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

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

Conflicts of interest disclosure

S.K.-A.: BioCryst, Biotest, CSL Behring, Ionis, KalVista, Pharvaris, Takeda, Otsuka; **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.:** no conflicts of interests to disclose relative to this work; **M.Sto.:** BioCryst, CSL Behring, KalVista, Pharming, Takeda; **A.V.:** AstraZeneca, Berlin-Chemie/Menarini Group, CSL Behring, KalVista, Novartis, Pharming, Pharvaris, Sobi, Takeda; **G.G., Y.L., P.L., J.S., M.Y.:** employees of Pharvaris, holds stocks/stock options in Pharvaris; **M.A.R.:** Astria, BioCryst, BioMarin, Celldex, CSL Behring, Cycle Pharma, Grifols, Intellia, Ionis, KalVista, Novartis, Pharming, Pharvaris, Sanofi-Regeneron, Takeda

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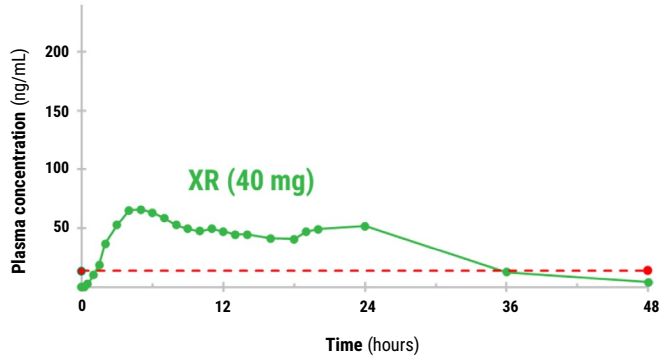
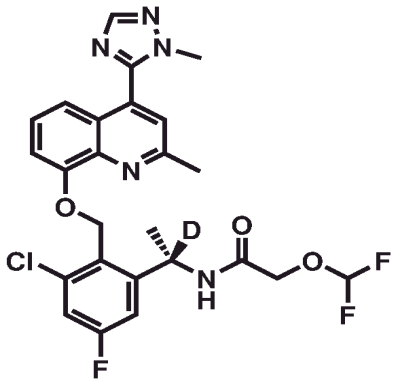
Deucrictibant is an investigational oral therapy for both the prophylactic and on-demand treatment of HAE attacks

DEUCRICTIBANT extended-release (XR) tablet

sustained absorption[1]



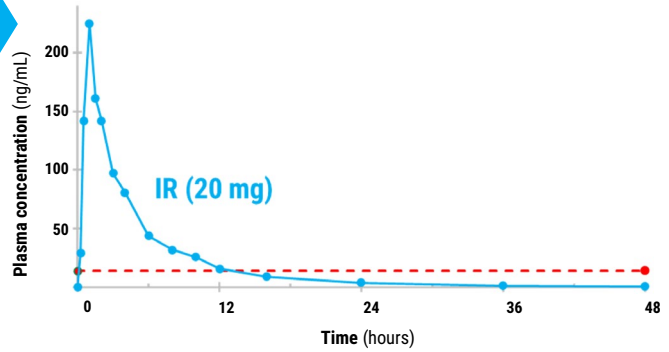
In studies, deucrictibant maintained sustained therapeutic exposure over 24 hours[1] from day 1, allowing for once-daily oral prevention HAE attacks[2]



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 October 28, 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 October 28, 2025. https://www.clinicaltrials.gov/study/NCT06343779.

