Long-Term Safety and Efficacy of Oral Deucrictibant for Prophylactic and On-Demand Treatment of Hereditary Angioedema Attacks: Results of the CHAPTER-1 and RAPIDe-2 Extension Trials

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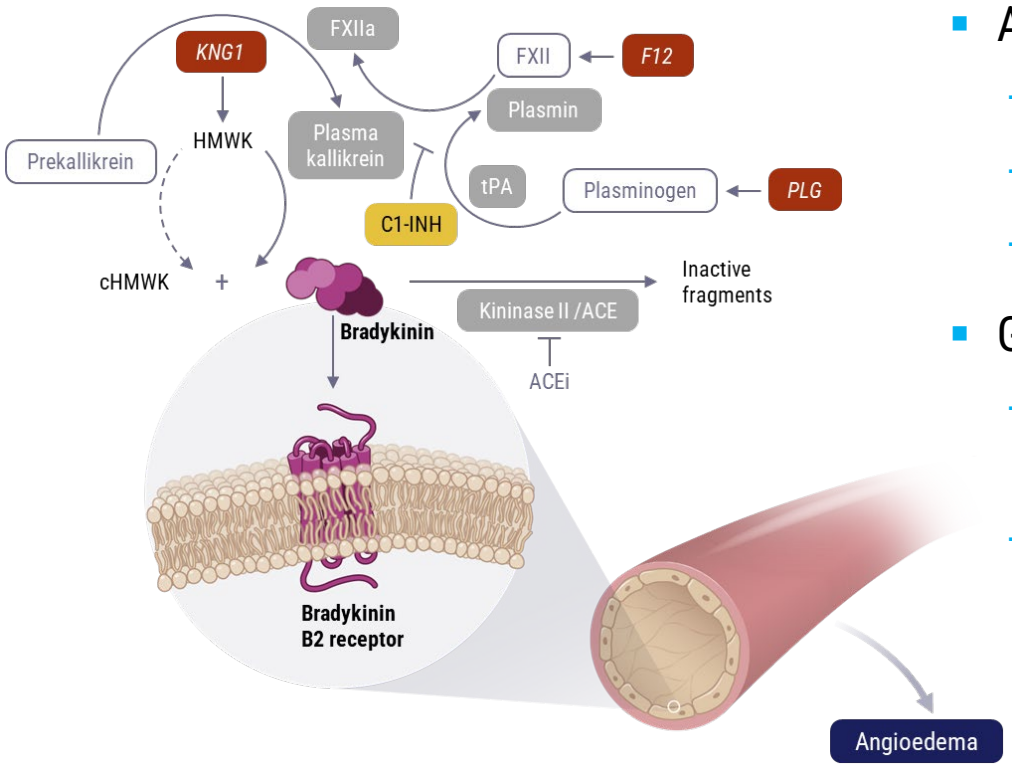
CHAPTER-1 and RAPIDe-2 are Pharvaris-sponsored clinical trials/studies. ClinicalTrials.gov identifiers: NCT05047185, NCT05396105.

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

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



- An unmet need remains for additional **prophylactic therapies** combining[1-4]:
  - Injectable-like efficacy
  - A well-tolerated profile
  - Ease of administration
- Guidelines recommend HAE attacks are treated as early as possible.[4,5]
  - Parenteral administration often leads to **on-demand treatment** of HAE attacks being delayed or forgone.[3,5-7]
  - A rapid and sustained response to on-demand treatment through to complete resolution is paramount to abate the physical, functional, and emotional burden of attacks.[5,7,8]

ACE, angiotensin converting enzyme; ACEi, ACE inhibitor; C1-INH, C1 inhibitor; cHMWK, cleaved HMWK; *F12*, gene encoding FXII; FXII, factor XII; FXIIa, factor XIIa; HAE, hereditary angioedema; HMWK, high-molecular-weight kininogen, *KNG1*, gene encoding HMWK; *PLG*, gene encoding plasminogen; tPA, tissue plasminogen activator.
1. Bouillet L, et al. *Allergy Asthma Proc*. 2022;43:406-12. **2**. Betschel SD, et al. *J Allergy Clin Immunol Pract*. 2023;11:2315-25. **3.** Covella B, et al. *Future Pharmacol*. 2024;4:41-53. **4.** Maurer M, et al. *Allergy*. 2022;77:1961-90. **5.** 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 August 25, 2025. **6.** Betschel SD, et al. *Allergy Asthma Clin Immunol*. 2024;20:43. **7.** Radojicic C, et al. *Allergy Asthma Proc*. 2021;42. **8.** Mendivil J, et al. Presented at: ACAAI; November 9–13, 2023; Anaheim, CA, USA.

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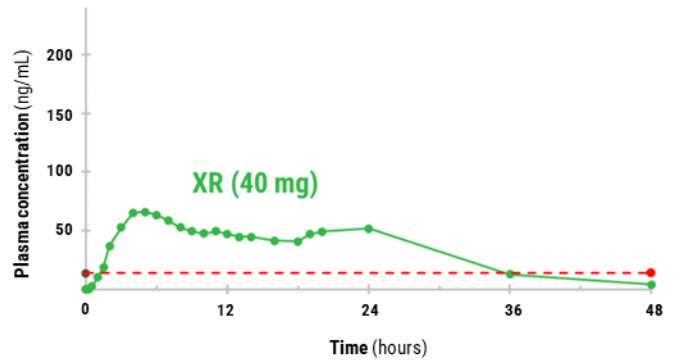
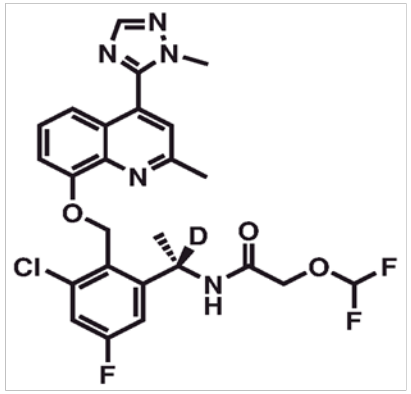
Deucrictibant is an investigational oral therapy for both the prophylactic and on-demand treatment of HAE attacks

DEUCRICTIBANT extended-release (XR) tablet

sustained absorption[1]



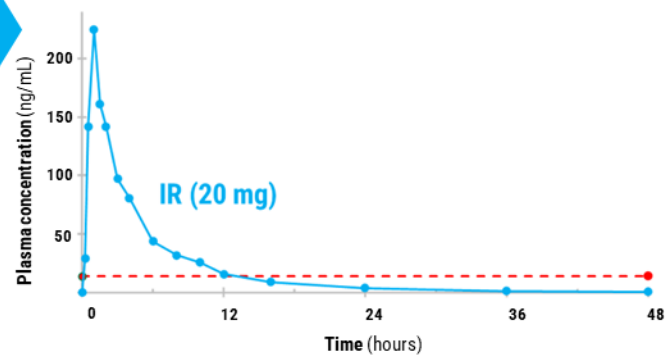
In studies, deucrictibant maintained sustained therapeutic exposure over 24 hours[1] from day one, allowing for once-daily oral prevention HAE attacks[2]



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]

HAE, hereditary angioedema; IR, immediate-release; XR, extended-release. **1.** Lesage A, et al. Presented at IDDST; May 22-24, 2024. **2.** CHAPTER-3. ClinicalTrials.gov identifier: NCT06669754. Accessed August 25, 2025. https://clinicaltrials.gov/study/NCT06669754. **3.** Maurer M, et al. Presented at AAAAI; Feb 24-27, 2023; San Antonio, TX, USA. **4.** RAPIDe-3. ClinicalTrials.gov identifier: NCT06343779. Accessed August 25, 2025. https://www.clinicaltrials.gov/study/NCT06343779.

