Oral Deucrictibant Extended-Release Tablet for Prophylaxis of Hereditary Angioedema Attacks: The Phase 3 CHAPTER-3 Trial

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Conflicts of interest disclosure

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CHAPTER-3 was a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: **NCT06669754.**

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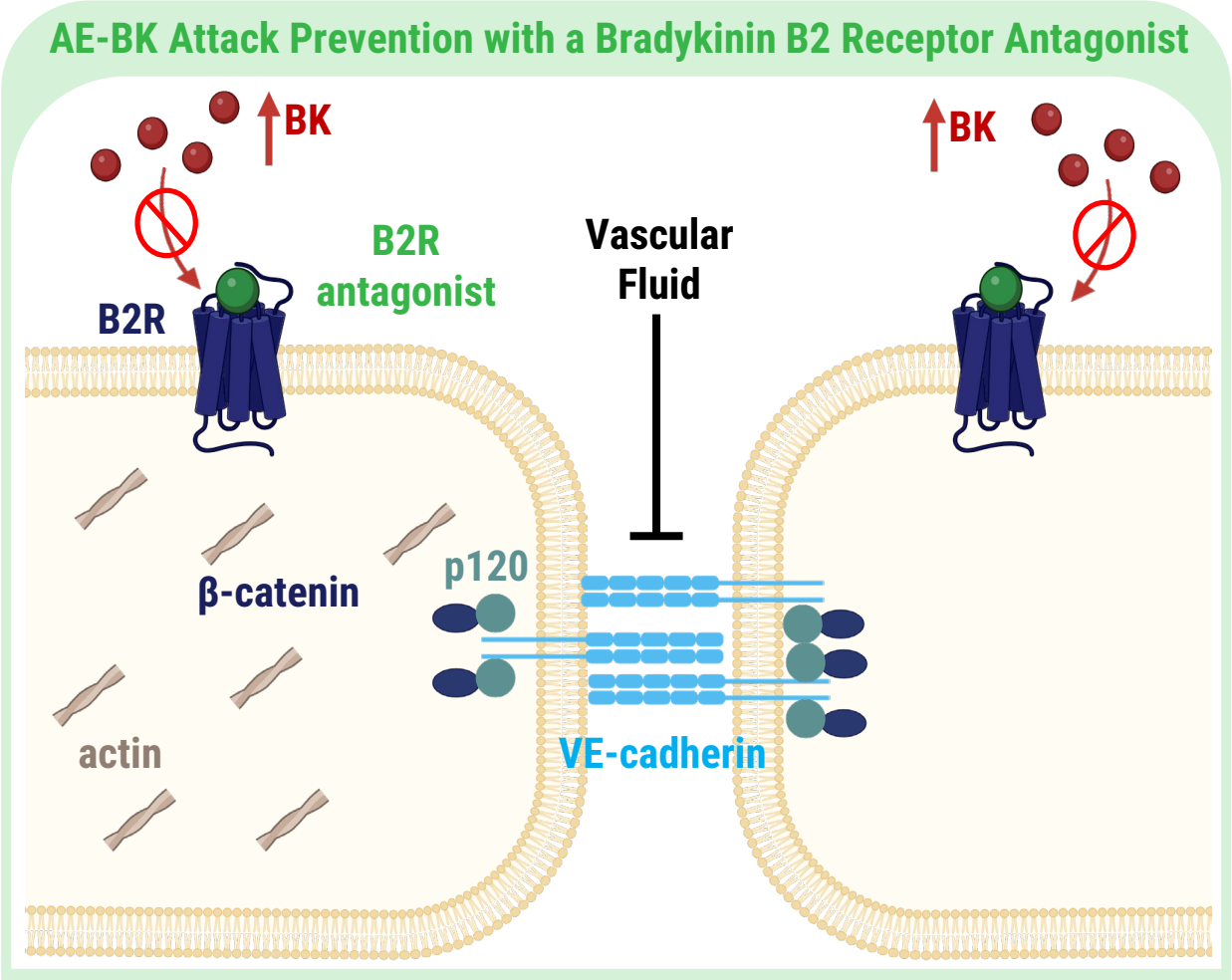
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Continuous bradykinin B2 receptor antagonism can inhibit excessive endothelial permeability and prevent AE-BK attacks

Long-term treatment with a bradykinin B2 receptor antagonist can:[1,2]

Prevent increased BK-mediated vascular permeability[1]

Sustain control of recurrent BK-B2R signaling for **long-term disease management**[2]



AE-BK, bradykinin-mediated angioedema; B2R, B2 receptor; BK, bradykinin; p120, p120-catenin; VE, vascular endothelial.

1. Terzuoli E, et al. *PLoS ONE*. 2014;9(1):e84358. 2. Aygören-Pürsün E, et al. *Lancet Haematol*. 2026;13(4) e215-e226.

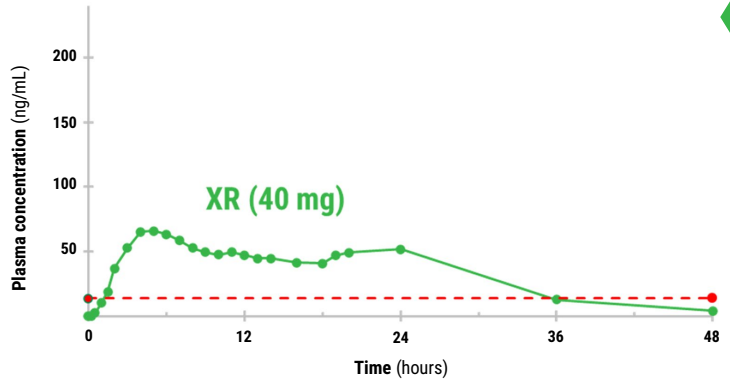
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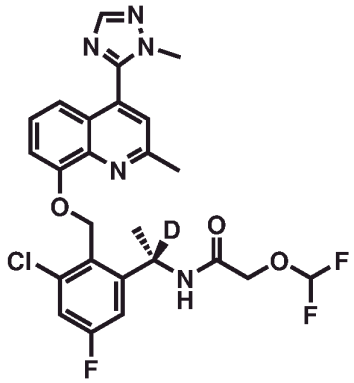
Deucrictibant is an investigational, orally administered, bradykinin B2 receptor antagonist in development for prophylactic and on-demand treatment of AE-BK attacks

