Results of the Phase 2 CHAPTER-1 Open-Label Extension Study on the Long-Term Safety and Efficacy of Oral Deucrictibant for Prophylaxis in Hereditary Angioedema

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

Conflicts of interest disclosure

S.K-A: BioCryst, Biotest, CSL Behring, Ionis, KalVista, Otsuka, Pharvaris, Takeda; **J.A.:** Astria, BioCryst, CSL Behring, Ionis, KalVista, Pharming, Pharvaris, Takeda; **F.A.:** BioCryst, CSL Behring, KalVista, Otsuka, Takeda; **M.C.:** BioCryst, CSL Behring, KalVista, Menarini, MSD, Novartis, Pharming, Pharvaris, Sobi, Takeda, UCB, Otsuka; **H.C.:** AstraZeneca (Alexion), CSL Behring, KalVista, Merck, Novartis, Pharming, Pharvaris, Roche, Sanofi, Sobi, Takeda; **N.C.:** BioCryst, CSL Vifor, GSK, Novartis, Pharming, Pharvaris, Takeda; **E.E.:** Biocryst, Dr. Falk Pharma, Novartis, Pharming, Pharvaris; **M.G.:** BioCryst, CSL Behring, Novartis; **S.G.:** Baxter, CSL Behring, Dyax, Grifols, Pharming/Swedish Orphan, Takeda, ViroPharma; **M.D.G.:** Biocryst, CSL Behring, Takeda; **P.G.:** BioCryst, CSL Behring, KalVista, Pharming, Takeda; **T.K.:** BioCryst, CSL Behring, KalVista, Otsuka, Pharvaris, Sanofi/Regeneron, Takeda; **M.M.:** Astria, BioCryst, CSL Behring, Intellia, KalVista, Novartis, Octapharma, Otsuka, Pharvaris, Takeda; **M.E.M.:** AstraZeneca, Astria, BioCryst, Blueprint, Celldex, Cogent, CSL Behring, GSK, Ionis, Intellia, KalVista, Merck, Novartis, Pharming, Pharvaris, Regeneron, Takeda, Teva; **M.S.:** BioCryst, CSL Behring, KalVista, Pharming, Pharvaris, Takeda; **M.D.T.:** none; **A.V.:** AstraZeneca, Berlin-Chemie/Menarini Group, CSL Behring, KalVista, Novartis, Pharming, Pharvaris, Sobi, Takeda; **H.J.W.:** BioCryst, BioMarin, CSL Behring, Genentech, GSK, Takeda; **W.H.Y.:** Aimmune Therapeutics, ALK Abello, AnaptysBio, Angioedema Centers of Reference and Excellence, Areteia, Aslan, AstraZeneca, Astria, BioCryst, Blueprint, Bristol Myers, Celgene, Celldex, CSL Behring, DBV Technologies, Dermira, Eli Lilly, Escient, Galderma, Genentech, GSK, Glenmark, Haleon, Hereditary Angioedema Canada, Incyte, Intellia, Ionis, Merck, Moderna, Novartis, Novavax, Pharvaris, Pharming, Providence, RAPT Therapeutics, Regeneron, Roche, Sanofi, Stallergenes, Takeda, Upstream Bio, VBI; **A.Z.:** Astria, BioCryst, CSL Behring, KalVista, Otsuka, Pharming, Pharvaris, Takeda; **R.C.:** employee of RC Consultancy and consultant to Pharvaris, holds stocks in Pharvaris; **S.M.:** employee of Mulders Clinical Consulting and consultant to Pharvaris; holds stocks in Pharvaris; **J.L., U.F., U.K, P.L.:** employees of Pharvaris, holds stocks in Pharvaris; **J.K.:** employee of JCK Consult and consultant to Pharvaris; holds stocks/stock options in Pharvaris; **A.L.:** employee of GrayMatters Consulting; consultant to Pharvaris; holds stocks/stock options in Pharvaris; advisor to Kosa Pharma; **E.A-P:** Astria, BioCryst, BioMarin, CSL Behring, Intellia, KalVista, Pharming, Pharvaris, Takeda; **M.A.R.:** Astria, BioCryst, BioMarin, Celldex, CSL Behring, Cycle Pharma, Grifols, Intellia, Ionis, KalVista, Novartis, Pharming, Pharvaris, Sanofi-Regeneron, Takeda.

