

Oral Deucritibant for Prophylaxis in Hereditary Angioedema: Long-Term Safety and Efficacy Results From the Phase 2 CHAPTER-1 Open-Label Extension Study

Markus Magerl

Institute of Allergology, Charité-Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin and Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Immunology and Allergology, Berlin, Germany

Coauthors: William H. Yang, Sorena Kiani-Alikhan, John Anderson, Francesco Arcoleo, Mauro Cancian, Hugo Chapdelaine, Niall Conlon, Efrem Eren, Mark Gompels, Sofia Grigoriadou, Maria D. Guarino, Padmalal Gurugama, Tamar Kinaciyan, Michael E. Manning, Marcin Stobiecki, Michael D. Tarzi, Anna Valerieva, H. James Wedner, Andrea Zanichelli, Rafael Crabbé, Susan Mulders, Jonathan Levy, Ulrich Freudensprung, Umar Katbeh, Jochen Knolle, Anne Lesage, Peng Lu, Emel Aygören-Pürsün, Marc A. Riedl

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Conflicts of interest disclosure

COI: M.M.: Argo, Astria, BioCryst, CSL Behring, Intellia, KalVista, Octapharma, Otsuka, Pharvaris, 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, Escient, Galderma, Genentech, Glenmark, GSK, Haleon, Hereditary Angioedema Canada, Incyte, Intellia, Ionis, Lilly, Merck, Moderna, Novartis, Novavax, Pharming, Pharvaris, Providence, RAPT Therapeutics, Regeneron, Roche, Sanofi, Stallergenes Greer, Takeda, Upstream Bio, VBI; **S.K.A.:** BioCryst, Biotest, CSL Behring, Ionis, KalVista, Otsuka, Pharvaris, Takeda; **J.A.:** Astria, BioCryst, CSL Behring, Intellia, Ionis, KalVista, Pharming, Pharvaris, Takeda; **F.A.:** BioCryst, CSL Behring, KalVista, Otsuka, Takeda; **M.C.:** BioCryst, CSL Behring, KalVista, Menarini, MSD, Novartis, Otsuka, Pharming, Pharvaris, Sobi, Takeda, UCB; **H.C.:** AstraZeneca (Alexion), CSL Behring, KalVista, Merck, Novartis, Pharming, Pharvaris, Roche, Sanofi, Sobi, Takeda; **N.C.:** BioCryst, CSL Vifor, GSK, Novartis, Pharvaris, Pharming, Takeda; **E.E.:** BioCryst, Dr Falk Pharma, Novartis, Pharming, Pharvaris; **M.G.:** BioCryst, CSL Behring, Novartis; **S.G.:** BioCryst, CSL Behring, KalVista, Neopharmed Gentili, Otsuka, Pharming, Pharvaris, Takeda; **M.D.G.:** BioCryst, CSL Behring, Takeda; **P.G.:** BioCryst, CSL Behring, KalVista, Pharming, Takeda; **T.K.:** ADARx, Astria, BioCryst, CSL Behring, KalVista, Otsuka, Pharvaris, Sanofi/Regeneron, Takeda; **M.E.M.:** AstraZeneca, Astria, BioCryst, Blueprint, Celldex, Cogent, CSL Behring, GSK, Intellia, Ionis, KalVista, Merck, Novartis, Pharming, Pharvaris, Regeneron, Takeda, Teva. **M.S.:** BioCryst, CSL Behring, KalVista, Pharming, Pharvaris, Takeda; **M.D.T.:** None to report; **A.V.:** AstraZeneca, Astria, Berlin-Chemie/Menarini Group, CSL Behring, Ewopharma, Ionis, KalVista, Novartis, Organon, Pharming, Pharvaris, Shire/Takeda, Sobi, Stallergenes Greer, Teva; **H.J.W.:** BioCryst, BioMarin, CSL Behring, Genentech, GSK, Takeda; **A.Z.:** Astria, BioCryst, CSL Behring, Intellia, 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., J.K., P.L.:** employee of Pharvaris, holds stocks in Pharvaris; **A.L.:** employee of GrayMatters Consulting and consultant to Pharvaris; holds stocks/stock options in Pharvaris; advisor to Kosa Pharma; **E.A.-P.:** Astria, BioCryst, BioMarin, CSL Behring, Intellia, KalVista, Otsuka, Pharming, Pharvaris, Takeda; **M.A.R.:** ADARx, Astria, BioCryst, BioMarin, Celldex, CSL Behring, Cycle Pharma, Grifols, Intellia, Ionis, KalVista, Novartis, Pharming, Pharvaris, Sanofi/Regeneron, Takeda.

CHAPTER-1 was a Pharvaris-sponsored clinical study. ClinicalTrials.gov identifier: NCT05047185.

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Continuous bradykinin B2 receptor antagonism can inhibit excessive endothelial permeability and prevent AE-BK attacks

