Sanfilippo Syndrome (pediatric) - FDA-Requested Listening Session

October 17, 2019

Objective of session

To better understand Mucopolysaccharidosis Type III (MPSIII), or Sanfilippo syndrome, burden and symptom progression, and to understand issues related to the barriers of being involved in clinical trials and natural history studies. For this session, the goal was to hear from families of patients who are 7 years old or younger.

Discussions in FDA Listening Sessions are informal and not meant to replace, but rather compliment, existing patient engagement opportunities in the Agency. 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 MPSIII, and the health effects and impacts, reflect those of the participants. This report is not meant to be representative of the views and experiences of the entire MPSIII patient population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.

Summary of discussion by question

1. ***When you are thinking about a potential treatment for Sanfilippo syndrome, what one activity of your child's daily life would you find most important to preserve? Why would you would choose that?***

    - The responses varied across the participants. When thinking about an important activity to preserve, the participants said sleep, mobility, speech/communication, and joy. Mobility was described as being important because the child is able to get or do what they want. Communication was described as important because the caregiver can understand the wants and needs of the child, reducing their guessing. Sleep was described as important because when the child lacks rest, all of their other functions are affected. It was commonly heard that the caregivers are open to anything that a potential treatment could address. They want to continue to see their child smile and have joy.

2. ***When thinking about a potential treatment, would you be willing to accept severe or life-threatening risks? Please explain why or why not?***

    - Half of the participants said they are willing to accept severe or life-threatening risks. While such risk is not ideal, they know that their child will succumb to the disease if left untreated, and therefore are willing to be more accepting of risk.

    - Others said the amount of risk they would be willing to accept depends on the potential benefit. For one participant, if a treatment showed the potential of a cure, they would be willing to accept more severe risk. They also might be willing to accept more severe risks as the disease progresses and their child loses functions, such as ambulating. Another participant indicated the risks they are willing to accept depends on the treatment or clinical trial. They would want to do research to be sure the treatment would cross or be administered beyond the blood brain barrier.

3. ***When you are thinking about the different types of clinical trials, does it make a difference to you if the clinical trial involves an experimental drug or gene therapy, and why?***

    - All participants indicated they would be open to participating in gene therapy clinical trials.

- Half of participates indicated they would be open to participating in an experimental drug clinical trial. Two of the three with this response have never been in a clinical trial.
- Three of the four who have been or are currently in a clinical trial said the trial they chose was the first available to them. The fourth person specifically chose a gene therapy trial because the treatment would be delivered beyond the blood brain barrier.
- Four participants mentioned that gene therapy only requires one administration, versus an experimental drug clinical trial requires regular administration. An experiment drug trial could be canceled, in which the patient no longer receives the product even if it seems to be working.
- Half of the participants indicated they would be open to doing gene therapy and enzyme replacement therapy simultaneously.
- Participants indicated that there are many unknowns about clinical trials, making them a difficult choice. The caregivers do a lot of research on their own. They consider that enrolling in a clinical trial often disqualifies the patient from other trial options. Participants shared that it is important that trials are accessible. Some participants do not have any clinical trial options. For those participating in a clinical trial, receiving a treatment is worth the associated burdens.

4. ***Would you participate in a randomized clinical trial, given there is a possibility your child may receive the placebo? Why?***
    - Five of the six participants shared they would not participate in a randomized clinical trial where their child might receive a placebo. The sixth participant indicated that they would participate, but it would be their last option.
    - Four participants shared that they are opposed to a placebo because it could waste time, which is already limited for their children. One person mentioned that participating in a randomized clinical trial could make them ineligible for other trials, even if they received the placebo.
5. ***Additional Comments:***
    - Many participants shared their concern about the endpoints that are selected for clinical trials. As parents, they often see progress not measured in the clinical trials, including progress beyond cognitive function.
    - It was suggested that videos of the child at home can help provide meaningful data because the children often act differently when tested outside the home. Parents believe they could objectively evaluate the child's sleep despite being fatigued the following day.
    - The thoughts around natural history studies was mixed. Generally, all acknowledge the importance of the natural history studies. There was concern about exposing their children to additional "poking and prodding". If the data collection was manageable, they would generally participate, particularly if it was a precursor for receiving an investigational medical product.

Partner organization

The National Organization for Rare Disorders (NORD) helped identify and prepare patient community participants. NORD was present during the listening session teleconference.

FDA divisions represented

- Office of the Commissioner, Patient Affairs Staff (organizer)

- Center for Drug Evaluation and Research (CDER), Division of Gastroenterology and Inborn Errors Products (DGIEP)
- Center for Biologics Evaluation and Research (CBER), Office of Tissues and Advanced Therapies (OTAT)

Patients represented

6 caregivers participated in the listening session representing MPSIII patients

- 3 patients were female
- 3 patients were male

Patient ages ranged from 4 years old to 6 years old

MPSIII Types A and B were present

- 3 patients were Type A
- 3 patients were Type B

Financial Interest

- Participants did not identify financial interests relevant to this meeting and are not receiving compensation for this listening session.