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

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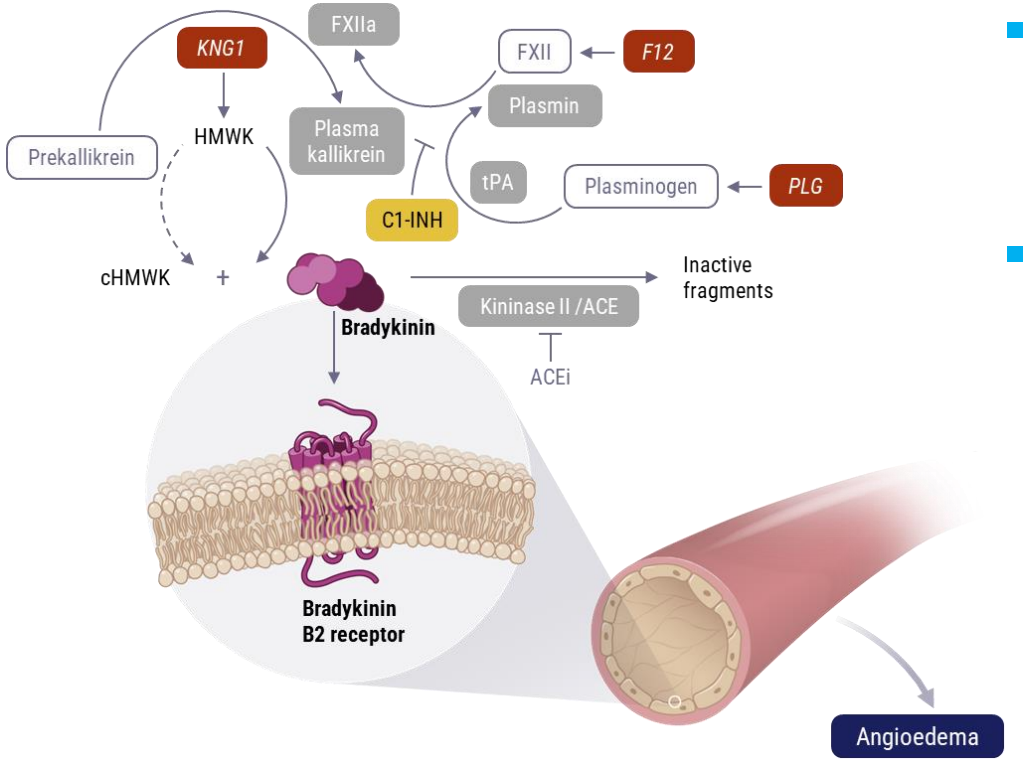
Hereditary angioedema (HAE) is a bradykinin-mediated condition with unmet medical needs



- 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.[2-5]
  - Clinical decision-making may be influenced by efficacy, patient experience, and 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. Accessed February 25, 2026. **5**. Covella B, et al. *Future Pharmacol*. 2024;4:41-53.

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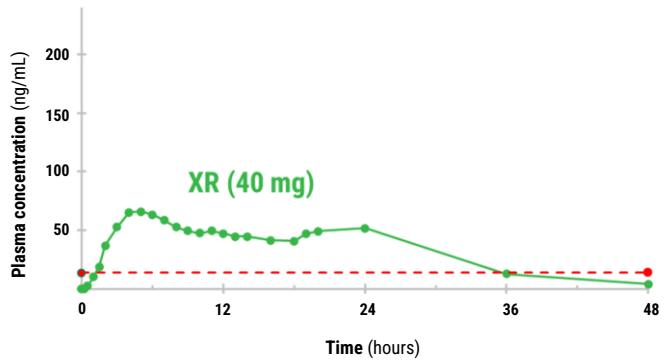
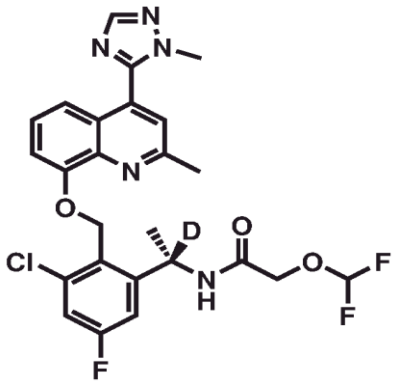
Deucrictibant is an investigational oral therapy for the prophylactic and on-demand treatment of bradykinin-mediated attacks

DEUCRICTIBANT extended-release (XR) tablet

sustained absorption[1]



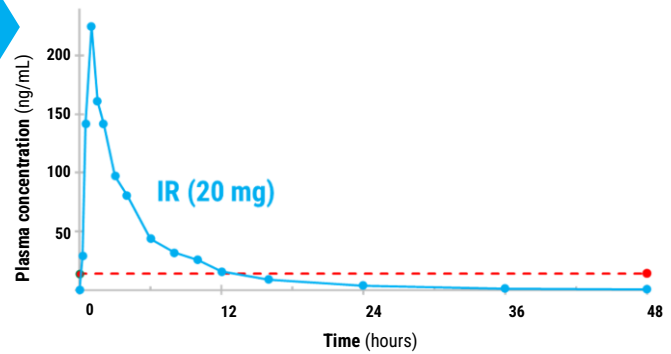
In studies, deucrictibant maintained sustained therapeutic exposure over 24 hours[1] from day 1, allowing for once-daily oral prevention of HAE attacks[2]



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 February 25, 2026. https://clinicaltrials.gov/study/NCT06669754. **3.** Maurer M, et al. Presented at AAAAI; February 24-27, 2023; San Antonio, TX, USA. **4.** RAPIDe-3. ClinicalTrials.gov identifier: NCT06343779. Accessed February 25, 2026. https://www.clinicaltrials.gov/study/NCT06343779.