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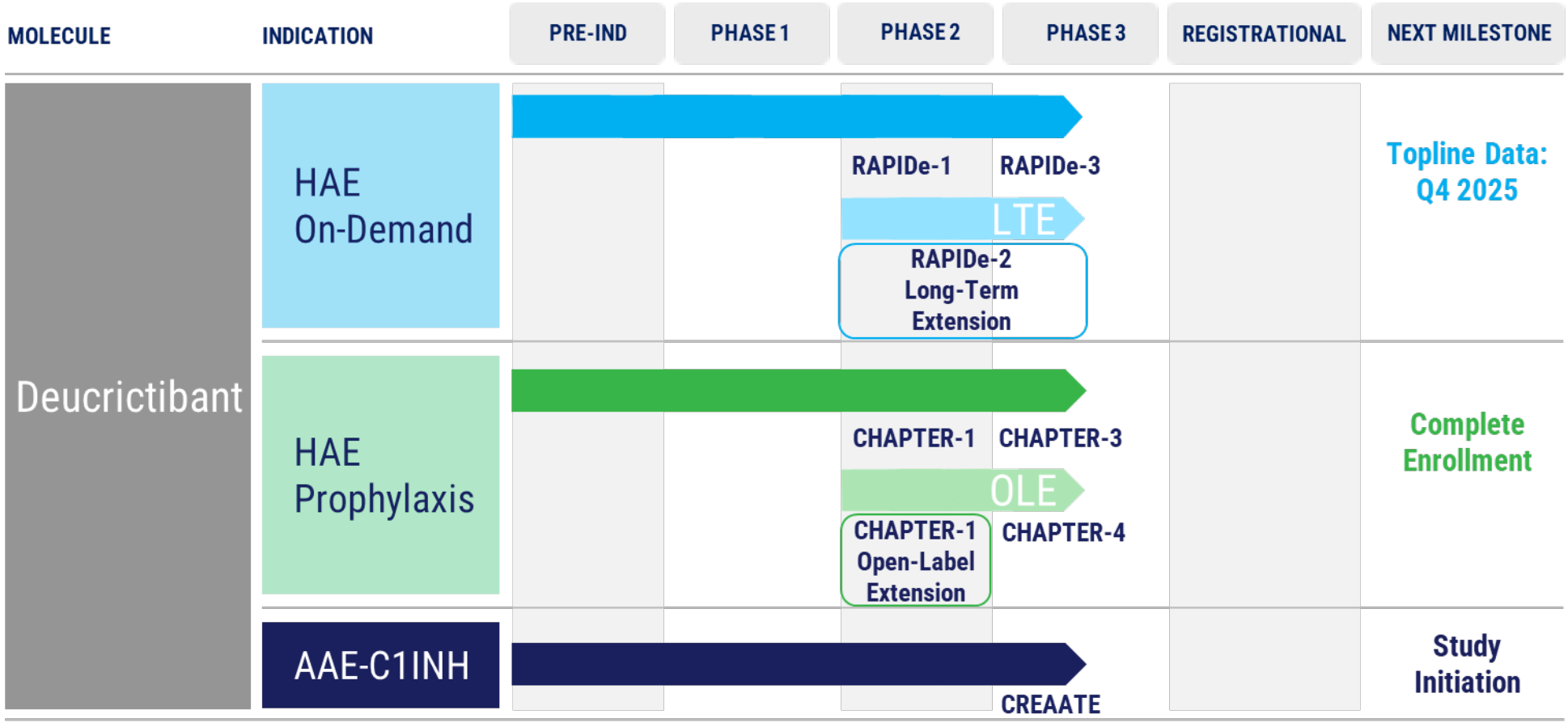
Deucrictibant development program in bradykinin-mediated angioedema



AAE-C1INH, acquired angioedema due to C1 inhibitor deficiency; HAE, hereditary angioedema; LTE, long-term extension; OLE, open-label extension; Q, quarter.
Study, ClinicalTrials.gov identifier: RAPIDe-1, NCT05396105; RAPIDe-2, NCT05396105; RAPIDe-3, NCT06343779; CHAPTER-1, NCT05047185; CHAPTER-3, NCT06669754. CHAPTER-4, NCT06679881.

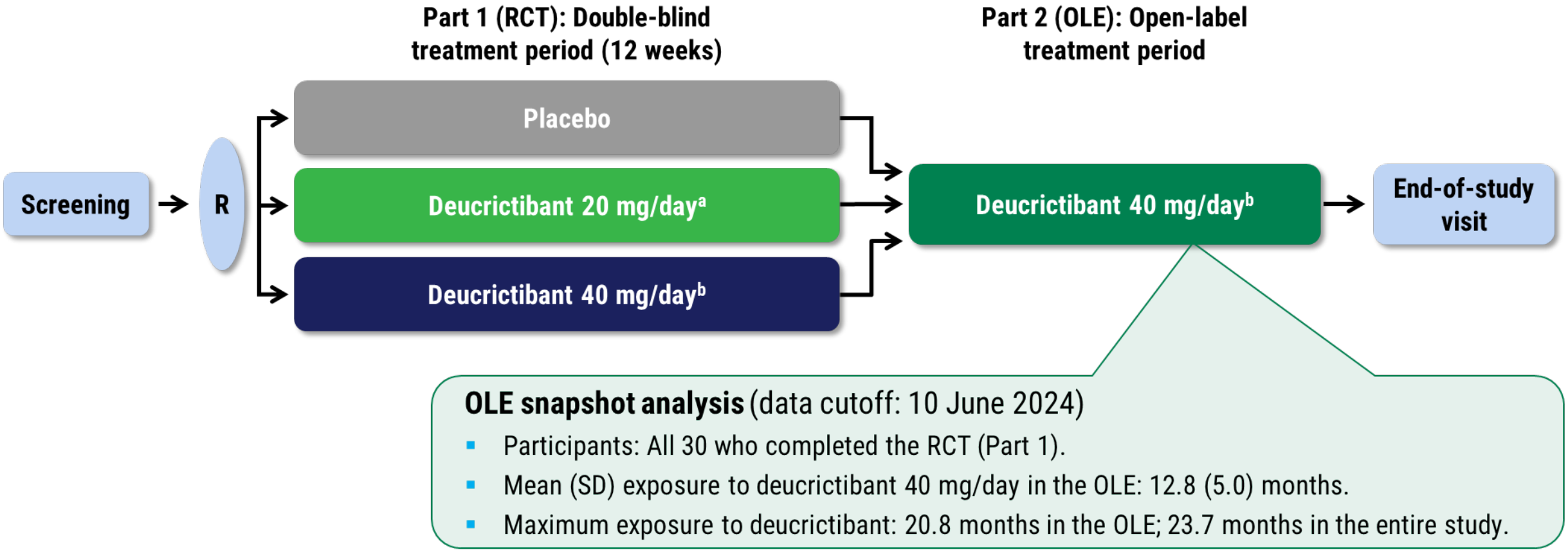
This presentation includes data for an investigational product not yet approved by regulatory authorities.

CHAPTER-1: Two-part, Phase 2 trial of deucrictibant

Prophylaxis

Key objectives in OLE:

Evaluate safety (primary objective) and efficacy of deucrictibant administered for long-term prophylaxis against HAE attacks.



IR, immediate-release; OLE, open-label extension; R, randomization; RCT, randomized controlled trial; SD, standard deviation. [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 25, 2025. https://www.clinicaltrials.gov/study/NCT05047185.

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CHAPTER-1: Deucrictibant was generally well tolerated with no safety signals in the OLE

Prophylaxis

- Deucrictibant was generally well tolerated with one treatment-related TEAE of tooth discoloration (investigator assessed).
  - No treatment-related serious or severe TEAEs.
  - No treatment-related TEAEs in laboratory parameters, vital signs (including blood pressure), or electrocardiogram findings, and no TEAEs leading to treatment discontinuation, study withdrawal, or death were reported.

