

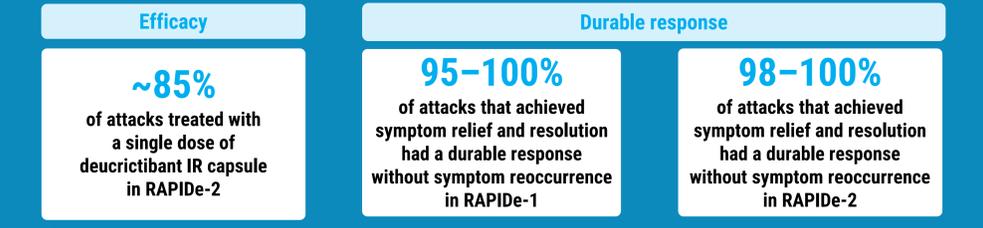
# Durability of Response to a Single Dose of Oral Deucricitbant for On-Demand Treatment of Hereditary Angioedema Attacks

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## Key takeaways

In a post-hoc analysis of two Phase 2 studies, the response to a single dose of deucricitbant immediate-release (IR) capsule was durable and the majority of hereditary angioedema (HAE) attacks that achieved symptom relief and resolution maintained a durable response without recurrence of symptoms.



## Background

- Hereditary angioedema (HAE):** a bradykinin-mediated condition with painful swelling attacks affecting multiple locations in the body.<sup>1</sup>
- Current landscape:** guidelines recommend HAE attacks are treated as early as possible.<sup>2-4</sup> Parenteral administration often leads to on-demand treatment of HAE attacks being delayed or forgone.<sup>5-9</sup>
- Treatment response:** a rapid and durable response to on-demand treatment 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.<sup>6,10</sup>
- Deucricitbant:** a selective, orally bioavailable, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of HAE attacks.<sup>11-18</sup>

## Objective

To assess the durability of effects following a single dose of deucricitbant immediate release (IR) capsule for treatment of HAE attacks in the placebo-controlled RAPiDe-1 trial (NCT04618211)<sup>11</sup> and in the RAPiDe-2 (NCT05396105)<sup>12</sup> extension study.

## Methods

- RAPiDe-1:** a Phase 2, double-blind, placebo-controlled, randomized, crossover, dose-ranging trial of deucricitbant IR capsule for on-demand treatment of angioedema attacks.
- Eligible participants:** adults with HAE type 1 or type 2 (HAE-1/2); ≥3 attacks in the last 4 months or ≥2 attacks in the last 2 months prior to screening; access to and experience with use of on-demand medications.
- RAPiDe-2:** a two-part, double-blind Phase 2/3 extension study. Part A participants were adults who completed RAPiDe-1.

Figure 1. RAPiDe-1 and RAPiDe-2 study design

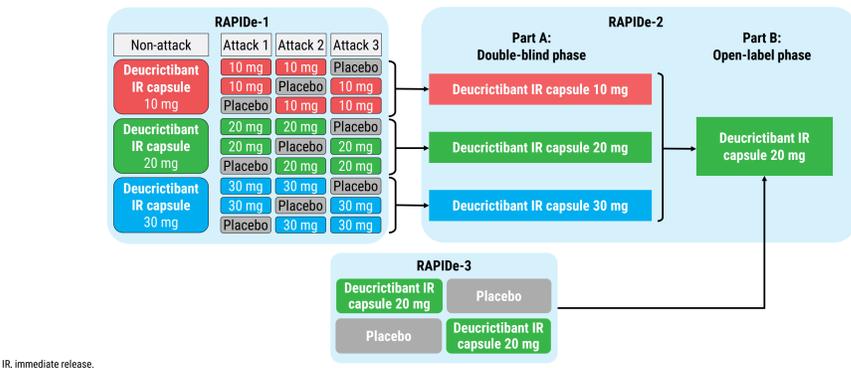
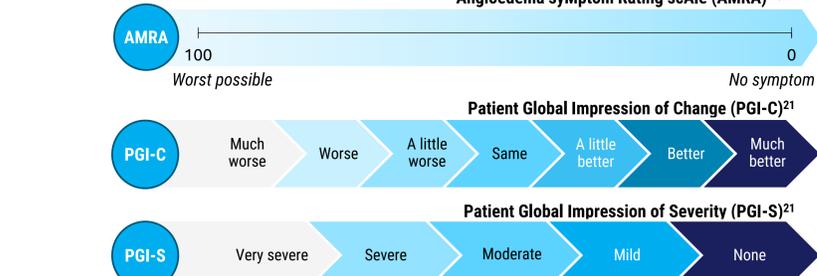


Figure 2. Efficacy assessment scales



## Post-hoc analysis of both studies

- Durability of response:** the achievement and maintenance of serial milestones of symptom relief and resolution without recurrence of symptoms following a single-dose of deucricitbant only.
- Symptom recurrence:** following the achievement of each pre-specified efficacy milestone, symptom recurrence was defined as any instance of the milestone no longer being met within 24 hours post-treatment.