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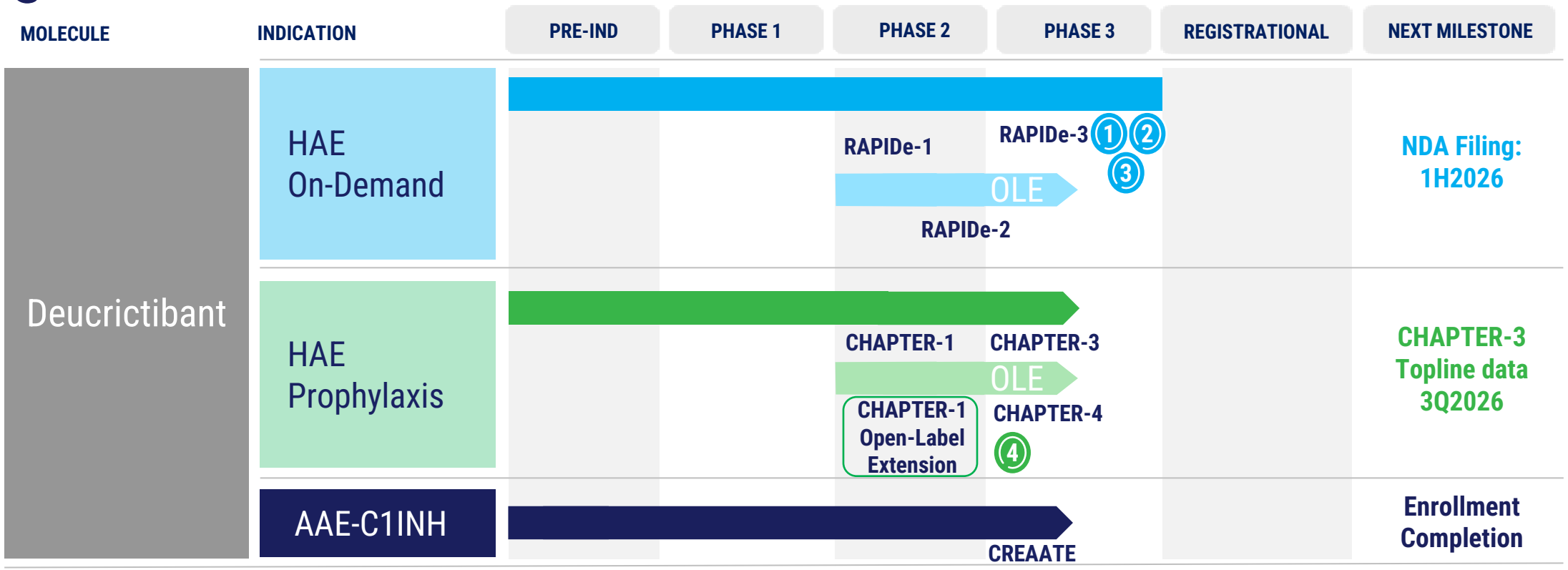
Deucrictibant development program in bradykinin-mediated angioedema



Other presentations at GALC 2026

1. Cohn D.M., et al. RAPIDe-3 Topline results
2. Riedl, M.A., et al. RAPIDe-3 End of progression
3. Tachdjian R, et al. RAPIDe-3 Qualitative interview concept elicitation
4. Zanichelli A, et al. CHAPTER-1 OLE Patient-reported outcomes (final data)

AAE-C1INH, acquired angioedema due to C1-inhibitor deficiency; HAE, hereditary angioedema; OLE, open-label extension. Study, ClinicalTrials.gov identifier: RAPIDe-1, NCT04618211; RAPIDe-2, NCT05396105; RAPIDe-3, NCT06343779; CHAPTER-1, NCT05047185; CHAPTER-3, NCT06669754; CHAPTER-4, NCT06679881; CREAATE, NCT07266805.

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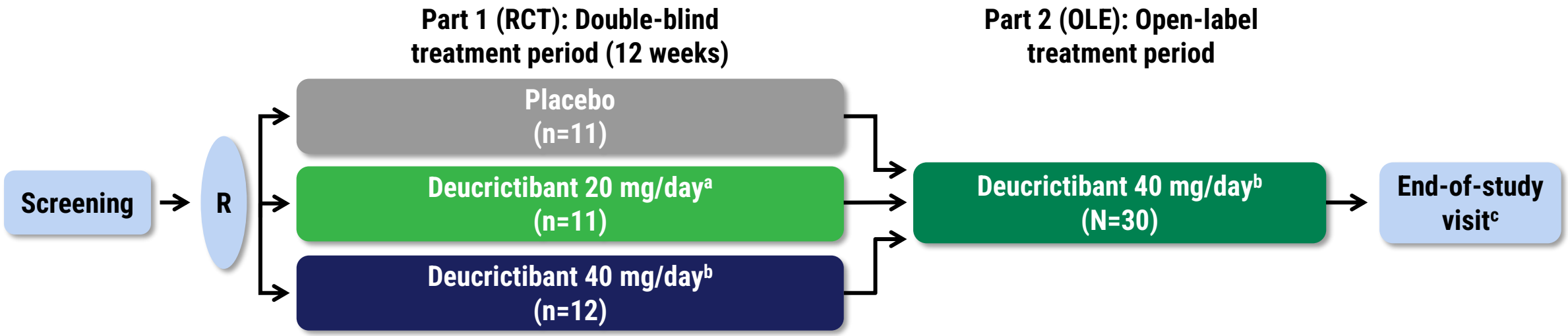
CHAPTER-1: Two-part, Phase 2 study of deucrictibant for long-term prophylaxis of HAE attacks



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 continued into the OLE.

