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Delayed On-demand Treatment of Hereditary Angioedema Attacks: Patient Perceptions and Associated Barriers

Sandra Christiansen[1], Maeve O'Connor[2], Julie Ulloa[3], Sherry Danese[3], Vibha Desai[4], Shawn Czado[4*], Paul Audhya[4], Paula Busse[5]

[1]University of California San Diego, La Jolla, CA, United States; [2]Allergy, Asthma, & Immunology Relief of Charlotte, Charlotte, NC, United States; [3]Outcomes Insights, Agoura Hills, CA, United States; [4]KalVista Pharmaceuticals, Cambridge, MA, United States; [5]The Mount Sinai Hospital, New York, NY, United States

*Employee of KalVista Pharmaceuticals at the time the study was conducted

Background

- Hereditary angioedema (HAE) is characterized by, unpredictable swelling attacks affecting cutaneous and submucosal tissues, which are typically painful debilitating and potentially fatal
- Treatment guidelines recommend the early use of on-demand treatment following the attack recognition to reduce morbidity and prevent mortality[1-3]
  - Currently available on-demand treatments for HAE attacks are administered subcutaneously or intravenously[3]
- Despite the recommendation for early treatment, recent research suggests that patients delay treatment of their HAE attacks[4]
- We assessed patient perceptions of "early" on-demand use vs. actual time to treatment, in conjunction with barriers contributing to treatment delay

Methods

- The US Hereditary Angioedema Association recruited patients with Type 1 or 2 HAE between April and June 2023
  - Recruitment was stratified to include 50% of patients taking on-demand only and 50% receiving LTP plus on-demand
- Participants completed a 20-minute, self-reported, online survey that inquired about their last treated HAE attack
- Participants were ≥12 years old and had to have treated ≥1 HAE attack within the prior 3 months using an approved on-demand therapy
- Respondents provided consent for their data to be used anonymously or in aggregate

Results

Table 1. Participant Demographics

	Total (N=94)	On-Demand Only Treatment (46% | n=43)	On-Demand Treatment +LTP (54% | n=51)	Adults (85% | n=80)	Adolescents (15% | n=14)
Current mean age, (SD)	39.4 (17.4)	42.6 (18.7)	36.7 (15.8)	43.8 (15.0)	14.4 (1.5)
Mean age of diagnosis, years (SD)	18 (12.6)	19 (12.7)	17 (12.5)	20 (12.5)	6 (4.1)
Gender					
Male	28%	23%	31%	21%	64%
Female	72%	77%	69%	79%	36%
Race/Ethnicity					
White	87%	91%	84%	89%	79%
Hispanic or Latino	9%	2%	14%	8%	14%
Black/African American	3%	2%	4%	3%	7%
American Indian or Alaskan Native	2%	2%	2%	–	14%
Asian	3%	5%	2%	4%	–
Other	1%	–	2%	1%	–
HAE Type					
Type 1	81%	79%	82%	81%	79%
Type 2	19%	21%	18%	19%	21%

Results

Figure 1. On-Demand Therapy Used for Last Treated Attack

On-Demand Therapy	On-Demand Only Treatment (n=43)	On-Demand Treatment + LTP (n=51)	Adults (n=80)	Adolescents (n=14)
Icatibant 65%	63%	66%	77%	NA*
Recombinant C1 Esterase Inhibitor 18%	21%	16%	13%	50%
Plasma Derived C1 Esterase Inhibitor 15%	14%	16%	9%	50%
Ecallantide 2%	2%	2%	3%	0%

% of Patients

*Not approved for patients under 18 years old.

- The most common on-demand treatments were icatibant (77%, branded and generic) for adults and recombinant C1 esterase inhibitor (50%) or plasma derived C1 esterase inhibitor (50%) for adolescents (**Figure 1**)

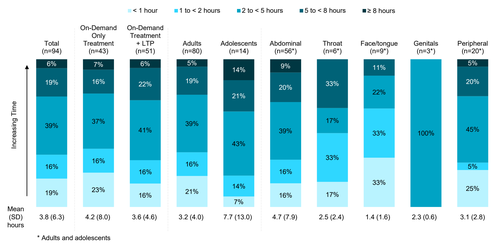
Figure 2. Long-Term Prophylaxis at Time of Last Treated Attack

Long-Term Prophylaxis	Adults (n=43)	Adolescents (n=8)
Lanadelumab 57%	63%	25%
Subcutaneous Human C1 Esterase Inhibitor 24%	26%	13%
Berotralstat 14%	9%	38%
Intravenous Human C1 Esterase Inhibitor 6%	2%	25%

% of Patients

- Among those on long-term prophylaxis at the time of the last treated attack (n=51; 54%), lanadelumab was the most common treatment among adults, whereas berotralstat was most common among adolescents (**Figure 2**)

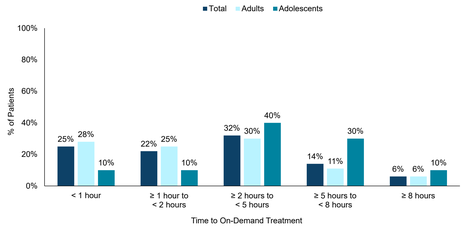
Figure 3. Time to Treatment with On-demand Therapy



