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From Symptoms to Decisions: How Patient-Reported Outcomes Shape Trustworthy Clinical Evidence

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Disclaimer

The opinions expressed reflect those of the speaker and are not the opinions or policies of their organization.

Orphan Drug Development & Review Timelines

244 days

Median FDA review time for novel orphan drugs (n=73)

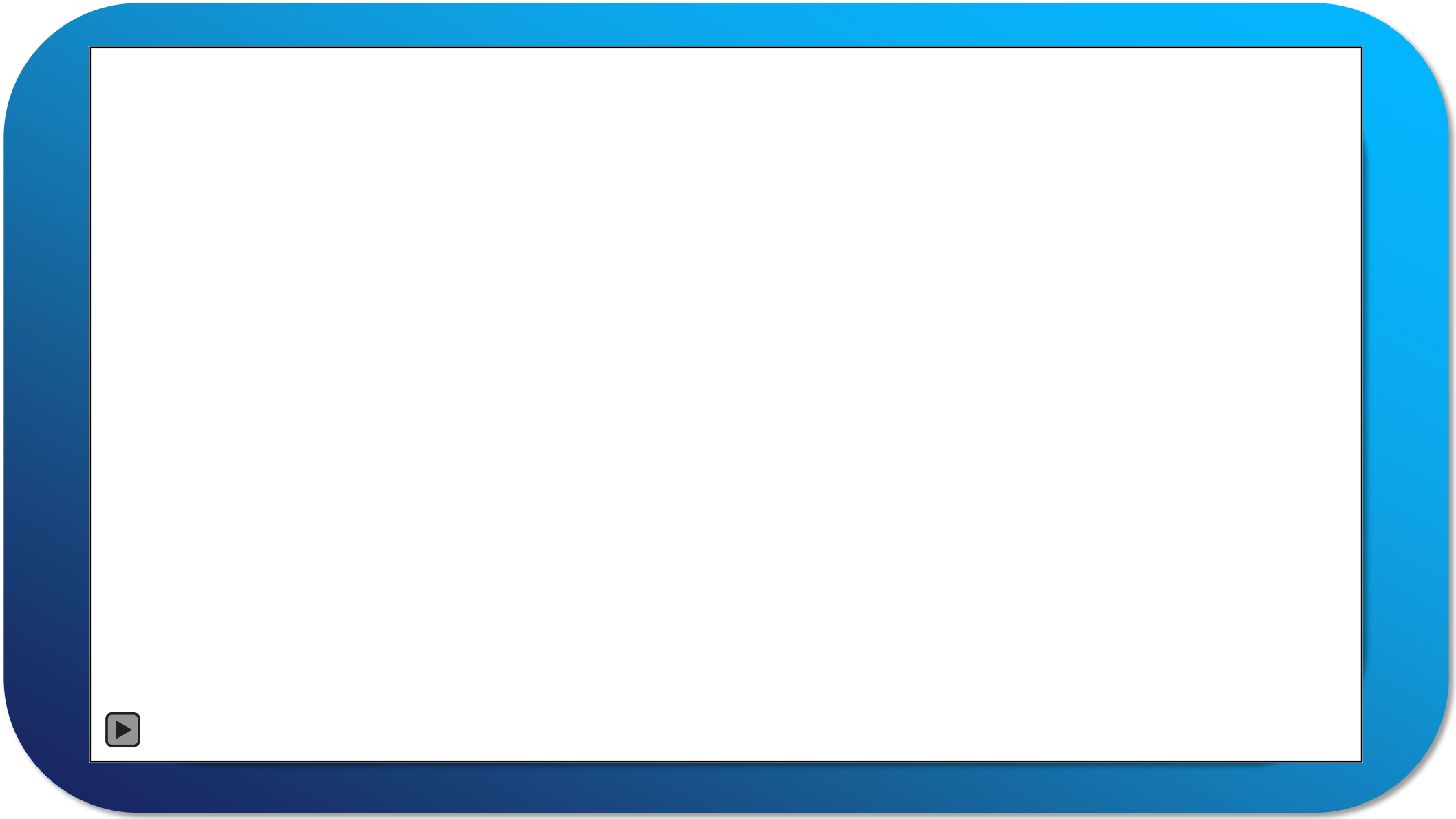
7.2 years

Median development time for novel orphan drugs (2020–2023)

