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Efficacy and Safety of Oral Deucrictibant, a Potent Bradykinin B2 Receptor Antagonist, in Prophylaxis of Hereditary Angioedema Attacks: Results of CHAPTER-1 Phase 2 Trial

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

Conflicts of interest disclosure

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

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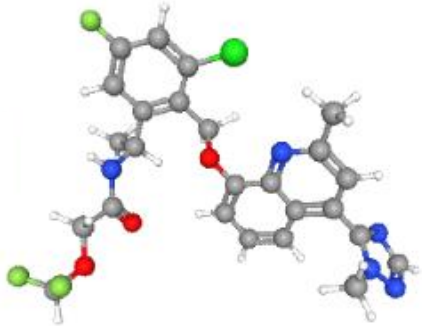
Two investigational oral therapies utilizing the same active ingredient for on-demand and prophylactic treatment of HAE

Deucrictibant
Immediate-release capsule

Rapid absorption

Aims to provide rapid and reliable symptom relief, through rapid exposure of attack-mitigating therapy in a convenient, small oral dosage form[a]

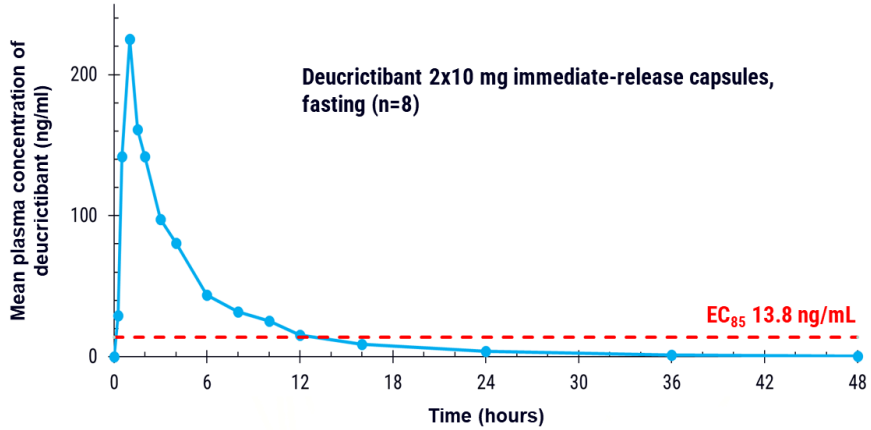


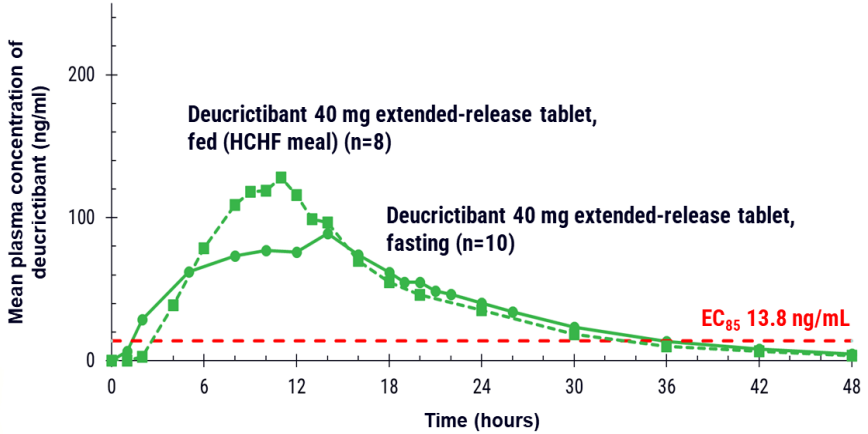
Deucrictibant
Extended-release tablet

Sustained absorption

Aims to provide sustained exposure of attack-preventing therapy in a convenient, small oral dosage form[a]

Deucrictibant





Adapted from: Groen K, et al. Presented at ACAAI 2022; November 10–14, 2022; Louisville, KY, USA. EC_{85}, concentration at which 85% of the maximum inhibitory effect is observed; HAE, hereditary angioedema; HCHF, high-calorie high-fat. [a]Aspirational; to be confirmed with clinical data.

