Long-Term Safety and Efficacy of Oral Deucrictibant for Treatment of Hereditary Angioedema Attacks: Results of the RAPIDe-2 Extension Study and Post-hoc Analysis on Durability of Response to a Single Dose of Oral Deucrictibant

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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 deucrictibant immediate-release (IR) capsule for treatment of repeat hereditary angioedema (HAE) attacks. In a post-hoc analysis, the response to a single dose of deucrictibant IR capsule was durable and the majority of HAE attacks that achieved symptom relief and resolution maintained a durable response without reoccurrence of symptoms.

Safety	Efficacy		Durable response
Deucrictibant was generally well tolerated with no treatment-related TEAEs	**1.1 Hours** Median time to onset of symptom relief	**86.9%** of attacks achieved complete symptom resolution at 24 hours	**>98%** of attacks that achieved symptom relief and resolution had a durable response without symptom reoccurrence

TEAE, treatment-related adverse event.

Background

- **Hereditary angioedema (HAE):** a bradykinin-mediated condition with painful swelling attacks affecting multiple locations in the body.[1]
- **Unmet need:** 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.[5-9]
- **Treatment response:** a rapid and durable response to on-demand treatment of an acute HAE attack through to complete resolution is paramount to abate the physical, functional, and emotional burden associated with symptoms and to enable the prompt restart of daily activities.[6,10]
- **Deucrictibant:** a selective, investigational, orally administered, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of bradykinin-mediated attacks.[11-20]

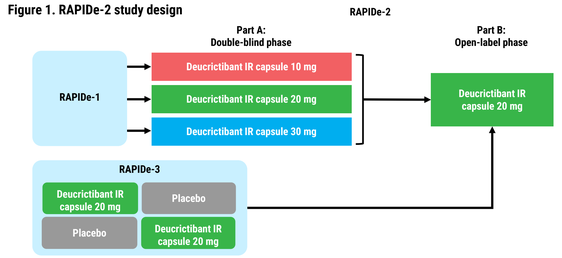
Objectives

- To evaluate the long-term safety and efficacy of deucrictibant IR capsule for on-demand treatment of repeat HAE attacks in Part A of the RAPIDe-2 (NCT05396105)* extension study.
- To assess the durability of effects following a single dose of deucrictibant IR capsule for treatment of HAE attacks in a post-hoc analysis of Part A of the RAPIDe-2 extension study.

Methods

- **RAPIDe-2 (NCT05396105)*:** a two-part, 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



IR, immediate-release.

Methods

- **Primary endpoint:** safety, including treatment-emergent adverse events (TEAEs), clinical laboratory tests, vital signs, and electrocardiogram (ECG) findings.
- **Secondary endpoints:** efficacy endpoints using patient-reported outcome tools.
- **Data collection:** pre-specified at pre-treatment, hourly for 6 hours, and at 8, 12, 24, and 48 hours post-treatment.

Figure 2. Efficacy assessment scales

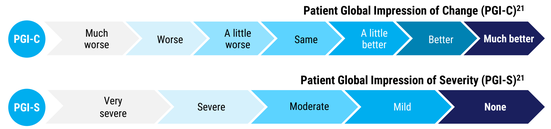


Table 1. Efficacy endpoints

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" at 24 hours[b]

PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]If 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. [b]Rescue 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 deucrictibant 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.

Results

Data

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

Table 2. Participant characteristics

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)

BMI, body mass index; HAE, hereditary angioedema; IR, immediate-release; SD, standard deviation. [a]All participants who received any dose of deucrictibant 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 (deucrictibant 10 mg, 20 mg, and 30 mg).

Results

Safety analysis

- Participants who received ≥1 dose of deucrictibant 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 electrocardiogram findings. No TEAEs leading to treatment discontinuation, study withdrawal, or death.

Table 3. TEAEs within 3 days of study drug administration

Adverse events	Deucrictibant 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

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]Tooth caries unrelated to treatment. Data for combined dose group shown (deucrictibant 10 mg, 20 mg, and 30 mg).

