Poster 696

Patient Preferences for Attributes of Prophylactic Treatment in Hereditary Angioedema: A Discrete-Choice Experiment

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BACKGROUND

- HAE is a genetic disorder that causes swelling in the limbs, face, abdomen, and/or other areas of the body and affects 1 in 67,000 people worldwide.[1,2] Treatments attempt to manage acute attacks and prevent future attacks based on known triggers or via a long-term plan to reduce the episode frequency/severity.[1]
- Several prophylactic treatments and indications have been approved/are in development for HAE.[3,4]
- The literature on people's preferences for HAE treatments is limited, and none quantify the tradeoffs patients are willing to make among treatment features.

OBJECTIVES

- Quantify patient preferences for the attributes of prophylactic HAE treatments and the tradeoffs people with HAE are willing to make among treatment features.
- Explore heterogeneity in preferences and the association between heterogeneity and patient characteristics.
- Understand the likelihood that people with HAE consider a switch from their current treatment to a different prophylactic treatment.

METHODS

- An online DCE survey was developed and pretested to elicit preference weights for 6 treatment features of unnamed prophylactic HAE treatments.
- This was administered to adults aged ≥ 18 years living in the USA with self-reported diagnosis of HAE who were recruited by a patient advocacy group.
- Respondents answered 12 experimentally designed DCE questions, each offering a choice between 2 hypothetical treatment profiles (Figure 1). Attributes and levels were based on product labels and clinical data (Table 1). Respondents also were asked a question about willingness to start a new prophylactic treatment and to complete the AECT.[5]
- Preference weights were estimated using a random-parameters logit model[6] and were used to calculate (1) CRAI (i.e., the percentage of total utility change accounted for by the attribute) and (2) MAR to estimate respondents' willingness to make tradeoffs.
- An LC model was used to explore heterogeneity in the DCE results. A logit model was used to explore associations between respondents' characteristics (Figure 2) and their willingness to start or switch to a new prophylactic treatment.

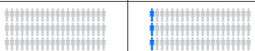
TABLE 1. Attributes and Levels for the Discrete-Choice Experiment

Technical attribute label	Patient-facing attribute label	Attribute levels
Time to maximum efficacy	Time until the preventative treatment provides full benefit	• 1 week • 2 weeks • 5 weeks • 10 weeks
Reduction in attack frequency (from a baseline frequency of 12 attacks over 6 months)	Reduction in attacks over 6 months once the treatment is providing full benefits	• 45% (average of around 6 or 7 attacks in the 6 months once the treatment provides full benefit) • 85% (average of around 2 attacks in the 6 months once the treatment is providing full benefits) • 90% (average of around 1 attack in the 6 months once the treatment is providing full benefits)
Mode of administration	How you take the treatment	• Tablet[a,b] • Vial and syringe • Prefilled syringe • Autoinjector
Dosing frequency	How often you take the treatment	• Once a day[a] • Twice a week[a] • Once every 4 weeks • Once every 8 weeks
Risk of ISR	Risk of a mild to moderate injection site reaction	• 0%[b] • 5% • 20% • 55%
Risk of a GI side effect (grade 1 or 2)	Risk of a mild to moderate GI side effect	• 0% • 7% • 15% • 25%

[a] The experimental design incorporated a restriction to ensure that the dosing frequency was always once a day or twice a week when the treatment was administered as a tablet.

[b] The experimental design incorporated a restriction to ensure that the risk of ISR was always 0% when the treatment was administered as a tablet.

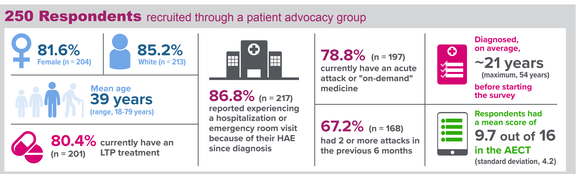
FIGURE 1. Choice Question Example

Treatment Feature	Treatment A	Treatment B
Time until the preventative treatment provides full benefit		
Reduction in attacks over 6 months once the treatment is providing full benefits	 Average of around **6 or 7 attacks** in the 6 months once the treatment provides full benefit	 Average of around **1 attack** in the 6 months once the treatment provides full benefit
How you take the treatment	 Tablet	 Vial and syringe
How often you take the treatment	**Once a day**	**Twice** a week
Risk of a mild-to-moderate injection site reaction	 0 out of 100 (0%)	 5 out of 100 (5%)
Risk of a mild-to-moderate gastrointestinal (GI) side effect	 7 out of 100 (7%)	 25 out of 100 (25%)
Which preventative treatment would you choose?		