353 days

Median EMA review time for novel orphan drugs (n=39)

Demirci E, et al. Front. Med. (2024);11:1404922. doi: 10.3389/fmed.2024.1404922



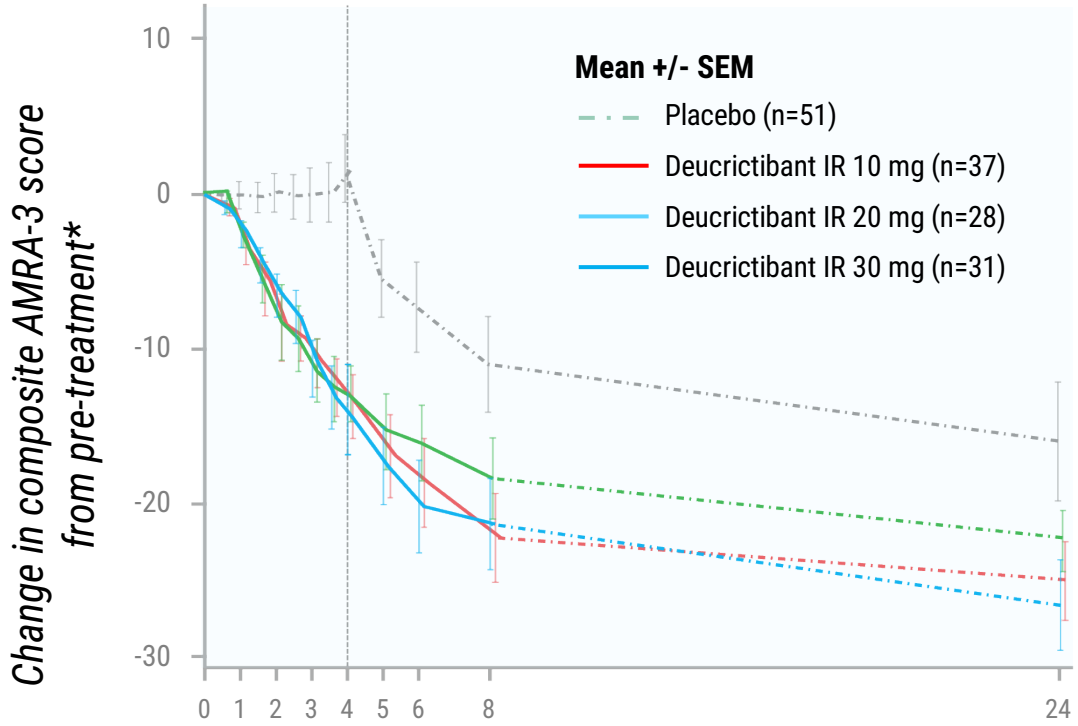
Patient-Reported Outcomes Measures Are Critical to Defining Primary Endpoints in On-Demand HAE Clinical Trials

Status	**Approved (year of approval)**			
Product	**pdC1INH** (2008/2009)	**Icatibant** (2008 [EU]/2009 [US])	**Ecallantide** (2009 [US])	**rhC1INH** (2010 [EU]/2014 [US])
Administration	IV	SC	SC	IV
PRO Measure	QUESTIONNAIRE	VAS-3 VAS-5	TOS MSCS	VAS TEQ
	Hospital-based data collection			

Modified from Cohn et al. JACI (2025);155 (3): 726-739

RAPIDe-1 Primary Endpoint: Deucrictibant IR Significantly Reduced Attack Symptoms by AMRA-3 at 4h

Reduction of attack symptoms by AMRA-3



Difference from placebo in change from pre-treatment to 4h post-treatment, LS mean (95% CI)

Deucrictibant IR **10 mg**	-16.75 (-21.52, -11.97)	P<0.0001†
Deucrictibant IR **20 mg**	-15.02 (-20.22, -9.81)	P<0.0001
Deucrictibant IR **30 mg**	-16.28 (-21.27, -11.29)	P<0.0001

Median **AMRA-3** at pre-treatment ranged from **24.33-27.00** across different dose levels

