during the OLE, and reoccurred by end of the OLE; ALT, AST, bilirubin, and ALP levels were normal
  - No treatment-related serious or severe TEAEs.
  - No TEAEs leading to study drug discontinuation, study withdrawal, or death.
- Mean (SD) treatment duration in the OLE was 22.2 (8.1) months.[a] Maximum deucrictibant exposure during the entire study was 33.8 months.[a]
- Twenty-one participants were on study at the time of CHAPTER-1 study end and all continued into the ongoing CHAPTER-4 OLE (NCT06679881) in which deucrictibant extended-release (XR) tablet, 40 mg, is administered. None of the 9 discontinuations in the CHAPTER-1 OLE were reported as due to reasons related to study drug.

	Placebo to 40 mg/day[b] (N=9)		**20 mg/day[c] to 40 mg/day[b]** (N=11)		**40 mg/day[b] to 40 mg/day[b]** (N=10)		**Total (N=30)**	
	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n
TEAEs	**8 (88.9)**	**40**	**8 (72.7)**	**45**	**8 (80.0)**	**25**	**24 (80.0)**	**110**
Treatment-related TEAEs	**0**	**0**	**0**	**0**	**1 (10.0)**	**1**	**1 (3.3)**	**1**
Gamma-glutamyltransferase increased	0	0	0	0	1 (10.0)	1	1 (3.3)	1
Serious TEAEs[d]	**0**	**0**	**1 (9.1)**	**2**	**1 (10.0)**	**1**	**2 (6.7)**	**3**
Tendon injury	0	0	0	0	1 (10.0)	1	1 (3.3)	1
Arthritis	0	0	1 (9.1)	1	0	0	1 (3.3)	1
Osteoarthritis	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**

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; OLE, open-label extension; SD, standard deviation; TEAE, treatment-emergent adverse event defined as adverse events that started or pre-existing adverse events that worsened during the period between first study dose in OLE and 4 weeks after last dose in OLE or the End of Study Visit, whichever was later; ULN, upper limit of normal. N = number of participants who received ≥1 dose of study treatment in the OLE by the cutoff date (10 June 2024). [a]1 month = 4 weeks. [b]Deucrictibant IR capsule, 20 mg twice daily. [c]Deucrictibant IR capsule, 10 mg twice daily. [d]Three serious TEAEs required reconstruction surgery, hip replacement, or knee replacement.

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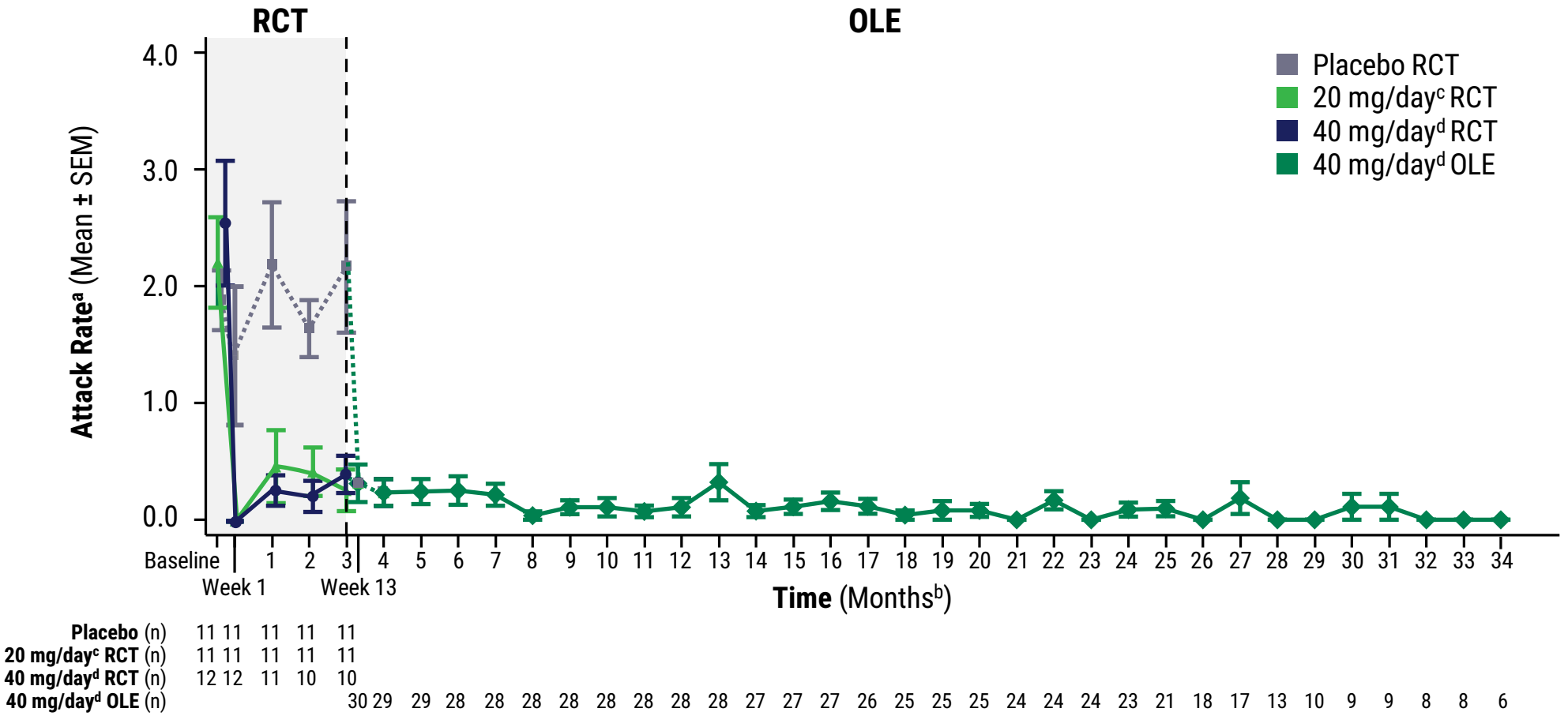
Attack rate reduced by week 1 and week 13 and remained low for up to ~34 months



IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial; SEM, standard error of the mean. [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.

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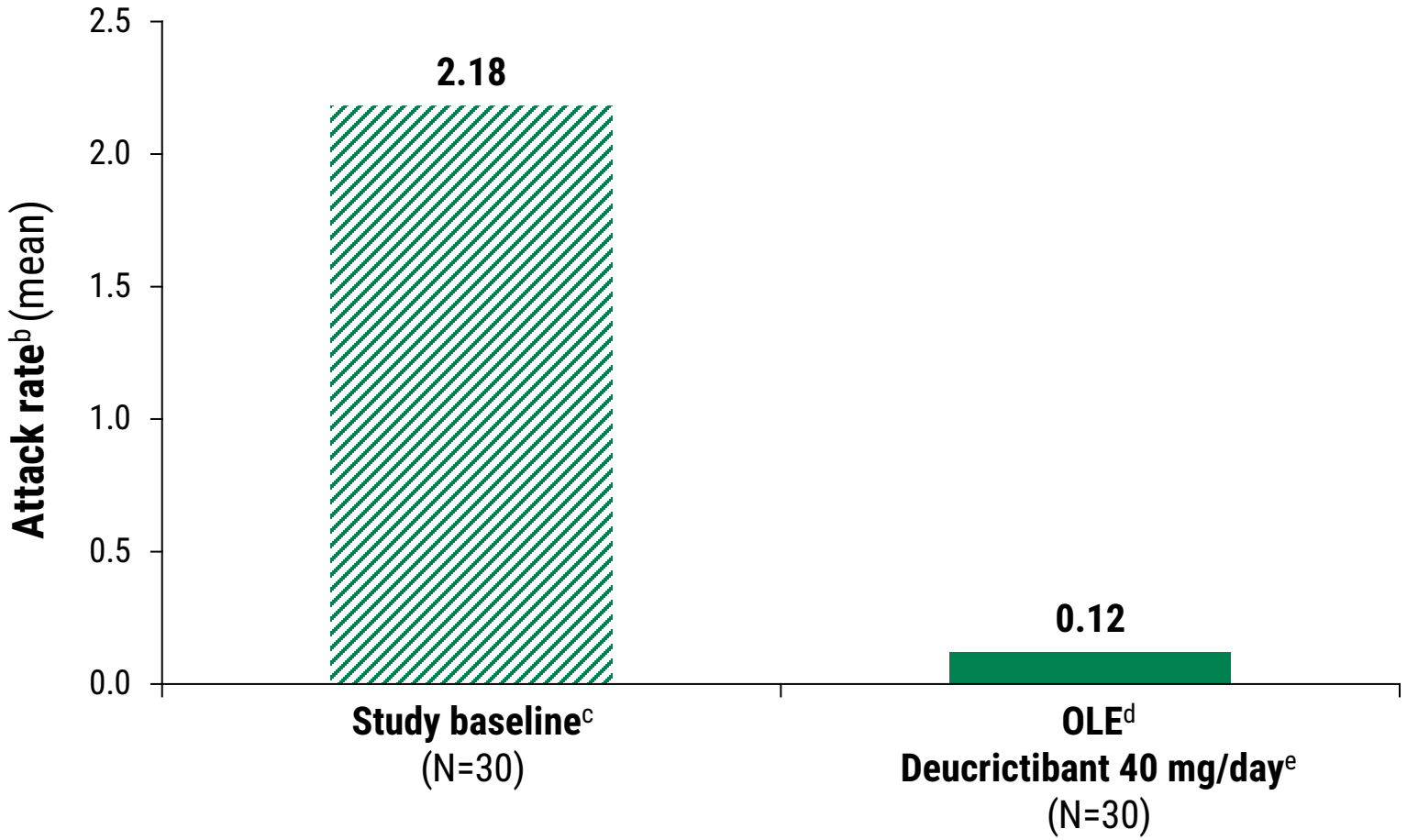
Average of 92.4% attack reduction from study baseline[a]



