

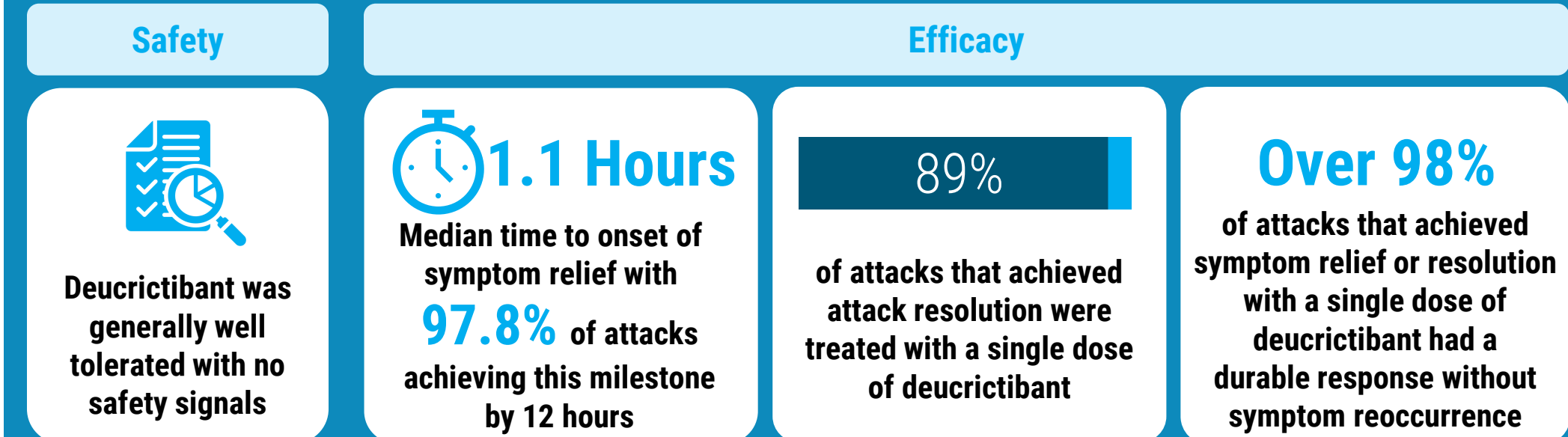
Long-Term Safety and Efficacy of Oral Deucricitbant for Treatment of Hereditary Angioedema Attacks: Results of the RAPIDe-2 Extension Study

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Key takeaways

Final Part A results from the RAPIDe-2 extension are consistent with the Phase 2 RAPIDe-1 study and provide further evidence on the long-term safety and efficacy of deucricitbant immediate-release (IR) capsule for 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.⁵⁻⁸
- Oral deucricitbant:** a selective, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of HAE attacks.⁹⁻¹⁶

