Sanfilippo Syndrome - FDA-Requested Listening Session
May 13, 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.

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 thinking about a potential treatment for MPSIII, what one activity of your child’s daily life would you find most important to preserve or to restore? What are you hoping that a potential treatment could address?

   • Over half of participants said that communication is an important activity to preserve or restore. Communication was described in several ways, including a patient being able to speak, a patient being able to express a need or feeling (including pain), and a patient being able to receive information such as verbal directions or safety information. There were caregivers representing patients from all age segments who discussed communication. Participants also indicated that they consider the inability to communicate or speak to be the most impactful symptom of MPSIII. While discussing how caregivers manage the patient’s pain when they are unable to communicate, participants indicated they often guess the source of the pain, they observe the patient’s facial expression while palpating the suspected source of pain, and they observe joint stiffness.

   • Almost half of participants said mobility is an important activity to preserve or restore. Mobility was described several ways, including the ability to walk or run independently, as well as ambulating with assistance. Some participants indicated that mobility allows their family to continue activities that make their children happy. There were caregivers representing patients from all age segments who discussed mobility.

   • Other activities that participants mentioned as being important to preserve or restore included sleeping, swallowing, cognitive ability, quality of life, and maintaining their current disease state by stopping disease progression.

2. In the event that a therapy is associated with severe or life-threatening risks, what is the minimal benefit that you find worthwhile to accept those risks and participate in an interventional clinical trial?
• Some caregivers found it too difficult to articulate an answer to this question because it depends. Four participants indicated they would try almost anything if there was a chance of benefit for their child.

3. **What would you consider when thinking about participating in a clinical trial for an experimental new therapy? How could clinical studies be better tailored for patients, parents, and caregivers?**

• Five participants indicated they would participate in a randomized clinical trial. When asked why:
  - Some said it is not a difficult choice because they know their child will succumb to the disease if left untreated.
  - Some said they think enrolling in a trial would help future patients.
  - Some said their child’s quality of life is currently good and/or stable, therefore they would feel comfortable enrolling in a trial.

• Four participants indicated they would not participate in a randomized clinical trial. When asked why:
  - Some said their child’s disease was too advanced to enroll in a trial and they worry it would cause more harm to their child.
  - Some said they feel it is unethical to have a placebo or to not receive a therapeutic dose.
  - Some said they are concerned it would disqualify them from participating in other trials, even if they do not receive the experimental new therapy.

• Participants were generally willing to participate in natural history studies. Compared to randomized clinical trials, some felt there were added benefits such as oversight by doctors who are knowledgeable in the disease area and the ongoing observation of the progression of the disease.

• When considering improvements that could be made to clinical studies, participants indicated:
  - There should be clinical trial locations available in each time zone because the time change can affect the patients.
  - Sponsors should provide letters for missing work or school allowing the patient and caregiver to be absent without penalty.
  - Sponsors should consider allowing more than one caregiver to travel with the patient because it is too challenging for one caregiver to travel with the patient alone.
  - Sponsors should consider subsidizing the cost for travel and time away from work.

4. **What worries you most about your loved one’s condition?**

5. A participant expressed concern about the primary endpoints selected for clinical trials. The endpoints should measure more than a cognitive test, such as mobility, eating, and pain.

6. A participant expressed concern that older children are not included in clinical trials and that access to treatments through compassionate use is very important.

7. A participant shared that it is important to talk to a spectrum of patients, including diversity in age and disease severity.

8. A participant shared the hope for an easy way to test for MPSIII because there is worry their family members or relatives have the disease.

**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

10 caregivers participated in the listening session representing 13 MPSIII patients
- 7 caregivers represented 1 patient; 3 caregivers represented 2 sibling patients
- 8 patients were female
- 5 patients were male

Patient ages ranged from 8 years old to 39 years old
- 2 patients were under 10 years old
- 3 patients were between the age of 10 and 19 years old
- 8 patients were 20 years old or older

All MPSIII Types were present
- 7 patients were Type A
- 2 patients were Type B
- 2 patients were Type C
- 2 patients were Type D

Financial Interest

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