

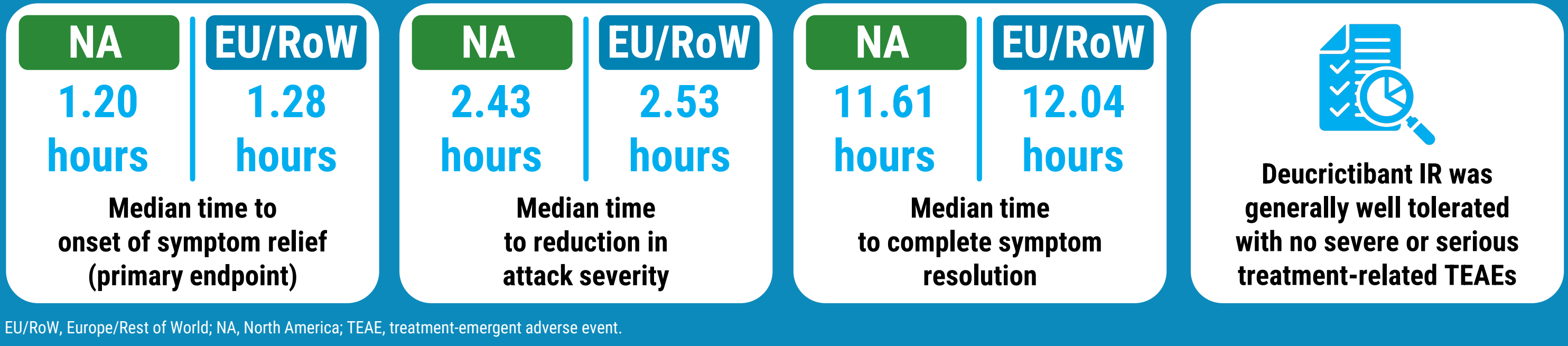
Oral Deucricitibant Immediate-Release Capsule for On-Demand Treatment of Hereditary Angioedema Attacks: Regional Subgroup Analysis From the Phase 3 RAPiDe-3 Trial

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Key takeaways

In this regional subgroup analysis of the pivotal RAPiDe-3 trial, deucricitibant immediate-release (IR) capsule, an orally administered bradykinin B2 receptor antagonist, provided faster onset of symptom relief, reduction in attack severity, and complete resolution in both the North America and Europe/Rest of World subgroups compared with placebo. Data were consistent across geographical locations and with the overall study population.



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

Background

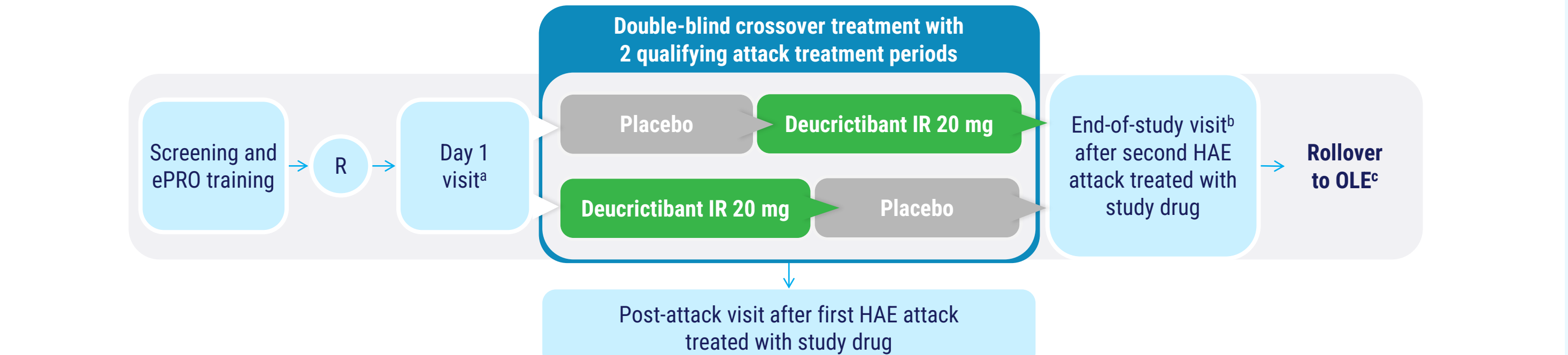
- Hereditary angioedema (HAE):** a bradykinin-mediated condition with painful swelling attacks affecting multiple locations in the body.¹
- Unmet need:** an unmet need remains for additional orally administered treatments combining ease of administration, rapid and sustained effects, and a well-tolerated safety profile.^{2,3}
- Oral deucricitibant:** a selective bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of bradykinin-mediated angioedema attacks.^{4,10}
- Primary analysis:** In the pivotal RAPiDe-3 trial, compared with placebo, deucricitibant immediate-release (IR) capsule provided significantly faster onset of symptom relief (1.28 hours vs >12 hours), reduction in attack severity (2.41 hours vs >12 hours), and complete resolution of HAE attacks (11.95 hours vs >48 hours) in 88 participants with paired treated attacks.⁶