DEUCRICTIBANT extended-release (XR) tablet

sustained absorption[1]



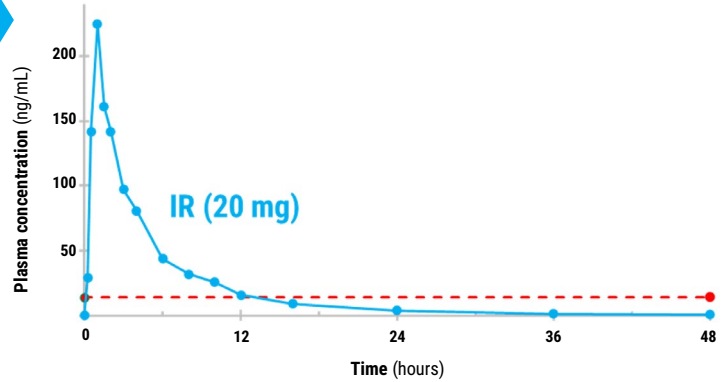
In studies, deucrictibant sustained therapeutic exposure over 24 hours[1] from day 1, allowing for once-daily oral prevention of HAE attacks[2]



Deucrictibant

DEUCRICTIBANT immediate-release (IR) capsule

rapid absorption[3]



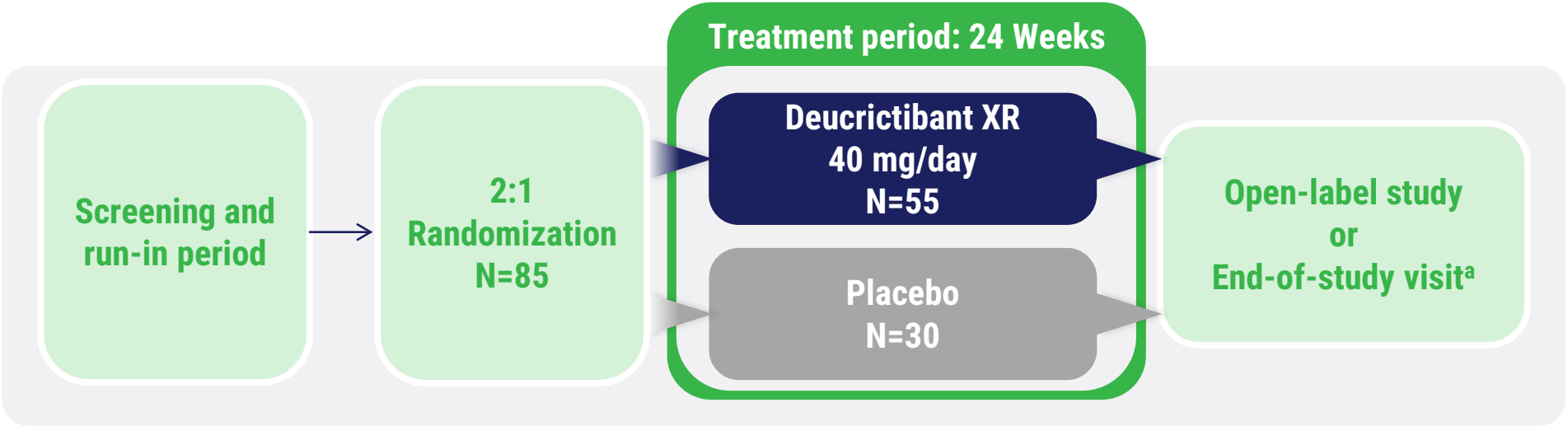
In studies, deucrictibant rapidly reached therapeutic exposure within 15–30 minutes[3], supporting on-demand oral treatment of HAE attacks[4]

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 October 22, 2026. 3. Maurer M, et al. *Lancet Haematol*. 2026;13(4):e200-e214. 4. Riedl MA, et al. *Lancet*. 2026. doi:10.1016/S0140-6736(26)01296-1.

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CHAPTER-3: a global, multicenter, Phase 3, randomized, double-blind, placebo-controlled trial



- **Key eligibility criteria:** adolescents or adults (≥12 years) with HAE-C1INH (type 1 or type 2) and HAE-nC1INH, and ≥3 attacks within 3 months before screening and ≥2 attacks during up to 8-week run-in period.
- **Primary endpoint:** time-normalized 'per four weeks' number of investigator-confirmed HAE attacks during the 24-week treatment period (monthly rate).
- **Secondary endpoints included:** HAE attacks treated with on-demand medication; moderate-to-severe HAE attacks; proportion of participants achieving ≥50%, ≥70%, and ≥90% reduction in HAE attack rate versus baseline; proportion of attack-free participants during the treatment period; change from baseline in AE-QoL; incidence of TEAEs.
- **Statistical analysis:** the primary endpoint, and 12 secondary endpoints, including HRQoL outcomes, were evaluated for statistical significance using a prespecified hierarchical testing procedure.

AE-QoL, Angioedema Quality of Life questionnaire; HAE, hereditary angioedema; HAE-C1INH, hereditary angioedema with deficiency or dysfunction of C1 inhibitor; HAE-nC1INH, hereditary angioedema with normal C1 inhibitor; HRQoL, health-related quality of life; TEAE, treatment-emergent adverse event; XR, extended-release. [a]After the 24-week treatment period, participants could continue into the CHAPTER-4 open-label study (ClinicalTrials.gov NCT06679881) or enter a 4-week end-of-study follow-up period.