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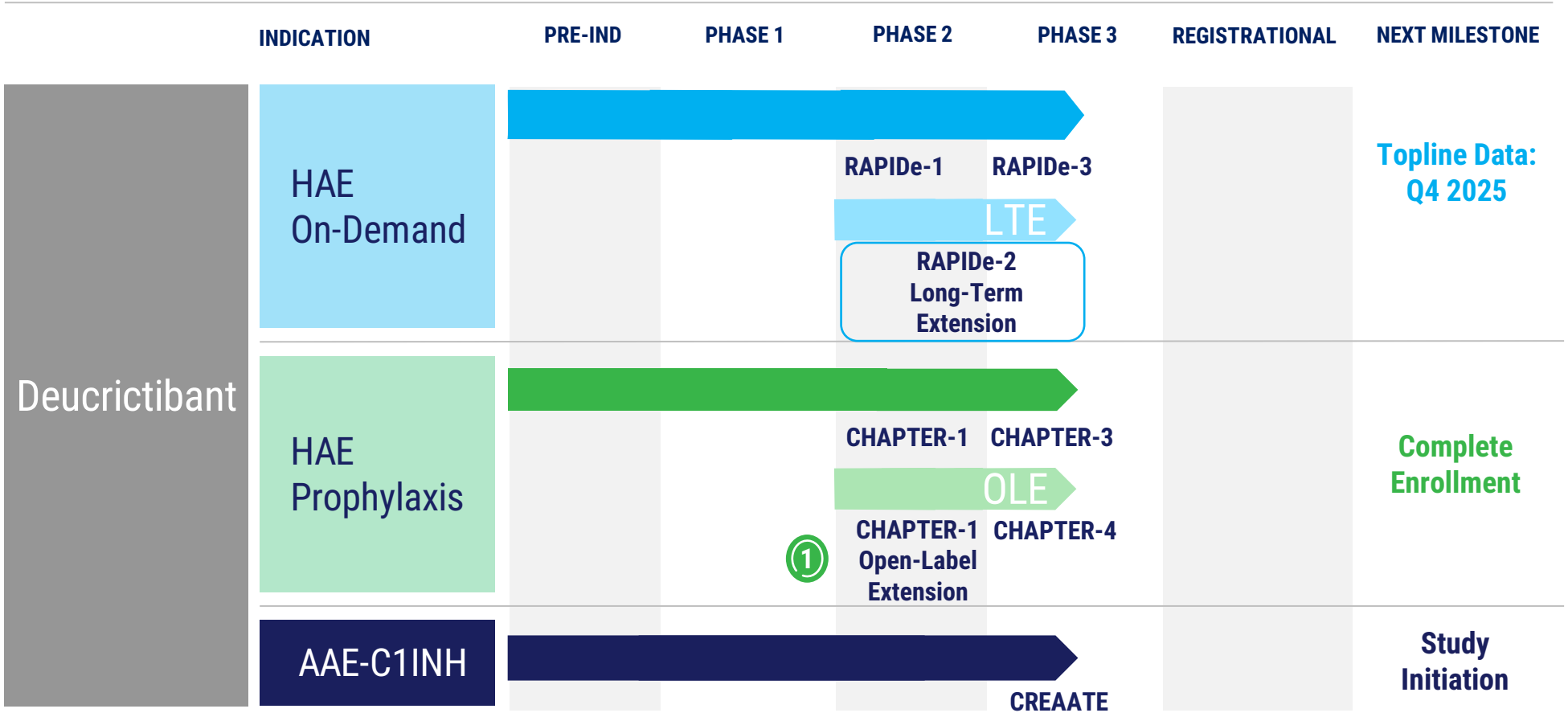
Deucrictibant development program in bradykinin-mediated angioedema



Poster presentation at BSI-CIPN: Dec 1 at 15:45-16:30

① Gurugama P, et al. CHAPTER-1 OLE Topline data

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, NCT04618211; RAPIDe-2, NCT05396105; RAPIDe-3, NCT06343779; CHAPTER-1, NCT05047185; CHAPTER-3, NCT06669754; CHAPTER-4, NCT06679881.