Note: This example shows the patient-facing labels for the treatment features included in the survey. There were 72 treatment pairs in the experimental design divided into 6 blocks of 12 treatment choice questions. Each respondent was randomly assigned to 1 block of 12 treatment choice questions.

RESULTS

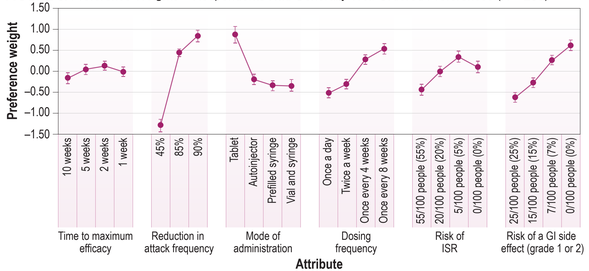
FIGURE 2. Respondent Characteristics



Preference Weights and Attribute Importance

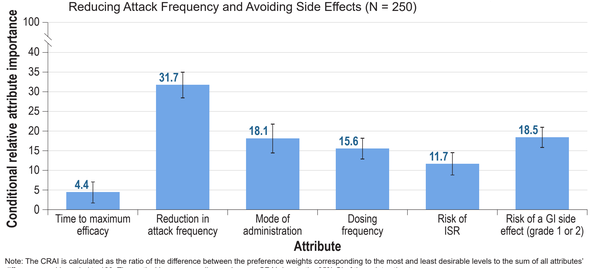
- Respondent preferences were generally well ordered with better attribute levels preferred to worse attribute levels (Figure 3).
- Overall, respondents had the strongest preferences for reduction in attack frequency (CRAI = 31.7%), reduced risk of a GI side effect (CRAI = 18.5%), treatments taken as an oral tablet versus injections (CRAI = 18.1%), treatments taken once every 8 weeks versus more frequently (CRAI = 15.6%), and treatments with a lower risk of ISR (CRAI = 11.7%) (Figure 4).
- Respondents placed the least importance on reducing the time to maximum efficacy (CRAI = 4.4%), and there was no statistically significant difference between the preference weights for 10 weeks versus 1 week to maximum efficacy, the shortest time to maximum efficacy presented in the survey.

FIGURE 3. Preference Weights – Respondents Had Generally Well-Ordered Preferences (N = 250)



Note: The preference weights are the estimated parameters corresponding to the effects-coded attribute levels. They are log odds distributed symmetrically around 0. The vertical bars surrounding each mean preference weight denote the 95% CI of the point estimate.

FIGURE 4. Conditional Relative Attribute Importance – Respondents Placed Greatest Importance on Reducing Attack Frequency and Avoiding Side Effects (N = 250)



Note: The CRAI is calculated as the ratio of the difference between the preference weights corresponding to the most and least desirable levels to the sum of all attributes' differences and is scaled to 100. The vertical bars surrounding each mean CRAI denote the 95% CI of the point estimate.

Maximum Acceptable Risk

- On average, respondents were willing to accept risks of ISR and GI side effects in exchange for improvements in other attribute levels included in the study (Table 2).
  - Respondents' willingness to accept increases in the risk of ISRs ranged from 11.1% (for an improvement in dosing frequency) to > 50% for the most valued improvements in other attributes (a reduction in attack frequency and a change in mode of administration).
  - Respondents' willingness to accept increases in the risk of GI side effects ranged from 5.0% to > 25% for the most valued improvements in other attributes.

TABLE 2. Maximum Acceptable Risk of Injection Site Reaction and a Gastrointestinal Side Effect (N = 250)

Attribute improvement		Mean MAR of ISR (95% CI)	Mean MAR of a GI side effect (95% CI)
From this level	To this level		
Reduction in attack frequency			
40 percentage-point improvement 45%	85%	> 50%[a]	> 25%[b]
5 percentage-point improvement 85%	90%	19.3% (0.0%-38.6%)	7.6% (4.0%-11.2%)
45 percentage-point improvement 45%	90%	> 50%[a]	> 25%[b]
Mode of administration			
Autoinjector	Tablet	> 50%[a]	17.5% (12.7%-22.3%)
Dosing frequency			
Once every 4 weeks	Once every 8 weeks	11.1% (0.4%-21.8%)	5.0% (0.7%-9.2%)

Note: Estimates of MAR were not extrapolated outside the risk range presented in the survey.

