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Oral Deucrictibant Immediate-Release Capsule for On-Demand Treatment of Hereditary Angioedema Attacks: End of Progression Results in the Phase 3 RAPIDe-3 Trial

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

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Disclosure

In relation to this presentation, I declare the following, real or perceived conflicts of interest:

Type	Company
Grant research support and/or speaker/consultancy fees	BioCryst, CSL Behring, KalVista, Pharming, Sobi, Takeda
Conferences and educational events	CSL Behring, Menarini, MSD, Novartis, Pharming, Takeda
Clinical trial/registry investigator	ADARx, BioCryst, Chiesi, CSL Behring, KalVista, NeoPharmed, Gentili, Novartis, Pharming, Pharvaris, Takeda, UCB, Otsuka

RAPIDe-3 was a Pharvaris-sponsored clinical study. ClinicalTrials.gov identifier: NCT06343779

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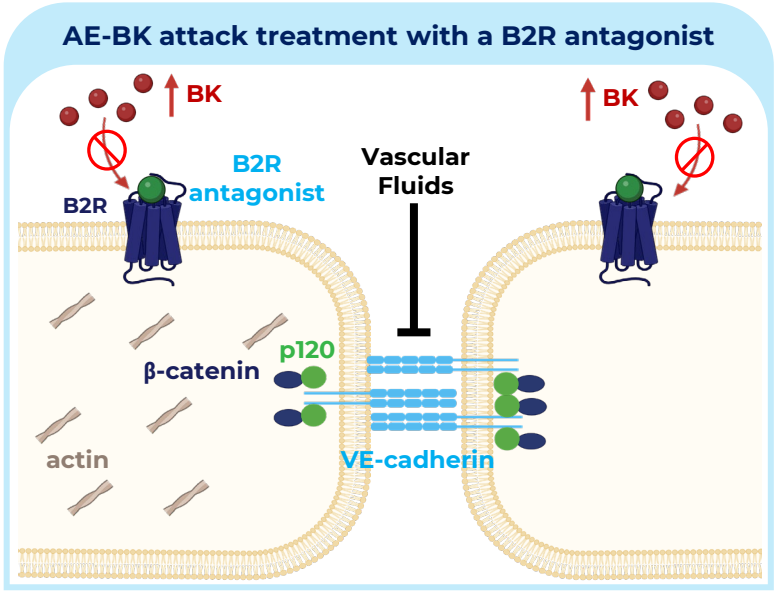
B2R antagonism inhibits downstream signaling and decreases excessive endothelial permeability during an AE-BK attack

Treatment with a B2R antagonist can end the progression of AE-BK attacks by:

- **Inhibiting excessive BK-mediated signaling that drives disruption of adherens and tight junctions[1,2]**
- **Preventing increased vascular permeability[1,2]**



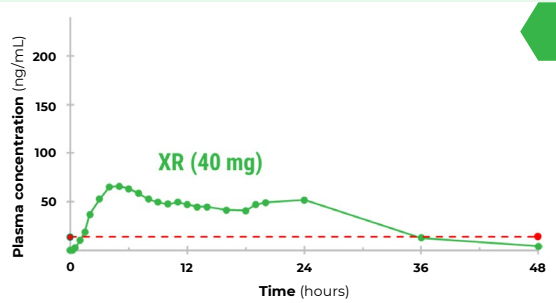
Bradykinin B2 receptor antagonism can effectively treat bradykinin-mediated angioedema attacks.[3-5]

AE-BK, bradykinin-mediated angioedema; BK, bradykinin; B2R, bradykinin B2 receptor; VE, vascular endothelial. **1.** Terzuoli E, et al. PLoS ONE 2014;9(1):e84358. **2.** Kempe S, et al. *Microcirculation.* 2019;27(2):e12592. **3.** Vázquez DO, et al. *World Allergy Organ J.* 2026 [online ahead of print]. **4.** Suffritti C, et al. *Clin Exp Allergy.* 2014;44(12):1503-1514. **5.** Maurer M, et al. *Lancet Haematol.* 2026; 13(4):e200-14.

