PHARVARIS

CHAPTER-1 Phase 2 Top-line Data

December 6, 2023

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Agenda

Introduction

Berndt Modig, *CEO Pharvaris*

Review of CHAPTER-1 top-line Phase 2 data

Peng Lu, M.D. PhD, *CMO Pharvaris*

KOL perspective

Marc A. Riedl, M.D., M.S., *Professor of Medicine, Clinical Director of the U.S. Hereditary Angioedema Association (HAEA) Angioedema Center at the University of California San Diego (UCSD), Clinical Service Chief for Allergy/Immunology at UCSD; principal investigator in the CHAPTER-1 study*

Closing Remarks, Q&A

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Closing Remarks, Q&A

People living with HAE are seeking highly effective, well-tolerated and less burdensome prophylactic therapies

Injectable-like **efficacy**

Well-tolerated

Easy, painless administration

An effective oral bradykinin B2 receptor antagonist has the potential to deliver on their hopes

Proprietary Pharvaris research, 2022 (representative sample of patients, n = 103, and doctors, n = 100)

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Closing Remarks, Q&A

CHAPTER-1, a Phase 2 prophylactic study of deucrictibant in HAE

Primary endpoint met: 84.5% (p=0.0008) reduction in monthly attack rate versus placebo*

- 92.3% reduction in occurrence of moderate and severe attacks*
- 92.6% reduction in occurrence of attacks treated with on-demand medication*
- Clinically meaningful results across primary, secondary, and health-related quality of life endpoints
- Deucrictibant well-tolerated at both doses

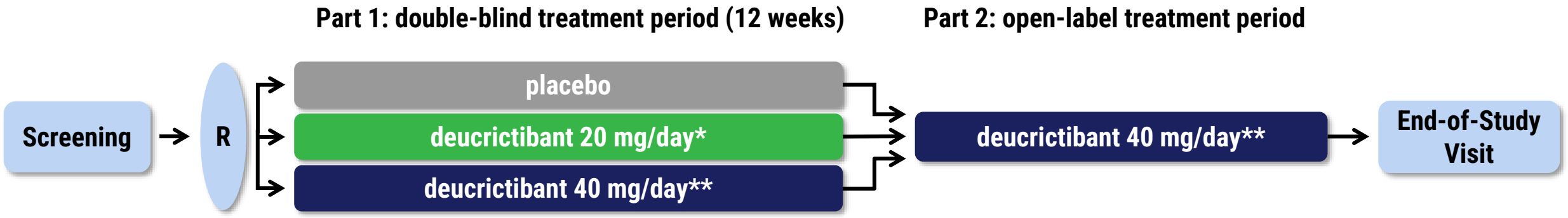
*40 mg/day deucrictibant treatment group; %reduction in monthly attack rate is based on a Poisson regression model

Note: all attacks reported herein are investigator-confirmed; attack rate is number of attacks per month of exposure, also referred to as time-normalized number of attacks; all statistical analyses comparing deucrictibant and placebo are made without adjustment for multiplicity.

CHAPTER-1 study design

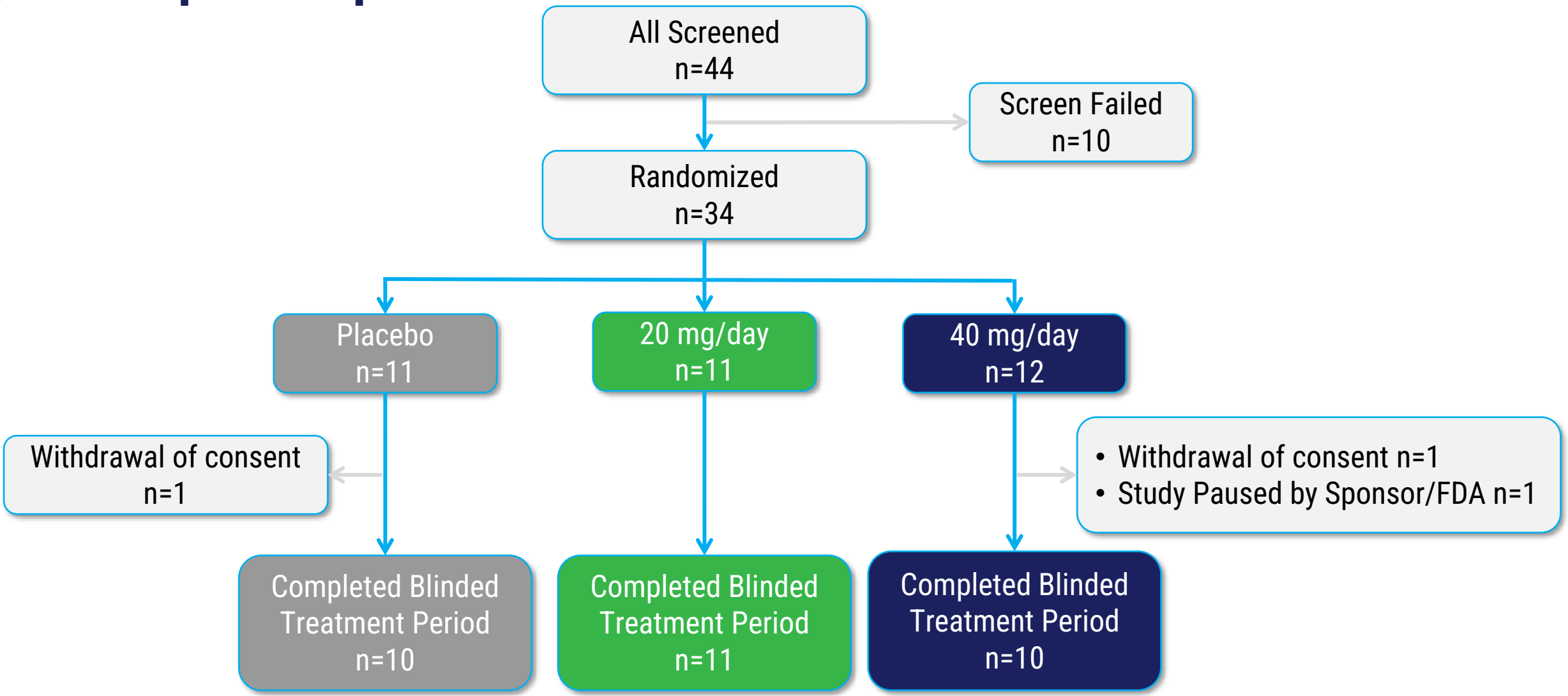
Double-blind, placebo-controlled Phase 2 study evaluating deucrictibant for long-term prophylaxis in HAE-1/2

