Long-Term Safety and Efficacy of Oral Deucrictibant for Treatment of Hereditary Angioedema Attacks: Results of the RAPIDe-2 Extension Study

M.A. Riedl, J. Anderson, E. Aygören-Pürsün, L. Bouillet, H. Chapdelaine, H. Farkas, D. Gobert, R. Hakl, J.S. Jacobs, R. Lleonart, M.E. Manning, A. Reshef, G. Spadaro, M. Staevska, M. Stobiecki, G. Giannattasio, Y. Li, P. Lu, J. Sun, M. Yu, A. Valerieva

C1-Inhibitor Deficiency & Angioedema Workshop, 2025
Budapest, Hungary, 29 May - 1 June 2025

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

Conflicts of interest disclosure

M.A.R.: Astria, BioCryst, BioMarin, Celldex, CSL Behring, Cycle Pharma, Grifols, Intellia, Ionis, KalVista, Novartis, Pharming, Pharvaris, Sanofi-Regeneron, Takeda; **J.A.:** BioCryst, BioMarin, CSL Behring, Cycle Pharma, KalVista, Pharming, Pharvaris, Takeda; **E.A-P.:** Astria, BioCryst, CSL Behring, Intellia, Kalvista, Otsuka, Pharvaris, Takeda; **L.B.:** BioCryst, Blueprint, CSL Behring, Novartis, Takeda; **H.C.:** AstraZeneca (Alexion), CSL Behring, KalVista, Merck, Novartis, Pharming, Pharvaris, Roche, Sanofi, Sobi, Takeda; **H.F.:** BioCryst, CSL Behring, Intellia, KalVista, ONO Pharmaceutical, Pharming, Pharvaris, Takeda; **D.G.:** Pharming, Takeda; **R.H.:** BioCryst, CSL Behring, KalVista, Pharvaris, Pharming, Takeda; **J.S.J.:** BioCryst, CSL Behring, Cycle Pharma, Oasis, Pharming, Pharvaris, Takeda; **R.L.:** BioCryst, CSL Behring, Ionis, KalVista, Novartis, Pharming, Pharvaris, Takeda; **M.E.M.:** Allakos, Amgen, AstraZeneca, BioCryst, Blueprint, CSL Behring, Cycle Pharma, Genentech, GSK, Merck, Novartis, KalVista, Pharming, Pharvaris, Sanofi/Regeneron, Takeda; **A.R.:** BioCryst, CSL Behring, Pharming, Pharvaris, Stallergens, Takeda, Teva; **G.S.:** Pharvaris, Takeda; **M.Sta.:** has no conflicts of interests to disclose relative to this work; **M.Sto.:** BioCryst, CSL Behring, KalVista, Pharming, Takeda; **G.G., Y.L., J.S., M.Y.:** employees of Pharvaris, holds stocks in Pharvaris; **P.L.:** employee of Pharvaris, holds stocks/stock options in Pharvaris; **A.V.:** AstraZeneca, Berlin-Chemie/Menarini Group, CSL Behring, KalVista, Novartis, Pharming, Pharvaris, Sobi, Takeda.

Acknowledgments: Medical writing services were provided by Jonny Turner, PhD, of Envision Pharma and funded by Pharvaris.

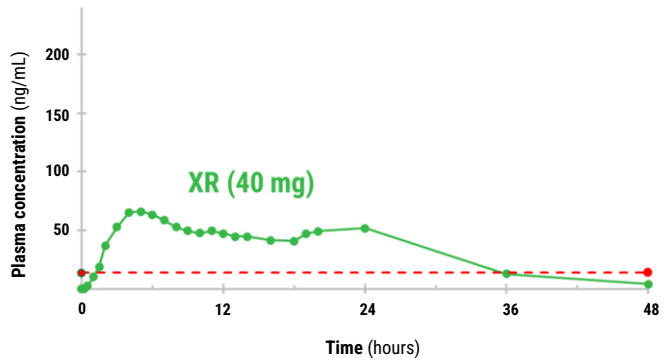
RAPIDe-2 is a Pharvaris-sponsored clinical study. ClinicalTrials.gov identifier: NCT05396105.

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

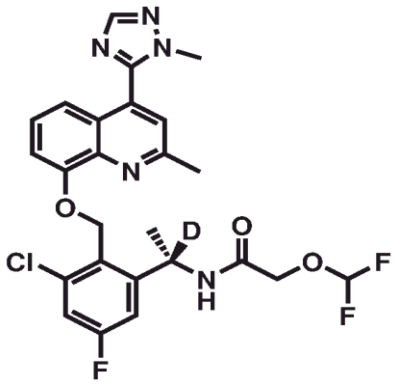
Deucrictibant is an investigational oral therapy for both the prophylactic and on-demand treatment of HAE attacks

DEUCRICTIBANT extended-release (XR) tablet

sustained absorption[1]



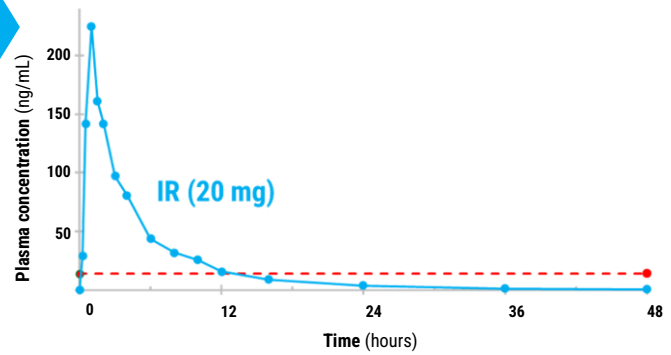
In studies, deucrictibant maintained sustained therapeutic exposure over 24 hours[1] from day one, allowing for once-daily oral prevention HAE attacks[2]



deucrictibant

DEUCRICTIBANT immediate-release (IR) capsule

rapid absorption[3]

