Attack Characteristics in Patients with Hereditary Angioedema Receiving Non-Androgen Long-term Prophylaxis

William R. Lumry[1], Alan Baptist[2], Daniel Soteres[3], Michael Manning[4], Lucy Earl[5], Hannah Connolly[5], Paul Audhya[6], Alice Wang[6], Tomas Andriotti[6], Vibha Desai[6]

[1]AARA Research Center, Dallas, TX, USA; [2]Henry Ford Health/Michigan State University, Detroit, USA; [3]Asthma & Allergy Associates, PC and Research Center, Colorado Springs, CO, USA.

[4]Allergy, Asthma & Immunology Associates, Ltd., Internal Medicine, UA College of Medicine-Phoenix, Scottsdale, Arizona, USA. [5]Adelphi Real World, Bollington, UK. [6]KalVista Pharmaceuticals, Cambridge, USA

Background

- Hereditary angioedema (HAE) is a rare genetic disease, most commonly caused by deficiency (type 1) or dysfunction (type 2) of the C1-inhibitor protein and subsequent uncontrolled activation of the kallikrein kinin system, resulting in attacks of tissue swelling [1-3]
- Despite reductions in the frequency of HAE attacks reported with non-androgen long-term prophylaxis (LTP), patients continue to experience attacks

Objectives

- To describe the proportion of non-androgen LTP users who reported ≥1 HAE attacks in the past 12 months
- To characterize reported attacks in non-androgen LTP users

Methods

- Data were derived from the Adelphi HAE Disease Specific Programme (DSP)™, a real-world, cross-sectional study with retrospective data collection in the US (January-November 2023)
- HAE treating physicians (eligible if they were responsible for the management of ≥1 HAE patient per month) utilized patients' medical charts and their diagnostic and clinical judgment to provide current and historic data on demographics, attack characteristics, and treatment
- The survey was conducted according to relevant guidelines and legislation, and the methodology has been previously published and validated [4-5]
- These analyses included HAE patients aged ≥12 with HAE type 1 or 2. All analyses were descriptive

Study sample

- Overall, 71 physicians (50.7% allergist/allergist-immunologist, 21.1% dermatologist, 12.7% pulmonologist, 8.5% ENT specialist, 7.0% haematologist) reported data for 288 patients with HAE
  - Cohort 1 included patients receiving non-androgen LTP for ≥12 months at the point of data collection (n=124)
  - Cohort 2 included patients who were receiving non-androgen LTP at the time of their last HAE attack and experienced ≥1 attack in the 12 months prior to data collection (n=103)

Results

Table 1. Cohort 1 - Patient baseline demographics, background characteristics and current treatment

	Overall (n=124)
Age (years), mean ± SD	35.4 ± 12.49
Female, n (%)	58 (46.8%)
Ethnicity, n (%)	
White	94 (75.8%)
Black African American/African or Caribbean	23 (18.5%)
Asian	5 (4.0%)
South or Central American Native	2 (1.6%)
Other	1 (0.8%)
Years since diagnosis, mean ± SD (n)	6.4 ± 8.48 (99)
HAE type, n (%)	
Type 1	80 (77.7%)
Type 2	23 (22.3%)
Current treatment, n (%)	
LTP only	29 (23.4%)
LTP and on-demand	95 (76.6%)
Time receiving LTP treatment (years), mean ± SD	2.9 ± 1.81
Time receiving on-demand treatment (years), mean ± SD	4.2 ± 3.26
Current LTP treatment, n (%)	
Lanadelumab	56 (45.2%)
Berotralstat	30 (24.2%)
Subcutaneous C1 esterase inhibitor	27 (21.8%)
Intravenous C1 esterase inhibitor	12 (9.7%)

Abbreviations: HAE; hereditary angioedema, LTP; long-term prophylaxis, SD; standard deviation

Table 2. Cohort 1 – Physician perceived frequency that patients reported attacks

	Overall (n=124)
Never, n (%)	5 (4.0%)
Rarely, n (%)	14 (11.3%)
Sometimes, n (%)	36 (29.0%)
Very often, n (%)	35 (28.2%)
Always, n (%)	34 (27.4%)

- In cohort 1, 75.0% of patients experienced at least one attack in the 12 months prior to data collection; however, only 27.4% of patients always reported their attacks (Table 2)

Table 3. Cohort 2 - Patient baseline demographics, background characteristics and treatment of most recent HAE attack

