

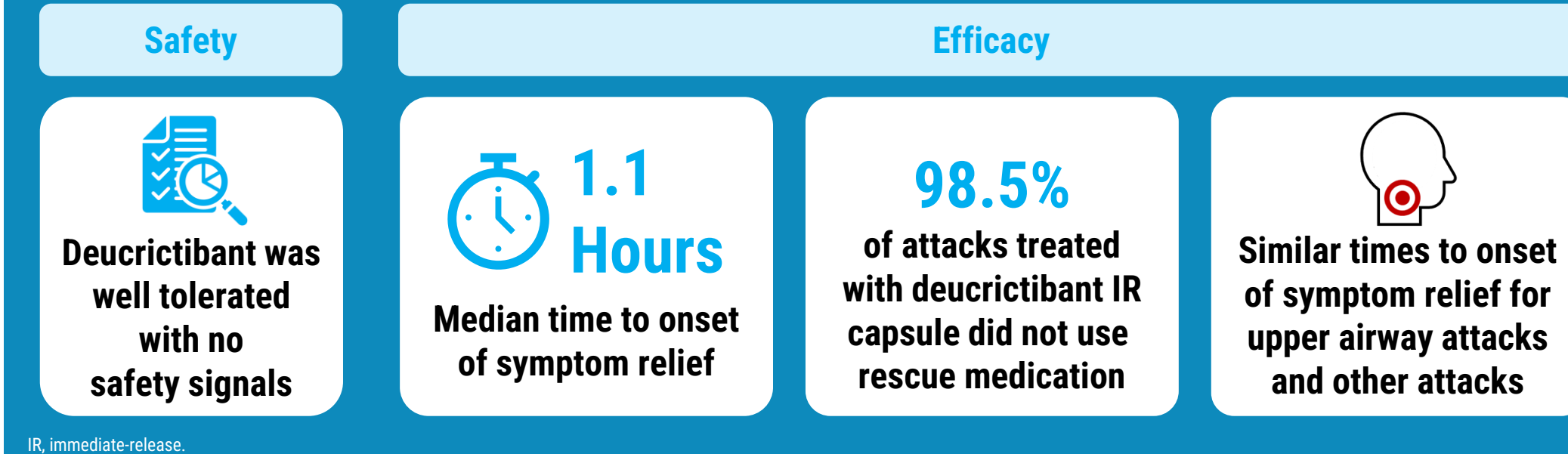
Long-Term Safety and Efficacy of Oral Deucricitbant for Treatment of Hereditary Angioedema Attacks: Results of the RAPiDe-2 Extension Study

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Key takeaways

The ongoing Phase 2/3 RAPiDe-2 extension study provides evidence on the long-term safety and efficacy of deucricitbant immediate-release (IR) capsule for on-demand treatment of repeat hereditary angioedema (HAE) attacks.



Background

- Hereditary angioedema (HAE):** a bradykinin-mediated condition with painful swelling attacks affecting multiple locations in the body.¹
- Current landscape:** guidelines recommend HAE attacks are treated as early as possible.²⁻⁴ Parenteral administration often leads to on-demand treatment of HAE attacks being delayed or forgone.⁵⁻¹⁴
- Oral deucricitbant:** a selective, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of HAE attacks.¹⁵⁻²²