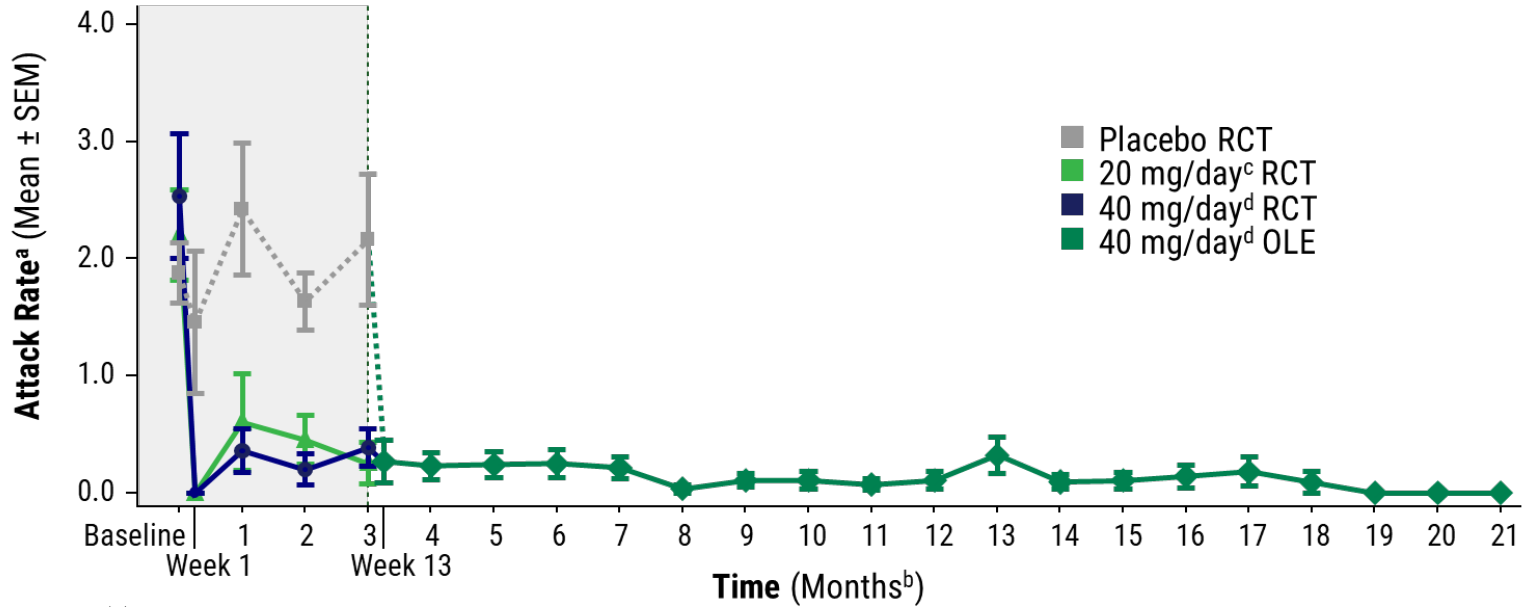
	Placebo to 40 mg/day[a] (N=9)		20 mg/day[b] to 40 mg/day[a] (N=11)		40 mg/day[a] to 40 mg/day[a] (N=10)		Total (N=30)	
	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n	Participants, n (%)	Events, n
TEAEs	**5 (55.6)**	**25**	**7 (63.6)**	**31**	**6 (60.0)**	**16**	**18 (60.0)**	**72**
Treatment-related TEAEs[c]	**1 (11.1)**	**1**	**0**	**0**	**0**	**0**	**1 (3.3)**	**1**
Tooth discoloration	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**
Tendon injury	0	0	0	0	1 (10.0)	1	1 (3.3)	1
Hip arthroplasty (arthritis)	0	0	1 (9.1)	1	0	0	1 (3.3)	1
Treatment-related serious TEAEs[c]	**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**

TEAE, treatment-emergent adverse event defined as adverse events that start or pre-existing adverse events that have worsened during the period between first study dose in OLE and 4 weeks after last dose in OLE or the End of Study Visit, whichever is later.
N = number of participants who received ≥1 dose of study treatment in the OLE by the cutoff date (10 June 2024). [a]Deucrictibant IR capsule, 20 mg twice daily. [b]Deucrictibant IR capsule, 10 mg twice daily. [c]Investigator assessed.

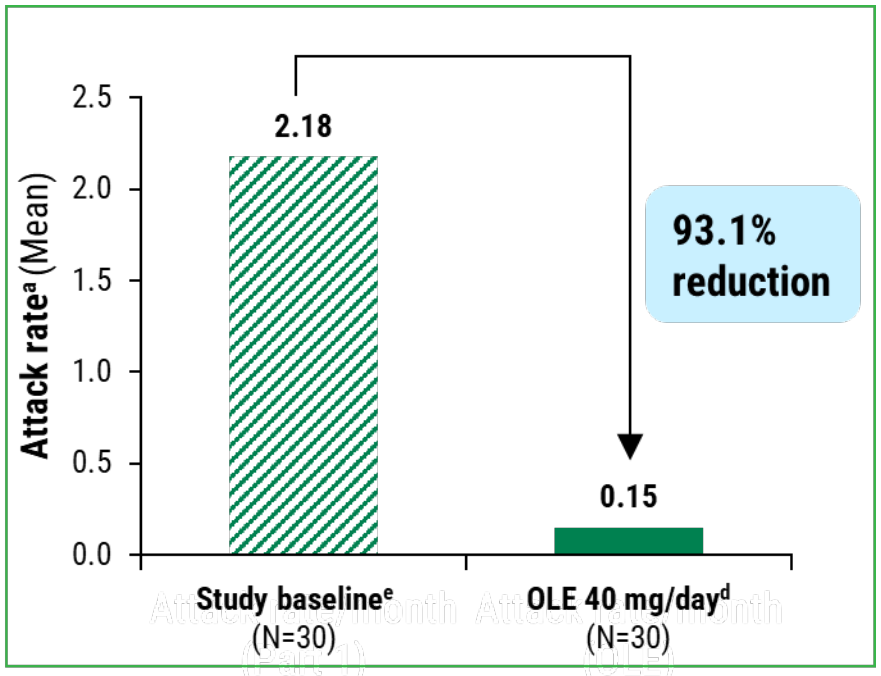
This presentation includes data for an investigational product not yet approved by regulatory authorities.

CHAPTER-1: Attack rate reduced by week 1 in the RCT and remained low through ≥1.5 years in the OLE

Prophylaxis



Placebo (n)	1111	11	11	11																			
20 mg/day[c] RCT (n)	1111	11	11	11																			
40 mg/day[d] RCT (n)	1212	11	10	10																			
40 mg/day[d] OLE (n)				30	29	29	28	28	28	28	28	28	28	28	28	21	19	16	11	11	10	9	7



IR, immediate release; LS, least squares; OLE, open-label extension; RCT, randomized controlled trial; SEM, standard error of the mean. n = number of participants at each timepoint. N = number of participants in the OLE. [a]Based on time normalized number of attacks per 4 weeks. [b]1 month = 4 weeks. [c]Deucrictibant IR capsule, 10 mg twice daily. [d]Deucrictibant IR capsule, 20 mg twice daily. [e]Baseline attack rate is raw (unadjusted) mean; OLE attack rate is LS mean. No multiplicity adjustment was applied.