Objective

To assess the efficacy, safety, and tolerability of oral deucricitibant IR capsule for on-demand treatment of attacks in adolescents and adults with HAE, including participants with HAE with normal C1 inhibitor (HAE-nC1INH). This analysis presents subgroup data from North America and Europe/Rest of World.

Methods

Figure 1. RAPiDe-3 trial design



ePRO, electronic patient-reported outcome; HAE, hereditary angioedema; IR, immediate-release; OLE, open-label extension; R, randomization. *Adolescent participants received a non-attack dose for pharmacokinetic sampling at Day 1 visit prior to randomization. *Data from end-of-study visit could be used to qualify the participant for an OLE study with deucricitibant. *Rollover to the OLE was optional. Riedl MA, et al. *Lancet*. 2026; doi: 10.1016/S0140-6736(26)01296-1.

- RAPiDe-3 (NCT06343779)*:** a global, Phase 3, randomized, double-blind, placebo-controlled trial.
- Participants:** adolescents (aged ≥12 to <18 years) and adults (aged ≥18 to ≤75 years) with HAE-C1INH type 1 or 2, or HAE-nC1INH. Participants on long-term HAE prophylaxis were also enrolled.
- Study drugs:** participants self-administered deucricitibant IR capsule 20 mg or placebo to treat two qualifying attacks in a crossover design. Qualifying attacks were defined as either a non-laryngeal attack with at least one symptom item score of ≥20 on the Angioedema Symptom Rating Scale (AMRA) assessment, or a non-severe laryngeal attack without breathing difficulties or stridor.
- Analysis sets:** subgroup analysis included all participants with treated attacks. Safety analysis included all participants who received ≥1 dose of study drug.

Table 1. Selected efficacy* and safety endpoints

Endpoint	Instrument	Definition
Primary endpoint		
Time to onset of symptom relief	PGI-C	Time to a PGI-C rating of at least "a little better" for 2 consecutive timepoints within 12 hours post-treatment
Secondary endpoints		
Proportion of attacks achieving onset of symptom relief	PGI-C	Proportion of study-drug treated attacks achieving a PGI-C rating of at least "a little better" at 4 hours post-treatment
Time to reduction in attack severity	PGI-S	Time to a ≥1-level reduction in PGI-S score from pre-treatment for 2 consecutive timepoints within 12 hours post-treatment
Time to complete symptom resolution	PGI-S	Time to PGI-S rating of "none" within 48 hours post-treatment
Safety endpoint		
TEAEs and serious TEAEs	–	TEAE defined as an adverse event from the first study drug administration through the end-of-study visit

PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity; TEAE, treatment-emergent adverse event. *The primary and 3 of 11 hierarchical order-ranked secondary endpoints.

Results

- In total, RAPiDe-3 enrolled 134 participants. The North American and European/Rest of World subgroups included 38 and 96 participants, respectively.
- In this analysis, 113 participants had ≥1 attack treated with study drug.
- Demographics and baseline characteristics were generally balanced across treatment groups.