Attacks in mITT Analysis Set refer to attacks treated with blinded study drug that had non-missing AMRA-3 result at pre-treatment and at least one non-missing AMRA-3 result post-treatment. Figure is based on descriptive summary of mean and SEM. Least squares mean differences, CIs, and *P* values come from a MMRM. Data after rescue medication use is not included. The referenced publication uses VAS-3 language as the label rather than AMRA.
* AMRA-3 assessed every 30 minutes up to 4 hours post-treatment, then at 5, 6, 8, 24, 48 hours; †Nominal *P* value.
AMRA, Angioedema Symptom Rating Scale; CI, confidence interval; IR, immediate-release; LS, least squares; mITT, modified intent-to-treat; MRMM, mixed-effects model with repeated measures; SEM, standard error of the mean.
Modified from Maurer M, et al. The Lancet Haematology, 2026; 13, e200-e214

“Given the variability in symptoms and primary attack locations, our current thinking is that use of a global instrument such as the Patient Global Impression of Change (PGI-C) may be more appropriate and easily interpretable as the primary outcome measure.”

– FDA feedback

Novel PRO or Legacy Measure — Which Endpoint Will Regulators Trust?

Patient **G**lobal **I**mpression of **C**hange[1,2]

PGI-C

Much worse → Worse → A little worse → Same → A little better → Better → Much better

Patient **G**lobal **I**mpression of **S**everity[1,2]

PGI-S

Very severe → Severe → Moderate → Mild → None

Angioedema sy**M**ptom **R**ating sc**A**le[2,3]

AMRA

100 Worst symptoms → No symptoms 0

AMRA, Angioedema Symptom Rating Scale; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity; PRO, patient-reported outcome.

1. Cohn DM, et al. *Clin Transl Allergy*. 2023;13(9):e12288; **2.** Mendivil J, et al. Presented at: GA²LEN UCARE Conference 2023; Dec 8, 2023; São Paulo, Brazil; **3.** McMillan CV, et al. *Patient*. 2012;5:113-126.