* Adults and adolescents

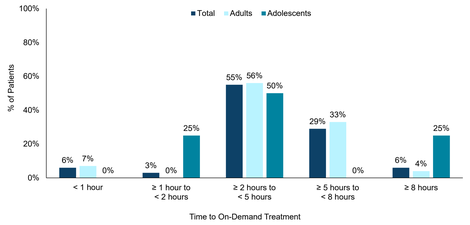
- Mean reported time from attack onset to on-demand treatment was 3.8 hours, with 19% treating in less than an hour (**Figure 3**)
- Time to treatment was fastest for attacks affecting the face/tongue, throat, and genitals
- Time to treatment was longer among adolescents (mean 7.7 hours) than adults (mean 3.2 hours), with only 7% of adolescents treating in less than an hour

Figure 4. Time to On-Demand Treatment Among Patients Who Said They Treated Their Attack "Early"



- The majority of participants (n=63; 67%) believed they treated their attack early, despite only 25% treating in less than one hour and 48% treating in less than 2 hours (**Figure 4**)
  - The mean (SD) time to treatment for these patients was 2.9 (4.5) hours

Figure 5. Time to On-Demand Treatment in Patients Who Said They Did Not Treat Attack Early



- 31 participants (33%) reported that they did not treat their attack early, with 90% of these patients waiting at least 2 hours to treat their attack (**Figure 5**)
  - The mean (SD) time to treatment for these patients was 5.7 (8.8) hours

Figure 6. Top Ranked Barriers to Treating Attack Early Among Patients that Reported a Barrier

	Ranked 1st	On-Demand Only Treatment (n=38)	On-Demand Treatment + LTP (n=47)	Adults (n=71)	Adolescents (n=14)
I was not certain it was a real / actual attack	53%	34%	26%	31%	21%
I thought the attack would be mild	39%	13%	17%	13%	29%
I wanted to save my on-demand treatment for a severe attack	32%	11%	9%	11%	–
I did not have my on-demand treatment with me	20%	5%	19%	16%	–
I wanted to avoid the burning, stinging or pain with the injection	19%	5%	2%	4%	–
I did not want to / could not interrupt what I was doing	17%	3%	4%	3%	7%
My on-demand treatment was expensive	15%	–	–	–	–
I waited to treat until the attack was severe	14%	11%	9%	10%	7%
I wanted to avoid the pain of the needle	14%	–	2%	–	7%
I did not have a private place to administer treatment	11%	5%	–	1%	7%
I did not have anyone to help me	9%	3%	2%	3%	–
I wanted to avoid the side effects of treatment	7%	5%	–	–	14%
I had to go to the hospital / emergency center for treatment	7%	–	–	–	–
I did not feel well enough to prepare and administer the treatment	6%	3%	–	1%	–

% of Patients

- 83 participants (88%) reported barriers to treating attacks early (**Figure 6**)
- Top ranked barriers included uncertainty whether the attack was "real" (53%), belief the attack was going to be mild (39%), desire to save on-demand treatment for a severe attack (32%), not having on-demand treatment with them (20%), and desire to avoid injection pain/stinging/burning (19%) (**Figure 6**)

Figure 7. Attack Severity at the Time of Treatment

	On-Demand Only Treatment (n=43)	On-Demand Treatment + LTP (n=51)	Adults (n=80)	Adolescents (n=14)
Mild 29%	28%	29%	33%	7%
Moderate 55%	63%	49%	56%	50%
Severe 13%	7%	18%	9%	36%
Very severe 3%	2%	4%	3%	7%

% of Patients

- The majority of attacks were treated only when they became moderate (55%), severe (13%), or very severe (3%) (**Figure 7**)

Conclusions

- **Despite their perception of treating attacks "early", many patients did not meet guideline recommendations for prompt on-demand treatment after recognition of an HAE attack**
- **Most common barriers to earlier treatment were uncertainty if attack was real, thinking the attack would be mild, and wanting to save treatment for a severe attack**
- **Our findings highlight a need to reinvigorate efforts regarding guideline implementation and proactively address barriers contributing to on-demand treatment delays**

Acknowledgments

The authors wish to thank Jason Allaire, PhD of Generativity Health Outcomes Research for his assistance with this poster. Funding for Dr. Allaire was provided by KalVista Pharmaceuticals.

Disclosures

Sandra Christiansen reports advisory boards: KalVista, BioCryst and US HAEA Medical Advisory Board. Maeve O'Connor reports speaker/consultant/advisor or research support: KalVista, Pharming, CSL, GSK, Blueprint, TEVA, AZ, Sanofi, Grifols, AbbVie. Julie Ulloa and Sherry Danese have received consulting fees from KalVista. Vibha Desai and Paul Audhya are employees of KalVista Pharmaceuticals. Shawn Czado was an employee of KalVista Pharmaceuticals. Paula Busse reports consulting fees: Takeda, KalVista, CVS Specialty, BioCryst, CSL, Behring, ADArx, Astria, Phavaris.

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Presented

AAAAI Annual Meeting 2024. February 23-26, 2024 in Washington DC

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