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Prophylaxis of Hereditary Angioedema Attacks With Oral Deucrictibant: Efficacy and Quality-of-Life Results from CHAPTER-1

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

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

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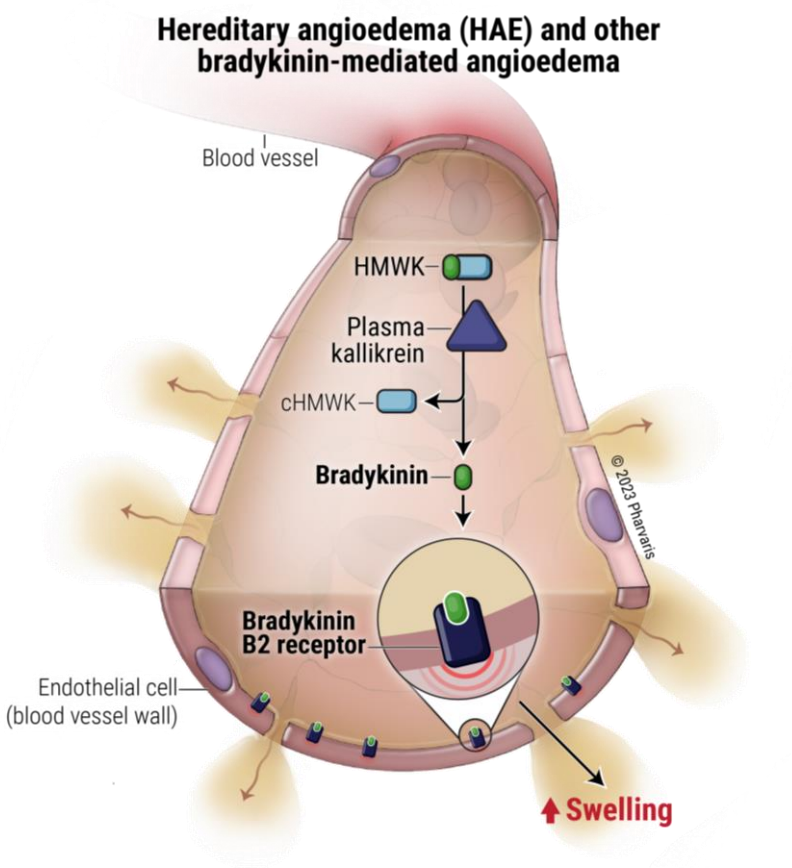
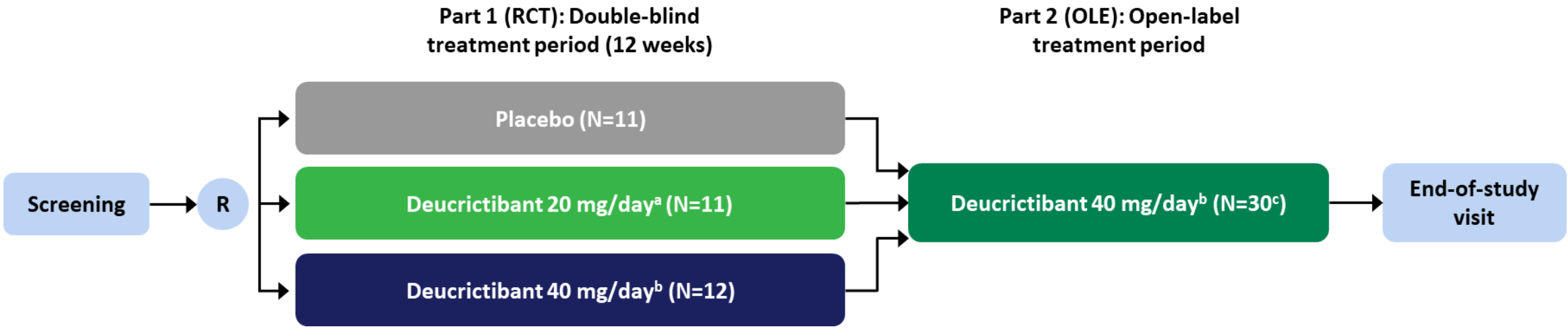
Hereditary angioedema (HAE) is a bradykinin-mediated condition with unmet medical needs



- Excess bradykinin is the main mediator of the clinical manifestations of bradykinin-mediated angioedema attacks, including HAE.[1,2]
- An unmet need remains for additional prophylactic treatments combining[3-6]:
  - Injectable-like efficacy
  - A well-tolerated profile
  - Ease of administration

cHMWK, cleaved HMWK; HMWK, high-molecular-weight kininogen. **1**. Frank MM. *J Allergy Clin Immunol.* 2010;125:S262-71. **2**. Busse PJ, et al. *N Engl J Med.* 2020;382:1136-48. **3**. Bouillet L, et al. *Allergy Asthma Proc.* 2022;43:406-12. **4**. Betschel SD, et al. *J Allergy Clin Immunol Pract.* 2023;11:2315-25. **5.** Covella B, et al. *Future Pharmacol.* 2024;4:41-53. **6**. US Food and Drug Administration, Center for Biologics Evaluation and Research. The voice of the patient – hereditary angioedema. May 2018. https://www.fda.gov/media/113509/download. Accessed November 13, 2024.