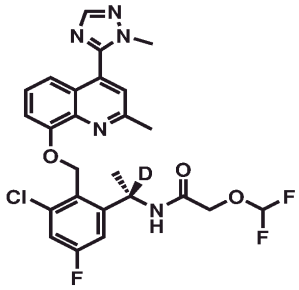
Deucrictibant is an orally administered, bradykinin B2 receptor antagonist in development for the prophylactic and on-demand treatment of bradykinin-mediated angioedema attacks

DEUCRICTIBANT extended-release (XR) tablet

sustained absorption[1]



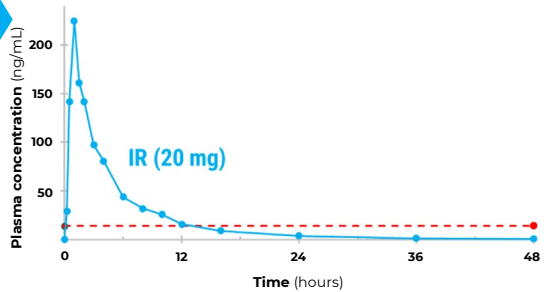
In studies, deucrictibant maintained sustained therapeutic exposure over 24 hours[1] from day 1, allowing for once-daily oral prevention of HAE attacks[2]



Deucrictibant

DEUCRICTIBANT immediate-release (IR) capsule

rapid absorption[3]

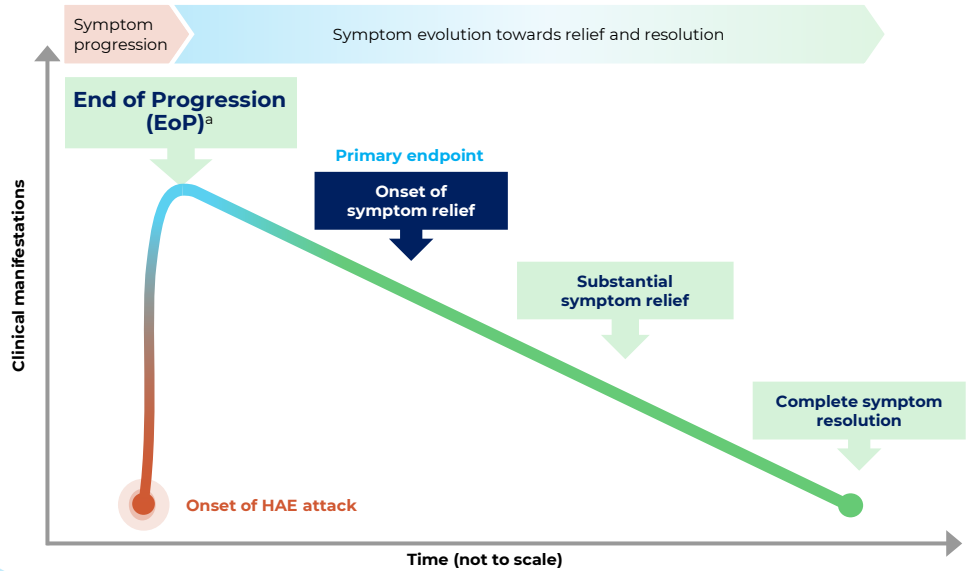


In studies, deucrictibant rapidly reached therapeutic exposure within 15–30 minutes[3], supporting on-demand oral treatment of HAE attacks[4, 5]

HAE, hereditary angioedema; IR, immediate-release; XR, extended-release. **1.** Zhang et al. Presented at C1INH Workshop; May 29-June 1, 2025. **2.** CHAPTER-3. ClinicalTrials.gov identifier: NCT06669754.. https://clinicaltrials.gov/study/NCT06669754. Accessed May 29, 2026 **3.** Maurer M, et al. *Lancet Haematol.* 2026; 13(4):e200-14. **4.** RAPIDe-3. ClinicalTrials.gov identifier: NCT06343779. https://www.clinicaltrials.gov/study/NCT06343779. Accessed May 29, 2026. **5.** Riedl MA, et al. Presented at the American Academy of Allergy, Asthma & Immunology (AAAAI) Annual Meeting; March 2026; Philadelphia, PA, USA.