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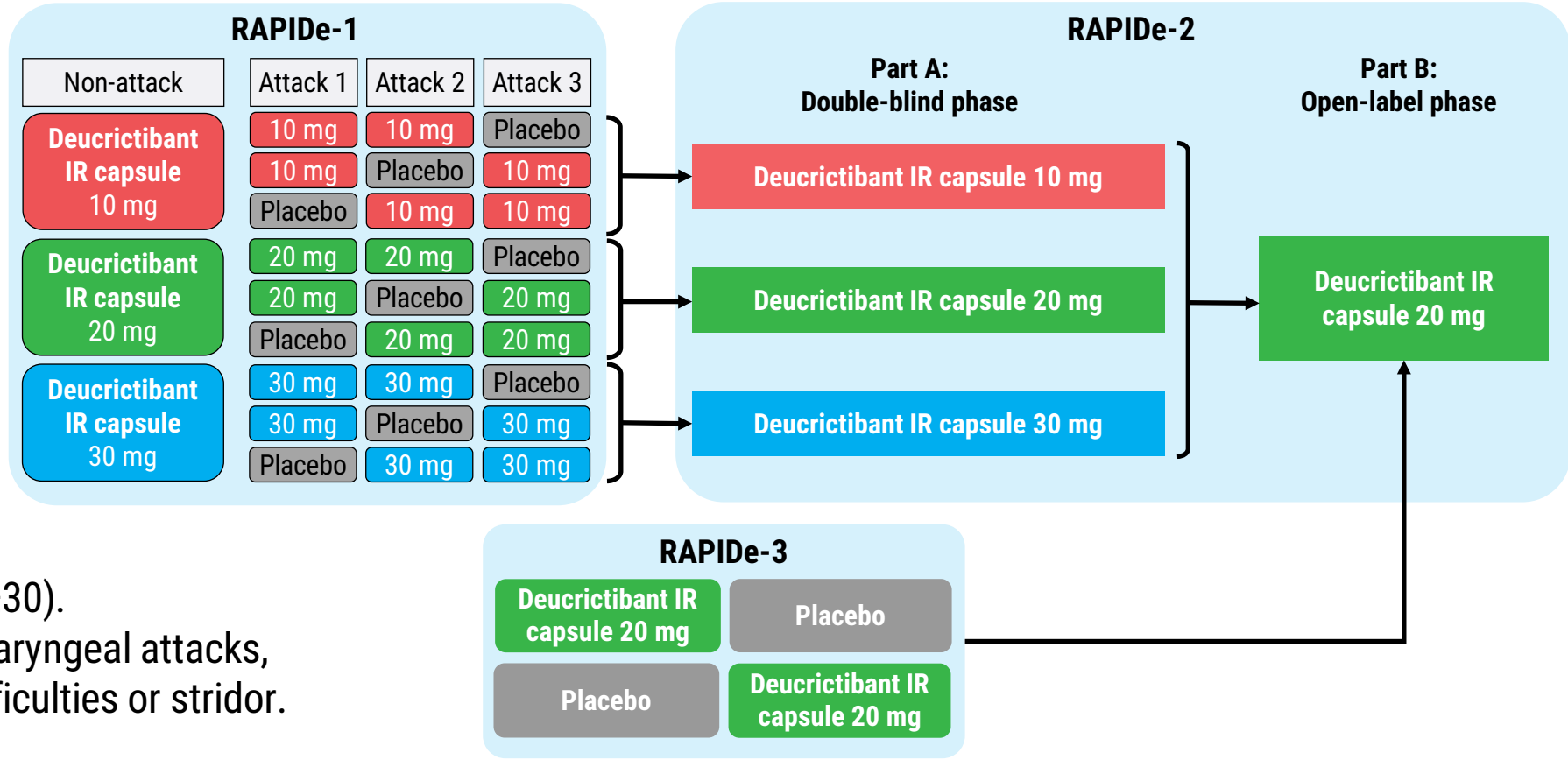
RAPIDe-2: a two-part, Phase 2/3 long-term extension study of deucrictibant for on-demand treatment of repeat HAE attacks

- **RAPIDe-2 Part A:** enrolled adult (aged ≥18 years) participant who completed RAPIDe-1 (NCT04618211).
- **Deucrictibant:** participants continued 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 score ≥30).
  - upper airway attacks, including laryngeal attacks, presenting without breathing difficulties or stridor.



AMRA-3, three symptom Angioedema syMptom Rating scAle; HAE, hereditary angioedema; IR, immediate-release. RAPIDe-1, ClinicalTrials.gov identifier: NCT04618211. Accessed October 28, 2025. https://www.clinicaltrials.gov/study/NCT04618211. RAPIDe-2, ClinicalTrial.org identifier NCT05396105. Accessed October 28, 2025. https://clinicaltrials.gov/study/NCT05396105.

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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.

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.

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Participant characteristics and HAE attacks

Participant characteristics	Deucrictibant IR capsule (Combined dose group[a]) (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[b] were similar to the final RAPIDe-1 Phase 2 trial population.

- 465 attacks from 19 participants included in the mITT efficacy[c] and safety[a] 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 received any dose of deucrictibant in the study. [b]Study baseline refers to results at the screening or enrollment 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 enrollment 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. [c]All participants who had ≥1 attack treated with deucrictibant and non-missing PGI-C results from ≥1 post-treatment timepoint.

Deucrictibant IR capsule well tolerated across all doses

TEAEs within 3 days of study drug administration

Adverse events	Deucrictibant IR capsule (Combined dose group) (N=19; A=465)
Attacks with any TEAE, a (%)	12 (2.6)
Treatment-related TEAEs, a	0
Serious TEAEs, a	1[a]
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.

A, number of treated attacks; a, number of treated attacks with an event; ECG, electrocardiogram; IR, immediate-release; N, number of participants; TEAE, treatment-emergent adverse event, defined as adverse event occurring from first study drug administration. [a]Tooth caries unrelated to treatment. Data for combined dose group shown (deucrictibant 10 mg, 20 mg, and 30 mg).

