

Route of administration preferences of people living with hereditary angioedema for on-demand treatment: A US-based qualitative study

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Background

- Hereditary angioedema (HAE) is characterized by recurrent and unpredictable episodes of subcutaneous or submucosal swelling which can affect the abdomen, extremities, genitals, face, and larynx¹
- All currently approved HAE on-demand treatments must be administered parenterally, which results in significant treatment burden

Objective

- The objectives of this qualitative study were to understand patients' likes and dislikes related to their current on-demand treatment, their attack experiences and route of administration (ROA) preferences for on-demand treatment

Methods

- The US Hereditary Angioedema Association (HAEA) recruited people living with type 1 or type 2 HAE to be interviewed
- Participants were not informed of the identity of the study sponsor
- Study population included both adults (18 to 69yrs) and adolescents (12 to 17yrs); has had at least one HAE attack within the past six months; currently taking on-demand treatment (C1-INH replacement or bradykinin receptor B2 antagonist or kallikrein inhibitor)
- The sampling plan aimed to obtain half of each age group currently taking both on-demand treatment and long-term prophylaxis (LTP) and half taking only on-demand treatment
- Open-ended questions were asked to participants to understand their likes and dislikes associated with their current on-demand treatment
- Open-ended questions were then asked to understand the trade-offs patients are willing to make when choosing a preferred ROA. Hypothetical self-administered injection and oral on-demand treatments were initially presented with similar efficacy and tolerability/mild side-effect risk profiles (Figure 1), which were then made better/worse depending upon participants' initial treatment choice
- Profiles were based on on-demand injection treatments' US package inserts and clinical trial data for oral on-demand treatment in development

Figure 1. Hypothetical Trade-off Scenario

Features	Treatment A	Treatment B
How you take the treatment	Self-injection administered at home	Pill
How long it takes to feel a little improvement in your symptoms?	Same	Same
Risk of mild to moderate pain after the injection	Yes, more than 9 out of 10 people	No
Increased risk of additional mild side effects (e.g., nausea, dizziness and headache)	Yes, fewer than 1 out of 10 people	Yes, fewer than 1 out of 10 people
Which option would you choose?	Treatment A <input type="checkbox"/>	Treatment B <input type="checkbox"/>

Results

Table 1. Respondent Characteristics				Table 3. Responses to Trade-off Scenarios			
Characteristics	Adolescents (n = 10)	Adults (n = 10)	Total (N = 20)		Adolescents (n = 10)	Adults (n = 10)	Total (N = 20)
Age, mean years (SD)	15.5 (1.5)	36.7 (16)	26.1 (8.9)	Treatment choice, n (%)			
[min-max]	[12-17]	[18-60]	[12-60]	Treatment A (self-administered injection)	—	—	—
Gender, n (%)				Treatment B (oral)	10 (100)	10 (100)	20 (100)
Female	5 (50)	6 (60)	11 (55)	Reasons for treatment B, n (%)^a			
Male	5 (50)	4 (40)	9 (45)	Less pain/burning	5 (30)	5 (50)	10 (50)
Race/ethnicity, n (%)				Convenient to take/carry	3 (30)	4 (40)	7 (35)
African American or Black	1 (10)	1 (10)	2 (10)	4 hours before second dose	4 (40)	2 (20)	6 (30)
Hispanic, Latin American, or Latinx	4 (30)	—	4 (20)	Safer (due to no injection/infusion)	1 (10)	—	1 (5)
Middle Eastern or North African	—	1 (10)	1 (5)	No needles	1 (10)	1 (10)	2 (10)
White	5 (50)	8 (80)	13 (65)	Less time to take	2 (20)	1 (10)	3 (15)
Age at HAE diagnosis, mean years (SD)	6.7 (4.3)	17.2 (12)	11.9 (8.3)	“What if” scenarios...			
HAE type 1, n (%)	10 (100)	7 (70)	17 (85)	Treatment A offered “substantial improvement” (vs. Treatment B, “little improvement”) within the same timeframe, n (%)			
Number of attacks, last 6 months, n (SD)	4.4 (5.1)	4.5 (5.0)	4.5 (5.0)	Treatment A choice	9 (90)	8 (80)	17 (85)
Most recent attack location, n (%)				Treatment B choice	1 (10)	2 (20)	3 (15)
Face	1 (10)	—	1 (5.0)	The risk for mild side effects was higher for Treatment B?			
Extremities	3 (30)	4 (40)	7 (35)	Odds before switching to Treatment A, n (%)^b			
Abdomen	5 (50)	4 (40)	9 (45)	< 5 in 10	2 (20)	3 (30)	5 (25)
Throat	1 (10)	2 (20)	3 (15)	≥ 5 in 10	8 (80)	7 (70)	15 (75)
Lifetime specific attack location, n (%)							
Abdominal	8 (80)	9 (90)	17 (85)				
Throat	4 (40)	6 (60)	10 (50)				
Current type of HAE treatment, n (%)							
On-demand treatment and LTPT	8 (80) ^c	5 (50)	13 (65)				
On-demand treatment only	2 (20)	5 (50)	7 (35)				
On-demand treatment used for most recent attack, n (%)							
Firazyr, icatibant ^a	1 (10)	8 (80)	9 (45)				
Berinert	3 (30)	1 (10)	4 (20)				
Ruconest, conestat alfa	3 (30)	—	3 (15)				
Used LTPT ^b	3 (30)	1 (10)	4 (20)				

LTPT = long-term prophylactic treatment; SD = standard deviation.

