Original Article

Health-Related Quality of Life with Subcutaneous C1-Inhibitor for Prevention of Attacks of Hereditary Angioedema

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What is already known about this topic? Hereditary angioedema with C1-inhibitor deficiency (C1-INH-HAE) remains a cause of health-related quality of life (HRQoL) impairments, including anxiety and productivity deficits, despite noted improvements over recent years concurrent with the availability of new targeted therapies.

What does this article add to our knowledge? This is the first analysis to evaluate HRQoL in patients with C1-INH-HAE using self-administered subcutaneous C1-inhibitor as routine prophylaxis. These findings supplement clinical efficacy outcomes reported recently from the randomized, phase III COMPACT (Clinical Studies for Optimal Management of Preventing Angioedema with Low-Volume Subcutaneous C1-Inhibitor Replacement Therapy) study.

How does this study impact current management guidelines? HAE consensus guidelines cite restoration of normal quality of life as a treatment goal, and these findings provide strong evidence that subcutaneous C1-INH has the potential to significantly improve a number of HRQoL measures.

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Abbreviations used
C1-INH- C1-inhibitor
C1-INH-HAE- Hereditary angioedema with C1-inhibitor deficiency
CI- Confidence interval
EQ-5D-3L- European Quality of Life-5 Dimensions Questionnaire
HADS- Hospital Anxiety and Depression Scale
HAE- Hereditary angioedema
HRQoL- Health-related quality of life
HSV- Health state value
IGART- Investigator Global Assessment of Response to Therapy
IV- Intravenous
MCID- Minimal clinically important difference
PRO- Patient-reported outcome
SC- Subcutaneous
SD- Standard deviation
SF- Short Form
SGART- Subject Global Assessment of Response to Therapy
TSQM- Treatment Satisfaction Questionnaire for Medication
VAS- Visual analog scale
WPAI- Work Productivity and Activity Impairment Questionnaire

BACKGROUND: Hereditary angioedema with C1-inhibitor deficiency (C1-INH-HAE) impairs health-related quality of life (HRQoL).
OBJECTIVE: The objective of this study was to assess HRQoL outcomes in patients self-administering subcutaneous C1-INH (C1-INH[SC]; HAEGARDA) for routine prevention of HAE attacks.
METHODS: *Post hoc* analysis of data from the placebo-controlled, crossover phase III COMPACT study (Clinical Studies for Optimal Management of Preventing Angioedema with Low-Volume Subcutaneous C1-Inhibitor Replacement Therapy). Ninety patients with C1-INH-HAE were randomized to 1 of 4 treatment sequences: C1-INH(SC) 40 or 60 IU/kg twice weekly for 16 weeks, preceded or followed by 16 weeks of twice weekly placebo injections. All HAE attacks were treated with open-label on-demand treatment as necessary. HRQoL assessments at week 14 (last visit) included the European Quality of Life-5 Dimensions Questionnaire (EQ-5D-3L), the Hospital Anxiety and Depression Scale (HADS), the Work Productivity and Activity Impairment Questionnaire (WPAI), and the Treatment Satisfaction Questionnaire for Medication (TSQM).
RESULTS: Compared with placebo (on-demand treatment alone), treatment with twice weekly C1-INH(SC) (both doses combined) was associated with better EQ-5D visual analog scale general health, less HADS anxiety, less WPAI presenteeism, work productivity loss, and activity impairment, and greater TSQM effectiveness and overall treatment satisfaction. More patients self-reported a "good/excellent" response during routine prevention with C1-INH(SC) compared with on-demand only (placebo prophylaxis) management. For each HRQoL measure, a greater proportion of patients had a clinically meaningful improvement during C1-INH(SC) treatment compared with placebo.
CONCLUSIONS: In patients with frequent HAE attacks, a treatment strategy of routine prevention with self-administered twice weekly C1-INH(SC) had a greater impact on improving multiple HAE-related HRQoL impairments, most notably anxiety and work productivity, compared with on-demand treatment alone (placebo prophylaxis). **(J Allergy Clin Immunol Pract 2018;■:■-■)**

Key words: *C1-inhibitor protein; Hereditary angioedema; Patient-reported outcomes; Quality of life; Productivity; Satisfaction; Subcutaneous; HAEGARDA*

Hereditary angioedema (HAE) with C1-inhibitor deficiency (C1-INH-HAE) is a debilitating and potentially life-threatening condition characterized by recurrent episodes of nonpruritic submucosal and/or subcutaneous edema.[1-4] C1-INH-HAE is a rare genetic disorder typified by a deficiency of C1-INH protein (HAE type 1; accounts for approximately 85% of cases) or abnormally functioning C1-INH in the presence of normal or elevated C1-INH levels (HAE type 2; approximately 15% of cases).

As a lifelong, unpredictable, and debilitating disease with an omnipresent potential for fatal laryngeal swelling, C1-INH-HAE can have profound effects on various aspects of health-related quality of life (HRQoL). A landmark study by Lumry et al,[5] conducted before the availability of HAE-specific medications in the United States, found significant impairment of both physical and mental HRQoL in patients with C1-INH-HAE. In that study, the mean attack frequency was 27 HAE attacks per year. Since 2009, after the introduction of a number of HAE-specific therapies, some studies have indicated better overall HRQoL in patients with C1-INH-HAE as measured by the Short-Form (SF)-12 or SF-36 instruments.[6-8] However, other research conducted among C1-INH-HAE populations with access to effective therapies has since reported continued negative impacts of HAE on various aspects of HRQoL.[9-16]

Anxiety continues to be a particular burden among patients with C1-INH-HAE, even in recent studies in which patients had access to current, HAE-specific medications for on-demand therapy and prophylaxis.[10,15,17,18] The unpredictability of HAE

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