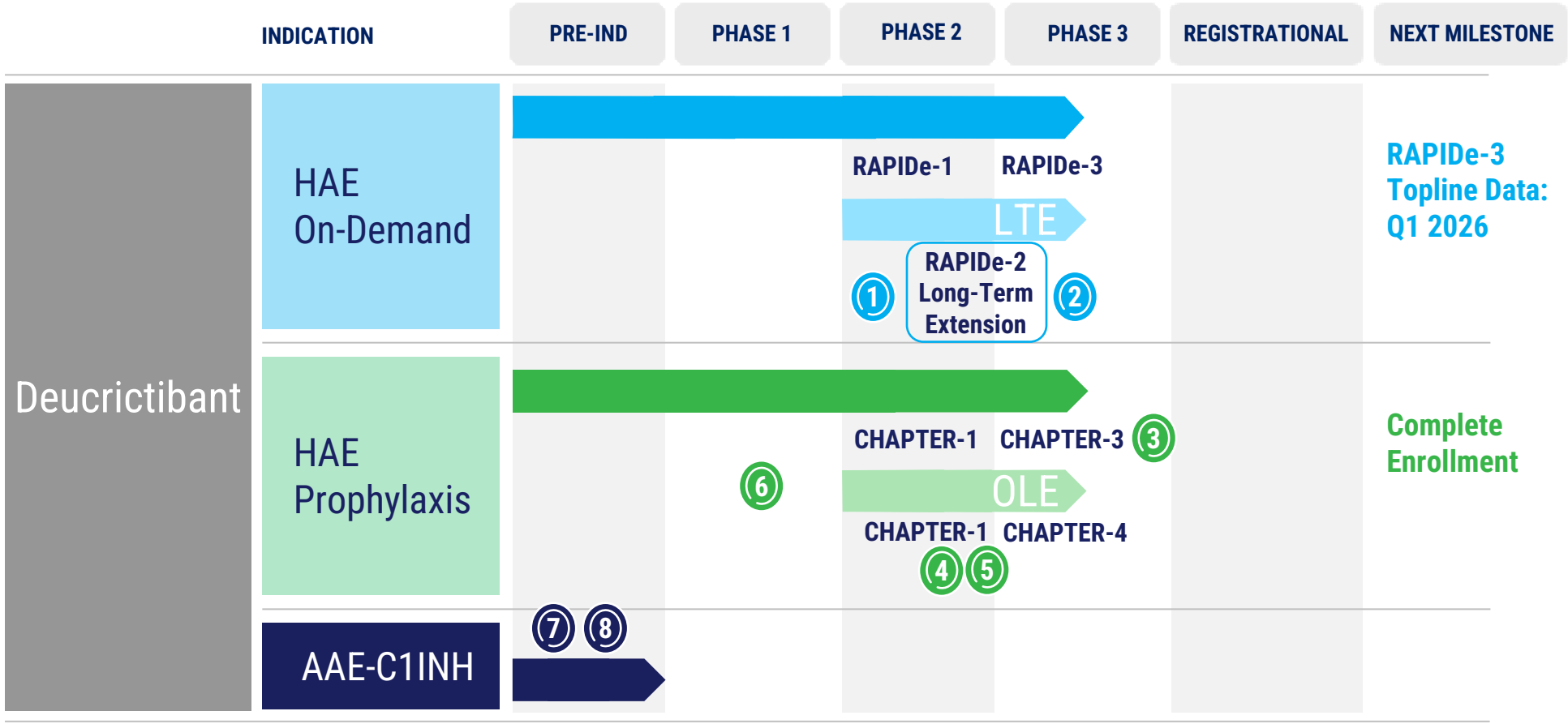


In studies, deucrictibant rapidly reached therapeutic exposure within 15-30 minutes[3], supporting on-demand oral treatment of HAE attacks[4]

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 May 13, 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 May 13, 2025. https://www.clinicaltrials.gov/study/NCT06343779.