^a While indicated for individuals aged 18 years and older, 1 adolescent (aged 15 years) reported recent first-time use of Firazyr for their on-demand treatment.

^b One adult (Haegarda) and 3 adolescents (Haegarda, Oriadeyo, Takhyro) reported using their LTPT as an on-demand treatment for their most recent attack. At screening, these participants reported use of Firazyr (n = 1) and Berinert (n = 3) as their current on-demand treatment.

^c Although the sampling plan aimed to obtain half of each age group currently taking both on-demand treatment and LTPT and half taking only on-demand treatment, this was not able to be achieved in the adolescent cohort.

Table 2. Reported “Likes” and “Dislikes” of Most Recent Acute Attack Treatment by Mode of Administration^a

Characteristic	Adolescents ^b , n (%)				Adults ^c , n (%)			Total, n (%)			
	SCI (n = 3)	IVI (n = 6)	Pill (n = 1)	Total (n = 10)	SCI (n = 9)	IVI (n = 1)	Total (n = 10)	SCI (n = 12)	IVI (n = 7)	Pill (n = 1)	Total (N = 20)
Likes^d, n (%)											
Effective/reliable; “it works”	—	4 (67)	1 (100)	5 (50)	8 (89)	—	8 (80)	8 (80)	4 (40)	1 (100)	13 (65)
Feeling of the medicine going in (emotional relief; mostly IV)	—	3 (50)	—	3 (30)	—	—	—	—	3 (30)	—	3 (15)
Easy to inject (intravenous and subcutaneous)	—	1 (17)	—	1 (10)	1 (11)	—	1 (10)	1 (10)	1 (10)	—	2 (10)
Familiar/comfortable	—	1 (17)	—	1 (10)	—	—	—	—	1 (10)	—	1 (5)
Easy to constitute (e.g., referenced previous more cumbersome process)	—	1 (17)	—	1 (10)	—	—	—	—	1 (10)	—	1 (5)
SCI (vs. IVI)	1 (10)	—	—	1 (10)	1 (11)	—	1 (10)	1 (10)	1 (10)	—	2 (10)
Cost (e.g., “affordable”)	—	—	—	—	1 (11)	—	1 (10)	1 (10)	—	—	1 (5)
Portable	—	—	1 (100)	1 (10)	2 (22)	—	2 (20)	2 (20)	—	1 (100)	3 (15)
Dislikes^d, n (%)											
Painful/burning injection	1 (33)	3 (50)	—	4 (40)	3 (33)	—	3 (30)	4 (40)	3 (30)	—	7 (35)
Takes too long to work (efficacy)	1 (33)	1 (17)	—	2 (20)	3 (33)	—	3 (30)	4 (40)	1 (10)	—	5 (25)
Cannot easily take with you (refrigeration and travel)	1 (33)	—	—	1 (10)	3 (33)	—	3 (30)	4 (40)	—	—	4 (20)
Needles/injections (fear/avoidance)	—	—	—	—	3 (33)	—	3 (30)	3 (30)	—	—	3 (15)
Burden/hassle of administration (i.e., time commitment; refrigeration; preparation)	—	2 (33)	—	2 (20)	2 (22)	1 (100)	3 (30)	2 (20)	3 (30)	—	5 (25)
Dependent on others for administration	—	2 (33)	—	2 (20)	—	—	—	—	2 (20)	—	2 (10)
Body-weight sensitive (i.e., 1 participant was administered too low of a dose due to a recent weight gain)	—	1 (17)	—	1 (10)	1 (11)	—	1 (10)	1 (10)	1 (10)	—	2 (10)
Same infusion site (e.g., they would like to be able to inject in other places)	1 (33)	1 (17)	—	2 (20)	—	—	—	1 (10)	1 (10)	—	2 (10)
High cost	—	—	—	—	1 (11)	—	1 (10)	1 (11)	—	—	1 (5)

IVI = intravenous infusion; SCI = subcutaneous injection.

^a Reported likes and dislikes were based on the treatment used for their most recent attack, including 4 participants who used a long-term prophylactic treatment.

^b Ten adolescents took Firazyr (n = 1, SCI), Haegarda (n = 1, SCI), Takhyro (n = 1, SCI), Berinert (n = 3, IVI), Ruconest (n = 3), and Oriadeyo (n = 1, pill).

^c Ten adults took Firazyr (n = 8, SCI), Haegarda (n = 1, SCI), and Berinert (n = 1, IVI).

^d Multiple response question; percentages sum to greater than 100% per column.

Conclusions

- All participants preferred the hypothetical oral on-demand treatment over hypothetical self-administered injection on-demand treatment when efficacy and tolerability/mild side-effect risk were the same
- In the hypothetical comparison, self-administered injection was only preferred over oral on-demand treatment if it offered substantially better efficacy over oral treatment, and only if the oral treatment had substantially worse tolerability/mild side-effect risk than observed in available clinical studies
- Quantitative analyses in a larger cohort are warranted to better refine on-demand treatment preferences, for shared decision-making

References

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