Lived Patient Experiences of Hereditary Angioedema Based on Attacks and Associated Symptoms: An Innovative Conceptual Model

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Key takeaways

Qualitative interviews embedded in clinical trial protocols are an expanding concept within the allergy/immunology field and are newly being applied to the study of hereditary angioedema (HAE).

In-trial qualitative interviews conducted with participants during RAPIDe-3 provide, among others, insights into the experiences of people living with HAE related to their attacks and associated symptoms.

HAE attack experience

- **Most participants reported peripheral 92.3% and abdominal attacks 86.8%**
- **90.1%** Skin swelling was the most reported symptom

HAE attack-related impacts

- **93.4%** Emotional wellbeing was the most reported HAE-related impact domain
- **73.6%** Most participants reported experiencing HAE-related fatigue

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 caused by excess bradykinin activating bradykinin B2 receptors that affects multiple locations in the body and negatively impacts health-related quality of life (HRQoL).[1-6]
- **Unmet need:** although both prophylactic and on-demand treatments are available for individuals with HAE, no published conceptual models have been developed using patient interview data collected as part of a randomized controlled trial to capture participants' lived experiences of the disease or with long-term prophylactic and on-demand therapies.[7,8]
- **Oral deucrictibant:** a selective, bradykinin B2 receptor antagonist under development for both prophylactic and on-demand treatment of bradykinin-mediated angioedema attacks.[9-17]

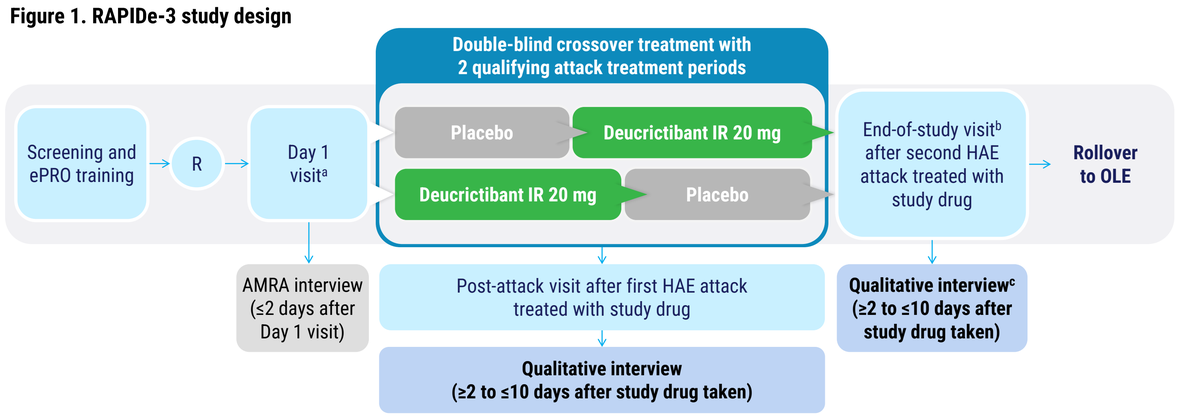
Objective

- To better understand the lived experiences of people with HAE, the RAPIDe-3 clinical trial was designed to include blinded qualitative interviews that explored participants' experiences living with HAE, including HAE attacks, related symptoms, and their physical and emotional impacts, to support development of a conceptual model of HAE.

Methods

- **RAPIDe-3 (NCT06343779)*:** a completed, global, Phase 3, randomized, double-blind, placebo-controlled, crossover trial that evaluated the efficacy and safety of deucrictibant immediate-release (IR) capsule 20 mg for on-demand treatment of HAE attacks in adolescents and adults.[11]
- **Eligible participants:** aged ≥12 to ≤75 years, diagnosed with HAE type 1/2 or HAE with normal C1 inhibitor, a history of at least two HAE attacks in the last 3 months before screening, and experience using standard-of-care treatment to manage HAE attacks.

Figure 1. RAPIDe-3 study design



AMRA, Angioedema SyMptom Rating scAle; ePRO, electronic patient-reported outcome; HAE, hereditary angioedema; 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 R. [b]Data from the end-of-study visit may be used to qualify the participant for an OLE study with deucrictibant. [c]The qualitative interview following the second treated attack must occur before completion of the end-of study visit.

