

Treatment of HAE attacks with oral deucricitbant: RAPIDe-2 extension results

Marcus Maurer^{1,2}, Emel Ayyören-Pürsün³, Laurence Bouillet⁴, Hugo Chapdelaine⁵, Henriette Farkas⁶, Delphine Gobert⁷, Roman Hakl⁸, Ramon Leonart⁹, Avner Reshef¹⁰, Giuseppe Spadaro¹¹, Maria Stavevska¹², Marcin Stobiecki¹³, Justin Sun¹⁴, Li Zhu¹⁴, Ming Yu¹⁴, Giorgio Giannattasio¹⁵, Peng Lu¹⁴, Anna Valerieva¹²

¹Charité - Universitätsmedizin Berlin, Institute of Allergology, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany; ²Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Immunology and Allergology, Berlin, Germany; ³University Hospital Frankfurt, Department for Children and Adolescents, Goethe University Frankfurt, Frankfurt, Germany; ⁴National Reference Center for Angioedema (CREAK), Department of Internal Medicine, Grenoble Alpes University, Laboratoire T-RAIG, UMR 5525 TIMC-IMAG (UGA-CNRS), Grenoble, France; ⁵CHU de Montréal, Université de Montréal, Montréal, QC, Canada; ⁶Hungarian Angioedema Center of Reference and Excellence, Department of Internal Medicine and Haematology, Semmelweis University, Budapest, Hungary; ⁷Sorbonne Université, Médecine Interne, AP-HP, Centre de référence des angioedèmes à kinines, Hôpital Saint-Antoine, Paris, France; ⁸St. Anne's University Hospital in Brno and Faculty of Medicine Department of Clinical Immunology and Allergy, Masaryk University, Brno, Czech Republic; ⁹Bellvitge University Hospital, Allergy Service, L'Hospitalet de Llobregat, Barcelona, Spain; ¹⁰Barzilai University Hospital, Allergy, Immunology and Angioedema Center, Ashkelon, Israel; ¹¹University of Naples Federico II, Department of Translational Medical Sciences and Center for Basic and Clinical Immunology Research (CISI), Napoli, Italy; ¹²Medical University of Sofia, Department of Allergology, Sofia, Bulgaria; ¹³Jagiellonian University Medical College, Department of Clinical and Environmental Allergy, Krakow, Poland; ¹⁴Pharvaris Inc., Lexington, MA, USA; ¹⁵Pharvaris GmbH, Zug, Switzerland