	Overall (n=103)	Adult patients (n=98)	Adolescent patients (n=5)
Age (years), mean ± SD	34.3 ± 12.03	35.2 ± 11.48	15.0 ± 1.22
Female, n (%)	50 (48.5%)	47 (48.0%)	3 (60.0%)
Ethnicity, n (%)			
White	74 (71.8%)	71 (72.4%)	3 (60.0%)
Black African American/African or Caribbean	22 (21.4%)	22 (22.4%)	0 (0%)
Asian	6 (5.8%)	4 (4.1%)	2 (40.0%)
South or Central American Native	2 (1.9%)	2 (2.0%)	0 (0%)
Other	1 (1.0%)	1 (1.0%)	0 (0%)
Years since diagnosis, mean ± SD (n)	6.4 ± 8.48 (99)	6.5 ± 8.65 (94)	4.1 ± 3.51 (5)
HAE type, n (%)			
Type 1	80 (77.7%)	75 (76.5%)	5 (100.0%)
Type 2	23 (22.3%)	23 (23.5%)	0 (0%)
Days since most recent HAE attack, mean ± SD	109.3 ± 82.92	111.5 ± 83.99	66.4 ± 42.95
Patients who treated their most recent HAE attack, n (%)	78 (76.5%)	75 (77.3%)	3 (60.0%)
On-demand treatment used to treat most recent HAE attack, n (%)			
Icatibant (branded and generic)	55 (53.9%)	52 (53.6%)	3 (60.0%)
Plasma derived C1 esterase inhibitor	10 (9.8%)	10 (10.3%)	0 (0%)
Recombinant C1 esterase inhibitor	8 (7.8%)	8 (8.2%)	0 (0%)
Ecallantide	5 (4.9%)	5 (5.2%)	0 (0%)
LTP at the time of most recent HAE attack, n (%)			
LTP only	22 (21.4%)	21 (21.4%)	1 (20.0%)
LTP and on-demand treatment	81 (78.6%)	77 (78.6%)	4 (80.0%)
Time receiving LTP treatment (years), mean ± SD	2.0 ± 1.54	2.1 ± 1.55	0.9 ± 0.61

Abbreviations: HAE; hereditary angioedema, LTP; long-term prophylaxis, SD; standard deviation

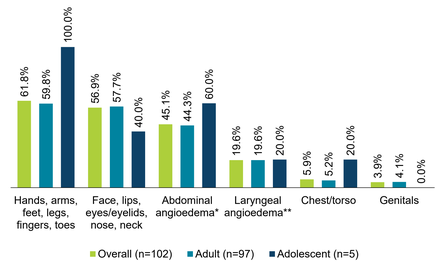
- Cohort 2 included 103 patients with a mean (± SD) age of 34.3±12.0 years, and 48.5% were female (**Table 3**)
- Most patients in cohort 2 (76.5%) treated their most recent HAE attack with on-demand treatment (**Table 3**)

Table 4. Cohort 2 - Non-androgen long-term prophylaxis treatment at the time of most recent HAE attack

	Overall (n=103)	Adult patients (n=98)	Adolescent patients (n=5)
LTP at the time of most recent HAE attack, n (%)			
Lanadelumab	43 (41.7%)	40 (40.8%)	3 (60.0%)
Berotralstat	26 (25.2%)	24 (24.5%)	2 (40.0%)
C1 esterase inhibitor (Haegarda)	22 (21.4%)	22 (22.4%)	0 (0%)
Intravenous C1 esterase inhibitor	13 (12.6%)	13 (13.3%)	0 (0%)

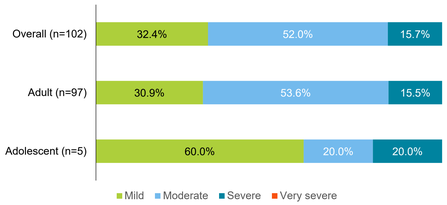
Abbreviations: HAE; hereditary angioedema, LTP; long-term prophylaxis

Figure 1. Cohort 2 - Location of most recent HAE attack



More than one response could be provided for attack location
* Abdominal pain, with or without abdominal distention, nausea, vomiting, diarrhea
** Stridor, dyspnea, difficulty speaking, difficulty swallowing, throat tightening, or swelling of the tongue, palate, uvula, larynx

Figure 2. Cohort 2 – What was the grade/severity of the attack?