Interviews

- The trial included 60-minute, semi-structured, qualitative interviews for concept elicitation regarding participants' descriptions of living with HAE, their attacks and associated symptoms, physical and emotional impacts of HAE, and fatigue/tiredness.
  - The interviews also captured participants' experiences with HAE medications (including the study drug), treatment satisfaction and preferences, other non-localized symptoms from HAE attacks (such as anxiety or depression), health status, and study experience. These data will be presented elsewhere.
- Interviews were conducted via a remote call ≥48 hours to ≤10 days following each of two HAE attacks treated with study drug.

HRQoL

- HRQoL was measured using the EuroQol 5 Dimension 5 Level (EQ-5D-5L) questionnaire.

Results

Study population

- A total of 141 interviews were conducted with 91 participants across 19 countries.
- Of these, 50 participants across 16 countries completed two interviews, while the remaining 41 participants completed a single interview.
- Participants had a mean (standard deviation [SD]) age of 36.7 (14.0) years and were predominantly female (n=49/91 [53.8%]) and White (n=71/91 [78.0%]).
- Most participants had HAE type 1 (n=82/91 [90.1%]), with a mean (SD) age at diagnosis of 19.6 (12.3) years.

Table 1. Participant baseline demographics and disease characteristics

Participant characteristics	Interviewed participants (N=91)	All participants in RAPIDe-3 (N=134)
Age, mean (SD), years	36.7 (14.0)	39.0 (14.7)
Sex: Female, n (%)	49 (53.8)	76 (56.7)
Race, n (%)		
White	71 (78.0)	93 (69.4)
Asian	5 (5.5)	19 (14.2)
Black or African American	5 (5.5)	10 (7.5)
American Indian or Alaska Native	1 (1.1)	1 (0.7)
Other	5 (5.5)	7 (5.2)
Not reported	4 (4.4)	4 (3.0)
Region, n (%)[a]		
Europe	46 (50.5)	56 (41.8)
Rest of World	19 (20.9)	40 (29.9)
North America	26 (28.6)	38 (28.4)
HAE type, n (%)		
HAE-C1INH-type 1	82 (90.1)	118 (88.1)
HAE-C1INH-type 2	6 (6.6)	10 (7.5)
HAE-nC1INH	2 (2.2)	4 (3.0)
Unspecified type 1 or 2	1 (1.1)	2 (1.5)

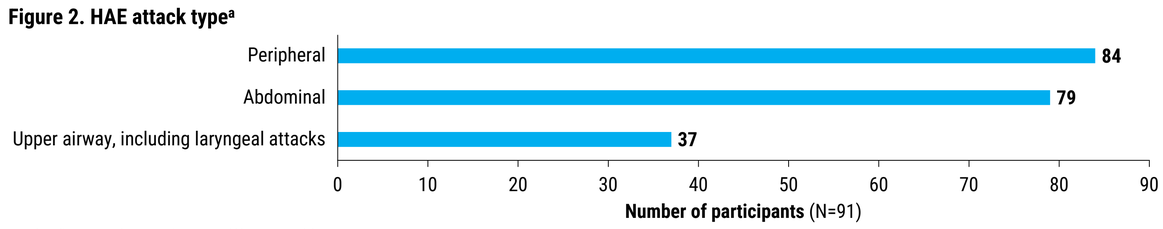
C1INH, C1 inhibitor; HAE, hereditary angioedema; nC1INH, normal C1INH; SD, standard deviation. [a]Geographic region of North America included Canada, Puerto Rico, and the United States of America; Europe included Austria, Bulgaria, Czech Republic, France, Germany, Hungary, Italy, Netherlands, Poland, Spain, Sweden, and the United Kingdom; Rest of World included Argentina, Australia, Brazil, Hong Kong, Japan, Saudi Arabia, South Africa, South Korea, and Turkey.

HAE attack experience

- Most participants (n=75/88 [85.2%]) reported the age at which they first experienced HAE attacks: 45.3% (n=34/75) reported onset before age 10 years, 33.3% (n=25/75) between ages 10 and 20 years, and 5.3% (n=4/75) between ages 21 and 29 years.
- Most participants reported peripheral (n=84/91 [92.3%]) and abdominal (n=79/91 [86.8%]) attacks (**Figure 2**).
- A range of attack triggers was reported across all attack types, with emotional stress as the most common trigger (**Figure 3**).
- A total of 27 symptoms were reported with the most common being skin swelling, abdominal pain, vomiting, and skin pain (**Figure 4**).

