PHARVARIS

Bradykinin data discussion

September 2024

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Agenda

Berndt Modig, CEO Pharvaris

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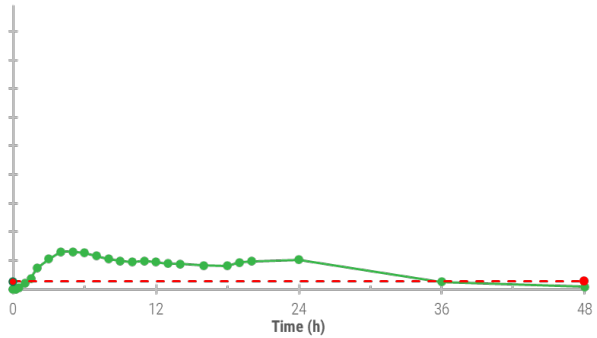
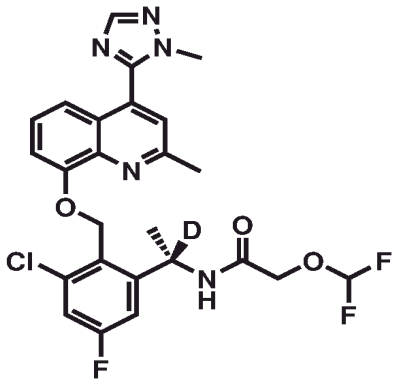
Deucrictibant has the potential to become a preferred therapy for people living with HAE

DEUCRICTIBANT extended-release (XR) tablet

sustained absorption[1]



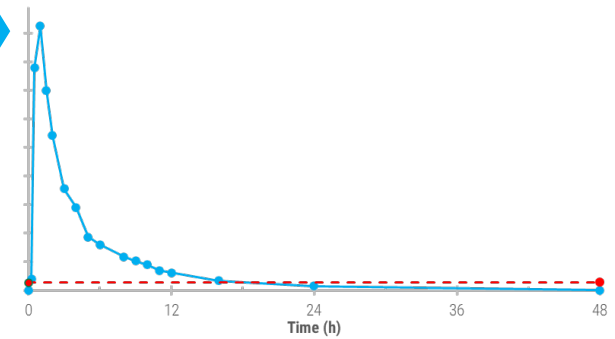
Maintains sustained therapeutic exposure over 24 hours[2] from day one, allowing for once-daily oral treatment to prevent HAE attacks*



deucrictibant

DEUCRICTIBANT immediate-release (IR) capsule

rapid absorption[3]



Rapidly reaches therapeutic exposure within 15-30 minutes[4], making it optimal for on-demand oral treatment of HAE attacks*

Two oral products with the same active ingredient for the prevention and treatment of HAE attacks

*To be confirmed with clinical data from Phase 3 studies

Source: [1]Company data: single-dose cross-over PK study in healthy volunteers (n=14) under fasting conditions. [2]Lesage A et al, IDDST 2024. [3]Crabbe et al, AAAAI 2021. [4]Maurer M et al, AAAAI 2023.

With injectable-like efficacy and oral convenience, deucrictibant shows potential to become a preferred therapy to manage HAE

Long-Term Prophylaxis (LTP)

Efficacy	Early-onset attack reduction sustained for over one year in ongoing OLE study[1]
Quality of Life	Improvement in disease control and health-related quality of life paralleled attack reduction in Phase 2[2,3]
Safety & Tolerability	Phase 2 safety and tolerability profile confirmed in ongoing OLE study[1,4]
Formulation	Commercial formulation for once-daily dosing ready for Phase 3

Potential preferred option for LTP

On-Demand Treatment (ODT)

Efficacy	Onset of symptom relief with median PGI-C "a little better" ~ 1.1 hour Symptom resolution with PGI-S "none" ~ 11.5 hours in ongoing LTE study[5] 85.8% of attacks achieved complete symptom resolution within 24 hours in ongoing LTE; 90.2% of which with single dose[5]
Safety & Tolerability	Phase 2 safety and tolerability profile confirmed in ongoing LTE study[5,6]

Potential preferred option for ODT

OLE: open-label extension. LTE: long-term extension. PGI-C: patient global impression of change. PGI-S: patient global impression of severity.

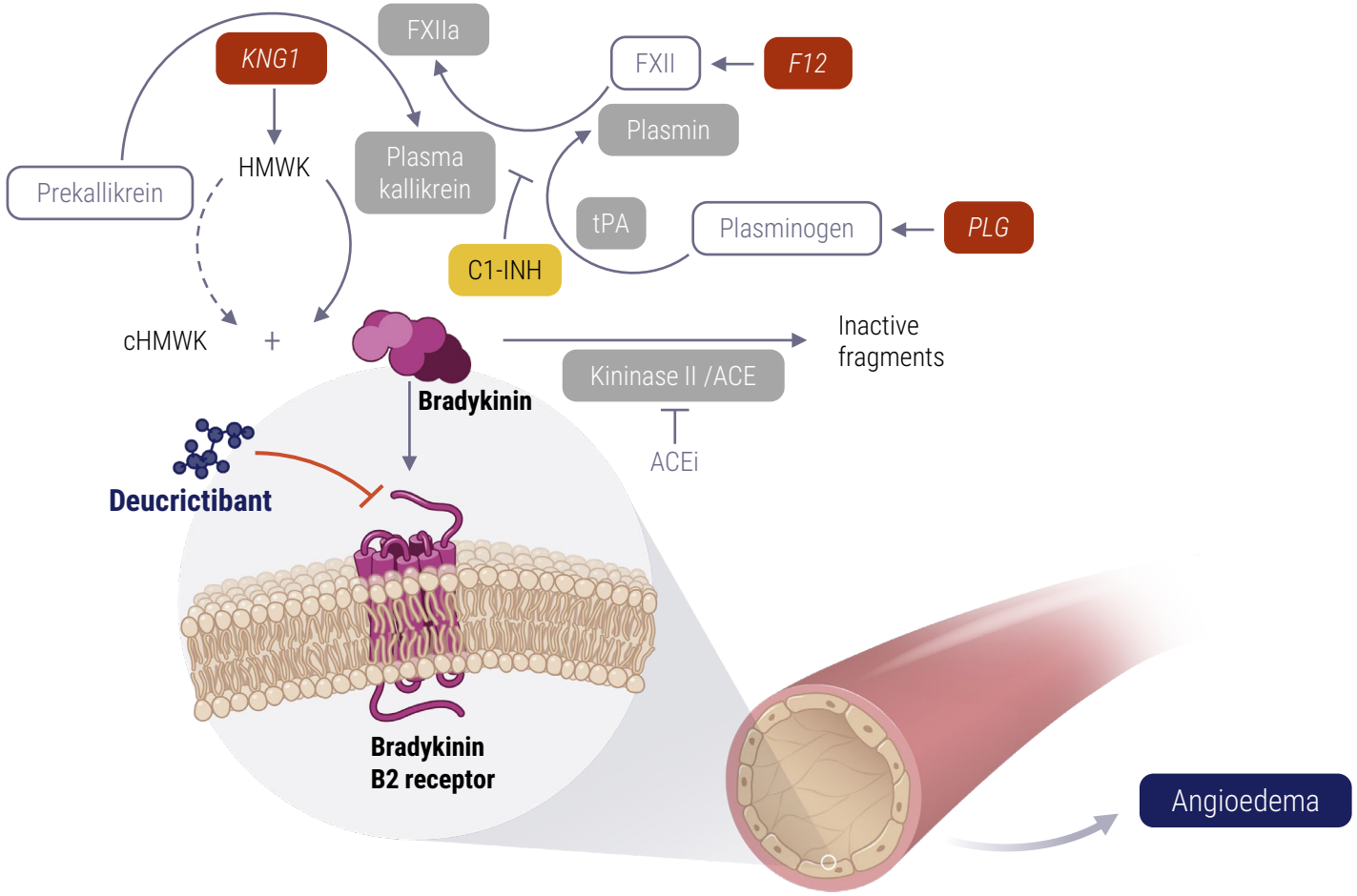
Source: [1]Riedl MA et al. BKS 2024. [2]Valerieva A et al. EAACI 2024. [3]Magerl M et al. BKS 2024. [4]Riedl MA et al. AAAAI 2024. [5]Maurer M et al. BKS 2024. [6]Maurer M et al. AAAAI 2023.

Pharvaris: Robust disclosure at 2024 Bradykinin Symposium

1. Bradykinin Challenge Model in Humanized Bradykinin B2 receptor Transgenic Rat; Jolanta Skarbaliene, Ph.D.
2. **LTP Prophylactic Treatment With Deucrictibant Improves HAE Disease Control and HRQoL; Markus Magerl, M.D.**
3. **LTP Long-Term Safety and Efficacy of Oral Deucrictibant for HAE Prophylaxis; Mark A. Riedl, M.D., M.A.**
4. **ODT Treatment of HAE Attacks With Oral Deucrictibant RAPIDe-2 Extension Results; Emel Aygören-Pürsün, M.D.**
5. Prophylaxis of Hereditary Angioedema Attacks With Oral Deucrictibant CHAPTER-1 Results; Emel Aygören-Pürsün, M.D.
6. **ODT Deucrictibant vs. Standard of Care in HAE Propensity Score-Matched Analysis; Mark A. Riedl, M.D., M.A.**
7. Clinical Trials Conformity with AURORA COSa systematic literature review; Remy Petersen, M.D. Ph.D.
8. **LTP Cardiovascular safety of repeated oral administration of the B2-receptor antagonist deucrictibant; Nieves Crespo, Ph.D.**
9. Deucrictibant inhibits carrageenan-induced edema in bradykinin B2 receptor transgenic rat; Anne Lesage, Ph.D.
10. The bradykinin challenge model translates across rat, monkey and human; Juan Bravo, Ph.D.
11. A novel kinin biomarker assay for characterization of bradykinin-mediated disorders; Evangelia Pardali, Ph.D.
12. A HMWK capillary immunoblotting assay to characterize bradykinin-mediated disorders; Evangelia Pardali, Ph.D.

Bradykinin B2 receptor antagonism is a foundational mechanism to treat and prevent bradykinin-mediated angioedema attacks[1,2]

- **Directly blocks the main mediator** of swelling and inflammation[1,3]
- Has the potential to prevent or treat bradykinin-mediated angioedema **irrespective of the source of bradykinin**[4-6]



Source: [1]Maurer M, et al. *Allergy.* 2022. [2]Zuraw BL *World Allergy Orphan J.* 2010. [3]Lumry WR et al. Allergy Asthma Proc. 2020. [4]Riedl MA et al. AAAAI 2024. [5]Maurer M et al. AAAAI 2023. [6]Petersen RS et al. *J Allergy Clin Immunol.* 2024.