Table 2. Participant demographics and baseline disease characteristics

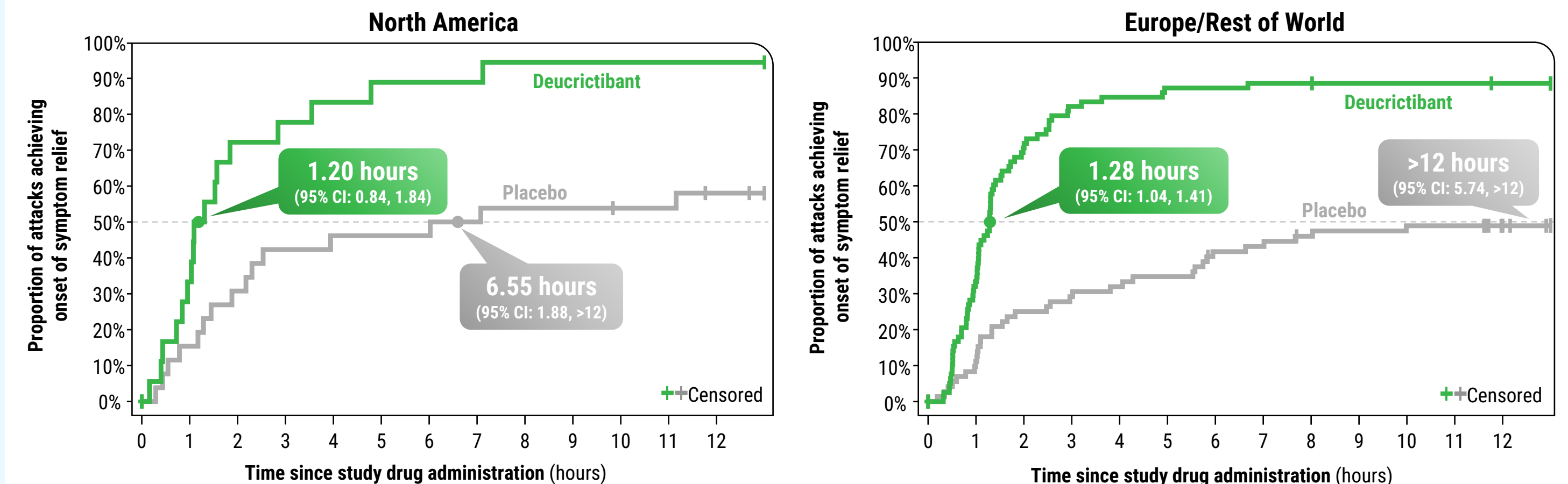
Participant characteristics	North America subgroup (N=38) ^a	Europe/Rest of World subgroup (N=96) ^a
Age in years, mean (SD)	39.0 (14.9)	39.0 (14.7)
≥12 to <18, n (%)	3 (7.9)	7 (7.3)
≥18 to <65, n (%)	34 (89.5)	82 (85.4)
≥65, n (%)	1 (2.6)	7 (7.3)
Sex: Female, n (%)	20 (52.6)	56 (58.3)
BMI, mean (SD)	29.2 (7.8)	25.5 (4.7)
Race, n (%)		
White	25 (65.8)	68 (70.8)
Asian	1 (2.6)	18 (18.8)
Black or African American	7 (18.4)	3 (3.1)
American Indian or Alaska Native	1 (2.6)	0
Other	3 (7.9)	4 (4.2)
Not reported	1 (2.6)	3 (3.1)
Years since HAE diagnosis, mean (SD)	20.6 (14.7)	16.5 (12.2)
Number of attacks within 3 months before screening, mean (SD)	3.4 (2.5)	4.8 (3.5) ^b
HAE type, n (%)		
HAE-C1INH type 1	35 (92.1)	83 (86.5)
HAE-C1INH type 2	0	10 (10.4)
Unspecified HAE-C1INH type 1 or 2	2 (5.3)	0
HAE-nC1INH ^c	1 (2.6)	3 (3.1)
Current LTP use, n (%)	13 (34.2) ^d	18 (18.9) ^e

BMI, body mass index; C1INH, C1 inhibitor; HAE, hereditary angioedema; LTP, long-term prophylaxis; nC1INH, normal C1 inhibitor; SD, standard deviation. ^aGeographic region of North America included Canada, Puerto Rico, United States of America; Europe included Austria, Bulgaria, Czech Republic, France, Germany, Hungary, Italy, Netherlands, Poland, Spain, Sweden, United Kingdom; Rest of world included Argentina, Australia, Brazil, Hong Kong, Japan, Saudi Arabia, South Africa, South Korea, Turkey. ^bn=94. ^cIncluded participants with HAE-nC1INH associated with a documented genetic variant. ^dLTP medication included lanadelumab (6 [15.8%]), complement C1 inhibitor (4 [10.5%]), berotralstat (2 [5.3%]), and other (1 [2.6%]). ^eLTP medication included lanadelumab (7 [7.3%]), complement C1 inhibitor (2 [2.1%]), berotralstat (6 [6.3%]), and other (3 [3.1%]).