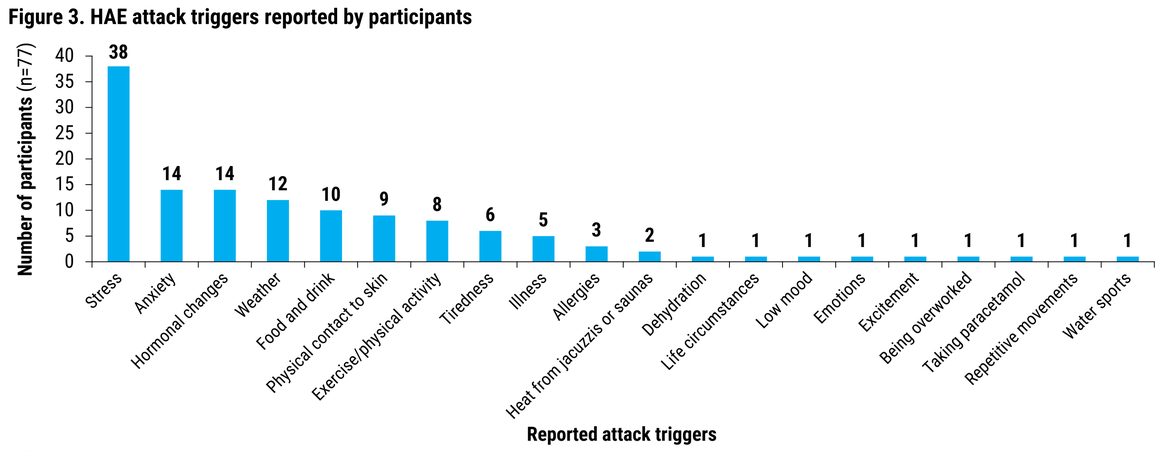
Results

Figure 2. HAE attack type[a]



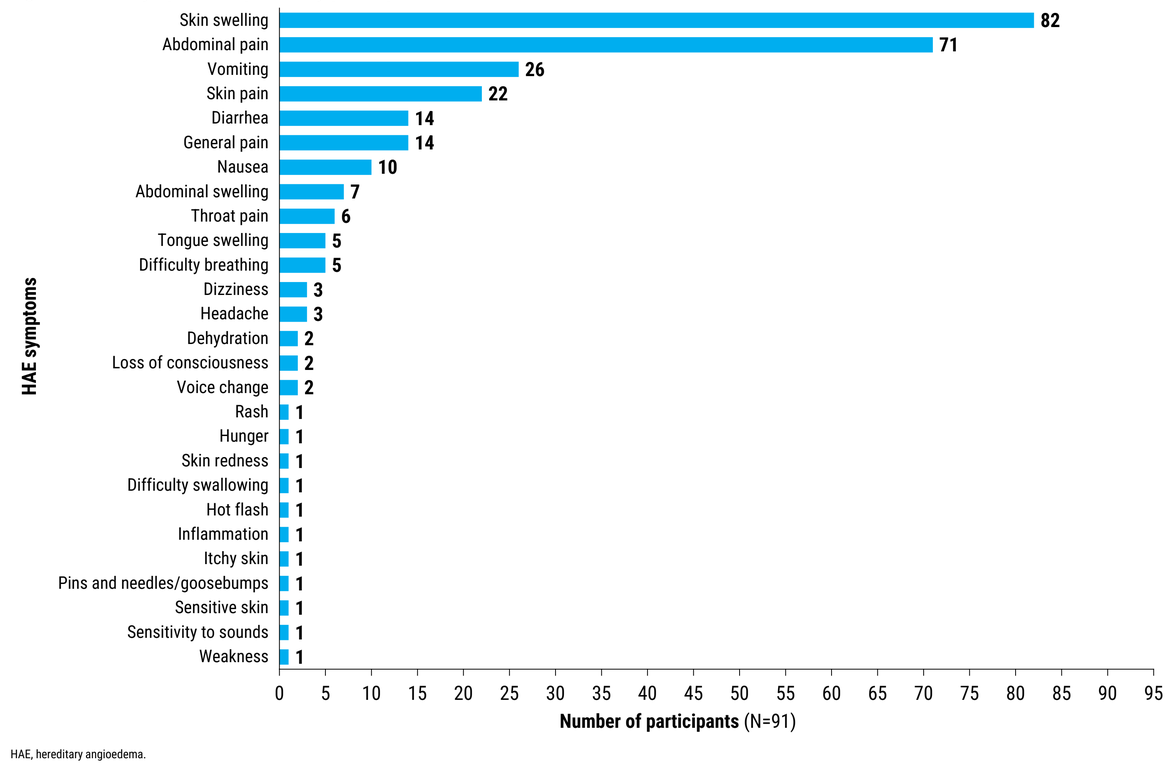
HAE, hereditary angioedema. [a]Participants could have ≥1 attack location.