Deucrictibant clinical development for LTP and ODT

Long-Term Prophylaxis (LTP)

CHAPTER-1	Phase 2[1]	Part 1: randomized controlled primary analysis (complete) Part 2: open-label extension (ongoing)
CHAPTER-3	Phase 3 pivotal	Start-up
CHAPTER-4	Phase 3 OLE	Start-up

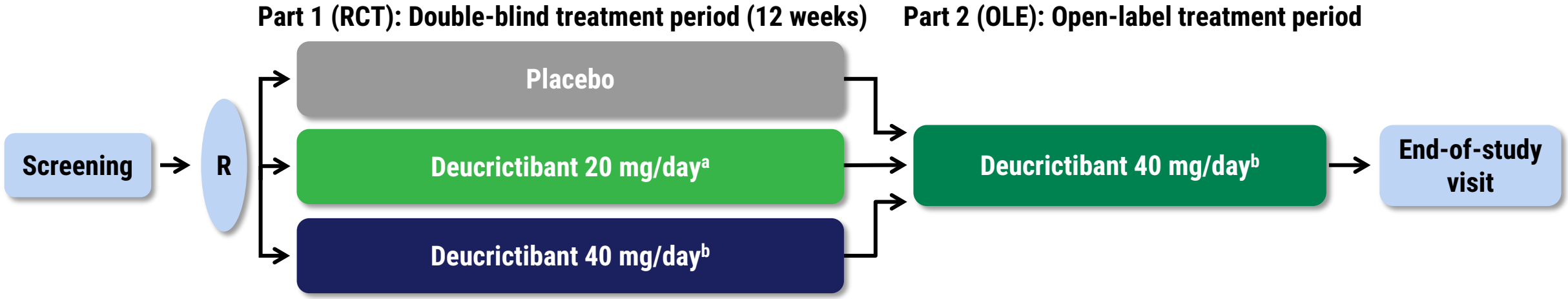
On-Demand Treatment (ODT)

RAPIDe-1	Phase 2[2]	Complete
RAPIDe-2	Phase 2/3 LTE[3]	Ongoing
RAPIDe-3	Phase 3 pivotal[4]	Ongoing

OLE: open-label extension. LTE: long-term extension.
Source: [1]NCT05047185. [2]NCT04618211. [3]NCT05396105. [4]NCT06343779.

CHAPTER-1 open-label extension

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



Open-Label Extension (OLE)

- Evaluate safety (primary objective) and efficacy of deucrictibant administered for long-term prophylaxis against HAE attacks
- **100% of CHAPTER-1 completers continued in OLE**
  - Data from RCT and OLE also presented for RCT completers for direct comparison

HAE, hereditary angioedema; OLE, open-label extension; IR, immediate-release; R, randomization; RCT, randomized controlled trial. [a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.
CHAPTER-1 is a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: NCT05047185. Accessed August 14, 2024. https://www.clinicaltrials.gov/study/NCT05047185.

Summary of safety data in LTP ongoing open-label extension

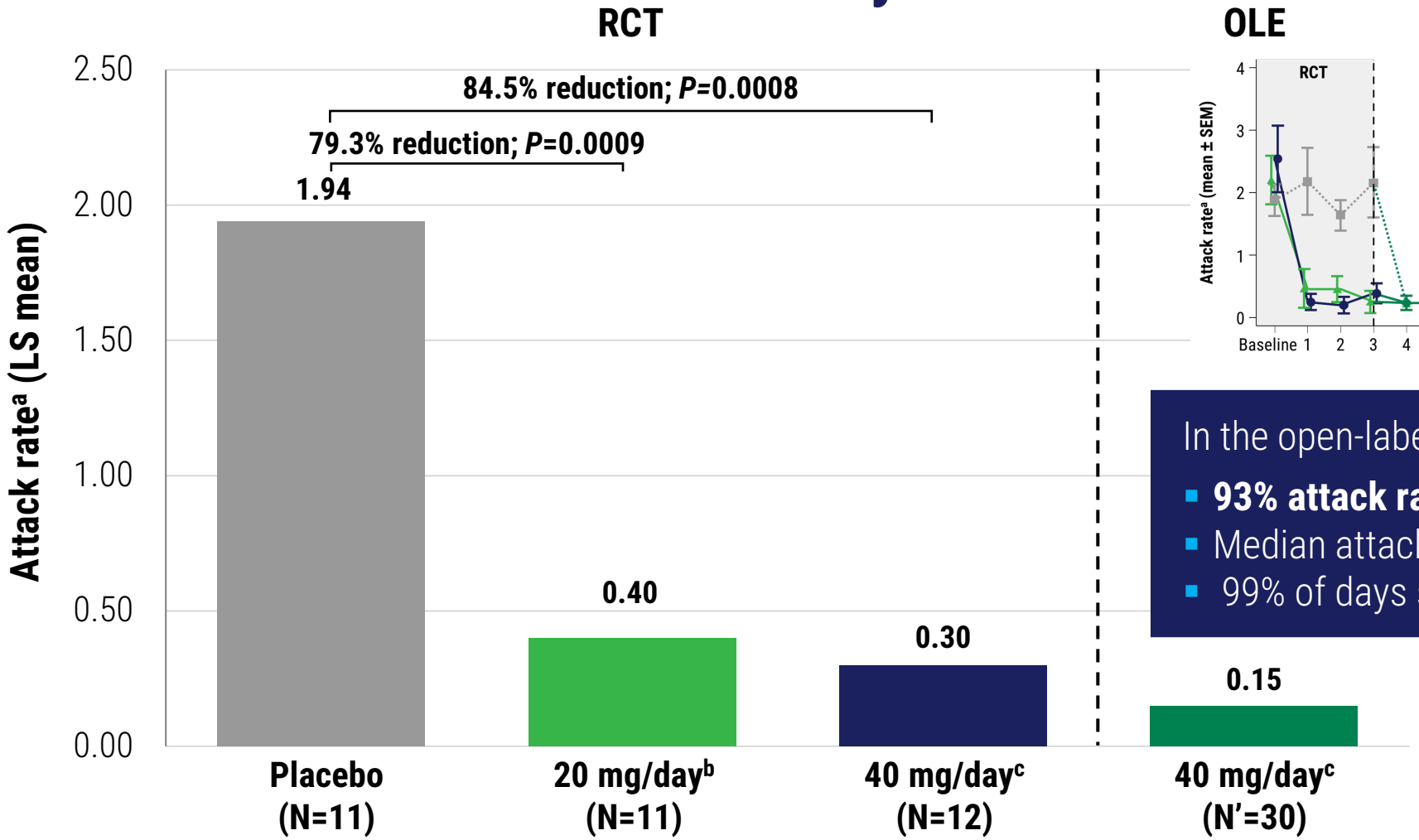
Adverse events	Placebo to 40 mg/day[a] (N=9)		20 mg/day[b] to 40 mg/day[a] (N=11)		40 mg/day[a] to 40 mg/day[a] (N=10)		Total (N=30)	
	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n
TEAEs	5 (55.6)	25	7 (63.6)	31	6 (60.0)	16	18 (60.0)	72
Treatment-related TEAEs	1 (11.1)	1*	0	0	0	0	1 (3.3)	1
Serious TEAEs	0	0	1 (9.1)	1	1 (10.0)	1	2 (6.7)	2
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

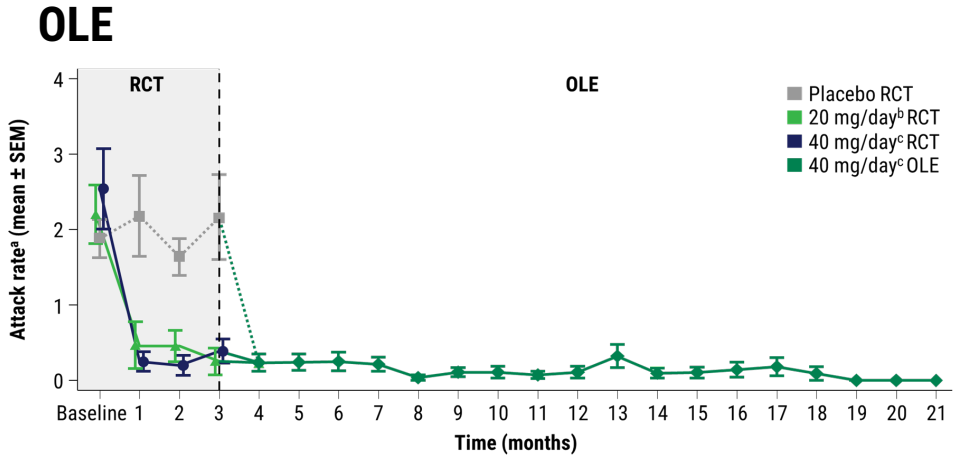
* One event of tooth discoloration is reported as treatment-related TEAEs

- No treatment-related serious or severe TEAEs
- No treatment-related TEAEs in laboratory parameters, vital signs, or ECG findings
- No TEAEs leading to treatment discontinuation, study withdrawal, or death

IR, immediate-release; TEAE, treatment emergent adverse event. N = number of participants who received at least 1 dose of blinded study treatment. [a]Deucrictibant IR capsule, 20 mg twice daily. [b]Deucrictibant IR capsule, 10 mg twice daily.

Continuing deucrictibant treatment sustained the early-onset attack reduction for over one year



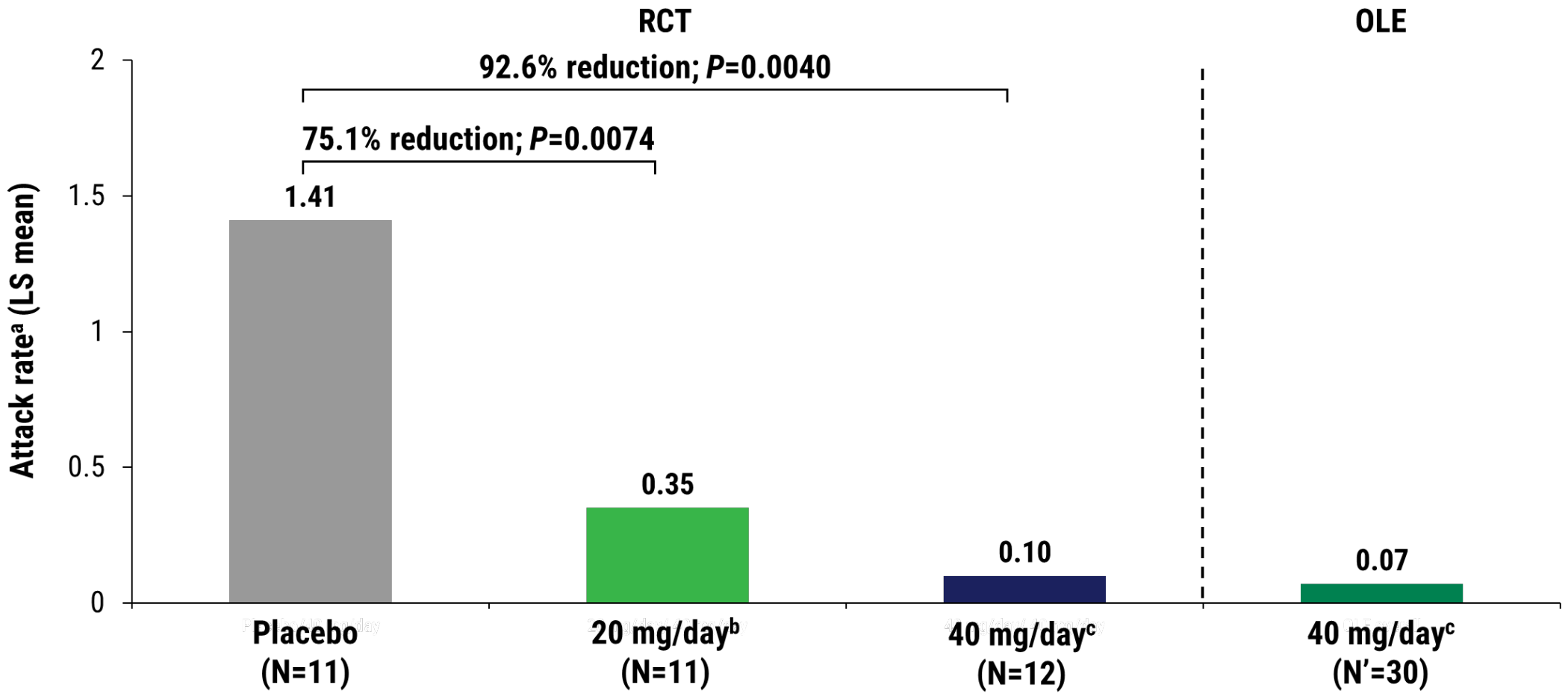


In the open-label extension up to 18 months:

- **93% attack rate reduction from baseline**
- Median attack rate = 0 for every month
- 99% of days symptom free

IR, immediate release; OLE, open label extension; RCT, randomized controlled trial. N = number of participants randomized in each treatment group in Part 1 of the study. N' = number of participants in the OLE. [a]1 month = 4 weeks. [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Deucrictibant IR capsule, 20 mg twice daily.