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Participant characteristics at baseline were generally balanced across both treatment groups

Participant characteristics	Deucrictibant XR N=55	Placebo N=30
Age, mean (SD), years	38.6 (13.7)	39.3 (16.1)
≥12 to <18 years, n (%)	4 (7.3)	4 (13.3)
18 to <65 years, n (%)	49 (89.1)	25 (83.3)
≥65 years, n (%)	2 (3.6)	1 (3.3)
Sex, female, n (%)	34 (61.8)	22 (73.3)
BMI, mean (SD), kg/m^2	28.7 (7.5)	25.5 (4.9)
Race,[a] n (%)		
White	35 (63.6)	24 (80.0)
Asian	13 (23.6)	3 (10.0)
Black or African American	1 (1.8)	1 (3.3)
HAE type, n (%)		
HAE-C1INH type 1 or type 2	52 (94.5)	28 (93.3)
HAE-nC1INH	3 (5.5)	2 (6.7)
HAE attack rate (attacks/month), mean (SD)	3.8 (2.0)	3.5 (1.8)

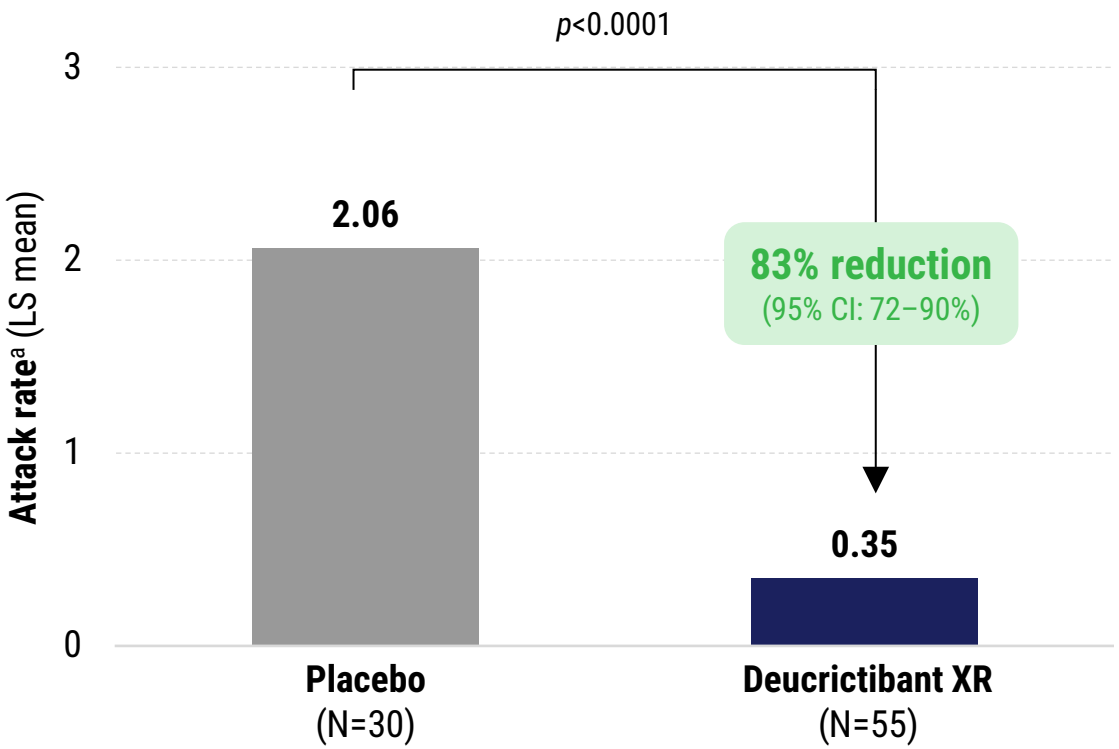
BMI, body mass index; HAE, hereditary angioedema; HAE-C1INH, hereditary angioedema with deficiency or dysfunction of C1 inhibitor; HAE-nC1INH, hereditary angioedema with normal C1 inhibitor; IQR, interquartile range; SD, standard deviation; XR, extended-release. [a]Also included: "Other", 2 (3.6) vs 1 (3.3); "Not reported", 3 (5.5) vs 1 (3.3); and "Multiple", 1 (1.8) vs 0.

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Deucrictibant XR reduced the attack rate vs placebo

All HAE types
(HAE-C1INH type 1 or type 2, and HAE-nC1INH)
Primary endpoint



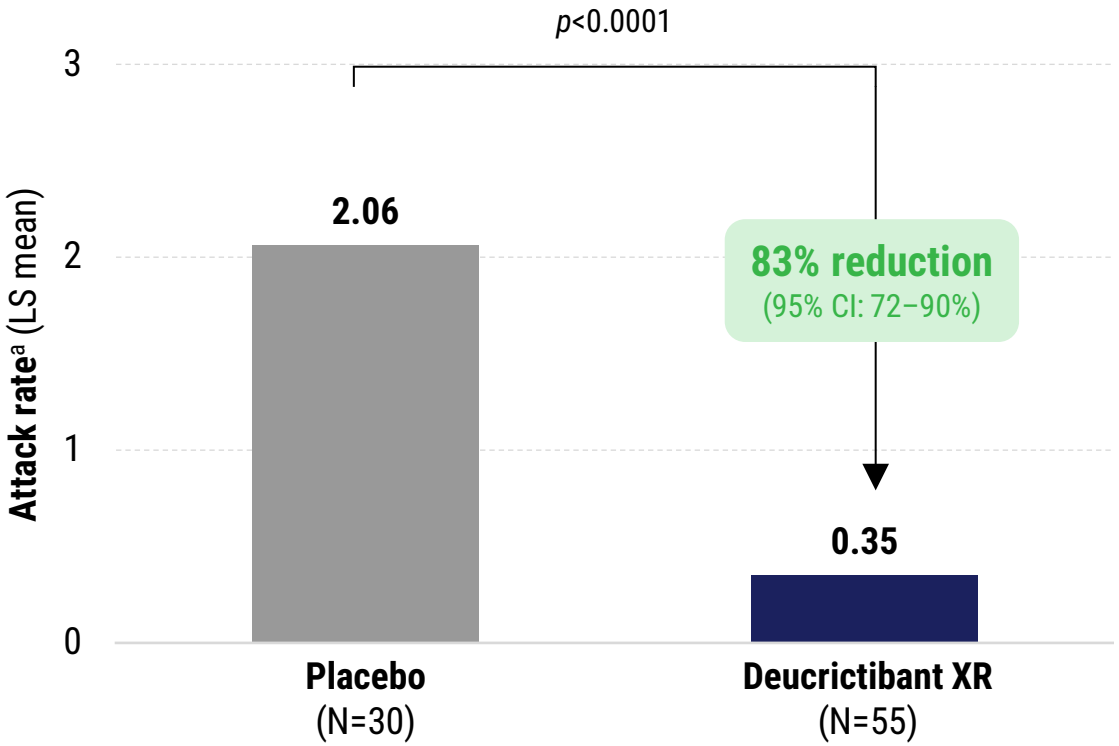
CI, confidence interval; HAE, hereditary angioedema; HAE-C1INH, hereditary angioedema with deficiency or dysfunction of C1 inhibitor; HAE-nC1INH, hereditary angioedema with normal C1 inhibitor; LS, least squares; XR, extended-release. [a]Attack rate = time-normalized (per 4 weeks) number of investigator-confirmed HAE attacks during the 24-week treatment period. Results based on a Poisson regression model adjusted for baseline attack rate and age group.