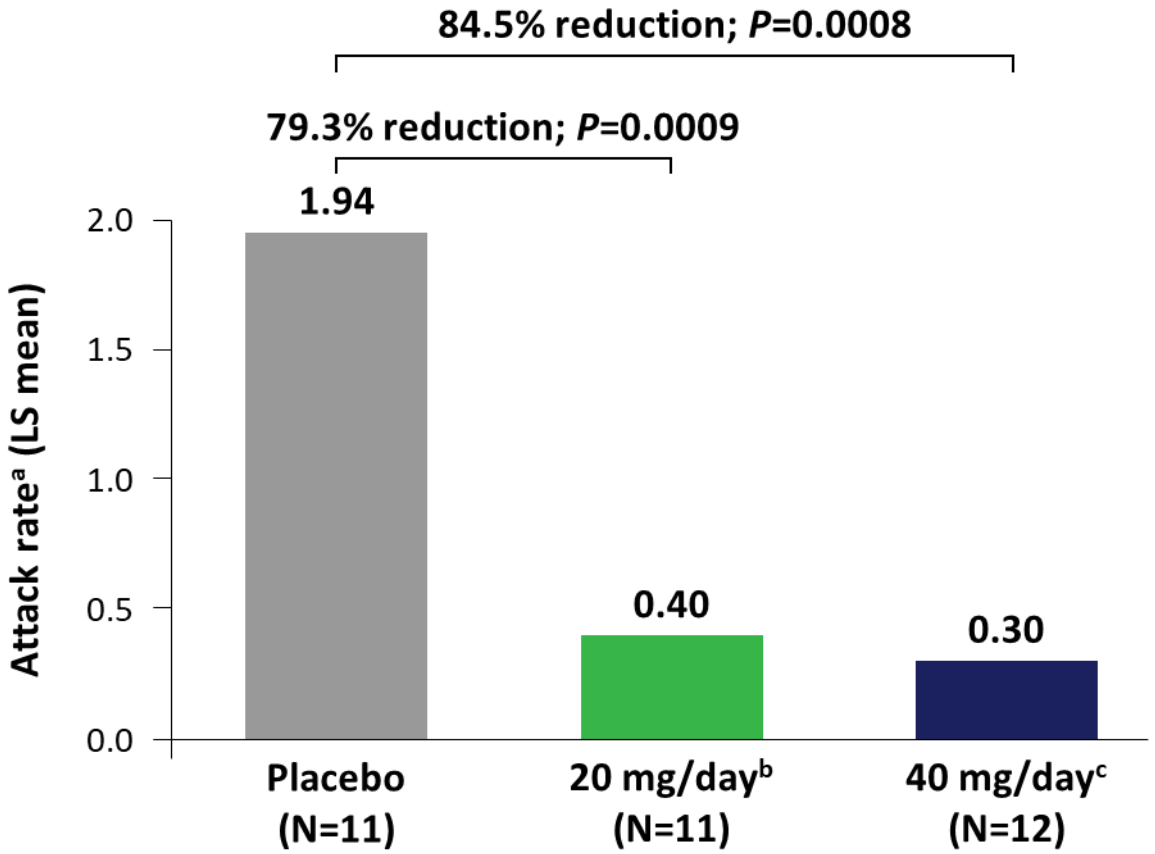
CHAPTER-1: Two-part, Phase 2 study of deucrictibant for long-term prophylaxis of HAE attacks



- RCT endpoints included:
  - Time-normalized number of investigator-confirmed HAE attacks (**HAE attack rate[d]**) – primary endpoint
  - Time-normalized number of **moderate and severe HAE attacks**
  - Time-normalized number of **HAE attacks treated with on-demand medication**
  - **Disease control** assessed using Angioedema Control Test (AECT) [1,2]
  - **Health-related quality of life (HRQoL)** assessed using Angioedema Quality of Life Questionnaire (AE-QoL)[3,4]

HAE, hereditary angioedema; IR, immediate-release; OLE, open-label extension; R, randomization; RCT, randomized controlled trial. CHAPTER-1 is a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: NCT05047185. https://www.clinicaltrials.gov/study/NCT05047185. Accessed November 13, 2024. **1.** Weller K, et al. *Allergy.* 2020;75:1165-77. **2.** Weller K, et al. *J Allergy Clin Immunol Pract.* 2020;8:2050-57. **3.** Weller K, et al. *Allergy.* 2012;67:1289-98. **4.** Weller K, et al. *Allergy.* 2016;71:1203-9. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily. [c]All 30 participants who completed Part 1 enrolled in Part 2. [d]Based on time normalized number of attacks per 4 weeks.