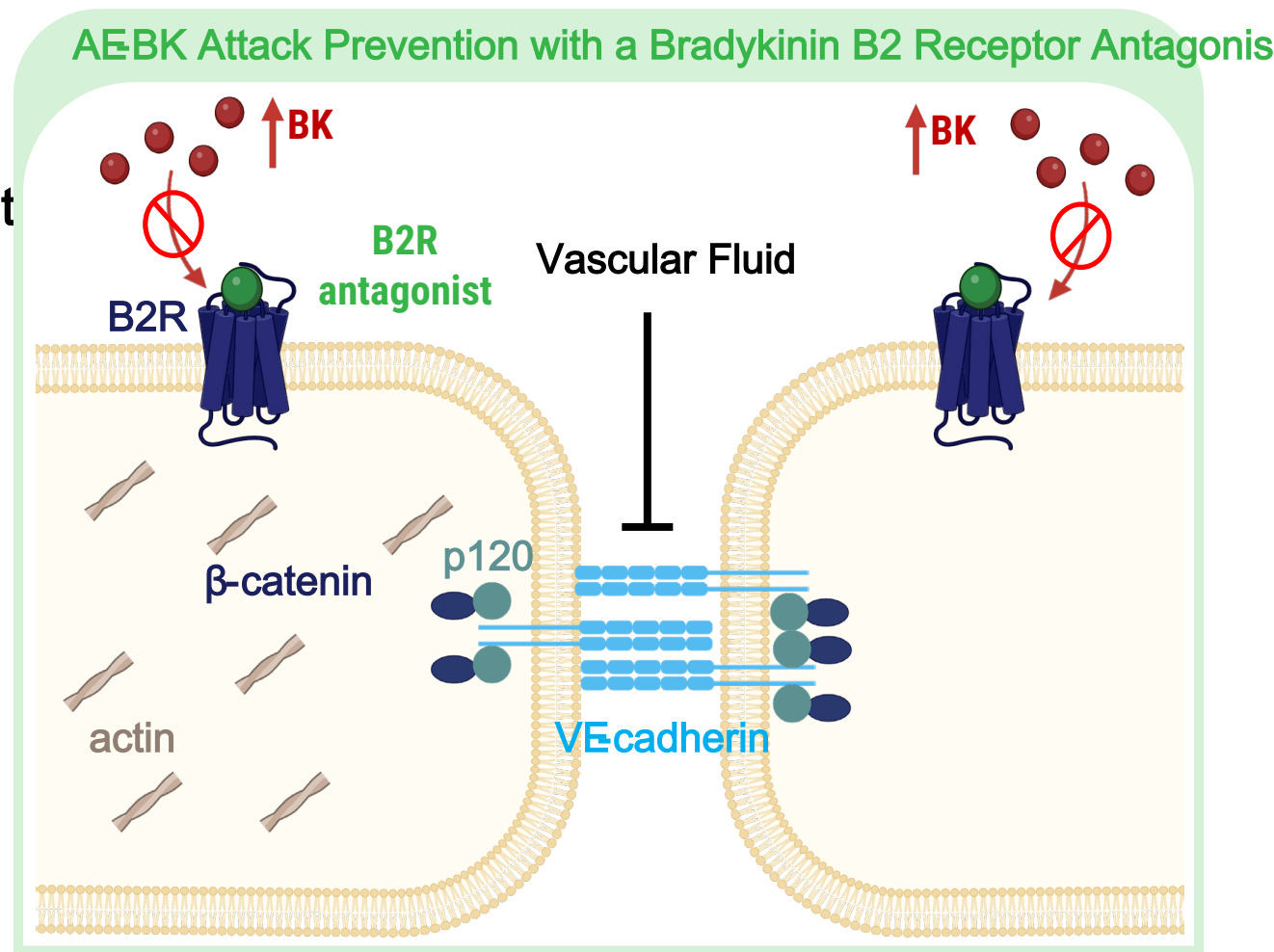
Longterm treatment with a bradykinin B2 receptor antagonist can:



Prevent increased vascular permeability¹



Sustain control of recurrent BK-signaling for long-term disease management²

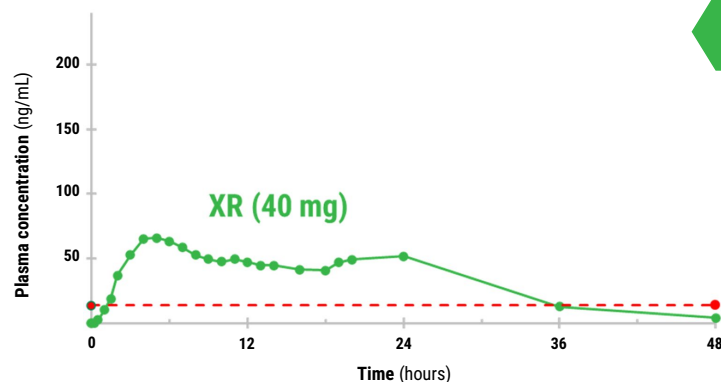


AE-BK, bradykinin-mediated angioedema; B2R, B2 receptor; BK, bradykinin; VE, vascular endothelial.

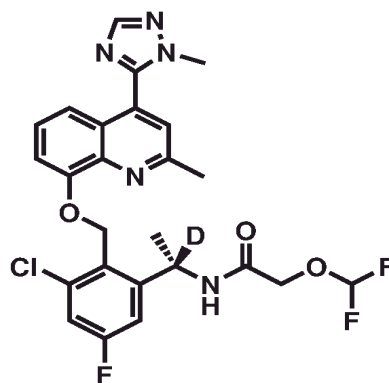
1. Terzuoli E, et al. PLoS ONE 2014;9(1):e84358. 2. Aygören-Pürsün E, et al. Lancet 2026;13(4) e215-e26.

Deucrictibant is an orally administered bradykinin B2 receptor antagonist in development for the prophylactic and on-demand treatment of AE-BK attacks

DEUCRICTIBANT extended-release (XR) tablet sustained absorption¹

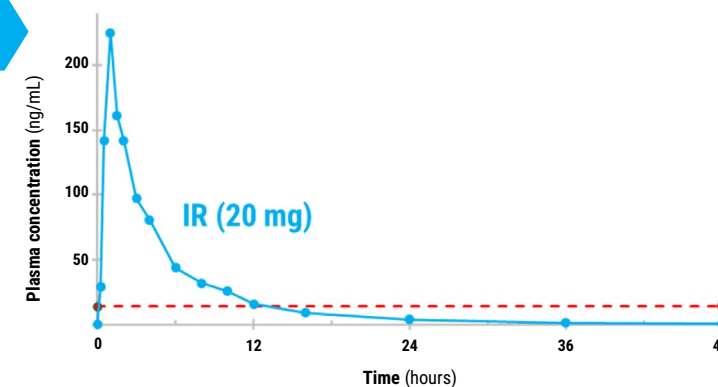


In studies, deucrictibant maintained sustained therapeutic exposure over 24 hours¹ from day 1, allowing for once-daily oral prevention of HAE attacks²