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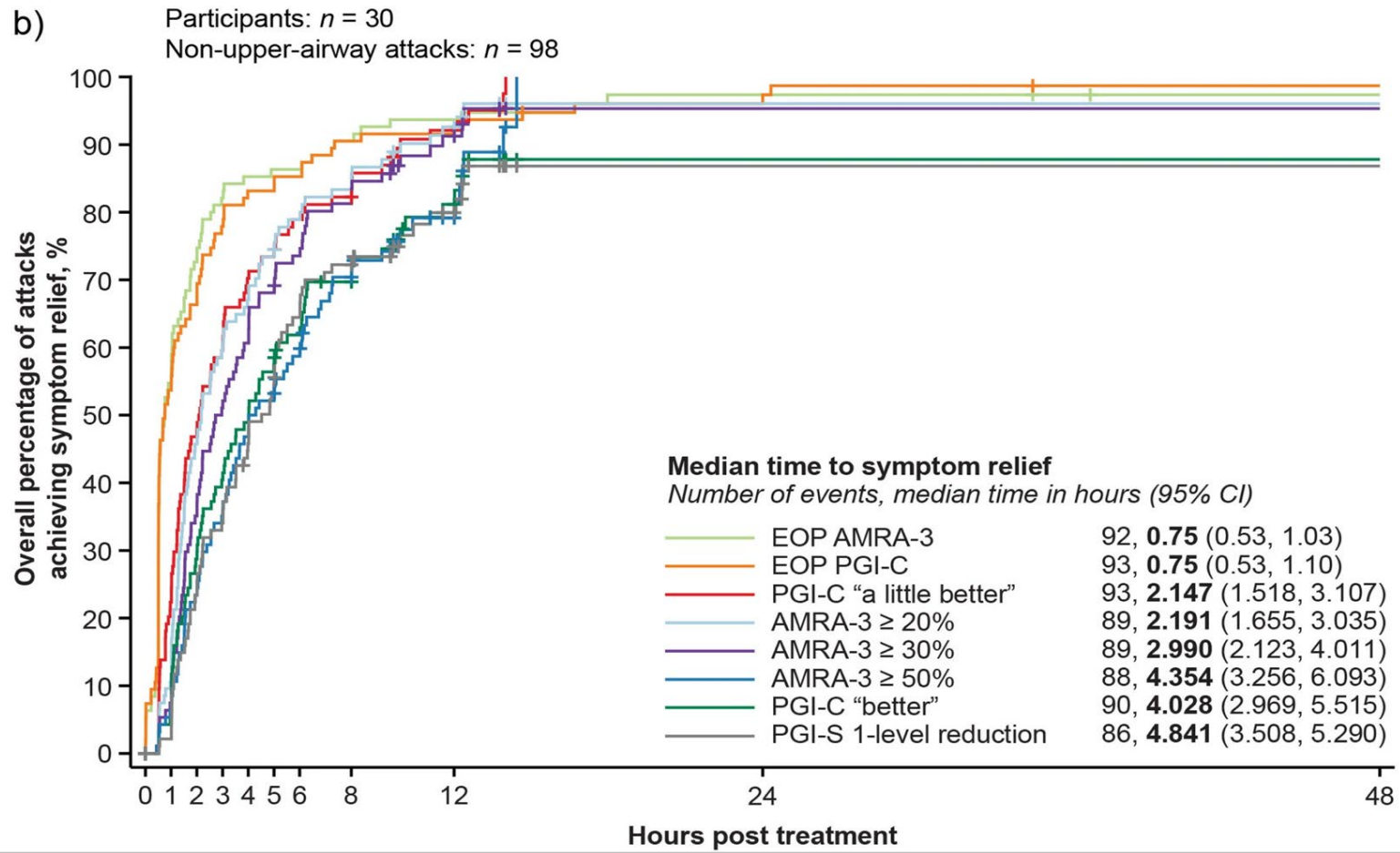
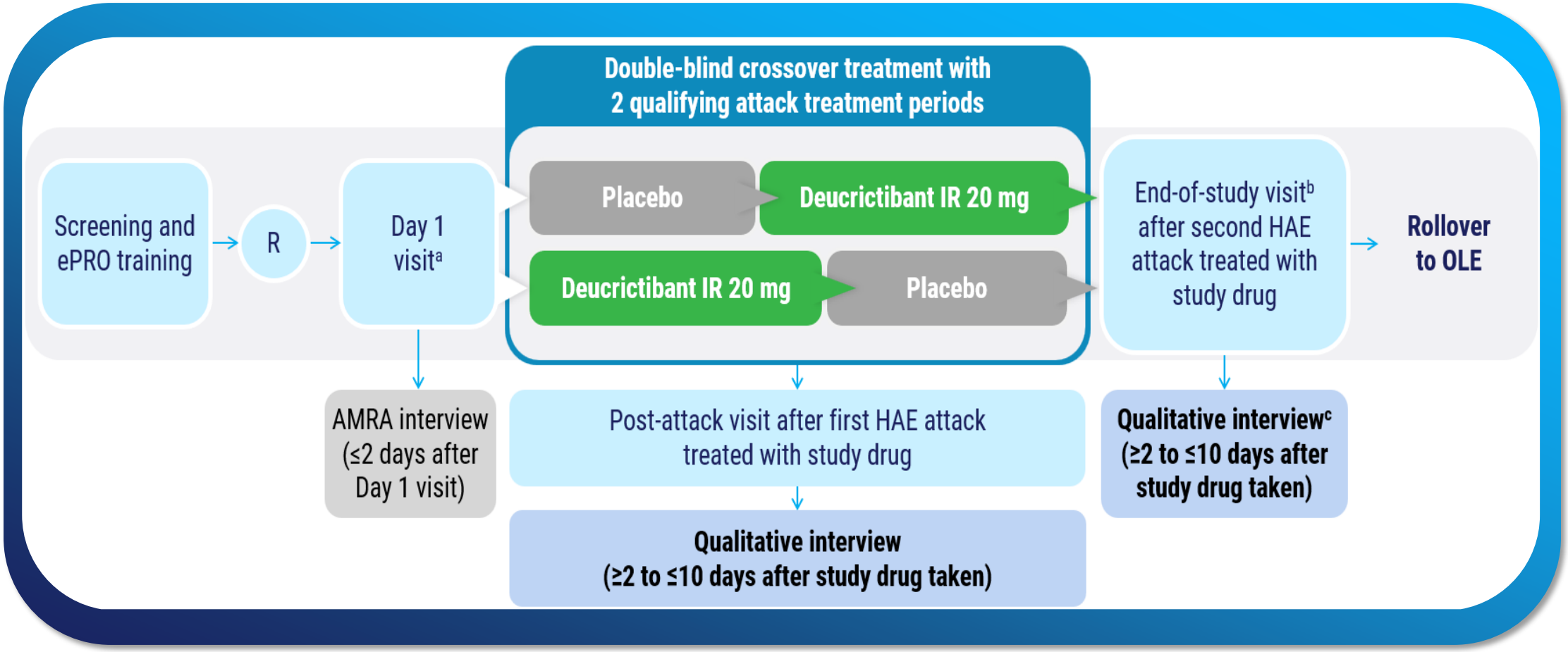
Derisking a Pivotal Trial by Generating Real-World Evidence