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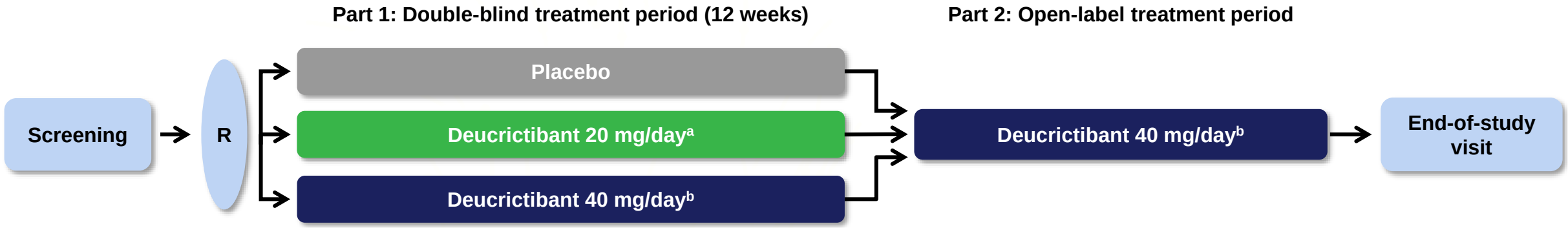
CHAPTER-1*: Two-part, Phase 2 study of deucrictibant for long-term prophylaxis of HAE attacks



- Primary endpoint
  - Time-normalized number of investigator-confirmed HAE attacks (**monthly[c] HAE attack rate**)
- Secondary endpoints
  - Time-normalized number of **moderate and severe HAE attacks**
  - Time-normalized number of **HAE attacks treated with on-demand medication**

HAE, hereditary angioedema; IR, immediate-release; R, randomization. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily. [c]1 month = 4 weeks.
*CHAPTER-1 is a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: NCT05047185. Accessed May 16, 2024. https://www.clinicaltrials.gov/study/NCT05047185.
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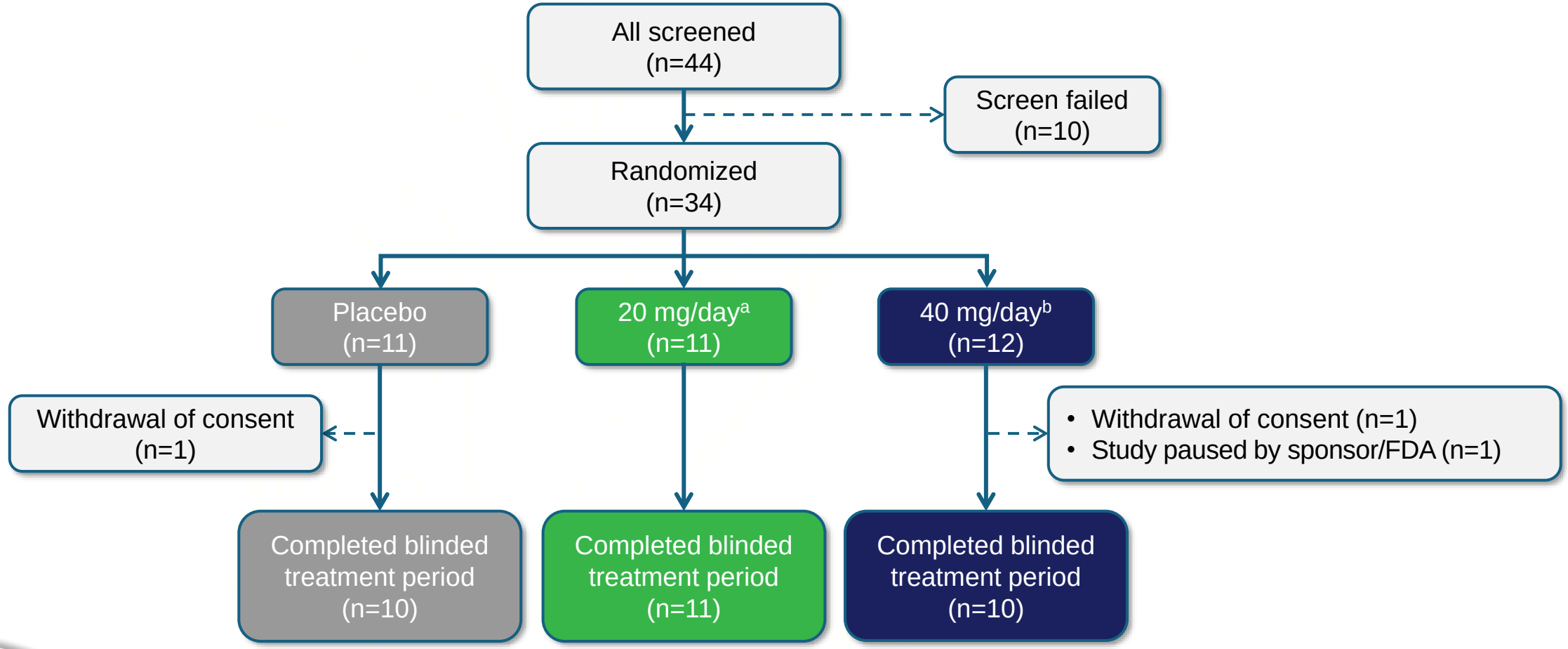
Participant disposition