Primary endpoint: Deucrictibant significantly reduced the overall attack rate



	Placebo (N=11)	Deucrictibant 20 mg/day[b] (N=11)	Deucrictibant 40 mg/day[c] (N=12)
Attack rate[a]			
BL, median	1.67	1.67	1.74
On study, median	2.15	0	0.15
Change from BL, median	0.33	–1.34	–1.59
% change from BL, median	17	–100	–96
Model-based inference			
LS mean	1.94	0.40	0.30
% reduction vs placebo	–	79.3	84.5
P value	–	0.0009	0.0008

BL, baseline; IR, immediate-release; LS, least squares. N = number of randomized participants. Model-based inferences are based on a Poisson regression model adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied. [a]Based on time normalized number of attacks per 4 weeks. [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily.

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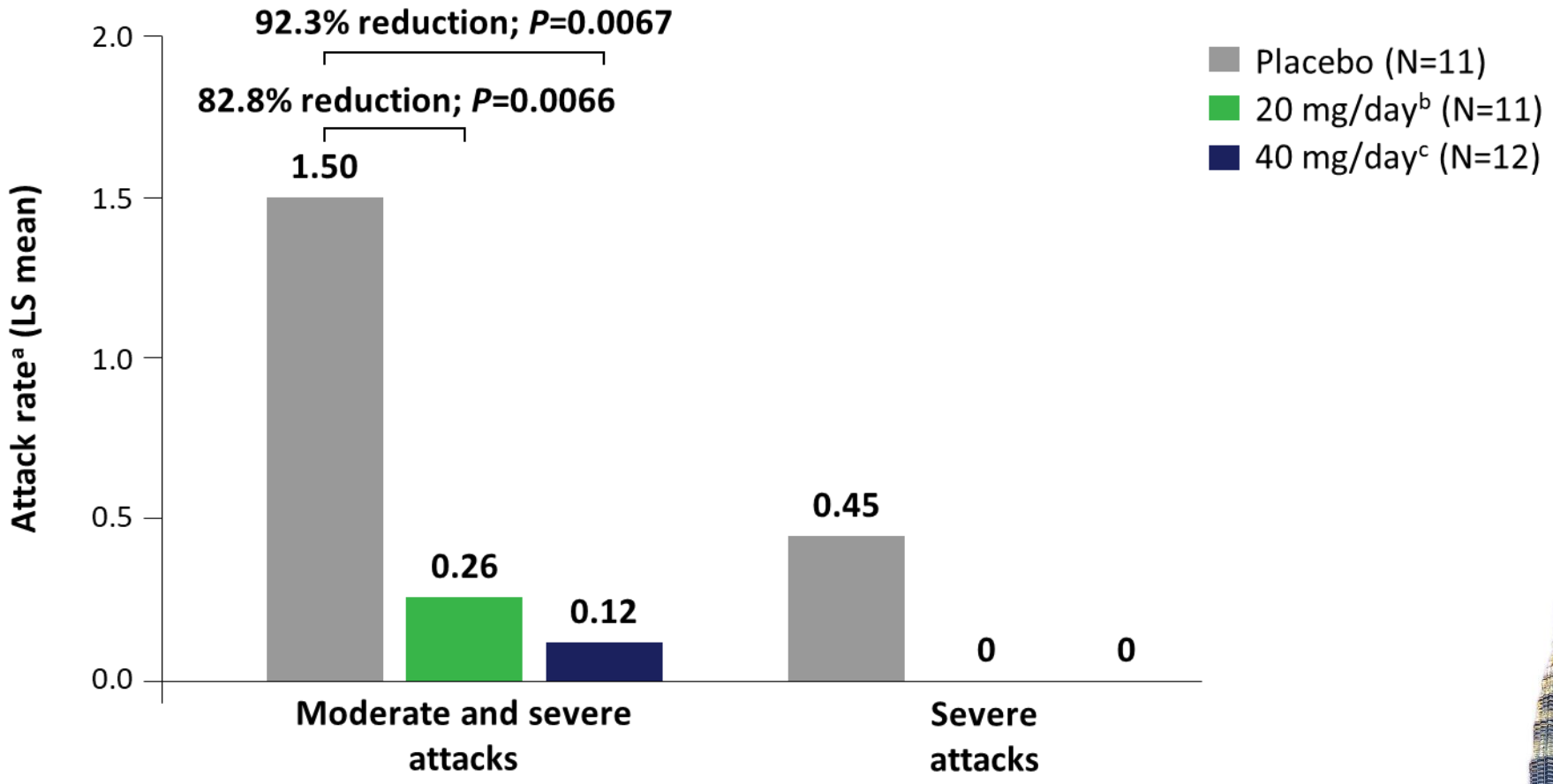
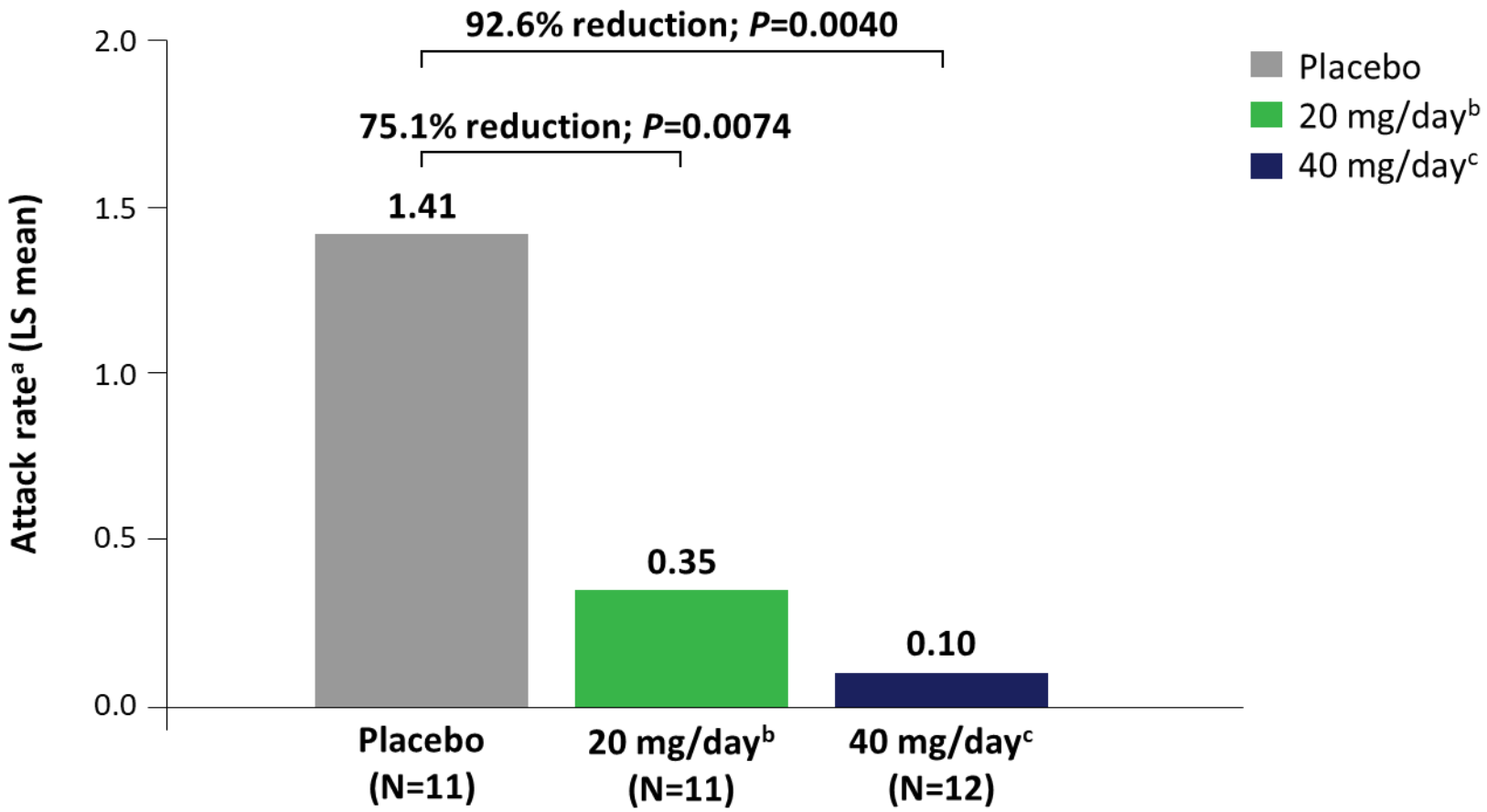
Deucrictibant reduced rates of “moderate and severe” attacks



