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

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Rationale: Heterogeneity in HAE attack locations, symptoms, severity, and temporal patterns make it difficult to identify an optimal patient-reported outcome (PRO) measure to evaluate the efficacy of on-demand treatments. In a phase 2 randomized controlled trial of sebetralstat, a range of novel and historic measures were utilized including patient global impressions of change (PGI-C), and severity (PGI-S), and a composite of three visual analogue scales (VAS) assessing abdominal pain, skin pain and skin swelling.

Methods: With support from the US Hereditary Angioedema Association, a virtual patient advisory board with US patients was conducted on November 12, 2020, during which 7 adults living with HAE were asked to provide feedback on the clinical meaningfulness of the various clinical measures utilized in the phase 2 sebetralstat trial. Follow-up 1:1 interviews were conducted to further evaluate their perspective.

Results: Participant ages ranged from 20s to 70s, four (57.1%) were female. Advisory board participants conveyed that all three PROs were acceptable for clinical trial use and captured endpoints that were of significance to HAE patients. A total of 71.4% of participants preferred PGI-C over PGI-S related to scale increments appropriately reflecting gradual change; none preferred VAS. Follow-up interviews focused on the PGI-C. All participants (100%) indicated that the beginning of symptom relief was clinically meaningful. To describe overall HAE attack symptoms on PGI-C at the moment when they noted the improvement after administration of on-demand medication following the onset of the attack, 71.4% (5/7) chose “A little better”, 14.2% (1/7) chose “Better”, and 14.2% (1/7) chose “Much better”.

Conclusions: The PGI-C is a patient-preferred PRO for the assessment of efficacy of on-demand treatments for HAE attacks. A rating of “A little better” is meaningful to patients and appropriately reports the clinically meaningful endpoint of beginning of symptom relief.