FDA, Food and Drug Administration; IR, immediate-release; n, number of participants. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.
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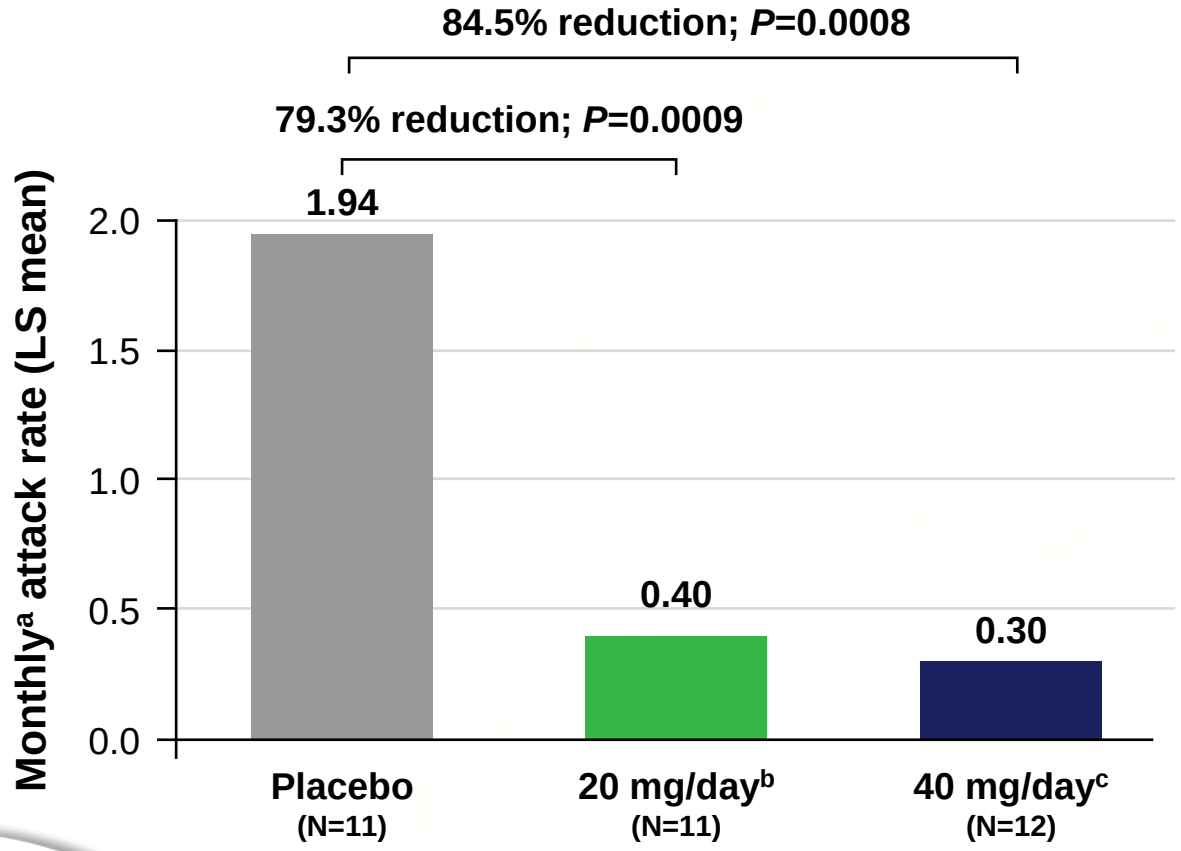
Balanced demographics and baseline characteristics