Insights from a Mixed Methods Study of Participants Receiving Standard-of-Care Treatments in the U.S.



Mendivil et al. Clinic Rev Allerg Immunol 69, 14 (2026)

RAPIDe-3: Embedding Patient Voices Directly Into HAE Trial Design



[a]Adolescent participants received a non-attack dose for pharmacokinetic sampling at Day 1 visit prior to R. [b]Data from the end-of-study visit might have been used to qualify the participant for an OLE study with deucrictibant. cThe qualitative interview following the second treated attack had to occur before completion of the end-of study visit.
AMRA, Angioedema SyMptom Rating scAle; ePRO, electronic patient-reported outcome; HAE, hereditary angioedema; IR, immediate-release; OLE, open-label extension; R, randomization.

RAPIDe-3 represents the **first Phase 3 HAE on-demand treatment trial** to comply with the AURORA consensus,[1] capturing **patient experience** across multiple domains while patients were still blinded to treatment, exemplifying **FDA[2] and EMA[3] Patient Experience Data philosophy[4]**

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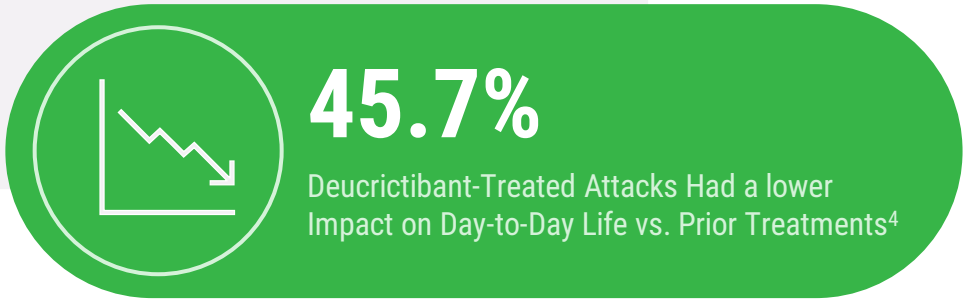
Embedded Contemporaneous Interviews Conducted Post-Attack



1. Petersen R, et al. JACI: In Practice, 2024; 12, 1614-1621 2. FDA. Patient-Focused Drug Development: Methods to Identify What Is Important to Patients. Guidance 2. February 2022. 3. EMA. Reflection Paper on Patient Experience Data (PED). EMA/CHMP/PRAC/148869/2025. September 2025. 4. Valerieva A, et al. Presented at: EAACI 2026; June 13, 2026; Istanbul, Turkey.

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How Could This Improve Patient Outcomes?

- Patient Focused Drug Development, Real-World Evidence and Patient Experience Data are concepts that can enrich Clinical Development Programs and then ultimately improve decision making and patient outcomes
- Real-World Evidence can reduce uncertainty, refining clinical trial endpoints to make them more patient-relevant
- The voice of patients or Patient Experience Data adds an extra dimension to quantitative information, providing a holistic picture of the treatment effect and what matters most to the patient
- The sum of high quality quantitative and qualitative data provides comprehensive insights into patient needs, preferences and priorities which can inform, guide and enhance shared-decision making

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Thank you.