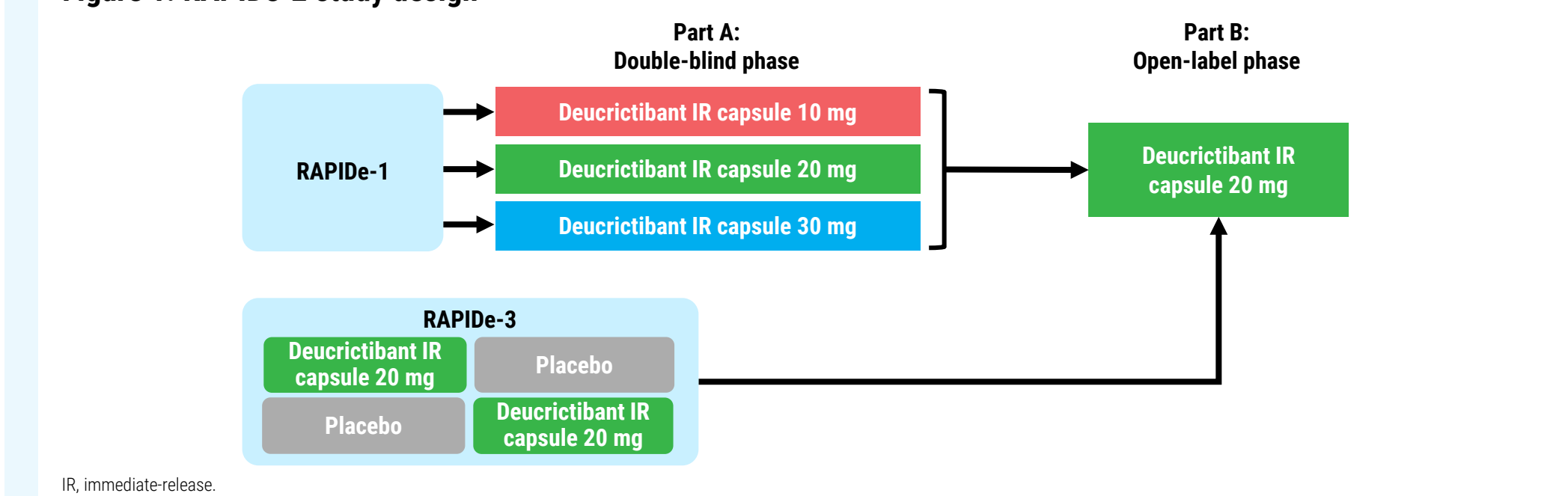
Objective

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.¹¹
- Part A eligible participants:** adults who completed RAPIDe-1 (NCT04618211).⁹
- Part A prophylaxis:** no long-term HAE prophylaxis treatment was allowed. Recent use of long-term HAE prophylaxis treatment prior to screening was allowed provided a pre-specified washout period was observed.

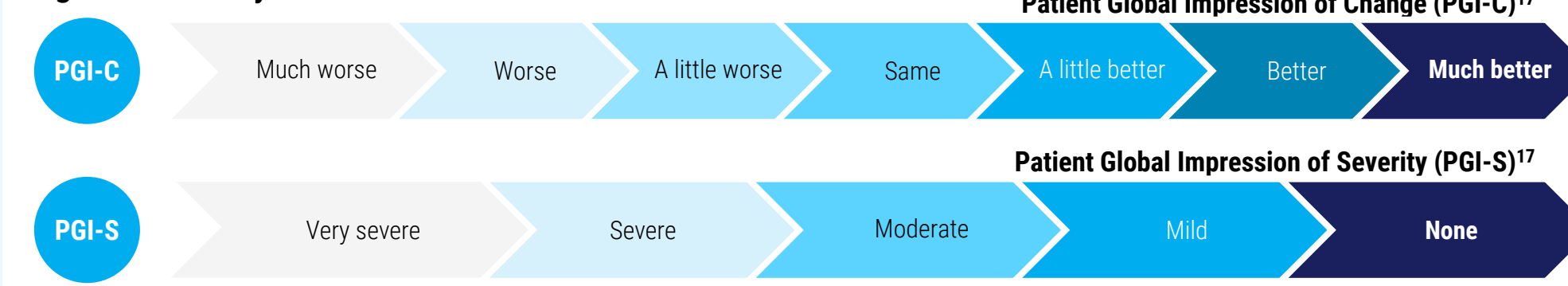
Figure 1. RAPIDe-2 study design



Methods

- Primary endpoint:** safety including treatment-emergent adverse events (TEAEs), clinical laboratory tests, vital signs, and electrocardiogram findings.
- Secondary endpoints:** efficacy endpoints using 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 and proportion of attacks achieving:	
Onset of symptom relief	PGI-C rating of at least "a little better" for 2 consecutive timepoints by 12 hours. ^a
Substantial symptom relief	PGI-C rating of at least "better" for 2 consecutive timepoints by 12 hours. ^a
Reduction in attack severity	≥1-level reduction in the PGI-S from pre-treatment for 2 consecutive timepoints by 12 hours. ^a
Complete attack resolution	PGI-S rating of "none" by 24 hours. ^b

PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. ^aIf rescue medication used within 14.5 hours post-treatment, time to event was censored at 14.5 hours regardless of whether event occurred within 12 hours post-treatment. ^bRescue medication use within 33.5 hours post-treatment was regarded as not achieving complete attack resolution at 24 hours.

Post-hoc analyses

- Durability of treatment response:** the achievement and maintenance of serial milestones of symptom relief and resolution without reoccurrence of symptoms following a single-dose of deucricitbant only.
 - Symptom reoccurrence:** following the achievement of each efficacy milestone, symptom reoccurrence was evaluated as any instance where the milestone was no longer being met within 24 hours.
- Upper airway attacks:** confirmed by investigators and defined as swelling of the lips/tongue or any sensation of lump in the throat, difficulty swallowing, or voice change (assessed with AMRA-5).

Results

Data:

- RAPIDe-2 Part A included 465 attacks from 19 participants. Combined dose-blinded group data shown.