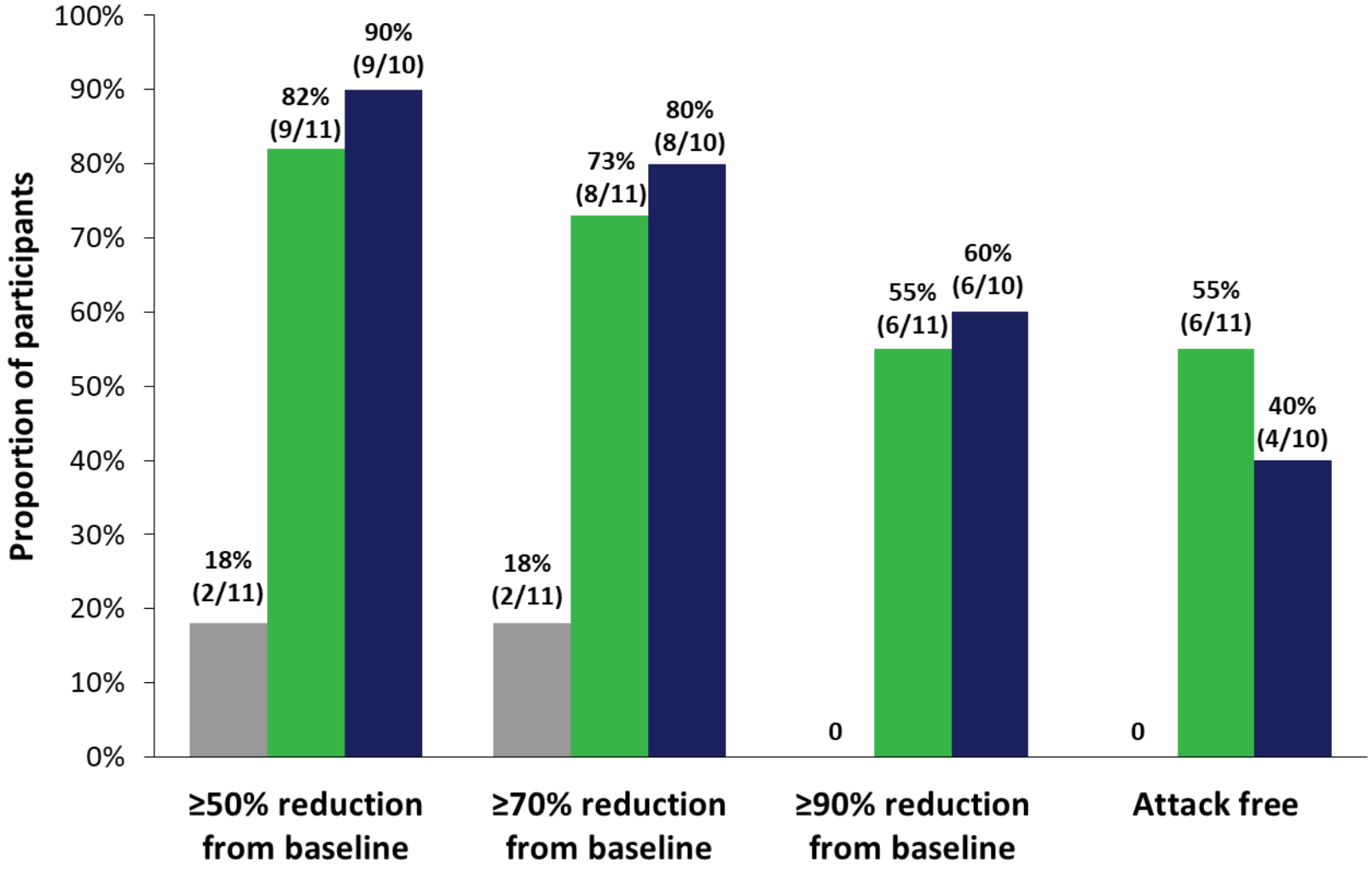
IR, immediate-release; LS, least squares. N = number of randomized participants. The *P* values in this figure are nominal. Model-based inferences are based on a Poisson regression model adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied. [a]Based on time normalized number of attacks per 4 weeks. [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily.