- On average, the most recent HAE attack of patients in cohort 2 occurred 109 days ago and most frequently caused swelling of the extremities (61.8%), face and neck (56.9%), abdominal viscera (45.1%), and larynx (19.6%) (**Figure 1**)
- The most recent HAE attack was reported as severe by 15.7% of patients and as moderate by 52.0% (**Figure 2**)
- For the most recent HAE attack, 11.7% of patients required an ER visit and 3.9% were admitted to hospital (**Table 5**)

Table 5. Cohort 2 - Emergency visits and hospitalization required for most recent HAE attack

	Overall (n=103)	Adult patients (n=98)	Adolescent patients (n=5)
Patient attended emergency room (ER)	12 (11.7%)	10 (10.2%)	2 (40%)
Patient was admitted to hospital	4 (3.9%)	4 (4.1%)	0 (0%)
Did not require ER or hospitalization	88 (85.4%)	85 (86.7%)	3 (60%)

Conclusions

- **Results show 75.0% of patients receiving non-androgen LTP reported ≥1 HAE attack in the 12 months prior to data collection**
- **Infrequent reporting of attacks to physicians and/or potential survivor bias from including long-term users of non-androgen LTP may have resulted in underestimation of frequency of attacks**
- **Of patients receiving non-androgen LTP, 23.4% of patients in Cohort 1 were not receiving an on-demand treatment, and 21.4% in Cohort 2 were not receiving an on-demand treatment or were choosing not to treat their attack**
- **In patients using non-androgen LTP, a high proportion of patients reported their most recent attack as moderate or severe, 19.6% of these attacks involved laryngeal swelling, and a considerable number of patients required ER visit/hospitalization**
- **Although non-androgen LTP reduces the frequency of attacks, all patients require ready access to on-demand treatment as per international guidelines**

Acknowledgments

Data collection was undertaken by Adelphi Real World (Bollington, UK) as part of an independent survey, entitled the Adelphi Hereditary Angioedema Disease Specific Programme (DSP)™. All data are the intellectual property of Adelphi Real World. KalVista subscribed to this survey and did not influence the original survey through either contribution to the design of questionnaires or data collection.

Editorial/medical writing support on behalf of Adelphi Real World (Bollington, United Kingdom) was provided by Dr Gary Sidgwick of Adelphi Real World, under the guidance of the authors and in accordance with Good Publication Practice 2022 (GPP 2022) guidelines

Disclosures

William R. Lumry: Advisory boards for BioCryst, CSL Behring, and Takeda; research grants from Astra Zeneca, Astria, Biomarin, CSL Behring, Grifols, Ionis, KalVista, Lilly, Novartis, Pharvaris, Takeda, Teva and Up Stream Bio; consulting fees from Astria, BioCryst, Biomarin, CSL Behring, Express Scripts / CVS, Intellia, KalVista, Magellan, Optum, Pharming, Pharvaris and Takeda; payments for lectures from BioCryst, CSL Behring, Pharming, Takeda, Grifols, Astra Zeneca, Sanofi and GSK; advisory board member of the US Hereditary Angioedema Association. Alan Baptist: Consultant for KalVista and Takeda; research support from BioCryst, Takeda, and Ionis. Daniel F. Soteres: Research investigator for BioCryst, Ionis, KalVista, Pharvaris, and Takeda; speaker and/or consultant for BioCryst, CSL Behring, Cycle Pharma, KalVista, and Takeda. Michael Manning: Consultant and research funding for KalVista, Takeda, Pharming, CSL Behring, BioCryst, Ionis, Pharvaris, Lucy Earl: Former employee of Adelphi Real World, Bollington, UK, Hannah Connolly: Employee of Adelphi Real World, Bollington, UK. Paul K. Audhya, Alice Wang, Tomas Andriotti and Vibha Desai: Employee of KalVista Pharmaceuticals, Cambridge, United States

This poster is intended for healthcare professionals

References

1. Busse PJ, Christiansen SC, Riedl MA, et al. J Allergy Clin Immunol Pract. 2021;9(1):132-150.e3.
2. Busse P, Kaplan A. J Allergy Clin Immunol Pract. 2022;10(3):716-722.
3. Bork K et al. Allergy Asthma Clin Immunol. 2021;17(1):40.
4. Anderson P et al. Current Medical Research and Opinion. 2023;39(12):1707-1715.
5. Anderson P et al. Current Medical Research and Opinion. 2008;24(11):3063-3072.

To view this poster after the presentation, visit KalVista Virtual Medical Booth.

KalVista Pharmaceuticals