Table 2. Participant characteristics

Participant characteristics	Deucricitbant 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)

BMI, body mass index; HAE, hereditary angioedema; IR, immediate-release; SD, standard deviation. ^aAll participants who received any dose of deucricitbant in the study. 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. Data for combined dose group shown (deucricitbant 10 mg, 20 mg, 30 mg).

Results

Safety analysis

- Participants who received ≥1 dose of deucricitbant IR capsule in the study.
- No treatment-related TEAEs.
- No treatment-related serious or severe TEAEs, no treatment-related TEAEs in laboratory parameters, vital signs, or ECG findings, and no TEAEs leading to treatment discontinuation, study withdrawal, or death.

Table 3. TEAEs within 3 days of study drug administration

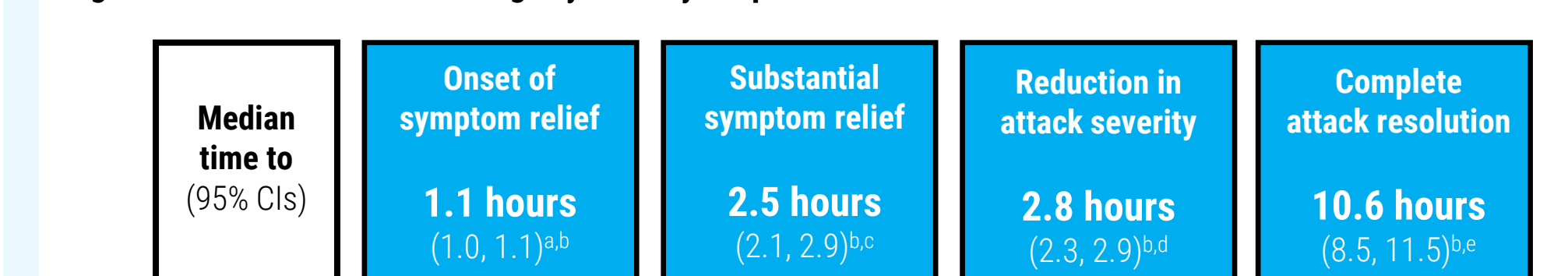
Adverse events	Deucricitbant IR capsule (combined dose group) (N=19; A=465)
Attacks with any TEAE, n (%)	12 (2.6)
Treatment-related TEAEs, n	0
Serious TEAEs, n	1 ^a
Treatment-related serious TEAEs, n	0
TEAEs leading to study drug discontinuation, study withdrawal, or death, n	0

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. ^aTeeth caries unrelated to treatment. Data for combined dose group shown (deucricitbant 10 mg, 20 mg, and 30 mg).

Efficacy analysis

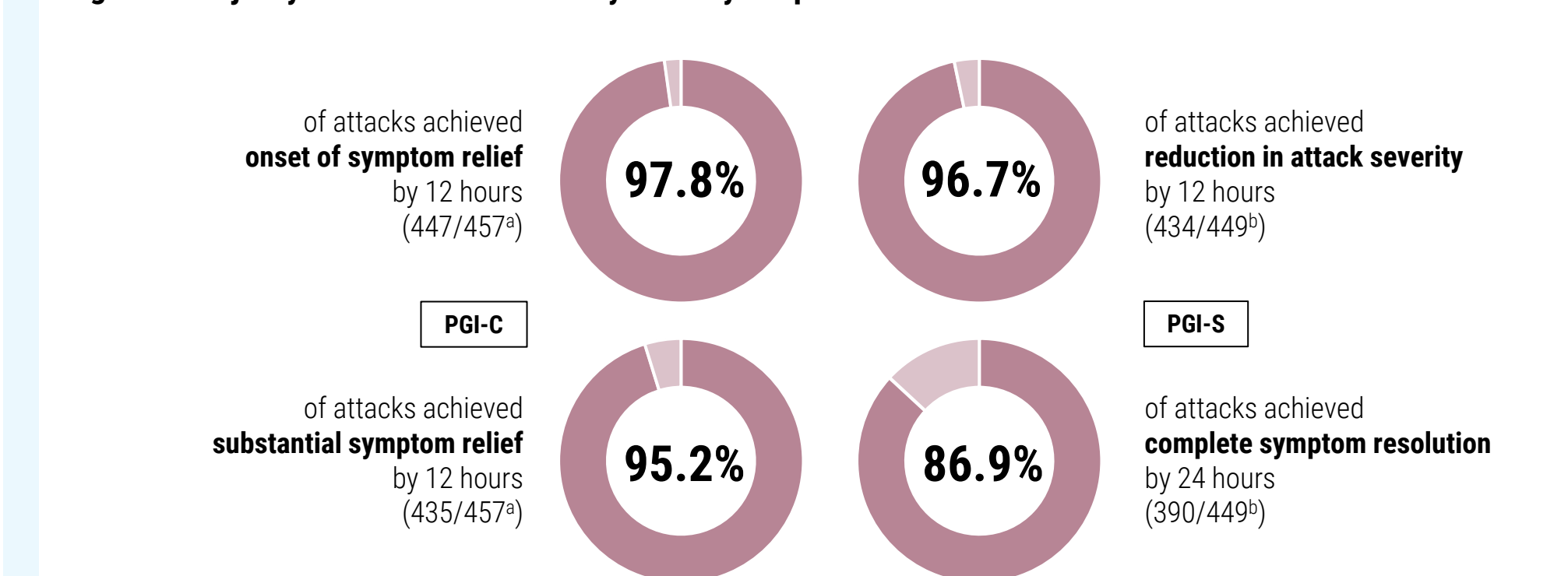
- Modified intention-to-treat analysis set: participants who treated ≥1 attack with deucricitbant IR capsule and non-missing PGI-C results from ≥1 post-treatment timepoint.