Deucrictibant

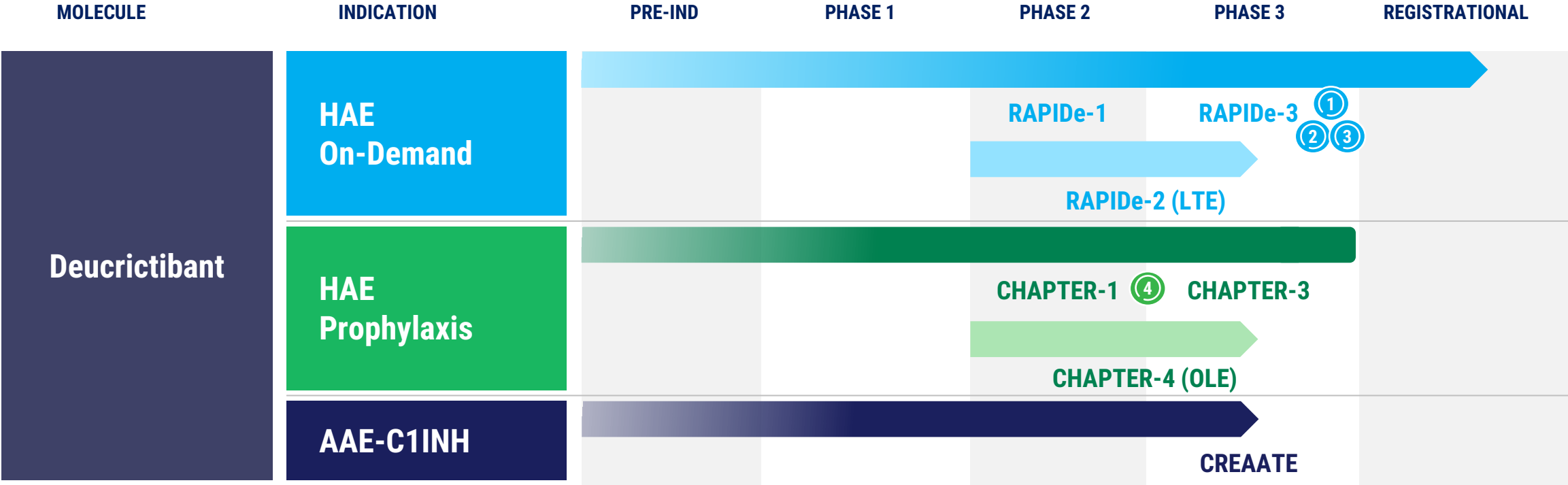
DEUCRICTIBANT immediate-release (IR) capsule rapid absorption³



In studies, deucrictibant rapidly reached therapeutic exposure within 15–30 minutes,³ supporting on-demand oral treatment of HAE attacks^{4,5}

AE-BK, bradykinin-mediated angioedema; 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. <https://clinicaltrials.gov/study/NCT06669754>. Accessed September 2, 2026. 3. Maurer M, et al. *Lancet Haematol.* 2026; 13(4):e200-14. 4. Riedl MA, et al. *Lancet.* 2026; doi:10.1016/S0140-6736(26)01296-1. 5. Riedl MA, et al. Presented at the American Academy of Allergy, Asthma & Immunology (AAAAI) Annual Meeting; March 2026; Philadelphia, PA, USA.

Deucrictibant development program in AE-BK

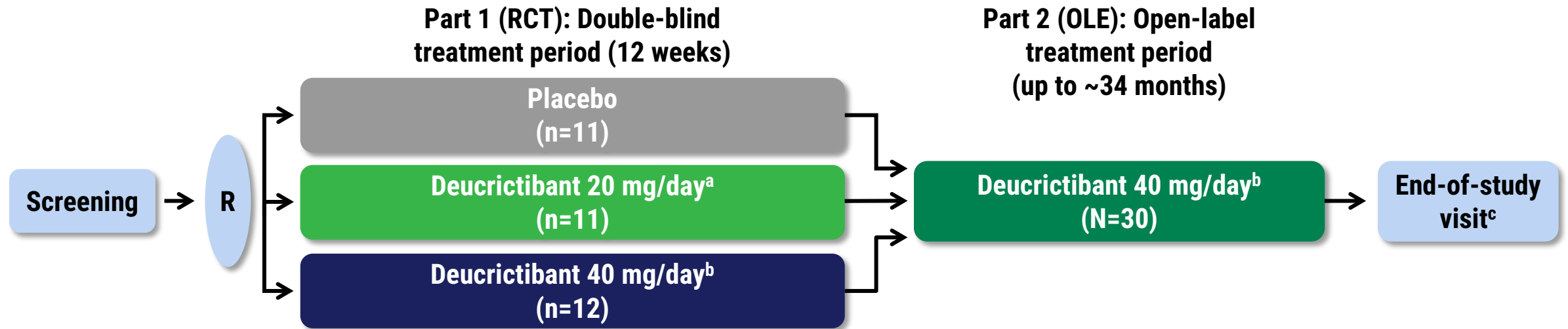


Other Presentations at 2026 HAEi Regional Conference Americas

- ① Adatia A, et al. RAPIDe-3 Regional subgroup analysis
- ② Grumach A, et al. RAPIDe-3 Qualitative interviews: Study attack experience
- ③ Tachdjian R, et al. RAPIDe-3 End of progression
- ④ Chapdelaine H, et al. CHAPTER-1 OLE patient-reported outcomes

AAE-C1INH, acquired angioedema due to C1 inhibitor deficiency; AE-BK, bradykinin-mediated angioedema; BK, bradykinin; HAE, hereditary angioedema; IND, Investigational New Drug; LTE, long-term extension; OLE, open-label extension.

CHAPTER-1: Two-part, Phase 2 study of deucricitibant 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:
 - Deucricitibant 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 deucricitibant for long-term prophylaxis of HAE attacks in adults in the OLE of the CHAPTER-1 study.
- Mean (SD) treatment duration in the OLE: 22.2 (8.1) months.
- Maximum deucricitibant exposure during the entire study: 33.8 months.
- Mean (SD) treatment duration for the 14 participants who were attack-free during the OLE: 22.4 (7.6) months.