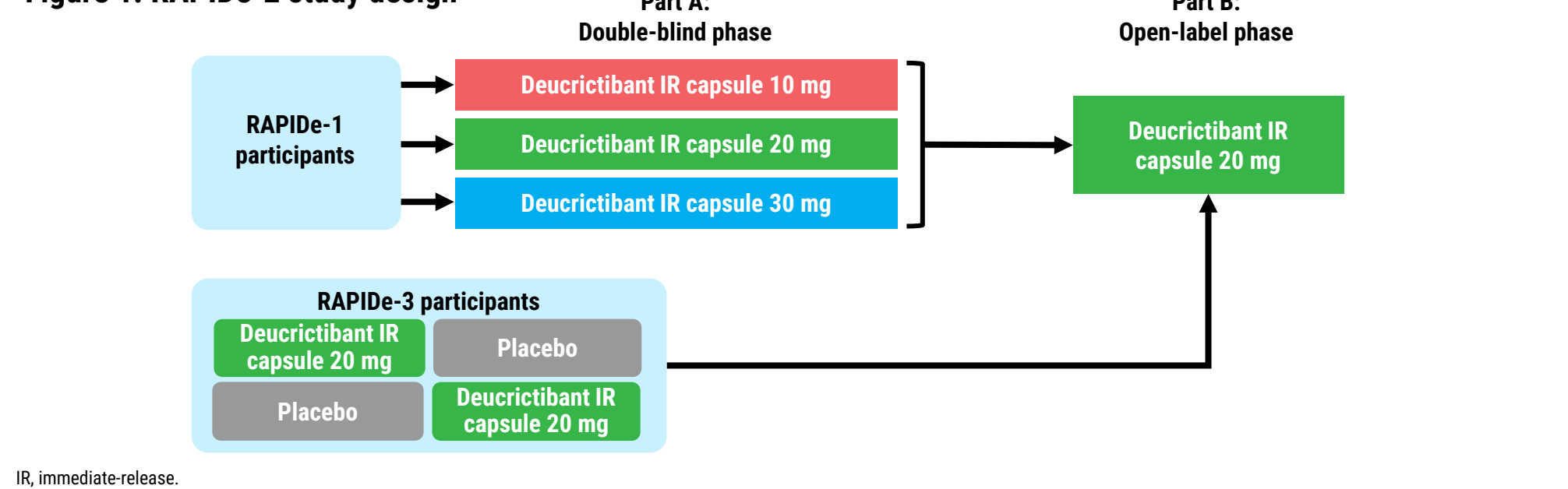
Objective

Evaluate the long-term safety and efficacy of deucricitbant IR capsule for on-demand treatment of repeat HAE attacks in the RAPiDe-2 extension study.

Methods

- RAPiDe-2 (NCT05396105)*:** a two-part, double-blind Phase 2/3 extension study.¹⁷
- Part A eligible participants:** adults who completed RAPiDe-1 (NCT04618211).¹⁵
- Part A prophylaxis:** no long-term HAE prophylaxis treatment is allowed. Recent use of long-term HAE prophylaxis treatment prior to screening is allowed provided a pre-specified washout period is observed.

Figure 1. RAPiDe-2 study design



COI: Research grant support, consultancy fees, speaker fees, advisory board, investigator, and/or clinical trial fees - M.E.M.: Allakos, Amgen, AstraZeneca, BioCryst, Blueprint, CSL Behring, Cycle Pharma, Genentech, GSK, KalVista, Merck, Novartis, Pharming, Pharvaris, Sanofi/Regeneron, Takeda; J.A.: BioCryst, BioMarin, CSL Behring, Cycle Pharma, KalVista, Pharming, Pharvaris, Takeda; E.A.P.: Astria, BioCryst, BioMarin, CSL Behring, Intellia, KalVista, Pharming, Pharvaris, Takeda; L.B.: BioCryst, Blueprint, CSL Behring, Novartis, Takeda; H.C.: AstraZeneca (Alexion), CSL Behring, KalVista, Merck, Novartis, Pharming, Pharvaris, Roche, Sanofi, Sobri, Takeda; H.F.: BioCryst, CSL Behring, Intellia, KalVista, ONO Pharmaceutical, Pharming, Pharvaris, Takeda; D.G.: Pharming, Takeda; R.H.: BioCryst, CSL Behring, KalVista, Pharming, Pharvaris, Takeda; J.S.J.: BioCryst, CSL Behring, Cycle Pharma, Oasis, Pharming, Pharvaris, Takeda; R.L.: BioCryst, CSL Behring, Ionis, KalVista, Novartis, Pharming, Pharvaris, Stalergens, Takeda, Teva; G.S.: Pharvaris, Takeda; M.Sta.: none; M.Sto.: BioCryst, CSL Behring, KalVista, Pharming, Takeda; A.V.: AstraZeneca, Berlin-Chemie/Menarini Group, CSL Behring, KalVista, Novartis, Pharming, Pharvaris, Sobri, Takeda; J.S., L.Z., M.Y., G.G.: employees of Pharvaris, hold stocks in Pharvaris; P.L.: employee of Pharvaris, holds stocks/stock options in Pharvaris; M.M.: Adverum, Attune, BioCryst, CSL Behring, KalVista, Pharming, Pharvaris, Takeda.