End of progression (EoP) of bradykinin-mediated angioedema attack symptoms

End of progression is defined as the earliest post-treatment timepoint after which attack manifestations stop worsening further, marking the earliest evidence of treatment response[1]



EoP:

- Serves as a clinically meaningful indicator of attacks evolving towards relief and resolution[1]
- Offers psychological reassurance by reducing the uncertainty associated with attack escalation[2]

EoP, end of progression, HAE, hereditary angioedema; IR, immediate-release; PGI-C, Patient Global Impression of Change. [a]In RAPIDe-3, EoP was defined as the earliest post-treatment timepoint after which all subsequent PGI-C ratings were stable or improved within 12 hours.

1. Petersen RS, et al. *J Allergy Clin Immunol Pract*. 2024;12(6):1614-21.
2. Jean-Baptiste, Milenka et al. *Orphanet J Rare Dis.* 2022; 17(1), 232.

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

Time to EoP was included in the Acute Treatment Outcomes in Hereditary Angioedema (AURORA) consensus project

The **AURORA Delphi consensus project** developed a set of five core outcomes for clinical trials of on-demand HAE treatment[1]

Patients, clinicians, researchers, industry representatives, and regulatory stakeholders were brought together to develop the core outcomes[1]

Time to **EoP** was included as one of the five core outcomes specified by the AURORA project[1]

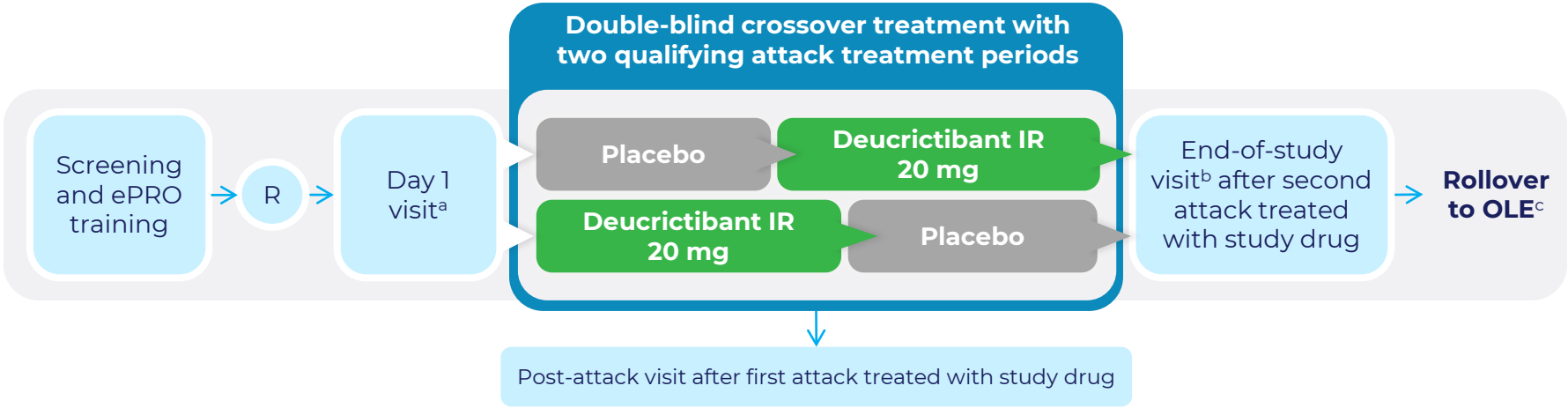
95%

of participants agreed to include time to EoP in the core outcomes set[1]

EoP[a] of attack manifestations was measured in the RAPIDe-3 trial for the first time as a pre-specified endpoint in an HAE on-demand trial

EoP, end of progression, HAE, hereditary angioedema; PGI-C, Patient Global Impression of Change. [a]In RAPIDe-3, EoP was defined as the earliest post-treatment timepoint after which all subsequent PGI-C ratings were stable or improved within 12 hours. **1**. Petersen RS, et al. *J Allergy Clin Immunol Pract*. 2024;12(6):1614-21.