On average less than one attack per year per participant was treated with rescue medication

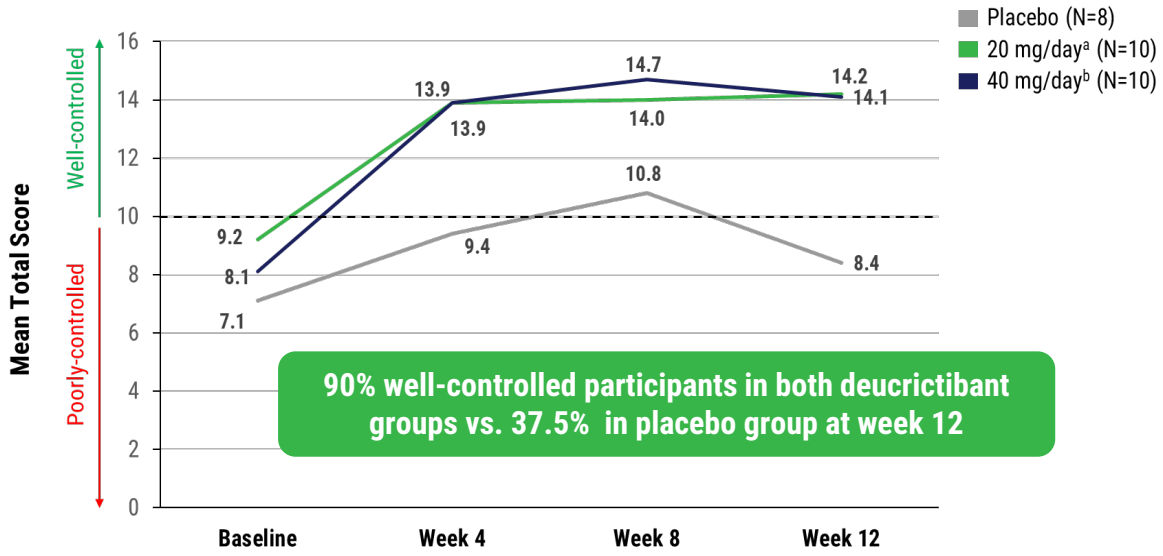


IR, immediate release; LS, least squares; OLE, open-label extension; RCT, randomized controlled trial. N = number of participants randomized in each treatment group in the RCT. N' = number of participants in the OLE. LS mean estimates of attack rate are based on Poisson regression models adjusted for baseline attack rate and time on treatment. No multiplicity adjustment was applied. The *P*-values in this figure are nominal. [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.

Improvements in disease control and health-related quality of life paralleled attack reduction during deucrictibant treatment[1,2]

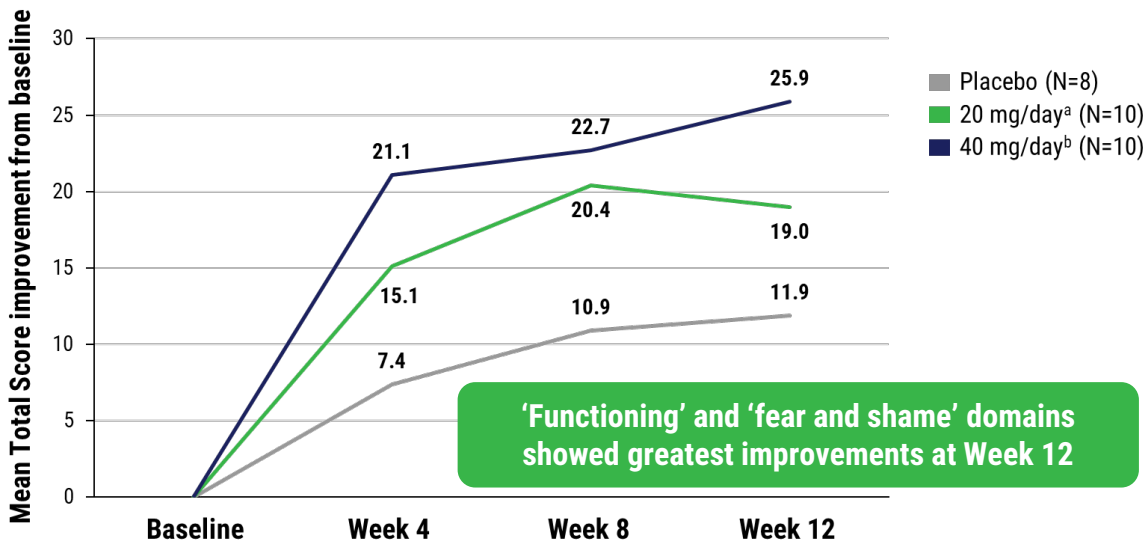
- The goals of HAE treatment are to achieve complete control of the disease and to normalize people's lives[3]
- This can currently only be achieved by long-term prophylaxis (LTP)

AECT score[1]



90% well-controlled participants in both deucrictibant groups vs. 37.5% in placebo group at week 12

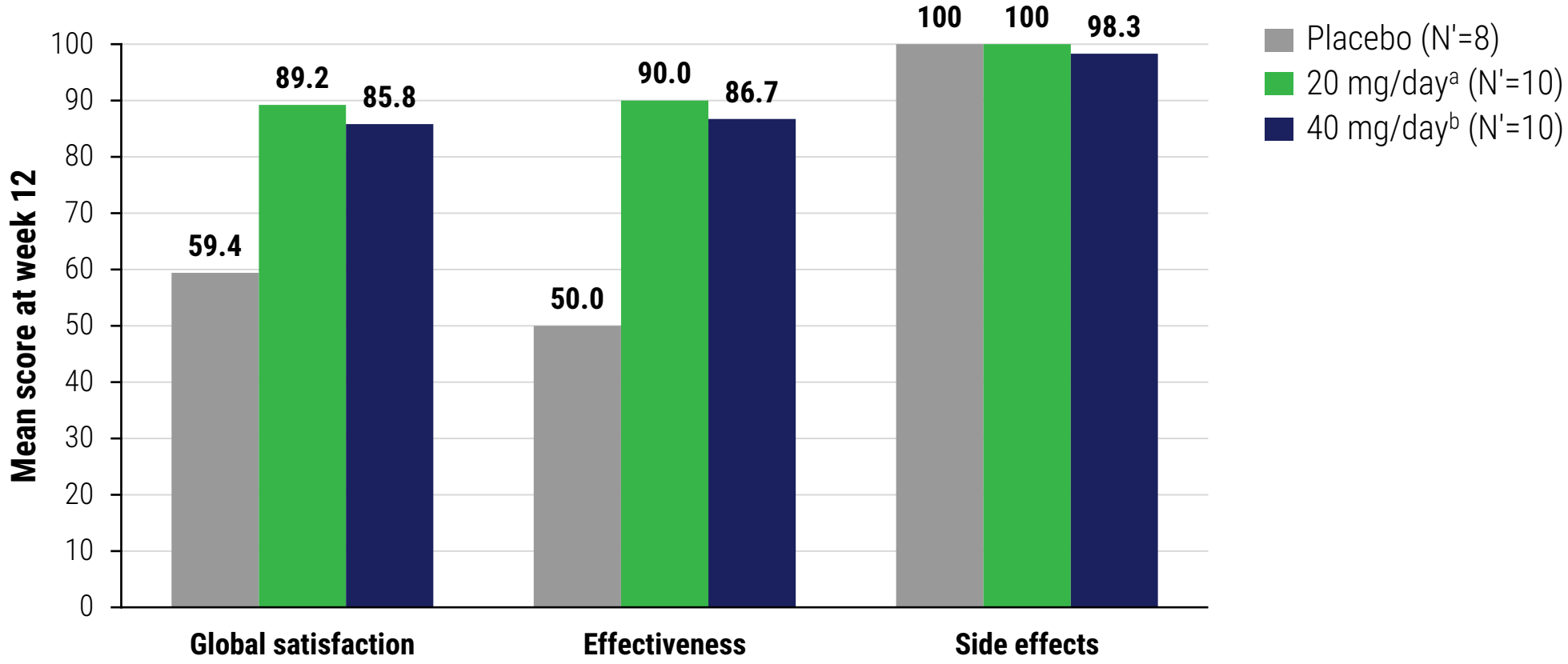
AE-QoL score[1]



'Functioning' and 'fear and shame' domains showed greatest improvements at Week 12

AE-QoL, Angioedema Quality of Life Questionnaire; 4-week AECT, Angioedema Control Test (4-week recall period); IR, immediate-release; RCT, randomized controlled trial. N = number of participants with AECT and AE-QoL data at week 12.
[a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily. **Source:** [1]Magerl M et al. 2024 BKS. [2]Zanichelli A et al. ITACA 2024. [3]Maurer M et al. 2022 Allergy.

Deucrictibant shows greater patient satisfaction versus placebo across effectiveness and side effects (TSQM instrument)



IR, immediate release; TSQM, Treatment Satisfaction Questionnaire for Medication. N' = number of participants with TSQM results at week 12.
[a]Deucrictibant IR capsule, 10 mg twice daily. [b]Deucrictibant IR capsule, 20 mg twice daily.