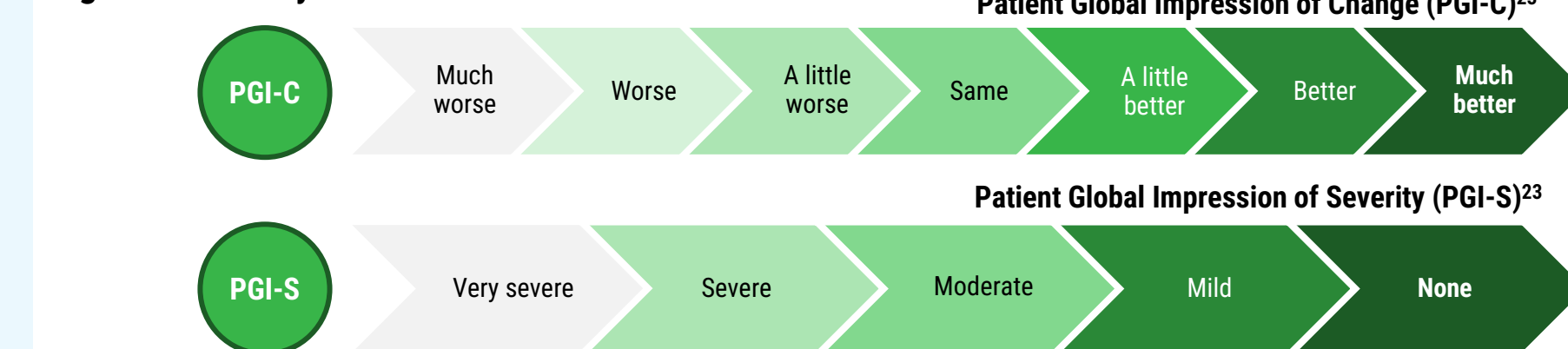
Acknowledgments: Medical writing support was provided by Natalie Haustруп, PhD, of Two Labs Pharma Services.

Methods

Primary endpoint: Safety including treatment-emergent adverse events (TEAEs), clinical laboratory tests, vital signs, and electrocardiogram findings.

Secondary endpoints: Efficacy endpoints using two patient-reported outcome tools.

Figure 2. Efficacy assessment scales



- Data collection pre-specified at pre-treatment, hourly for 6 hours, and at 8, 12, 24, and 48 hours post-treatment.

Table 1. Efficacy endpoints

Key efficacy endpoints	Defined as
Time to	
Onset of symptom relief	By 12 hours, PGI-C rating of at least "a little better" for 2 consecutive timepoints
Reduction in attack severity	By 12 hours, ≥ 1 -level reduction in the PGI-S from pre-treatment for 2 consecutive timepoints
Substantial symptom relief	By 12 hours, PGI-C rating of at least "better" for 2 consecutive timepoints
Proportion of attacks achieving	
Complete attack resolution	By 24 hours, PGI-S rating of "none"

PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity.

Post hoc analyses: Safety and efficacy for on-demand treatment of upper airway attacks, including laryngeal attacks without breathing difficulties.

- Upper airway attacks confirmed by investigators as per protocol definition: Swelling of the lips/tongue or any sensation of lump in the throat, difficulty swallowing, or voice change.
- Difficulty swallowing and voice change were assessed using the 5-symptom composite Angioedema symptom Rating scAle (AMRA-5).

Results

Data:

- Data snapshot from RAPiDe-2 Part A. Combined dose-blinded group data shown.

