Patient and Caregiver Preferences for Attributes of Treatment in Hemophilia A: Literature Review and Qualitative Research

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Introduction

- Extended half-life (EHL) and non-factor therapies have changed the treatment landscape for hemophilia A through, for example, more convenient and less frequent infusion schedules amongst other reasons. These products vary in characteristics that may affect a patient's willingness to use them.
- Quantifying patient and caregiver preferences for different characteristics of EHL and non-factor hemophilia A treatments may inform treatment selection.
- Such preferences can be elicited via a discrete choice experiment (DCE).[1]
- Identifying key treatment attributes (i.e., characteristics) and levels (i.e., variations in attributes) via rigorous qualitative methods is a critical step in DCE studies.[2]

Objectives

- To use qualitative research methods to identify key attributes and levels to be used in a DCE that evaluates hemophilia A patients' and caregivers' preferences in treatment decision-making.

Methods

- A literature review and consultation with a clinical expert was conducted to identify a preliminary list of attributes that were then assessed via in-depth, cognitive interviews with hemophilia A patients.
- Recruitment of interview participants (patients and caregivers) was conducted by Rare Patient Voice (RPV).
- Patients and caregivers were eligible if they fulfilled the criteria listed in Table 1
- A semi-structured interview guide was used, and included 3 main components:
  1. Discussion on clarity and comprehensibility of attributes and descriptions of attributes
  2. Ranking and rating exercise of attributes:
     - Ranking: 1 to 6, where 1 = "most important", and 6 = "least important"
       - A unique rank was assigned to each attribute and allows for differentiation of attributes in order of importance.
     - Rating: range of 0 to 10, where 0 = "not important", and 10 = "very important"
       - Measured how important one attribute was over another on the same scale.
  3. Discussion on meaningfulness and relevance of range of levels for each attribute
- Each interview lasted ~60 minutes and was conducted by a trained interviewer.

Table 1. Eligibility Criteria

	Inclusion criteria	Exclusion criteria
Patients (N=5)	• Self-reported diagnosis of hemophilia A • 18 years or older • Able to read and speak English	• Unwilling to provide written informed consent
Caregivers (N=5)	• Providing care for a patient (below 18 years of age) who has a caregiver-reported diagnosis of hemophilia A • 18 years or older • Able to read and speak English	• Unwilling to provide written informed consent

Results

Literature Review

- 18 treatment characteristics were initially identified.[3-9]
- Based on discussions with the clinical expert, the following 6 characteristics were included in the subsequent qualitative interviews:
  - Bleed protection
  - Joint health
  - Safety
  - Dosing
  - Length of time product has been approved for use
  - Product type (Factor and non-factor therapy)

Qualitative Interviews

- Patient (N=5) and caregiver (N=5) cognitive interviews confirmed that all 6 attributes were important drivers of decision-making for hemophilia A treatment (Table 2).
- The 3 top ranked attributes by patients and caregivers were (Table 2):
  - bleed protection (average rank: 1.4),
  - safety (2.9), and
  - joint health (3.5)
- Following the completion of interviews, the attribute descriptions and labels were revised to improve clarity and ensure that differences in levels were meaningful to participants.
  - For example, dosing attribute levels expanded from 1, 2, and 3 times per week to 1, 2, and 4 times per week. Some participants stated that they were accustomed to infusions 2-3 times a week. Therefore, the difference from 2 to 3 was not meaningful to them.
- Participants feedback, the revised/final list of attribute labels, levels and descriptions are presented in Table 3.This list was used to construct the DCE choice tasks that were used in the subsequent quantitative preference survey.