HAE, hereditary angioedema; IR, immediate-release; ODT, on-demand treatment; 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. ^aDeucricitibant IR capsule, 10 mg twice daily. ^bDeucricitibant IR capsule, 20 mg twice daily. ^cTwenty-one participants rolled over to the ongoing CHAPTER-4 (NCT06679881) open-label study in which deucricitibant extended-release tablet is self-administered. CHAPTER-1 was a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: NCT05047185. <https://www.clinicaltrials.gov/study/NCT05047185>. Accessed September 2, 2026. CHAPTER-4 is a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: NCT06679881. <https://clinicaltrials.gov/study/NCT06679881>. Accessed September 2, 2026.

Deucrictibant was well tolerated, with no safety signals in the OLE

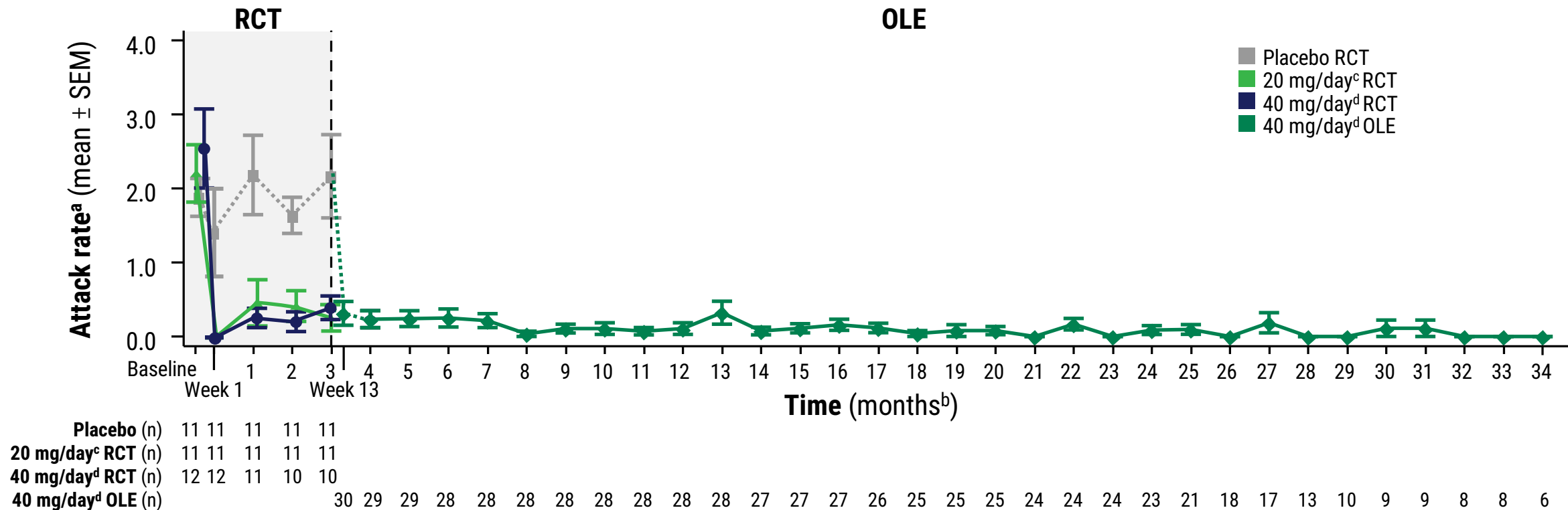
- Deucrictibant was generally well tolerated with one treatment-related TEAE reported: isolated, mild, asymptomatic increased gamma-glutamyltransferase (<2 ULN).
 - No clinically significant abnormalities in laboratory parameters, vital signs, or ECG findings. Blood pressure remained stable during the OLE.
 - No treatment-related severe or serious TEAEs were reported.
 - No TEAEs leading to study drug discontinuation, study withdrawal, or death were reported.
- 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 nine discontinuations in the CHAPTER-1 OLE were reported as treatment-related or associated with an adverse event.

	Placebo to deucrictibant 40 mg/day ^a (N=9)		Deucrictibant 20 mg/day ^b to deucrictibant 40 mg/day ^a (N=11)		Deucrictibant 40 mg/day ^a to deucrictibant 40 mg/day ^a (N=10)		Total (N=30)	
	Participants, n (%)	Events, no.	Participants, n (%)	Events, no.	Participants, n (%)	Events, no.	Participants, n (%)	Events, no.
Any TEAE	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 event that started or pre-existing adverse event 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. ^aDeucrictibant IR capsule, 20 mg twice daily.