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

Deucrictibant development program in bradykinin-mediated angioedema



Other oral presentations

4 Aygoren-Pursun, et al. CHAPTER-1 OLE May 31, 15:30-15:45

Poster presentations at C1-Inhibitor Workshop

1 Valerieva A, et al. RAPIDe-1/2 durability of treatment response

2 Lleonart R, et al. RAPIDe-2 upper airway attack outcomes

3 Zanichelli A, et al. CHAPTER-3 study design

5 Magerl M, et al. CHAPTER-1 OLE patient-reported outcomes

6 Zhang Z-Y, et al. Once-daily XR tablet for prophylaxis

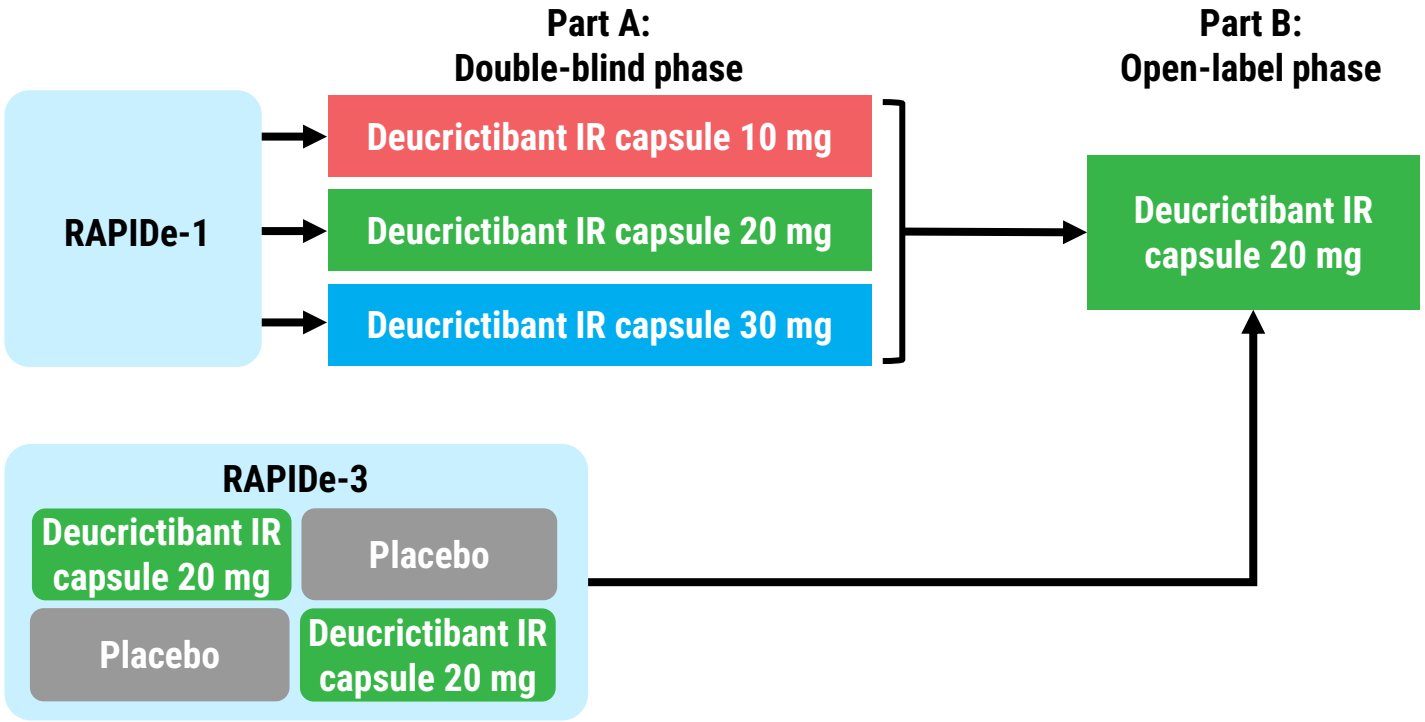
7 Aygören-Pürsün E, et al. Epidemiology in European population

8 Zanichelli A, et al. Qualitative interviews

AAE-C1INH, acquired angioedema due to C1-inhibitor deficiency; HAE, hereditary angioedema; LTE, long-term extension; OLE, open-label extension; Q, quarter; XR, extended release. Study, ClinicalTrials.gov identifier: RAPIDe-1, 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.

RAPIDe-2: a two-part, Phase 2/3 extension study of deucrictibant for on-demand treatment of repeat HAE attacks



- **RAPIDe-2 Part A:** enrolled adult (≥18 years) participants who completed RAPIDe-1.
- **Deucrictibant:** participants continue to self-administer the same double-blind dose of deucrictibant IR capsule received in RAPIDe-1 to treat qualifying:
  - non-upper airway attacks (≥1 symptom with AMRA-3 score ≥30), and
  - upper airway attacks, including laryngeal attacks, presenting without breathing difficulties.

AMRA-3, three symptom Angioedema syMptom Rating scAle; HAE, hereditary angioedema; IR, immediate-release. RAPIDe-1, ClinicalTrials.gov identifier: NCT04618211. Accessed May 13, 2025. https://www.clinicaltrials.gov/study/NCT04618211. RAPIDe-2, ClinicalTrial.org identifier NCT05396105. Accessed May 13, 2025. https://clinicaltrials.gov/study/NCT053961052.

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

Study endpoints

- **Primary endpoint:** Safety, including TEAEs, clinical laboratory tests, vital signs, and ECG findings.
- **Efficacy:** Assessed using PRO tools.
- **Secondary efficacy endpoints included**:
  - **Time to onset of symptom relief**:
    PGI-C rating of at least "a little better" for 2 consecutive timepoints by 12 hours post-treatment.
  - **Time to substantial symptom relief:**
    PGI-C rating of at least "better" for 2 consecutive timepoints by 12 hours post-treatment.
  - **Time to reduction in attack severity**:
    ≥1-level reduction in PGI-S from pre-treatment for 2 consecutive timepoints by 12 hours post-treatment.
  - **Proportion of attacks achieving complete attack resolution**:
    PGI-S rating of "none" at 24 hours post-treatment.
- **Post-hoc analyses:**
  - Durability of response to treatment.
  - Treatment outcomes of upper airway attacks.

Patient Global Impression of Change (PGI-C)[1]

Patient Global Impression of Severity (PGI-S)[1]

ECG, electrocardiogram; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity; PRO, patient-reported outcome; TEAE, treatment-emergent adverse event. **1.** Cohn DM, et al. *Clin Transl Allergy*. 2023;e12288.

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

Participant characteristics and HAE attacks

Participant characteristics	Deucrictibant IR capsule (Combined dose group[b]) (N=19)
Age in years, mean (SD)	44.4 (17.6)
Sex: Male/female, n (%)	7 (36.8) / 12 (63.2)
Race: White/other, n	18 / 1
BMI, mean (SD)	26.8 (4.0)
Years since HAE diagnosis, mean (SD)	23.3 (15.2)
HAE type, n (%)	
HAE-1	17 (89.5)
HAE-2	2 (10.5)

- Baseline characteristics[c] were similar to the final RAPIDe-1 Phase 2 trial population.

- 465 attacks from 19 participants included in the mITT efficacy[a] and safety[b] analysis sets.
  - 14 of 465 attacks were upper airway, including laryngeal, attacks.
  - Manifestations of 6 attacks included difficulty in swallowing and/or voice change before treatment, assessed using AMRA-5.
  - No difficulties were reported in administering the capsule, including during upper airway attacks.

AMRA-5, five-symptom composite Angioedema syMptom Rating scAle; BMI, body mass index; HAE, hereditary angioedema; IR, immediate-release; mITT, modified intention-to-treat; SD, standard deviation. [a]All participants who had ≥1 attack treated with deucrictibant and non-missing PGI-C results from ≥1 post-treatment timepoint. [b]All participants who received any dose of deucrictibant in the study. [c]Study baseline refers to results at the screening or enrolment visit of RAPIDe-2 Part A. For parameters whose values remain constant over time, baseline values from RAPIDe-1 were used. For parameters without results at the screening or enrolment visit of RAPIDe-2 or for parameters not collected at that time, the last available assessment in RAPIDe-1 was used as the baseline values. Data for combined dose group shown (deucrictibant 10 mg, 20 mg and 30 mg).