Table 2. Mean Attribute Rating, Ranking, and Verbatim Quotes of Participant Perception

Attributes (Ranking/Rating)	Mean Ranking	Mean Rating	Examples of verbatim quotes of participant's perception
Bleed protection	*1.4*	*9.4*	• *"I think about preventing my joints from getting worse, and what causes that is bleeds**. I think the goal of replacing the factor,…, is to avoid the bleeding episodes**. That is on the top of my mind" – PT* • *"If I am taking a medication, I want it to work. **That's the whole point of the reason why I am taking a medication, to control my bleeds**."— PT*
Safety	*2.9*	*8.0*	• *"For me **I wanna know if it's safe**, what are the risks that come with it" – CG* • *"I wanna make sure that **there's nothing really strong to be concerned** about by switching to that product." – PT*
Joint Health	*3.5*	*7.2*	• *"Joint studies are usually more long term,…, you don't just find out how well your joints are doing after 2 to 3 treatments so **I want to see how long people that have been on the product for a certain period of time, how their joints are doing**…" – PT*
Dosing	*4.2*	*6.5*	• *"We want to **infuse as little as possible** and still be safe" – CG* • *"The things that are going to move the needle and make me change factors are you know, **less infusions and effective infusions**" - CG.*
Length of time product has been approved for use	*4.2*	*6.9*	• *"If I could I would want it [medication] as **been studied more or been out for a bit**" -CG* • *"I would definitely **prefer minimum of two years** in the field. Major complications will surface. I feel like two would be minimum …*-PT
Product Type and Use	*4.8*	*6.1*	• *"Knowing what I know about the non-factor-based products, I know they are not used for **if you actually get injured, you still have to use your normal medicine** and it is one of those things where am I happy to have 2 types of products in stock or just 1 type of product in stock" – PT*

Abbreviations: PT, patient; CG, caregiver.
Ranking: 1 (most important) and 6 (least important).
Rating scale: 0 (not important) to 10 (very important)

Conclusions & Future Research

- Bleed protection, joint health, safety, dosing, length of time product has been approved for use, and product type were important characteristics that hemophilia A patients and caregivers consider in their preference for different treatments.
- Of the 6 attributes assessed, bleed protection, safety and joint health, in that order, were ranked as the most important characteristics to patients and caregivers.
- When talking about bleed protection, participants focused on bleeds from trauma and joint bleeds.
- The qualitative study results provided preliminary insight on patient and caregiver preferences of treatment related attributes in hemophilia A.
- The feedback elicited from these interviews was used to refine the attributes, descriptions and levels. These were then included in a subsequent quantitative online DCE survey study among hemophilia A patients and caregivers (N = ~200) to further understand trade-offs among these 6 characteristics in their preference for different treatments.

Table 3. Preliminary and Revised Attributes, Labels, Levels, and Top-line Participant Feedback