- 34 participants enrolled in North America and Europe



R = randomization;
*deucrictibant 20 mg/day = deucrictibant immediate-release capsules (PHVS416) 10 mg twice daily
**deucrictibant 40 mg/day = deucrictibant immediate-release capsules (PHVS416) 20 mg twice daily

Participant disposition



20 mg/day = deucrictibant immediate release (IR) capsules 10 mg twice daily; 40 mg/day = deucrictibant IR capsules 20 mg twice daily; n = number of participants.

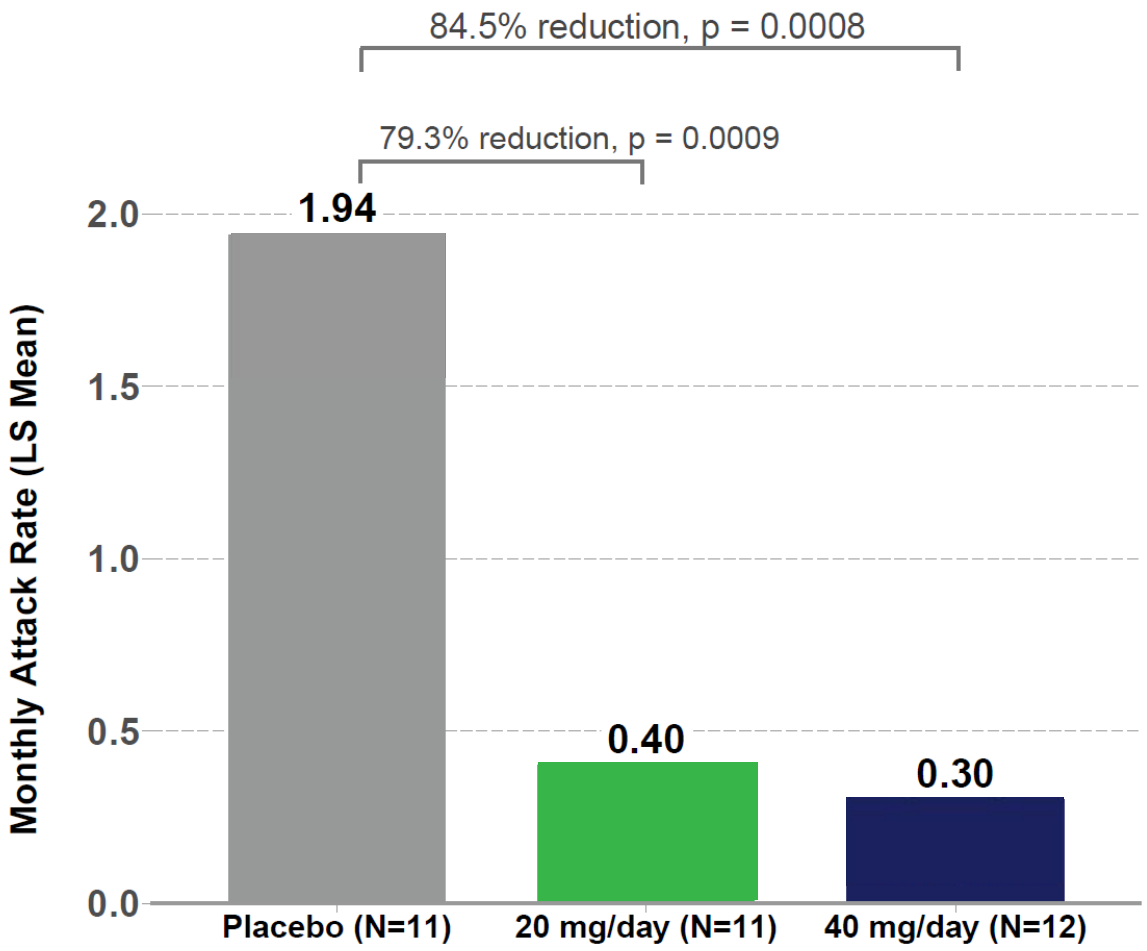
Balanced demographics and baseline characteristics

	Placebo N=11	20 mg/day N=11	40 mg/day N=12	All N=34
Age in years – Mean	41.4	38.4	40.8	40.2
Sex: M/F – n	3/8	6/5	4/8	13/21
Race: White – n (%)	11 (100)	11 (100)	12 (100)	34 (100)
BMI (kg/m2) – 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 HAE attack rate per month				
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 HAE attack rate categories – n (%)				
1 to < 2 attacks per 4 weeks	6 (54.5)	7 (63.6)	7 (58.3)	20 (58.8)
2 to < 3 attacks per 4 weeks	3 (27.3)	1 (9.1)	1 (8.3)	5 (14.7)
≥ 3 attacks per 4 weeks	2 (18.2)	3 (27.3)	4 (33.3)	9 (26.5)

20 mg/day = deucrictibant immediate release (IR) capsules 10 mg twice daily.
40 mg/day = deucrictibant IR capsules 20 mg twice daily.
N = number of randomized participants.