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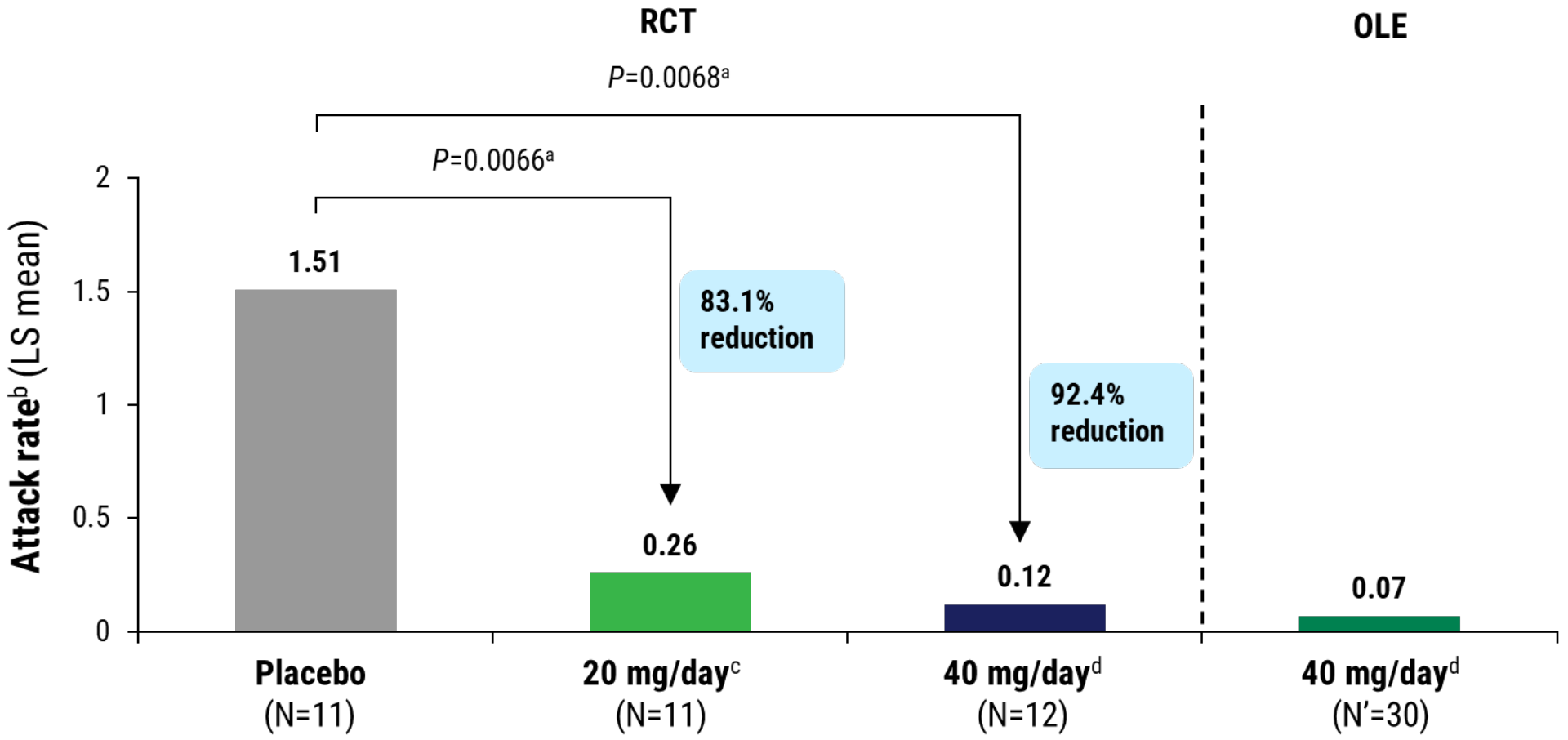
CHAPTER-1: “Moderate and severe” attack rate reduced in the RCT and remained low in the OLE

Prophylaxis



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. [a]The *P*-values in this figure are nominal. [b]Based on time-normalized number of attacks per 4 weeks. [c]Deucrictibant IR capsule, 10 mg twice daily. [d]Deucrictibant IR capsule, 20 mg twice daily.

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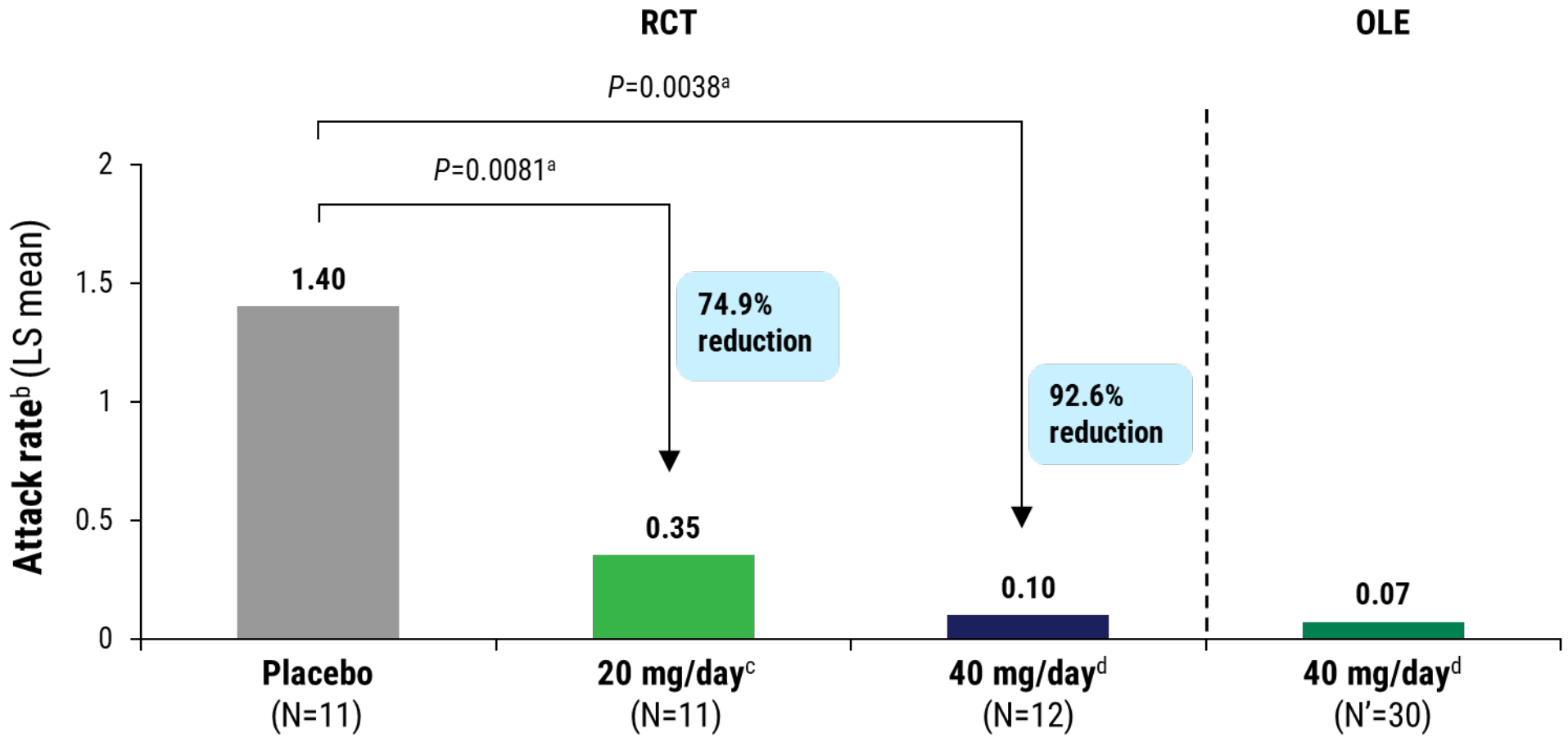
CHAPTER-1: On-demand treated attack rate reduced in the RCT and remained low in the OLE

Prophylaxis



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. [a]The *P*-values in this figure are nominal. [b]Based on time-normalized number of attacks per 4 weeks. [c]Deucrictibant IR capsule, 10 mg twice daily. [d]Deucrictibant IR capsule, 20 mg twice daily.