Efficacy analysis

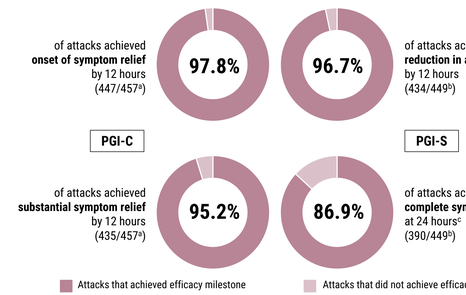
- Modified intention-to-treat analysis set: participants who treated ≥1 attack with deucrictibant IR capsule and non-missing PGI-C results from ≥1 post-treatment timepoint.

Figure 3. Median time to achieving key efficacy endpoints

Median time to (95% CI)	Onset of symptom relief	Substantial symptom relief	Reduction in attack severity	Complete attack resolution
	1.1 hours (1.0, 1.1)[a,b]	2.5 hours (2.1, 2.9)[b,c]	2.8 hours (2.3, 2.9)[b,d]	10.6 hours (8.5, 11.5)[b,e]

CI, confidence interval; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [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]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. [d]≥1 point reduction in PGI-S from pre-treatment for 2 consecutive timepoints by 12 hours post-treatment and without rescue medication use. [e]PGI-S rating of "none" within 48 hours post-treatment and without rescue medication use.

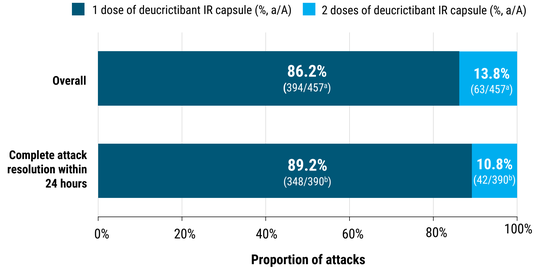
Figure 4. Majority of attacks achieved key efficacy endpoints



PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]457 attacks have at least 1 post-treatment PGI-C result. [b]449 attacks have non-missing pre-treatment PGI-S and at least 1 post-treatment PGI-S. [c]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.

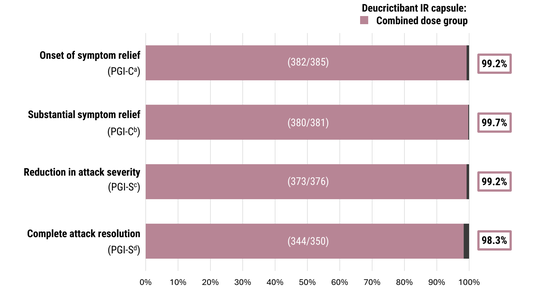
Results

Figure 5. Majority of attacks treated with a single dose of deucrictibant IR capsule and without rescue medication



IR, immediate-release. a = number of attacks with specified outcome. A = number of attacks. 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.

Figure 6. RAPIDe-2: Over 98% of attacks that achieved symptom relief and resolution with a single dose of deucrictibant IR capsule maintained a durable response without reoccurrence of symptoms



IR, immediate-release; PGI-C, patient global impression of change; PGI-S, patient global impression of severity. [a]Onset of symptom relief defined as PGI-C rating of at least "a little better" for 2 consecutive timepoints by 12 hours post-treatment; reoccurrence of symptoms defined as subsequent rating of "same" or lower within 24 hours. [b]Substantial symptom relief defined as PGI-C rating of "better" for 2 consecutive timepoints by 12 hours post-treatment; reoccurrence of symptoms defined as subsequent rating of "a little better" or lower within 24 hours. [c]Reduction in attack severity defined as PGI-S ≥1 point reduction from pre-treatment by 12 hours post-treatment; reoccurrence of symptoms defined as subsequent occurrence of less than 1-point reduction within 24 hours. [d]Complete attack resolution defined as PGI-S rating of "none" at 24 hours post-treatment; reoccurrence of symptoms defined as subsequent occurrence of rating above "none" within 24 hours. Data for combined dose group shown (deucrictibant 10 mg, 20 mg, and 30 mg).