Primary endpoint met: deucrictibant significantly reduced attack rate

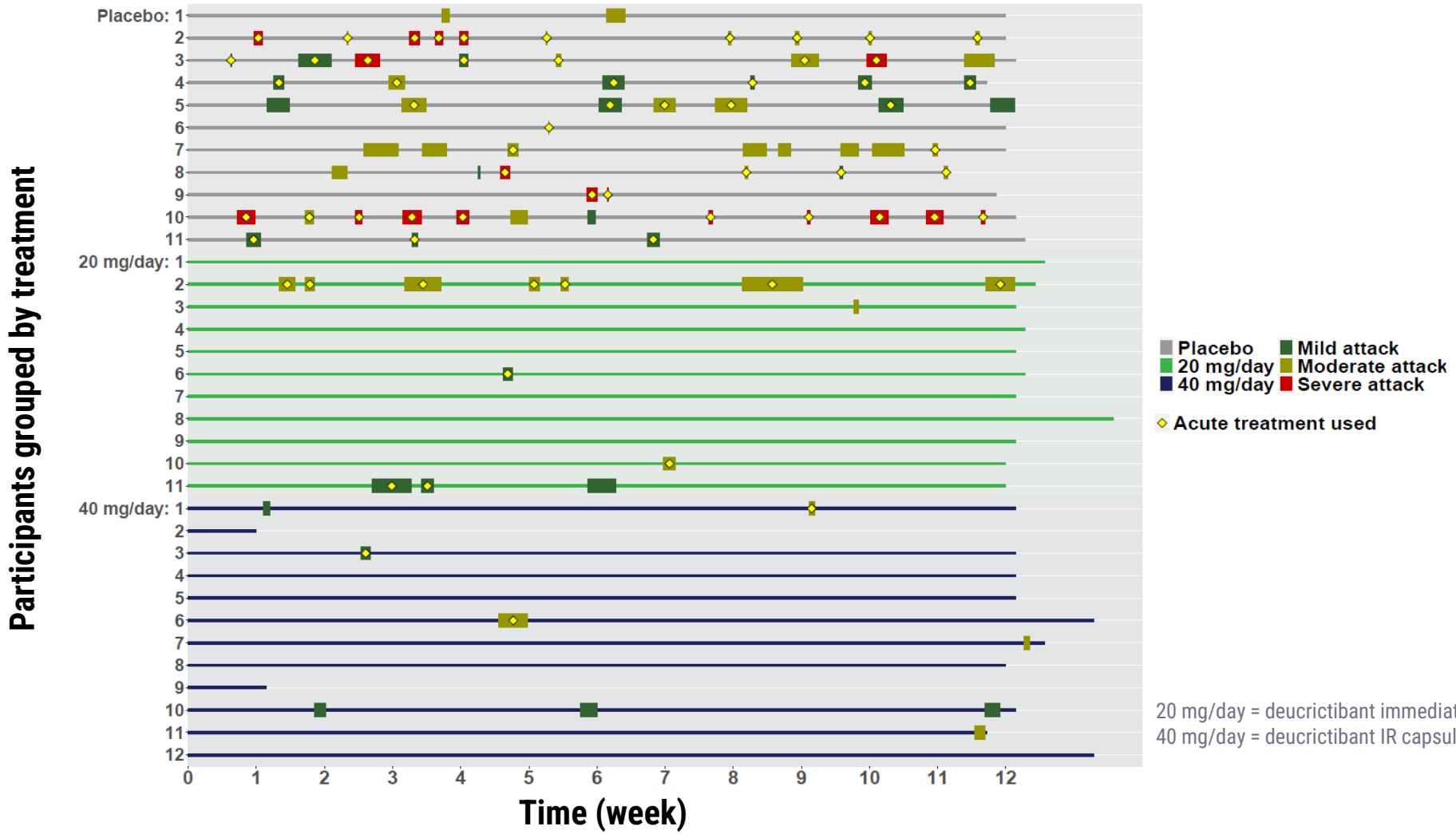
Monthly attack rate measured as time-normalized number of investigator confirmed HAE attacks



	Placebo N=11	20 mg/day N=11	40 mg/day N=12
Monthly attack rate – Median			
Baseline	1.67	1.67	1.74
On study	2.15	0	0.15
Change from baseline	0.33	-1.34	-1.59
% change from baseline	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

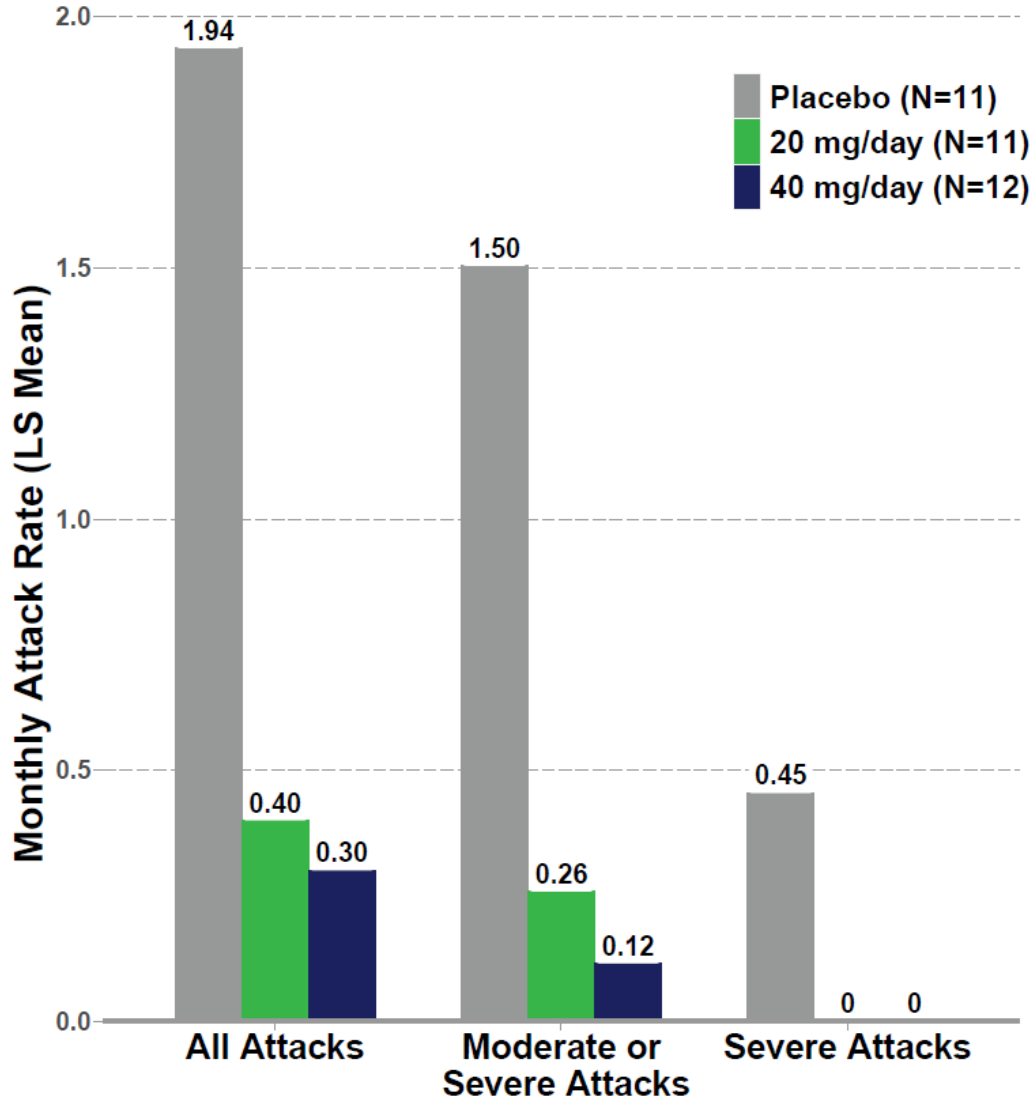
20 mg/day = deucrictibant immediate release (IR) capsules 10 mg twice daily.
40 mg/day = deucrictibant IR capsules 20 mg twice daily.
N = number of randomized participants.
LS mean = least squares mean. Model-based inferences are based on a Poisson regression model adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied.