Deucrictibant IR capsule well tolerated across all doses

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

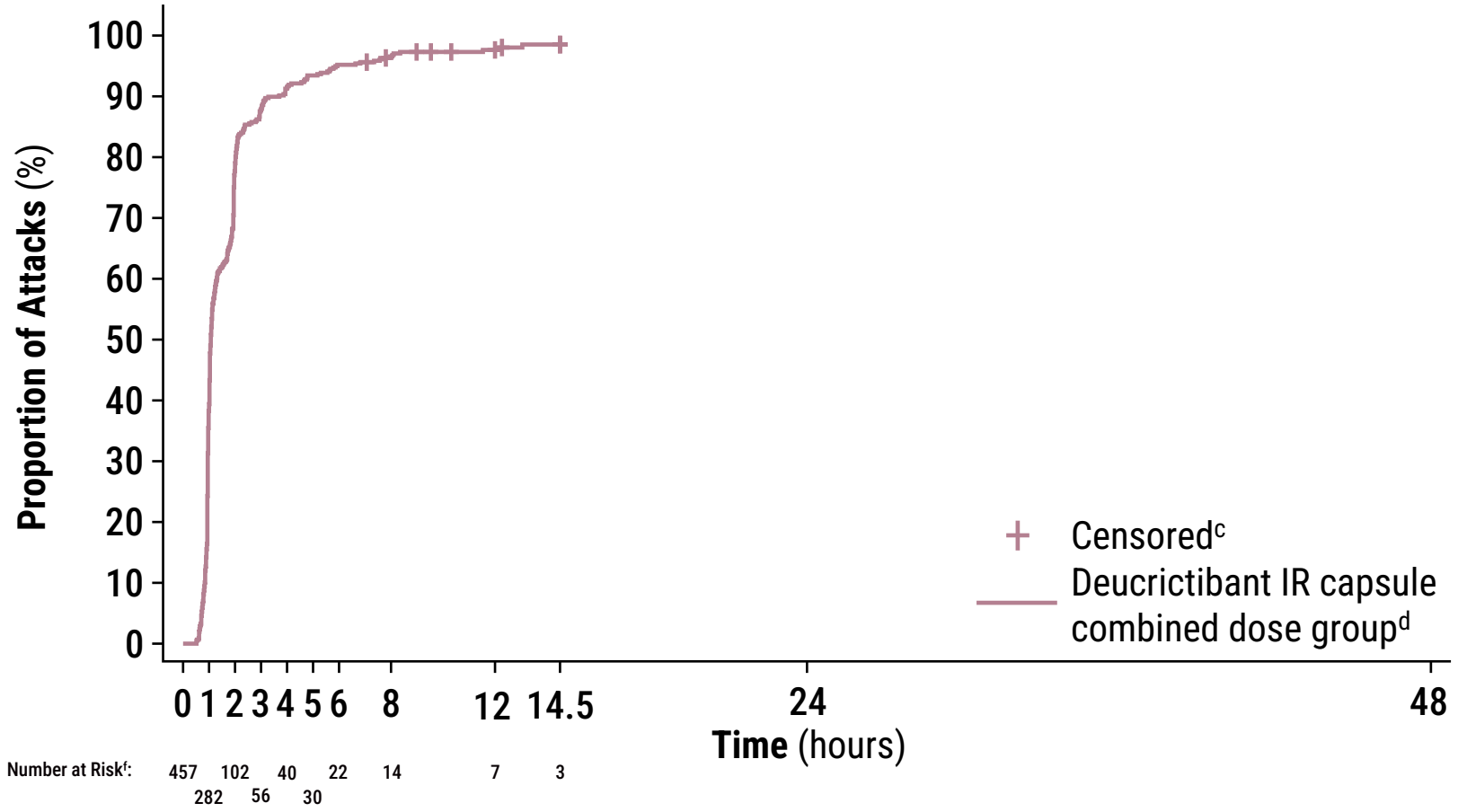
- No treatment-related TEAEs.
- No treatment-related serious or severe TEAEs.
- No treatment-related TEAEs in laboratory parameters, vital signs, or ECG findings.
- No TEAEs leading to treatment discontinuation, study withdrawal, or death.

ECG, electrocardiogram; 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]Deucrictibant IR capsule 10, 20 and 30 mg. [b]Tooth caries unrelated to treatment. Data for combined dose group shown (deucrictibant 10mg, 20mg and 30mg).

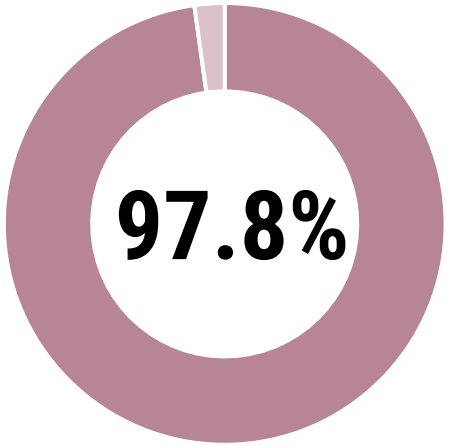
This presentation includes data for an investigational product not yet approved by regulatory authorities.