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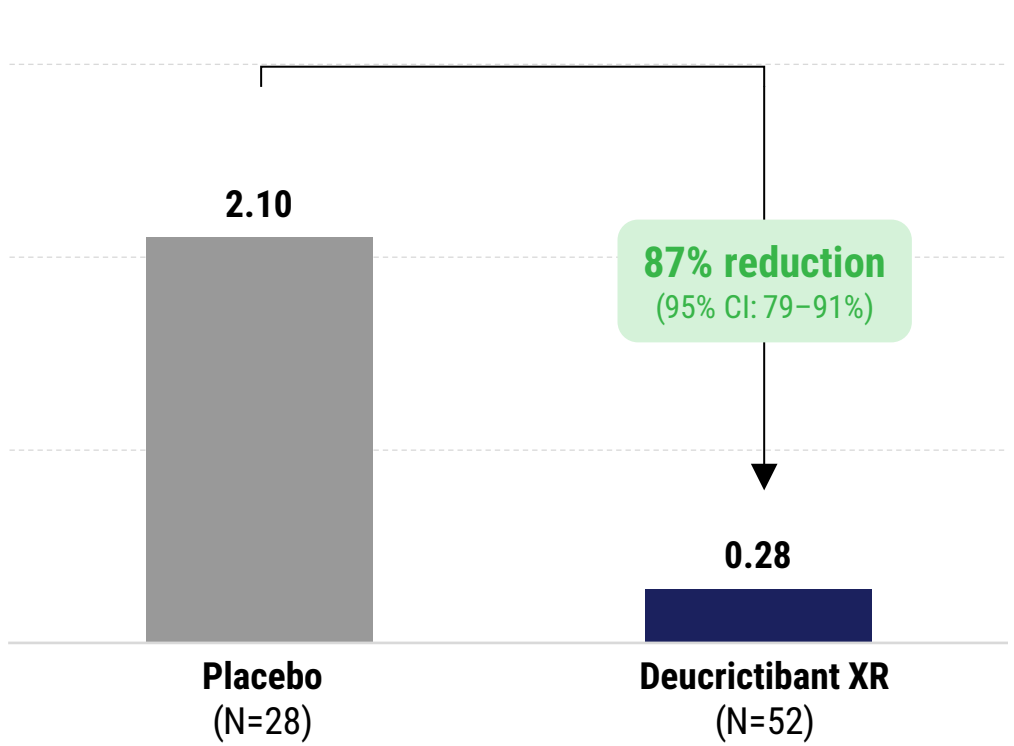
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Deucrictibant XR reduced the attack rate vs placebo

All HAE types (HAE-C1INH type 1 or type 2, and HAE-nC1INH)
Primary endpoint



HAE-C1INH type 1 or type 2
Post hoc analysis[b]