Preliminary Attribute, Label and Levels	Top-line Participant Feedback	Revised Attribute, Label and Levels	Revised Description
Bleed Protection *Number of bleeding episodes per year* • 0 per year • 1 per year • 3 per year • 5 per year	• Participants often asked what kind of bleeds were referred to – spontaneous versus trauma	**Bleed Protection** *Number of bleeding episodes a year* • 0 per year • 1 per year • 3 per year • 5 per year	• The goal of hemophilia A treatment is to reduce the number of bleeding episodes that a person with hemophilia A experiences in a year. • A bleeding episode can either be due to an injury/trauma or can be spontaneous (i.e. sudden bleeding inside the body for no clear reason).
Joint Health *Available studies reporting improvement in joint health (e.g. less swelling, better strength, and better range of motion)* • Yes • No	• Participants suggested simplifying the attribute label. Some were focused on available studies while some were focused on joint improvement • Participants suggested simplifying the description	**Joint health** *Improvement in joint health (e.g. less swelling, better strength, and better range of motion) shown in scientific studies* • Yes (improvement in joint health shown in studies) • No (no studies showing improvement in joint health)	• Joint damage can result from repeated bleeding into joint(s) over time, which is an important concern in hemophilia A. • Hemophilia A patients with joint damage can have problems with strength, swelling, range of motion, etc. • Some treatments have been shown in scientific studies to improve joint health (e.g. less swelling, better strength, and better range of motion).
Safety *Additional safety concerns* • Additional safety risk of excessive blood clots forming when not bleeding • Overall safe, no additional safety concerns	• Most participants did not immediately think of clotting issues as a safety concern as they thought that treatment was supposed to facilitate clotting. • Some found the level "excessive blood clots forming when not bleeding" confusing • Participants suggested clarifying in the attribute description that while the treatment is supposed to help with clotting, sometimes too much clotting can happen that then becomes a safety issue	**Safety** *Safety concerns about too much clotting* • Safety concerns about too much clotting • No safety concerns about too much clotting	• All hemophilia A treatments come with some risks or side effects. Sometimes, there are additional risks present. • For a patient with hemophilia A, blood is supposed to clot to prevent bleeding when a treatment is given. • However, sometimes the treatment may result in too much clotting at other places such as the legs, kidney, brain, etc. which may affect daily function. • For example, if blood clots develop in the legs, a hemophilia A patient may experience swelling and may need to get a medical procedure to remove the clot.
Dosing *How often the treatment is given in the clinical setting* • 1 time a week • 2 times a week • 3 times a week	• Most find the term "clinical setting" very confusing – they think this refers to treatment being administered at a treatment center or doctor's office (instead of at home) • Participants suggested using "How the treatment is given/administered" • Some participants were doing infusions 2-3 times a week, and therefore think a greater difference in levels is needed for the difference to be meaningful	**Dosing** *How often this treatment is given* • 1 time per week • 2 times per week • 4 times per week	• Hemophilia A treatments differ in how often they are given to the patient. Some treatments are given more frequently than others.
Length of time product has been approved for use *Number of years this treatment has been used in the clinical setting* • Less than 1 year • Between 1 and 3 years • Between 4 and 6 years • More than 6 years	• Participants interpreted this as how long the treatment is used in the doctor's office or healthcare provider setting • Some also interpreted this as the number of years the treatment has been studied in clinical trials, while other interpreted it as the number of years it has been used after approval for use in the public	**Length of time product has been approved for use** *Number of years the treatment has been approved for use in hemophilia A patients* • Less than 1 year • Between 1 and 3 years • Between 4 and 6 years • More than 6 years	• Different hemophilia A treatments have been approved for use in patients over the years by the regulatory government agency (i.e. the Food and Drug Administration [FDA]). As a result, treatments can differ in the number of years that they have been available for use in Hemophilia A patients. • In general, if the treatment has been available for a longer period of time, more studies will be available to understand the treatment and the more physicians have experience with the treatment.
Product Type and Use *What type of treatment product is this and how it is used?* • Factor therapy. It can be used to prevent bleeding, stop bleeding, and during surgery • Non-factor therapy. It can only be used to prevent bleeding. It can NOT be used to stop bleeding or during surgery	• Participants interpreted the label in several ways. Some thought of this as type of product (short versus long-acting), some thought of "how it is used" as route of administration –subcutaneous vs intravenous • Suggested label change "what type of treatment product it is and how it is administered" • Not all participants understood the difference between factor and non-factor products	**Product type** *Type of treatment product (factor replacement versus non-factor therapy)* • Factor replacement therapy (It can be used to prevent bleeding, stop bleeding, and during surgery) • Non-factor therapy (It can be used to prevent bleeding, but NOT be used to stop bleeding or during surgery)	There are different types of treatments for hemophilia A: factor replacement therapy or non-factor therapy. Both therapies differ in the way they work, and how they can be used. • Factor replacement therapy works by replacing the clotting factor in the body. It can be used to prevent future bleeds. If bleeding occurs, it can be used to stop bleeds. It can also be used during surgery. • Non-factor therapy works by helping with the clotting process without the need to replace the clotting factor. It can be used to prevent future bleeds. However, if a bleed occurs, it cannot be used to stop the bleed. It also cannot be used during surgery.

Disclosures

- This study was sponsored by Bioverativ, a Sanofi company.
- Li N was an employee of Bioverativ, a Sanofi company when this study was conducted.
- Jain N and Su J are employees of Bioverativ, a Sanofi company.
- BM, JN, NX, HE and SR are employees of Pharmerit International LP and paid consultants on this study.

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