Part 2 - OLE: Key objectives

- To evaluate the safety and efficacy of deucrictibant for long-term prophylaxis of HAE attacks in adults in the OLE of the CHAPTER-1 study.

HAE, hereditary angioedema; IR, immediate-release; OLE, open-label extension; R, randomization; RCT, randomized controlled trial. n = number of participants randomized in each treatment group in the RCT. N = number of participants.
[a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily. [C]Twenty-one participants rolled over to the ongoing CHAPTER-4 (NCT06679881) OLE in which deucrictibant extended-release tablet is self-administered.
CHAPTER-1 is a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: NCT05047185. https://www.clinicaltrials.gov/study/NCT05047185. Accessed February 25, 2026. CHAPTER-4 is a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: NCT06679881. https://clinicaltrials.gov/study/NCT06679881. Accessed February 25, 2026.

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Deucrictibant was well tolerated with no safety signals in the OLE

- Deucrictibant was generally well tolerated with one treatment-related TEAE reported: mild, asymptomatic increased gamma-glutamyltransferase (<2 ULN).
  - No clinically significant abnormalities in laboratory parameters, vital signs, or ECG findings.
  - No treatment-related severe or serious TEAEs were reported.
  - No TEAEs leading to study drug discontinuation, study withdrawal, or death.
- Mean (SD) treatment duration in the OLE was 22.2 (8.1) months. Maximum deucrictibant exposure during the entire study was 33.8 months.
- Twenty-one participants were on study at the time of CHAPTER-1 study end, and all continued into the ongoing CHAPTER-4 OLE (NCT06679881),[1] in which deucrictibant XR tablet, 40 mg, is self-administered. None of the 9 discontinuations in the CHAPTER-1 OLE were reported as treatment-related or associated with an adverse event.

	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	**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[c]	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**

ECG, electrocardiogram; IR, immediate-release; OLE, open-label extension; SD, standard deviation; TEAE, treatment-emergent adverse event; ULN, upper limit of normal; XR, extended-release. TEAE 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. N = number of participants who received ≥1 dose of study treatment in the OLE. [a]Deucrictibant IR capsule, 20 mg twice daily. [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Started during the RCT, resolved while continuing deucrictibant treatment during the OLE, and reoccurred by end of the OLE; alanine aminotransferase, aspartate aminotransferase, bilirubin, and alkaline phosphatase levels were normal. [d]Three serious TEAEs required reconstruction surgery, hip replacement, or knee replacement. These were not considered treatment-related.

1. CHAPTER-4. https://clinicaltrials.gov/study/NCT06679881. Accessed February 25, 2026.

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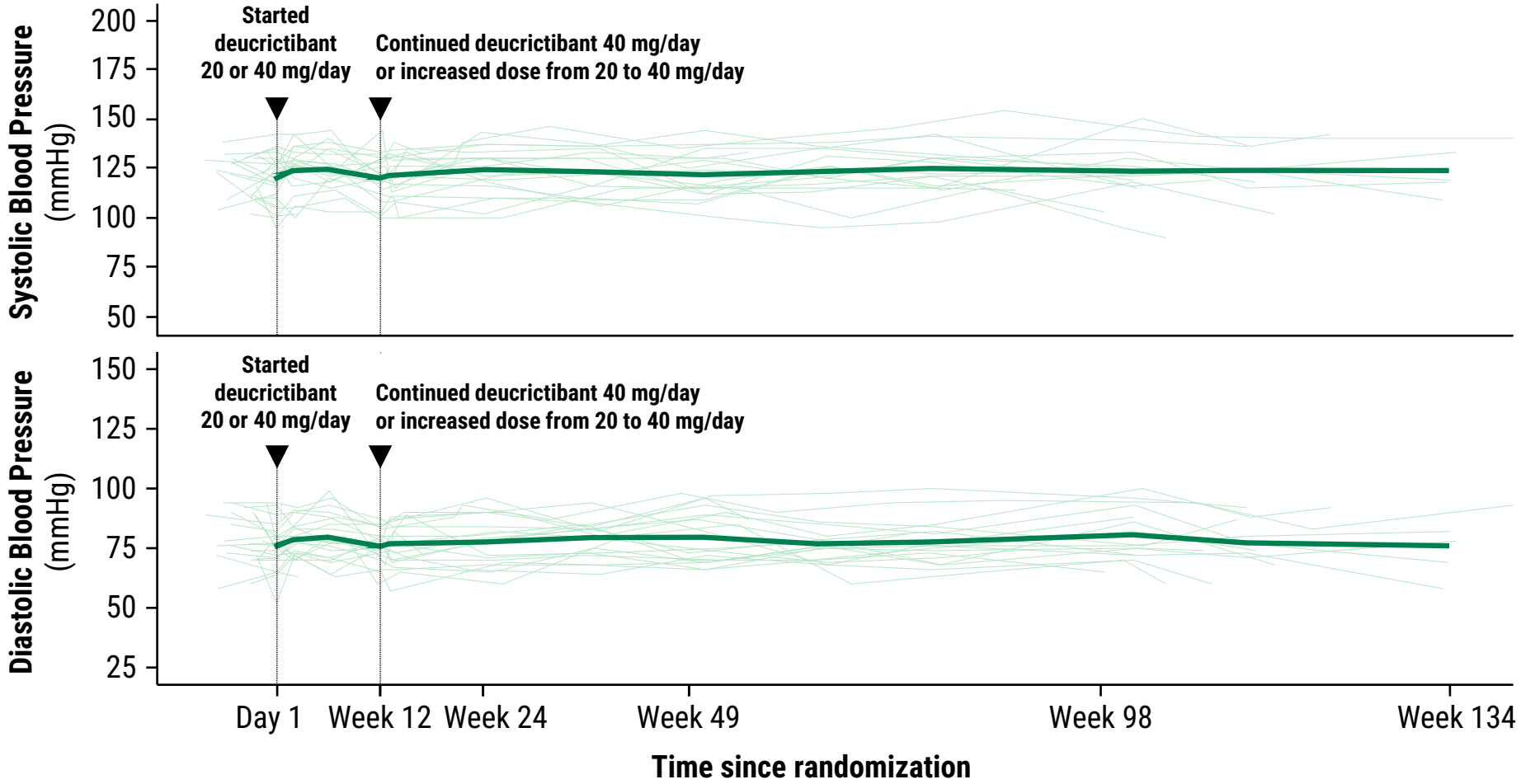
Blood pressure remained stable during long-term treatment with deucrictibant