Deucrictibant reduced occurrence of attacks treated with on-demand medication



IR, immediate-release; LS, least squares. N = number of randomized participants. The *P*-values in this figure are nominal. Model-based inferences are based on a Poisson regression model adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied. [a]Based on time normalized number of attacks per 4 weeks. [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily.

Deucrictibant substantially reduced attack rate from baseline



IR, immediate-release. N = Participants with ≥4 weeks of treatment. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

Measuring disease control and HRQoL

Angioedema Control Test (AECT)[1,2] **:** a four-item questionnaire with a five-point response scale developed and validated to retrospectively quantify disease control and to aid treatment decisions in patients with recurrent angioedema.
AECT-4Wk – four-week recall used.

0 | 1 | 2 | 3 | 4

- *How often have you had angioedema in the last four weeks?*
- *How much has your quality of life been affected?*
- *How much has the unpredictability bothered you?*
- *How well has your angioedema been controlled by therapy?*

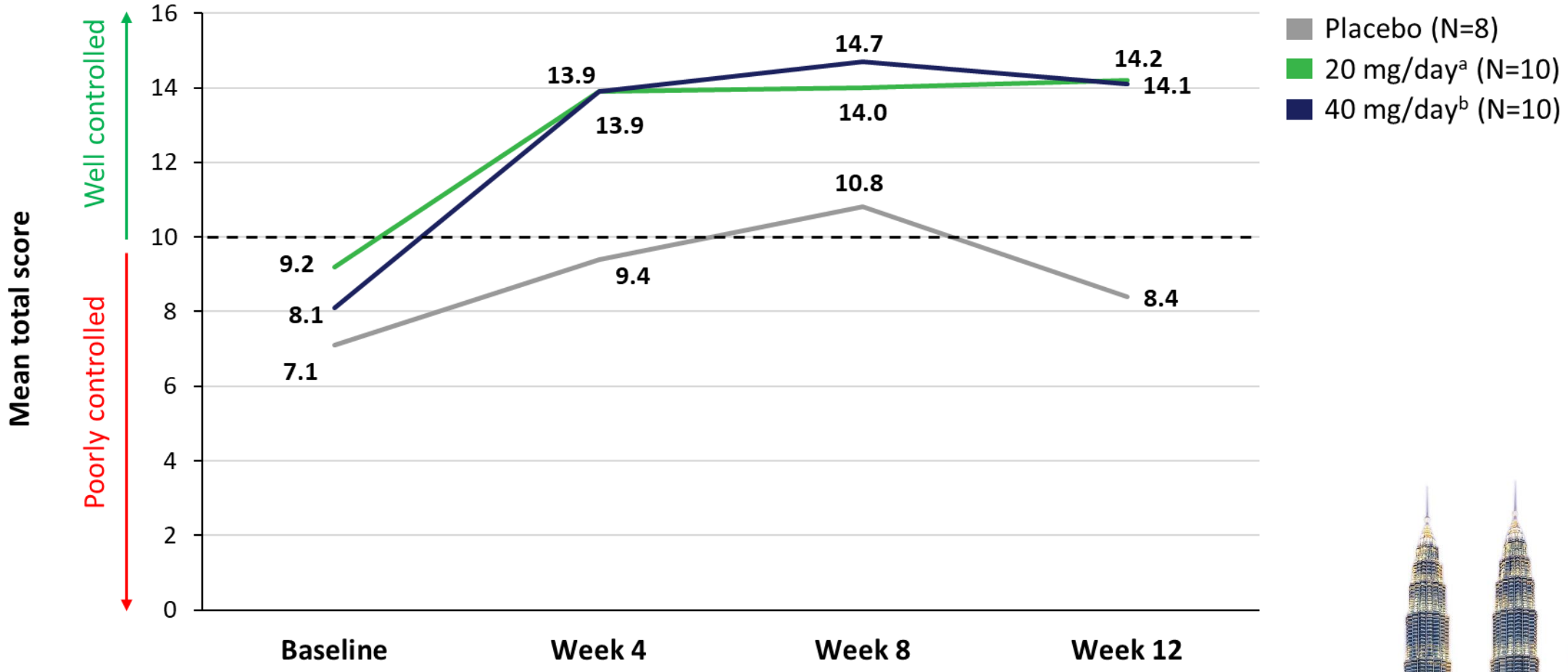
Angioedema Quality of Life Questionnaire (AE-QoL)[3-5]:
A tool validated for HAE and comprising a 17-item questionnaire with a five-point response scale across four domains:

(1) functioning
(2) fatigue/mood
(3) fear/shame
(4) nutrition

Never | Rarely | Sometimes | Often | Very often

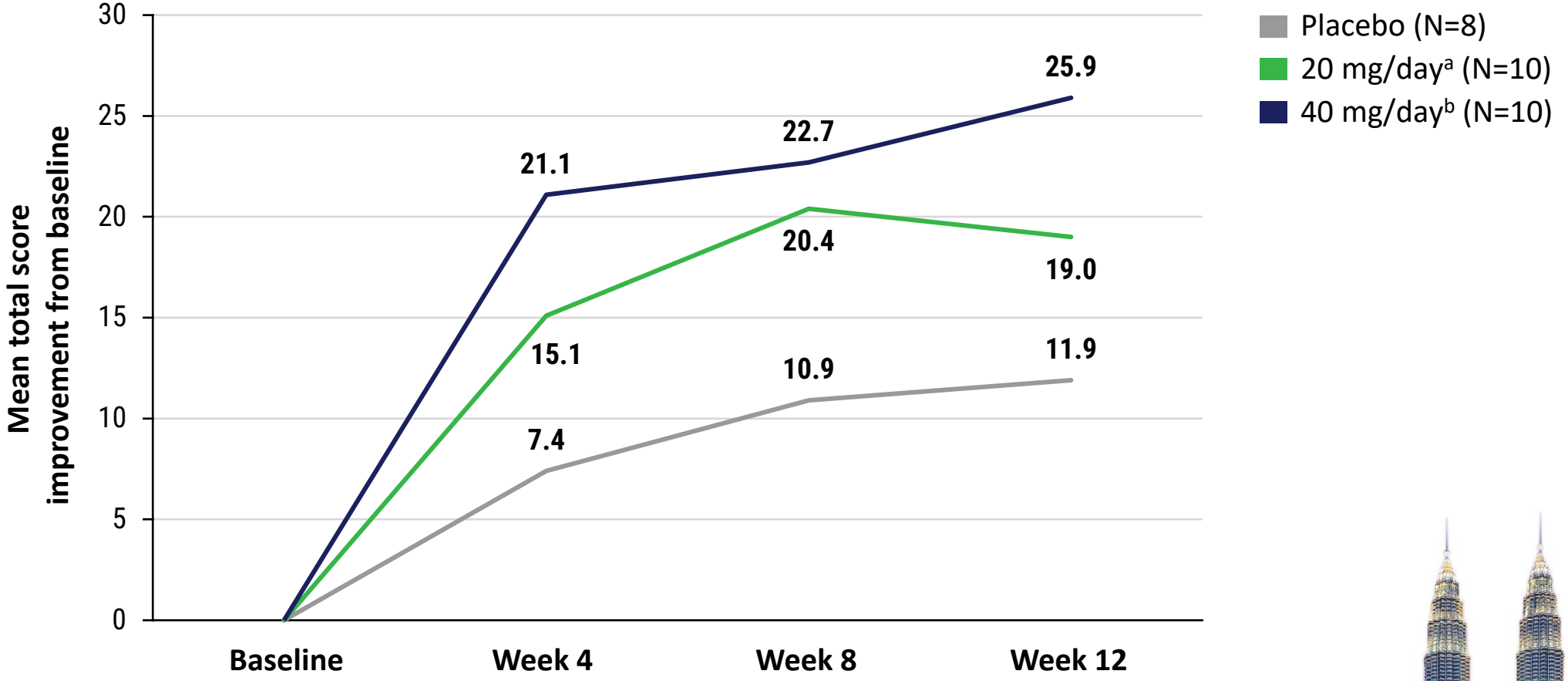
HAE, hereditary angioedema; HRQoL, health-related quality of life. **1.** Weller K, et al. *Allergy*. 2020;75:1165-77. **2.** Weller K, et al. *J Allergy Clin Immunol Pract*. 2020;8:2050-57. **3.** Weller K, et al. *Allergy*. 2012;67:1289-98. **4**. Weller K, et al. *Allergy*. 2016;71:1203-9. **5.** Vanya M, et al. *J Patient Rep Outcomes*. 2023; 7:33.