Significant attack reduction and no severe attacks with deucrictibant



20 mg/day = deucrictibant immediate release (IR) capsules 10 mg twice daily.
40 mg/day = deucrictibant IR capsules 20 mg twice daily.

92.3% reduction in moderate or severe attacks at 40 mg/day dose



	Placebo N=11	20 mg/day N=11	40 mg/day N=12
Monthly attack rate of moderate or severe attacks			
LS mean	1.50	0.26	0.12
% reduction vs placebo		**82.8%**	**92.3%**
Nominal p-value		0.0066	0.0067

20 mg/day = deucrictibant immediate release (IR) capsules 10 mg twice daily.
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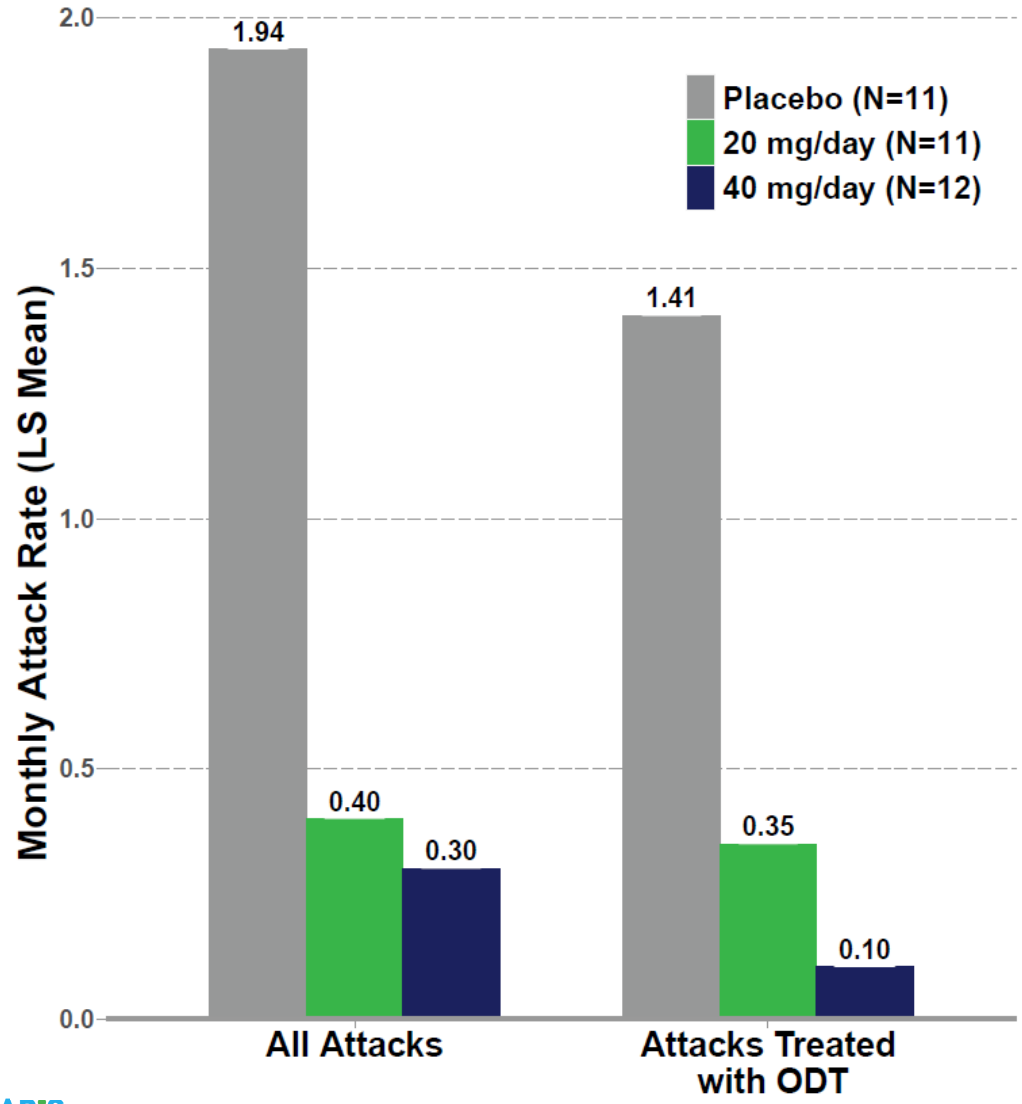
N = number of randomized participants.
LS mean = least squares mean. Monthly attack rates are based on a Poisson regression model adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied.