Safety analysis

- Participants who received ≥ 1 dose of deucricitbant IR capsule in the study at data cutoff (10 June 2024).
- 337 attacks from 19 participants.

Table 2. TEAEs within 5 days of study drug administration

Adverse events	Deucricitbant IR capsule (Combined dose group)
Attacks with any TEAE, n (%)	13 (3.9)
Treatment-related TEAEs, n	0
Serious TEAEs, n	1 ^a
Treatment-related serious TEAEs, n	0
TEAEs leading to study drug discontinuation, study withdrawal, or death, n	0

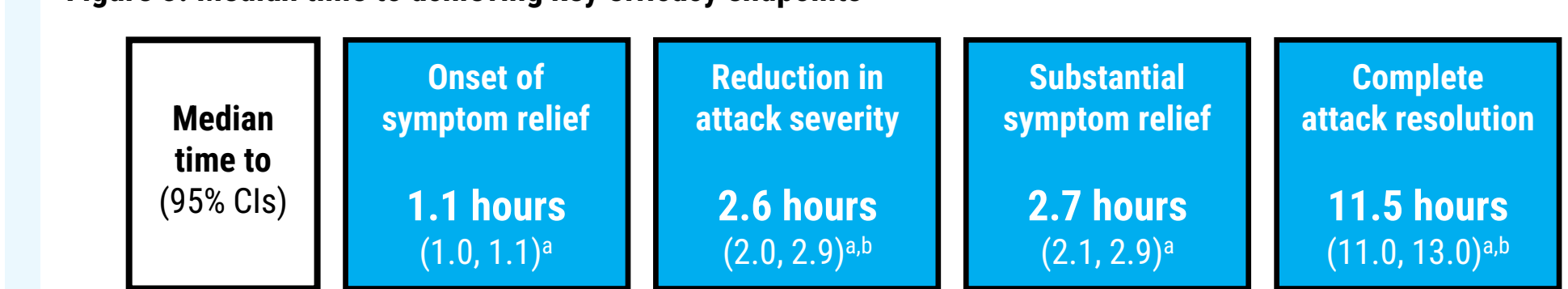
IR, immediate-release; TEAE, treatment-emergent adverse event (defined as adverse event occurring during time window from first study drug administration). ^aTooth caries unrelated to treatment.

Results

Efficacy analysis

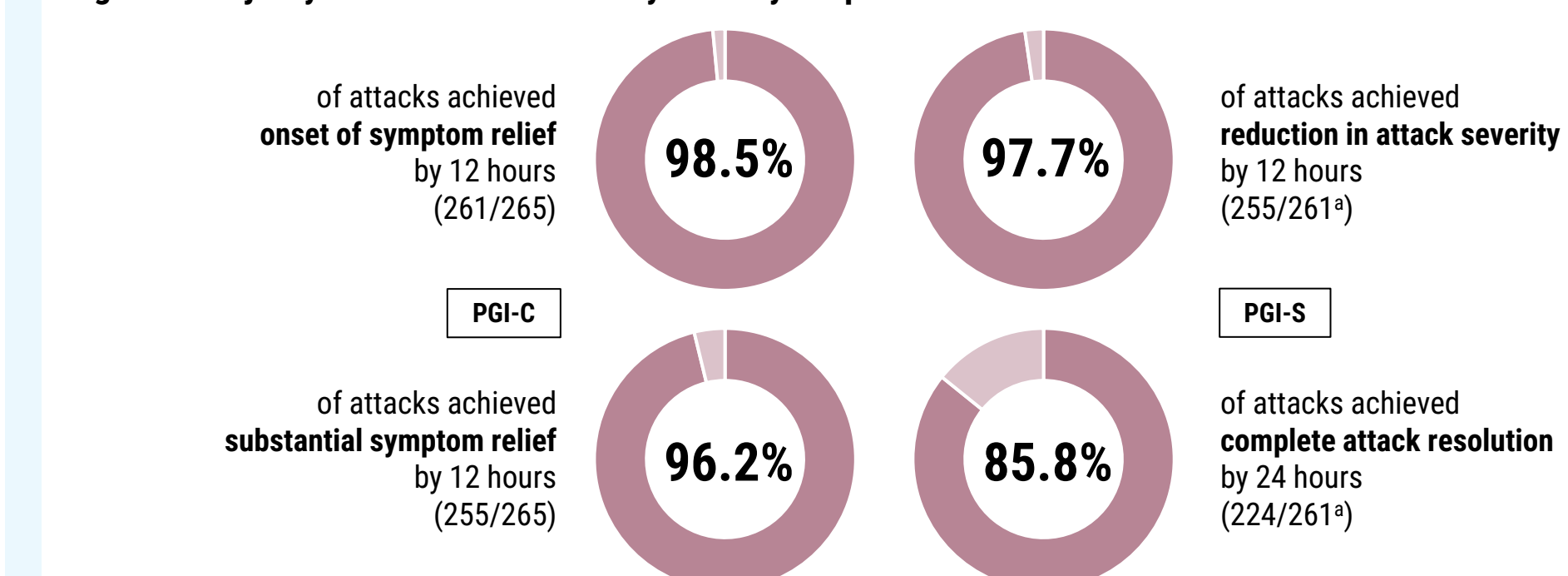
- Modified intention-to-treat analysis set: participants who treated ≥ 1 attack with deucricitbant IR capsule and non-missing PGI-C results from ≥ 1 post-treatment timepoint at data cutoff (01 March 2024).
- 265 attacks from 17 participants.