Thin lines represent individual participant blood pressure. Thick lines represent the group mean blood pressure.

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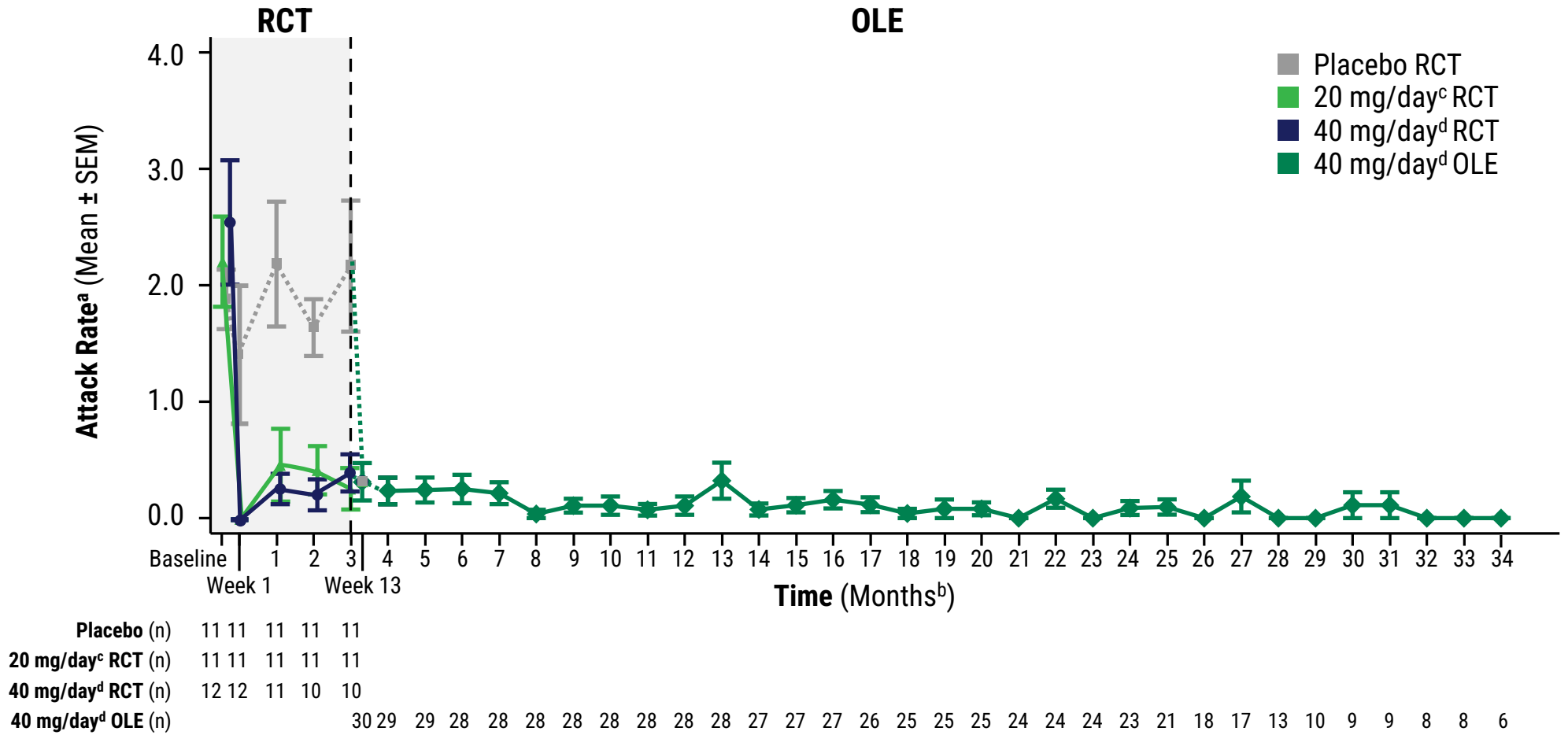
Attack rate reduced by week 1 and week 13 and remained low for up to ~34 months



