

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

Sandra Christiansen¹, Maeve O'Connor², Julie Ulloa³, Sherry Danese³, Vibha Desai⁴, Paul Audhya⁴, Paula Busse⁵

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

Abstract

- Rationale:** Hereditary angioedema (HAE) is characterized by debilitating swelling attacks affecting cutaneous and submucosal tissues. Prompt on-demand treatment is essential to limit disease morbidity and mortality. We assessed patient perceptions of "early" on-demand use vs. actual time to treatment, in conjunction with barriers contributing to treatment delay.
- Methods:** People with Type 1 or 2 HAE were recruited between April and June 2023 by the US Hereditary Angioedema Association to complete a 20-minute, self-reported, online survey. Participants were ≥12 years old and had to have treated ≥1 HAE attack within prior 3 months with an approved on-demand therapy.
- Results:** Respondents included 80 adults and 14 adolescents, 54% on long-term prophylaxis (LTP) at the time of their most recent treated attack. Mean reported time from attack onset to on-demand treatment was 3.8 hours, with 19% treating in <1 hour. Time to treatment among adolescents (mean 7.7 hours) and for abdominal attacks (mean 4.7 hours) revealed the longest treatment delays. A total of 67% reported their perception of time to treatment as "early" despite only 26% treating in less than 1hr and 48% treating in less than 2 hours (mean 2.9 hours). Barriers delaying treatment included uncertainty whether the attack was "real" (53%), belief the attack was going to be mild (39%), not having on-demand treatment with them (20%), and desire to avoid injection pain/stinging/burning (19%).
- Conclusions:** Despite their perception of treating attacks "early," many patients do not meet guideline recommendations for prompt on-demand treatment of HAE attacks. Our findings highlight a need to educate patients on treating at the earliest recognition of an attack and proactively addressing barriers contributing to treatment delays.

Background

- 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 attack recognition to reduce morbidity and prevent mortality.¹⁻³ Currently available on-demand treatments for HAE attacks are administered subcutaneously or intravenously³
- Despite the recommendation for early treatment, recent research suggests that patients delay on-demand treatment of their HAE attacks⁴
- 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 participants with Type 1 or 2 HAE between April and June 2023
 - Recruitment was stratified to include 50% of participants 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 (n=43) (46%)	On-demand Treatment +LTP (n=51) (54%)	Adults (n=80) (85%)	Adolescents (n=14) (15%)
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 at 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%

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%	NA*
Recombinant C1 Esterase Inhibitor	18%	21%	16%	50%
Plasma Derived C1 Esterase Inhibitor	15%	14%	9%	50%
Ecallantide	2%	2%	3%	0%

*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 the Time of Last Treated Attack

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

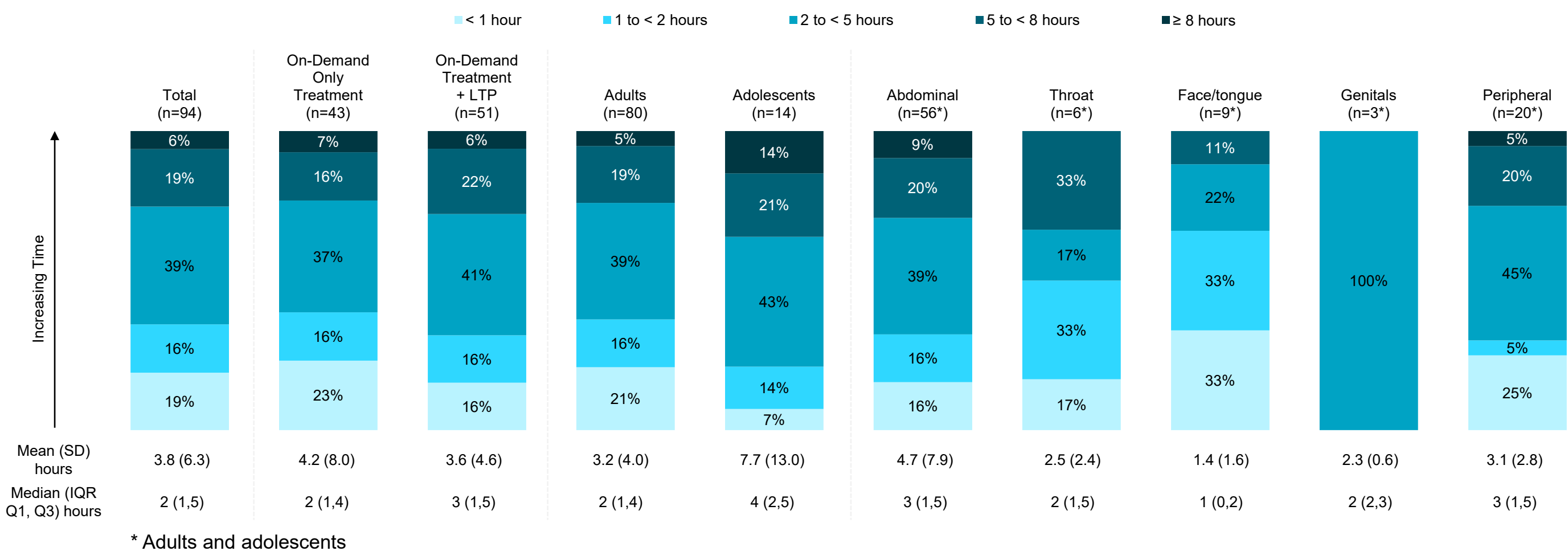
- Among those on long-term prophylaxis at the time of the last treated attack (n=51; 54%), lanadelumab was the most common treatment among adults, whereas bertralstat was most common among adolescents (Figure 2)