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

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- **Treatment response:** a rapid and durable response to on-demand treatment of an acute HAE attack through to complete resolution is paramount to abate the physical, functional, and emotional burden associated with symptoms and to enable the prompt restart of daily activities.[6,10]
- **Deucrictibant:** a selective, investigational, orally administered, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of bradykinin-mediated attacks.[11-20]

1. Busse PJ, et al. *N Engl J Med.* 2020;382:1136-48. **2.** Betschel S, et al. *Allergy Asthma Clin Immunol.* 2019;15:72. **3.** Busse PJ, et al. *J Allergy Clin Immunol Pract.* 2021;9:132-50. **4.** Maurer M, et al. *Allergy.* 2022;77:1961-90.**5.** Center for Biologics Evaluation and Research. The voice of the patient–hereditary angioedema. US Food and Drug Administration; May 2018. https://www.fda.gov/media/113509/download. Accessed August 07, 2025. **6.** Betschel SD, et al. *Allergy Asthma Clin Immunol*. 2024;20:43. **7.** Covella B, et al. *Future Pharmac.* 2024;4:41-53. **8.** Christiansen S, et al. *Ann Allergy Asthma Immunol* 2025;May;134(5):570-579. **9.** Mendivil J, et al. Presented at: ACAAI; November 9–13, 2023; Anaheim, CA, USA. **10.** Petersen RS, et al. *J Allergy Clin Immunol Pract.* 2024;1614:1621. **11.** RAPIDe-1 https://www.clinicaltrials.gov/study/NCT04618211. Accessed August 07, 2025. **12.** Maurer M, et al. Presented at: AAAAI; February 24–27, 2023; San Antonio, TX, USA. **13**. RAPIDe-2. https://clinicaltrials.gov/study/NCT05396105. Accessed August 07, 2025. **14.** RAPIDe-3 https://www.clinicaltrials.gov/study/NCT06343779. Accessed August 07, 2025. **15.** CHAPTER-1. https://www.clinicaltrials.gov/study/NCT05047185. Accessed August 07, 2025. **16.** CHAPTER-3. https://clinicaltrials.gov/study/NCT06669754. Accessed August 07, 2025. **17.** CHAPTER-4. https://clinicaltrials.gov/study/NCT06679881. Accessed August 07, 2025. **18.** Aygören-Pürsün E, et al. Presented at: EAACI; May 31–June 3, 2024; Valencia, Spain. **19**. Lesage A, et al. *Front Pharmacol*. 2020;11:916. **20**. Lesage A, et al. *Int Immunopharmacol*. 2022;105:108523.

