

# Patient Perspectives on an Optimal Outcome Measure to Assess Efficacy in the Acute Treatment of Hereditary Angioedema Attacks

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## Introduction

- Clinical trials assessing the efficacy of on-demand treatments for hereditary angioedema (HAE) attacks have used a large variety of clinical endpoints,<sup>1</sup> and there is no consensus regarding optimal standardized endpoints and/or patient-reported outcomes (PROs)
- Sebetralstat, an investigational oral plasma kallikrein inhibitor in development for on-demand treatment of HAE attacks, was studied in a phase 2, randomized, double-blind, placebo-controlled trial and demonstrated improvements in several PROs, including the Patient Global Impression of Change (PGI-C), Patient Global Impression of Severity (PGI-S), and composite visual analog scale (VAS)<sup>2,3</sup>
- A post hoc analysis of the trial data showed that improvements reported with the PGI-C were generally in agreement with the other PRO measures, supporting the PGI-C as a meaningful measure of efficacy in patients with HAE from a patient perspective<sup>3</sup>
- We sought to further understand the perspectives of patients with HAE with C1-inhibitor deficiency (C1-INH-HAE) on the PGI-C through a series of direct patient engagements

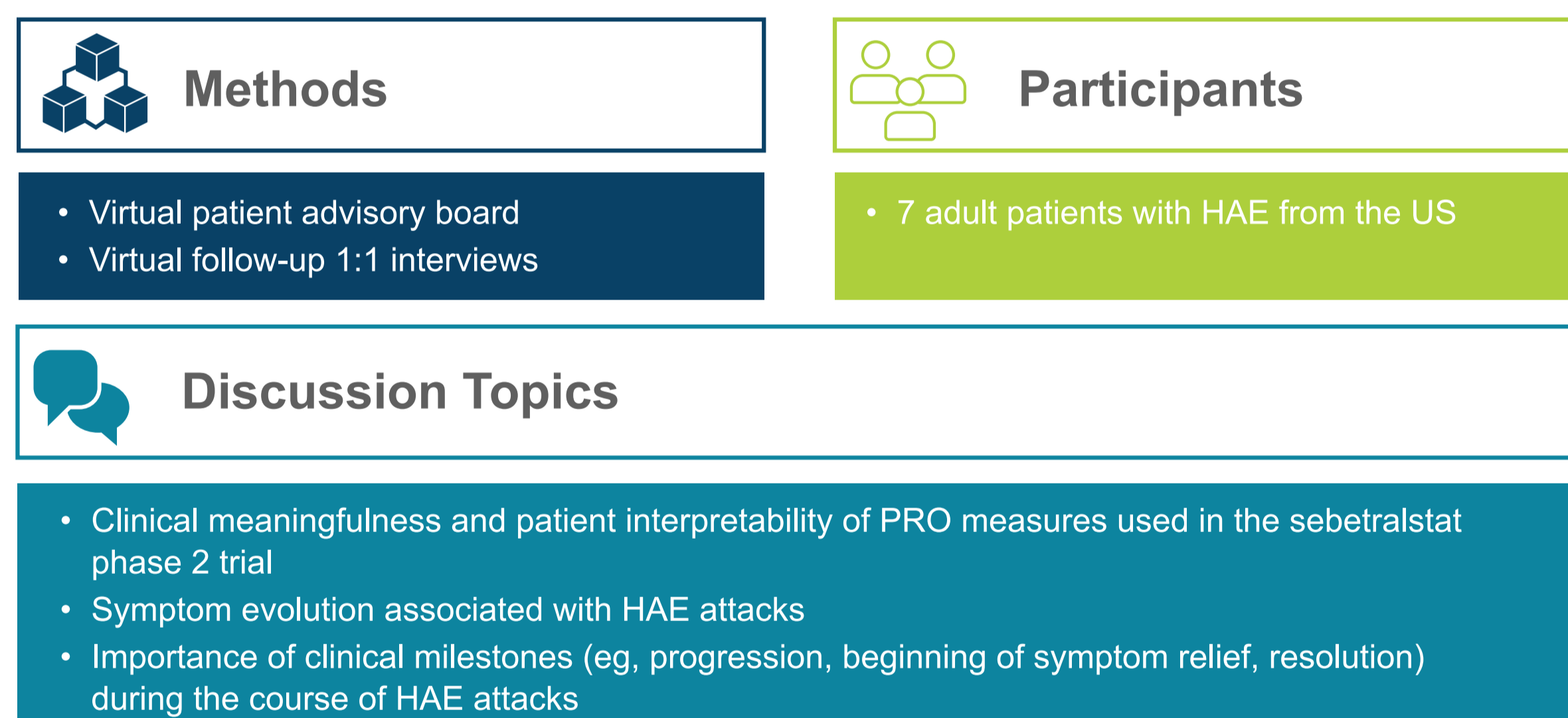
## Objective

- To assess patient perspectives on assessments of efficacy for on-demand treatments for HAE