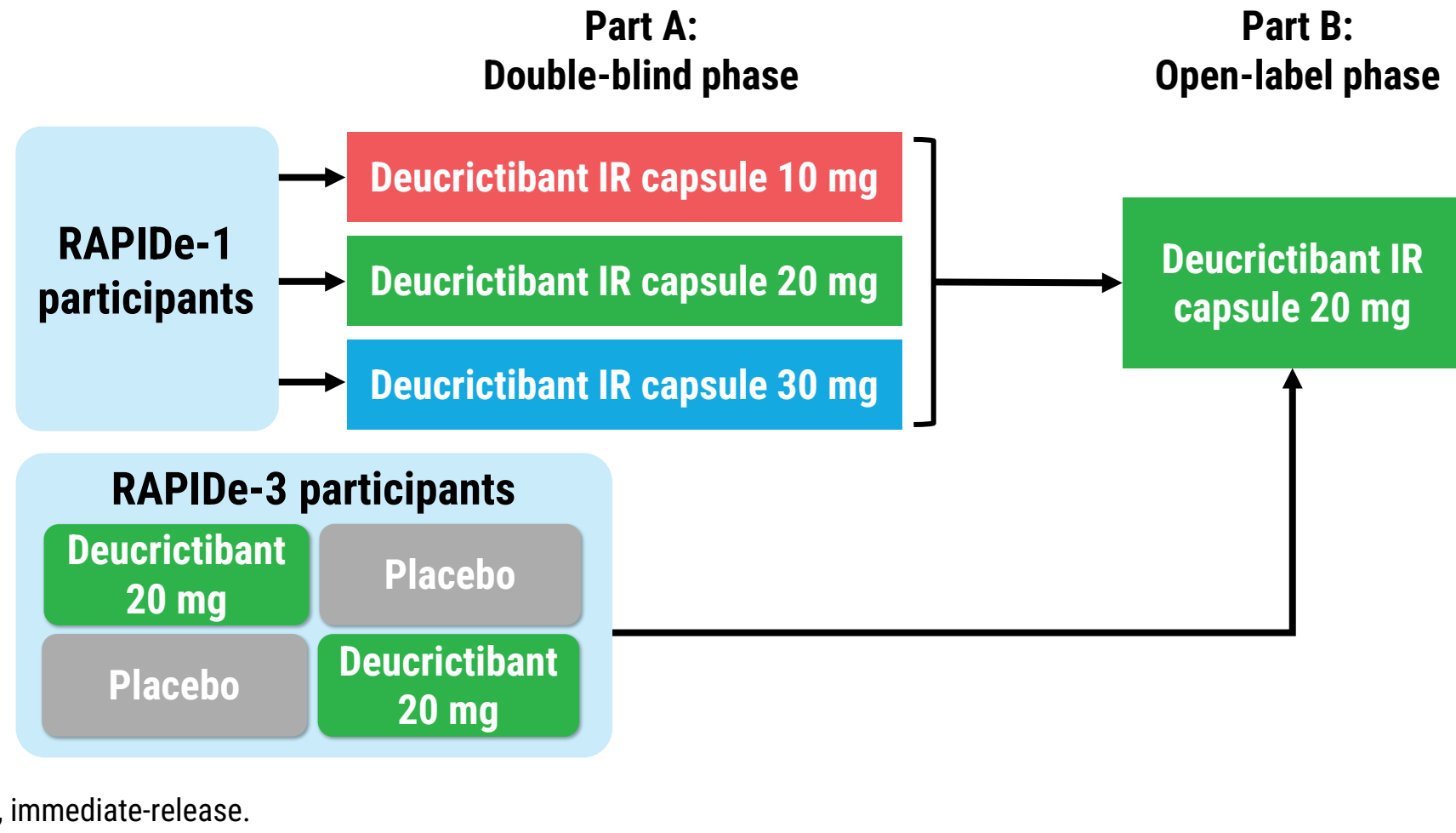
Rationale

- International guidelines recommend that hereditary angioedema (HAE) attacks are treated as early as possible.¹⁻³
- The burden associated with parenteral administration of currently approved on-demand medications⁴⁻⁸ often leads to treatment of HAE attacks being delayed or forgone.⁹⁻¹³
- An unmet need exists for on-demand oral therapies that are effective and well-tolerated and may reduce the treatment burden by enabling prompt administration.¹³
- Deucricitbant is a selective, orally administered bradykinin B2 receptor antagonist under development for prophylactic and on-demand treatment of HAE attacks.¹⁴⁻¹⁹
- In the RAPIDe-1 Phase 2 trial (NCT04618211),¹⁴ deucricitbant immediate-release (IR) capsule reduced time to onset of symptom relief and to resolution of HAE attacks vs placebo; treatment was well-tolerated.¹⁵