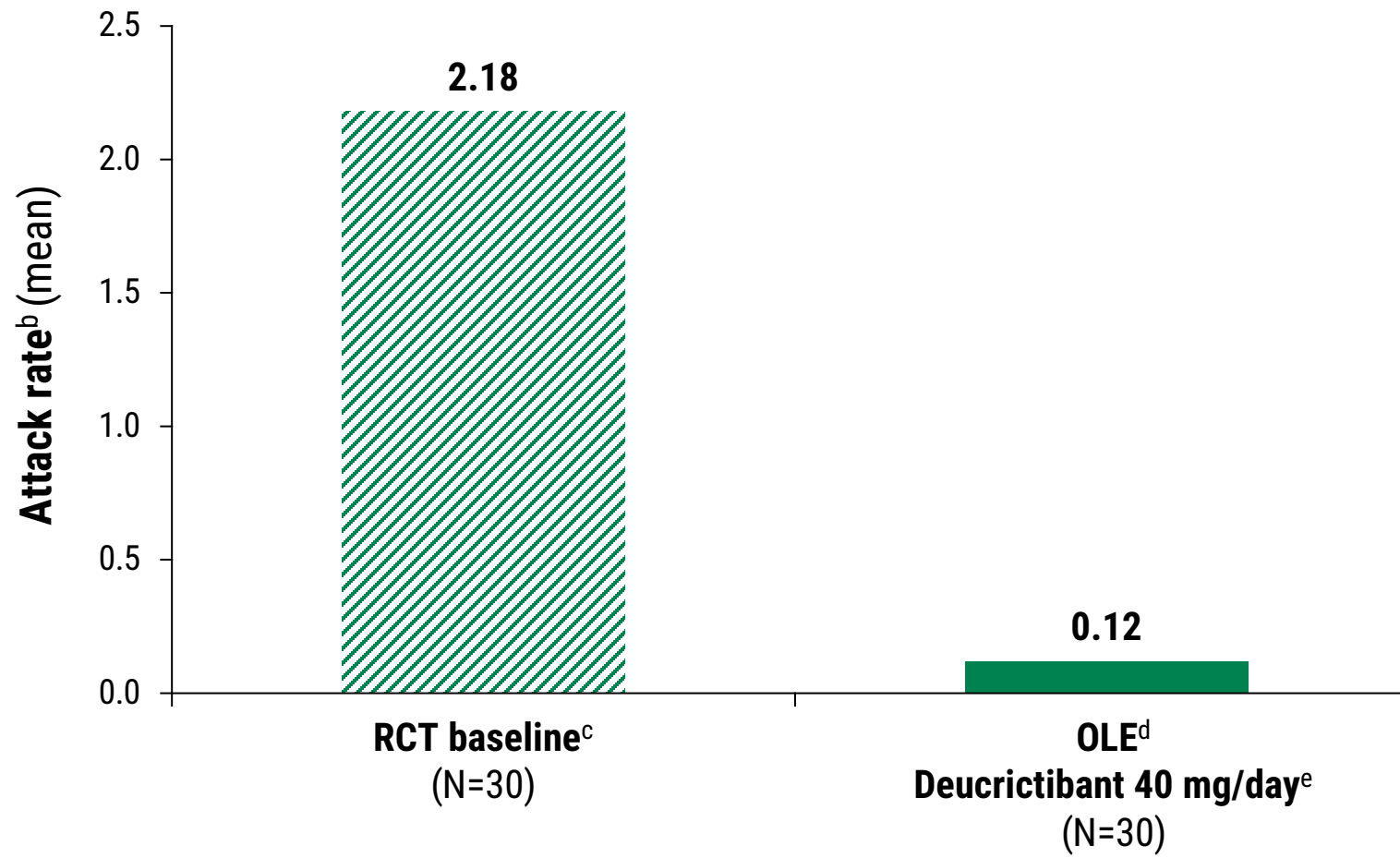
^bDeucrictibant IR capsule, 10 mg twice daily. ^cStarted during the RCT, resolved while continuing deucrictibant treatment during the OLE, and reoccurred by end of the OLE; alanine aminotransferase, aspartate aminotransferase, bilirubin, and alkaline phosphatase levels were normal. ^dThree serious TEAEs required reconstruction surgery, hip replacement, or knee replacement. These were not considered treatment-related. 1. CHAPTER-4. <https://clinicaltrials.gov/study/NCT06679881>. Accessed September 2, 2026.

Attack rate was reduced within the first week of treatment with deucricitbant and remained low for up to ~34 months



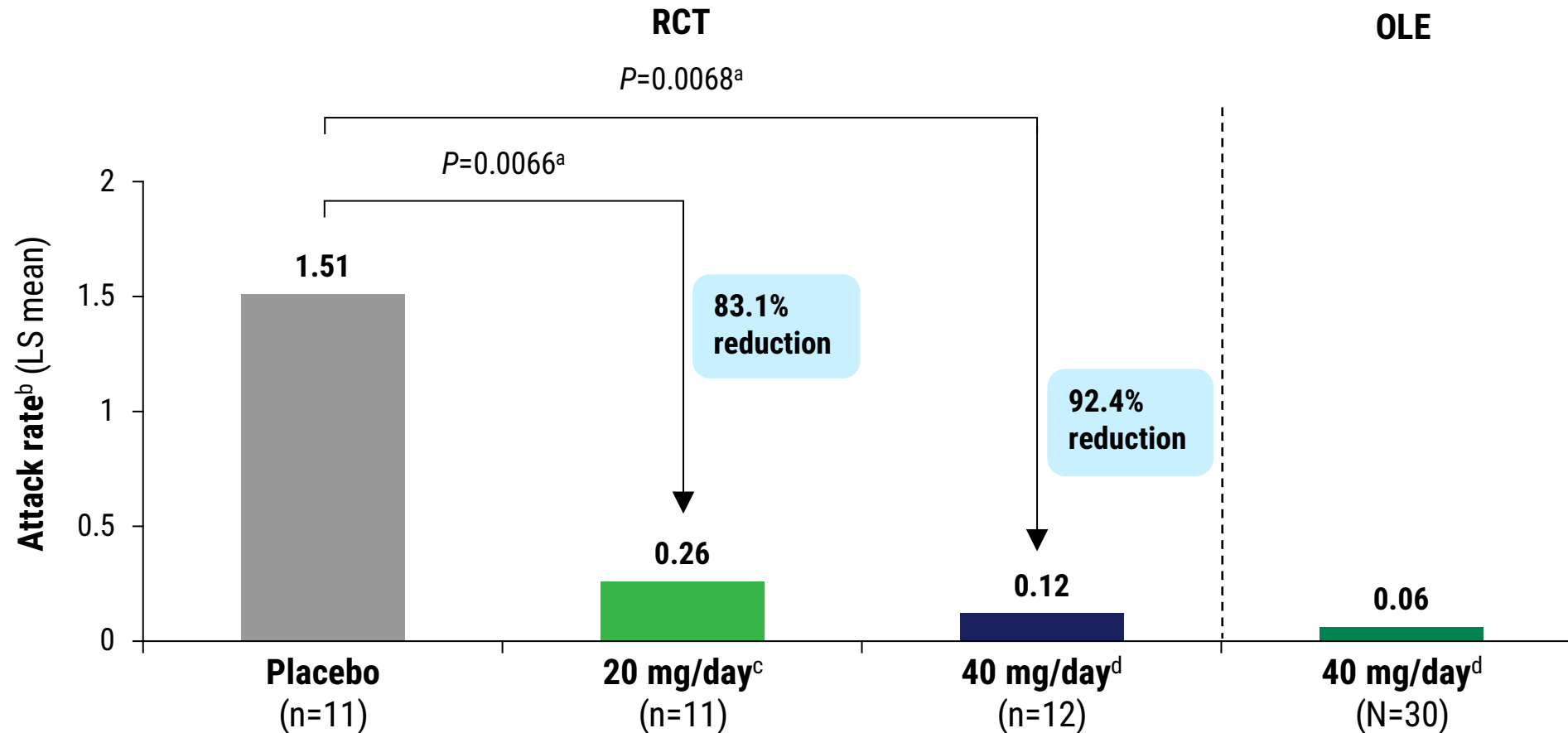
IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial; SEM, standard error of the mean. n = number of participants analyzed at each timepoint. ^aBased on time normalized number of attacks per 4 weeks. ^b1 month = 4 weeks. ^cDeucricitbant IR capsule, 10 mg twice daily. ^dDeucricitbant IR capsule, 20 mg twice daily.