## Methods

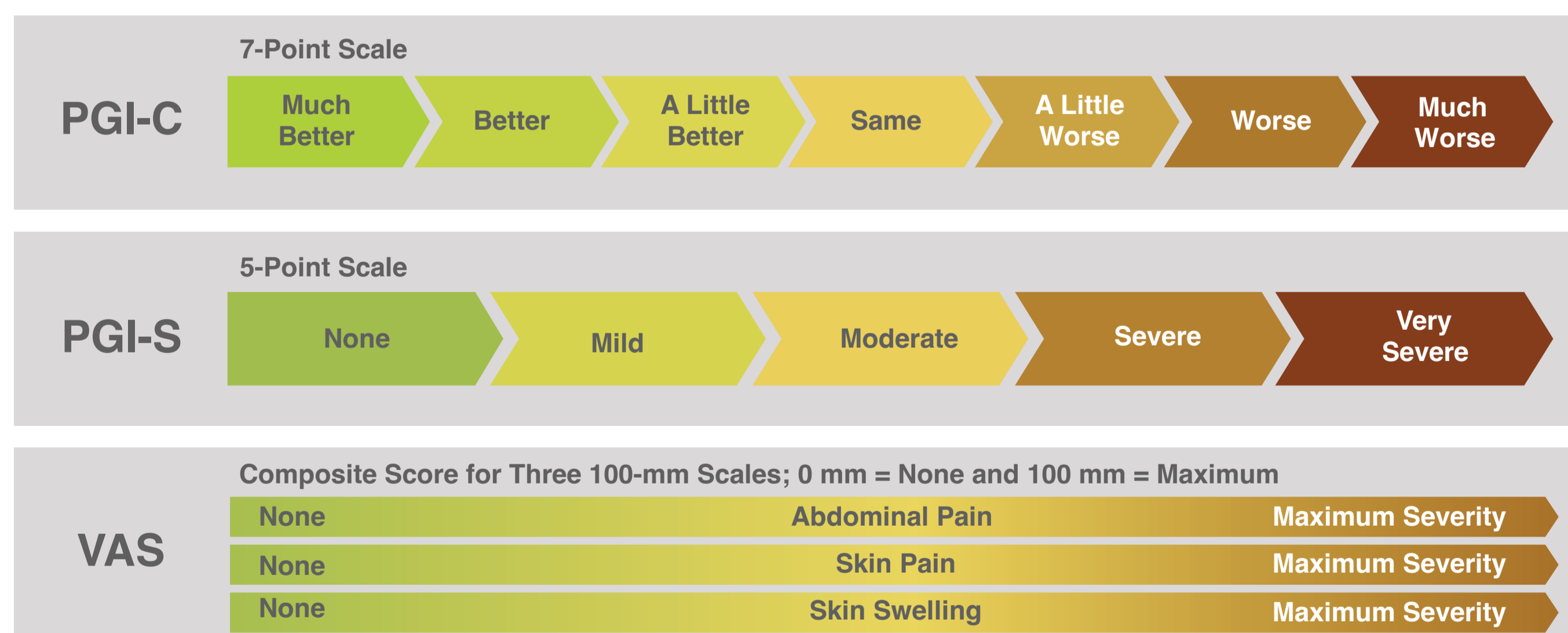
- Patient insights were collected during a virtual patient advisory board and 1:1 follow-up interviews (Figure 1)
  - The patient advisory board and subsequent individual follow-ups were conducted with the support of the US Hereditary Angioedema Association, which was responsible for patient recruitment
- Feedback was collected on outcome measures used in the sebetralstat phase 2 trial (Figure 2), symptom evolution, and the spectrum of symptom relief experienced over the course of HAE attacks

Figure 1. Collection of Patient Insights



HAE, hereditary angioedema; PRO, patient-reported outcome.

