Retrospective Analysis of Patient Outcomes Associated with Subcutaneous C1INH Prophylaxis for Hereditary Angioedema

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CONCLUSIONS

- **This hybrid chart review/qualitative research study was uniquely designed to assess clinical and disease burden outcomes using parallel methods of medical chart data retrieval supplemented with patient interviews analyzed using qualitative methods.**
- **Limitations of this study include incomplete data for certain outcomes in medical charts, possible patient recall bias, and a relatively small cohort.**
- **Despite these limitations, the findings support that implementation of LTP with C1INH(SC) resulted in decreased HAE attack frequency, markedly lessened severity of breakthrough attacks, reduced on demand medication needs, and improvements in multiple facets of QoL.**

BACKGROUND

- The humanistic burden of hereditary angioedema (HAE) is considerable and multi-faceted, affecting not only physical and emotional well-being, but exerting a broad, negative impact on quality-of-life-related factors such as education, career, work productivity, and social interactions on both patients and their families.[1–4]
- Consensus guidelines state that treatment goals are to "achieve total control of the disease, normalize patients' lives"[5], "lesson the burden of illness, and provide patients with HAE with a normal quality of life (QoL)."[6]
- At present, long-term prophylaxis (LTP) with medication is the only way to prevent attacks and reduce the burden of the disease.[5]
- Subcutaneous C1INH replacement therapy (C1INH[SC]; HAEGARDA®) is a first-line option for LTP.[5,6]
- C1INH(SC) is typically self-administered by the patient or a caregiver. Breakthrough attacks can be treated at home, also, using on-demand medications that are kept on hand.
- In today's treatment environment, in which patients with HAE have increasing autonomy in their disease management, an assessment of real-world outcomes of self-administered LTP therapy may be difficult to capture sufficiently through medical chart data alone.
- The purpose of this study was to gain a more holistic understanding of the clinical and QoL impacts of routine C1INH(SC) used as LTP in patients with HAE, as well as on-demand medication use patterns, using a combination of patient interviews and medical chart review data.

METHODS

Study Design and Patients

- This study was a hybrid design combining semi-structured, qualitative interviews used in parallel with a retrospective medical records review.
- Participants were adults (≥18 years) with HAE type 1 or 2 who had been using C1INH(SC as LTP for at least 1 year and who had been using on demand treatments only for at least 1 year prior to C1INH(SC).
- Patients were identified from the practice populations of 7 clinician-investigators who were all highly experienced in the treatment of patients with HAE.

Data Collection

- Medical records were reviewed by trained site staff for the period 12 months prior and 12 months after starting C1INH(SC) LTP (index date) for data relating to HAE attacks, attack treatment, and patient impact.
- Patient interviews were conducted by telephone.
  - Each interview was 30 minutes in length and conducted by a trained interviewer from ICON plc using a semi-structured interview format with open-ended questions.
  - Patients received a $75 gift card as compensation for participation.
  - Interviews were thematically analyzed using qualitative methods (MaxQDA software) to identify themes and information relating to HAE attacks, attack treatment, and patient impact.

RESULTS

Study Cohort

- The study included 36 patients (**Table 1**) ranging in age from 24–77 years (mean age, 47.9).
- A majority of patients (n=34; 94%) had HAE type 1.

C1INH(SC) dosing and administration

- The most commonly prescribed C1INH(SC) doses were 60 IU/kg (n=27; 75%) and 40 IU/kg (n=5; 14%); prescribed doses in the remaining 4 (11%) patients were 50, 50, 30, and 21 IU/kg.
- Dosing frequency was biweekly (24 patients), every 3-4 days (11 patients), and not reported in 1 patient.

Annualized Attack Frequency

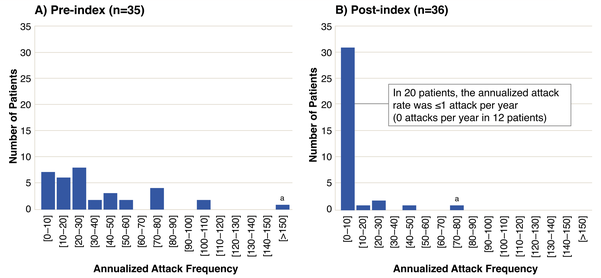
- Pre-index and post-index annualized HAE attack frequency distributions are presented in **Fig. 1**.
- Pre-index annualized attack frequencies ranged from 1-198 attacks per year.
- Post-index, 20 patients had 0 or <1 annualized attacks and 12 of these patients reported 0 attacks.
  - One patient had 78 annualized attacks post-index, but this reflected a 60% decrease from 198 annualized attacks pre-index.