RAPIDe-3 trial design

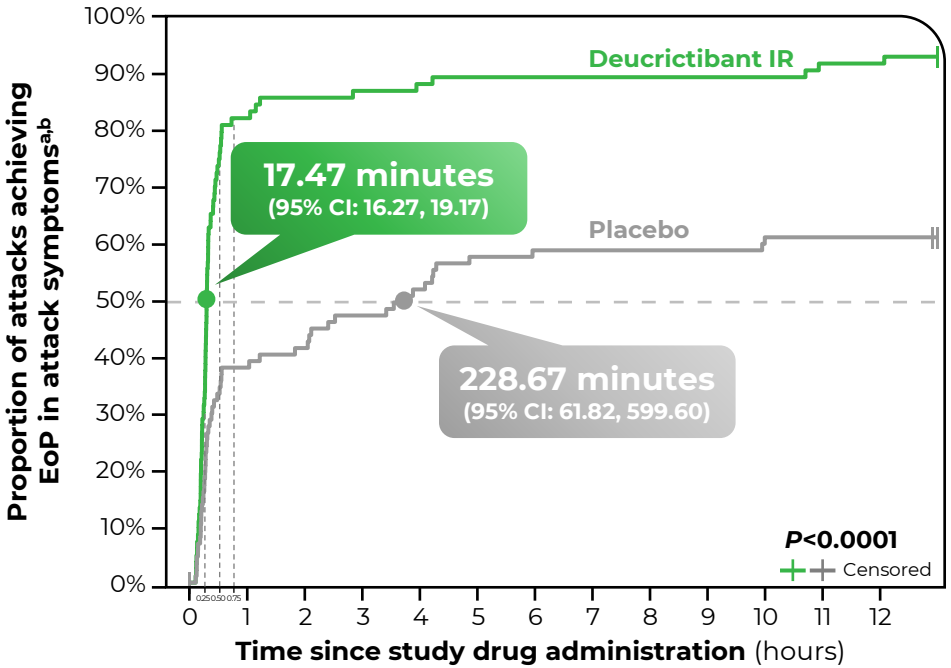


- **Participants:** adolescents (aged ≥12 to <18 years) and adults (aged ≥18 to ≤75 years) with HAE-C1INH Type 1 or 2, or HAE with normal C1 inhibitor (HAE-nC1INH). Participants on long-term HAE prophylaxis were also enrolled.
- **Qualifying attacks:** defined as either non-laryngeal or non-severe laryngeal attacks without breathing difficulties or stridor, and with at least one symptom item score of ≥20 on the Angioedema syMptom Rating scAle (AMRA) assessment.
- **Analysis set:** primary efficacy analysis included all randomized participants who treated both attacks with study drug in accordance with the crossover design.

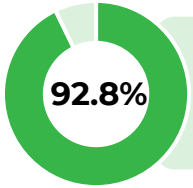
ePRO, electronic patient-reported outcome; HAE, hereditary angioedema; HAE-nC1INH, HAE with normal C1 inhibitor; IR, immediate-release; OLE, open-label extension; R, randomization.
[a]Adolescent participants received a non-attack dose for pharmacokinetic sampling at Day 1 visit prior to randomization. [b]Data from end-of-study visit could be used to qualify the participant for an OLE study with deucrictibant. [c]Rollover to the OLE was optional.
RAPIDe-3 was a Pharvaris-sponsored clinical study. ClinicalTrials.gov identifier: NCT06343779.

17.47 minutes median time to end of progression in attack symptoms with deucrictibant IR

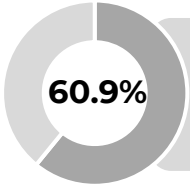
Earliest post-treatment timepoint after which all subsequent PGI-C ratings are stable or improved



Proportion of attacks achieving EoP of attack symptoms by 12 hours[a,b]



Deucrictibant IR (77/83[c])