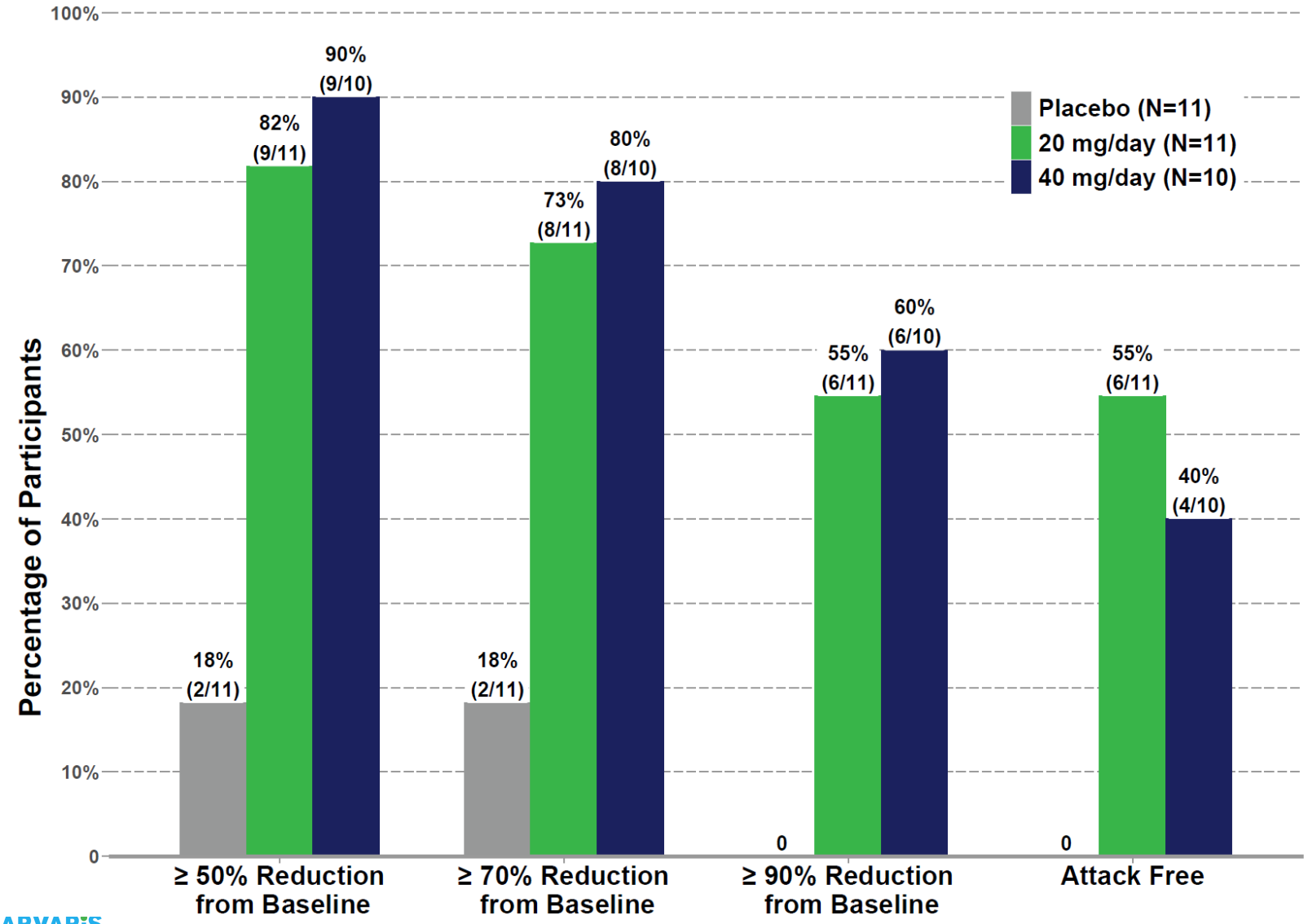
92.6% reduction in attacks treated with ODT at 40 mg/day dose



	Placebo N=11	20 mg/day N=11	40 mg/day N=12
Monthly attack rate of attacks treated with ODT			
LS mean	1.41	0.35	0.10
% reduction vs placebo		**75.1%**	**92.6%**
Nominal p-value		0.0074	0.0040

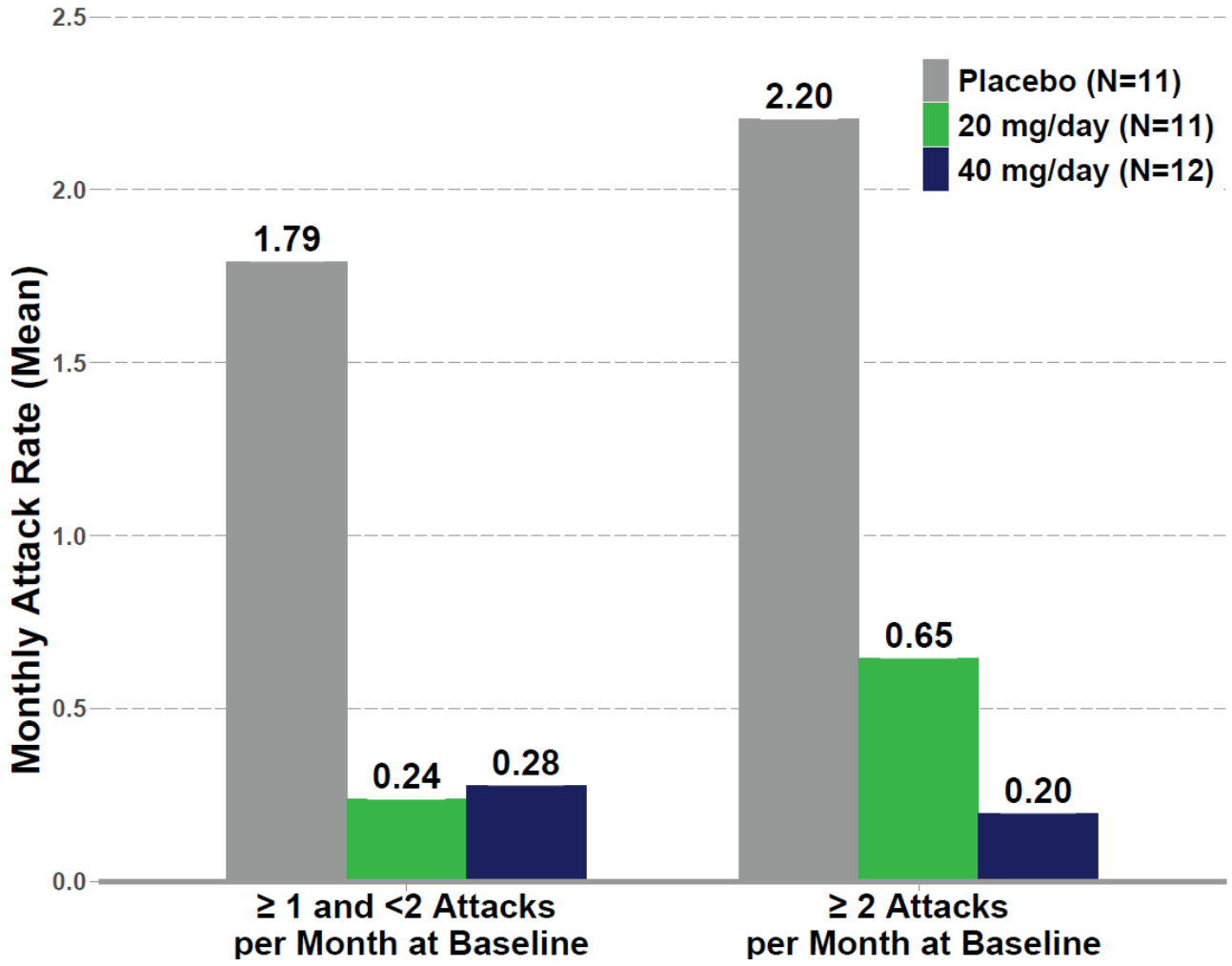
ODT = on-demand treatment (icatibant, C1-inhibitor (C1-INH))
20 mg/day = deucrictibant immediate release (IR) capsules 10 mg twice daily;
40 mg/day = deucrictibant IR capsules 20 mg twice daily.
N = number of randomized participants.
LS mean = least squares mean. Monthly attack rates are based on a Poisson regression model adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied.