	Placebo (N=11)	20 mg/day[a] (N=11)	40 mg/day[b] (N=12)	All (N=34)
Age (years), mean	41.4	38.4	40.8	40.2
Sex: Male/Female, n	3/8	6/5	4/8	13/21
Race: White, n (%)	11 (100)	11 (100)	12 (100)	34 (100)
BMI (kg/m^2), mean	26.7	29.5	25.4	27.1
HAE type, n				
Type 1	10	9	12	31
Type 2	1	2	0	3
Baseline monthly[c] HAE attack rate				
Mean	1.9	2.1	2.5	2.2
Median (min, max)	1.7 (0.7, 3.7)	1.7 (1.0, 5.3)	1.7 (1.0, 6.7)	1.7 (0.7, 6.7)
Randomized baseline monthly[c] HAE attack rate categories, n (%)				
1 to <2 attacks	6 (54.5)	7 (63.6)	7 (58.3)	20 (58.8)
2 to <3 attacks	3 (27.3)	1 (9.1)	1 (8.3)	5 (14.7)
≥3 attacks	2 (18.2)	3 (27.3)	4 (33.3)	9 (26.5)

BMI, body mass index; HAE, hereditary angioedema; IR, immediate-release; N, number of randomized participants. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily. [c]1 month = 4 weeks. *This presentation includes data for an investigational product not yet approved by regulatory authorities.*