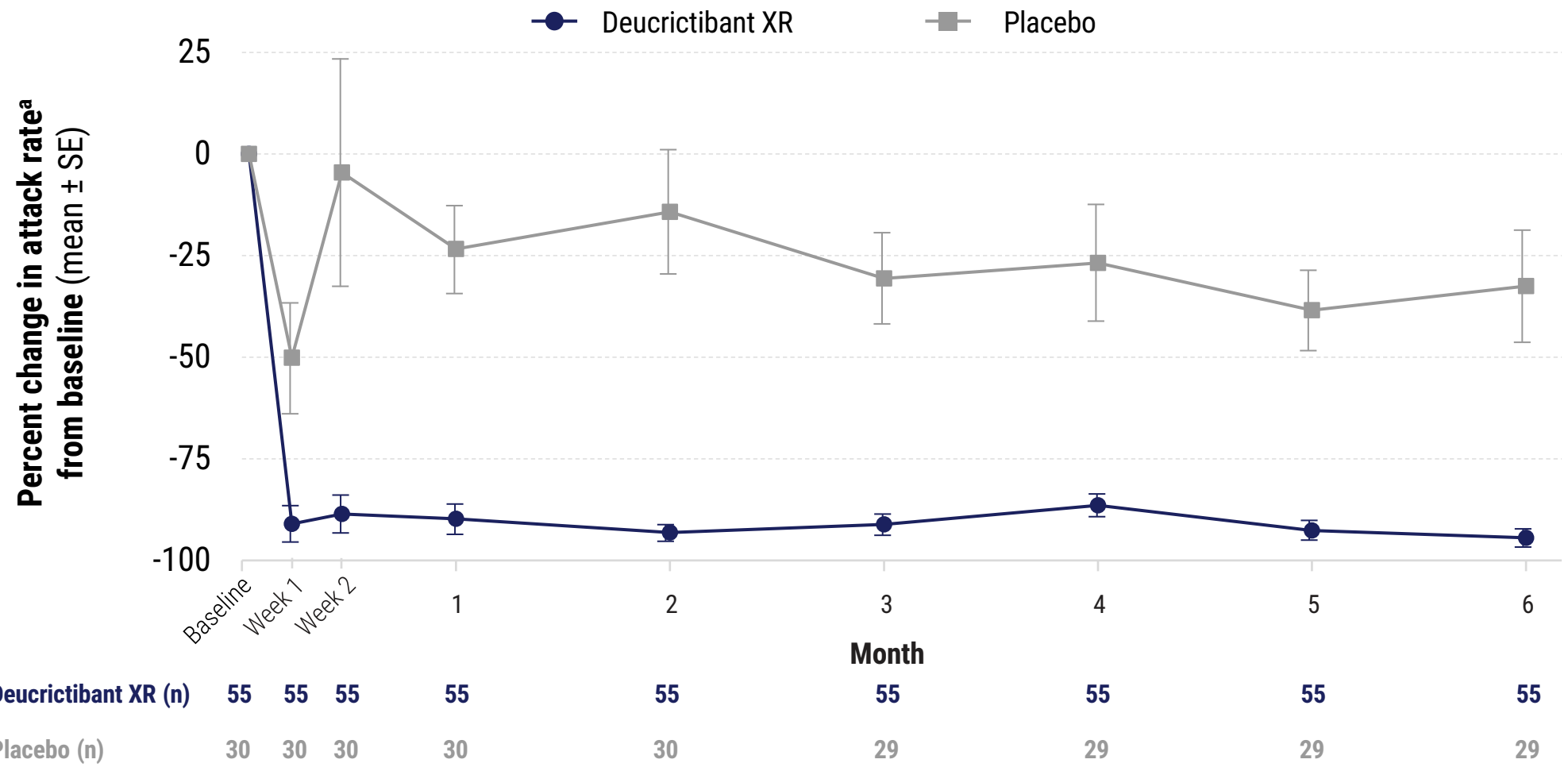


CI, confidence interval; HAE, hereditary angioedema; HAE-C1INH, hereditary angioedema with deficiency or dysfunction of C1 inhibitor; HAE-nC1INH, hereditary angioedema with normal C1 inhibitor; LS, least squares; XR, extended-release. [a]Attack rate = time-normalized (per 4 weeks) number of investigator-confirmed HAE attacks during the 24-week treatment period. Results based on a Poisson regression model adjusted for baseline attack rate and age group. [b]Post hoc analysis in participants with HAE-C1INH type 1 or type 2, using the same model as the primary analysis.

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Deucrictibant XR reduced attack rate within the first week and had durable effects throughout the study



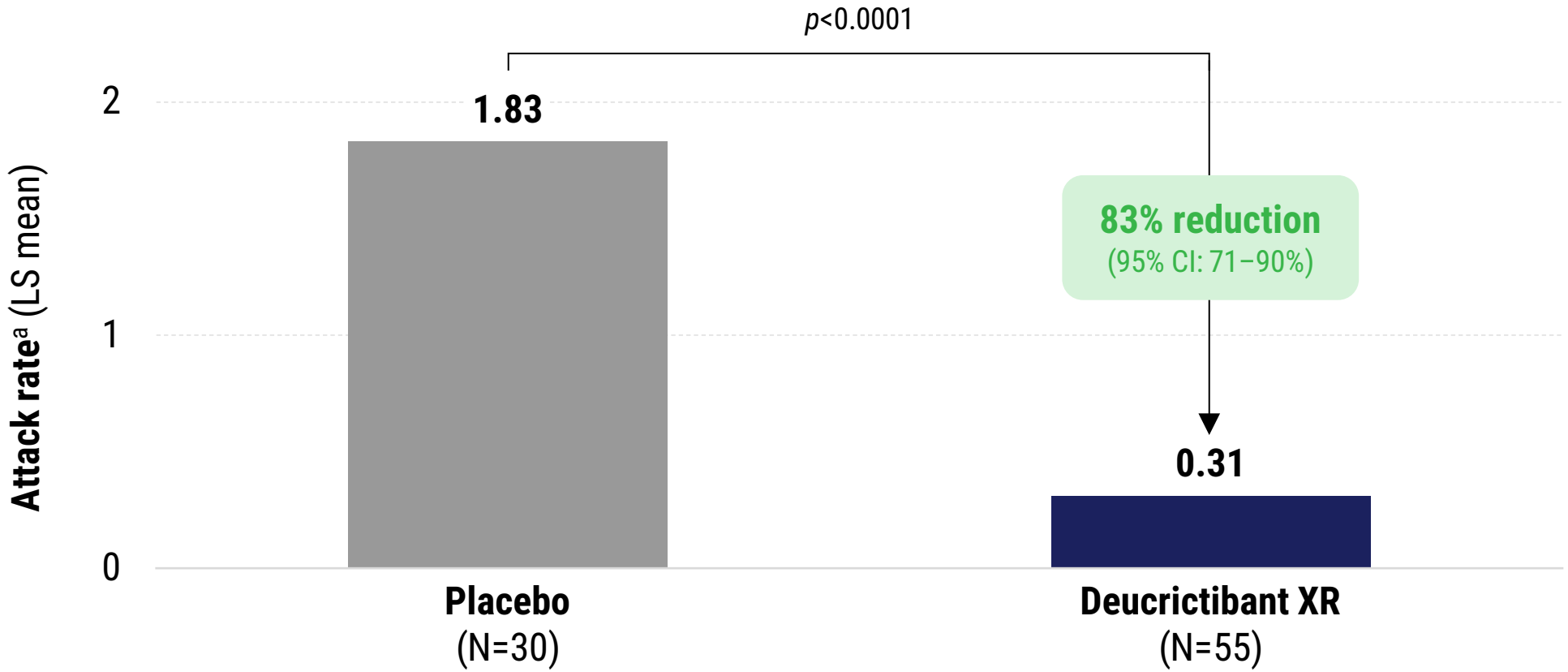
Deucrictibant XR (n)	55	55	55	55	55	55	55	55	55
Placebo (n)	30	30	30	30	30	29	29	29	29

HAE, hereditary angioedema; SE, standard error; XR, extended-release. [a]Attack rate was calculated as the number of investigator-confirmed attacks occurring over days 1–7 and 8–14 for Week 1 and Week 2, respectively, over days 15–28 for Month 1, and for the remaining 4-week intervals the attack rate was calculated as the number of investigator-confirmed attacks during that interval divided by number of days the participant contributed to that interval multiplied by 28 days.

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Deucrictibant XR significantly reduced the rate of attacks treated with on-demand medication vs placebo