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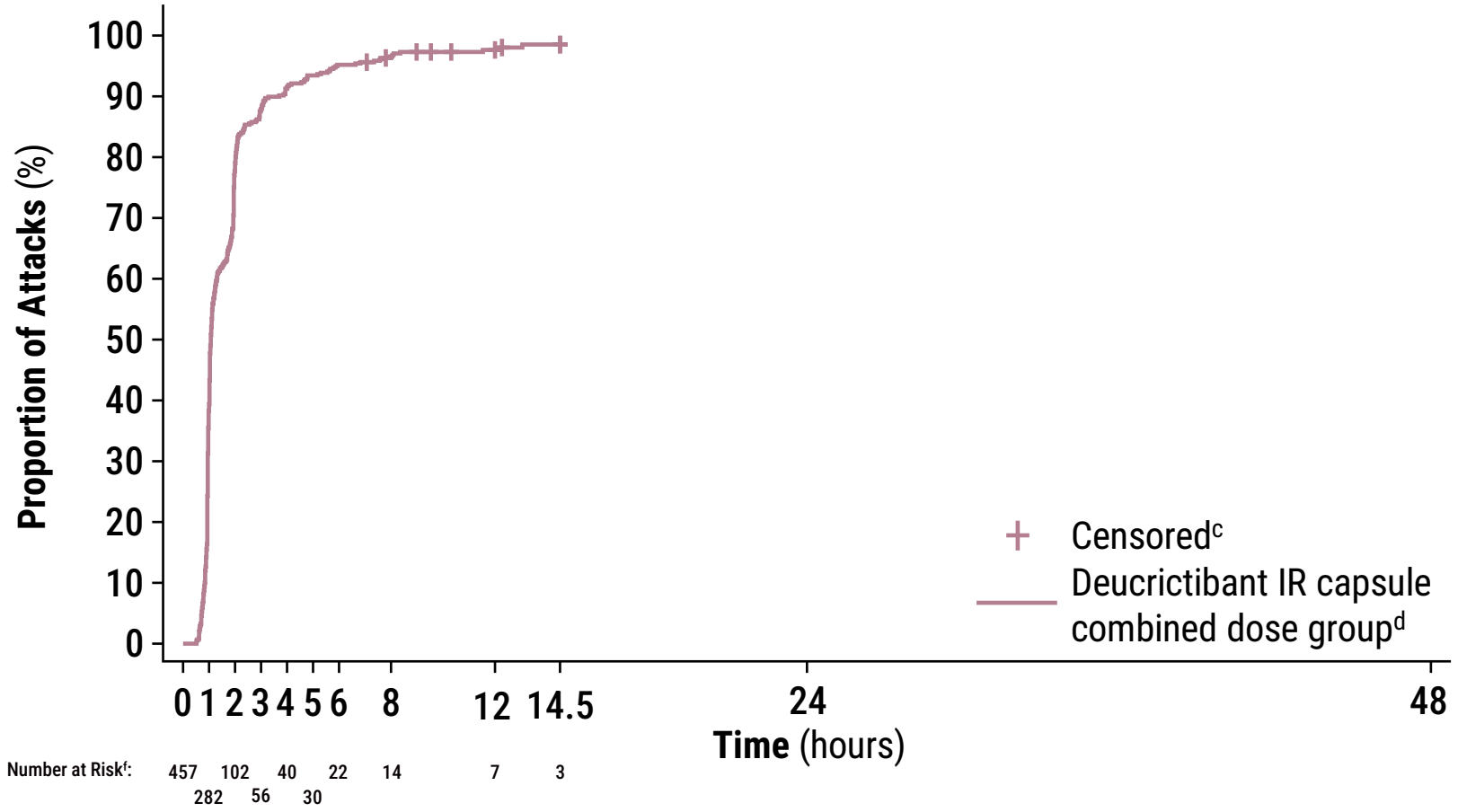
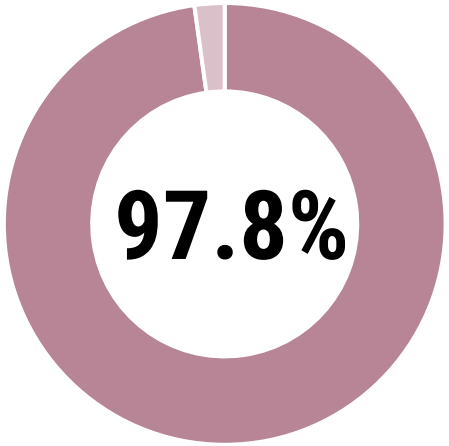
1.1 hours median time to onset of symptom relief

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]PGI-C rating of at least “a little better” for 2 consecutive timepoints by 12 hours post-treatment, 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 ≥1 post-treatment PGI-C result. [f]Pooled evaluable attacks.