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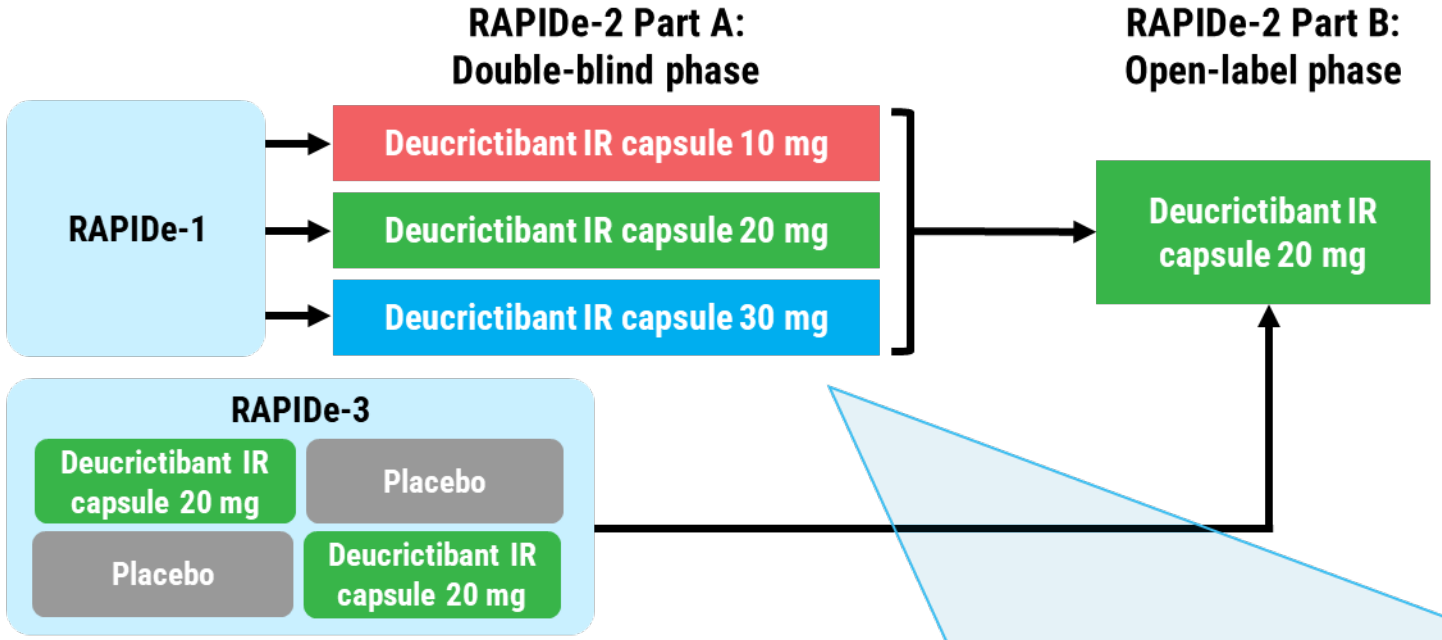
RAPIDe-2: Phase 2/3 extension study of deucrictibant

On-demand

Key objectives: Evaluate long-term safety and efficacy of deucrictibant for on-demand treatment of repeat HAE attacks.



Final RAPIDe-2 Part A data

- Deucrictibant: participants continue self-administering the same double-blinded dose received in RAPIDe-1 to treat qualifying attacks.
- Qualifying attacks: non-upper airway attacks (≥1 symptom with AMRA-3 score ≥30), and upper airway attacks, including laryngeal attacks presenting without breathing difficulties.
- Data: Results shown for combined dose group.

AMRA-3, Angioedema syMptom Rating scAle (used to measure skin swelling, skin pain, and abdominal pain); IR, immediate-release. RAPIDe-1. NCT04618211, https://www.clinicaltrials.gov/study/NCT04618211 Accessed August 25, 2025. RAPIDe-2. NCT05396105. https://clinicaltrials.gov/study/NCT053961052 Accessed August 25, 2025. RAPIDe-3. NCT06343779. https://clinicaltrials.gov/study/NCT06343779 Accessed August 25, 2025. RAPIDe-2 is a Pharvaris-sponsored clinical study.

RAPIDe-2: Deucrictibant well tolerated across all doses

On-demand

TEAEs within 3 days of study drug administration

Adverse events	Deucrictibant IR capsule (Combined dose group[a]) (N=19; A=465)
Attacks with any TEAE, a (%)	12 (2.6)
Treatment-related TEAEs, a	0
Serious TEAEs, a	1[b]
Treatment-related serious TEAEs, a	0
TEAEs leading to study drug discontinuation, study withdrawal, or death, a	0

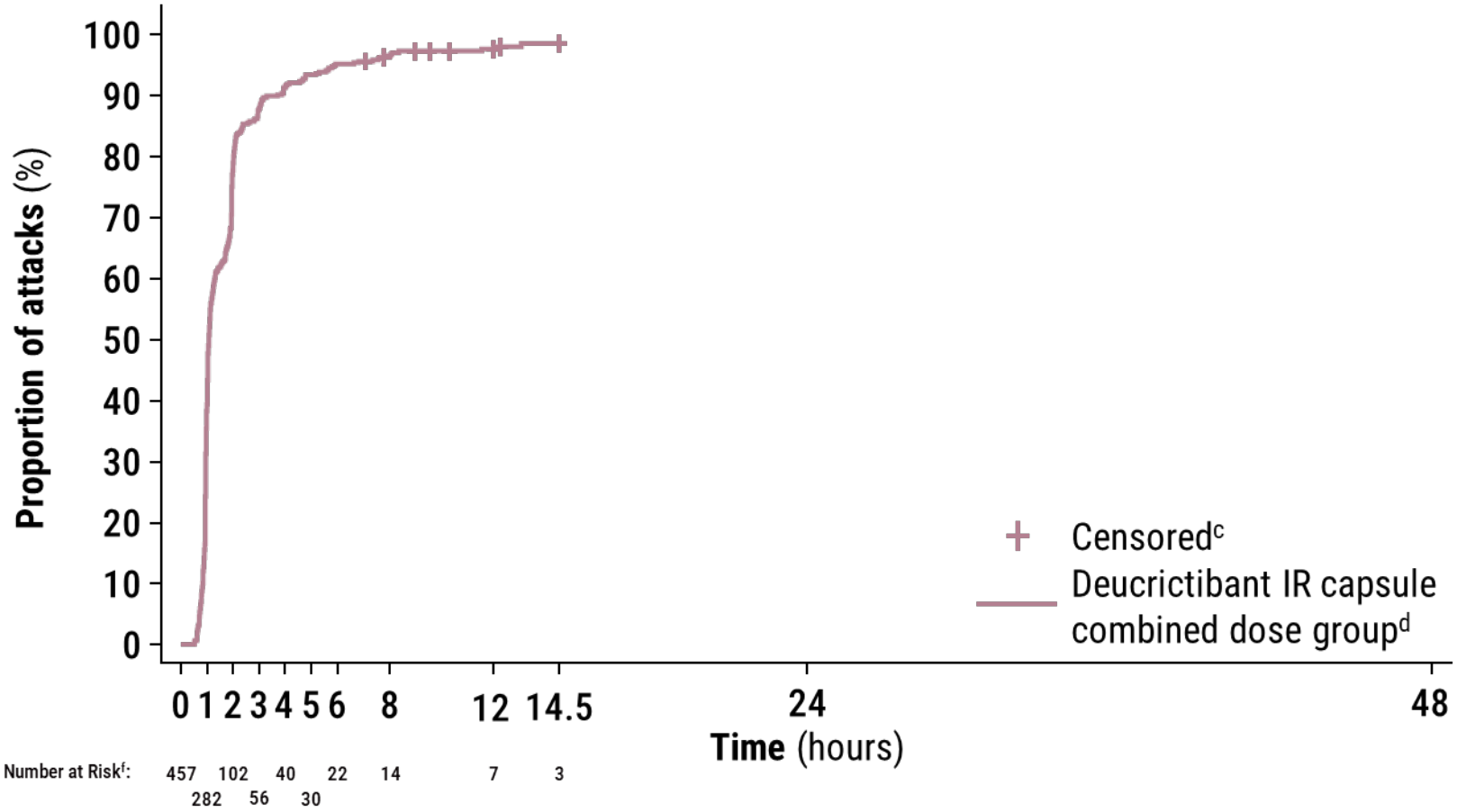
- No treatment-related TEAEs.
- No treatment-related serious or severe TEAEs.
- No treatment-related TEAEs in laboratory parameters, vital signs, or electrocardiogram (ECG) findings.
- No TEAEs leading to treatment discontinuation, study withdrawal, or death.