Figure 3. Median time to achieving key efficacy endpoints



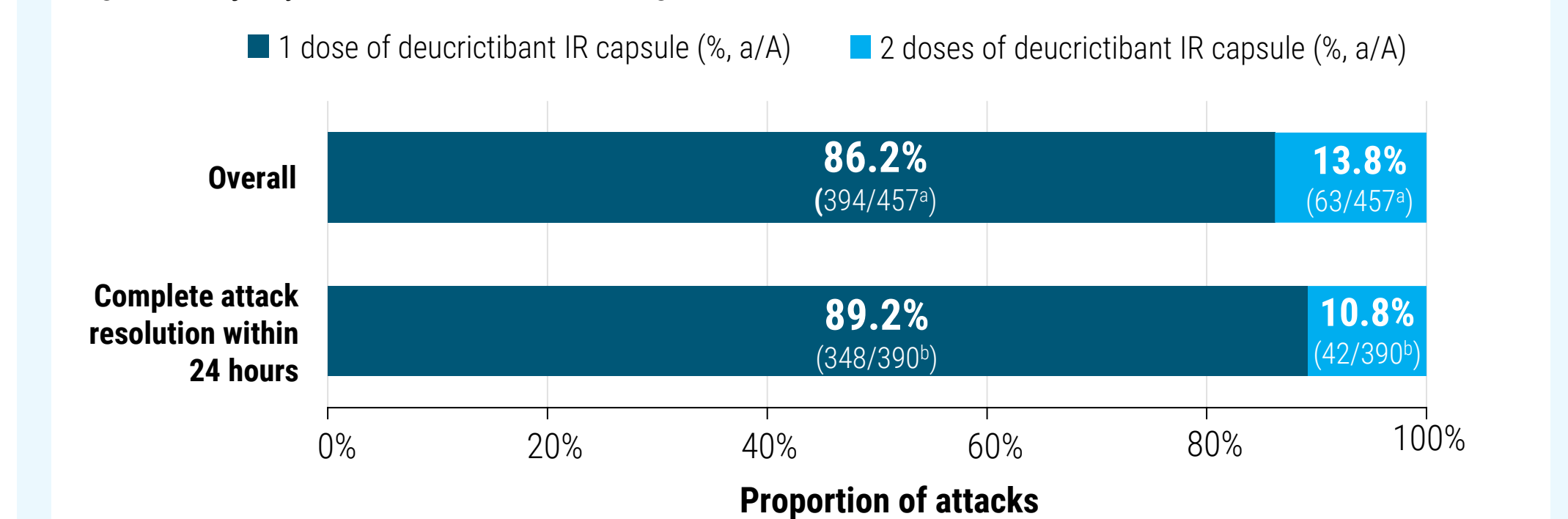
CI, confidence interval; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. ^aPGI-C rating of at least "a little better" for 2 consecutive timepoints by 12 hours post-treatment regardless of any missing intervening assessments and without rescue medication use. ^bWithin-participant correlation was not accounted for in all Kaplan-Meier estimates. ^cPGI-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. ^d≥1 point reduction in PGI-S from pre-treatment for 2 consecutive timepoints by 12 hours post-treatment and without rescue medication use. ^ePGI-S rating of "none" at 24 hours post-treatment and without rescue medication use.