Disclosures

- In relation to this presentation, the authors declare the following, real or perceived conflicts of interest:
 - Receipt of grants/research support: Maeve O'Connor: KalVista Pharmaceuticals, Pharming, CSL, GSK, Blueprint, TEVA, AZ, Sanofi, Grifols, AbbVie, Paula Busse: Takeda, KalVista, CVS Specialty, BioCryst, CSL, Behring, ADARx, Astria, Phavaris
 - Receipt of honoraria or consultation fees: Sandra Christiansen: KalVista Pharmaceuticals, BioCryst, US HAEA Medical Advisory, Maeve O'Connor: KalVista, Pharming, CSL, GSK, Blueprint, TEVA, AZ, Sanofi, Grifols, AbbVie, Julie Ulloa and Sherry Danese: KalVista Pharmaceuticals
 - Participation in sponsored speaker bureau: No conflicts of interest
 - Stock/shareholder: Vibha Desai and Paul Audhya: KalVista Pharmaceuticals
 - Vibha Desai and Paul Audhya are employees of KalVista Pharmaceuticals

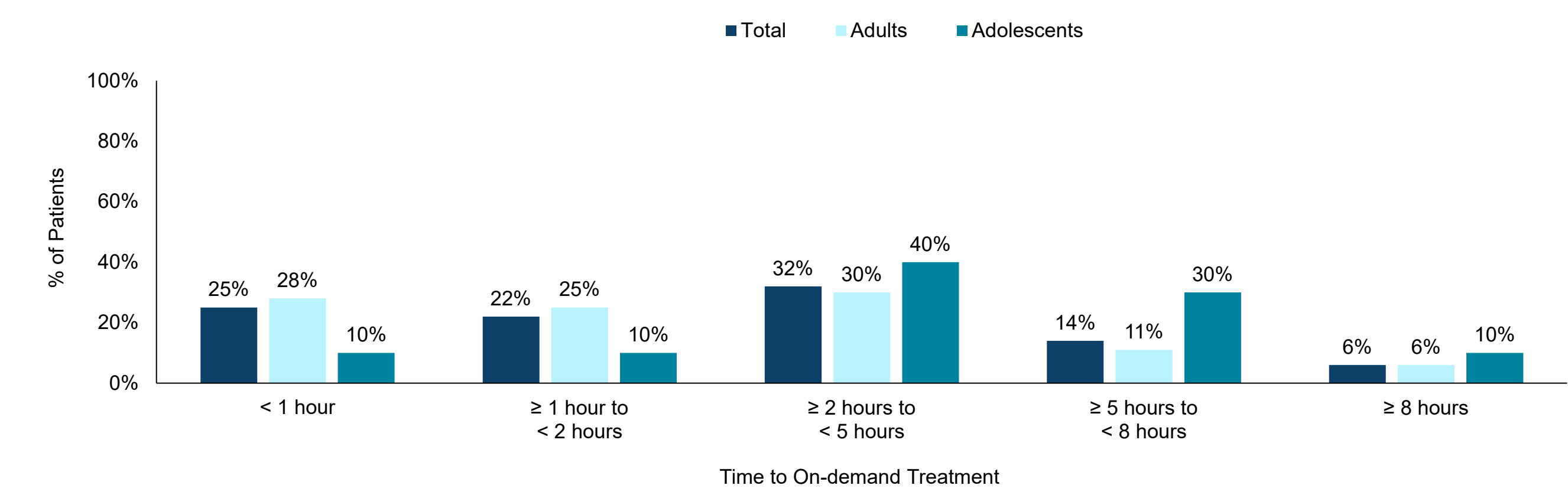
Results

Figure 3. Time to Treatment with On-demand Therapy



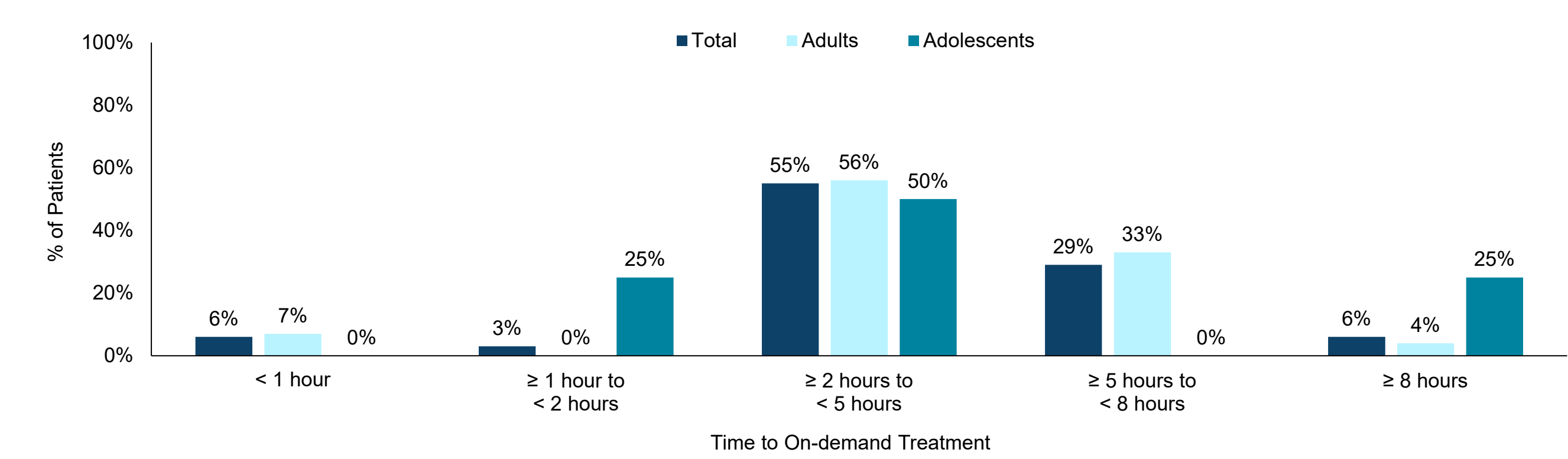
- Mean reported time from attack onset to on-demand treatment was 3.8 hours, with 19% treating in less than an hour (Figure 3)
- Time to treatment was fastest for attacks affecting the face/tongue, throat, and genitals
- Time to treatment was longer among adolescents (mean 7.7 hours) than adults (mean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

Barrier	Ranked 1 st			
	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	34%	26%	31%	21%
I thought the attack would be mild	13%	17%	13%	29%
I wanted to save my on-demand treatment for a severe attack	11%	9%	11%	–
I did not have my on-demand treatment with me	5%	19%	16%	–
I wanted to avoid the burning, stinging or pain with the injection	5%	2%	4%	–