Substantial reduction of attack rate from baseline



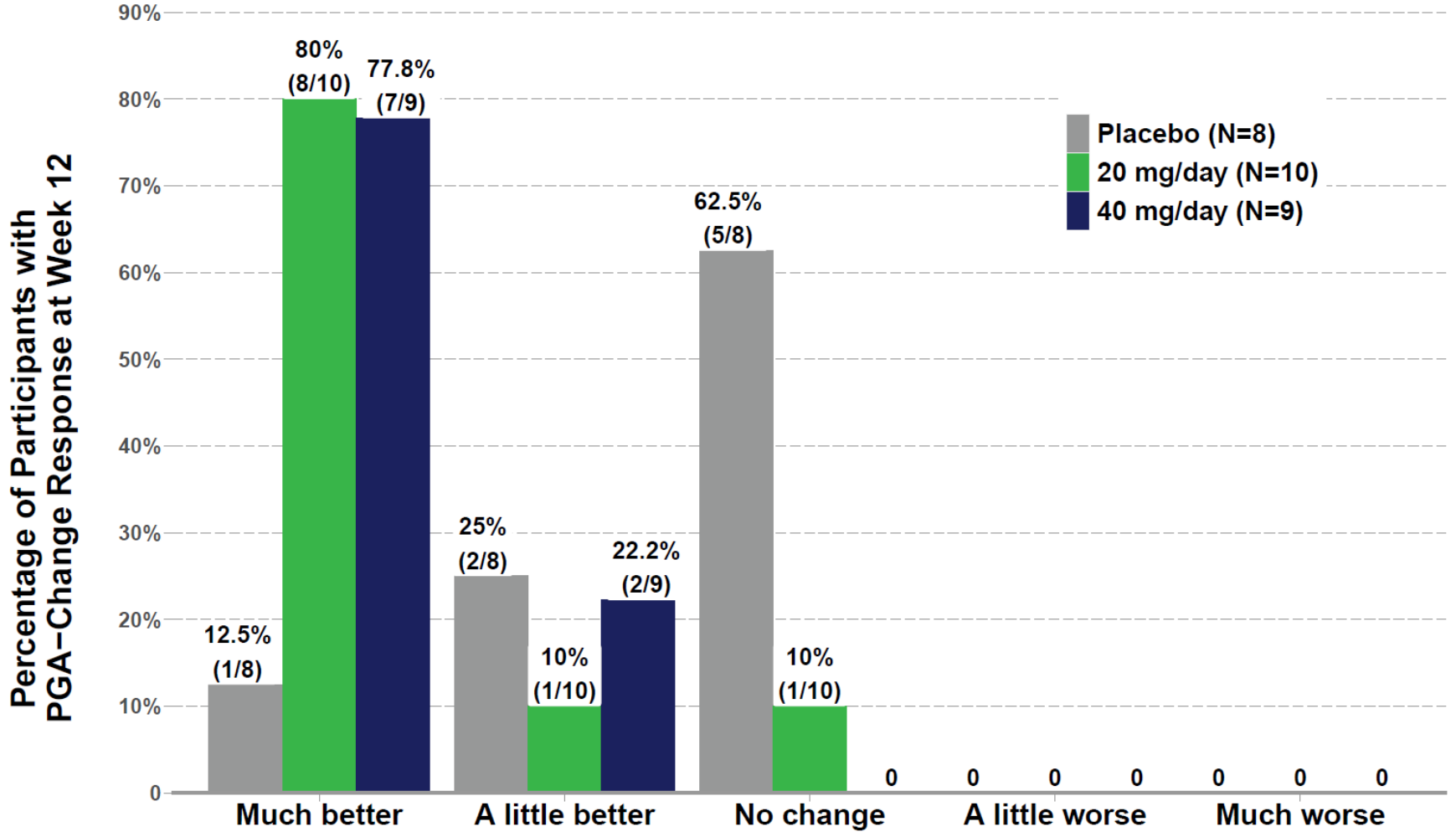
20 mg/day = deucrictibant immediate release (IR) capsules 10 mg twice daily.
40 mg/day = deucrictibant IR capsules 20 mg twice daily.
N = number of randomized participants.
Results based on participants with at least 4 weeks of treatment.