Results

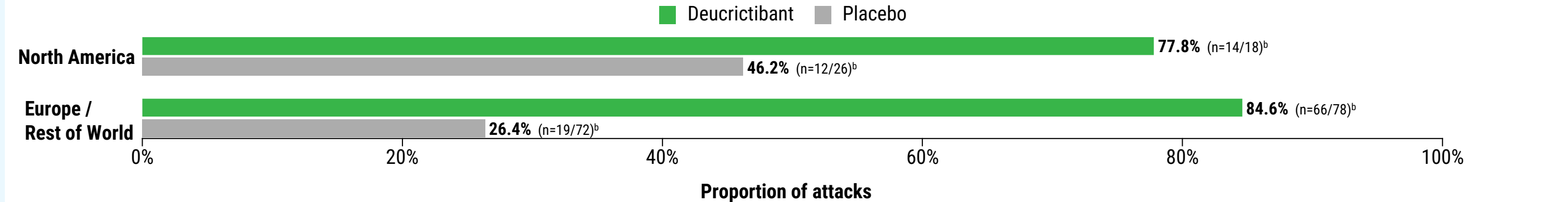
Efficacy

Figure 2. Deucricitibant-treated attacks were shown to achieve onset of symptom relief faster than placebo-treated attacks in both subgroups^{a,b}



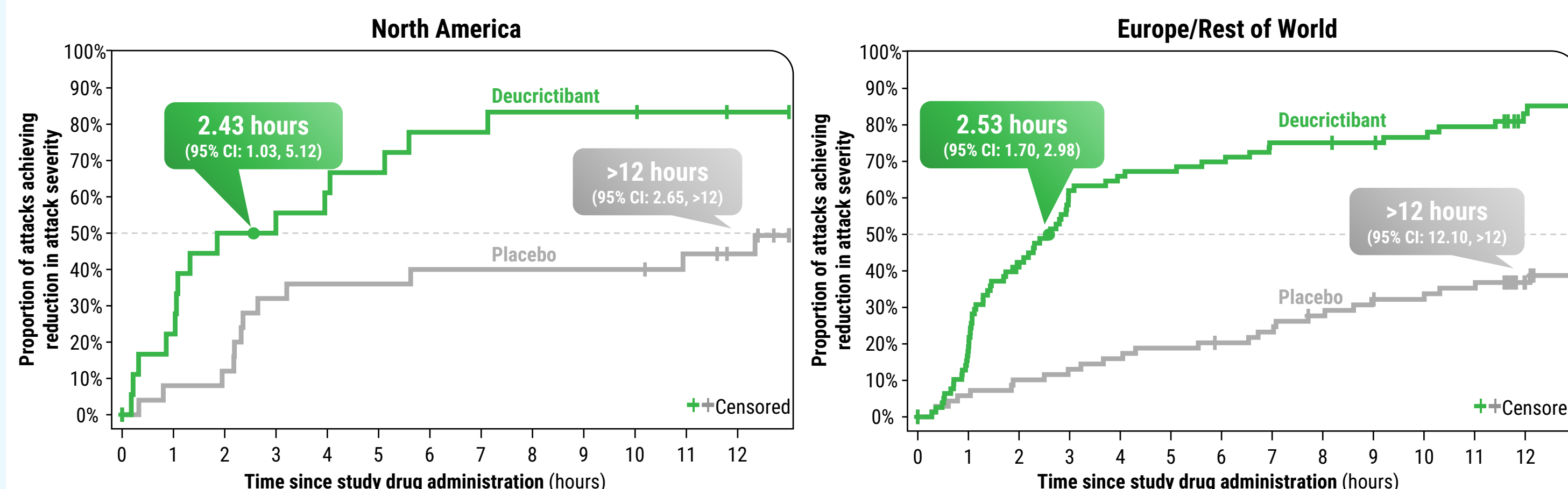
CI, confidence interval; PGI-C, Patient Global Impression of Change. *If the event of interest was not achieved within the pre-specified timeframe, the attack was right censored at the last observation before the upper end of the data entry window. For attacks with rescue medication use, they were treated as right censored at the upper end of the data entry window. ^bPGI-C rating of at least "a little better" for 2 consecutive timepoints within 12 hours post-treatment.