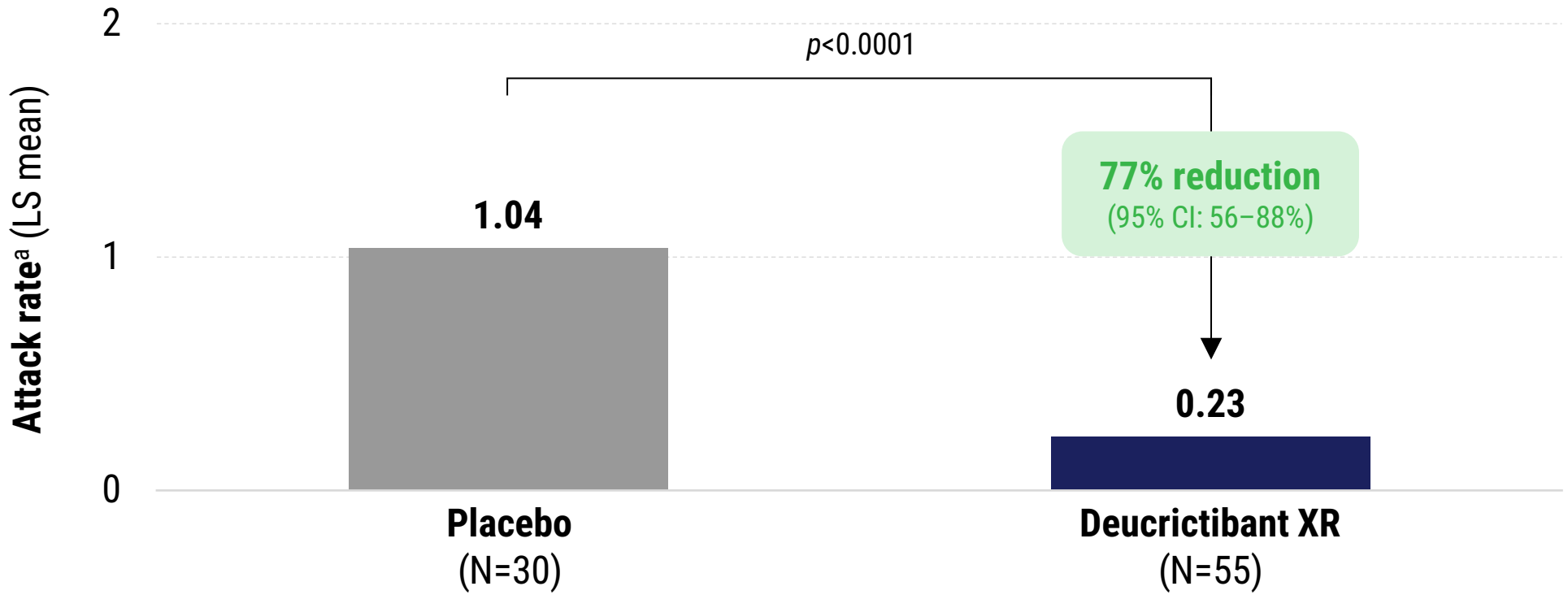


CI, confidence interval; HAE, hereditary angioedema; LS, least squares; XR, extended-release. [a]Attack rate = time-normalized (per 4 weeks) number of investigator-confirmed HAE attacks during the 24-week treatment period. Results based on a Poisson regression model adjusted for baseline attack rate and age group.

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Deucrictibant XR significantly reduced the rate of moderate-to-severe attacks vs placebo

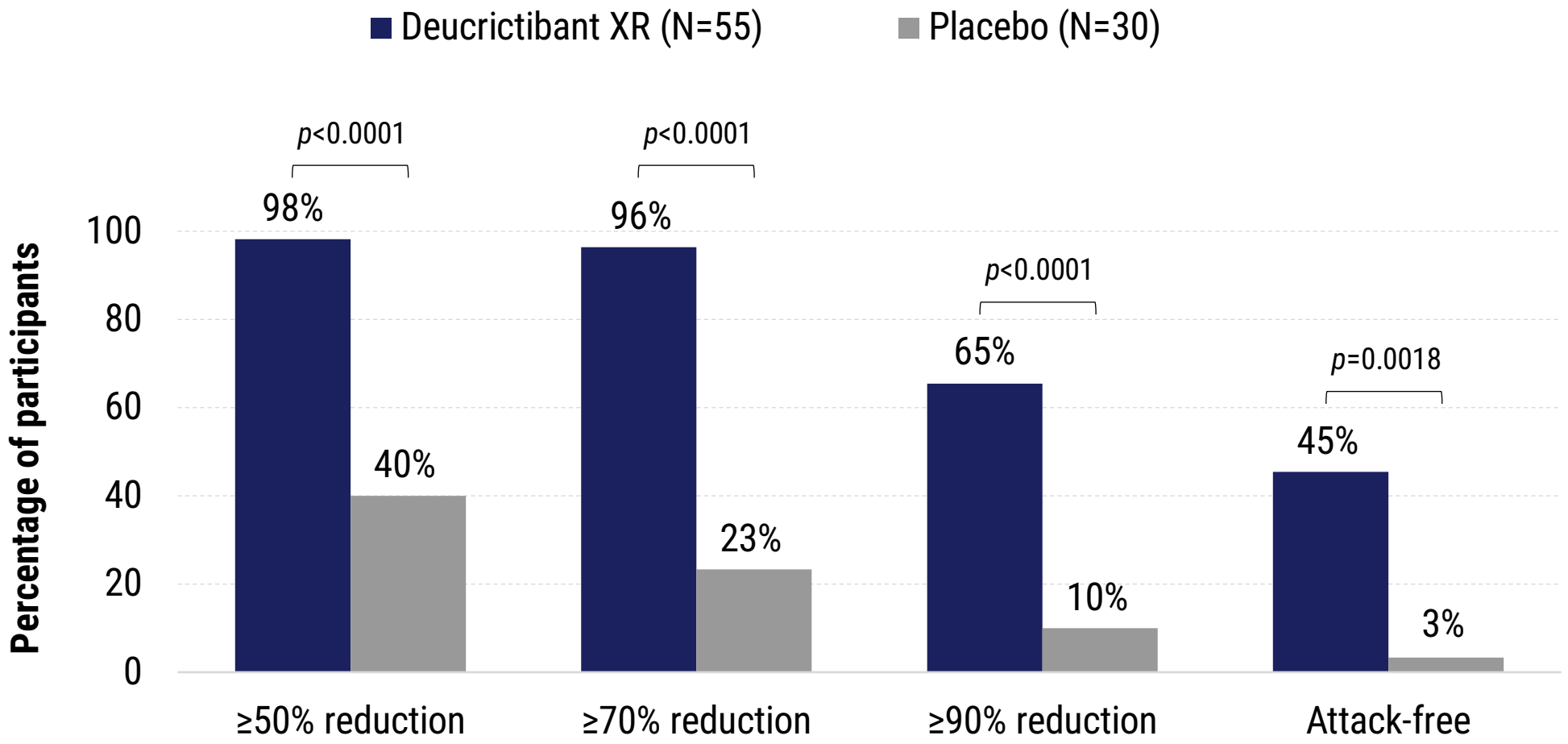


CI, confidence interval; HAE, hereditary angioedema; LS, least squares; XR, extended-release. [a]Attack rate = time-normalized (per 4 weeks) number of investigator-confirmed HAE attacks during the 24-week treatment period. Results based on a Poisson regression model adjusted for baseline attack rate and age group.