Figure 3. Median time to achieving key efficacy endpoints



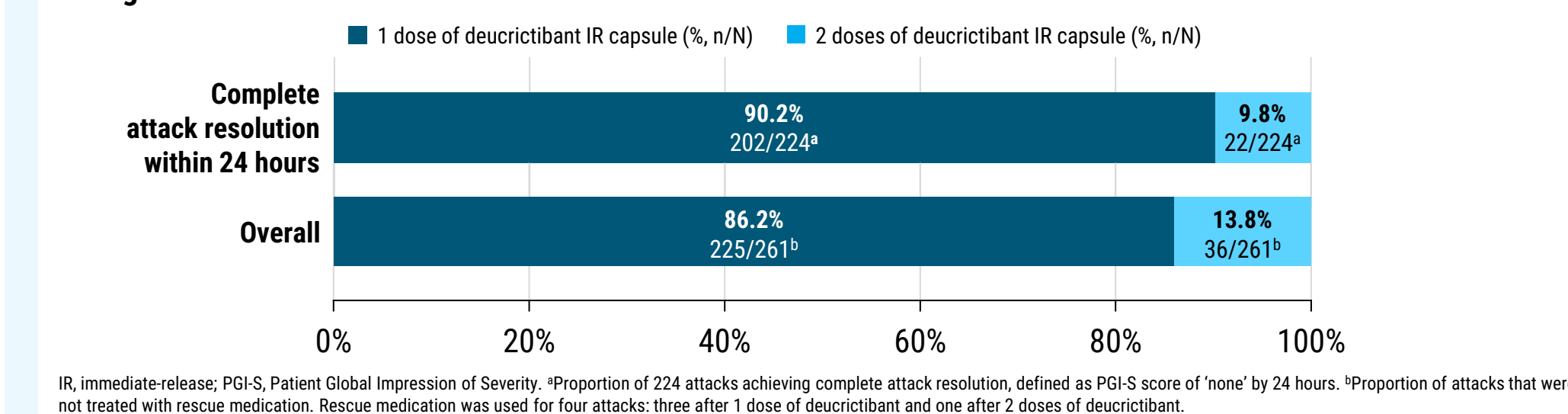
CI, confidence interval; PGI-S, Patient Global Impression of Severity. ^aAnalysis included participants in the modified intention-to-treat efficacy analysis set at data cutoff (01 March 2024); 265 attacks from 17 participants. ^b261 attacks have non-missing pre-treatment PGI-S. ^cWithin-participant correlation was not accounted for in all Kaplan-Meier estimates.