In non-clinical and clinical studies, deucrictibant has shown no cardiac effects

Non-Clinical Studies

- Deucrictibant had no evident effects on cardiac electrophysiology, morphology, or hemodynamic parameters in chronic in vivo preclinical studies in NHP
  - Male and female NHP up to 39 weeks

Clinical Studies

- Deucrictibant showed no evident effects on cardiac electrophysiology or hemodynamic parameters in clinical studies in humans completed to date
  - Single- and multiple-dose Phase 1 clinical studies
  - Prophylactic treatment up to 12 weeks of administration in the Phase 2 clinical trial and up to one year in the ongoing OLE

Source: Crespo et al, Bradykinin Symposium 2024

Positive Phase 3 data could position deucrictibant to become a preferred LTP with injectable-like efficacy and the oral convenience of a daily tablet

	Cinryze® (pdC1INH)	Haegarda® (pdC1INH)	Takhzyro® (lanadelumab)	Orladeyo® (berotralstat)	garadacimab	donidalorsen	deucrictibant	
Mechanism of Action	Plasma-deriveed C1NH	Plasma-derived C1INH	Anti-plasma kallikrein mAb	Plasma kallikrein inhibitor	Anti-FXIIa mAb	Plasma kallikrein inhibitor	Bradykinin B2 receptor antagonist	
Clinical Trial(s)	Ph 3§ (500 U, 1,000 U)	Ph 3§§ (60 IU/Kg)	Ph 3† (300mg q2w / q4w)	Ph 3†† (150mg)	Ph 3†	Ph 3¶ (80 mg q4w, q8w)	Ph 2‡ (40mg)	Ph 2/3 LTE
Mean monthly attack reduction vs. placebo	71-85%[1]	84%[2]	73-87%[4]	44%[6,7]	89%[8]	55-81%[9]	85%[10,11]	93%¤[12]
Mean reduction in use of ODT vs. placebo	-	89%[2]	74-87%[4]	54%[7]	88%[8]	67-92%¶¶[9]	93%[10,11]	pending publication
≥50% attack reduction	-	90%#[2,3]	100-100% vs. 32%[4,5]	58% vs. 25%[6,7]	95% vs. 33%[8]	83-93% vs. 27%¶¶[9]	90% vs. 18%[11]	pending publication
≥70% attack reduction	-	83%#[2,3]	76-89% vs. 10%[4,5]	50% vs. 15%[6,7]	92% vs. 17%[8]	65-92% vs. 18%¶¶[9]	80% vs. 18%[11]	pending publication
≥90% attack reduction	-	58%#[2,3]	55-67% vs. 5%[4,5]	23% vs. 8%[6,7]	74% vs. 8%[8]	48-62% vs. 9%¶¶[9]	60% vs. 0%[11]	pending publication
% patients attack-free vs. placebo	-	40% vs. 0%[2,3]	31-44% vs. 2%[4,5]	10% vs. 2.5%[6]	62% vs. 0%[8]	35-53% vs. 9%¶¶[9]	40% vs. 0%[11]	pending publication

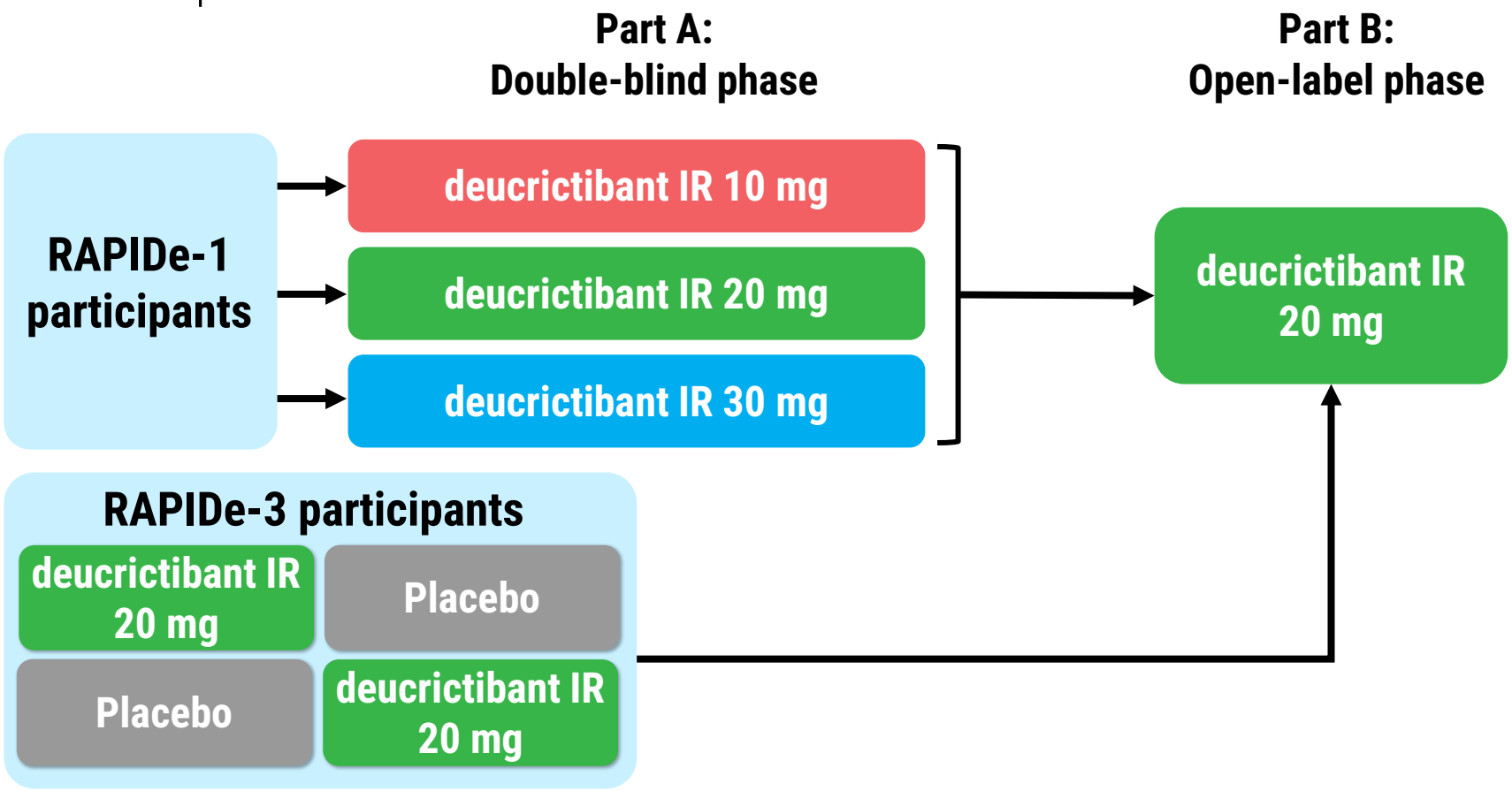
§ Crossover, 12 weeks/treatment. §§ Crossover, 16 weeks/treatment (results reported for weeks 3-16 for each treatment arm). †Parallel-arms, 26 weeks. ††Parallel-arms, 24 weeks. ¶ Parallel-arms, 25 weeks. ‡Parallel-arms, 12 weeks. # vs. placebo. ¶¶ Weeks 5-25. ¤ vs. RCT Part 1 baseline.

1. Cinryze® US PI, Feb 2023. 2. Longhurst H et al. 2017 N Engl J Med. 3. Haegarda® US PI, Jan 2022. 4. Takhzyro® US PI, Feb 2023. 5. Banerji A et al. 2018 JAMA. 6. Zuraw B et al. 2021 J Allergy Clin Immunol. 7. Orladeyo® US PI, Nov 2023. 8. Craig TJ et al. 2023 Lancet. 9. Riedl MA et al. 202 N Engl J Med. 10. Aygören-Pürsün E et al. 2024 EAACI. 11 Aygören-Pürsün E et al. 2024 KS. 12. Riedl MA et al. 2024 BKS.

RAPIDe-2 long-term extension

RAPIDe-2 study design and objective[1]

Objective: To evaluate the long-term safety and efficacy of orally administered deucrictibant immediate-release capsule for the treatment of HAE attacks[a]



IR, immediate-release. [a]Including laryngeal attacks (without breathing difficulties). Source: [1]Maurer M et al. BKS 2024.

Summary of safety profile[1]

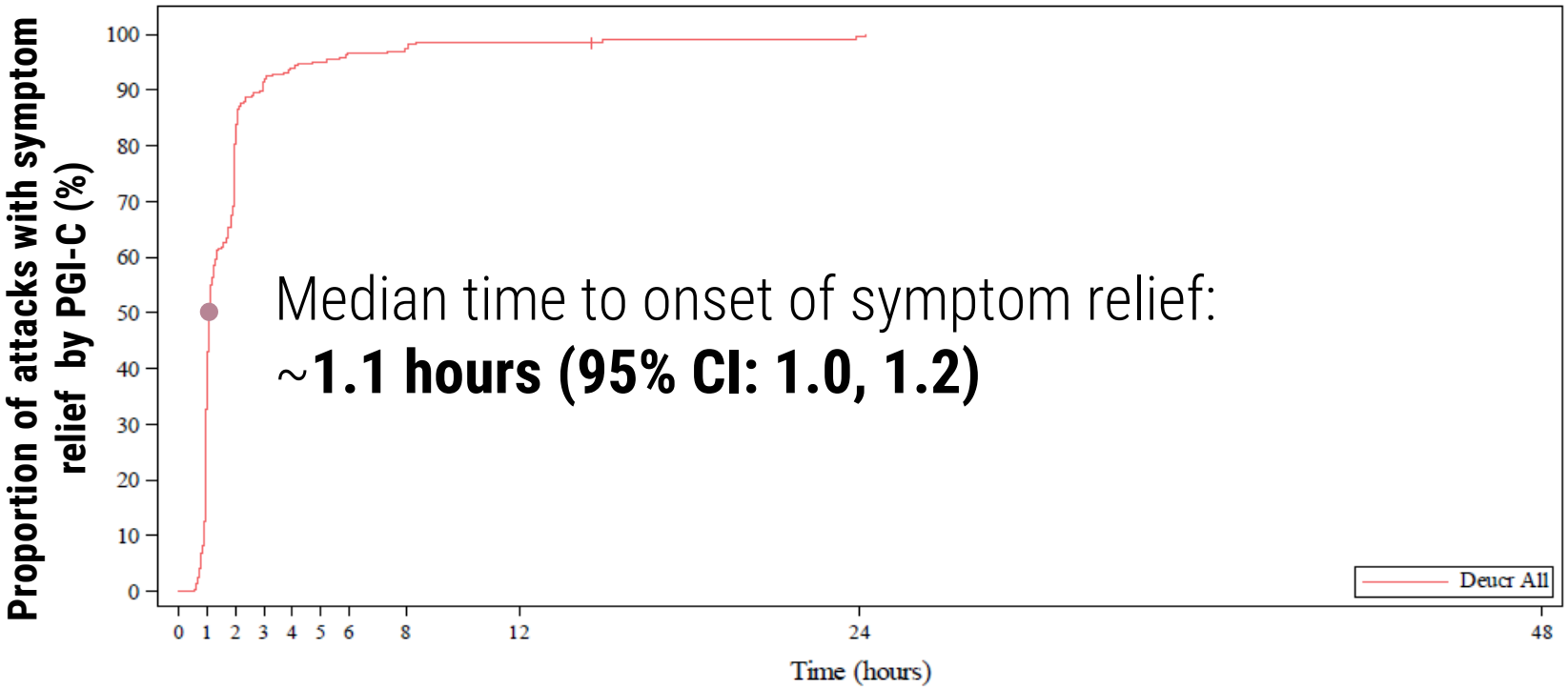
Adverse events	Deucrictibant IR capsule (All doses)
Number of patients (safety analysis population)	N=19
Number of attacks treated	N'=337
Attacks with any TEAE, n (%)	13 (3.9)
Treatment-related TEAEs, n	0
Serious TEAEs, n	1
Treatment-related serious TEAEs, n	0
TEAEs leading to study drug discontinuation, study withdrawal, or death, n	0