Methods

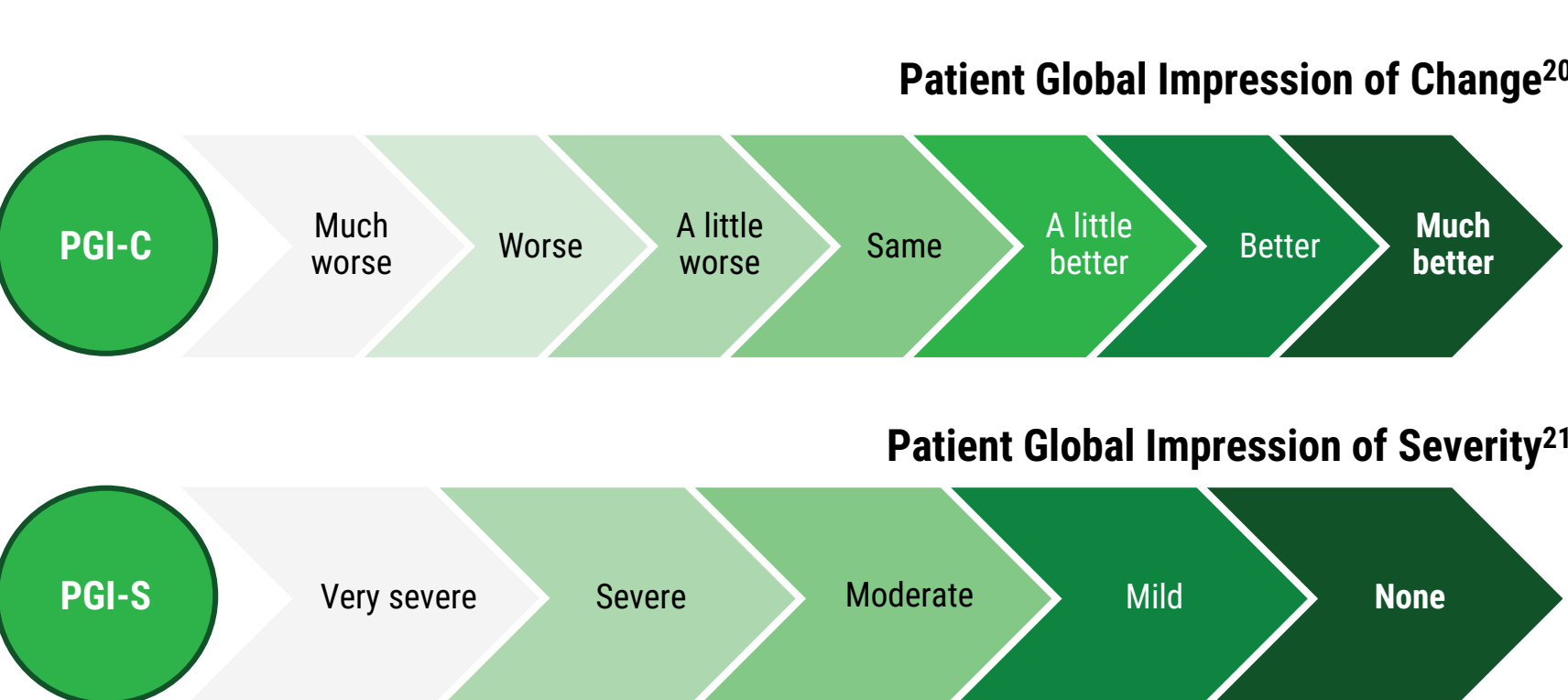
- RAPIDe-2 (NCT05396105)^{16*} is an ongoing two-part Phase 2/3 extension study evaluating long-term safety and efficacy of orally administered deucricitbant IR capsule for the treatment of HAE attacks.
- Part A enrolls adult (≥18 years) participants who completed RAPIDe-1. Participants continue self-administering the same double-blinded dose of deucricitbant IR capsule (10 mg, 20 mg, or 30 mg) received in RAPIDe-1 to treat qualifying nonlaryngeal attacks (≥1 symptom with Visual Analogue Scale score ≥30), and laryngeal attacks presenting without breathing difficulties (Figure 1).

Figure 1. RAPIDe-2 study design



- The primary endpoint assesses safety, including treatment-emergent adverse events (TEAEs), clinical laboratory tests, vital signs, and electrocardiogram (ECG) findings.
- Patient-reported outcome (PRO) tools are used to assess efficacy (Figure 2), with data collection pre-specified at pre-treatment, every hour up to 6 hours, and then at 8, 12, 24, and 48 hours, from administration of deucricitbant IR capsule.
- Key efficacy endpoints (Figure 2) include:
 - Onset of symptom relief, defined as Patient Global Impression of Change (PGI-C) rating of at least "a little better" for 2 consecutive timepoints by 12 hours post-treatment.
 - Time to reduction in attack severity, defined as achieving ≥1 point reduction in the Patient Global Impression of Severity (PGI-S) from pretreatment for 2 consecutive timepoints by 12 hours post-treatment.
 - Proportion of attacks achieving complete attack resolution, defined as achieving PGI-S rating of "none" at 24 hours post-treatment.