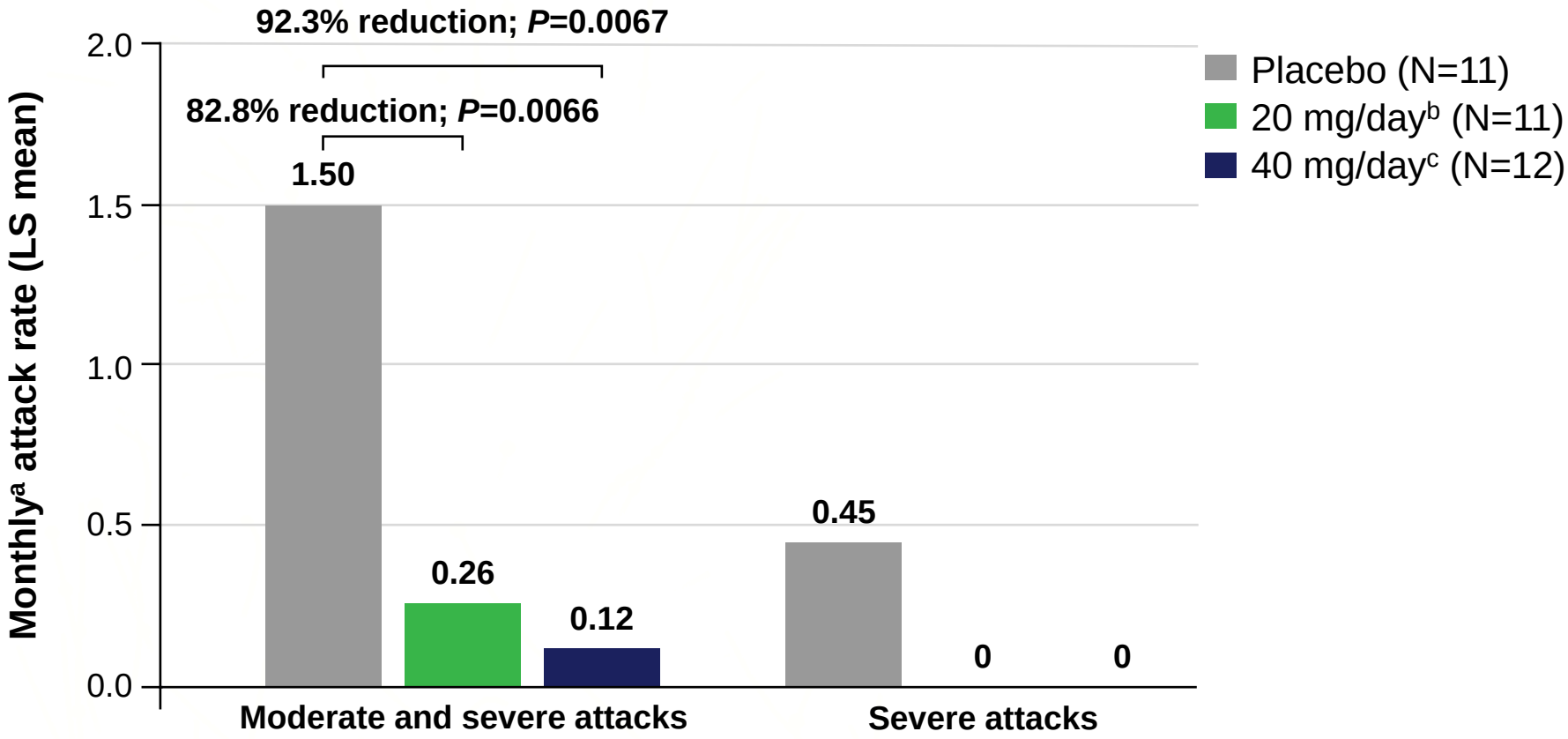
Primary endpoint: deucrictibant significantly reduced the monthly attack rate



	Placebo (N=11)	Deucrictibant 20 mg/day[b] (N=11)	Deucrictibant 40 mg/day[c] (N=12)
Monthly[a] attack rate			
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	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