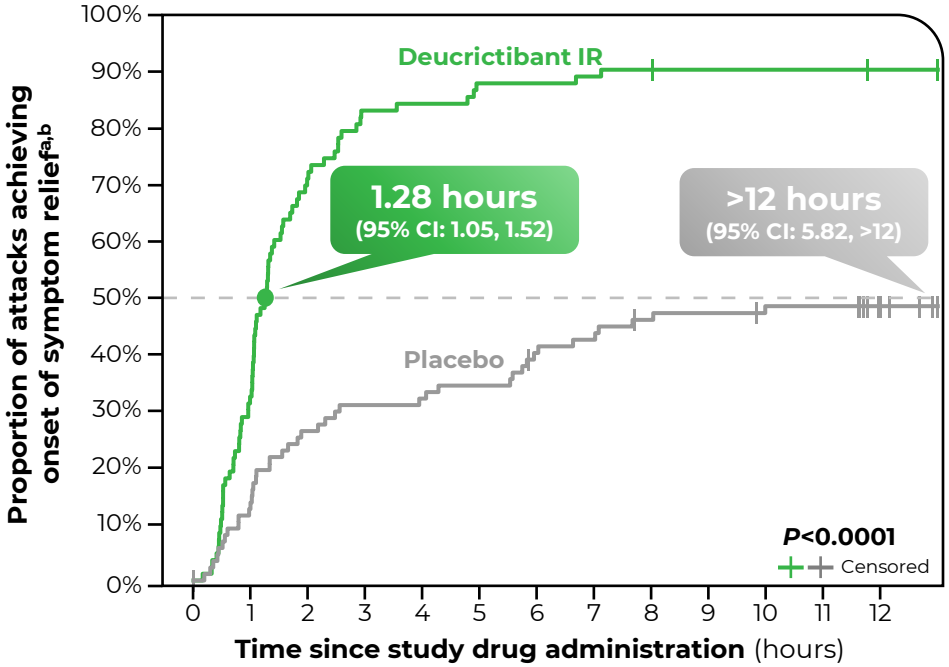


Placebo (53/87[c])

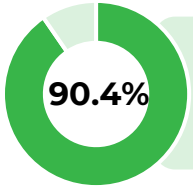
CI, confidence interval; EoP, end of progression; IR, immediate-release; PGI-C, Patient Global Impression of Change. [a]If the event of interest was not achieved within the pre-specified timeframe, the attack was right censored at the last observation before the upper end of the data entry window. For attacks with rescue medication use, they were treated as right-censored at the upper end of the data entry window. [b]Time to EoP of attack manifestations was the earliest post-treatment timepoint after which all subsequent PGI-C ratings were stable or improved. [c]Number of attacks with post-treatment data within the pre-specified timeframe.

1.28 hours median time to onset of symptom relief with deucrictibant IR

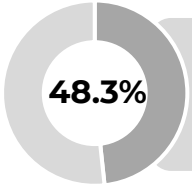
PGI-C rating of at least “a little better” for two consecutive timepoints within 12 hours post treatment



Proportion of attacks achieving onset of symptom relief[a,b] by 12 hours



Deucrictibant IR (75/83[c])

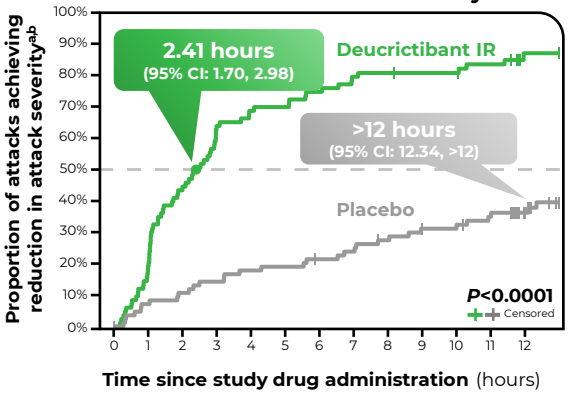


Placebo (42/87[c])