Figure 2. Efficacy assessment scales



Results

- The RAPIDe-2 Part A combined-dose group results are reported here.
- A total of 265 attacks from 17 participants were included in the modified intention-to-treat efficacy analysis set (data cutoff: 1 March 2024), defined as all participants who had ≥1 attack treated with deucricitbant and non-missing PGI-C results from ≥1 post-treatment timepoint.
- A total of 337 attacks from 19 participants were included in the safety analysis set (data cutoff: 10 June 2024), defined as all participants who received any dose of deucricitbant in the study.
 - 7 of 337 attacks were laryngeal.
- Baseline characteristics were consistent with the RAPIDe-1 Phase 2 trial (Table 1).

Results

Table 1. Baseline characteristics

	Deucricitbant IR capsule (All doses)
Number of attacks treated ^a	337
Number of participants ^a	19
Age in years, mean (SD)	42.7 (17.6)
Sex: Male/female, n (%)	7 (36.8) / 12 (63.2)
Race: White/other	18 / 1
BMI, mean (SD)	27.0 (3.8)
Years since HAE diagnosis, mean (SD)	21.7 (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. ^aNumber by the cutoff date of 10 June 2024.

Safety

- Deucricitbant was well-tolerated across all doses, with no treatment-related TEAEs (Table 2).
- 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 were reported.

Table 2. TEAEs within 5 days after administration of study drug

Adverse events	Deucricitbant IR capsule (All doses)
Number of attacks treated ^a	337
Number of participants ^a	19
Attacks with any TEAE, n (%)	13 (3.9)
Treatment-related TEAEs, n	0
Serious TEAEs, n	1 ^b
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). ^aNumber in the safety analysis set (data cutoff: 10 June 2024). ^bTooth caries unrelated to treatment.

Efficacy

- The median time to onset of symptom relief was 1.1 hours (95% CI, 1.0, 1.2) (Figure 3, Table 3).
- 98.5% (261/265) of attacks achieved onset of symptom relief by 12 hours (Table 3, Figure 4).