Figure 4. Majority of attacks achieved key efficacy endpoints within timeframe



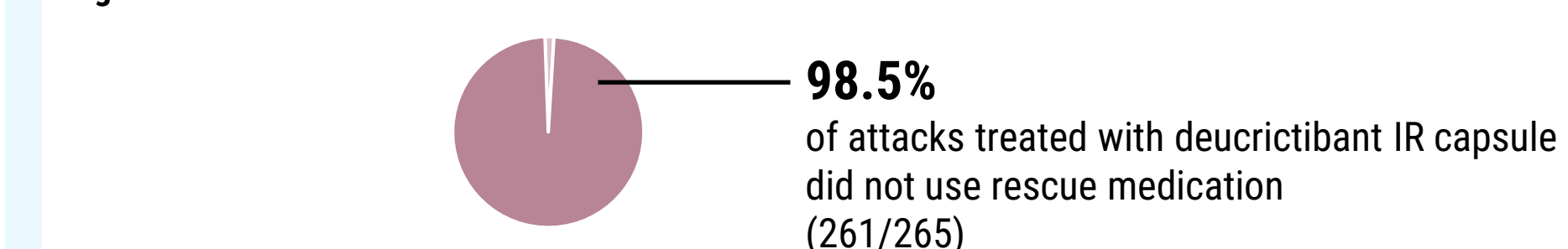
PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. ^a261 attacks had non-missing pre-treatment PGI-S.

Figure 5. Over 90% of attacks achieving complete attack resolution within 24 hours were treated with a single dose of deucricitbant



IR, immediate-release; PGI-S, Patient Global Impression of Severity. ^aProportion of 224 attacks achieving complete attack resolution, defined as PGI-S score of "none" by 24 hours. ^bProportion of attacks that were not treated with rescue medication. Rescue medication was used for four attacks: three after 1 dose of deucricitbant and one after 2 doses of deucricitbant.

Figure 6. 98.5% of attacks treated with deucricitbant did not use rescue medication



IR, immediate-release.

Results

Upper airway attacks analysis

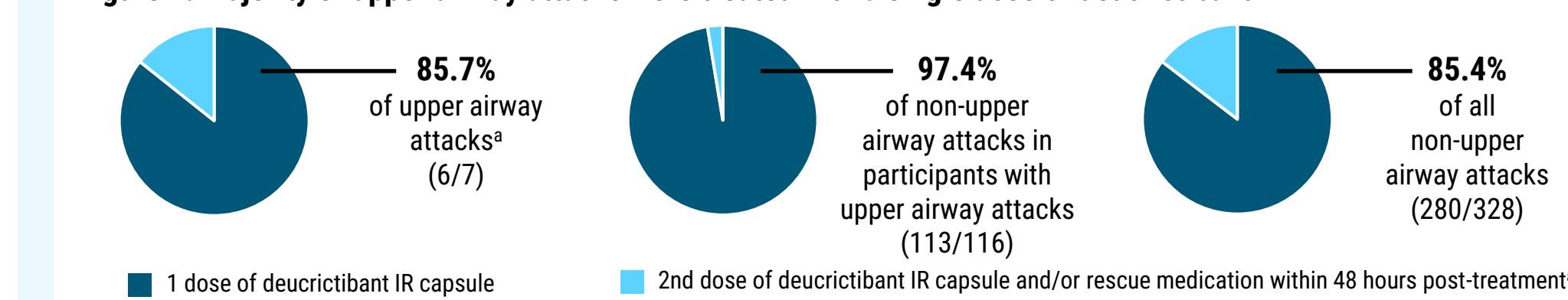
- 337 attacks at data cutoff (31 May 2024), of which 7 were upper airway, including laryngeal, attacks.
 - Difficulty in swallowing and/or voice change were reported for 3 attacks.