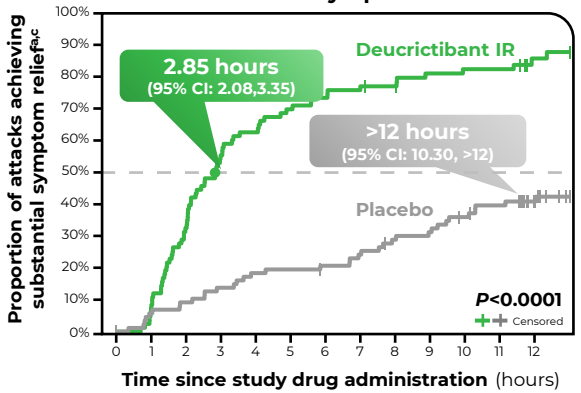
CI, confidence interval; IR, immediate-release; PGI-C, Patient Global Impression of Change. [a]If the event of interest was not achieved within the pre-specified timeframe, the attack was right-censored at the last observation before the upper end of the data entry window. For attacks with rescue medication use, they were treated as right-censored at the upper end of the data entry window. [b]PGI-C rating of at least “a little better” for two consecutive timepoints within 12 hours post treatment. [c]Number of attacks with post-treatment data within the pre-specified timeframe.

Deucrictibant-treated attacks achieved both symptom relief and complete symptom resolution faster than placebo-treated attacks

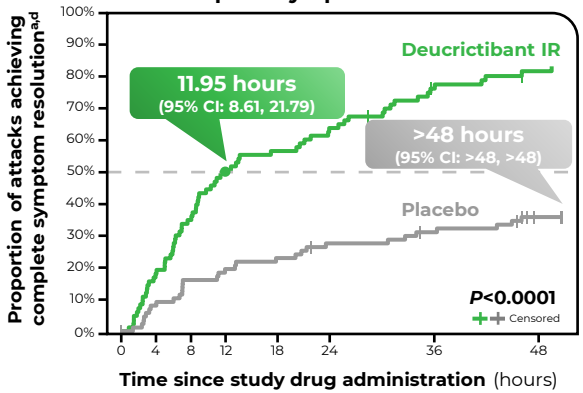
Reduction in attack severity



Substantial symptom relief



Complete symptom resolution



Reduction in attack severity by 12 hours[a,b]

85.5%	(n=71/83[e])
38.1%	(n=32/84[e])

Substantial symptom relief by 12 hours[a,c]

85.5%	(n=71/83[e])
41.4%	(n=36/87[e])

Complete symptom resolution by 48 hours[a,d]

81.9%	(n=68/83[e])
36.8%	(n=32/87[e])

Achieved milestone with deucrictibant IR Achieved milestone with placebo

CI, confidence interval; IR, immediate-release PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity. [a]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. [b]≥1-level reduction in PGI-S from pre-treatment for two consecutive timepoints within 12 hours post-treatment. [c]PGI-C rating of at least "better" for two consecutive timepoints within 12 hours post treatment. [d]PGI-S rating of "none" within 48 hours post treatment. [e]Number of attacks with post-treatment data within the pre-specified timeframe.