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

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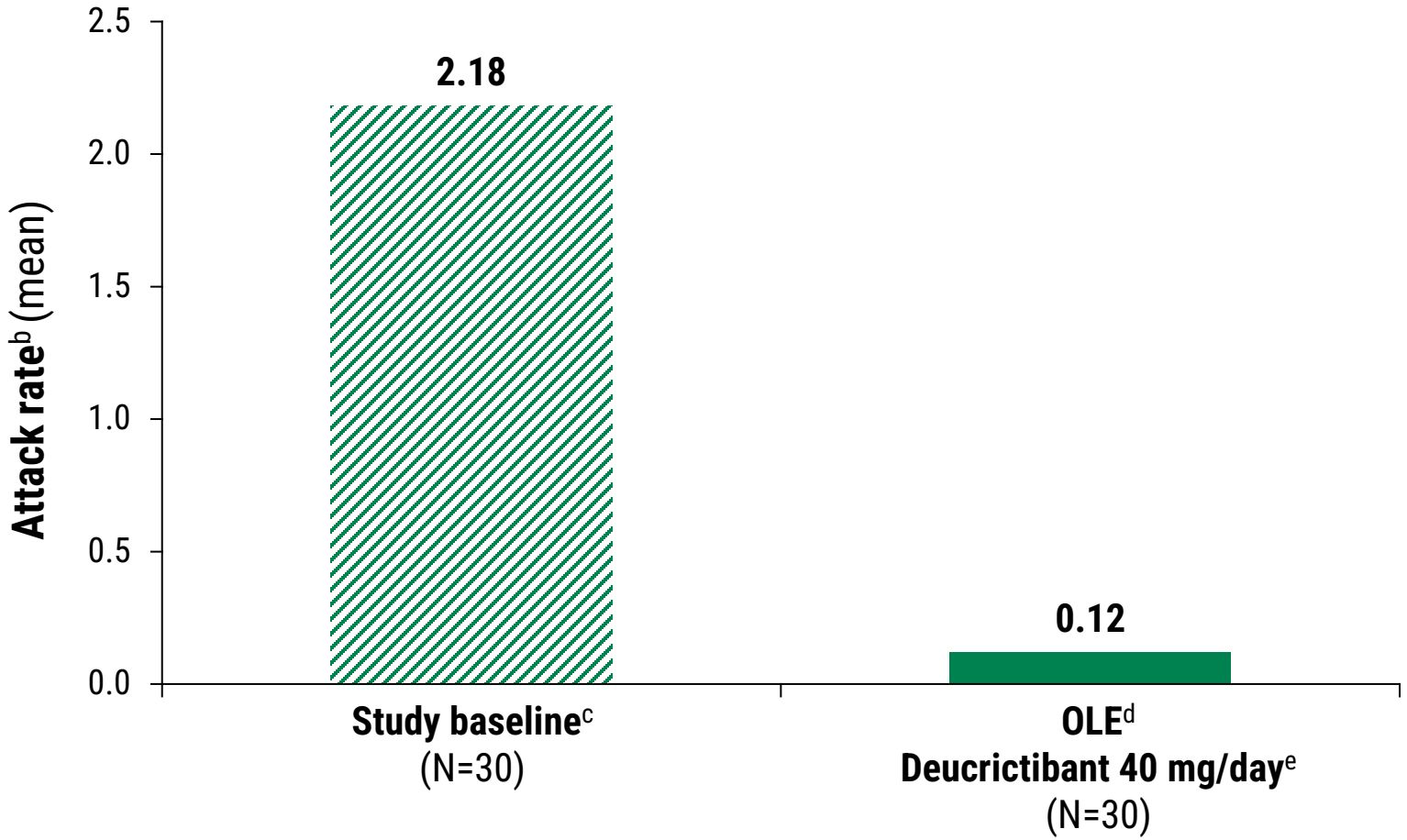
Average of 92.4% attack reduction from study baseline[a]



IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial. N = number of participants in the OLE. [a]92.4% is the average patient-level reduction from CHAPTER-1 RCT baseline and excludes one participant 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 the OLE. [e]Deucrictibant IR capsule, 20 mg twice daily.