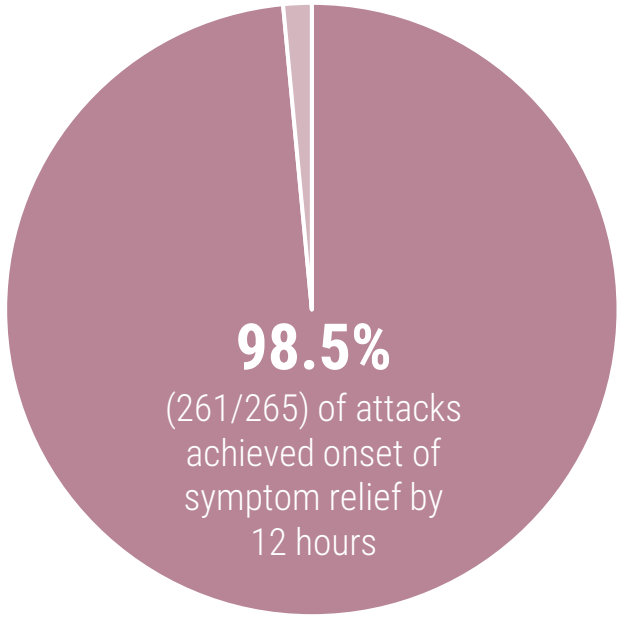
- No treatment-related serious or severe TEAEs
- No treatment-related TEAEs in laboratory parameters, vital signs, or ECG findings were reported
- No TEAEs leading to treatment discontinuation, study withdrawal, or death

IR, immediate-release; TEAE, treatment-emergent adverse event (defined as AE occurring during time window from first study drug administration; TEAEs within 5 days post-treatment were analyzed); N= Number of participants treated with study drug, N' = Number of attacks treated with study drug. Data snapshot for safety analysis population: 10 June 2024. **Source:** [1]Maurer M et al. BKS 2024.

Rapid median onset of symptom relief at ~1.1 hours: 98.5% of attacks achieved onset of symptom relief by 12 hours[1]

- Time to onset of symptom relief is defined as PGI-C rating of at least 'a little better' for two consecutive timepoints post-treatment[a]



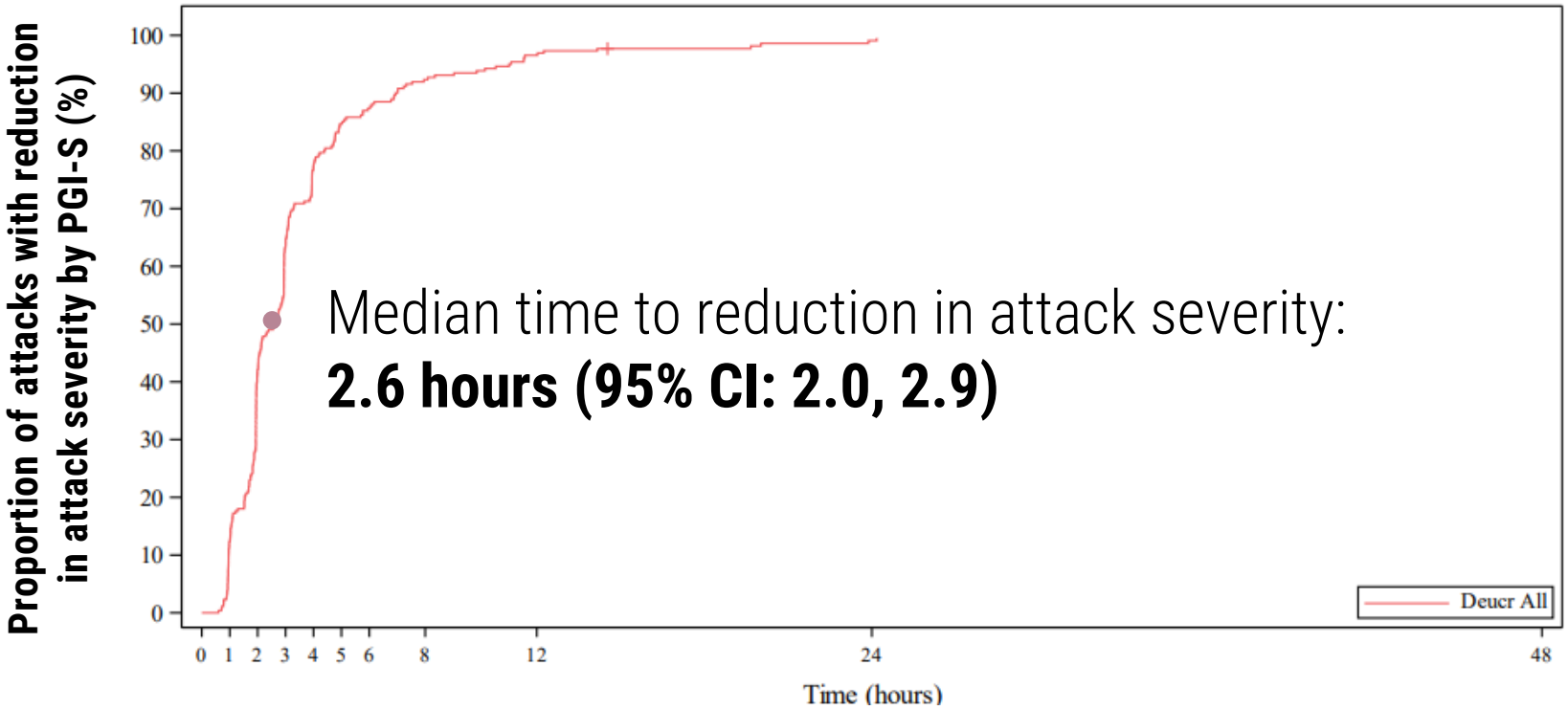


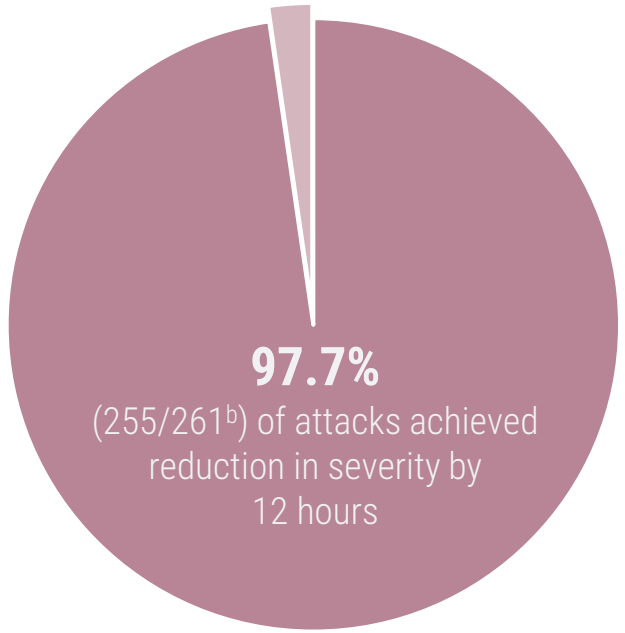
PGI-C, Patient Global Impression of Change. [a]Symptom relief is also considered as achieved if PGI-C rating reached at least a 'little better' at the last scheduled time point (48 h) provided no rescue medication used within 48h after the last time point. The time is censored at the time of the last post-treatment PGI-C assessment prior to intake of HAE rescue medication, or a medication not allowed for treating an attack.

Source: [1]Maurer M et al. BKS 2024.

Rapid median reduction in attack severity at 2.6 hours: 97.7% of attacks achieved a reduction in severity by 12 hours[1]

- Reduction in attack severity is defined as achieving ≥1 point reduction in PGI-S from pre-treatment for two consecutive time points[a]



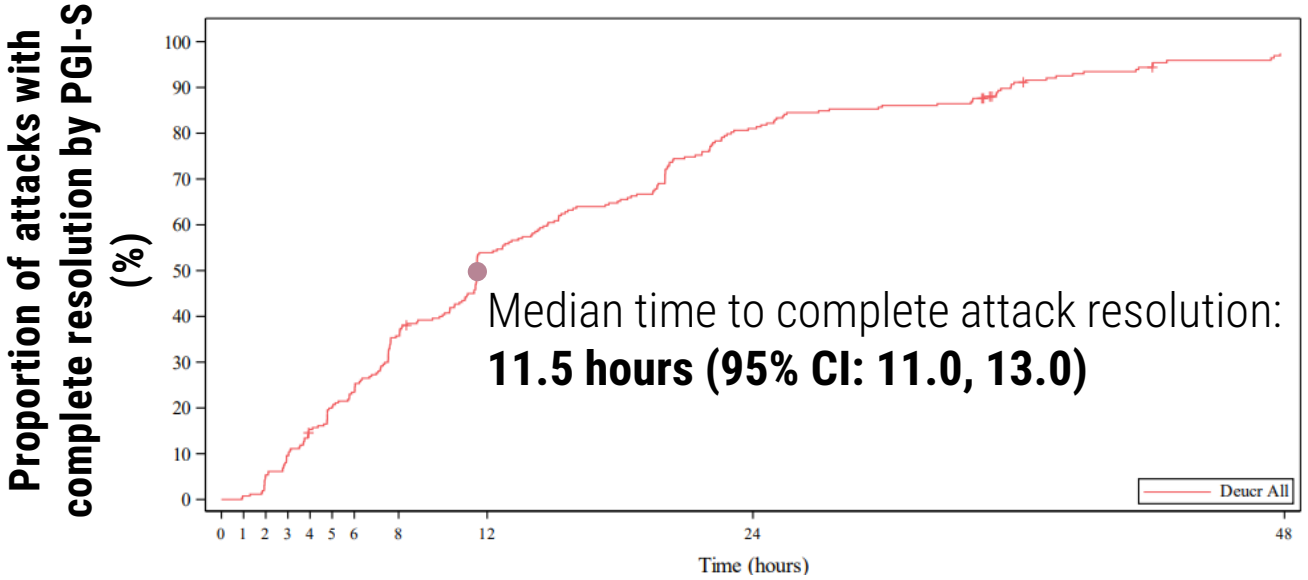


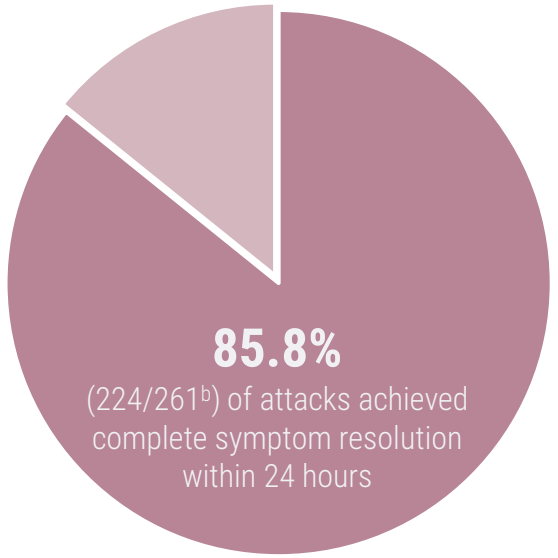
PGI-S, Patient Global Impression of Severity. [a]Reduction in attack severity is also considered as achieved if ≥ 1 point reduction in PGI-S from pre-treatment at the last scheduled time point (48 h) provided no rescue medication used within 48h after the last time point. [b]261 attacks have non-missing pre-treatment PGI-S.