Table 1. Sociodemographic and Clinical Characteristics of Study Cohort

Characteristic	N=36
Age at Interview (years), mean (SD), range	47.9 (15.6), 24-77
Sex, Female	23 (64%)
Race/Ethnicity	
White	32 (89%)
Black or African American	3 (8%)
Other[a]	1 (3%)
Working Status	
Working full-time	22 (61%)
Retired	6 (17%)
Looking after home / family or unemployed / seeking work	2 (6%)
Self-employed	2 (6%)
Permanently unable to work / disability	2 (6%)
Working part-time	2 (6%)
Insurance Type[b]	
Private health insurance	25 (69%)
Medicare/Medicaid	11 (31%)
Other	5 (17%)
Patient Medical History	
Weight, last recorded (lbs), mean, range	199.3, 123–375 (n=28)
HAE Type 1	34 (94%)
HAE Type 2	2 (6%)
Age at initial HAE diagnosis (years), mean, range	17.1, 4–44 (n=32)
Family history of HAE	29 (81%) (n=34)

Data are n (%) unless noted otherwise. N=36 unless noted otherwise. ""Other" reported as multiracial (White/Native Hawaiian/Hispanic/Latino)
[b]Some patients reported multiple forms of insurance. HAE, hereditary angioedema; SD, standard deviation

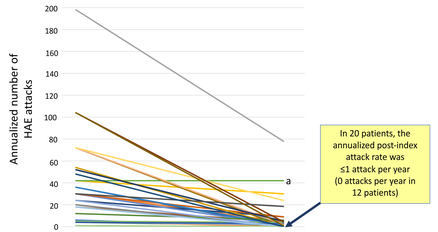
Figure 1. Histograms of patient distribution according to annualized HAE attack frequency A) pre-index and B) post-index. Index = initiation of LTP with C1INH(SC)



[a] One outlier patient with particularly burdensome disease reported experiencing a pre-index annualized frequency of ~198 attacks per year (15–18 attacks per month). Post-index, the annualized rate decreased to 78 attacks per year (6–7 per month)

- The mean (SD) attack frequency decreased significantly from 38.8 (38.8) attacks per year pre-index to 7.0 (15.3) attacks per year (P<0.00005).
  - This represented an 82.0% decrease in the number of attacks (mean of 31.8 fewer attacks per patient per year)
- The median annualized attack rate decreased from 30 to 1 attack per year (96.7% decrease).

Figure 2. Annualized HAE attack frequencies by individual patients, pre- and post-index (n=35). Data as reported in patient interviews. Index = initiation of LTP with C1INH(SC)



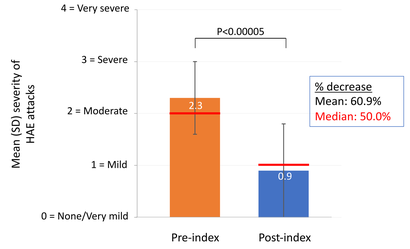
	Pre-Index	Post-Index	% Reduction
Mean (SD) no. of attacks	38.8 (38.8)	7.0 (15.3)*	82.0%
Median no. of attacks	30	1	96.7%

[a] This patient reported ~42 severe attacks per year pre-index. Frequency and severity were not notably different post-index, but the patient reported that the attacks resolved more quickly while using C1INH(SC) prophylaxis. It should also be noted that this patient's medical chart noted a post-index attack frequency of one attack per month
HAE, hereditary angioedema; LTP, long-term prophylaxis; SD, standard deviation
*P<0.00005, pre-index vs post-index

Attack Severity

- Overall, the mean (SD) severity of attacks decreased significantly from 2.3 (0.7) pre-index to 0.9 (0.9) post-index (P<0.00005), on a scale ranging from 0=none/mild to 4=very severe (**Fig. 3**).
  - 1 patient was on C1INH(SC) throughout a pregnancy and reported increased attack frequency and severity during the pregnancy.

Figure 3. Mean reported severity of HAE attacks[a] (n=35), pre- and post-index. Index = initiation of LTP with C1INH(SC). Red lines represent median values.

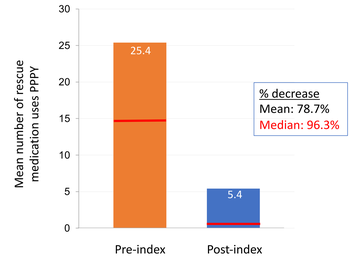


[a] Severity of attacks was captured from patient interviews; narrative descriptions of severity were translated into numerical severity scores based on a scale of 0=none/very mild, 1=mild, 2=moderate, 3=severe, and 4=very severe. Responses which include a combination of severities were scored as the middle point between the two numerical scores for the stated severities (e.g., "mild to moderate" was given a severity score of 1.5; "moderate to severe" was given a severity score of 2.5)
HAE, hereditary angioedema; LTP, long-term prophylaxis; SD, standard deviation

Rescue (On-demand) Medication Use

- Mean annualized rescue medication use decreased by 78.7% from an estimated 25.4 uses per patient per year (PPPY) pre-index to an estimated 5.4 uses PPPY post-index (**Fig. 4**).
  - Median pre- and post-index values were 14.7 and 0.6 (96.3% decrease).

Figure 4. Mean rescue medication use per patient per year (PPPY) pre-index vs post-index. Index = initiation of LTP with C1INH(SC). Red lines represent median values.

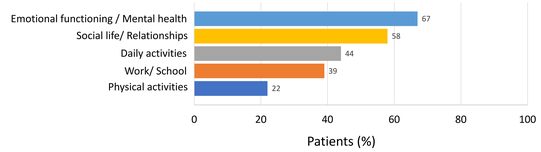


LTP, long-term prophylaxis; PPPY, per patient per year

Quality of Life

- While using C1INH(SC), substantial proportions of patients indicated experiencing improvement in many QoL domains, including emotional functioning/mental health, social life/relationships, daily activities, work/school, and physical activities (**Fig. 5**).

Figure 5. Patient-reported subjective improvements related to quality of life domains while using C1INH(SC). Data represent the proportion of patients whose interview content included mention of improved aspects of life categorized within one of the five QoL domains.



DISCLOSURES

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