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. ^a92.4% is the average patient-level reduction from CHAPTER-1 RCT baseline and excludes one participant with 4 days of OLE treatment and no attacks. ^bBased on time-normalized number of attacks per 4 weeks. ^cCrude mean attack rate at baseline. ^dCrude mean attack rate in the OLE. ^eDeucricitibant IR capsule, 20 mg twice daily.

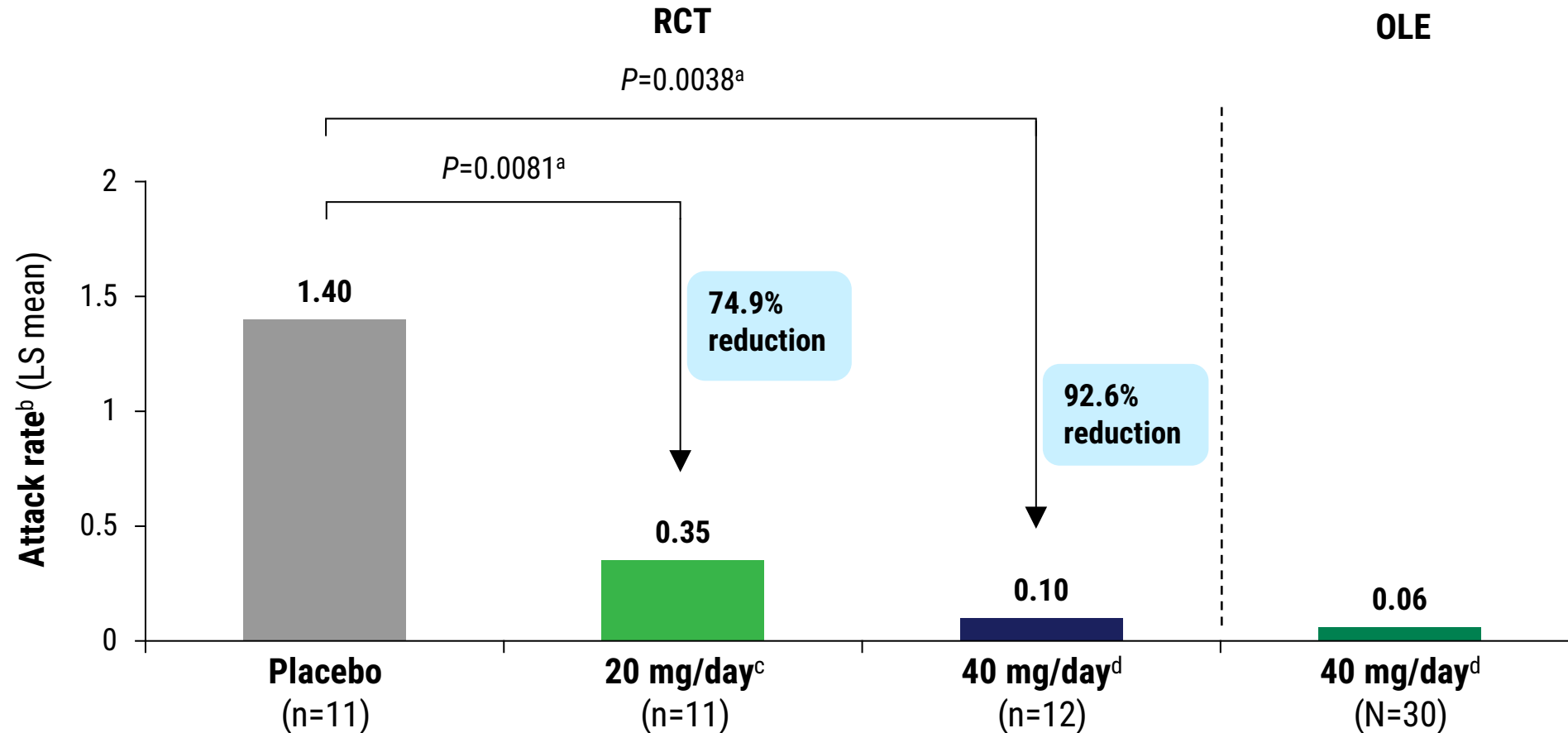
Rate of moderate-to-severe attacks was reduced in the RCT and remained low in the OLE



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. ^aThe P-values in this figure are nominal. ^bBased on time-normalized number of attacks per 4 weeks.

^cDeucricitabant IR capsule, 10 mg twice daily. ^dDeucricitabant IR capsule, 20 mg twice daily.