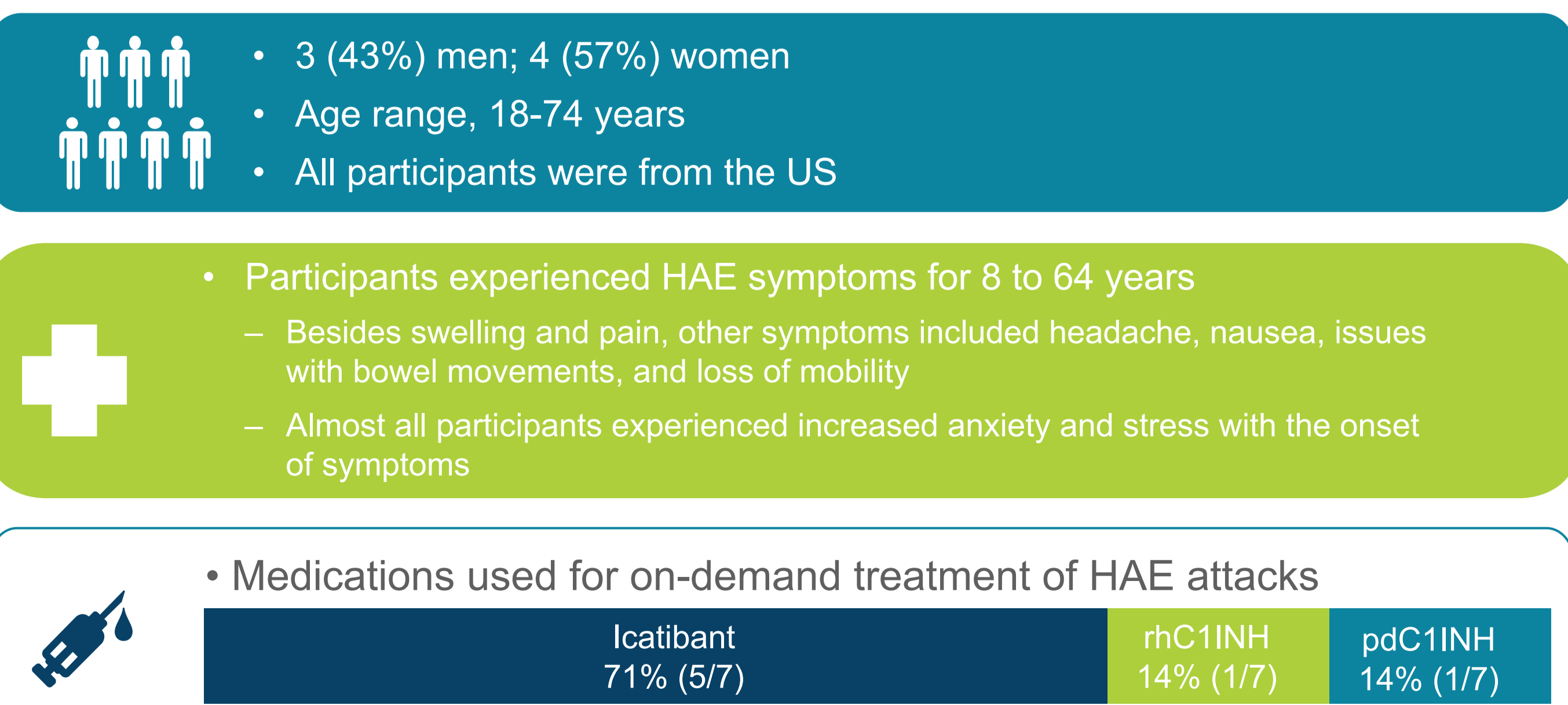
Figure 2. PROs in the Sebetralstat Phase 2 Trial



PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity; PRO, patient-reported outcome; VAS, visual analog scale.