IR, immediate-release; OLE, open-label extension. N = number of participants in the OLE. [a]92.4% is the average patient-level reduction from CHAPTER-1 RCT baseline and excludes one patient with 4 days of OLE treatment and no attacks. [b]Based on time-normalized number of attacks per 4 weeks. [c]Crude mean attack rate at baseline. [d]Crude mean attack rate in OLE. [e]Deucrictibant IR capsule, 20 mg twice daily.

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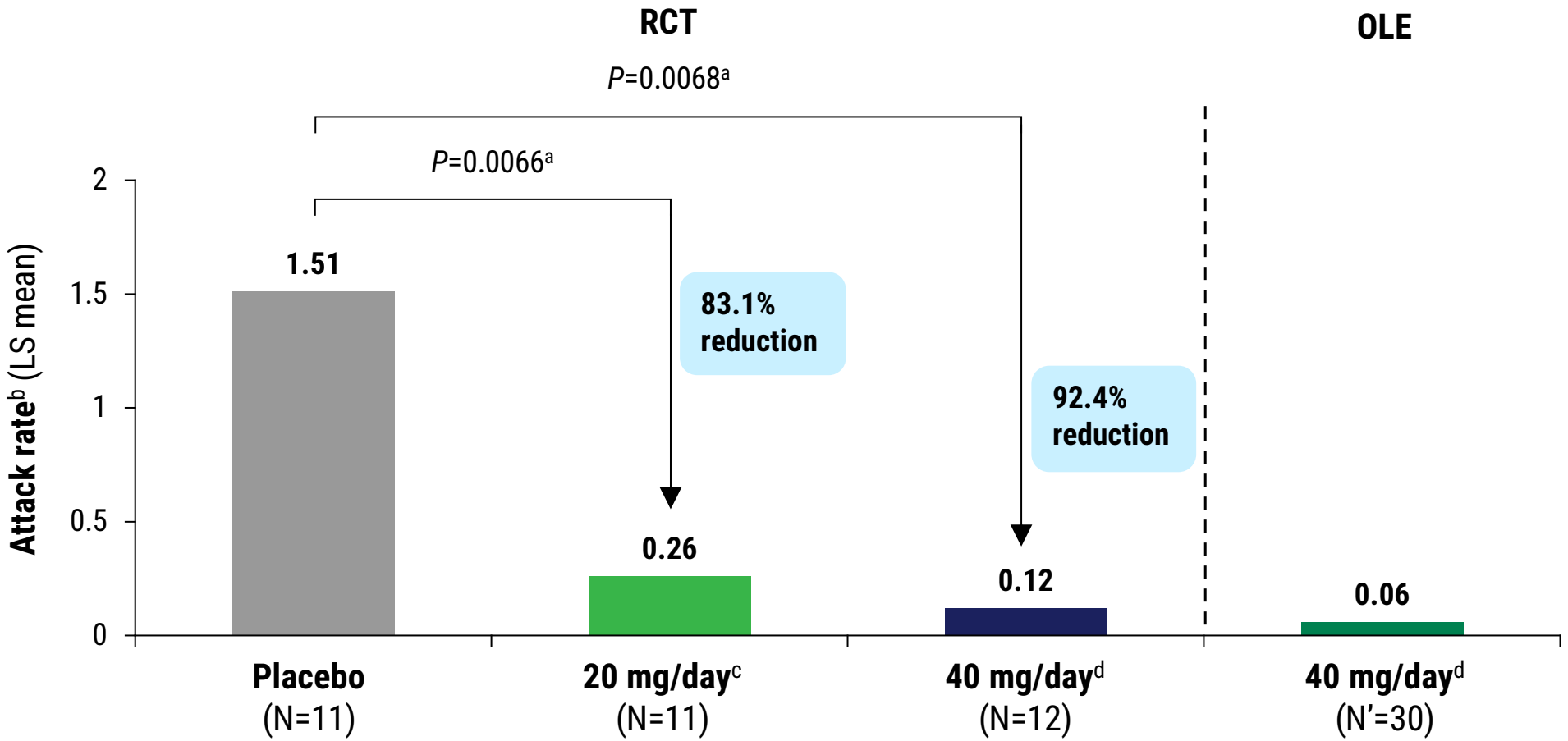
“Moderate and severe” attack rate reduced in the RCT and remained low in the OLE



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.