AECT: Treatment with deucrictibant resulted in well-controlled HAE by week 4 and throughout treatment



AECT, Angioedema Control Test; HAE, hereditary angioedema; IR, immediate-release. N = number of participants with AECT data at week 12. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

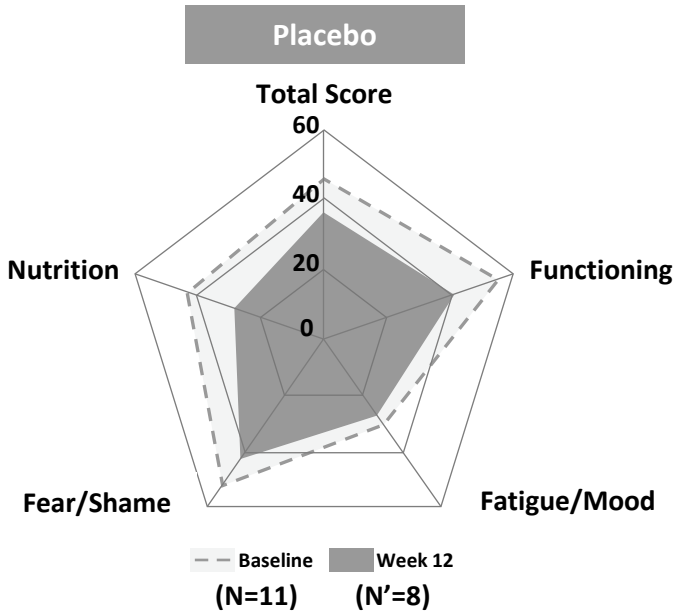
AE-QoL: Total score improved from baseline by week 4 and throughout treatment