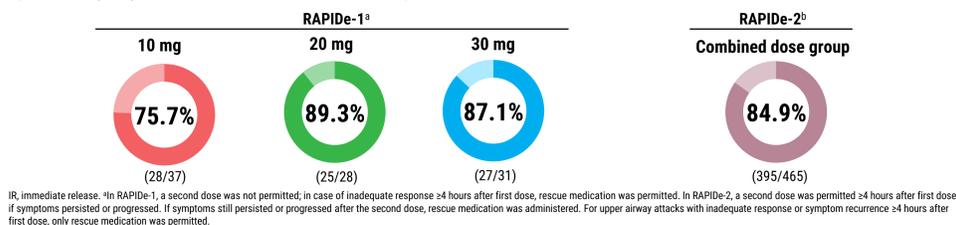
## Results

### Data

- These final RAPiDe-1 results included 96 HAE attacks treated with deucricitbant by 57 participants.
- These final RAPiDe-2 Part A results included 465 HAE attacks treated with deucricitbant by 19 participants.
- Combined dose group data are shown.

### Efficacy

Figure 3. Majority of attacks were treated with a single dose of deucricitbant IR capsule within 24 hours



IR, immediate release. <sup>11</sup>RAPiDe-1, a second dose was not permitted; in case of inadequate response 24 hours after first dose, rescue medication was permitted. In RAPiDe-2, a second dose 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. For upper airway attacks with inadequate response or symptom recurrence ≥4 hours after first dose, only rescue medication was permitted.

## Results

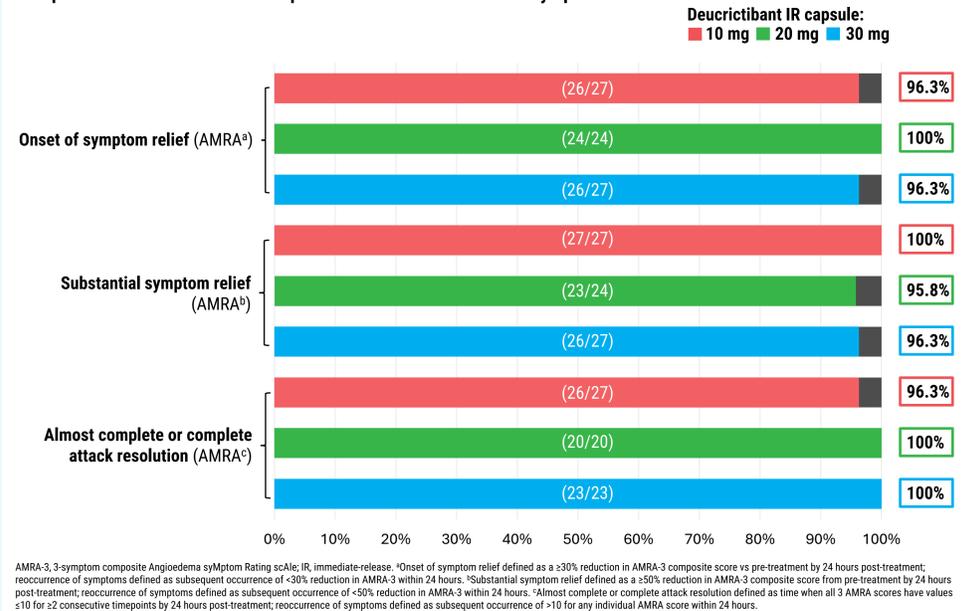
Table 1. Majority of attacks treated with a single dose of deucricitbant IR capsule achieved key efficacy endpoints

Attack milestone	Pre-specified efficacy milestone	RAPiDe-1			RAPiDe-2
		10 mg	20 mg	30 mg	Combined
Onset of symptom relief	AMRA: ≥30% reduction in AMRA-3 from pre-treatment <sup>a</sup>	96.4% (27/28)	96.0% (24/25)	100% (27/27)	95.2% (376/395)
	PGI-C: PGI-C rating of at least "a little better" for 2 consecutive timepoints <sup>b</sup>				97.5% (385/395)
Substantial symptom relief	AMRA: ≥50% reduction in AMRA-3 from pre-treatment <sup>a</sup>	96.4% (27/28)	96.0% (24/25)	100% (27/27)	94.2% (372/395)
	PGI-C: PGI-C rating of at least "better" for 2 consecutive timepoints <sup>b</sup>				96.5% (381/395)
Reduction in attack severity	PGI-S: ≥1 point reduction in PGI-S score <sup>b</sup>				95.2% (376/395)
Almost complete or complete attack resolution	AMRA: All 3 AMRA item scores (skin pain, skin swelling, and abdominal pain) ≤10 for 2 consecutive timepoints <sup>c</sup>	96.4% (27/28)	80.0% (20/25)	85.2% (23/27)	91.4% (361/395)
	PGI-S: PGI-S rating "none" <sup>c</sup>				88.6% (350/395)

AMRA, Angioedema symptom Rating scale (skin pain, skin swelling, and abdominal pain); IR, immediate-release; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. <sup>a</sup>Achieved by 24 hours post-treatment in RAPiDe-1 and by 12 hours post-treatment in RAPiDe-2. <sup>b</sup>Achieved by 12 hours post-treatment. <sup>c</sup>Achieved by 24 hours post-treatment.