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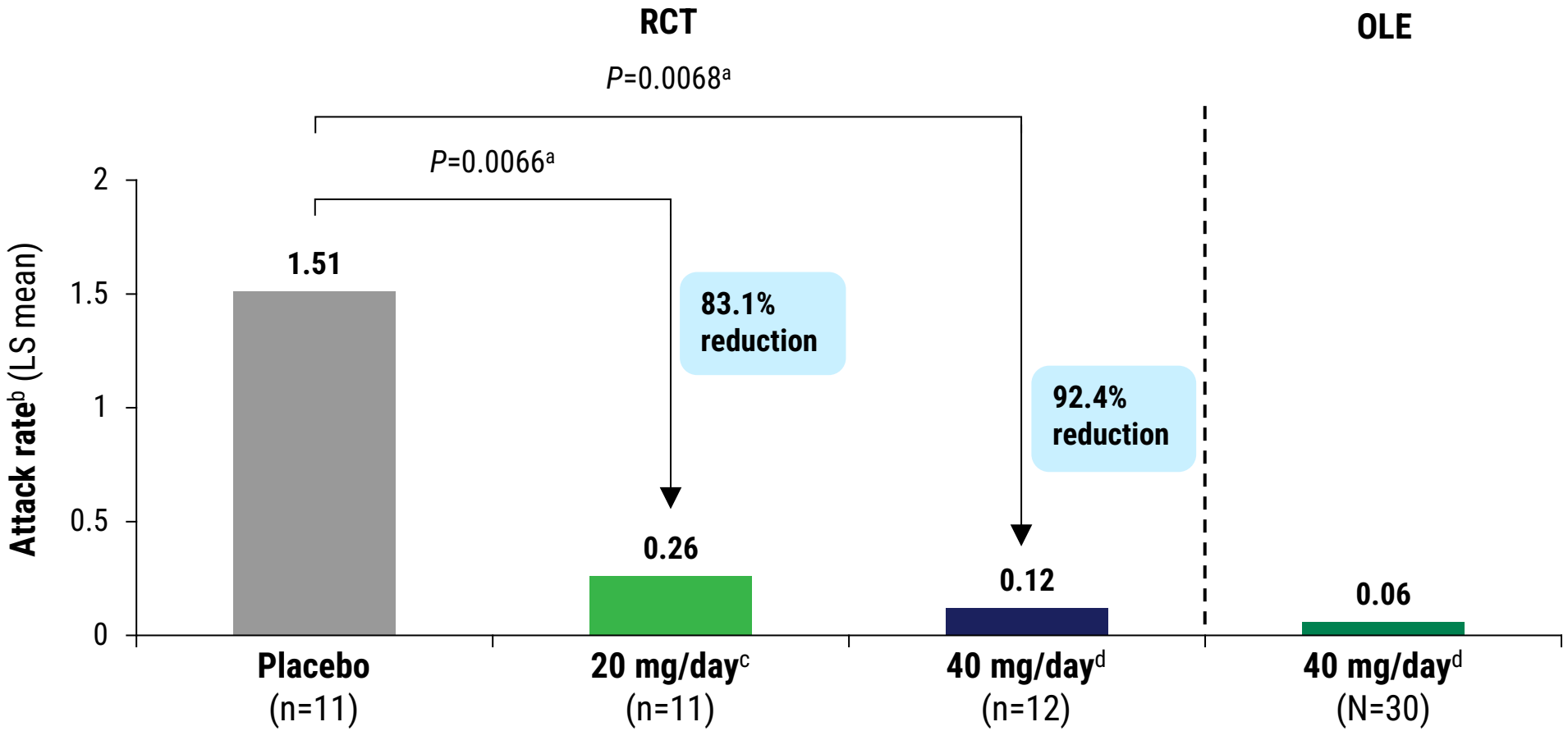
“Moderate and severe” attack rate reduced in the RCT and remained low in the OLE



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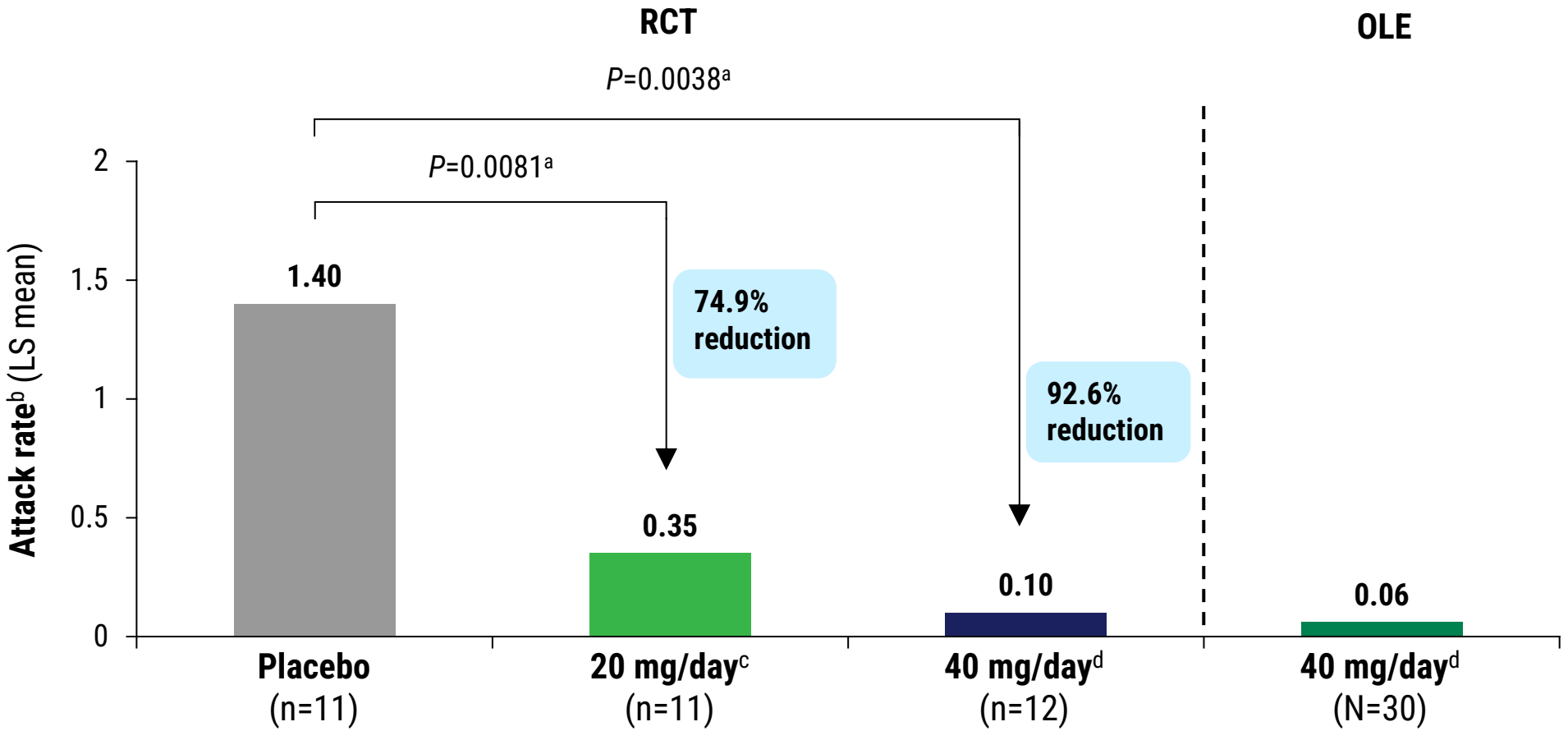
On-demand treated attack rate reduced in the RCT and remained low in the OLE