Figure 3. Kaplan-Meier plot of time to onset of symptom relief

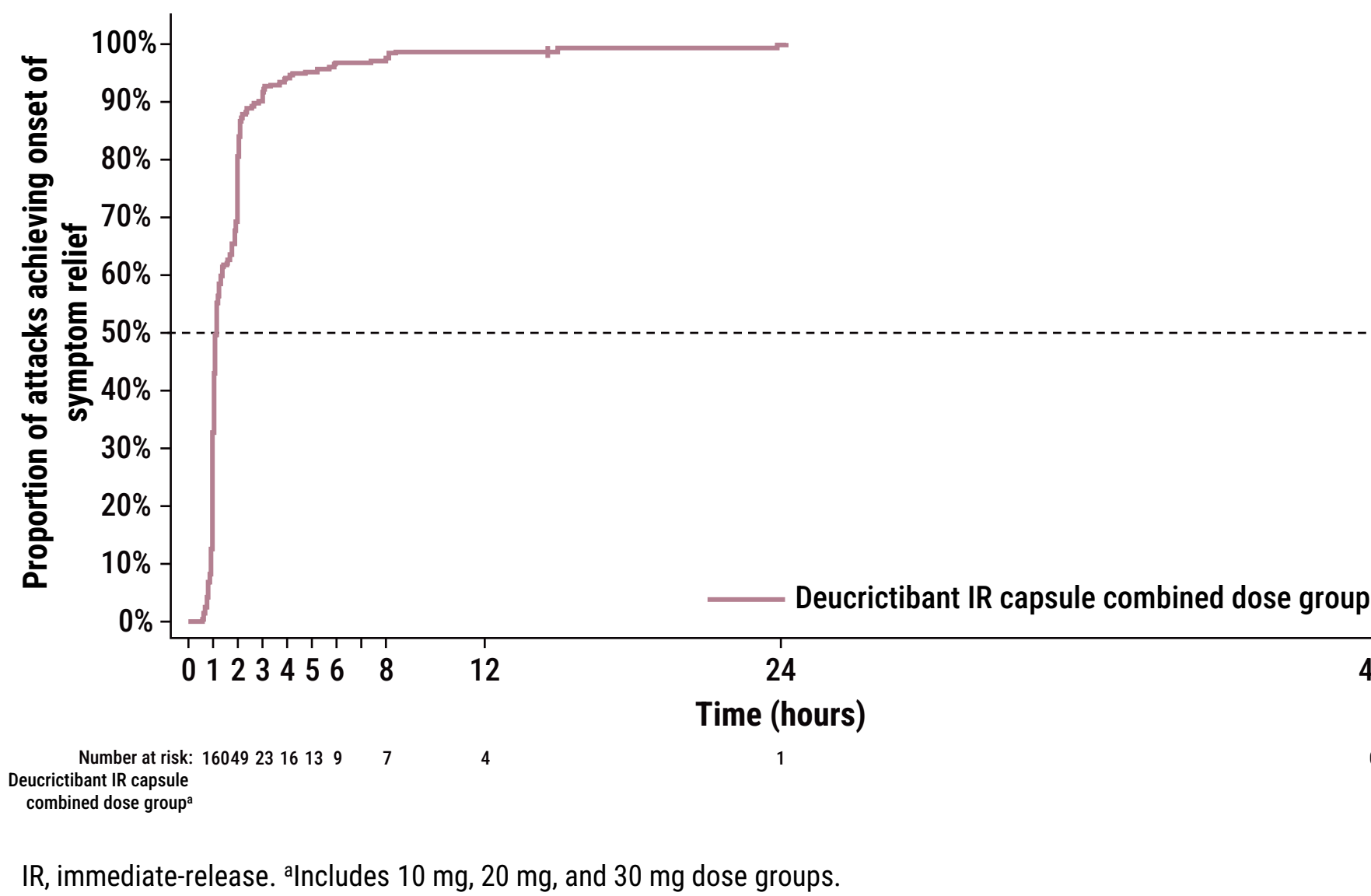


Table 3. Median time to achieving key efficacy endpoints

	Deucricitbant IR capsule (All doses)
Number of attacks treated ^a	265
Number of participants with treated attacks ^a	17
Median time to onset of symptom relief by PGI-C, hours (95% CI)	1.1 (1.0, 1.2)
Median time to reduction in attack severity by PGI-S, ^b hours (95% CI)	2.6 (2.0, 2.9)
Median time to complete attack resolution by PGI-S, ^b hours (95% CI)	11.5 (11.0, 13.0)

IR, immediate-release; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. ^aNumber in the modified intention-to-treat efficacy analysis set (data cutoff: 01 March 2024). ^b261 attacks have non-missing pre-treatment PGI-S.

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

Results

- 85.8% (224/261) of attacks achieved complete attack resolution within 24 hours (Figure 4). 90.2% (202/224) of attacks achieved this milestone with a single dose of deucricitbant IR capsule (Figure 5).