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Objectives and study design

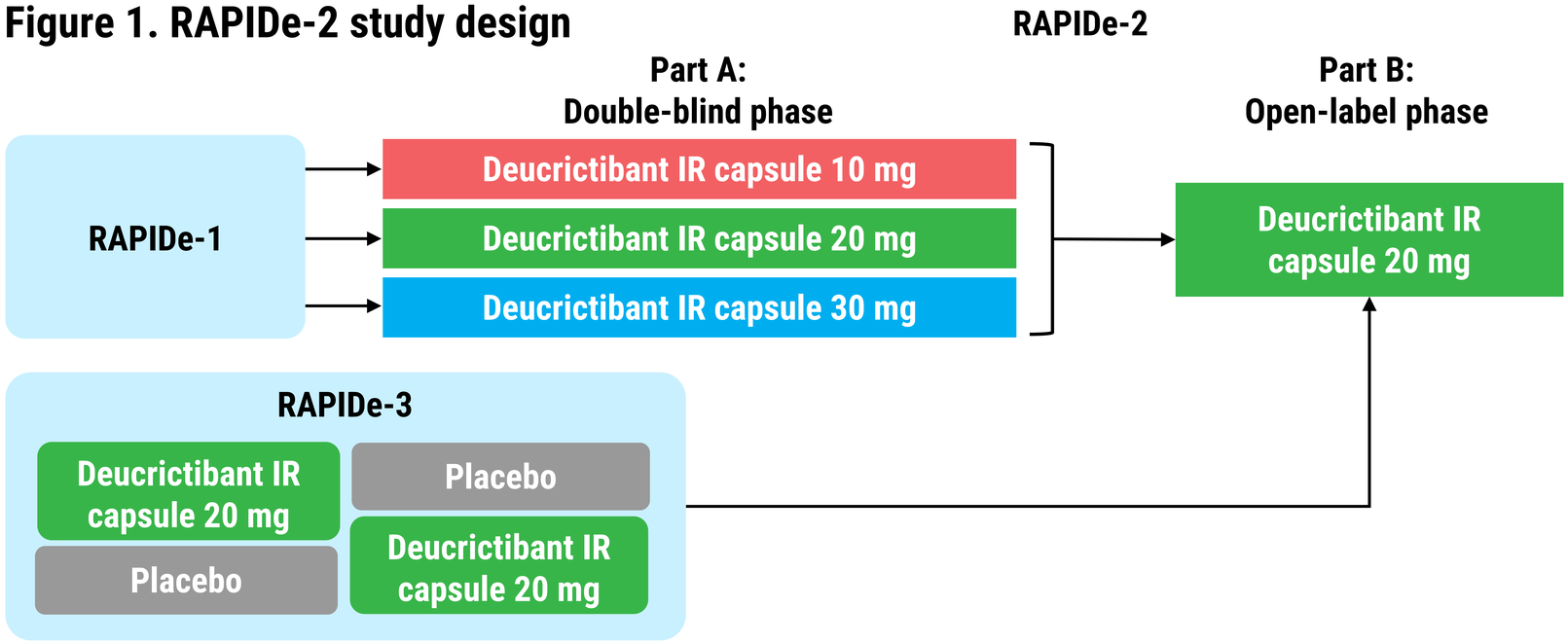
Objectives

- To evaluate the long-term safety and efficacy of deucrictibant IR capsule for on-demand treatment of repeat HAE attacks in Part A of the RAPIDe-2 (NCT05396105)* extension study.
- To assess the durability of effects following a single dose of deucrictibant IR capsule for treatment of HAE attacks in a post-hoc analysis of Part A of the RAPIDe-2 study.

Study design

- **RAPIDe-2 (NCT05396105)*:** a two-part, 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



HAE, hereditary angioedema; IR, immediate-release. *RAPIDe-2. ClinicalTrials.gov identifier: NCT05396105. **9.** Mendivil J, et al. Presented at: ACAAI; November 9–13, 2023; Anaheim, CA, USA. **11.** RAPIDe-1 https://www.clinicaltrials.gov/study/NCT04618211. Accessed August 07, 2025.

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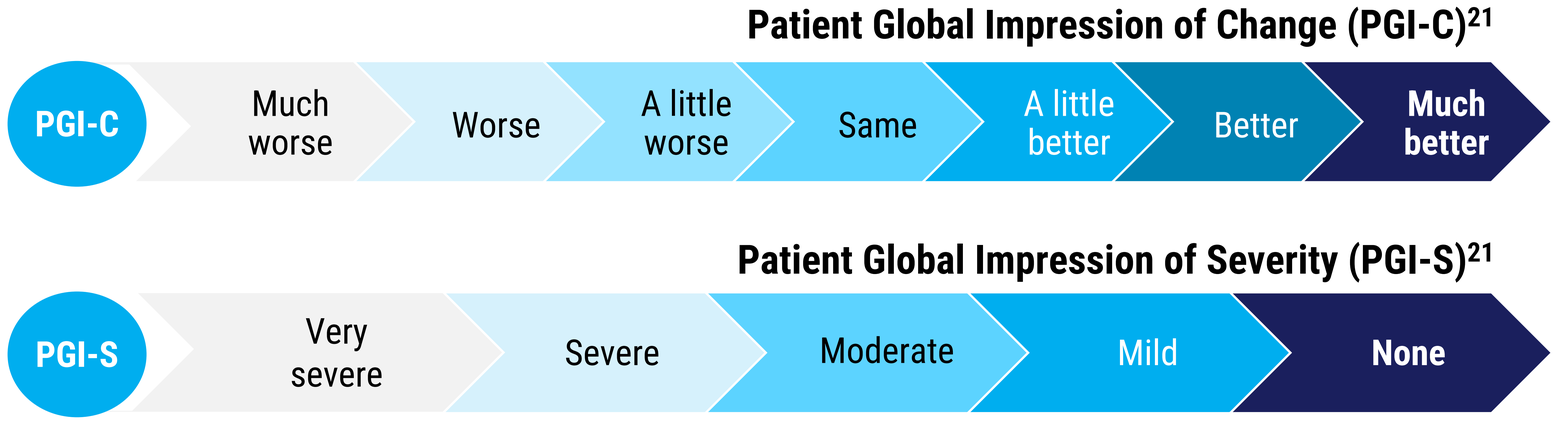
Methods