1.1 hours median time to onset of symptom relief

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]



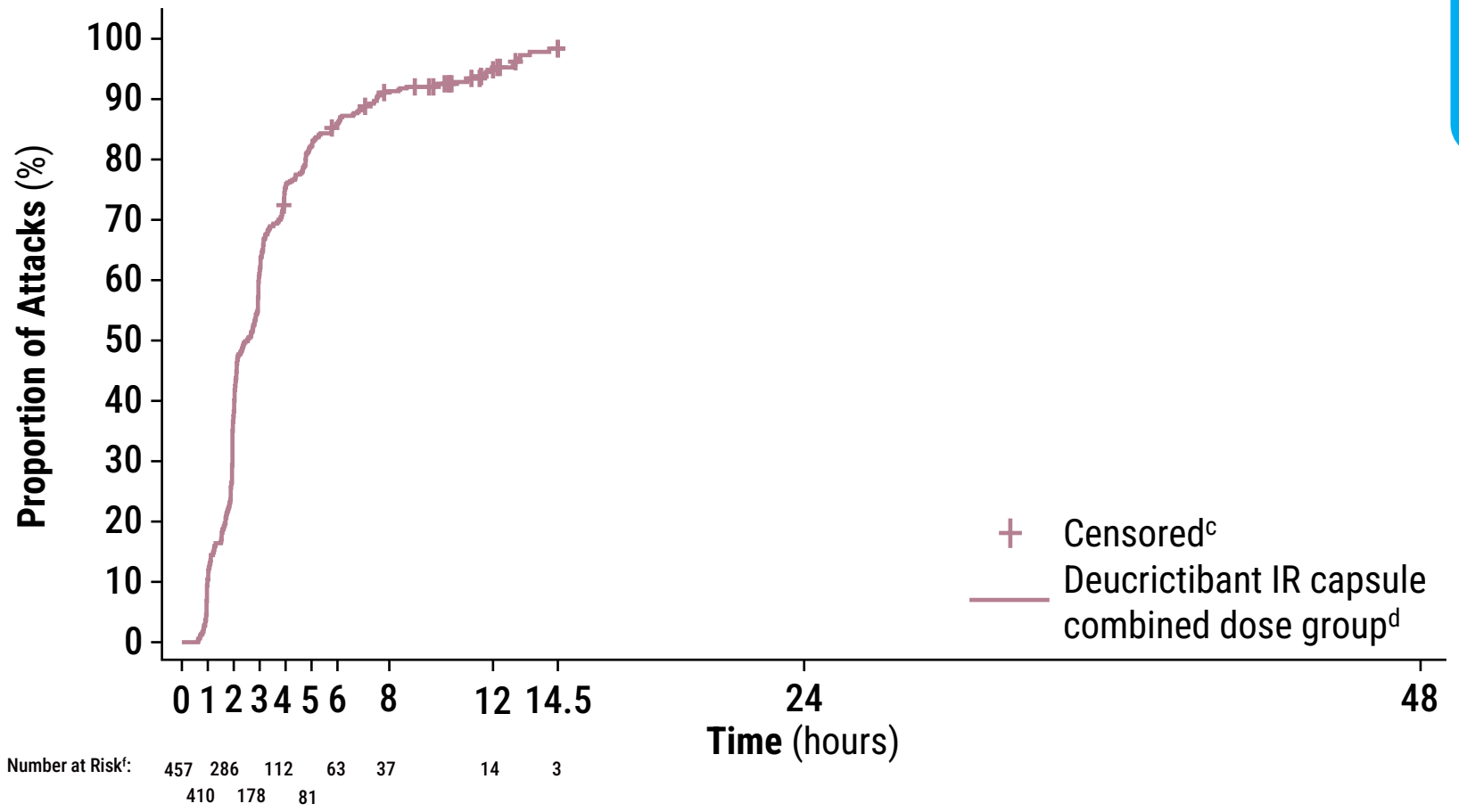
of attacks achieved **onset of symptom relief by 12 hours** (447/457[e])

CI, confidence interval; IR, immediate-release; PGI-C, Patient Global Impression of Change. [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.

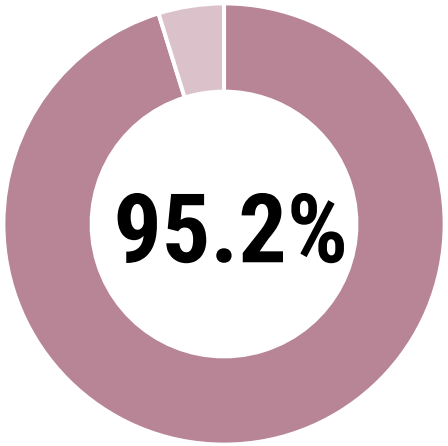
This presentation includes data for an investigational product not yet approved by regulatory authorities.