## Results

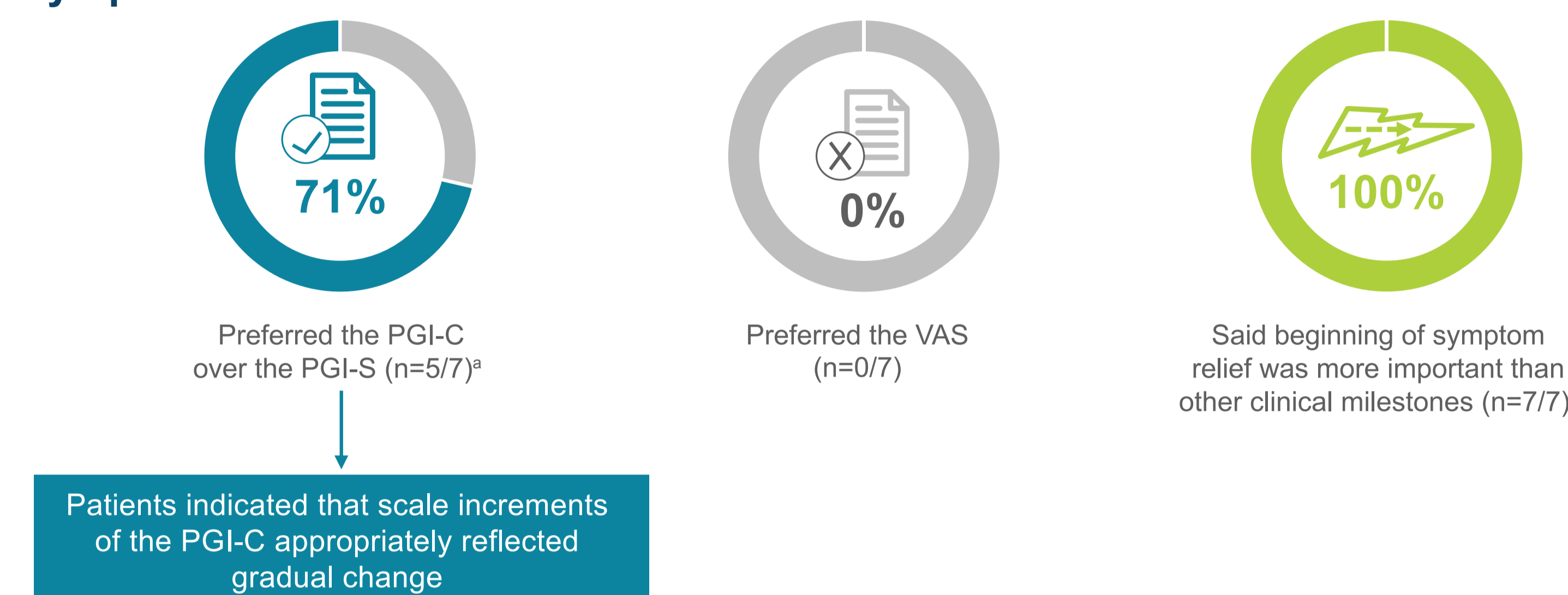
### Participant and Attack Characteristics



HAE, hereditary angioedema; pdC1INH, plasma-derived C1-inhibitor; rhC1INH, recombinant human C1-inhibitor.

- Patients indicated that all PRO measures (Figure 2) used in the sebetralstat phase 2 trial were acceptable and measured outcomes that were meaningful to patients with HAE
- Most patients preferred the PGI-C over the PGI-S (Figure 3)
  - None preferred the VAS
- All patients indicated that the beginning of symptom relief after treatment was more important than other clinical milestones during an attack, including complete resolution (Figure 3)

Figure 3. Patient Feedback on PRO Measures and the Importance of Early Symptom Relief



PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity; PRO, patient-reported outcome; VAS, visual analog scale.

<sup>a</sup> Two patients did not have strong opinions about the scale.

- Most patients selected "A Little Better" from the PGI-C when asked how HAE attack symptoms were when they first noticed improvement after use of on-demand treatment (Figure 4)

Figure 4. Patient Description of Overall HAE Attack Symptoms When They First Noticed Improvements After Use of On-Demand Treatment<sup>a</sup>

Much Better	14.2% (1/7)
Better	14.2% (1/7)
A Little Better	71.4% (5/7)
Same	0% (0/7)
A Little Worse	0% (0/7)
Worse	0% (0/7)
Much Worse	0% (0/7)

HAE, hereditary angioedema.

<sup>a</sup> Question: "At the moment when you first notice the medicine is beginning to work, how would you describe your overall HAE attack symptoms?"

## Conclusions

- These survey data support the PGI-C as a patient-preferred PRO for assessing the efficacy of on-demand treatments for HAE attacks
- The beginning of symptom relief measured as the PGI-C rating of "A Little Better" after treatment was the most important clinical milestone during HAE attacks
- These findings are consistent with post hoc analyses of the sebetralstat phase 2 trial, which found that the PGI-C was a sensitive measure of efficacy and was in agreement with other measures of improvement and attack resolution<sup>3</sup>
- Limitations of this study include the small number of participants and inclusion of participants from a single country
- These data support the use of the PGI-C rating of "A Little Better" as the primary endpoint in the ongoing sebetralstat phase 3 KONFIDENT trial (NCT05259917) for on-demand treatment of HAE attacks in patients with C1-INH-HAE<sup>4</sup>

### References

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