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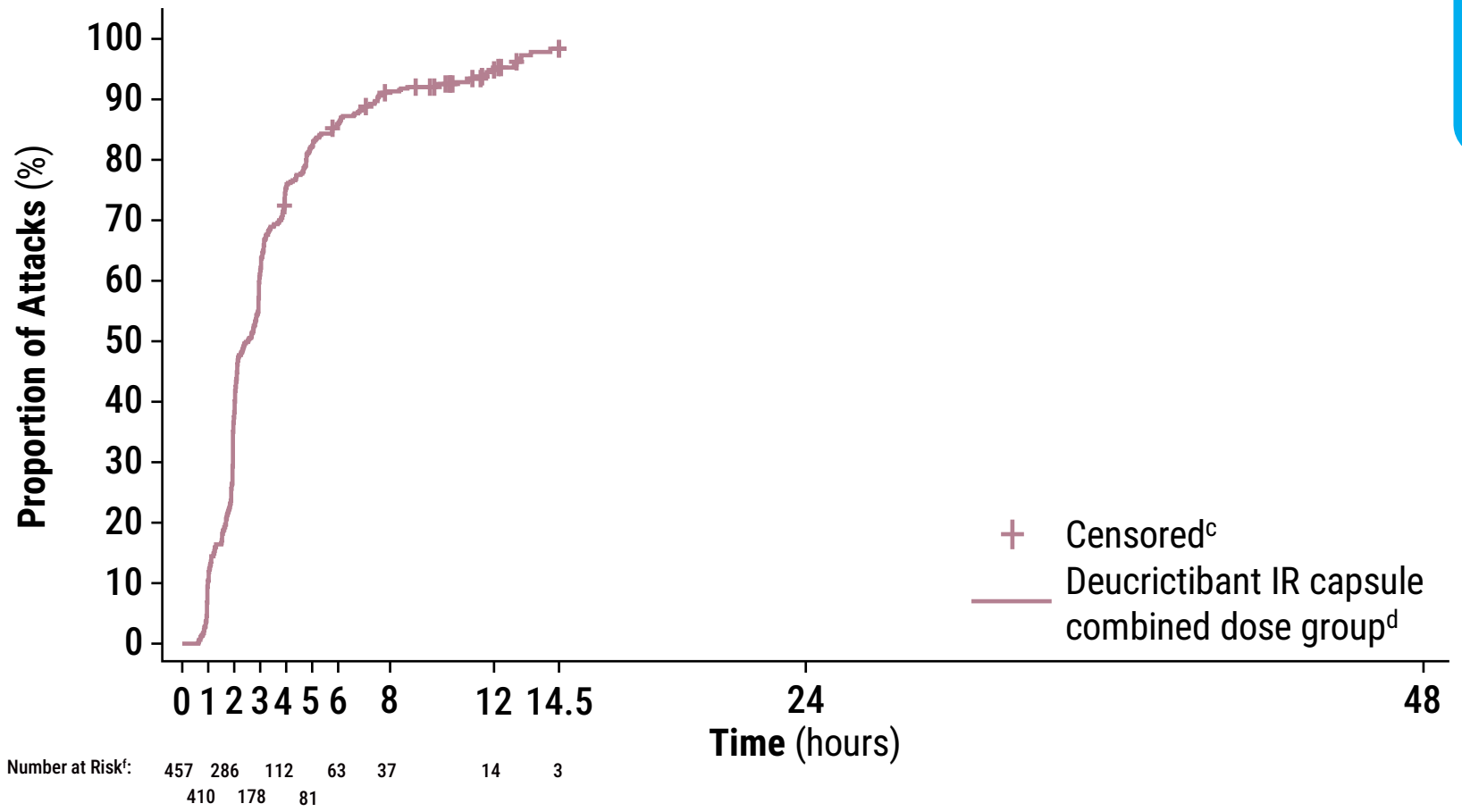
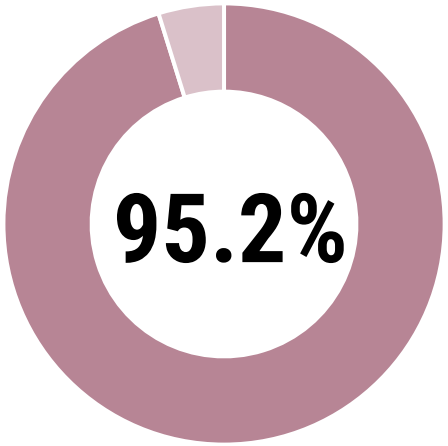
2.5 hours median time to substantial symptom relief

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



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]PGI-C rating of at least "better" for 2 consecutive timepoints by 12 hours post-treatment, 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 ≥1 post-treatment PGI-C result. [f]Pooled evaluable attacks.