IR, immediate-release; TEAE, treatment-emergent adverse event, defined as adverse event occurring from first study drug administration. A = number of treated attacks. N = number of participants.
[a]Combined dose group includes deucrictibant IR capsule 10mg, 20mg and 30mg. [b]Tooth caries unrelated to treatment.

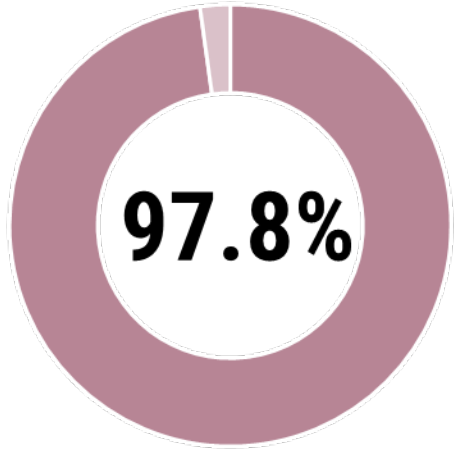
1.1 hours median time to onset of symptom relief

On-demand

Patient Global Impression of Change (PGI-C) rating of at least “a little better” for 2 consecutive timepoints by 12 hours post-treatment



1.1 hours (95% CI, 1.0, 1.1) median time to onset of symptom relief[a,b]



of attacks achieved **onset of symptom relief by 12 hours** (447/457[e])

CI, confidence interval; IR, immediate-release. [a]regardless of any missing intervening assessments and without rescue medication use. [b]Within-participant correlation was not accounted for in all Kaplan-Meier estimates. [c]Attacks that used rescue medication within 12 hours post-treatment were censored at 14.5 hours; attacks that did not reach milestone and without rescue medication within 12 hours post-treatment were censored at the last assessment time within 12 hours post-treatment. [d]Includes 10 mg, 20 mg, and 30 mg dose groups. [e]457 attacks have at least one post-treatment PGI-C result. [f]Pooled evaluable attacks.

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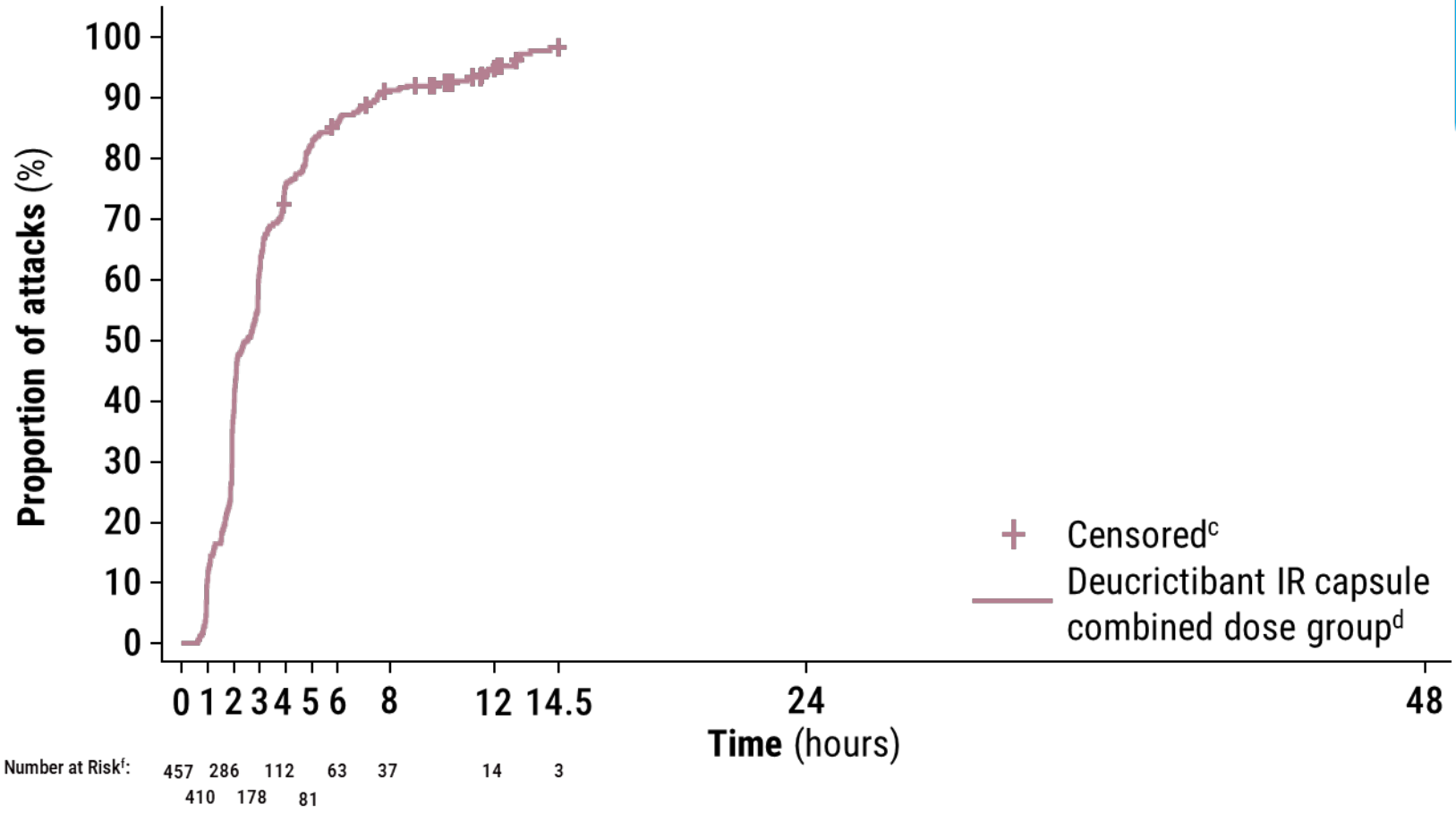
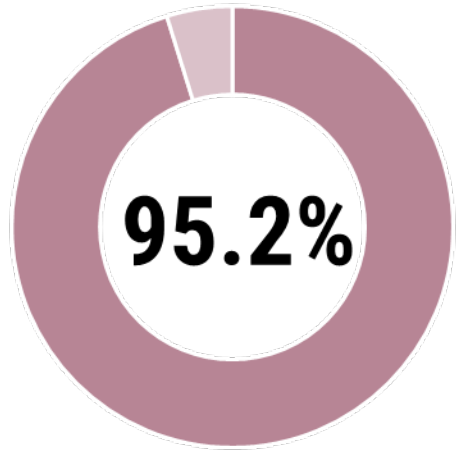
2.5 hours median time to substantial symptom relief

PGI-C rating of at least "better" for 2 consecutive timepoints by 12 hours post-treatment

On-demand



2.5 hours (95% CI, 2.1, 2.9) median time to substantial symptom relief[a,b]



of attacks achieved **substantial symptom relief by 12 hours** (435/457[e])

CI, confidence interval; IR, immediate-release. [a]regardless of any missing intervening assessments and without rescue medication use. [b]Within-participant correlation was not accounted for in all Kaplan-Meier estimates. [c]Attacks that used rescue medication within 12 hours post-treatment were censored at 14.5 hours; attacks that did not reach milestone and without rescue medication within 12 hours post-treatment were censored at the last assessment time within 12 hours post-treatment. [d]Includes 10 mg, 20 mg, and 30 mg dose groups. [e]457 attacks have at least one post-treatment PGI-C result. [f]Pooled evaluable attacks.