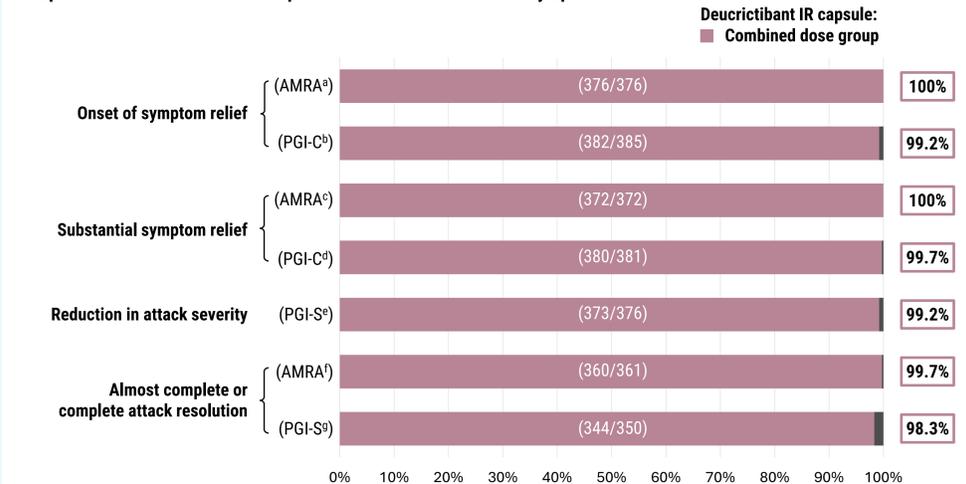
## Durability of response

Figure 4. RAPiDe-1: 95–100% of attacks that achieved symptom relief and resolution with a single dose of deucricitbant IR capsule maintained a durable response without recurrence of symptoms



AMRA-3, 3-symptom composite Angioedema symptom Rating scale; IR, immediate-release. <sup>a</sup>Onset of symptom relief defined as a ≥30% reduction in AMRA-3 composite score vs pre-treatment by 24 hours post-treatment; recurrence of symptoms defined as subsequent occurrence of <30% reduction in AMRA-3 within 24 hours. <sup>b</sup>Substantial symptom relief defined as a ≥50% reduction in AMRA-3 composite score from pre-treatment by 24 hours post-treatment; recurrence of symptoms defined as subsequent occurrence of <50% reduction in AMRA-3 within 24 hours. <sup>c</sup>Almost complete or complete attack resolution defined as time when all 3 AMRA scores have values ≤10 for ≥2 consecutive timepoints by 24 hours post-treatment; recurrence of symptoms defined as subsequent occurrence of >10 for any individual AMRA score within 24 hours.

Figure 5. RAPiDe-2: 98–100% of attacks that achieved symptom relief and resolution with a single dose of deucricitbant IR capsule maintained a durable response without recurrence of symptoms



AMRA-3, 3-symptom composite Angioedema symptom Rating scale; IR, immediate-release; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. <sup>a</sup>Onset of symptom relief defined as a ≥30% reduction in AMRA-3 composite score from pre-treatment by 24 hours post-treatment; recurrence of symptoms defined as subsequent occurrence of <30% reduction in AMRA-3 within 24 hours. <sup>b</sup>Onset of symptom relief defined as PGI-C rating of at least "a little better" for 2 consecutive timepoints by 12 hours post-treatment; recurrence of symptoms defined as subsequent occurrence of "same" or lower within 24 hours. <sup>c</sup>Substantial symptom relief defined as a ≥50% reduction in AMRA-3 composite score from pre-treatment by 24 hours post-treatment; recurrence of symptoms defined as subsequent occurrence of <50% reduction in AMRA-3 within 24 hours. <sup>d</sup>Substantial symptom relief defined as PGI-C rating of "better" for 2 consecutive timepoints by 12 hours post-treatment; recurrence of symptoms defined as subsequent rating of "a little better" or lower within 24 hours. <sup>e</sup>Reduction in attack severity defined as PGI-S ≥1 point reduction from pre-treatment by 12 hours post-treatment; recurrence of symptoms defined as subsequent occurrence of <1 point reduction within 24 hours. <sup>f</sup>Almost complete or complete attack resolution defined as time when all 3 AMRA scores have values ≤10 for ≥2 consecutive timepoints by 24 hours post-treatment; recurrence of symptoms defined as subsequent occurrence of >10 for any individual AMRA score within 24 hours. <sup>g</sup>Complete attack resolution defined as PGI-S rating of "none" at 24 hours post-treatment; recurrence of symptoms defined as subsequent occurrence of rating above "none" within 24 hours. Data for combined dose group shown (deucricitbant 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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