- **Primary endpoint:** safety, including treatment-emergent adverse events (TEAEs), clinical laboratory tests, vital signs, and electrocardiogram (ECG) findings.
- **Secondary endpoints:** efficacy endpoints using patient-reported outcome tools.
- **Data collection:** pre-specified at pre-treatment, hourly for 6 hours, and at 8, 12, 24, and 48 hours post-treatment.

Methods

Figure 2. Efficacy assessment scales



21. Cohn DM, et al. *Clin Transl Allergy*. 2023;e12288.

Methods

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” at 24 hours[b]

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 deucrictibant 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.

PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]If 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. [b]Rescue medication use within 33.5 hours post-treatment was regarded as not achieving complete attack resolution at 24 hours.

Results

Data

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

Table 2. Participant characteristics

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)

BMI, body mass index; HAE, hereditary angioedema; IR, immediate-release; SD, standard deviation. [a]All participants who received any dose of deucrictibant 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 (deucrictibant 10 mg, 20 mg, and 30 mg).

Results: Safety analysis

- Participants who received ≥1 dose of deucrictibant 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.
- No TEAEs leading to treatment discontinuation, study withdrawal, or death.

Table 3. TEAEs within 3 days of study drug administration

Adverse events	Deucrictibant 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.
[a]Tooth caries unrelated to treatment. Data for combined dose group shown (deucrictibant 10 mg, 20 mg, and 30 mg).

Results: Efficacy analysis

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

Figure 3. Median time to achieving key efficacy endpoints

Median time to (95% CI)	Onset of symptom relief	Substantial symptom relief	Reduction in attack severity	Complete attack resolution
	1.1 hours (1.0, 1.1)[a,b]	**2.5 hours** (2.1, 2.9)[b,c]	**2.8 hours** (2.3, 2.9)[b,d]	**10.6 hours** (8.5, 11.5)[b,e]

CI, confidence interval; IR, immediate-release; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [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]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. [d]≥1 point reduction in PGI-S from pre-treatment for 2 consecutive timepoints by 12 hours post-treatment and without rescue medication use. [e]PGI-S rating of "none" within 48 hours post-treatment and without rescue medication use.