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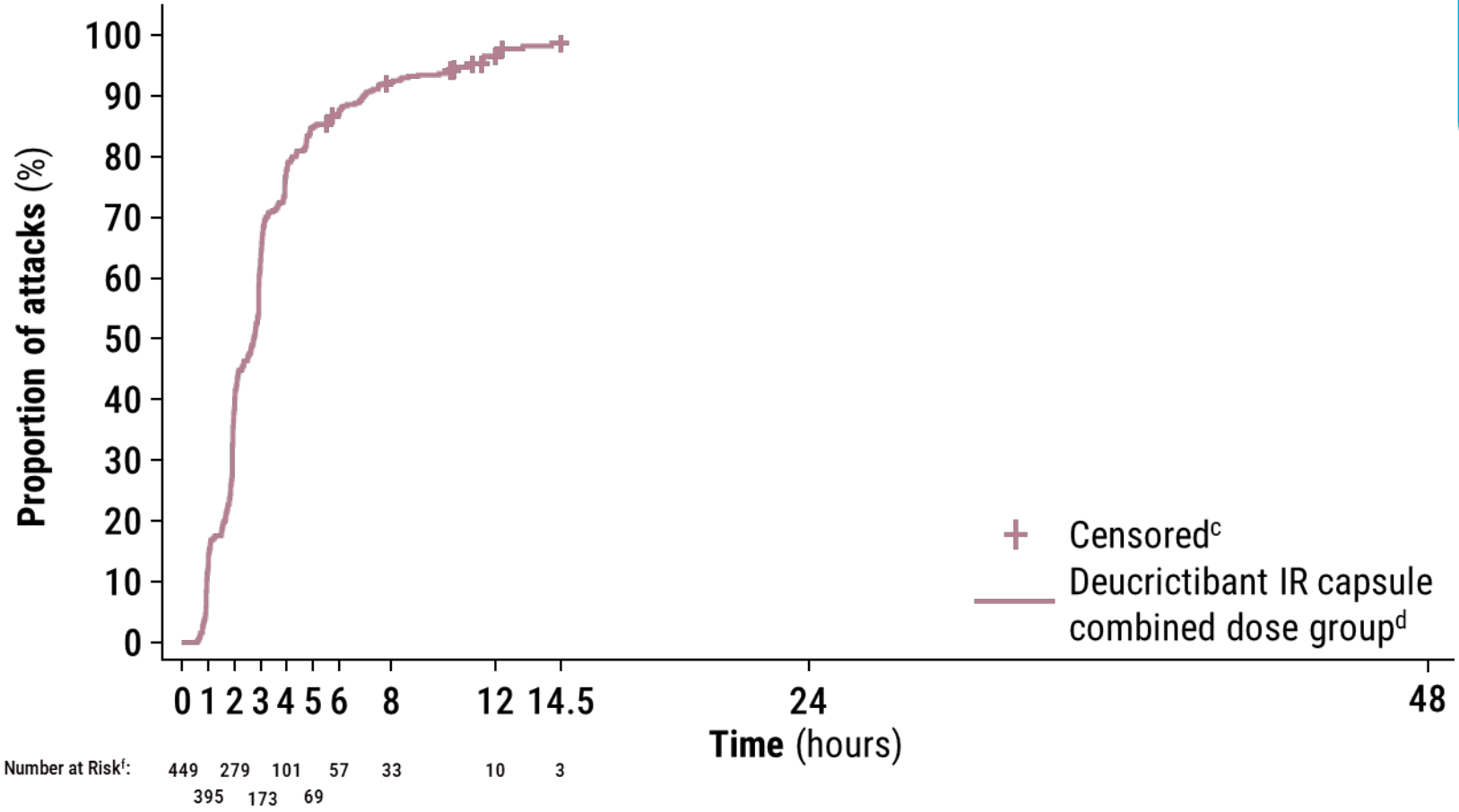
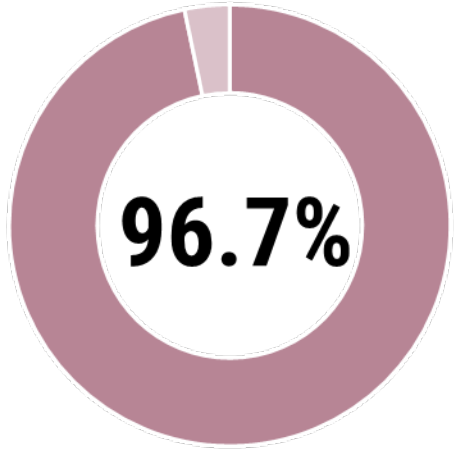
On-demand

2.8 hours median time to reduction in attack severity

≥1-level reduction in Patient Global Impression of Severity (PGI-S) from pre-treatment for 2 consecutive timepoints by 12 hours post-treatment



2.8 hours (95% CI, 2.3, 2.9) median time to reduction in attack severity[a,b]



of attacks achieved **reduction in attack severity by 12 hours** (434/449[e])

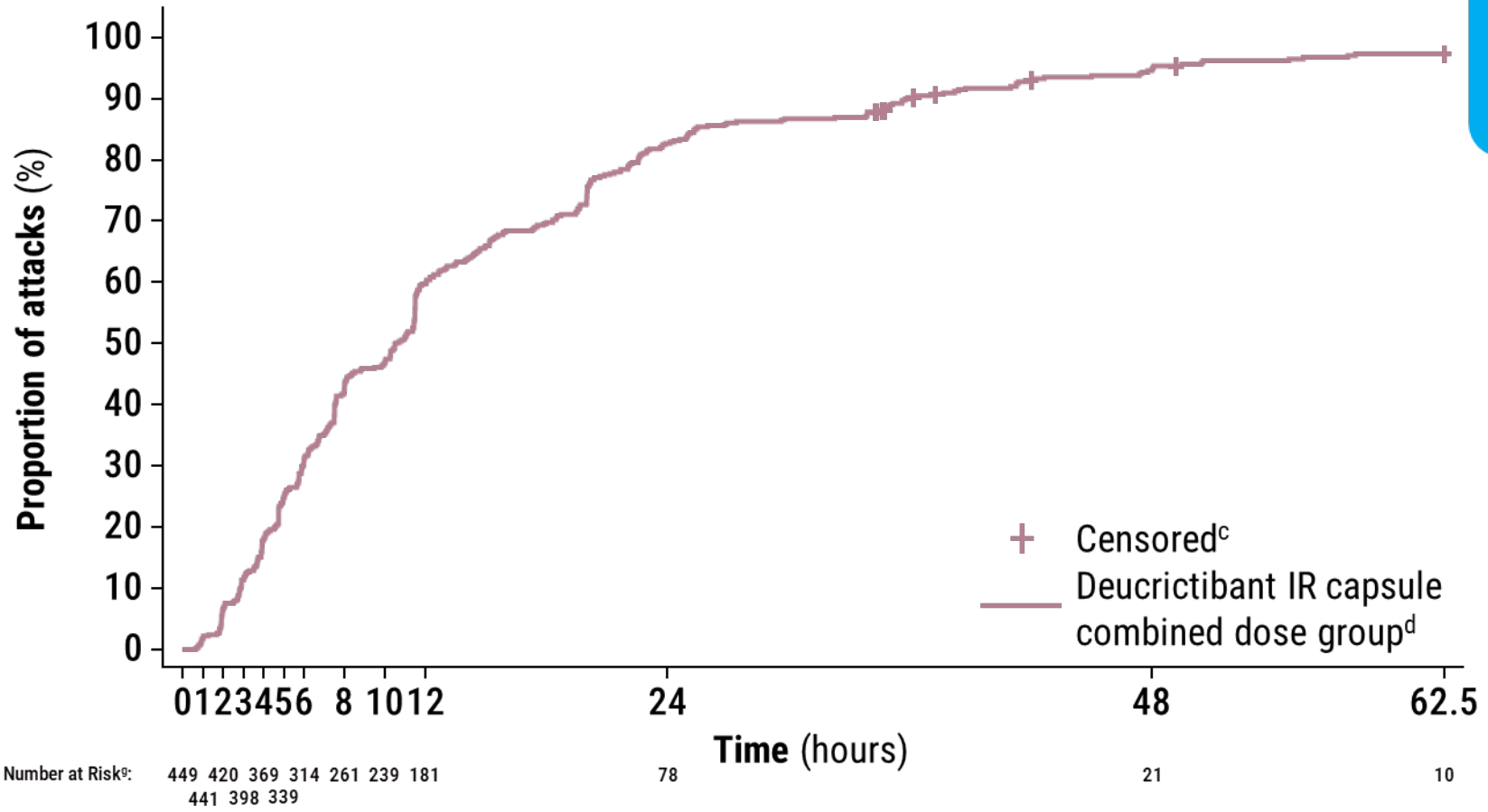
CI, confidence interval; IR, immediate-release. [a]without rescue medication use. [b]Within-participant correlation was not accounted for in all Kaplan-Meier estimates. [c]Attacks that used rescue medication within 12 hours were censored at 14.5 hours; attacks that did not reach milestone and without rescue medication within 12 hours were censored at the last assessment time within 12 hours. [d]Includes 10 mg, 20 mg, and 30 mg dose groups. [e]449 attacks have non-missing pre-treatment PGI-S and at least one post-treatment PGI-S. [f]Pooled evaluable attacks.