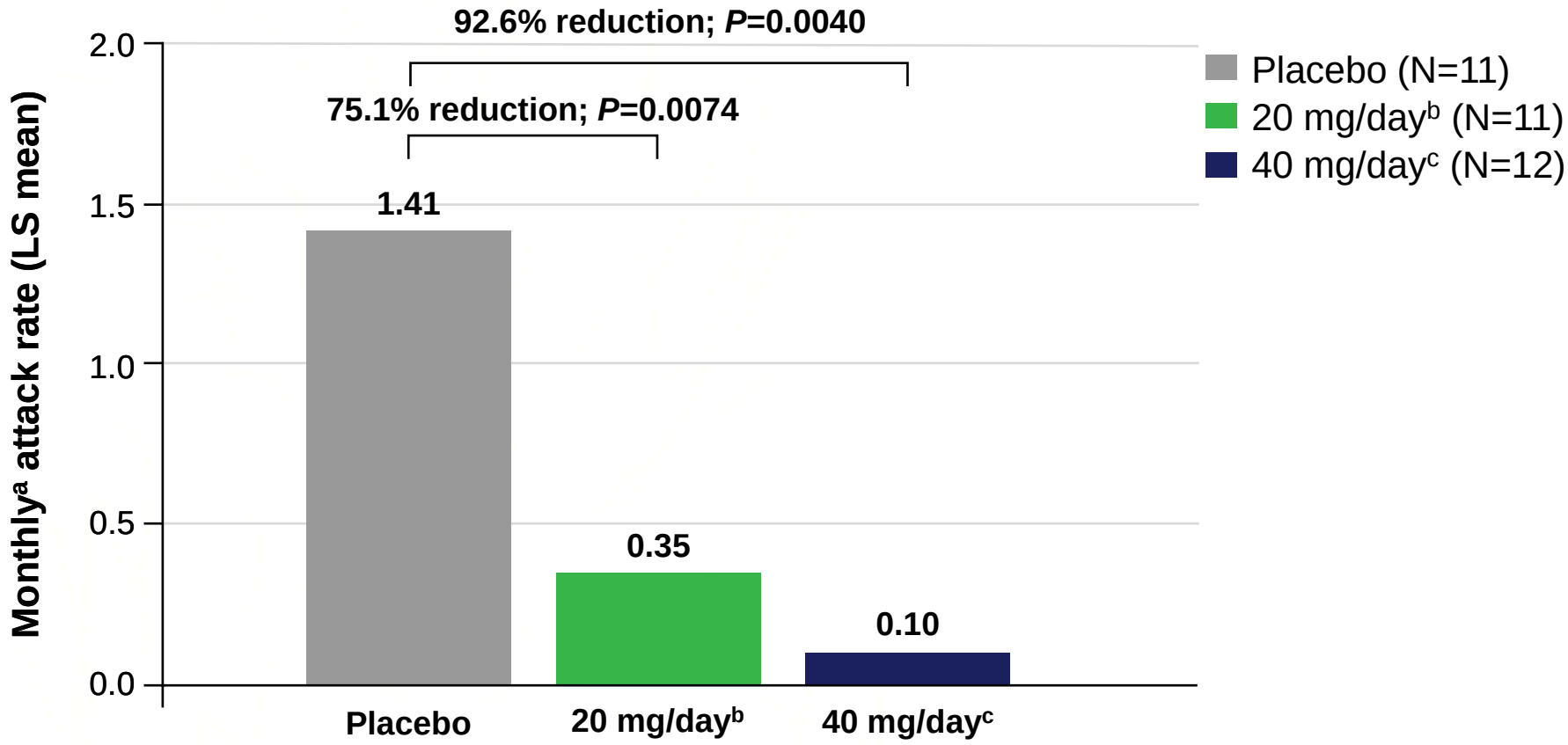
BL, baseline; IR, immediate-release; LS, least squares; N, number of randomized participants. Model-based inferences are based on a Poisson regression model adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied. [a]1 month = 4 weeks. [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily. *This presentation includes data for an investigational product not yet approved by regulatory authorities.*

Deucrictibant reduced occurrence of moderate and severe attacks



IR, immediate-release; LS, least squares; N, number of randomized participants. The *P* values in this figure are nominal. [a]1 month = 4 weeks. [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily. *This presentation includes data for an investigational product not yet approved by regulatory authorities.*