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



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



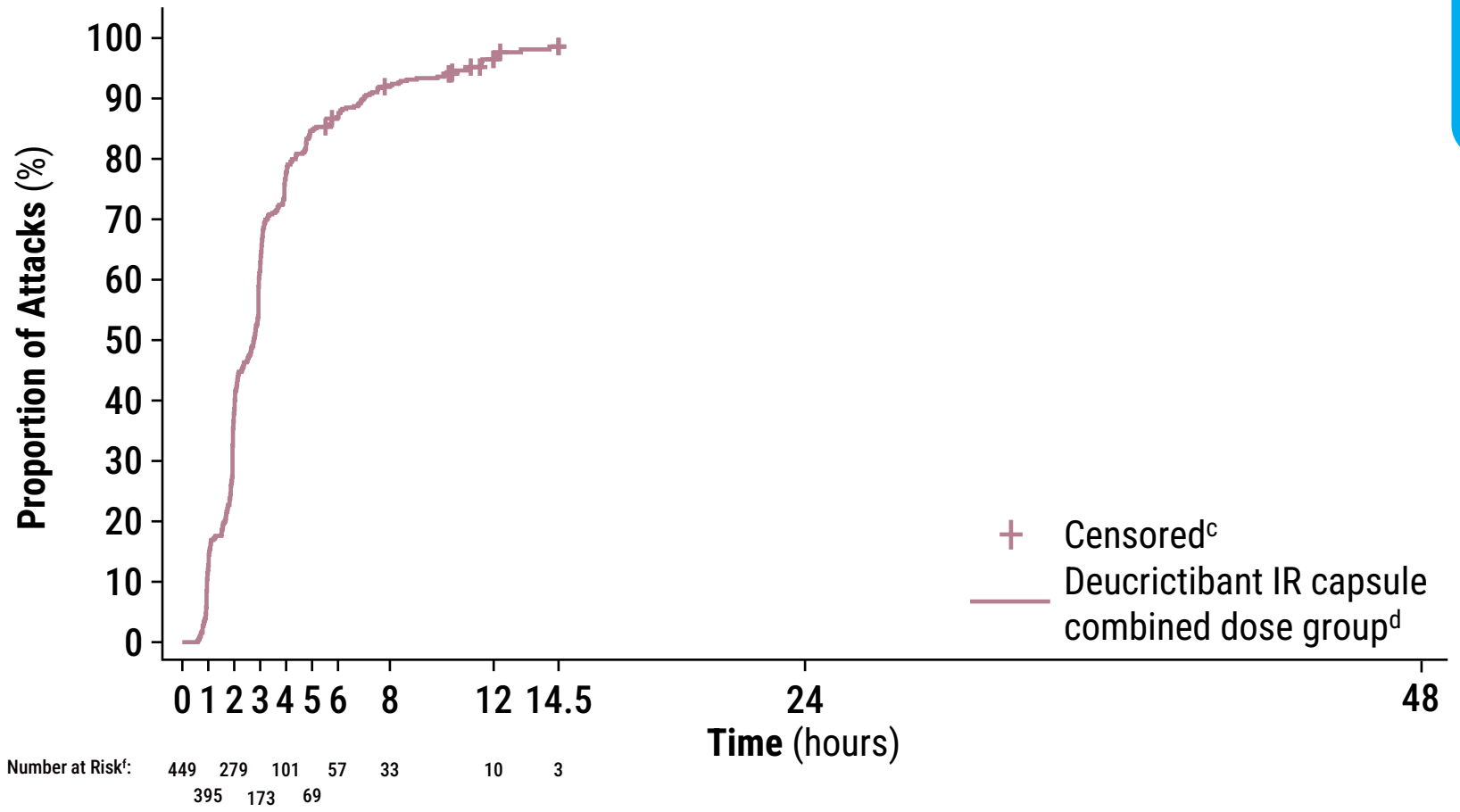
of attacks achieved **substantial symptom relief by 12 hours** (435/457[e])

CI, confidence interval; IR, immediate-release; PGI-C, Patient Global Impression of Change. [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.

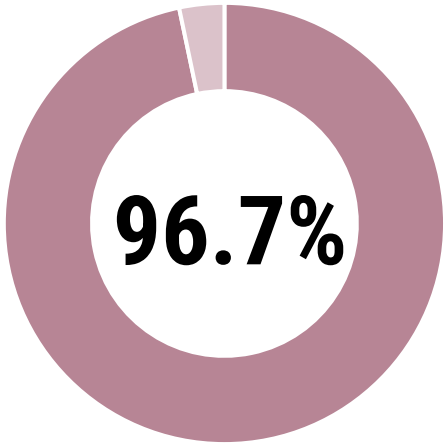
This presentation includes data for an investigational product not yet approved by regulatory authorities.

2.8 hours median time to reduction in attack severity

≥1-level reduction in 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]



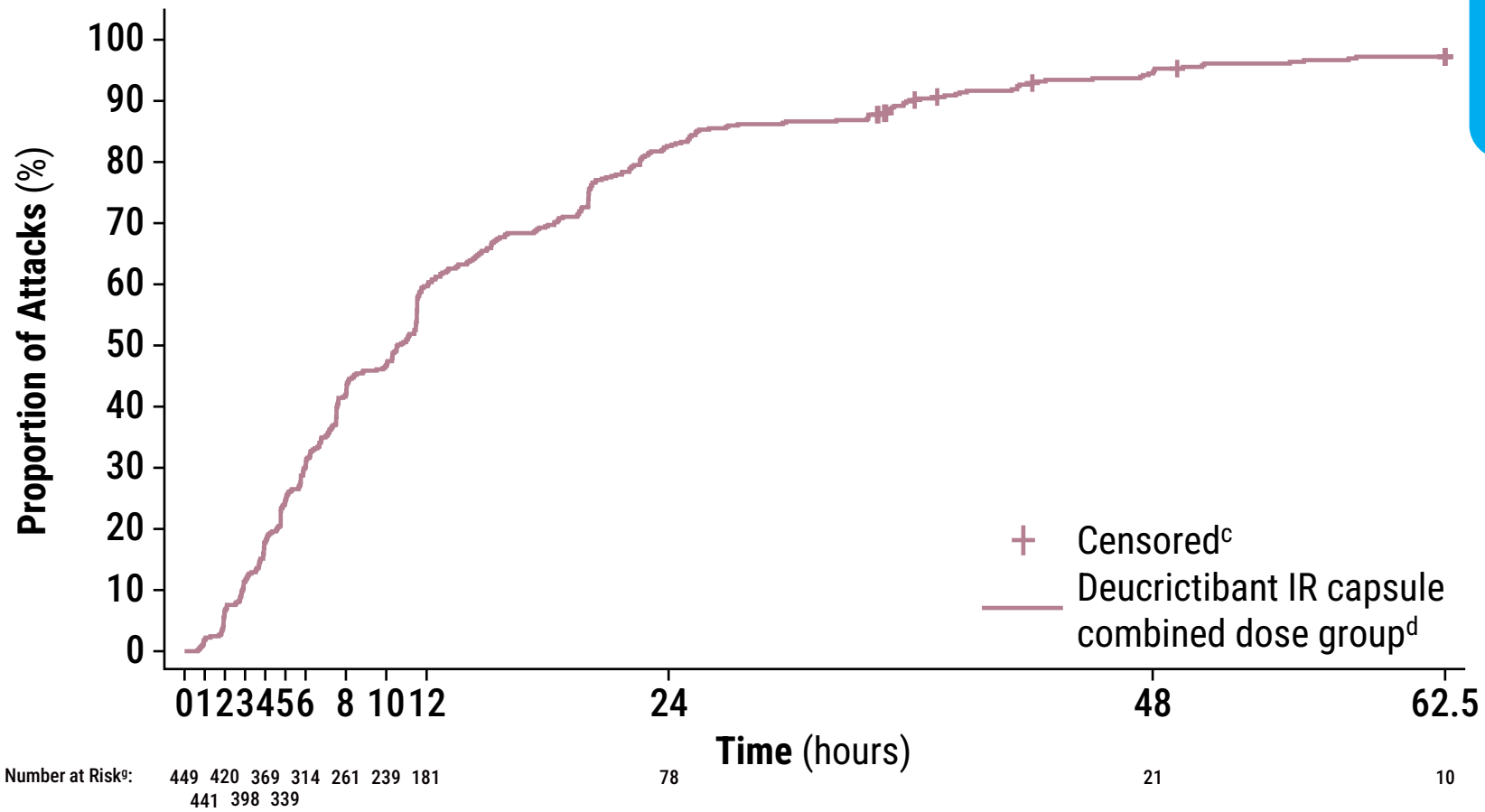
of attacks achieved **reduction in attack severity by 12 hours** (434/449[e])