Source: [1]Maurer M et al. BKS 2024.

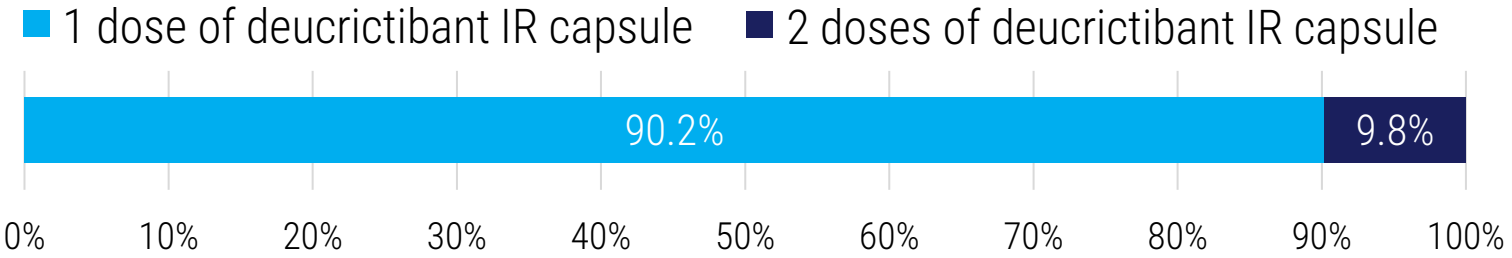
Median attack resolution time 11.5 hours: 85.8% of attacks completely resolved within 24 hours (90.2% of which with one only dose)[1]

- Time to complete attack resolution is defined as the time to post-treatment PGI-S rating achieving 'none'





Attacks treated with 1 or 2 doses of deucrictibant prior to achieving complete attack resolution (% of 224 attacks)



PGI-S, Patient Global Impression of Severity.
[a]261 attacks have non-missing pre-treatment PGI-S.
Source: [1]Maurer M et al. BKS 2024.

Mixed-methods study: Non-interventional collection of HAE attack symptoms assessments following treatment with standard of care

Participants recruited by HAEA

PGI-C, PGI-S, and AMRA-3/ AMRA-5 data collected via mobile app

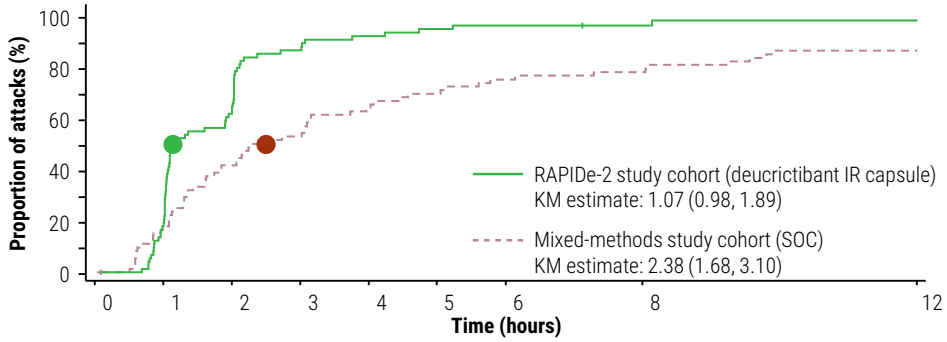
- At pre-treatment
- Every hour up to 4 hours following treatment administration
- Then at 8, 12, 24, and 48 hours

Qualitative interviews with a subset of participants

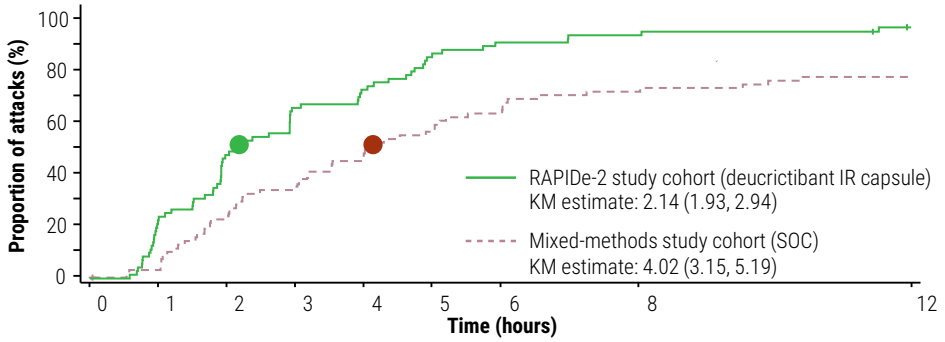
Note: Standard of care was icatibant or plasma derived/recombinant C1-Inhibiitor

In a propensity-score-matching analysis, deucrictibant showed favorable symptom relief outcomes versus standard of care[1]

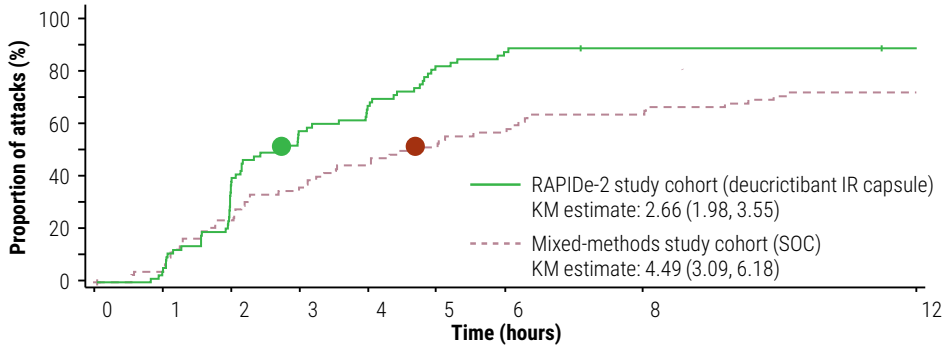
A. Time to symptom relief defined as PGI-C "A little better"



B. Time to reduction in attack severity defined as PGI-S ≥1 point reduction



C. Time to symptom relief defined as PGI-C "Better"



Time to symptom relief in hours, median (95% CI)	RAPIDe-2 cohort (deucrictibant; N=73)	Mixed-methods cohort (SOC; N=73)
A PGI-C – "A little better"	1.07 (0.98, 1.89)	2.38 (1.68, 3.10)
B PGI-S – ≥1 point reduction	2.14 (1.93, 2.94)	4.02 (3.15, 5.19)
C PGI-C – "Better"	2.66 (1.98, 3.55)	4.49 (3.09, 6.18)

AMRA, Angioedema syMptom Rating scAle; CI, confidence interval; IR, immediate-release; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. N=73 for both cohorts. Parameters: The first 10 consecutive attacks were selected for each participant; Greedy Nearest Neighbor 1:1 matching was used with Caliper = 0.5; participants were matched for sex, age, baseline attack severity (defined by AMRA score), and exact attack primary location. Source: [1]Riedl MA et al. BKS 2024.

Positive Phase 3 data could position deucrictibant to become a preferred ODT with rapid-onset and complete symptom resolution with a single oral capsule

		sebetralstat tablet	deucrictibant IR capsule			Standard of Care Berinert® (pdC1INH), Firazyr® (icatibant), Ruconest® (rhC1INH)
Mechanism of Action		Plasma kallikrein inhibitor	Bradykinin B2 receptor antagonist			Plasma-derived C1NH (23%) - Icatibant (60%) – Recombinant hC1INH (9%) - Other (9%)
Clinical Trial(s)		**Ph 3* (300mg, 600mg)**	**Ph 2 (10mg, 20mg, 30 mg pooled)**	**Ph 2/3 Ext.* (10mg, 20mg, 30mg pooled)**	**Ph 2/3 Ext. PSM Analysis (10mg, 20mg, 30mg pooled)**	**PSM Analysis of Mixed Methods Study[9]**
Time to onset of symptom relief (median)	**VAS/AMRA[a]**	-	**2.4 vs. 8.0 h[3]**	-	-	-
	TOS[b]	-	**2.0 vs. 7.6 h[4,5]**	-	-	-
	PGI-C[c]	**1.6-1.8 vs. 6.7 h[1]**	-	**1.1 h[7]**	**1.1 h[8]**	**2.4 h[8]**
Time to ≥50% VAS reduction (median)		**Not reported yet[2]**	**3.9 vs. 22.8 h[3]**	-	-	-
Time to reduction in attack severity (median)[d]		**7.7-9.3 vs. > 12 h[1]**	-	**2.6 h[7]**	**2.1 h[8]**	**4.0 h[8]**
Time to symptom resolution (median)	**VAS/AMRA[e]**	-	**7.5 vs. 42.0 h[3]**	-	-	-
	TOS[f]	-	**5.2 vs. 23.3 h[4,5]**	-	-	-
	PGI-S[g]	**≥24.0 vs. >24 h[1]**	-	**11.5 h[7]**	**12.3 h[8]**	**13.5 h[8]**
% attacks resolved within 24 h with 1 dose		**42.5-49.5% vs. 27.4%#[1]**	**75.0% vs. 15.7†[6] 81.7% vs. 22.4%‖[6]**	**90.2%[7]**	-	-
% attacks treated with 1 dose of study drug (no additional doses of study drug and/or rescue med.)		**≤60.2-≤60.9 vs. ≤44.0%[1]**	pending publication	**86.0%§[7]**	-	-