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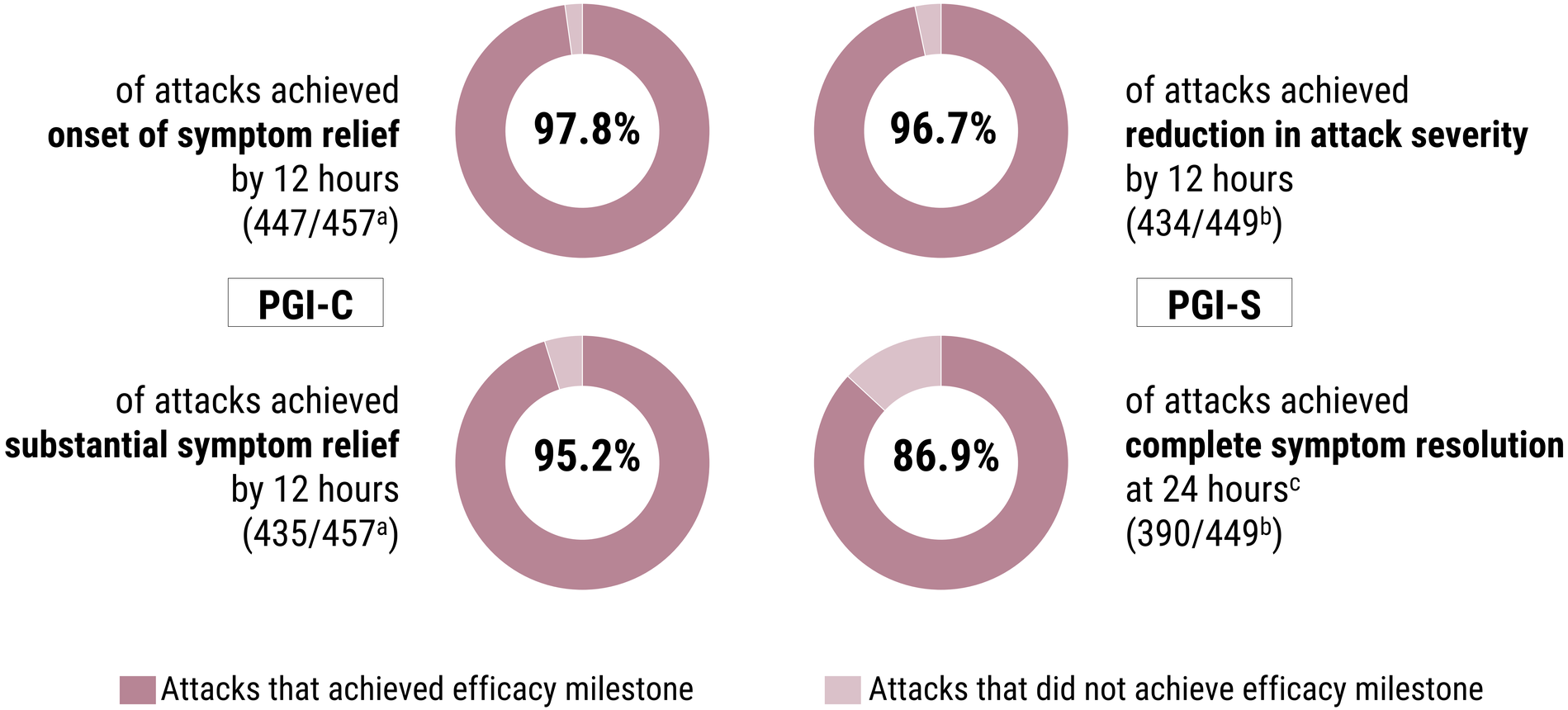
Results