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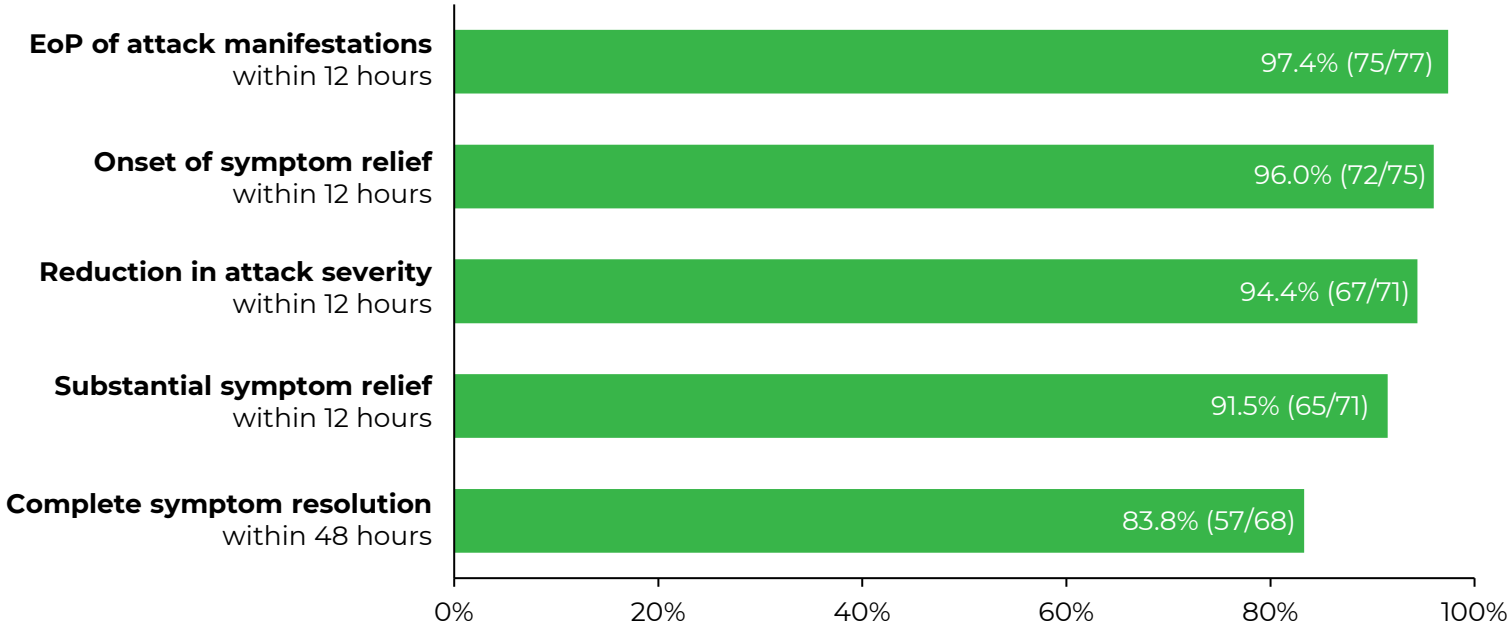
Majority of deucrictibant-treated attacks achieved efficacy endpoints with a single capsule



EoP, End of progression.

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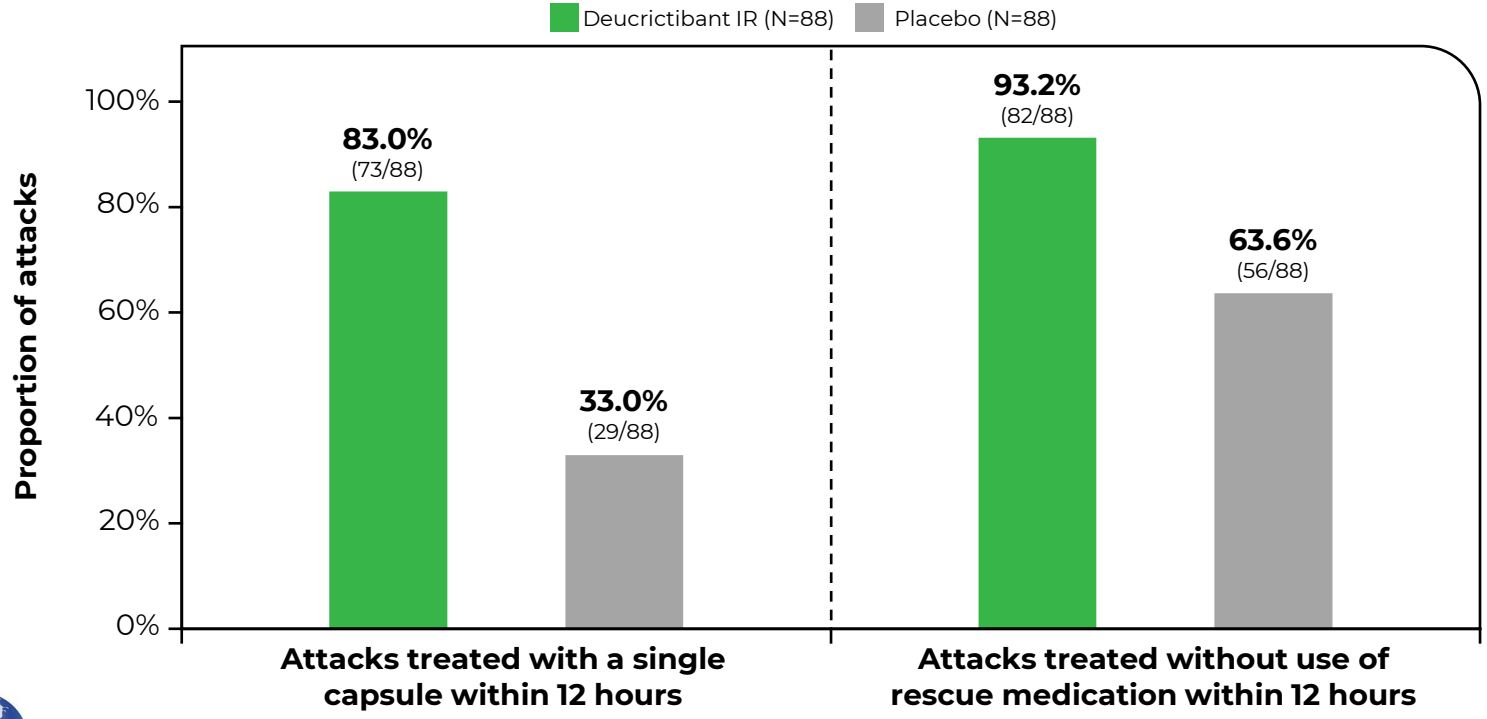
More than 80% of deucrictibant-treated attacks were treated with a single capsule and more than 90% did not require rescue medication