Figure 4. Majority of attacks achieved key efficacy endpoints



Results

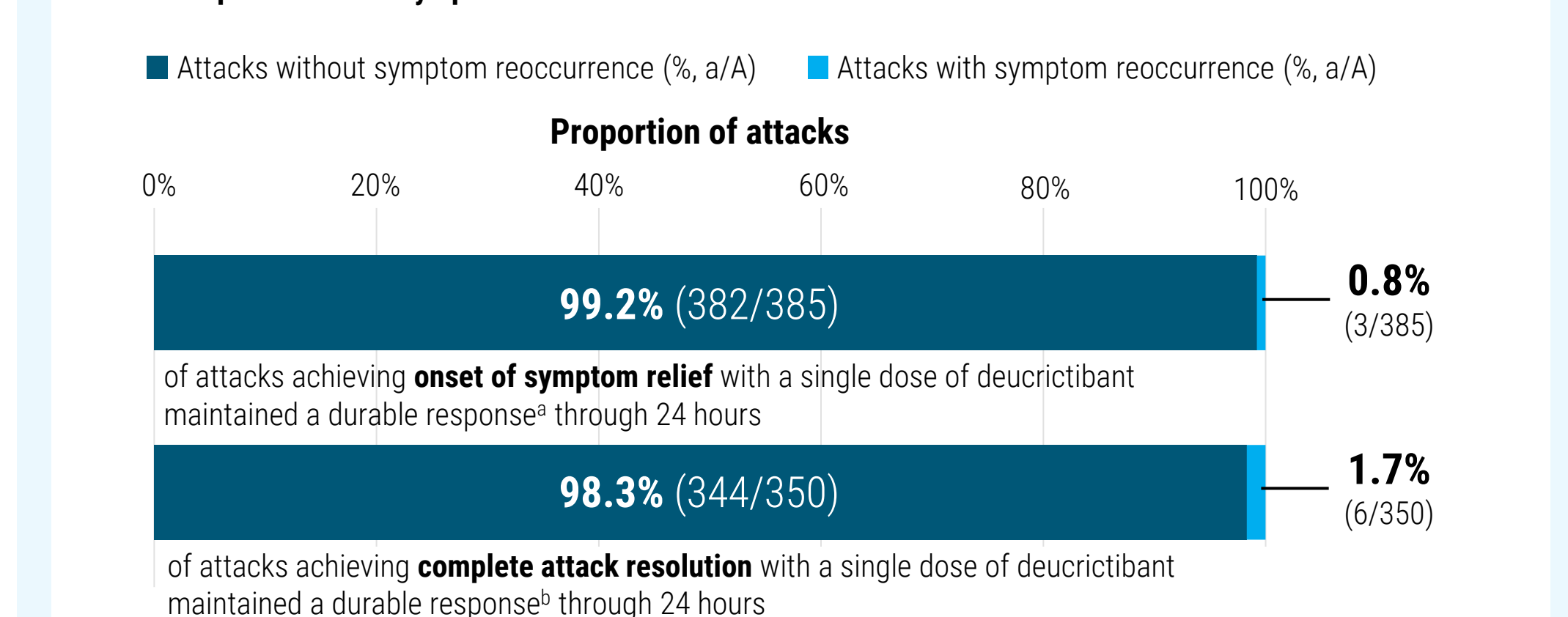
Figure 5. Majority of attacks treated with a single dose of deucricitbant and without rescue medication



IR, immediate-release; PGI-S, Patient Global Impression of Severity. A = number of attacks. Data for combined dose group shown (deucricitbant 10 mg, 20 mg, and 30 mg). ^aProportion of attacks that were not treated with rescue medication within 24 hours post-treatment. ^bAttacks used rescue medication within 24 hours post-treatment. ^cProportion of attacks achieving complete attack resolution, defined as PGI-S score of "none" by 24 hours and without rescue medication use.

Durability of response to treatment

Figure 6. Over 98% of attacks that achieved symptom relief or resolution with a single dose of deucricitbant had a durable response without symptom reoccurrence



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 deucricitbant. ^aDefined as PGI-C rating remaining "same" or "better" within 24 hrs after reaching "a little better" for 2 consecutive timepoints within 12 hours post-treatment. ^bDefined as PGI-S rating better than "none" within 24 hours after reaching "none" within 24 hours post-treatment. Combined dose group data shown (deucricitbant 10 mg, 20 mg, and 30 mg).

Treatment outcomes of upper airway attacks

- Of 465 attacks, 14 were upper airway, including laryngeal, attacks without breathing difficulties.
- Similar times to symptom relief and resolution were observed for upper airway attacks and other attacks.

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

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