Consistent efficacy regardless of baseline attack rate



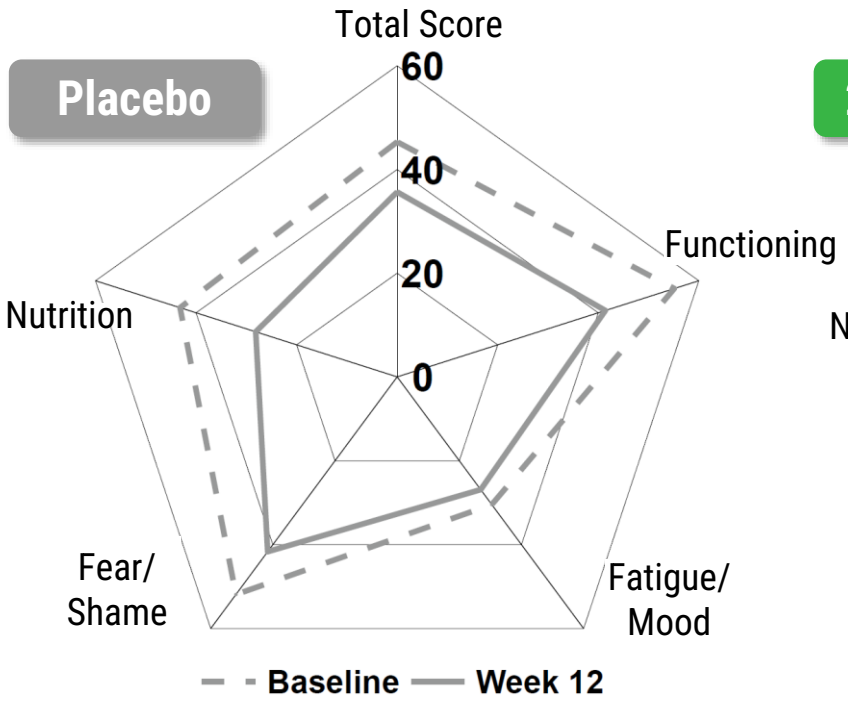
20 mg/day = deucrictibant immediate release (IR) capsules 10 mg twice daily.
40 mg/day = deucrictibant IR capsules 20 mg twice daily.
N = number of randomized participants.

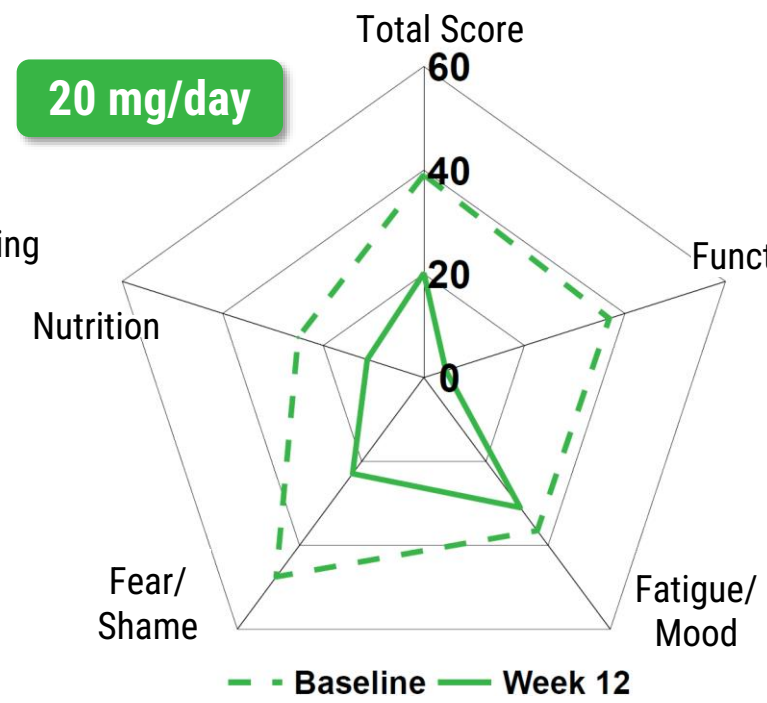
All 40 mg/day participants reported an improvement in PGA-Change

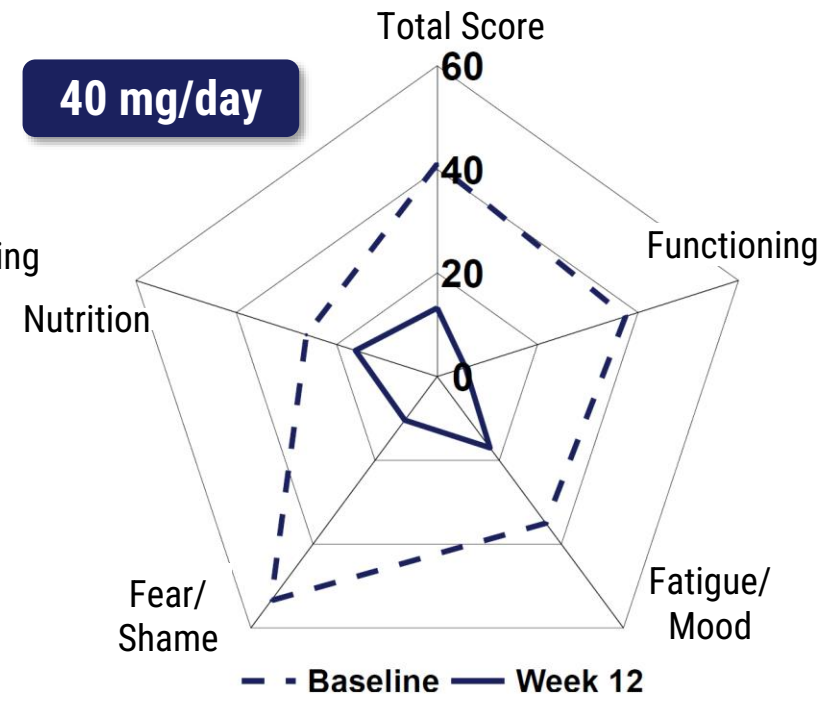


20 mg/day = deucrictibant immediate release (IR) capsules 10 mg twice daily. 40 mg/day = deucrictibant IR capsules 20 mg twice daily.
PGA-Change = patient global assessment of change (question). N = number of participants with PGA-Change results at Week 12.