Table 3. Similar times to symptom relief for upper airway and other attacks

	Upper airway attacks	Non-upper airway attacks in participants with upper airway attacks	Total non-upper airway attacks
Number of participants	5	5	19
Total number of attacks treated ^a	7	116	328
Time to onset of symptom relief ^{b,c}			
Number of attacks ^d	7	112	318
Median hours (95% CI)	0.9 (0.5, 2.0)	1.0 (1.0, 1.1)	1.1 (1.0, 1.1)
Time to reduction in attack severity ^{c,e}			
Number of attacks ^f	6	111	312
Median hours (95% CI)	3.0 (0.9, NE)	2.0 (2.0, 2.7)	2.7 (2.1, 2.9)

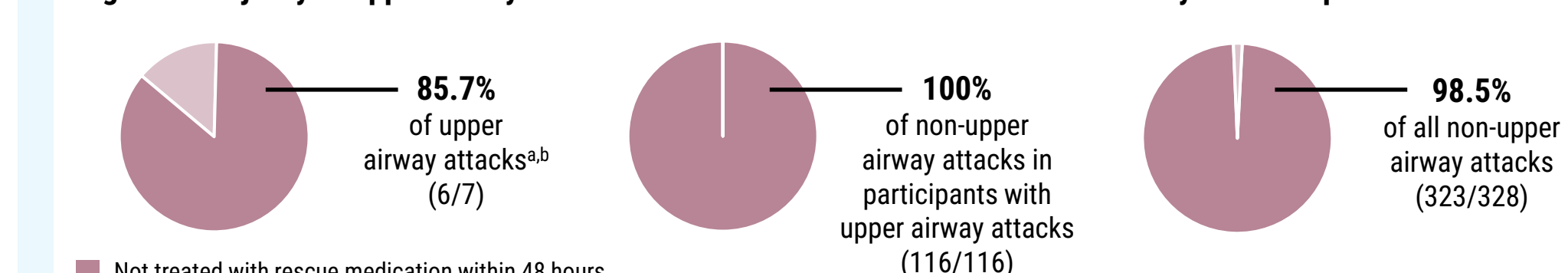
CI, confidence interval; NE, not estimable (insufficient data to calculate reliable estimate); PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. ^a337 attacks treated by 19 participants at data cutoff (31 May 2024). ^bPGI-C rating of at least "a little better" for 2 consecutive timepoints by 12 hours post-treatment. ^cWithin-participant correlation not accounted for in all Kaplan-Meier estimates. ^dEvaluable attacks include deucricitbant-treated attacks with ≥ 1 post-treatment PGI-C assessment. ^e ≥ 1 -level reduction in PGI-S from pre-treatment for 2 consecutive timepoints by 12 hours. ^fEvaluable attacks included deucricitbant-treated attacks with a pre- and ≥ 1 post-treatment PGI-S assessment.

Figure 7. Majority of upper airway attacks were treated with a single dose of deucricitbant



HAE, hereditary angioedema; IR, immediate-release. ^aFor upper airway attacks with inadequate response or symptom recurrence ≥ 4 hours after first dose of deucricitbant, only rescue medication was permitted. If needed, patients could use HAE rescue medication for an upper airway attack at any time. For other attacks, a second dose of deucricitbant was permitted ≥ 4 hours after first dose if symptoms persisted or progressed. If symptoms still persisted or progressed after the second dose of deucricitbant, rescue medication was administered.

Figure 8. Majority of upper airway and other attacks did not use rescue medication by 48 hours post-treatment



HAE, hereditary angioedema. ^aFor upper airway attacks with inadequate response or symptom recurrence ≥ 4 hours after first dose of deucricitbant, only rescue medication was permitted. If needed, patients could use HAE rescue medication for an upper airway attack at any time. For other attacks, a second dose of deucricitbant was permitted ≥ 4 hours after first dose if symptoms persisted or progressed. If symptoms still persisted or progressed after the second dose, rescue medication was administered. ^bOne participant used rescue medication for one upper airway attack and used a single dose of deucricitbant to treat two subsequent upper airway attacks.

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

*RAPiDe-2 is a Pharvaris-sponsored clinical trial. [ClinicalTrials.gov](https://clinicaltrials.gov) identifier: NCT05396105.