Barriers to Timely On-Demand Treatment of Hereditary Angioedema Attacks in Italian Patients

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Introduction

- Hereditary angioedema (HAE) is characterized by unpredictable swelling attacks affecting mucosal and subcutaneous tissues, which are typically painful, debilitating, and potentially fatal
- WAO/EAACI guidelines recommend the early use of on-demand treatment following recognition of an HAE attack to reduce morbidity and prevent mortality[1-3]
- Despite the recommendation for early treatment, recent research suggests that patients delay on-demand treatment of their attacks[4]

Methods

- Individuals with Type 1 or 2 HAE due to C1 inhibitor deficiency were recruited through the Italian Network for Hereditary and Acquired Angioedema (ITACA) between September 2023 and January 2024
- Respondents enrolled were ≥12 years old and had to have treated with an approved on-demand therapy ≥1 HAE attack within 3 months prior to the survey
- The survey was self-reported, and took respondents approximately 20 minutes to complete
- Recruitment was stratified to include 50% of participants taking on-demand treatment only and 50% taking on-demand treatment + long-term prophylaxis (LTP)

Results

Table 1. Respondent Characteristics

	Total (n = 101)	On-Demand Only (n = 48)	On-Demand + LTP (n = 53)	Adults (n = 87)	Adolescents (n = 14)
Current Mean Age, Years (SD)	38 (16.2)	40 (16.5)	37 (15.9)	42 (14.0)	15 (1.6)
Diagnosis Mean Age, Years (SD)	17 (14.7)	20 (16.8)	14 (11.7)	18 (15.2)	7 (3.1)
Gender					
Male	39.6%	43.8%	35.8%	37.9%	50.0%
Female	60.04%	56.2%	64.2%	62.1%	50.0%
HAE Type					
Type 1	93.1%	93.8%	92.4%	93.1%	92.8%
Type 2	6.9%	6.2%	7.6%	6.9%	7.2%
Days Since Last Attack, Mean (SD)	19.0 (17.7)	17.6 (16.5)	20.2 (18.9)	18.3 (15.6)	23.0 (28.1)

LTP: long-term prophylaxis

- Respondents included 14 adolescents (14%) with an average age of 15 years and 87 adults (86%) with an average age of 42 years (**Table 1**)
- Overall, respondents were predominately female (60.04%) with an average of 19 days since last HAE attack

Results

Figure 1. On-Demand Treatment at Time of Last Treated Attack

	Treatment Used (n = 101)	On-Demand Only (n = 48)	On-Demand + LTP (n = 53)	Adults (n = 87)	Adolescents (n = 14)
Icatibant (Firazyr and generic)	55%	54%	55%	59%	29%
Plasma derived C1 esterase inhibitor (Berinert)	44%	46%	42%	39%	71%
Plasma derived C1 esterase inhibitor (Cinryze)	2%	–	4%	2%	–
Recombinant C1 esterase inhibitor (Ruconest)	0%	–	–	–	–

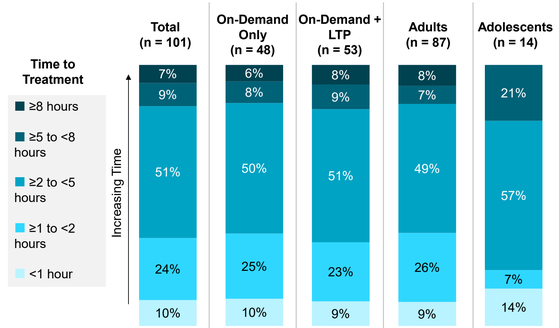
- The most commonly used initial on-demand treatment was icatibant (branded and generic) for adults and plasma derived C1 esterase inhibitor (Berinert) for adolescents (**Figure 1**)
- Among both the on-demand only and on-demand plus long-term prophylaxis groups, icatibant (branded and generic) was the most frequently used treatment, closely followed by plasma derived C1 esterase inhibitor (Berinert)

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

	Adults (n = 44)	Adolescents (n = 9)
Plasma derived C1 esterase inhibitor (Berinert)	34%	27%	67%
Lanadelumab	30%	34%	11%
Berotralstat	11%	11%	11%
Danazol	11%	14%	–
Plasma derived C1 esterase inhibitor (Cinryze)	8%	7%	11%
Tranexamic acid	6%	7%	–

- Among those on long-term prophylaxis at the time of the last treated attack, plasma derived C1 esterase inhibitor (Berinert) was the most common treatment among adolescents, whereas adults were most often treated with lanadelumab (**Figure 2**)