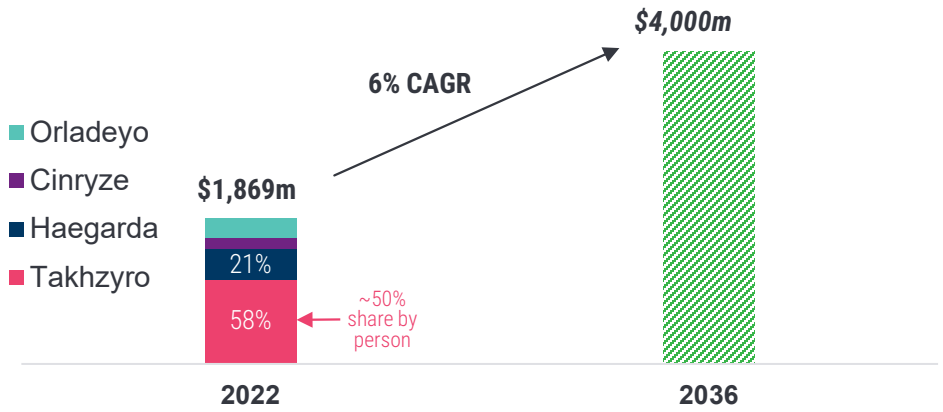
References on following slide

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

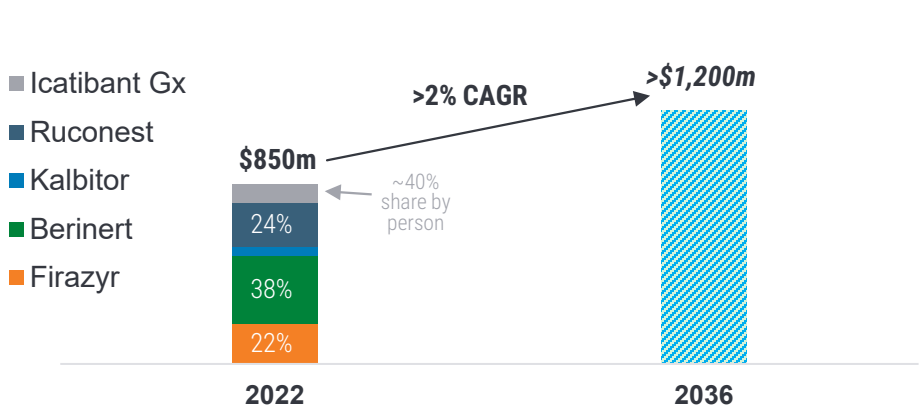
Commercial vision

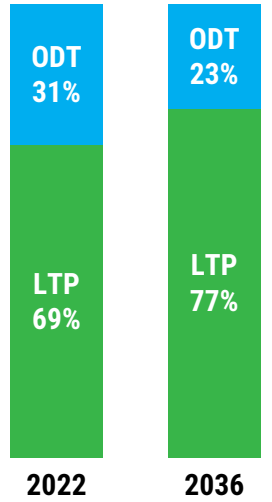
In the U.S., significant growth in the long-term prophylaxis (LTP) and on-demand therapy (ODT) market is expected over the next decade[1]

Value of prophylaxis[1-3]



Value of on-demand[1-3]





Growth expected to be driven by:

- New options
- Increased convenience
- Continued paradigm shift from ODT to LTP

Growth expected to be driven by:

- New options
- Increased convenience
- Increased treatment rate

LTP to further grow as the dominant treatment paradigm in the US market through to 2036[1]

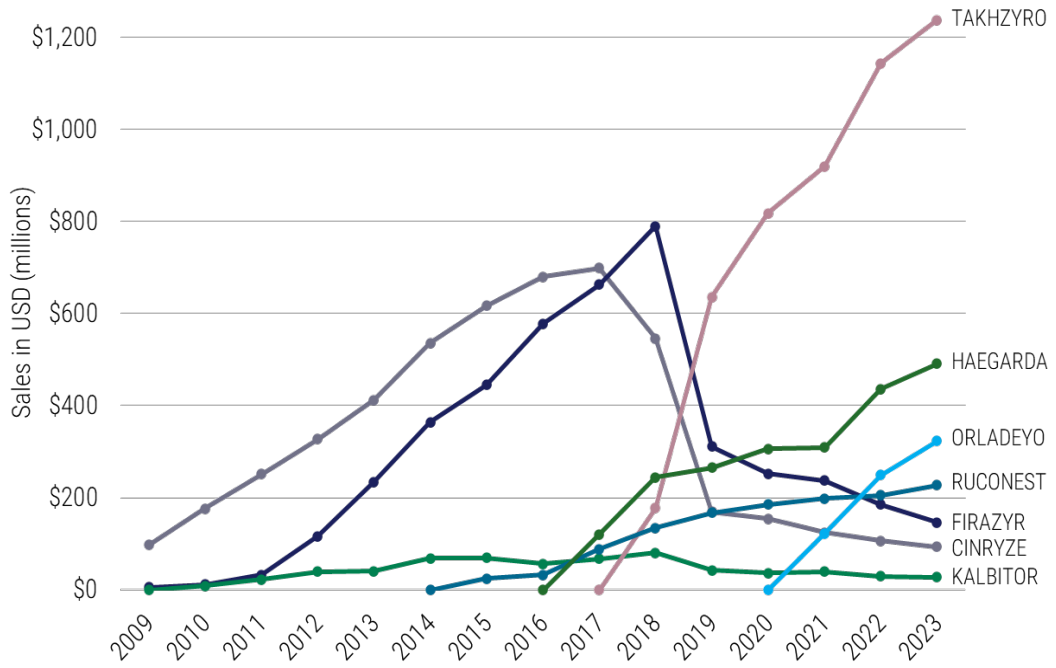
HAE market growth will be driven by increased efficacy and convenience of new therapies

Source: [1]IQVIA market evolution and company data. [2]Evaluate Pharma uptake curves 2008-2023. [3]SEC filings (BioCryst, CSL Behring, Pharming, Takeda).

Despite treatment satisfaction, the U.S. HAE market is dynamic, with people actively seeking a better[1] product

People actively switch therapies[2,3]: first-to-market is no guarantee for long-term market leadership

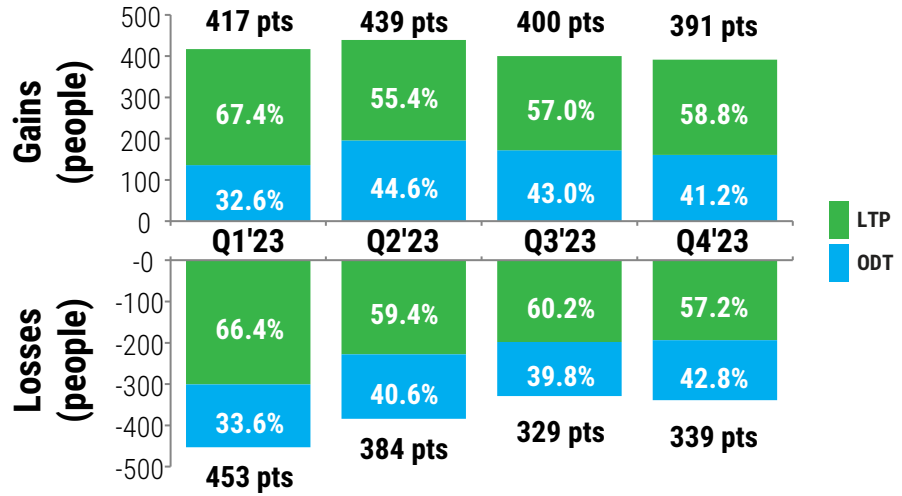
Evolution of HAE product sales[1,2]



Across ~7,000 people with HAE, there were over >1,500 unique counts of treatment initiation in 2023[4]

- Preference for convenient administration
- ODT-only to LTP switches dominate
- Most LTP gains went to Takhzyro and Orladeyo

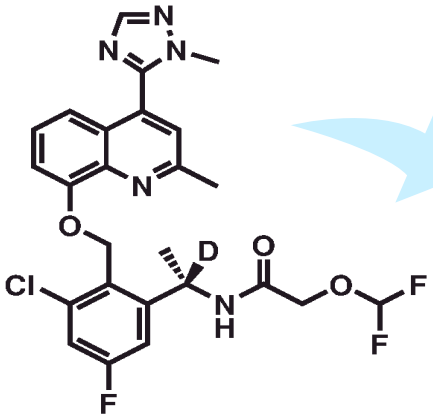
U.S. HAE switches, gains ↑ and losses ↓[3]



# of new Rx	-36	+55	+70	+52

[1]Treatment selection is driven by physicians and patient preference.
Source: [2]Evaluate Pharma uptake curves 2008-2023 [3]SEC filings (BioCryst, CSL Behring, Pharming, Takeda). [4]U.S. Chart Audit 2023.

Deucrictibant: Only compound today[1] with the potential to deliver injection-like efficacy orally across both LTP and ODT



Deucrictibant XR

Extended-release tablet

Sustained absorption[2]

*Maintains sustained therapeutic exposure over 24 hours[3] from initial dose, allowing for once-daily oral treatment to prevent HAE attacks**

- Highly **effective** at **preventing** attacks*[,4,5]
- **Rapid protection[2]** and elimination[6]
- **Well-tolerated**[4,5]
- **Easy oral** administration**[,7]

Deucrictibant IR

Immediate-release capsule

Rapid absorption[6]

*Rapidly reaches therapeutic exposure within 15-30 minutes[9], making it optimal for on-demand oral treatment of HAE attacks**

- **Rapid** onset of action[11,12]
- **Single dose** resolution[11]
- **Ease of oral** administration**[,7]

*To be confirmed with clinical data from Phase 3 studies. **Patient preference varies.

Source: [1]Company research. [2]Company data: target threshold exceeded on first day in single-dose cross-over PK study in healthy volunteers (n=14) under fasting conditions. [3]Lesage A et al, IDDST 2024. [4]Riedl MA et al. AAAAI 2024. [5]Riedl MA et al. BKS 2024. [6]Maurer M et al. HAEi Workshop, 2022. [7]Lesage et al. *Int. Immunopharmacology*, 2022. [8]Crabbe et al, AAAAI 2021. [9]Maurer M et al, AAAAI 2023. [10]Maurer M et al. AAAAI 2023. [11]Maurer M et al. BKS 2024.

Our strategy is to become a market leader in HAE

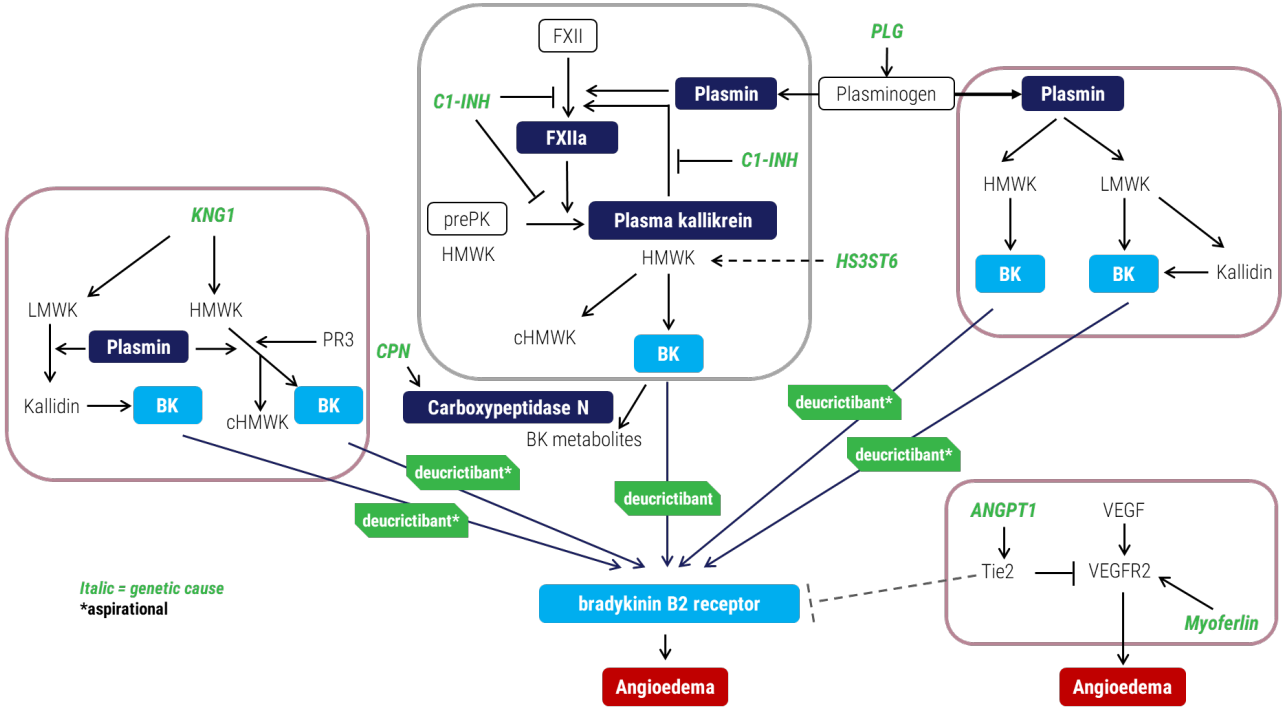
Rooted in a deep commitment to engage with the HAE community