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Significantly more participants achieved ≥50%, ≥70%, and ≥90% reduction in attack rate or were attack-free from baseline with deucrictibant XR vs placebo

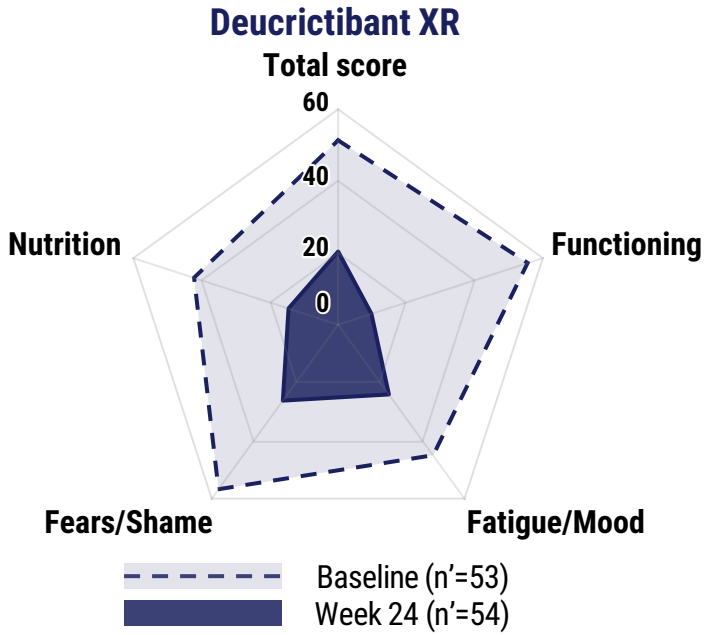


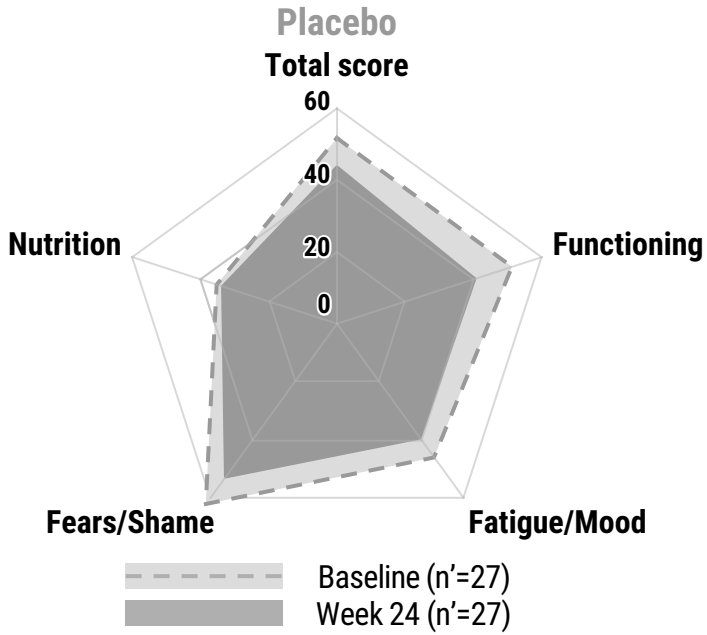
HAE, hereditary angioedema; XR, extended-release. Attack rate = time-normalized (per 4 weeks) number of investigator-confirmed HAE attacks during the 24-week treatment period. Results based on a logistic regression model adjusted for baseline attack rate and age group.

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Deucrictibant XR resulted in greater improvements in mean AE-QoL total score and all domain scores vs placebo





AE-QoL Total Score	Deucrictibant XR	Placebo
Baseline, mean (SD)	51.3 (18.0) (n'=53)	51.7 (14.4) (n'=27)
Week 24, mean (SD)	20.3 (19.3) (n'=54)	43.5 (17.7) (n'=27)
Change from baseline at Week 24, LS mean[a]	−32.2	-8.7
Difference vs placebo (95% CI)[a]	−23.5 (−32.2, −14.9)	
p-value[a]	*p*<0.0001	

AE-QoL, Angioedema Quality of Life questionnaire; CI, confidence interval; LS, least squares; SD, standard deviation; XR, extended-release. AE-QoL domains and total scores range from 0 to 100, with higher scores indicating greater impairment. n' represents the number of patients with AE-QoL data at the specific visit. n=28 at baseline for Functioning, Fears/Shame, and Nutrition scores in the placebo group. [a]Results based on a mixed-effect model with repeated measures with fixed effects of visit, treatment, treatment-visit interaction, age group, baseline HAE attack rate, and baseline score.

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Deucrictibant XR was generally well tolerated

Participants with event, n (%)	Deucrictibant XR N=55	Placebo N=30
Any TEAE[a]	42 (76.4)	17 (56.7)
Maximum Grade 1	15 (27.3)	6 (20.0)
Maximum Grade 2	23 (41.8)	11 (36.7)
Maximum Grade 3	3 (5.5)	0
Maximum Grade 4	1 (1.8)	0
Maximum Grade 5	0	0
Any treatment-related TEAE[b]	11 (20.0)	3 (10.0)
Any serious TEAE	1 (1.8)	0
Any treatment-related serious TEAE	0	0
Any TEAE leading to study drug discontinuation	1 (1.8)	1 (3.3)
Most common (≥10% of participants) TEAEs by preferred term		
Upper respiratory tract infection	9 (16.4)	2 (6.7)
Nasopharyngitis	7 (12.7)	4 (13.3)
Headache	5 (9.1)	4 (13.3)
Diarrhea	2 (3.6)	3 (10.0)