CI, confidence interval; IR, immediate-release; PGI-S, Patient Global Impression of Severity. [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.

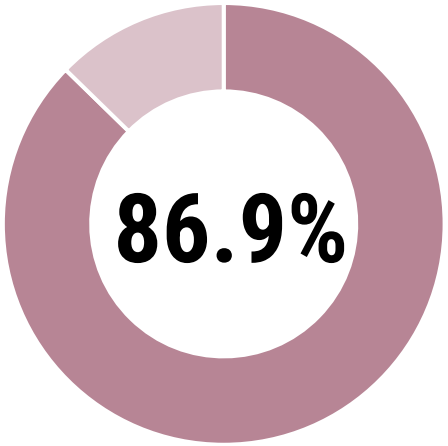
This presentation includes data for an investigational product not yet approved by regulatory authorities.

10.6 hours median time to complete attack resolution

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



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; PGI-S, Patient Global Impression of Severity. [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.

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

Upper airway attacks: Similar times to symptom relief and resolution for upper airway and other attacks

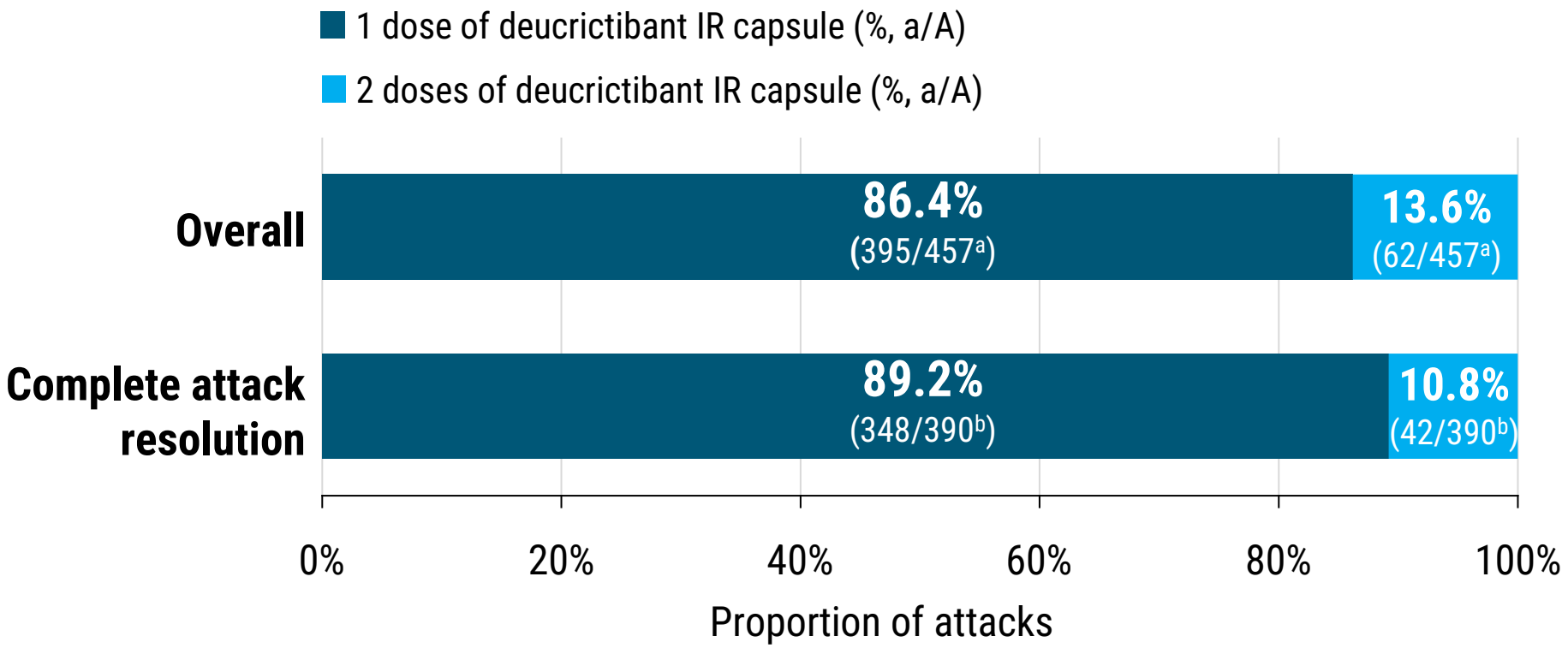
For more details, please see
Lleonart R, et al.
May 31st, Poster Session II, P55