Figure 4. Proportion of attacks achieving key efficacy endpoints

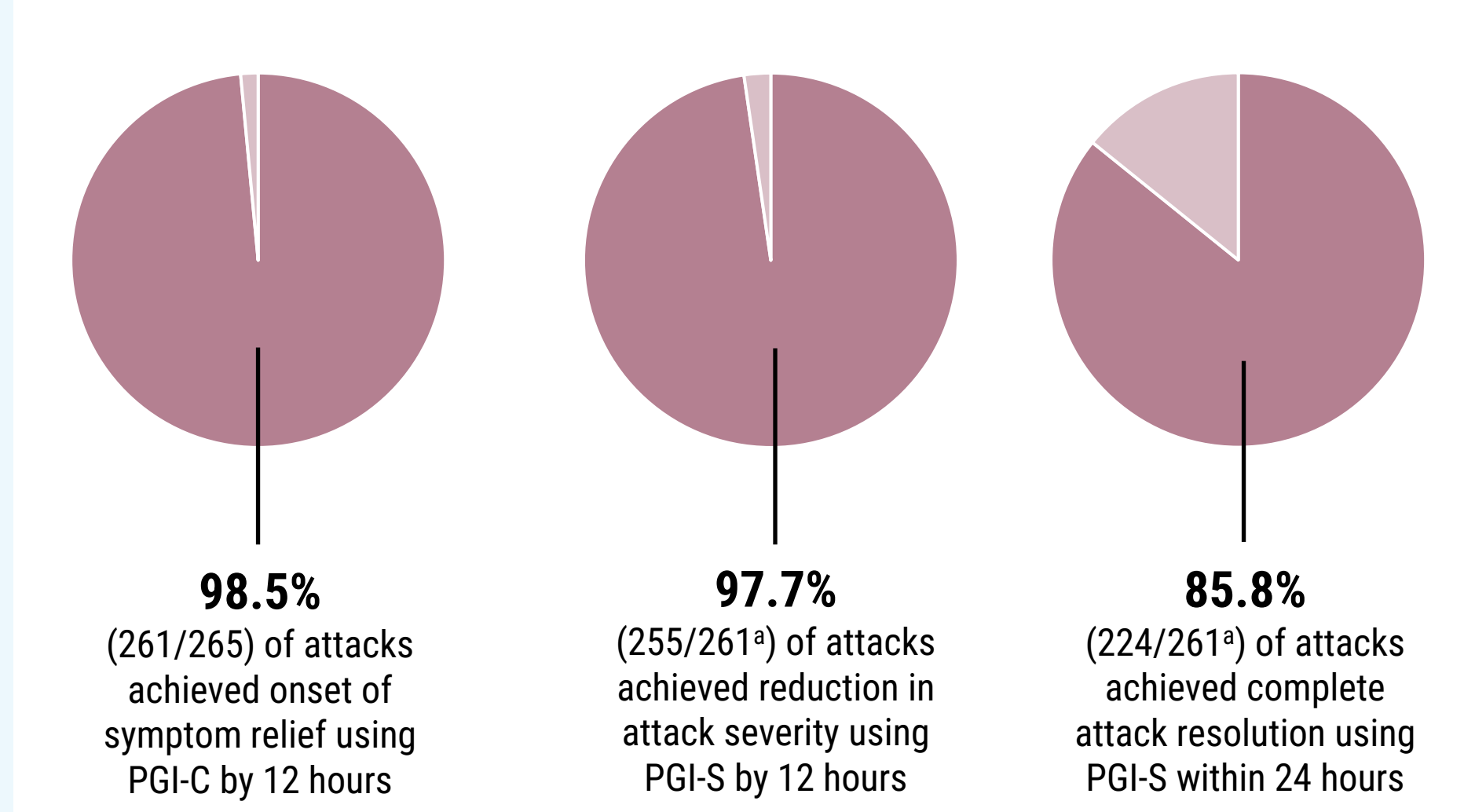
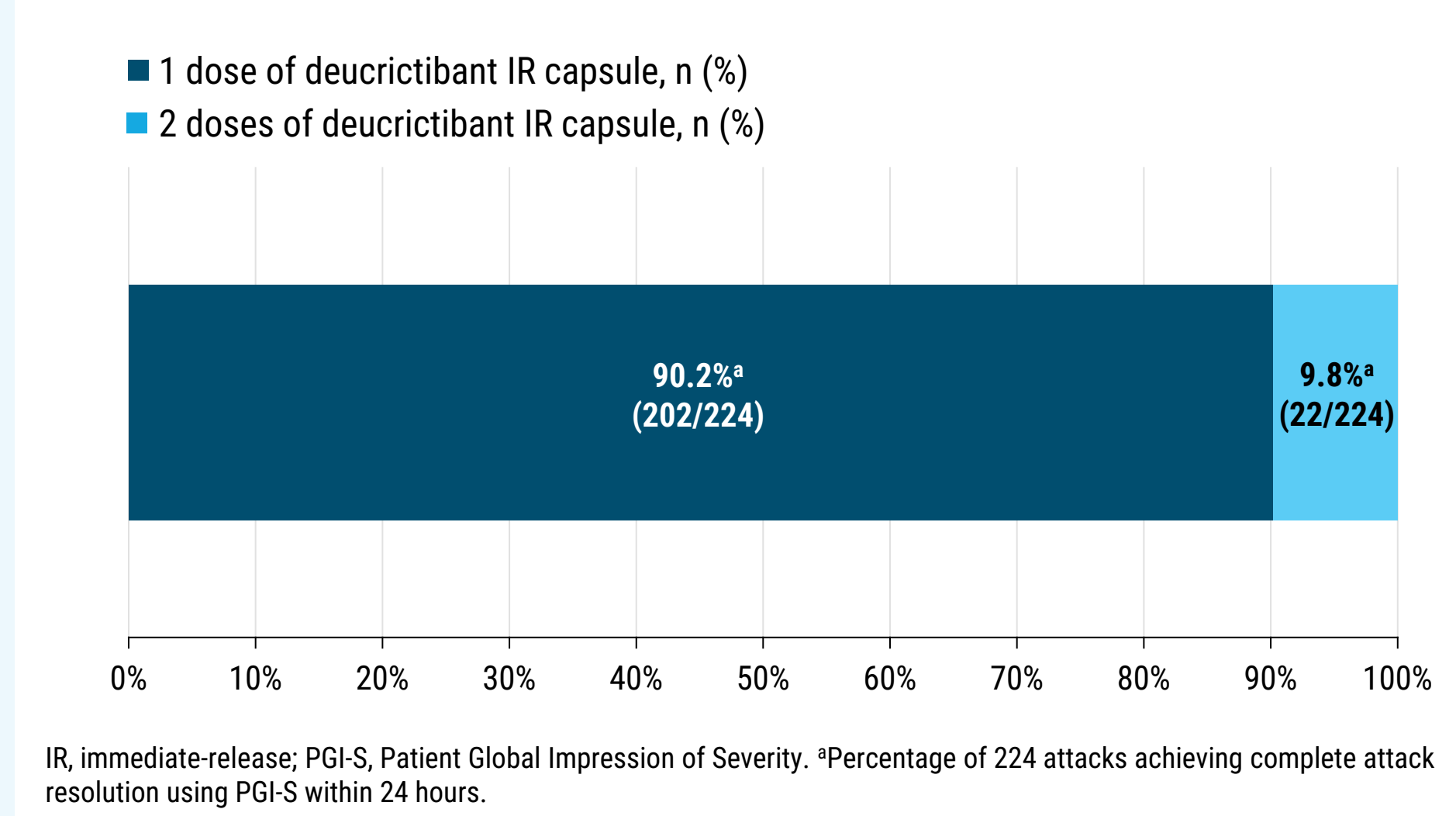
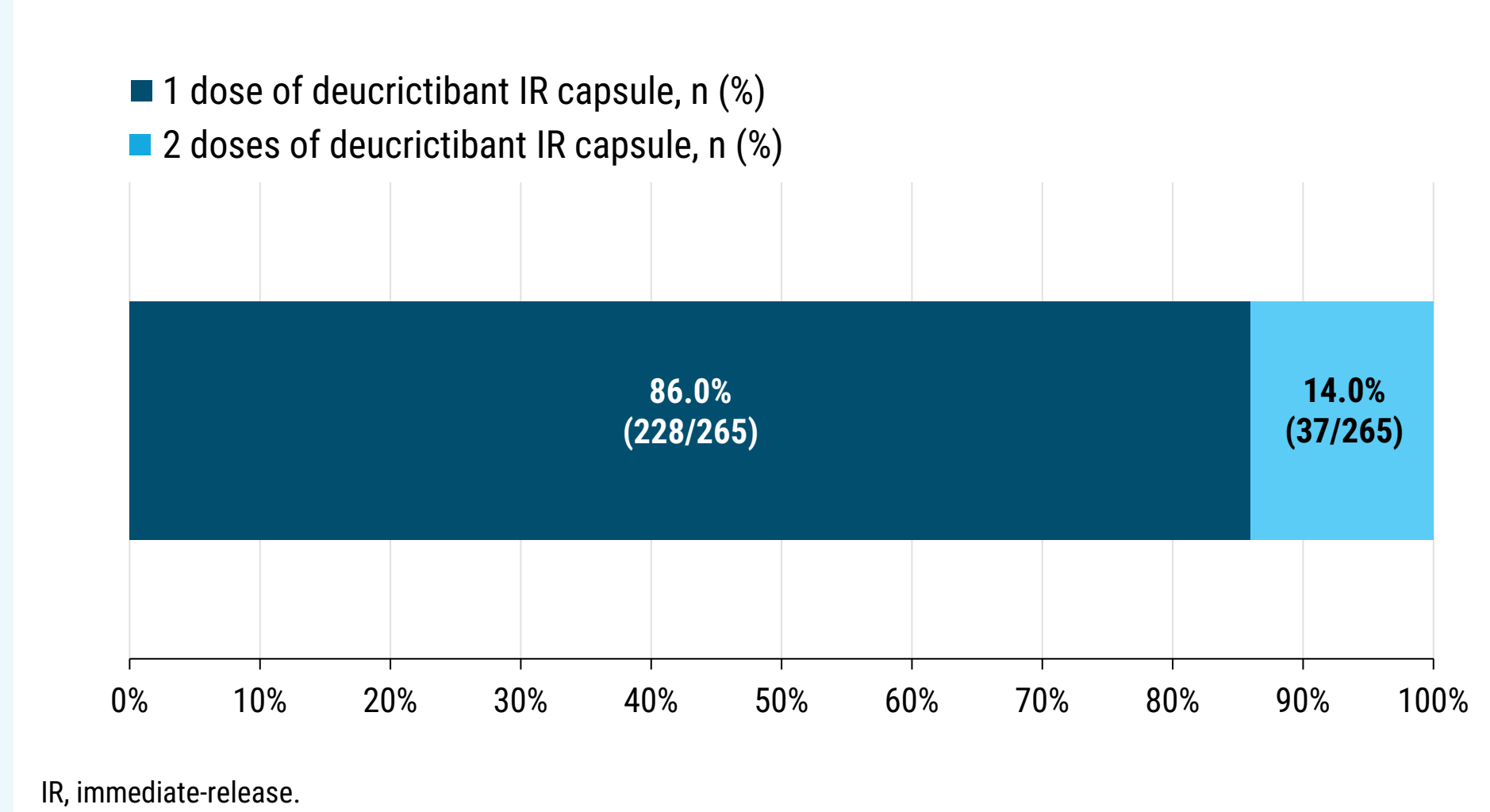


Figure 5. Attacks treated with 1 or 2 doses of deucricitbant prior to achieving complete attack resolution



- A total of 86.0% (228/265) of all attacks were treated with a single dose of deucricitbant IR capsule (Figure 6).

Figure 6. Attacks treated with 1 or 2 doses of deucricitbant



Conclusions

- In the current analysis of the ongoing RAPIDe-2 Phase 2/3 extension study, deucricitbant IR capsule was well-tolerated for all studied doses with no new safety signals observed.
- Efficacy analysis showed:
 - 1.1 hours median time to onset of symptom relief by PGI-C – 98.5% of attacks by 12 hours.
 - 2.6 hours median time to reduction in attack severity by PGI-S – 97.7% of attacks by 12 hours.
 - 11.5 hours median time to complete attack resolution by PGI-S – 85.8% of attacks within 24 hours.
 - 86.0% of attacks were treated with a single dose of deucricitbant IR capsule.
- Results from the ongoing RAPIDe-2 extension are consistent with the Phase 2 RAPIDe-1 study and provide evidence on the long-term safety and efficacy of deucricitbant IR capsule for repeat treatment of HAE attacks.

References

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