One AE of laryngeal dyskinesia, deemed not related to study drug

- Participant recovered during study

GI AEs were mild or moderate in severity and balanced between treatment groups

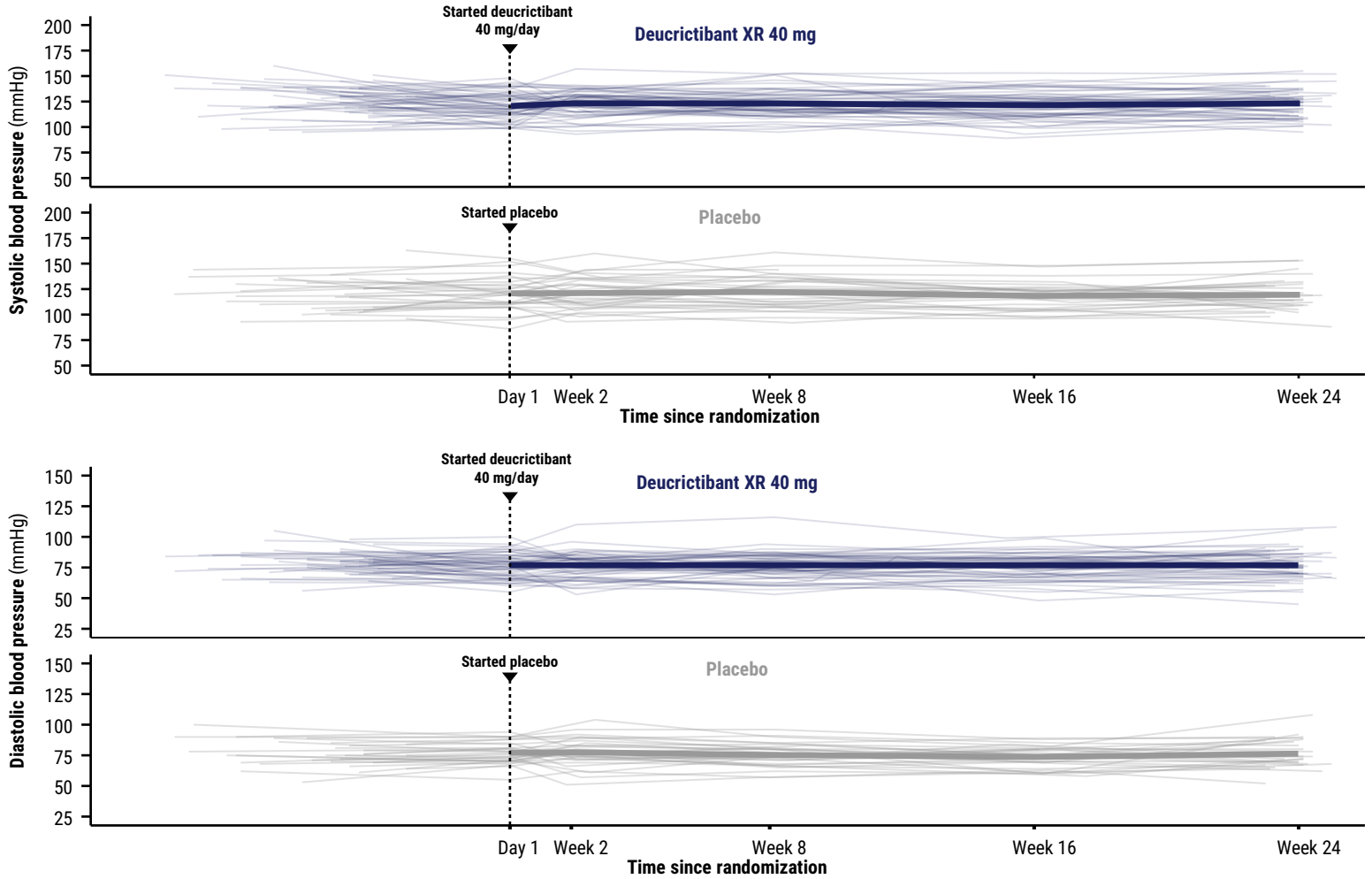
- They were deemed treatment-related in 1 (1.8%) deucrictibant- and 2 (6.7%) placebo-treated participants.

AE, adverse event; CRF, case report form; CTCAE, Common Terminology Criteria for Adverse Events; GI, gastrointestinal; MedDRA, Medical Dictionary for Regulatory Activities; NCI, National Cancer Institute; TEAE, treatment-emergent adverse event; XR, extended-release. [a]TEAEs were defined as AEs that started after the first administration of study drug, or medical conditions that were present prior to the first administration of study drug but worsened following the first administration of study drug. AE reported terms were coded using MedDRA version 29.0. Severity of AEs according to NCI CTCAE version 5.0. [b]Relatedness to study drug based on investigator's assessment as indicated on the CRF. Treatment-related TEAEs in the deucrictibant group were dry throat, erythema, fatigue, increased liver function test, nausea, oscillopsia, pruritus, and somnolence, vs dyspepsia, dysphagia, nausea, odynophagia, and urticaria in the placebo group.

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Peripheral blood pressure remained stable with deucrictibant XR treatment across the study period



- No treatment-related cardiovascular adverse events were reported with deucrictibant XR treatment.
- There were no treatment-related clinically significant abnormalities in heart rate, systolic and diastolic peripheral blood pressure, or ECG findings.
- No evidence of increased risks of cardiovascular events, consistent with previous findings from up to ~34 months of deucrictibant treatment in the Phase 2 CHAPTER-1 study.[1]

For further information on cardiovascular outcomes across the deucrictibant clinical program, please see poster R111.

ECG, electrocardiogram; XR, extended-release.

1. Lesage A, et al. Presented at the American College of Allergy, Asthma and Immunology (ACAAI) Annual Meeting; November 2026; Phoenix, AZ, USA.

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Conclusions

- The pivotal CHAPTER-3 trial met the primary and all secondary endpoints.
- Deucrictibant XR provided early and durable reduction in attack rate.

Attack reduction with deucrictibant XR vs placebo

83%

In HAE-C1INH and HAE-nC1INH (primary endpoint)

Attack rate

87%

In HAE-C1INH[a] (post hoc)



Deucrictibant XR provided reductions in attack rate within the first week of treatment



Deucrictibant XR was generally well tolerated

The Authors and the sponsor would like to thank all the people with HAE as well as all study site staff who participated in the CHAPTER-3 trial.

HAE, hereditary angioedema; HAE-C1INH, hereditary angioedema with deficiency or dysfunction of C1 inhibitor; HAE-nC1INH, hereditary angioedema with normal C1 inhibitor; XR, extended-release. [a]Additional post hoc analysis of HAE-C1INH type 1 or type 2, not adjusted for multiplicity.

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