Notes: Aspirational, to be confirmed with Phase 3 clinical data

Going Beyond HAE

Bradykinin B2 receptor inhibition is broadly applicable across angioedema

Type/Endotype	Mechanism	Name/Acronym
AE-MC Mast-cell mediated	Mast cell degranulation	AE-URT
		AE-ANA
AE-BK Bradykinin mediated	**Hereditary C1INH deficiency**	**HAE-C1INH (Type 1, 2)**
	Acquired C1INH deficiency	**AAE-C1INH**
	KKS pathway mutations	**HAE-FXII*, HAE-PLG*, HAE-KNG***
AE-VE Vascular endothelium	Intrinsic vascular endothelium dysfunction	HAE-ANGPT*, HAE-MYOF*, **HAE-HSST***, SCLS
AE-DI Drug induced	Drug adverse reactions (various mechanisms)	**AE-ACEI**, **AE-tPA**, **AE-DPPIV**, AE-NSAID, etc.
AE-UNK Unknown	Unknown aetiology or mechanism	AE-UNK, HAE-UNK*, EAE

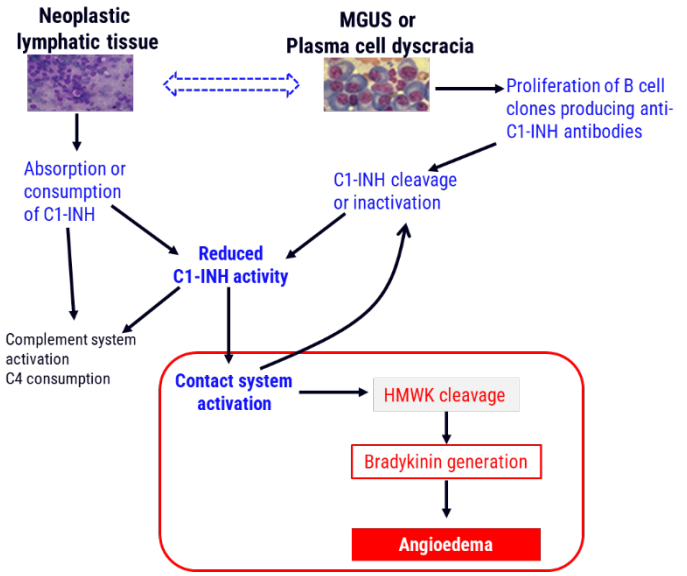


Source: Busse 2020 J Allergy Clin Immunol Pract; Bork et al 2021 J Allergy Clin Immunol; Zanichelli et al 2012 Allergy; Longhurst et al 2016 Clin. Exp. Immunol.; Otani, Banerji 2017 Immunol. Allergy Clin. N. Am.; Bova et al 2018 Int. Arch. Allergy Immunol.; Petersen et al 2024 J Allergy Clin Immunol; Shi et al 2021 Clin Immunol; Rashef et al 2024 J Allergy Clin Immunol

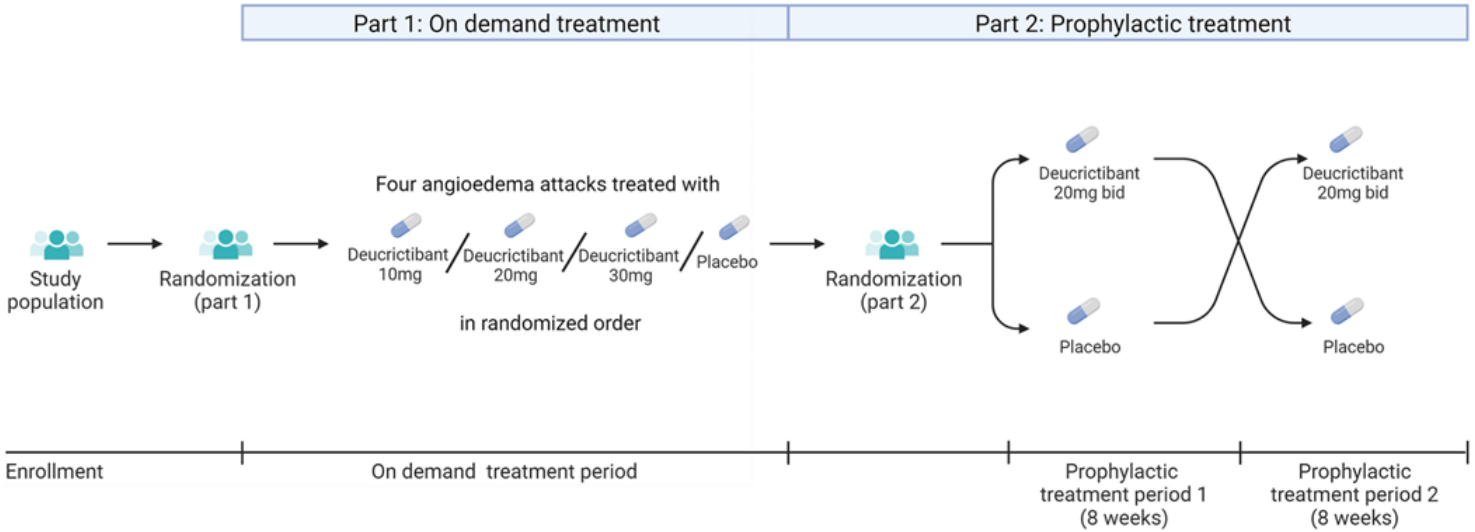
Notes: bold = known or potential role for bradykinin involvement in disease. *also designated as Normal C1INH Angioedema (HAE-nC1INH); HMWK: high-molecular-weight kininogen; cHMWK: cleaved high-molecular-weight kininogen; FXII(a): Factor XII(a); ACE(i): angiotensin-converting enzyme (inhibitor); tPA: tissue plasminogen activator; KNG1: gene encoding HMWK; PLG: gene encoding plasminogen; FXII: gene encoding FXII; ANGPT: gene encoding angiopoietin; MYOF: gene encoding myoferlin; HSST: gene encoding heparan sulfate sulfotransferase; SCLS: systemic capillary leak syndrome

Deucrictibant proof-of-concept in angioedema due to acquired C1-INH deficiency (AAE)[1]

- Estimated prevalence of 1:100,000 to 1:500,000 or ~ 10% of HAE type 1/2
- Currently, no therapies approved for AAE
- Investigator-initiated trial (IIT) by the Amsterdam UMC



JACI The Journal of Allergy and Clinical Immunology



Source: [1]Petersen RS et al. *J Allergy Clin Immunol.* 2024.

POP-AID investigator-initiated study: Deucrictibant prevention and treatment of acquired angioedema

Attacks per month	Patient 1	Patient 2	Patient 3
Baseline	1.2	1.2	0.9
Placebo	2.0	0.6	1.0
Deucrictibant	0	0	0

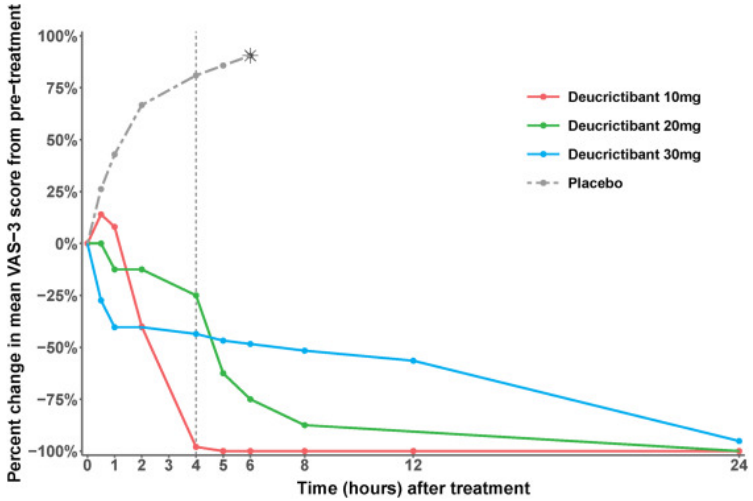


TABLE III. Summary of treatment-emergent adverse events

Event	Incidence in 4-wk period, no. (%)	
	Deucrictibant	Placebo
Any adverse event	5 (0.8)	4 (0.7)
Any drug-related adverse event	1 (0.2)*	0
Any serious adverse event	0	0
Treatment discontinued owing to an adverse event	0	0
Headache	1 (0.2)	0 (0)
Viral infection	0 (0)	2 (0.3)
Upper abdominal pain	1 (0.2)	0
Rash erythematous (sunburn-like)	1 (0.2)	0
Fatigue (heavy feeling throughout the whole body)	1 (0.2)	1 (0.2)
Dysgeusia (bitter taste)	1 (0.2)	1 (0.2)

Adverse events are reported as the preferred term using the Medical Dictionary for Regulatory Activities, version 23.0.
*Upper abdominal pain after ingestion of study treatment without water.

Antagonism of the bradykinin B2 receptor with deucrictibant has the potential to effectively and safely treat and prevent angioedema due to acquired C1-inhibitor deficiency

Source: [1]Petersen RS et al. *J Allergy Clin Immunol.* 2024.

PHVS has the ambition to realize the potential of deucrictibant to become the preferred option for bradykinin-mediated conditions

HAE → Long-term extension data[1,2] reinforces our belief that deucrictibant has the potential to become the preferred option for the management of HAE

AAE → Based on the community's interest[3] and the initial intriguing data[4], PHVS plans to pursue development of deucrictibant in AAE

nC1 → Leveraging B2-receptor mechanism[5], potential for application to normal C1-INH hereditary angioedema

Source: [1]Riedl MA et al. BKS 2024. [2]Maurer M et al. BKS 2024. [3]Company research. [4]Petersen RS et al. *J Allergy Clin Immunol.* 2024. [5]Lesage et al. *Int. Immunopharmacology,* 2022.

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