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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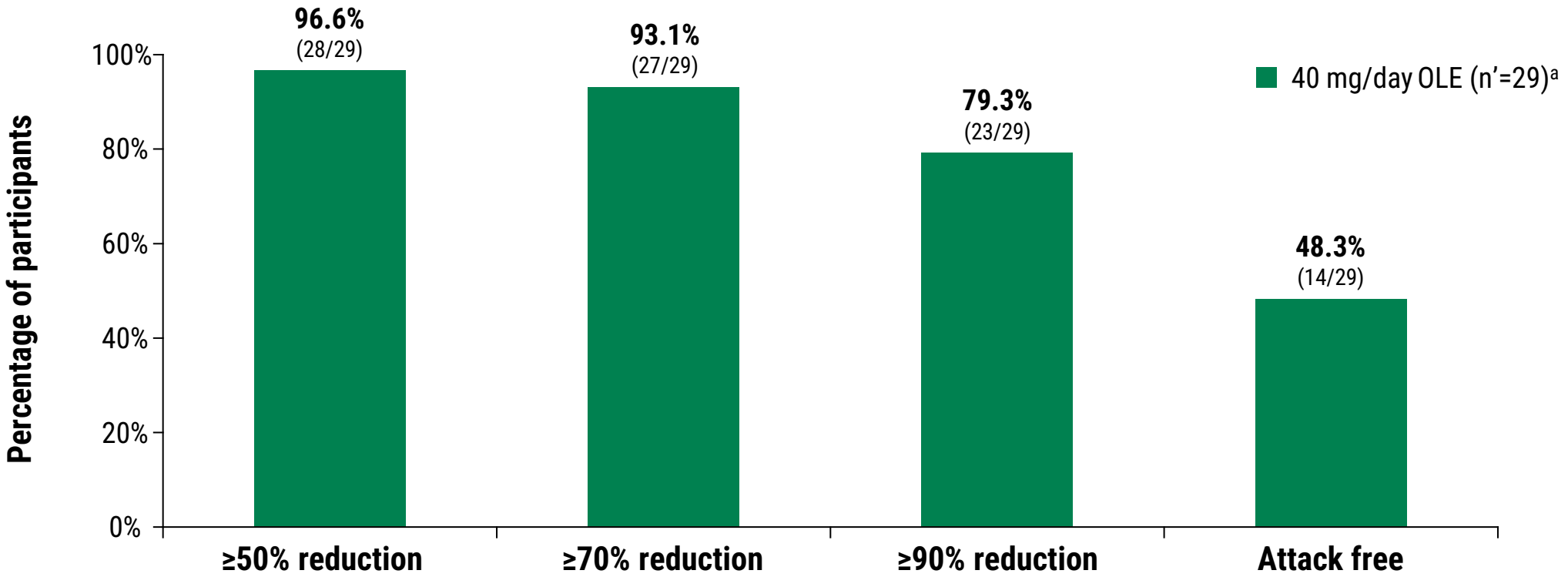
Attack rate reduced relative to RCT study baseline with approximately half of participants attack free during the OLE



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).

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Conclusions

Final data from the completed open-label extension (OLE) of the Phase 2 CHAPTER-1 study investigating daily oral deucrictibant administration provide first evidence on the long-term safety and efficacy of bradykinin B2 receptor antagonism for prophylaxis against bradykinin-mediated angioedema attacks.

Deucrictibant was generally well tolerated with no safety signals observed in laboratory parameters, vital signs, or ECG findings

Up to ~34 months

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

0.12

Overall on-study mean attack rate during the OLE

Attack free

Approximately half of participants were attack free 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.

ECG, electrocardiogram; HAE, hereditary angioedema; OLE, open-label extension.