AE-QoL: improvement in health-related quality of life







AE-QoL Total Score		Placebo	20 mg/day	40 mg/day
Baseline	N	11	10	12
	Mean	45.3	39.1	41.1
	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	10	10
	Mean	35.7	20.2	13.2
	Median (Q1, Q3)	37.5 (19.1, 49.3)	18.4 (7.4, 33.8)	12.5 (10.3, 17.7)

20 mg/day = deucrictibant immediate release (IR) capsules 10 mg twice daily. 40 mg/day = deucrictibant IR capsules 20 mg twice daily.
AE-QoL = angioedema quality of life (questionnaire). N = number of randomized participants. N' = number of participants with AE-QoL data at Week 12.

Deucrictibant well-tolerated at both doses

	Placebo (N=11)		20 mg/day (N=11)		40 mg/day (N=12)	
	Subjects n (%)	Number of events	Subjects n (%)	Number of events	Subjects n (%)	Number of events
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
Serious TEAEs	0	0	0	0	0	0
Treatment related Serious TEAEs	0	0	0	0	0	0
TEAEs leading to study drug discontinuation	0	0	0	0	0	0
TEAEs leading to withdrawal from study	0	0	0	0	0	0
TEAEs leading to death	0	0	0	0	0	0

20 mg/day = deucrictibant immediate release (IR) capsules 10 mg twice daily. 40 mg/day = deucrictibant IR capsules 20 mg twice daily.
N = number of participants randomized and dosed. n = number of participants having a treatment emergent adverse event.
TEAE = treatment-emergent adverse event, defined as adverse events that occur after the first administration of blinded study treatment.

All treatment-related adverse events were mild

System Organ Class Preferred Term	Placebo (N=11)	20 mg/day (N=11)	40 mg/day (N=12)
Participants with at least one treatment-related TEAE	**1 (9.1%)**	**2 (18.2%)**	**1 (8.3%)**
Gastrointestinal disorders	**0**	**1 (9.1%)**	**0**
Nausea	0	1 (9.1%)	0
Investigations	**0**	**0**	**1 (8.3%)**
Gamma-glutamyltransferase increased	0	0	1 (8.3%)
Nervous system disorders	**1 (9.1%)**	**1 (9.1%)**	**0**
Dizziness postural	0	1 (9.1%)	0
Headache	1 (9.1%)	0	0

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N = number of participants randomized and dosed.
TEAE = treatment-emergent adverse event, defined as adverse events that occur after the first administration of blinded study treatment.

Main efficacy results

	Placebo N=11	20 mg/day N=11	40 mg/day N=12
Monthly attack rate – LS Mean (95% CI)*			
All attacks (primary endpoint)	**1.94 (1.31, 2.87)**	**0.40 (0.17, 0.92)**	**0.30 (0.11, 0.82)**
% reduction vs placebo, p-value		**79.3%, p=0.0009**	**84.5%, p=0.0008**
Moderate or severe attacks	1.50 (0.91, 2.50)	0.26 (0.08, 0.81)	0.12 (0.02, 0.67)
Attacks treated with on-demand medication	1.41 (0.88, 2.24)	0.35 (0.14, 0.85)	0.10 (0.02, 0.57)
Achieving threshold reduction of attack rate from baseline**			
>=50% reduction	2/11 (18%)	9/11 (82%)	9/10 (90%)
>=70% reduction	2/11 (18%)	8/11 (73%)	8/10 (80%)
>=90% reduction	0	6/11 (55%)	6/10 (60%)
Attack free during treatment period	0	6 /11(55%)	4/10 (40%)

20 mg/day = deucrictibant immediate release (IR) capsules 10 mg twice daily; 40 mg/day = deucrictibant IR capsules 20 mg twice daily. N = number of randomized participants.
LS mean = least squares mean. CI = confidence interval.

*Results of monthly attack rates are based on Poisson regressions adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied. Nominal p-value < 0.01 for all secondary endpoints included in this section comparing deucrictibant with placebo.
**Participants with <4 weeks of treatment (2 participants on 40 mg/day) were not included in the summaries of proportions achieving threshold reduction of attack rate from baseline. Nominal p-value < 0.05 for all secondary endpoints included in this section comparing deucrictibant with placebo.

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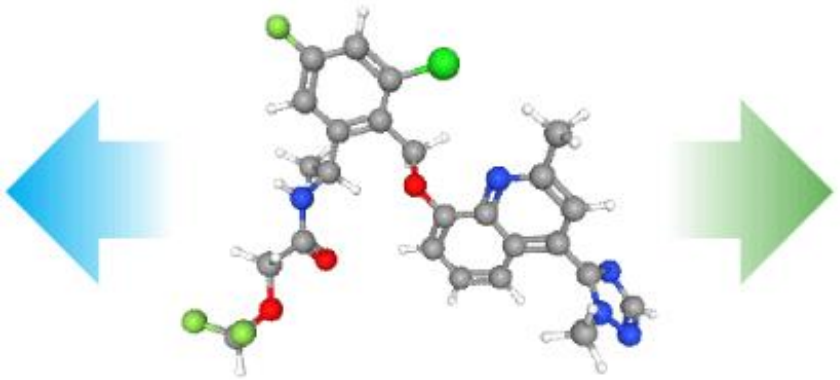
Closing Remarks, Q&A

Managing HAE with two oral products utilizing the same active ingredient for on-demand and prophylactic treatment

deucrictibant
Immediate release capsule
PHVS416
rapid absorption

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



deucrictibant

deucrictibant
Extended-release tablet
PHVS719
sustained absorption

Aim to provide sustained exposure of attack-preventing therapy in a convenient, small oral dosage form*

Based on the results in RAPIDe-1 and CHAPTER-1 deucrictibant has the potential to become the preferred option to treat and prevent HAE attacks

*Aspirational; to be confirmed with clinical data

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