Gene Therapy as a Treatment Modality for Hemophilia
October 23, 2018

FDA held a Listening Session with hemophilia patients and caregivers on October 23rd, 2018 to understand patient/caregiver concerns, perceived risks and benefits, and expectations of gene therapy as a treatment modality for hemophilia. The objective of the session is to understand perspectives of patients/caregivers who may be interested in using gene therapy as a treatment modality for hemophilia.

Patient Listening Sessions are intended to be a resource for the medical product Centers to expeditiously engage with patients or their advocates. Listening Sessions can either be FDA-requested (in cases where FDA has a specific set of questions to ask of a particular patient sub-population) or patient-led (when a patient community wants to share some perspectives with the FDA), and are generally focused on conditions of interest to staff across the medical product Centers.

Discussions in FDA Rare Disease Listening Sessions are informal. All opinions, recommendations, and proposals are unofficial and nonbinding on FDA and all other participants. This report summarizes the input provided by patients and patient representatives at the meeting. To the extent possible, the terms used in this summary to describe specific manifestations of hemophilia, health effects and impacts, and treatment experiences, reflect those of the participants. This report is not meant to be representative of the views and experiences of the entire hemophilia patient population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.

Summary of topics discussed

1. **Risks and benefits of gene therapy: While the patient/caregiver perspective varies in openness for enrolling in a gene therapy clinical trial, there was consistent interest in understanding the risks and benefits associated with gene therapy:**
    - Patients/caregivers indicated that the decision to enroll in a clinical trial affects many people beyond the patient. This could include their spouse, children, parents/siblings, and other dependents, all of whom should be involved in the decision to enroll. If a clinical trial were available for children, the child should be old enough to be involved in the decision and understand the commitment of the trial.
    - Patient/caregiver's interest in new therapy is partly dependent on the success of their current treatment modality.
    - Some patients/caregivers are less likely to enroll themselves or their child in a clinical trial if their current prophylaxis treatment is working and manageable.
    - Some patients/caregivers are interested in gene therapy but feel there is still too much unknown information about the treatment, including inconsistency about the achieved coagulation factor level and its persistence, and the unknown long-term safety. Some patients/caregivers would feel more comfortable enrolling in a clinical trial if there were more consensus about the advantages and risks.
    - Some of the benefits considered when thinking about enrolling in a clinical trial include not having to do infusions, the ability to be more active, the prevention of additional pain and joint deterioration, and helping the next generation of hemophilia patients.

2. **Safety monitoring: While patients/caregivers acknowledge that aspects of enrolling in clinical trials can be burdensome, the frequency of safety monitoring was not seen as a high priority when deciding whether to enroll in a clinical trial:**
    - The frequency of visits to the treatment center is burdensome in the beginning of the clinical trial but becomes less burdensome overtime when the frequency decreases.

Distance from where the patient/caregiver lives to the treatment center also determines how burdensome the visits are.
    - Patients/caregivers had consistent interest in prioritizing safety in clinical trials and are open to frequent safety monitoring visits to ensure risks are caught early and addressed quickly.
    - The requirement for long-term follow up procedures once a year are generally not considered burdensome. This may include invasive procedures such as a liver biopsy and non-invasive procedures such as an MRI.
    - Patients and caregivers prioritize success of the clinical trial more so than the burden of frequent treatment center visits.

3. **<u>Measuring success:</u> Defining and measuring success of gene therapy as a treatment modality for hemophilia varies across the patients/caregivers:**
    - Patients/caregivers had varying responses when asked what level and duration of Factor activity they would be satisfied with after receiving gene therapy.
    - Some patients/caregivers would be satisfied with Factor IX levels of 5-10% while others indicated they hope for levels of 40% or more.
    - Some patients/caregivers would be satisfied with a duration of elevated Factor levels for 5 years, while others indicated they hope for a duration of more than 10 years.

4. **<u>Other considerations:</u> Patients/caregivers consistently prioritize accurate and complete information about gene therapy and hemophilia:**
    - It is important that patients and caregivers are provided accurate non-biased information that clearly explains the risks and benefits of gene therapy. The available information should clearly set expectations for hemophilia A and B specifically.
    - Women with bleeding manifestations should also be included and targeted in educational materials and clinical trials.
    - Some are concerned about the unknown cost reimbursement for gene therapy.

<u>Partner organization</u>
National Organization for Rare Disorders

<u>FDA divisions represented</u>
- Office of the Commissioner, Patient Affairs Staff (organizer)
- Center for Biologics Evaluation and Research (CBER), Office of Tissues and Advanced Therapies (OTAT), Division of Clinical Evaluation and Pharmacology/Toxicology (DCEPT)

<u>Patients represented</u>
7 patients and caregivers

<u>Patient segments</u>
- Segment of adults with hemophilia enrolled in a gene therapy clinical trial
- Segment of adults with hemophilia not enrolled in a gene therapy clinical trial
- Segment of caregivers to children with hemophilia

<u>Conflict of Interest</u>
- No conflicts of interest were indicated by the participants