I did not want to / could not interrupt what I was doing	3%	4%	3%	7%
My on-demand treatment was expensive	–	–	–	–
I waited to treat until the attack was severe	11%	9%	10%	7%
I wanted to avoid the pain of the needle	–	2%	–	7%
I did not have a private place to administer treatment	5%	–	1%	7%
I did not have anyone to help me	3%	2%	3%	–
I wanted to avoid the side effects of treatment	5%	–	–	14%
I had to go to the hospital / emergency center for treatment	–	–	–	–
I did not feel well enough to prepare and administer the treatment	3%	–	1%	–

- 83 participants (88%) reported barriers to treating attacks early
- 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

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

- 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

References

- Betschel S, Badiou J, Binkley K, et al. The International/Canadian Hereditary Angioedema Guideline. *Allergy, Asthma & Clinical Immunology*. 2019;11(25):15(1):72. doi:10.1186/s13223-019-0376-8
- Busse PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. *The Journal of Allergy and Clinical Immunology In Practice*. Jan 2021;9(1):132-150.e3. doi:10.1016/j.jaip.2020.08.046
- Maurer M, Magerl M, Betschel S, et al. The international WAO/EAACI guideline for the management of hereditary angioedema-The 2021 revision and update. *WAO*. Jul 2022;77(7):1961-1990. doi:10.1111/all.15214
- Radojicic, Cristine et al. Patient Perspectives On Early Use Of On-demand Treatment For Hereditary Angioedema (HAE) Attacks to Reduce Severity and Duration. *Journal of Allergy and Clinical Immunology*. Volume 151, Issue 2, AB143

Presented:

2024 HAEi Regional Conference Americas. March 15-17, 2024, in Panama City, Panama

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