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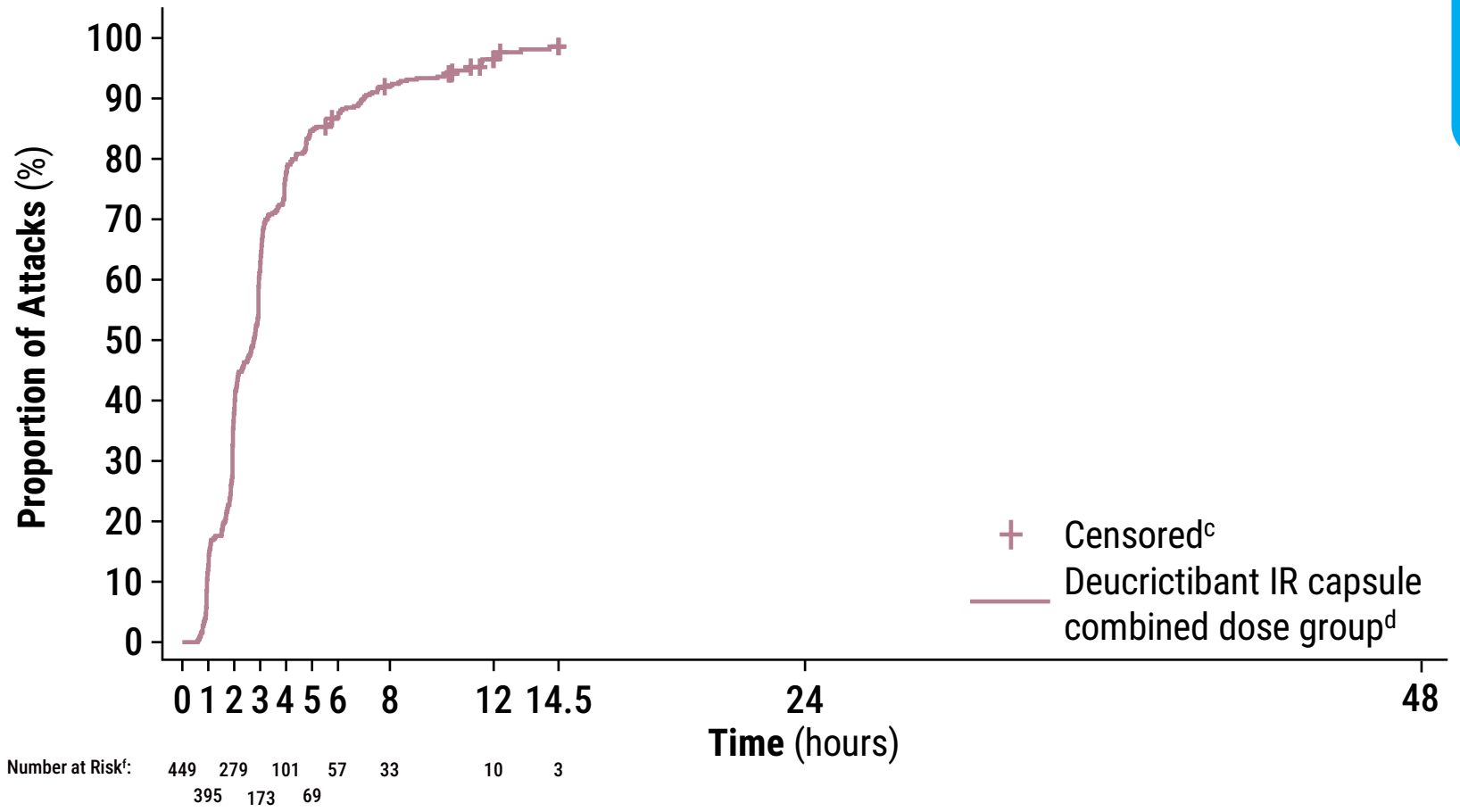
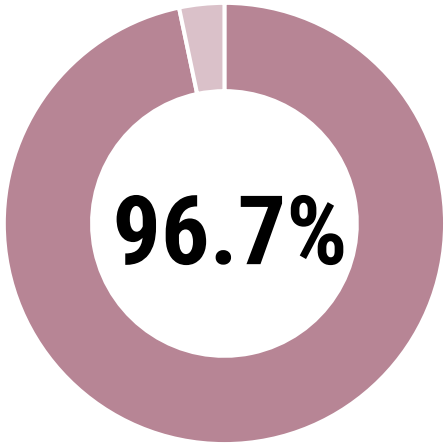
2.8 hours median time to reduction in attack severity

≥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]≥1-level reduction in PGI-S from pre-treatment for 2 consecutive timepoints by 12 hours post-treatment 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 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 ≥1 post-treatment PGI-S. [f]Pooled evaluable attacks.

