Childhood Cerebral Adrenal Leukodystrophy (CCALD) - FDA-Requested Listening Session

November 13, 2019

Objectives of session

- To better understand the disease burden and symptom progression.
- To understand issues related to barriers of being involved in clinical trials and natural history studies.
- To understand what meaningful function is important to preserve.

Discussions in FDA Listening Sessions are informal and not meant to replace, but rather complement 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 those representing patients with CCALD at the meeting. To the extent possible, the terms used in this summary to describe specific manifestations of CCALD, 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 CCALD 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 CCALD, what one activity of your child's daily life would you find most important to preserve? Why would you would choose that?***

    - The caregiver responses varied. Responses included: quality of life, "being a kid", cognitive function, vision, and communication.

    - Cognitive function was described as important by two caregivers, who indicated that cognitive function "makes us who we are".

    - Communication was described as important by two caregivers, who indicated it is important to understand whether their child experiences pain, anxiety, or other negative thoughts or feelings (e.g., anger, sadness, etc.) Communication was described by the caregivers as speech, hand gestures, blinking, or any other way to express thoughts or feelings.

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

    - A majority of the participants indicated they would be willing to accept severe or life-threatening risks. Three of the four people who said this added that they know their child will succumb to the disease if left untreated, therefore they are open to any opportunity. The one caregiver who would not accept severe risks at this time indicated that their child's disease is already too advanced, and they do not want to add any additional suffering.

3. ***Would you participate in a randomized clinical trial, given there is a possibility your child may receive the placebo, and why? Would your answer change: 1.) If the patient did not yet have symptoms or if the symptoms were mild? In this scenario, the patient would either receive the standard-of-care (i.e., hematopoietic stem cell transplant (HSCT)) or the medical product that is being tested; or 2.) Based on the duration of the trial in which they could receive a placebo? For example, if a trial lasted 1 year vs. 2 years vs. 3 years.***

- One participant indicated they would participate in a randomized clinical trial because they look for any opportunity for their child. A study that was over the course of multiple years may change the decision. If their child was declining, the caregiver indicated they would want to do the standard of care instead. If their child was stable, they might be more inclined to do a longer study.
- One participant would not want to participate in a randomized clinical trial, however the duration of the trial might change this decision.
- Three participants said they would not want to participate in a randomized clinical trial, and the duration of the trial and severity of the disease would not affect their decision.

4. ***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?***
   - A majority of the participants said clinical trial enrollment depends on the data and information available.
   - Some participants were more likely to prefer gene therapy because it gives them more hope for a cure as opposed to management of the disease. Some are also concerned about the stem cell therapy's risk of graft-versus-host disease, a sometimes-serious complication that occurs when the donor stem cells view the patient's healthy cells as foreign and attacks them.
5. ***If a treatment intervention study was not available, would you consider enrolling your child in a natural history study?***
   - A majority of the participants indicated they would be willing to enroll in a natural history study. The one caregiver who would not enroll at this time indicated that their child's disease is already too advanced, and they do not want to add any additional suffering.
   - One caregiver indicated if the disease became very advanced, they would not enroll and would instead focus on enjoying the remaining time with their son.
   - Some caregivers mentioned that children should be able to enroll in both a clinical trial and a natural history study at the same time.
   - Some caregivers suggested that instead of a placebo, data should be obtained from natural history studies or from children who never received treatment.
6. ***Additional Comments:***
   - Some caregivers emphasized that they hope diverse medical products will continue to be developed for CCALD patients. They hope that medical product developers will not "give up" on finding cures or treatments for patients who are not eligible to have gene therapy.
   - Some expressed hope for more studies for patients with a more advanced disease. Some do not currently meet the inclusion criteria for clinical trials due to having a high Loes score, and therefore are not eligible for clinical trials. A Loes score is a severity rating through an MRI evaluation of abnormalities in the brain due to CCALD. The scores range between 0 to 34.
   - Some shared that they are willing to help FDA, medical product developers, researchers, etc. in any way they can.

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 and caregivers represented

5 caregivers participated in the listening session representing CCALD male patients.

- 4 caregivers shared their child's most recent Loes scores. The scores varied, and included scores ranging from 1-2, 4-8, and 13-16.
- Patient ages ranged from 6 years old to 12 years old
- 2 patients were currently enrolled in a clinical trial, 2 patients had previously been in a clinical trial, and 1 patient had never been in a clinical trial.

Prior to the Listening Session, caregivers shared:

- Burdensome symptoms: challenges with communication, cognitive and behavioral issues, and declining motor skills.
- Management of CCALD and/or its symptoms: bone marrow transplant, gene therapy, and other medications including seizure medications and steroids.

Financial Interest

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