Figure 3. Time to On-Demand Treatment After Attack Onset



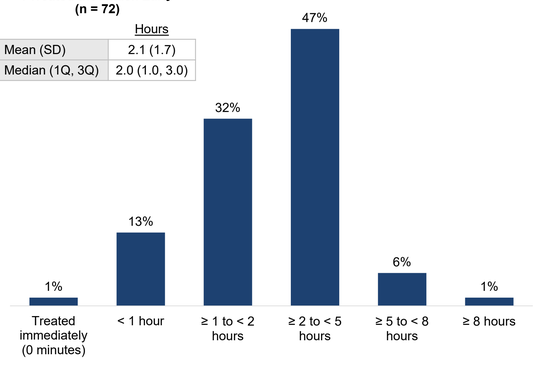
	Total (n = 101)	On-Demand Only (n = 48)	On-Demand + LTP (n = 53)	Adults (n = 87)	Adolescents (n = 14)
Mean (SD) (hour)	2.9 (2.7)	2.7 (2.7)	3.1 (2.7)	2.9 (2.8)	2.9 (1.9)
Median (1Q, 3Q)	2.0 (1.0, 4.0)	2.0 (1.0, 3.0)	2.0 (1.0, 4.0)	2.0 (1.0, 4.0)	2.5 (2.0, 4.0)
Min-Max	0-12	0-12	0-12	0-12	0-6

- The mean time (SD) to treatment during the most recent attack was 2.9 hours (2.7), with 10% (10/101) treating in <1 hour (**Figure 3**)

Figure 4. Perception of Time to Treatment Versus Actual Time to Treatment for Those Who Perceived They Treated Early

"I Treated the Attack Early" (n = 72)

	Hours
Mean (SD)	2.1 (1.7)
Median (1Q, 3Q)	2.0 (1.0, 3.0)



- 71% of respondents (72/101) believed they treated their attack early, despite only 14% of them treating in less than one hour (**Figure 4**)
- The mean time to treatment for those who believed they treated early was 2.1 hours

Figure 5. Barriers to Treating Attack Early Excluding Those Who Treated the Attack Immediately (n = 81; excludes those who treated attacks immediately)

Ranked Top 5

Barriers (Detailed) (Excluding those who treated the attack immediately, ranked top 5)		On-Demand Only (n=40)	On-Demand + LTP (n=41)	Adults (n=70)	Adolescents (n=11)
I was not certain it was a real / actual attack	40%	38%	42%	39%	46%
I thought the attack would be mild	37%	30%	44%	40%	18%
I wanted to save my on-demand treatment for a severe attack	22%	18%	27%	23%	18%
I waited to treat until the attack was severe	20%	18%	22%	19%	27%
I did not want to / could not interrupt what I was doing	16%	23%	10%	16%	18%
I did not have anyone to help me	12%	13%	12%	9%	36%
I did not have my on-demand treatment with me	9%	10%	7%	7%	18%
I did not have a private place to administer the treatment	9%	13%	5%	9%	9%
I had to go to the hospital / emergency centre for treatment	7%	13%	2%	7%	9%
I wanted to avoid the burning, stinging or pain with injection	5%	5%	5%	3%	18%
I wanted to avoid the pain of the needle	4%	3%	5%	3%	9%
I wanted to avoid the side effects of treatment	3%	5%	–	3%	–
I did not feel well enough to prepare and administer the treatment	3%	3%	2%	3%	–
My on-demand treatment was expensive	1%	–	2%	1%	–

- Eighty-one respondents (80%) who did not treat immediately ranked their top 5 reasons for not treating earlier (**Figure 5**)
- The most common barriers to treating sooner were uncertainty the attack was real (40%), thinking the attack would remain mild (37%), and wanting to save on-demand treatment for a severe attack (22%)
- Treatment administration-related barriers (e.g., not wanting to interrupt what they were doing, not having anyone to help with administration) were reported by 38% of respondents as their top reason for delaying treatment

Conclusions

- **Most respondents did not meet guideline recommendations for immediate on-demand treatment following HAE attack onset**
- **Uncertainty the attack was real, hoping the attack would stay mild, and wanting to save treatment for a severe attack were the most common reasons for delaying treatment**
- **A substantial proportion reported treatment administration barriers, including not wanting to interrupt what they were doing, not having anyone to help, and not having a private place to administer treatment**
- **These findings highlight a need to proactively address barriers contributing to treatment delays and to develop less invasive on-demand treatment options**

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Presented

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