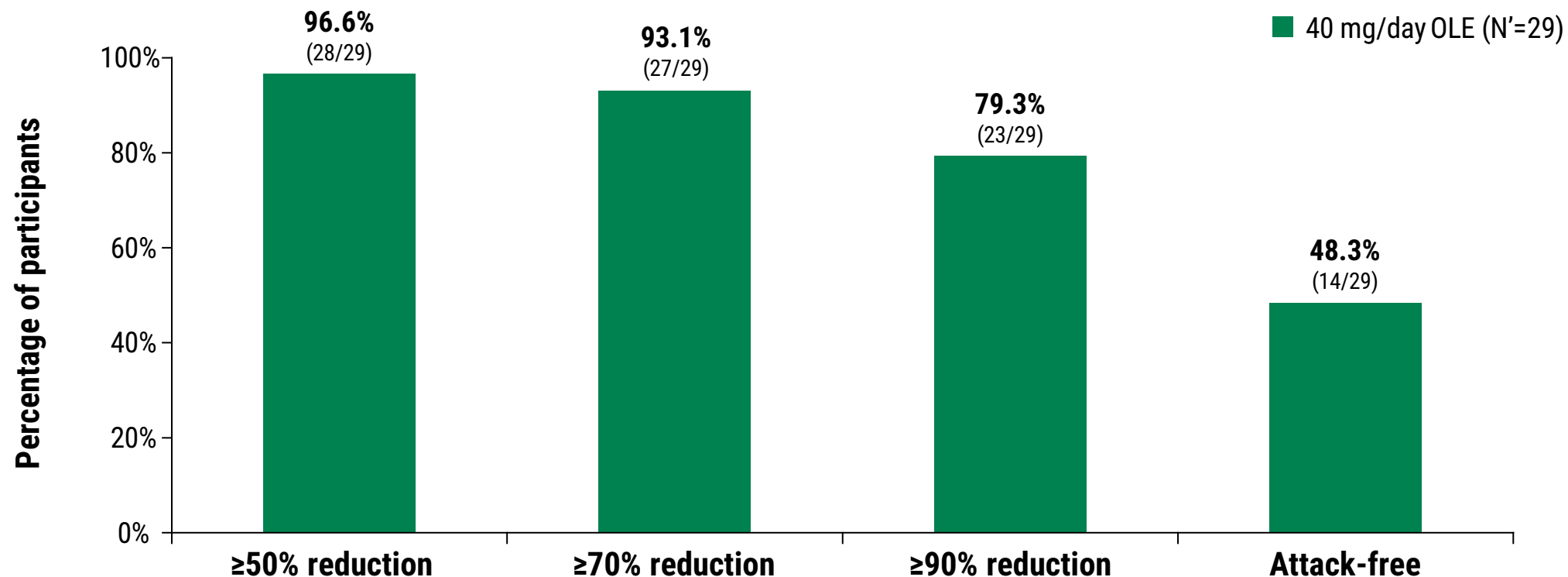
Rate of on-demand treated attacks was reduced in the RCT and remained low in the OLE



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. ^aThe P-values in this figure are nominal. ^bBased on time-normalized number of attacks per 4 weeks.

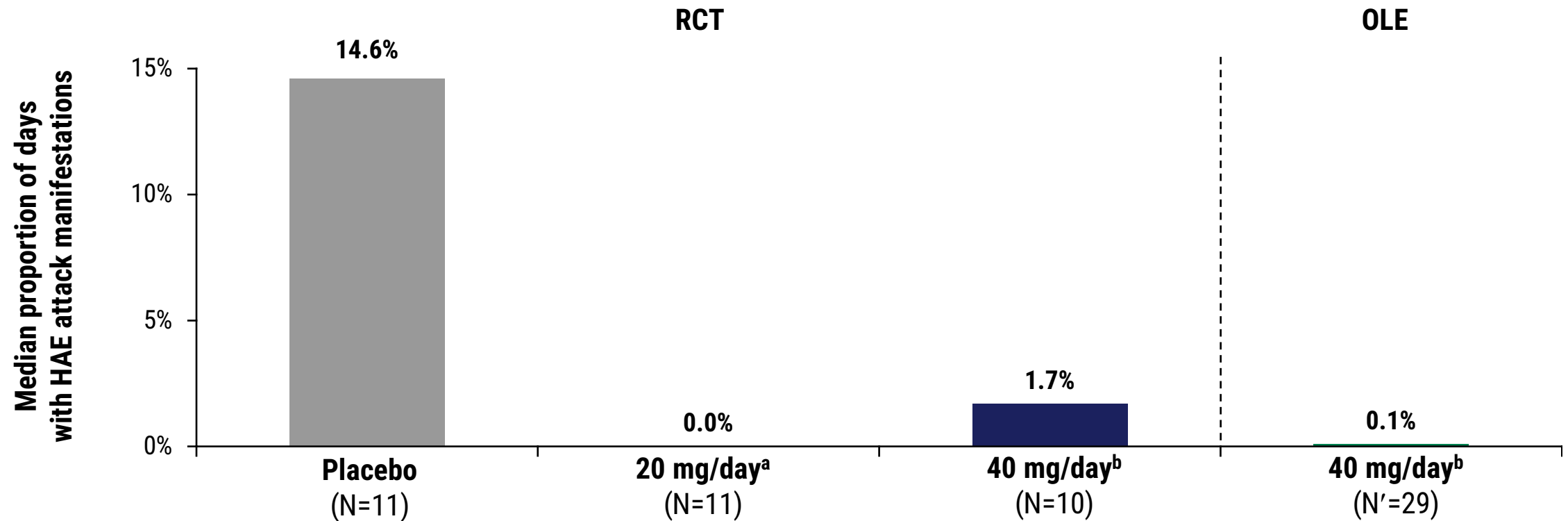
^cDeucricitabant IR capsule, 10 mg twice daily. ^dDeucricitabant IR capsule, 20 mg twice daily.

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. N' = Number of participants with ≥4 weeks of treatment in the OLE.

Median proportion of days with HAE attack manifestations was reduced in the RCT and remained low in the OLE



HAE, hereditary angioedema; IR, immediate-release; OLE, open-label extension; RCT, randomized controlled trial. N = Number of participants with ≥ 4 weeks of treatment in the RCT. N' = Number of participants with ≥ 4 weeks of treatment in the OLE.
^aDeucricitabant IR capsule, 10 mg twice daily. ^bDeucricitabant IR capsule, 20 mg twice daily.