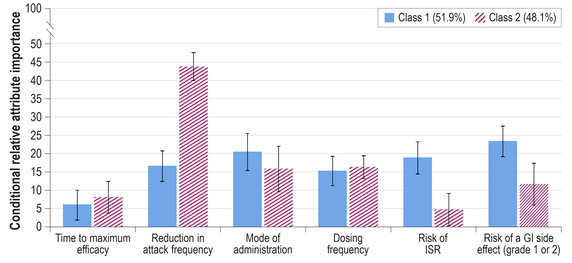
[a] The preference weight for 0% risk of ISR was disordered to 5% risk of ISR and not statistically different from 20% risk of ISR. Therefore, MARs of ISR were calculated using a 5% risk of ISR as the baseline risk instead of 0% (as for risk of a GI side effect). Estimates of MAR were not extrapolated outside the risk range presented in the survey. Hence, a mean MAR of ISR reported to be > 50% represents a total risk estimate > 55% (55% risk of ISR − 5% risk of ISR = 50% risk of ISR).

[b] Means that are reported to be > 25% represent MAR estimates > 25% risk of a GI side effect, which was the maximum level of the risk of GI side effect presented in the study.

Latent Class Analysis

- LC analysis identified 2 classes. Figure 5 presents the CRAI for each class.
  - Class 1 "burden minimizers" accounted for 51.9% of the sample, which prioritized avoiding risks of ISR and GI side effects, as well as mode and frequency of administration. Class 1 was more likely to have ever experienced an HAE attack in the groin or genitals and to have poorly controlled HAE as given by an AECT score < 10.
  - Class 2 "efficacy maximizers" accounted for 48.1% of the sample, which focused on treatments offering the largest reductions in attack frequency. Class 2 respondents were more likely to have selected only White as a race or ethnicity category or to have ever experienced mild to moderate GI symptoms because of HAE.

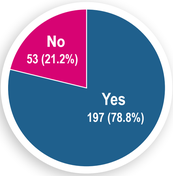
FIGURE 5. Latent Class Model: Burden Minimizers and Efficacy Maximizers (N = 250)



Willingness to Start or Switch to a New Prophylactic Treatment: Logit Analysis

- Characteristics associated with higher likelihood of considering a new LTP:
  - Poorly controlled HAE (AECT score < 10)[7]
  - Treated for less time in ER or hospital for HAE
  - Have autoinjector but never used it
  - Currently taking Berinert as LTP
  - Self-identify as African American or Black
- Characteristics associated with lower likelihood of considering a new LTP:
  - Older age
  - Self-identify as Hispanic, Latin American, or Latinx
  - Receive Medicare benefits
  - Receive co-pay assistance
  - Diagnosed with GI conditions
  - Experience with intravenous infusion treatment
  - Previous change in LTP

FIGURE 6. Responses to Treatment Starting/Switching Question



CONCLUSIONS

- Patients with HAE face preference-sensitive decisions over prophylactic treatments that differ across multiple dimensions, including their efficacy, safety, and administrative burdens.
- The results from this survey suggest that, on average, reduction in attack frequency is the most important treatment feature for people with HAE.
  - The risk of side effects, mode of administration, and dosing frequency also were important but less so than the reduction in attack frequency.
  - GI side effect risks were more important than ISR risks for the patients included in this study.
  - Respondents placed relatively lower importance on the time until treatment provides full benefits (the onset of action).
- Further analysis revealed preferences were heterogeneous and identified classes of "burden minimizers" and "efficacy maximizers" in the patterns of responses.
- Most respondents reported being willing to switch to a new prophylactic treatment, and those with poorly controlled HAE were more likely to consider switching.
  - Using appropriate tools, like the AECT, may help physicians identify these patients.
- The results of this study, particularly the heterogeneity in perspectives, highlight the need for conversations between physicians and patients when making decisions about initiating a new long-term prophylactic treatment for HAE.

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DISCLOSURES

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ABBREVIATIONS

AECT = Angioedema Control Test; CI = confidence interval; CRAI = conditional relative attribute importance; DCE = discrete-choice experiment; ER = emergency room; GI = gastrointestinal; HAE = hereditary angioedema; ISR = injection site reaction; LC = latent class; MAR = maximum acceptable risk; USA = United States of America.

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