Deucrictibant immediate-release capsule reduces time to end of progression of hereditary angioedema attacks' manifestations

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Position guide

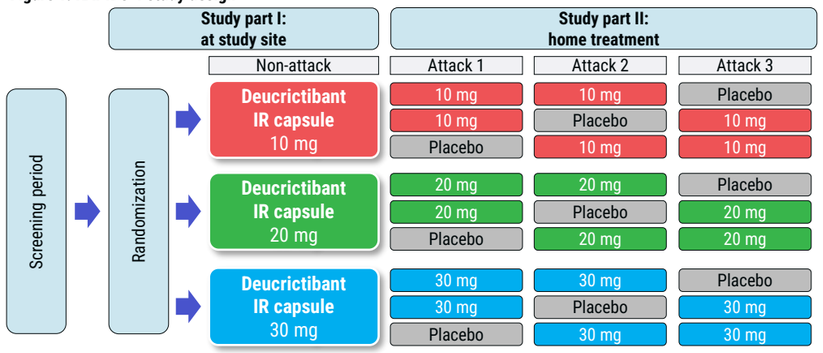
Introduction

- The US HAEA (Hereditary Angioedema Association) Medical Advisory Board 2020 Guidelines for the management of HAE state that "The key to reducing HAE morbidity is to arrest the progression of swelling to prevent disruption to a patient's life."[1]
- Observation of the end of progression (EoP) of angioedema manifestations is the first in-time event documenting treatment response and the initial evidence of attacks starting to evolve towards relief and resolution. A recent consensus study established EoP as a key core outcome score that should be measured and reported in all clinical trials for on-demand treatment of HAE.[2]
- In the phase 2 RAPIDe-1 trial (NCT04618211),[3,*] deucrictibant immediate-release (IR) capsule (PHVS416) reduced time to onset of symptom relief and to resolution of HAE attacks and substantially reduced use of rescue medication.[4,5]
- A post-hoc analysis was conducted to assess time to EoP of HAE attack manifestations in the RAPIDe-1 trial.

Methods

- RAPIDe-1 was a phase 2, double-blind, placebo-controlled, randomized, crossover, dose ranging trial of deucrictibant IR capsule for the on-demand treatment of angioedema attacks in patients with HAE-1/2 (**Figure 1**).
- Time to EoP was defined as the earliest post-treatment timepoint with the highest 3-symptom composite (skin pain, skin swelling, abdominal pain) visual analogue scale (VAS-3) score with no use of rescue medication.
- Post-treatment VAS scores were assessed every 30±10 min from 0 to 4 h, and at 5±0.5, 6±0.5, 8±1, 24±4 and 48±6 h.
- Participants using rescue medication were censored at the last assessment before use of rescue medication.

Figure 1. RAPIDe-1 study design



Results

- The EoP analysis included 147 qualifying HAE attacks treated by 62 participants with double-blinded placebo or deucrictibant IR capsule 10, 20, or 30 mg.
- Attacks treated with deucrictibant IR capsule (all dose groups) achieved EoP at a median time of 25-26 minutes vs 20 hours for attacks treated with placebo (**Table 1** and **Figure 2**).
- Within 24 hours after treatment, 78.4%, 89.3%, and 93.5% of HAE attacks treated with deucrictibant IR capsule 10, 20, and 30 mg, respectively, achieved EoP vs 29.4% of the attacks treated with placebo (**Table 1** and **Figure 3**).

Figure 2. Kaplan-Meier plot of time to EoP in RAPIDe-1

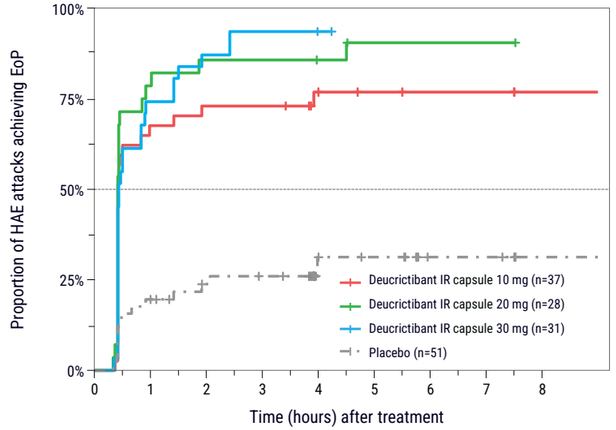
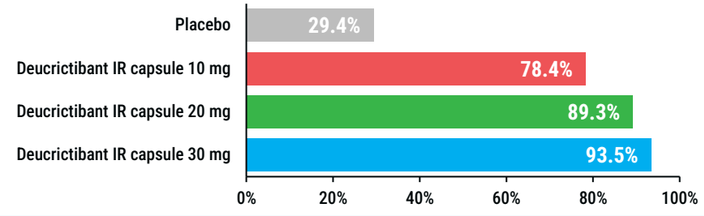


Table 1. HAE attacks achieving EoP in RAPIDe-1

	Placebo	Deucrictibant IR capsule 10 mg	Deucrictibant IR capsule 20 mg	Deucrictibant IR capsule 30 mg
Number of participants with treated attacks	51	21	16	20
Number of treated attacks	51	37	28	31
Attacks achieving EoP within 24 hours, n (%)	15 (29.4)	29 (78.4)	25 (89.3)	29 (93.5)
Kaplan-Meier estimate				
Median time to EoP (95% CI)	20.0 h (NE, NE)	25 min (25, 59)	25 min (25, 26)	26 min (25, 50)
Marginal Cox proportional hazard model*				
Hazard ratio vs placebo (95% CI)		3.87 (2.15, 6.98)	5.09 (2.98, 8.72)	5.23 (2.93, 9.33)
Nominal *P* value		<0.0001	<0.0001	<0.0001

CI, confidence interval; EoP, end of progression; HAE, hereditary angioedema; IR, immediate release; NE, not evaluable.
*Hazard ratio >1 favors treatment vs placebo.

Figure 3. Proportion of attacks achieving EoP within 24 hours



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Conclusions

- **In this post-hoc analysis of the RAPIDe-1 trial, treatment of HAE attacks with deucrictibant IR capsule reduced the time to achieve EoP of attacks' clinical manifestations.**
- **Results of the EoP analysis provide additional evidence on the early onset of effects of deucrictibant IR capsule for on-demand treatment of HAE attacks.**

The FDA has placed a hold on clinical trials of deucrictibant for long-term prophylaxis in the U.S.
For the latest information and updates visit: https://ir.Pharvaris.com/

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*RAPIDe-1 was a Pharvaris-sponsored clinical trial. ClinicalTrials.gov identifier: NCT04618211.

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