Figure 3. A higher proportion of attacks were shown to achieve onset of symptom relief at 4 hours* with deucricitibant compared with placebo in both subgroups



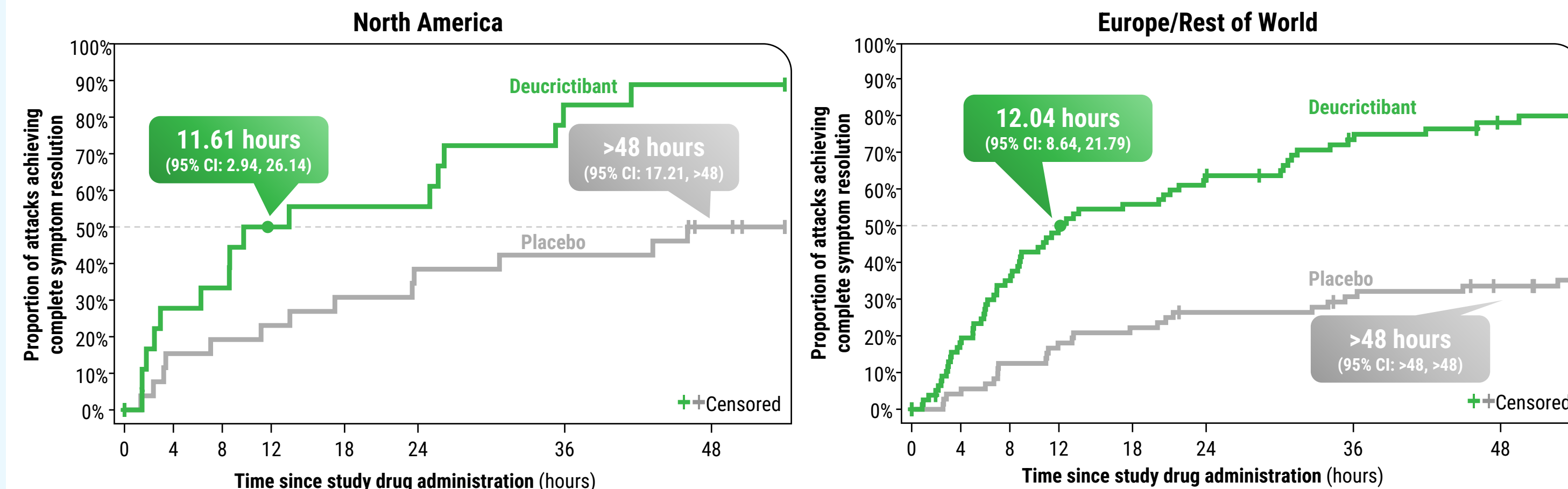
PGI-C, Patient Global Impression of Change. *Onset of symptom relief was considered achieved at 4 hours if for an attack, the last or the second-to-last available value of PGI-C prior to 4 hours post-treatment achieved "a little better" or "higher response" ("better" or "much better") and was sustained for 2 consecutive timepoints. Attacks with no PGI-C recorded within 4 hours post-treatment were excluded from the analysis, unless there was an intercurrent event for that attack, in which case the attack was considered as not achieving PGI-C "a little better" at 4 hours. *Number on participants with PGI-C data within 4 hours post-treatment.

Figure 4. Deucricitibant-treated attacks were shown to achieve reduction in attack severity faster than placebo-treated attacks in both subgroups^{a,b}



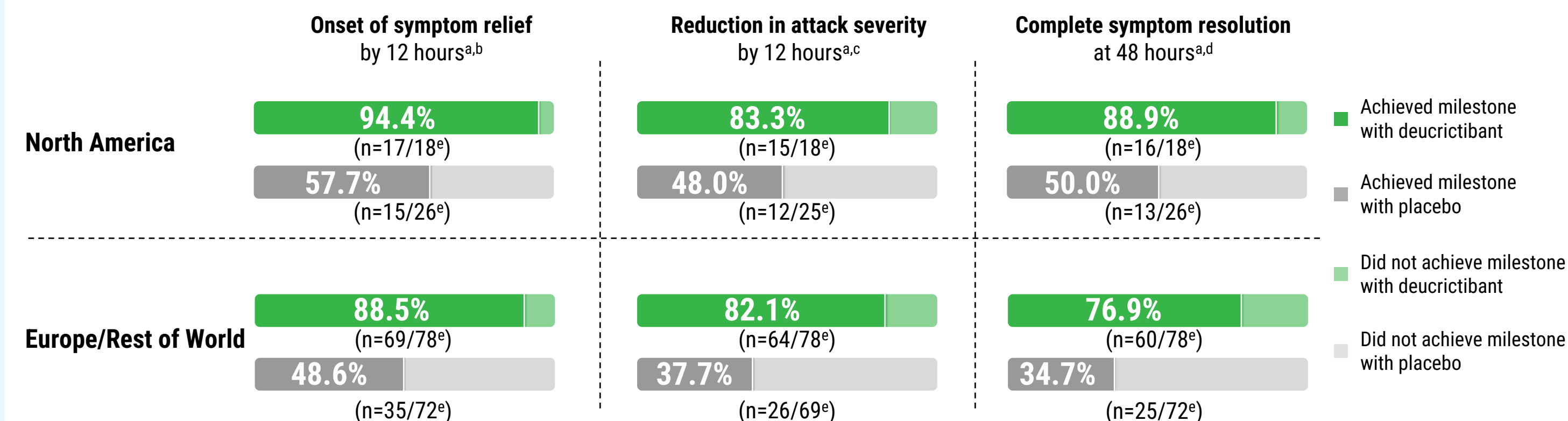
CI, confidence interval; PGI-S, Patient Global Impression of Severity. *If the event of interest was not achieved within the pre-specified timeframe, the attack was right censored at the last observation before the upper end of the data entry window. For attacks with rescue medication use, they were treated as right censored at the upper end of the data entry window. ^a≥1-level reduction in PGI-S score from pre-treatment for 2 consecutive timepoints within 12 hours post-treatment.