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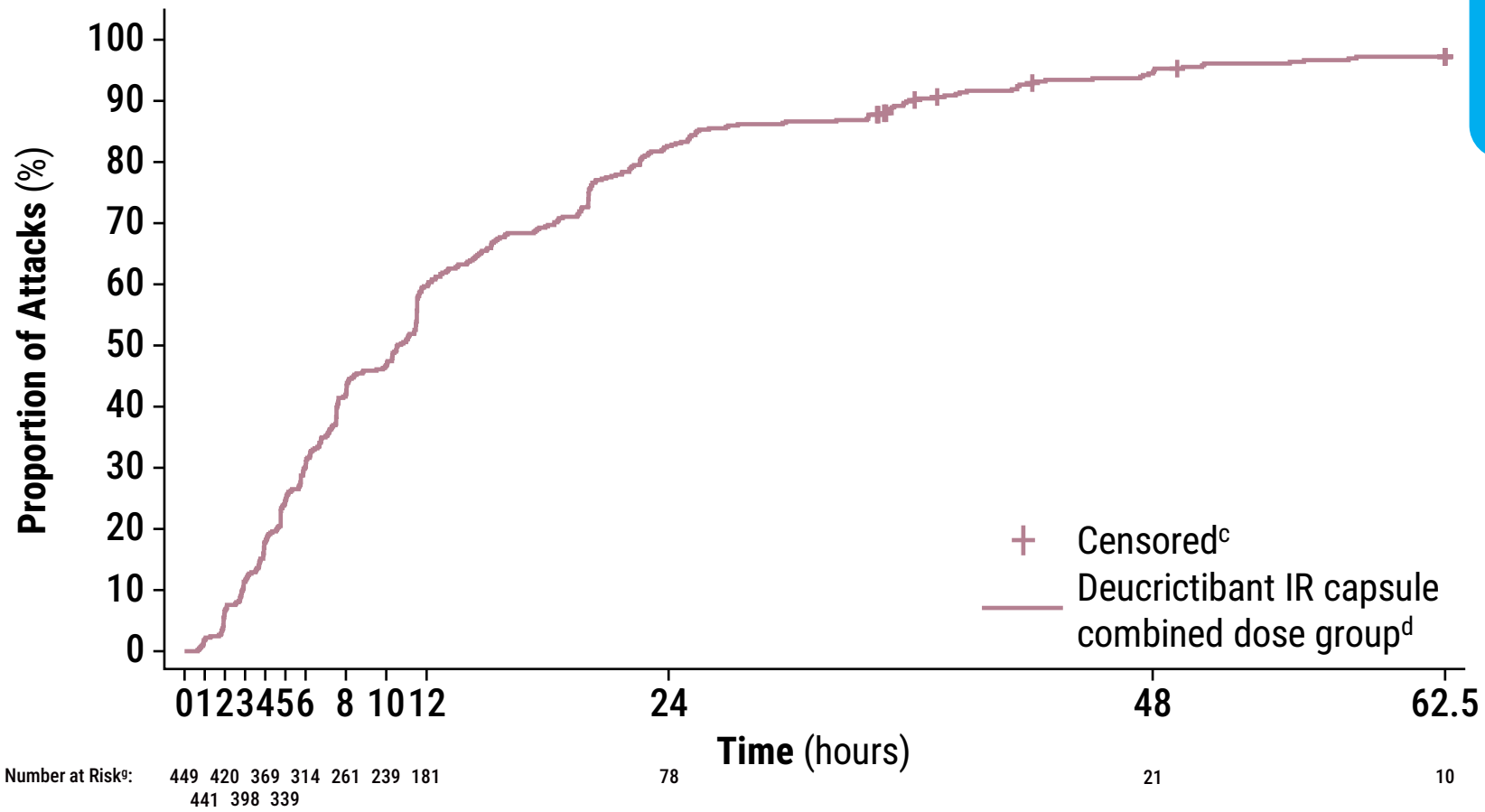
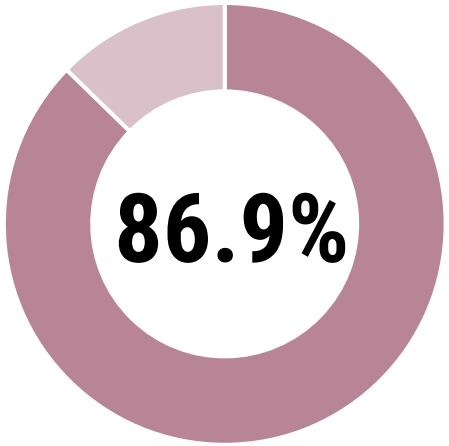
10.6 hours median time to complete attack resolution

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]PGI-S rating of “none” within 48 hours post-treatment 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 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 achieved at the last available timepoint before or at 24 hours post-treatment without rescue medication use. [f]449 attacks have non-missing pre-treatment PGI-S and at ≥1 post-treatment PGI-S. [g]Pooled evaluable attacks.