Figure 4. Majority of attacks achieved key efficacy endpoints



PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]457 attacks have at least 1 post-treatment PGI-C result. [b]449 attacks have non-missing pre-treatment PGI-S and at least 1 post-treatment PGI-S. [c]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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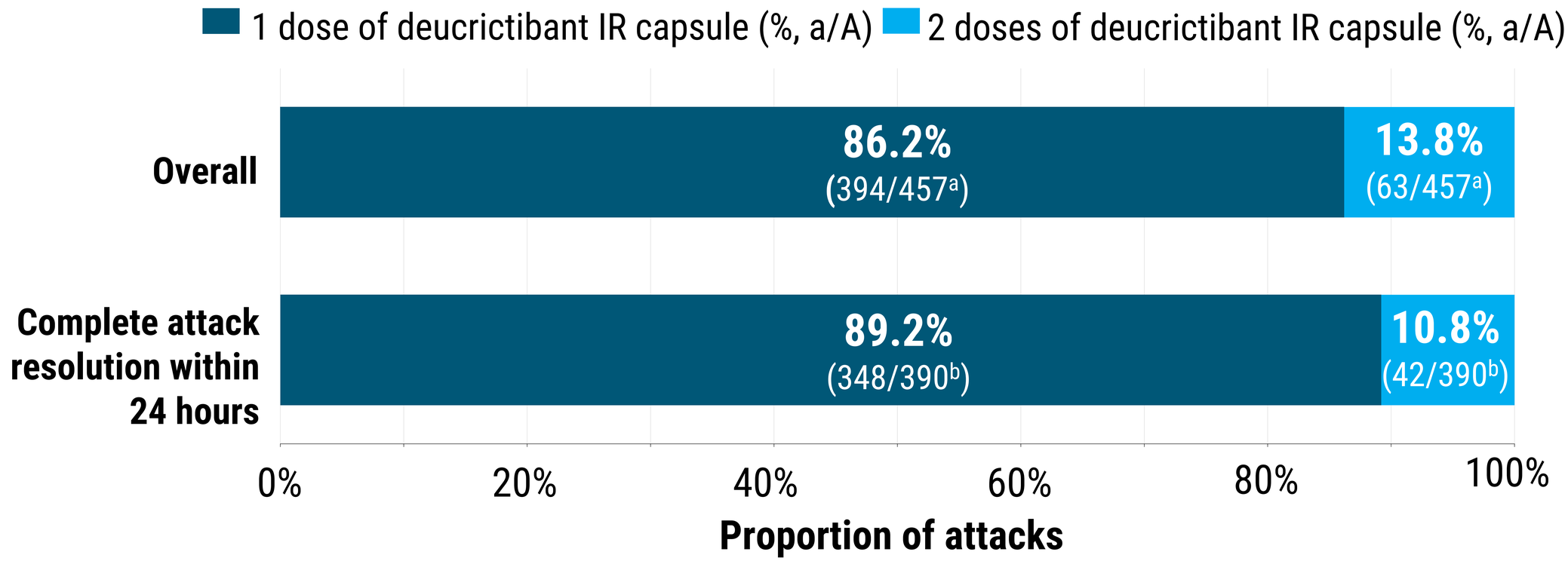
Results