Deucrictibant reduced occurrence of attacks treated with on-demand medication



IR, immediate-release; LS, least squares; N, number of randomized participants. [a]1 month = 4 weeks. [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily.
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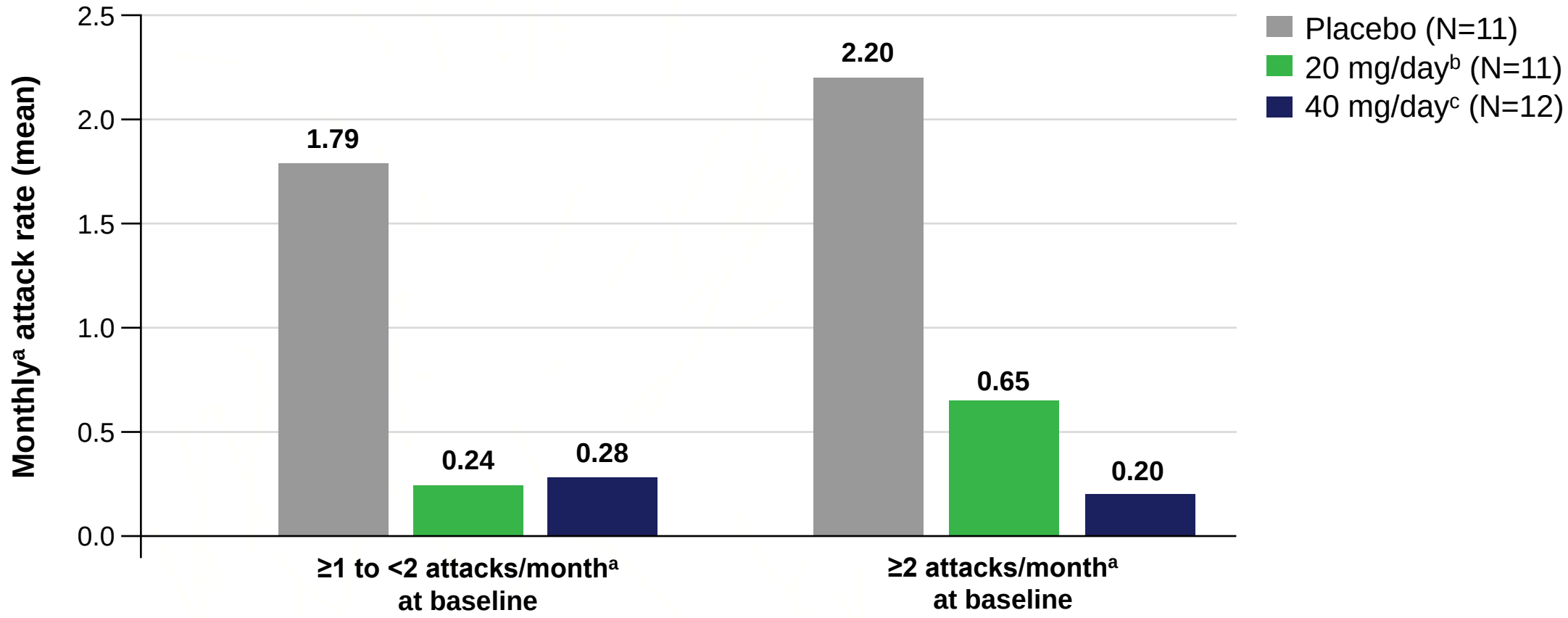
Deucrictibant reduced monthly attack rate regardless of baseline attack rate



IR, immediate-release; N, number of randomized participants. [a]1 month = 4 weeks. [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily.
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Deucrictibant was well tolerated at both doses

- All reported treatment-related treatment-emergent adverse events (TEAEs) were mild in severity

Adverse events	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; N, number of participants who received at least 1 dose of blinded study treatment. [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.*

Conclusions

- Prophylactic treatment with deucrictibant significantly reduced the occurrence of HAE attacks
- Primary endpoint was met: 84.5% (*P*=0.0008) reduction in monthly attack rate vs placebo[a]
- Consistent reduction in the occurrence of HAE attacks regardless of baseline attack rate
- Secondary endpoints
  - 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 tested were well-tolerated
- These data support further development of deucrictibant as a potential prophylactic therapy for HAE

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-1 trial.

HAE, hereditary angioedema. [a]40 mg/day deucrictibant treatment group. *This presentation includes data for an investigational product not yet approved by regulatory authorities.*

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