Mean duration of attacks treated with icatibant once as conventional on-demand treatment during the RCT and OLE (post hoc analysis^a)

	Icatibant-treated attacks in placebo treatment group (RCT)		Icatibant-treated attacks in deucricitibant treatment group (RCT and OLE)	
Attack severity	Number of participants (n) Number of attacks (a)	Mean (SD) duration of attack, ^b days	Number of participants (n') Number of attacks (a')	Mean (SD) duration of attack, ^b 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'=12	0.96 (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'=21	1.01 (0.97)

OLE, open-label extension; RCT, randomized controlled trial; SD, standard deviation. n = number of participants in the placebo group who used icatibant as conventional on-demand treatment. a = number of attacks in the placebo treatment group treated once with icatibant. n' = number of participants in deucricitibant treatment group who used icatibant as conventional on-demand treatment. a' = number of attacks in the deucricitibant treatment group treated once with icatibant. ^aDuration of attacks was not a pre-specified CHAPTER-1 measure and was calculated post hoc based on available data for attacks that used icatibant once only as conventional ODT. ^bDuration was assessed from the reported onset of attack manifestations to the reported complete resolution of the attack as recorded in the electronic diary. Adapted from "Oral deucricitibant for prophylaxis of hereditary angioedema attacks (CHAPTER-1): primary analysis of a randomised, double-blind, placebo-controlled, phase 2 trial" by Aygören-Pürsün E, which is licensed under CC BY 4.0.¹

1. Aygören-Pürsün E, et al. *Lancet Haematol*. 2026;13(4):e215-26.

Conclusions

Final data from the completed OLE of the Phase 2 CHAPTER-1 study investigating daily oral deucricitibant administration provide first evidence on the long-term safety and efficacy of bradykinin B2 receptor antagonism for prophylaxis against AE-BK attacks.



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



**Up to
~34 months**

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

0.12

Overall on-study mean monthly attack rate during the OLE



Attack-free

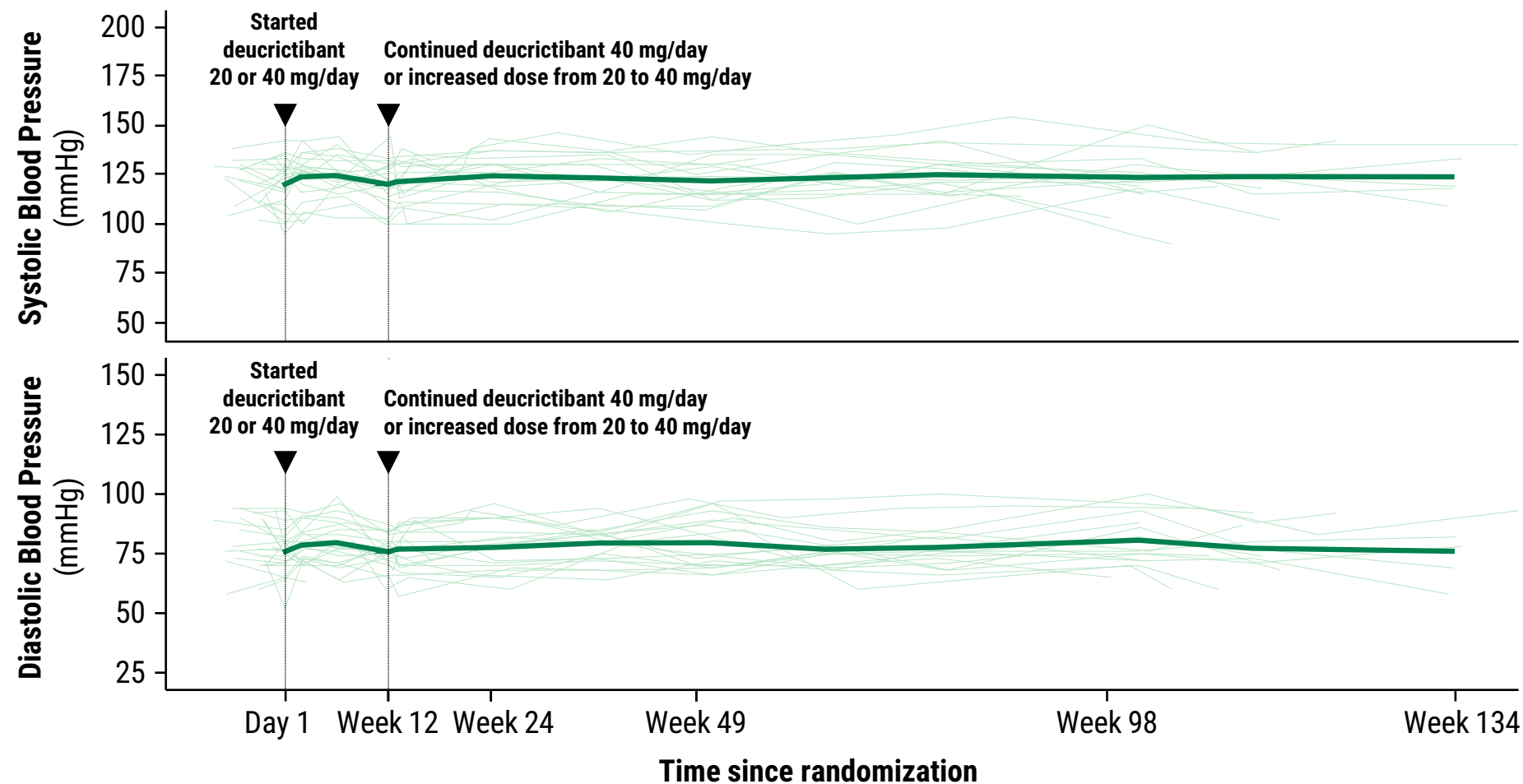
Approximately half of participants were attack-free during the OLE

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.



Back-up slides

Blood pressure remained stable during long-term treatment with deucricitbant



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

Positive topline data from CHAPTER-3 pivotal study of deucricitibant XR for prophylaxis of HAE Attacks

Data disclosed on September 8, 2026



Primary endpoint met: **83% attack rate reduction versus placebo ($P < 0.0001$)** in the first and only prophylaxis Phase 3 study in all three types of HAE

- **87% attack rate reduction versus placebo** observed in people with HAE type 1 or type 2



All secondary efficacy endpoints met with statistical significance



Deucricitibant XR was generally well tolerated

HAE, hereditary angioedema; XR, extended-release.

Pharvaris Press Release. CHAPTER-3 Topline Results. <https://ir.pharvaris.com/news-releases/news-release-details/pharvaris-announces-positive-topline-data-chapter-3-pivotal>. Accessed September 24, 2026.