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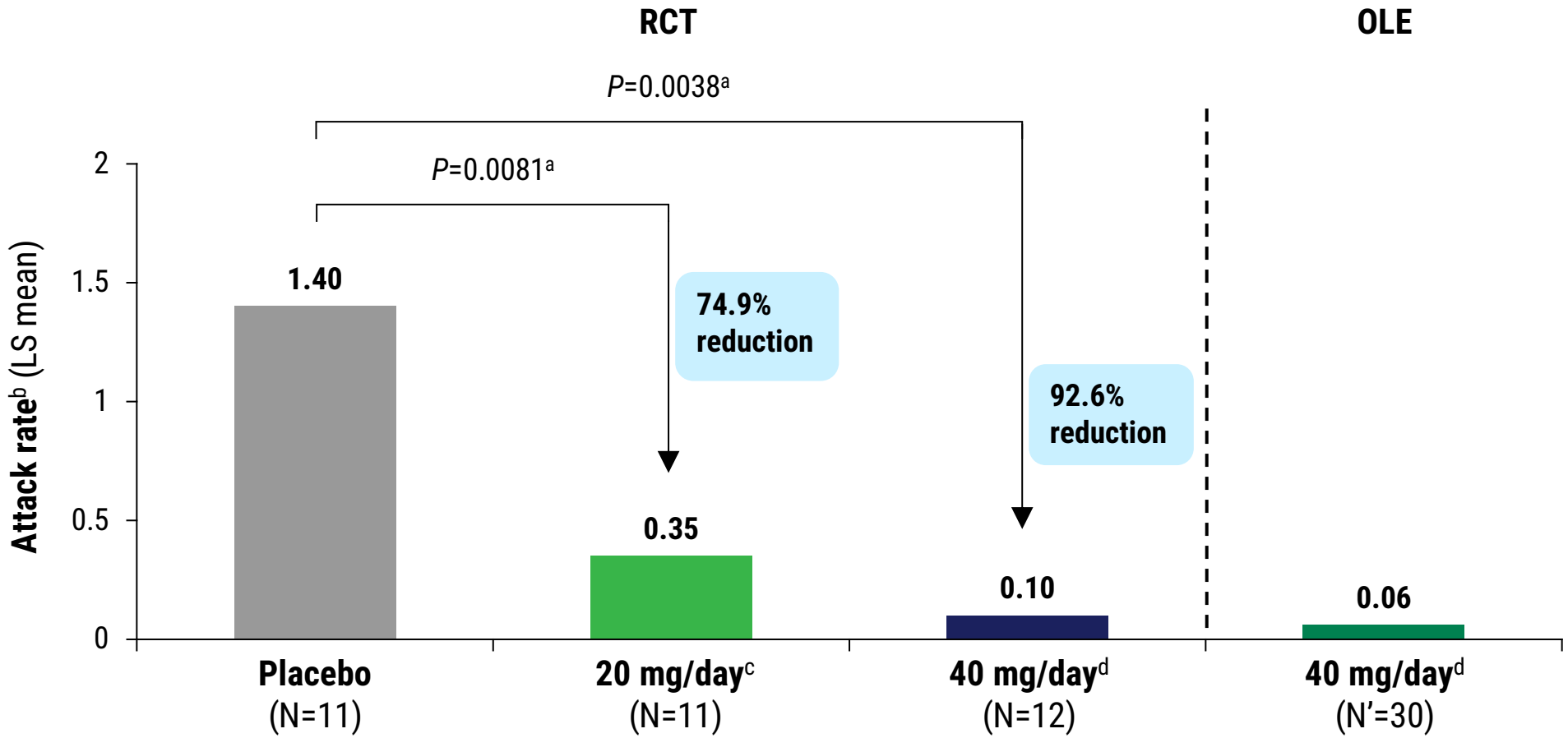
On-demand treated attack rate reduced in the RCT and remained low in the OLE



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.

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Conclusions

Final data from the completed Phase 2 CHAPTER-1 OLE study provide further evidence on the long-term safety and efficacy of oral deucrictibant for prevention of HAE attacks.

Deucrictibant was generally well tolerated with one treatment-related TEAE of asymptomatic increased GGT

Up to ~34 months

Attack rate reduced by week 1 and remained low for ~34 months in CHAPTER-1 RCT + OLE

0.12

Overall on-study attack rate during the OLE

0.06

Rate of "moderate and severe" attacks and of attacks treated with on-demand medication during the OLE

The Authors and the Sponsor would like to thank all the people with HAE as well as all study site staff who have been participating in the CHAPTER-1 trial.

GGT, gamma-glutamyltransferase; HAE, hereditary angioedema; OLE, open-label extension; RCT, randomized controlled trial; TEAE, treatment-emergent adverse event.

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