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

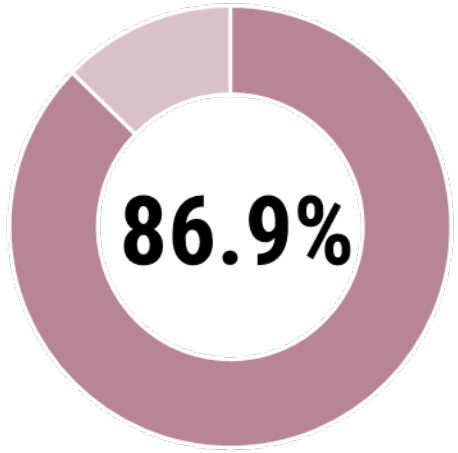
10.6 hours median time to complete attack resolution

PGI-S rating of “none” within 48 hours post-treatment

On-demand



10.6 hours (95% CI, 8.5, 11.5) median time to complete attack resolution[a,b]



of attacks achieved **complete symptom resolution at 24 hours[e]** (390/449[f])

CI, confidence interval; IR, immediate-release. [a]without rescue medication use. [b]Within-participant correlation was not accounted for in all Kaplan-Meier estimates. [c]Attacks that used rescue medication within 48 hours post-treatment were censored at 62.5 hours; attacks that did not reach milestone and without rescue medication within 48 hours post-treatment were censored at the last assessment time within 48 hours post-treatment. [d]Includes 10 mg, 20 mg, and 30 mg dose groups. [e]Symptom resolution is defined as achieving PGI-S rating of "none" at the last available timepoint before or at 24 hours post-treatment without use of rescue medication. [f]449 attacks have non-missing pre-treatment PGI-S and at least one post-treatment PGI-S. [g]Pooled evaluable attacks.

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Conclusions

Prophylaxis: CHAPTER-1 OLE	On-demand: RAPIDe-2
Overall results: ▪ Evidence on the long-term safety and efficacy of deucrictibant for prevention and treatment of HAE attacks. ▪ Support further investigation of deucrictibant as a potential prophylactic and on-demand therapy for HAE.	
Safety: All studied doses of deucrictibant were generally well tolerated, with one treatment-related TEAE of tooth discoloration in CHAPTER-1 OLE (investigator assessed).	
Efficacy: Deucrictibant 40 mg/day treatment: – OLE vs RCT baseline: attack rate reduced by 93.1%. – "Moderate and severe" attack rate was 0.07. – On-demand-treated attack rate was 0.07.	**Efficacy:** Combined dose (deucrictibant 10, 20 and 30 mg): Median times to – Onset of symptom relief: 1.1 hours 97.8% of attacks by 12 hours. – Substantial symptom relief: 2.5 hours 95.2% of attacks by 12 hours. – Reduction in attack severity: 2.8 hours 96.7% of attacks by 12 hours. – Complete attack resolution: 10.6 hours 86.9% of attacks at 24 hours.

The Authors and the Sponsor would like to thank all the people with HAE,
as well as all study site staff who have been participating in the CHAPTER-1 trial and RAPIDe-2 study.

HAE, hereditary angioedema; OLE, open-label extension; RCT, randomized controlled trial; TEAE, treatment-emergent adverse event.

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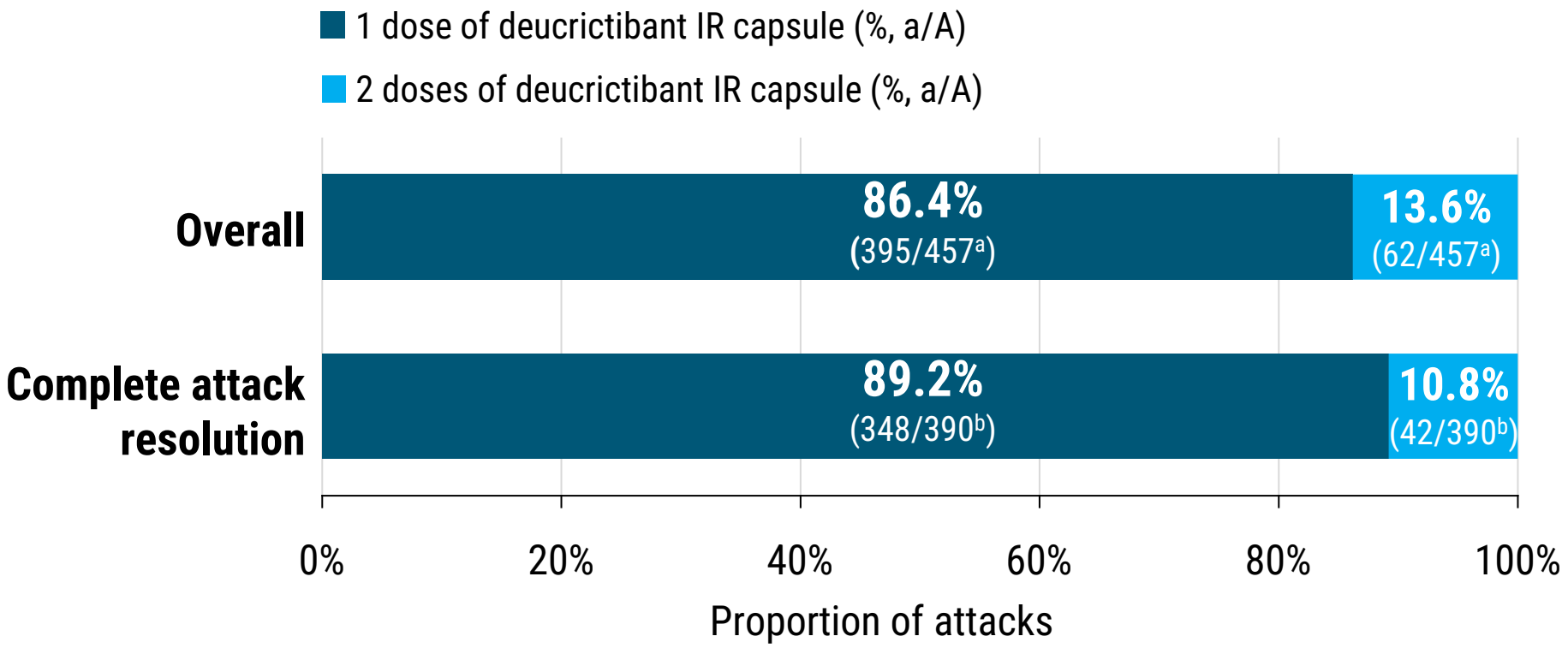
Majority of attacks treated with a single dose of deucrictibant and without rescue medication within 24 hours

On-demand



IR, immediate-release; PGI-S, Patient Global Impression of Severity. A = number of attacks. Data for combined dose group shown (deucrictibant 10mg, 20mg and 30mg). [a]Proportion of attacks that were not treated with rescue medication within 24 hours post-treatment; 8 attacks used rescue medication within 24 hours post-treatment. [b]Proportion of attacks achieving complete attack resolution, defined as achieving PGI-S rating of "none" at the last available timepoint before or at 24 hours post-treatment without use of rescue medication.

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