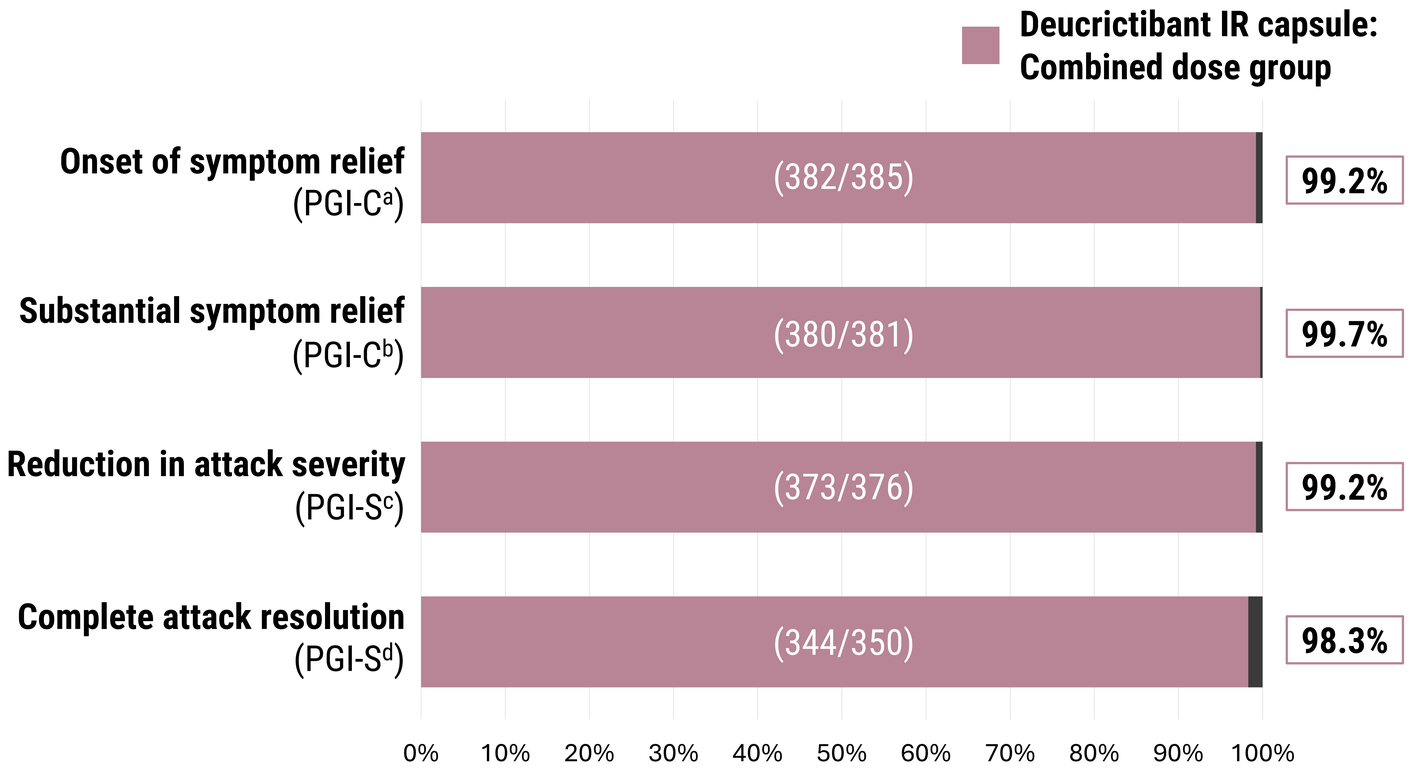
Figure 5. Majority of attacks treated with a single dose of deucrictibant IR capsule and without rescue medication



IR, immediate-release. a = number of attacks with the specified outcome. A = number of attacks. 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.

Results

Figure 6. RAPIDe-2: 98-100% of attacks that achieved symptom relief and resolution with a single dose of deucrictibant IR capsule maintained a durable response without reoccurrence of symptoms



IR, immediate-release; PGI-C, patient global impression of change; PGI-S, patient global impression of severity. [a]Onset of symptom relief defined as PGI-C rating of at least "a little better" for 2 consecutive timepoints by 12 hours post-treatment; reoccurrence of symptoms defined as subsequent rating of "same" or lower within 24 hours. [b]Substantial symptom relief defined as PGI-C rating of "better" for 2 consecutive timepoints by 12 hours post-treatment; reoccurrence of symptoms defined as subsequent rating of "a little better" or lower within 24 hours. [c]Reduction in attack severity defined as PGI-S ≥1 point reduction from pre-treatment by 12 hours post-treatment; reoccurrence of symptoms defined as subsequent occurrence of less than 1-point reduction within 24 hours. [d]Complete attack resolution defined as PGI-S rating of "none" at 24 hours post-treatment; reoccurrence of symptoms defined as subsequent occurrence of rating above "none" within 24 hours. Data for combined dose group shown (deucrictibant 10 mg, 20 mg, and 30 mg).

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Conclusions

- 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 deucrictibant IR capsule for treatment of repeat HAE attacks.
- In a post-hoc analysis, the response to a single dose of deucrictibant IR capsule was durable and the majority of HAE attacks that achieved symptom relief and resolution maintained a durable response without reoccurrence of symptoms.

Safety

Deucrictibant was generally well tolerated with no treatment-related TEAEs

Efficacy

1.1 Hours

Median time to onset of symptom relief

86.9%

of attacks achieved complete symptom resolution at 24 hours

Durable response

>98%

of attacks that achieved symptom relief and resolution had a durable response without symptom reoccurrence

The Authors and the Sponsor would like to thank all the people with HAE as well as all study site staff who participated in the RAPIDe-1 and RAPIDe-2 studies.

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

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