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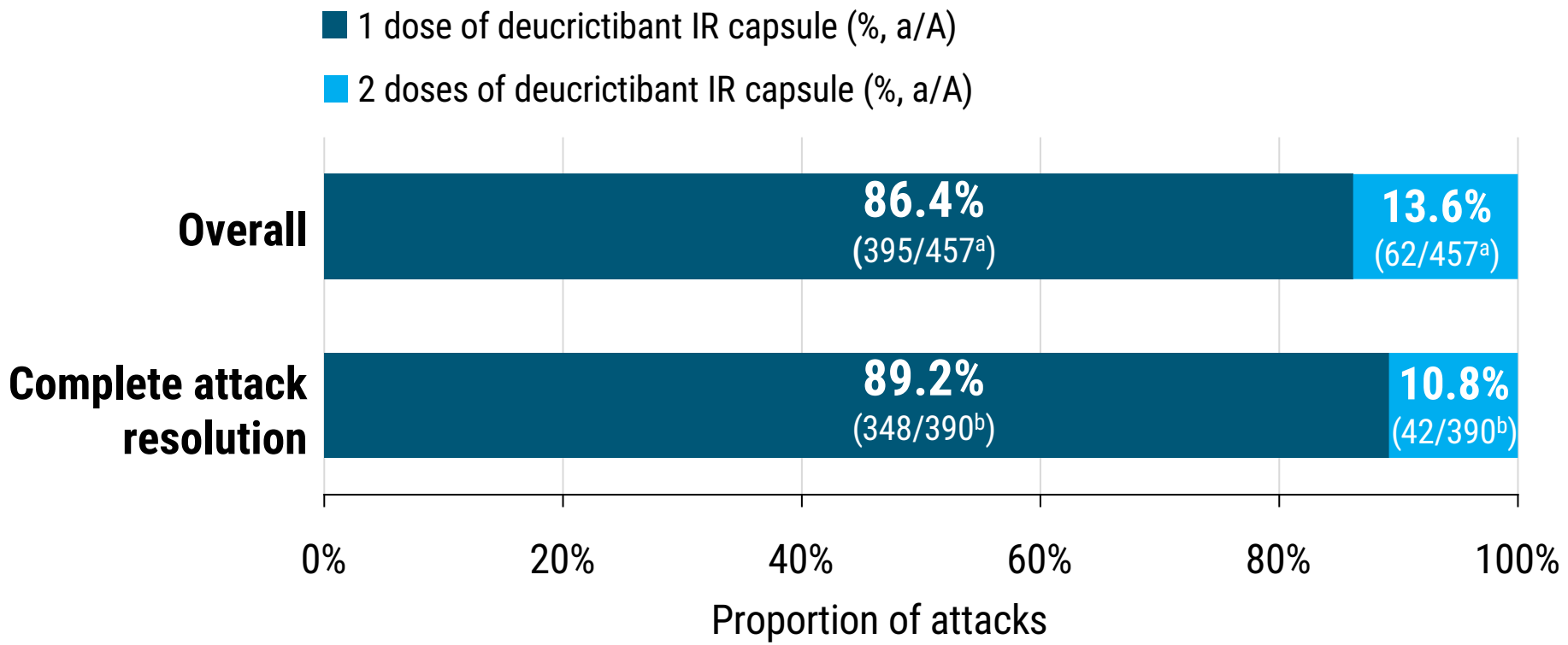
Majority of attacks treated with a single dose of deucrictibant and without rescue medication at 24 hours



A, number of attacks; a, number of evaluable attacks with an event; IR, immediate-release; PGI-S, Patient Global Impression of Severity. Data for combined dose group shown (deucrictibant 10 mg, 20 mg, and 30 mg). [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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Conclusions

Final results from Part A of the RAPIDe-2 extension study are consistent with the Phase 2 RAPIDe-1 study and provide further 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

of attacks that achieved complete resolution at 24 hours were treated with a single dose of deucrictibant

10.6 Hours

Median time to complete attack resolution

86.9%

of attacks achieved complete symptom 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.

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