	Upper airway attacks (n=7)	Non-upper airway attacks in participants with upper airway attacks (n=7)	Total non-upper airway attacks (n=19)
Total number of attacks treated[a]	14	177	451
Time to onset of symptom relief[b]			
Number of attacks[c]	14	171	443
Median hours (95% CIs)	**1.4** (0.8, 3.0)	**1.0** (1.0, 1.2)	**1.1** (1.0, 1.1)
Time to substantial symptom relief[b]			
Number of attacks[c]	14	171	443
Median hours (95% CIs)	**3.6** (2.0, 6.1)	**2.7** (2.1, 3.0)	**2.4** (2.1, 2.8)
Time to reduction in attack severity[b]			
Number of attacks[d]	12	169	437
Median hours (95% CIs)	**1.8** (0.9, 3.0)	**2.1** (2.0, 2.8)	**2.8** (2.4, 2.9)
Time to complete attack resolution[b]			
Number of attacks[d]	12	169	437
Median hours (95% CIs)	**8.9** (3.9, 36.3)	**8.0** (7.3, 10.7)	**10.6** (8.5, 11.5)

CI, confidence interval; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]465 attacks treated by 19 participants. [b]Within-participant correlation not accounted for in all Kaplan-Meier estimates. [c]Evaluable attacks include deucrictibant-treated attacks with ≥1 post-treatment PGI-C assessment. [d]Evaluable attacks included deucrictibant-treated attacks with a pre- and ≥1 post-treatment PGI-S assessment.

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

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



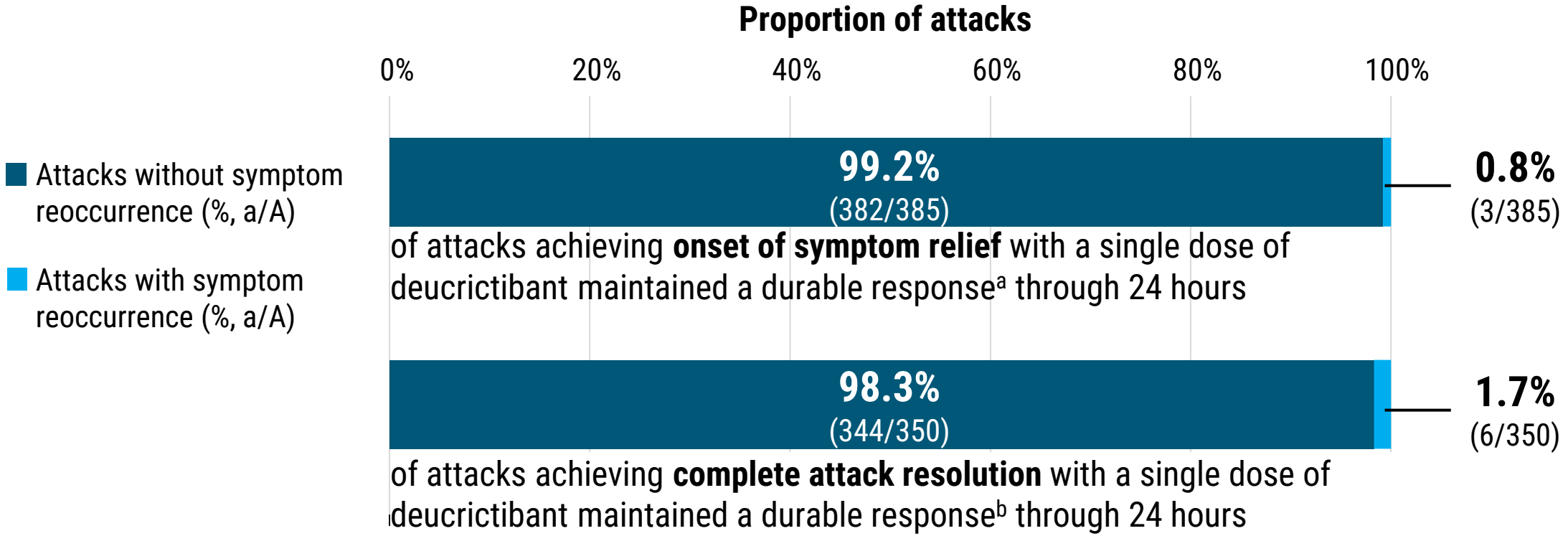
IR, immediate-release; PGI-S, Patient Global Impression of Severity. A= number of attacks. Data for combined dose group shown (deucrictibant 10mg, 20mg and 30mg). [a]Proportion of attacks that were not treated with rescue medication within 24 hours post-treatment; 8 attacks used rescue medication within 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.

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

Over 98% of attacks that achieved symptom relief or resolution with a single dose of deucrictibant had a durable response without symptom reoccurrence

For more details, please see **Valerieva A, et al. May 31st, Poster Session II, P56**

Following the achievement of each pre-defined efficacy milestone, symptom reoccurrence was evaluated as any instance where the milestone was no longer being met within 24 hours post-treatment.



PGI-C, patient global impression of change; PGI-S, patient global impression of severity. A= number of study-drug treated attacks that achieved the efficacy milestone with a single dose of deucritibant. [a]defined as PGI-C rating remaining 'same' or better within 24 hrs after reaching 'a little better' for two consecutive timepoints within 12 hrs post-treatment. [b]defined as PGI-S rating remaining as 'none' within 24 hrs after reaching 'none' within 24 hrs post-treatment. Combined dose group data shown (deucrictibant 10mg, 20mg and 30mg).

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

Conclusions

For more details, please see following posters at **Session II on May 31st :**
- Lleonart R, et al. RAPIDe-2 upper airway attack outcomes. **Poster P55**
- Valerieva A, et al. RAPIDe-1/2 durability of treatment response. **Poster P56**

Final results from Part A of the RAPIDe-2 extension are consistent with the Phase 2 RAPIDe-1 study and provide evidence on the long-term safety and efficacy of deucrictibant IR capsule for treatment of repeat HAE attacks.

Deucrictibant was generally well tolerated with no treatment related TEAEs

1.1 Hours
Median time to onset of symptom relief

97.8%
of attacks achieved onset of symptom relief by 12 hours

89%
of attacks that achieved attack resolution were treated with a single dose of deucrictibant

10.6 Hours
Median time to complete attack resolution

86.9%
of attacks achieved complete attack resolution 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 RAPIDe-2 study.

HAE, hereditary angioedema; IR, immediate-release; TEAE, treatment-emergent adverse event.

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