IR, immediate-release.

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Deucrictibant was generally well tolerated, with no serious adverse events, no severe TEAEs, and no discontinuations due to TEAEs[a,b]

- The only event reported more than once within 3 days post treatment was fatigue: a single event was reported by two participants, one of which 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.

Adverse events occurring within 3 days post-treatment	Non-attack: deucrictibant (N=10)[c]		Treated attacks: deucrictibant (N=100)		Treated attacks: placebo (N=101)	
	n (%)[d]	no. of events	n (%)[e]	no. of events	n (%)[e]	no. of events
Any TEAE	0	0	15 (15.0)	17	2 (2.0)	3
Treatment-related TEAEs[f]	0	0	5 (5.0)	6	1 (1.0)	1
Any severe TEAE[g]	0	0	0	0	0	0
Serious TEAEs	0	0	0	0	0	0
TEAEs leading to study drug discontinuation, study withdrawal, or death	0	0	0	0	0	0

AE, adverse event; TEAE, treatment-emergent adverse event. N refers 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. [a]Data based on safety analysis set. [b]TEAE defined as an AE from the first study drug administration through the end of study visit. [c]Adolescent participants only. [d]Defined as the number of participants with an AE that began within 3 days post treatment of non-attack period and before the next administration of study drug. [e]Defined as the number of attacks with an AE that started within 3 days post treatment of attack. [f]One event each of dyspepsia, fatigue, lethargy, brain fog, headache, and somnolence in deucrictibant-treated participants, and 1 event of pruritus in placebo-treated participants. [g]All reported TEAEs were graded 1 (mild) or 2 (moderate) and there were no reported TEAEs graded 4 (life-threatening), or 5 (fatal).

Conclusions

- Results from the pivotal RAPIDe-3 trial for treatment of attacks in multiple types of hereditary angioedema provide further evidence on the rapid and sustained efficacy, safety, and tolerability of the orally administered bradykinin B2 receptor antagonist deucrictibant immediate-release capsule. This trial met the primary and all 11 secondary efficacy endpoints.[a]
- EoP of attack manifestations was measured in the RAPIDe-3 trial for the first time as a pre-specified endpoint in an HAE on-demand trial.

17.47 minutes

Median time to end of progression of attack symptoms

97.4%

of the participants who achieved EoP used only one dose of deucrictibant IR

1.28 hours

Median time to onset of symptom relief

11.95 hours

Median time to complete symptom resolution

Deucrictibant IR was generally well tolerated with no severe or serious treatment-related TEAEs

The Authors and the Sponsor would like to thank all the people with HAE as well as all study site staff who have been participating in the RAPIDe-3 trial.

EoP, end of progression; HAE, hereditary angioedema; IR, immediate-release; TEAE, treatment-emergent adverse event. [a]The primary and first 5 of 11 hierarchical order-ranked secondary endpoints are included in this presentation.


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