Figure 5. Deucricitibant-treated attacks were shown to achieve complete symptom resolution faster than placebo-treated attacks in both subgroups^{a,b}



CI, confidence interval; PGI-S, Patient Global Impression of Severity. *If the event of interest was not achieved within the pre-specified timeframe, the attack was right censored at the last observation before the upper end of the data entry window. For attacks with rescue medication use, they were treated as right censored at the upper end of the data entry window. ^aPGI-S rating of "none" within 48 hours post-treatment.

Figure 5. Proportion of attacks achieving efficacy endpoints within pre-specified timeframes



PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. *If the event of interest was not achieved within the pre-specified timeframe, the attack was right censored at the last observation before the upper end of the data entry window. For attacks with rescue medication use, they were treated as right censored at the upper end of the data entry window. ^aPGI-C rating of at least "a little better" for 2 consecutive timepoints within 12 hours post-treatment. ^b≥1-level reduction in PGI-S score from pre-treatment for 2 consecutive timepoints within 12 hours post-treatment. ^cPGI-S rating of "none" within 48 hours post-treatment. ^dNumber of participants with post-treatment data within specified timeframe.

Safety

- The only event reported more than once within 3 days post-treatment was fatigue: a single event was reported by 2 participants, one of which was deemed unrelated to treatment by the investigator.
- No adverse events occurring within 3 days post-treatment were assessed as severe or serious, led to treatment discontinuation, or were associated with changes in clinical laboratory, vital signs, or electrocardiogram parameters.

Table 3. Adverse events occurring within 3 days post-treatment (North America and Europe/Rest of World)

	Non-attack deucricitibant ^a		Treated attack deucricitibant		Treated attack placebo	
	NA (N=3)	EU/RoW (N=7)	NA (N=21)	EU/RoW (N=79)	NA (N=26)	EU/RoW (N=75)
	n (%) ^b	events	n (%) ^b	events	n (%) ^b	events
Any TEAE	0	0	0	0	6 (28.6)	7
Treatment-related TEAEs^d	0	0	0	0	1 (4.8)	1
Any severe TEAE^e	0	0	0	0	4 (5.1)	5
Serious TEAEs	0	0	0	0	0	0
TEAEs leading to study drug discontinuation, study withdrawal, or death	0	0	0	0	0	0

EU/RoW, Europe/Rest of World; NA, North America; TEAE, treatment-emergent adverse event. ^aRefers to the total number of participants who received ≥1 dose of study drug. Percentage is calculated based on the N in the header; percentage = 100 x n/N where N is the number of participants. ^bAdolescent participants only. ^cDefined as the number of participants with an adverse event that began within 3 days post-treatment of non-attack period and before the next administration of study drug. ^dDefined as the number of participants with an adverse event that started within 3 days post-treatment of attack. ^eOne related TEAE of headache in deucricitibant-treated participants in the North America subgroup, and one related TEAE each of dyspnea, fatigue, lethargy, brain fog, and somnolence in deucricitibant-treated participants, and 1 event of pruritus in placebo-treated participants in the European/Rest of World subgroup. ^fAll reported TEAEs were graded 1 (mild) or 2 (moderate) and there were no reported TEAEs graded 4 (life-threatening) or 5 (fatal).

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