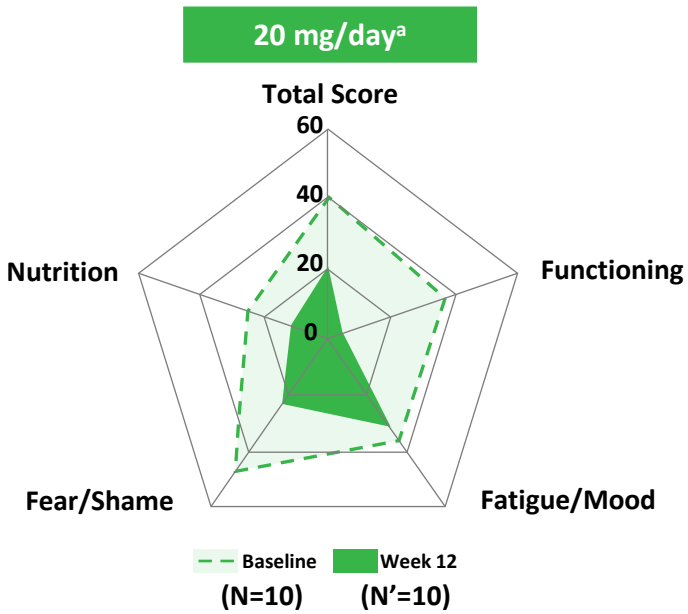


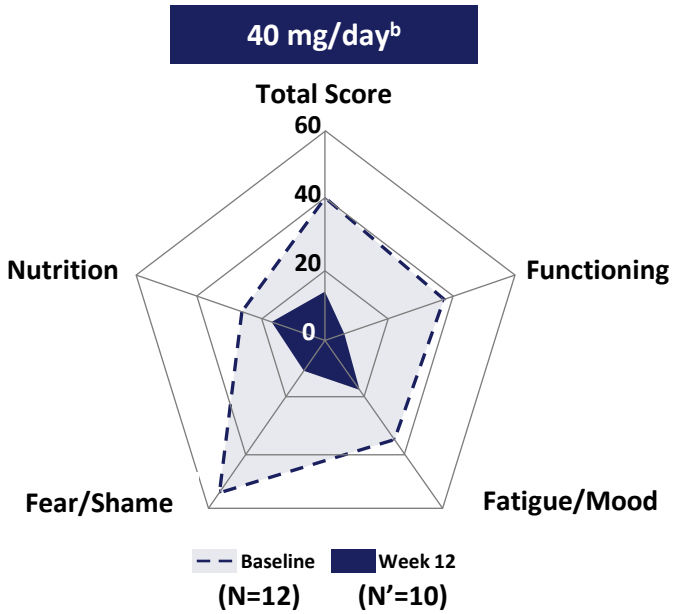
AE-QoL, Angioedema Quality of Life Questionnaire; IR, immediate-release. N = number of participants with AE-QoL data at week 12. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

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

AE-QoL: HRQoL improved across all domains







AE-QoL Total Score	Placebo	Deucrictibant 20 mg/day[a]	Deucrictibant 40 mg/day[b]
Baseline	**N=11**	**N=10**	**N=12**
Mean (SD)	45.3 (18.5)	39.1 (22.0)	41.1 (15.5)
Median (Q1, Q3)	42.6 (29.4, 57.4)	37.5 (16.2, 55.9)	40.4 (31.6, 49.3)
Week 12	**N'=8**	**N'=10**	**N'=10**
Mean (SD)	35.7 (19.6)	20.2 (15.6)	13.2 (6.9)
Median (Q1, Q3)	37.5 (19.1, 49.3)	18.4 (7.4, 33.8)	12.5 (10.3, 17.7)

AE-QoL, Angioedema Quality of Life Questionnaire; IR, immediate-release; HRQoL, health-related quality of life. N = number of randomized participants with AE-QoL data at baseline. N' = number of participants with AE-QoL data at week 12. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

Deucrictibant was well tolerated at both doses

- All reported treatment-related treatment-emergent adverse events (TEAEs) were mild in severity.
- No reports of serious TEAEs, severe TEAEs, or TEAEs leading to treatment discontinuation, study withdrawal, or death.

Adverse events in the RCT	Placebo (N=11)		Deucrictibant 20 mg/day[a] (N=11)		Deucrictibant 40 mg/day[b] (N=12)	
	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n
TEAEs	**7 (63.6)**	**16**	**6 (54.5)**	**11**	**7 (58.3)**	**12**
Treatment-related TEAEs	**1 (9.1)**	**1**	**2 (18.2)**	**2**	**1 (8.3)**	**1**
Nausea	0	0	1 (9.1)	1	0	0
Increased GGT	0	0	0	0	1 (8.3)	1
Dizziness postural	0	0	1 (9.1)	1	0	0
Headache	1 (9.1)	1	0	0	0	0
Serious TEAEs	**0**	**0**	**0**	**0**	**0**	**0**
Treatment-related serious TEAEs	**0**	**0**	**0**	**0**	**0**	**0**
TEAEs leading to study drug discontinuation, study withdrawal, or death	**0**	**0**	**0**	**0**	**0**	**0**

GGT, gamma-glutamyltransferase; IR, immediate-release; RCT, randomized controlled trial; TEAE, treatment-emergent adverse event (defined as adverse event occurring during time window from first study drug administration). N = number of participants who received ≥1 dose of blinded study treatment. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

Conclusions

- Prophylactic treatment with deucrictibant significantly reduced the occurrence of HAE attacks together with improved disease control and health-related quality of life.
  - Primary endpoint was met: 84.5% (p=0.0008) reduction in monthly attack rate vs placebo.[a]
  - 92.3% reduction in occurrence of “moderate and severe” attacks.[a]
  - 92.6% reduction in occurrence of attacks treated with on-demand medication.[a]
  - Both doses of deucrictibant were well tolerated.
  - Deucrictibant improved disease control and health-related quality of life within 4 weeks.
- CHAPTER-1 open-label extension data providing evidence that the attack rate remained low through >1 year are also presented at APAAACI 2024.

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

HAE, hereditary angioedema. [a]Deucrictibant 40mg/day treatment group.