Figure 3. HAE attack triggers reported by participants



HAE, hereditary angioedema.

Figure 4: HAE symptoms reported by participants

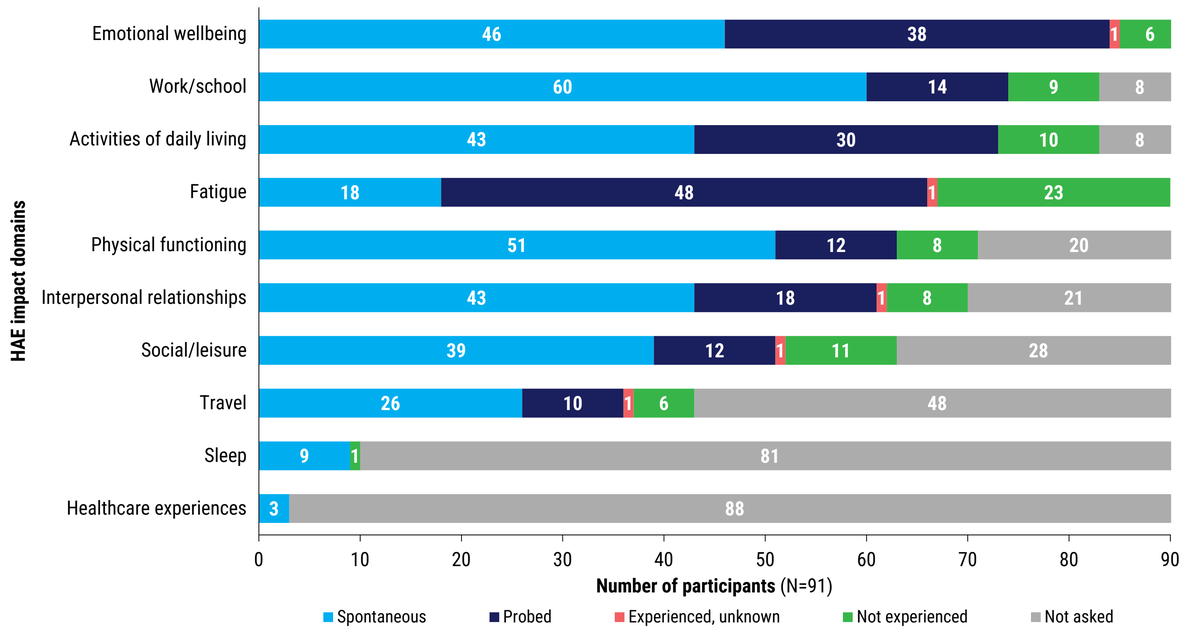


HAE, hereditary angioedema.

HAE attack-related impacts

- Participants described a total of 10 HAE-related impact domains with the most frequently reported being emotional wellbeing (n=85/91 [93.4%]), work/school (n=74/91 [81.3%]), and activities of daily living (n=73/91 [80.2%]) (**Figure 5**).

Figure 5. HAE-related impact domains as reported by participants[a]



HAE, hereditary angioedema. [a]Participants were asked specific questions about HAE impact on day-to-day life, HAE-related fatigue, HAE-related anxiety, and HAE-related depression/low mood during the initial interview.

- Emotional wellbeing impacts were commonly reported by participants, with anxiety being the most prevalent (n=74/85 [87.1%]), followed by depression or low mood (n=56/85 [65.9%]), and feelings of embarrassment or self-consciousness (n=19/85 [22.4%]).
- Several physical functioning concepts were reported by participants, most commonly limitations in physical functioning and difficulty with specific movements (both n=35/63 [55.6%]).
- Most participants reported experiencing HAE-related fatigue (n=67/91 [73.6%]), most commonly during attacks (n=24), but also before (n=20) and after (n=14) HAE attacks.
  - Fatigue was often associated with swelling (n=22) and pain (n=19).
  - Views on whether fatigue differed from tiredness were mixed, although more participants considered them distinct concepts (n=33/67 [49.3%]).

References

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