Glycogen Storage Disease Type 1 Caregivers to Pediatric Patients—FDA-Requested Listening Session

March 25, 2021

Objectives of Session

- To gain a better understanding of GSD Type 1 patient and caregiver perspectives on:
    - The burden of the disease and its various symptoms.
    - How currently available therapies are used to prevent hypoglycemia and the burden of these therapies, particularly cornstarch and glycoside.
    - Concerns and risk tolerance for a gene therapy that potentially could improve but not cure their disease.

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 GSD1a at the meeting. To the extent possible, the terms used in this summary to describe specific manifestations of GSD1a, 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 GSD1a 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. ***How has your child's condition and symptoms changed since they were first diagnosed with GSD1a?***

    - A majority of the caregiver participants indicated that their child(ren)'s symptoms varied according to several factors including stage of their development (i.e., often worsening in puberty), how well they could tolerate cornstarch or glycosade, illness, and activity levels. Half of caregivers indicated that the symptoms improved with increasing age, while the other half indicated that the symptoms worsened with age. Caregivers with younger children "made a mental note" about issues with puberty that were brought up by the other participants.

    - Four caregivers with multiple children with GSD1a mentioned that the symptoms differed from child to child. The symptoms varied depending on the age of diagnosis. Generally speaking, caregivers with multiple children thought that later diagnosis was associated with more severe manifestations such as enlarged liver, brain damage, depression, weight gain or decreased energy. The three participants indicated that they learned to manage the symptoms with time, and their second (or subsequent) child(ren) had been diagnosed earlier so they managed the symptoms much better than the older child diagnosed with GSD1a.

    - All caregivers of GSD1a patients agreed that the symptoms were constantly changing, and it was a constant struggle to manage them. One participant described GSD1a as a "roller coaster ride." One participant described the burden of raising children with GSD 1a as "24/7."

2. ***Follow-up question from CBER, Office of Tissues and Advanced Therapies (OTAT): What do you mean by "tolerated (cornstarch) better"?***

- This question was addressed to the caregiver, who mentioned their younger child tolerated cornstarch better, and the caregiver responded that it meant that the child did not have problems with bowel movements or vomiting compared to their older child.

3. ***Follow up question from CBER, Office of Tissues and Advanced Therapies (OTAT): Teenagers can sometimes be rebellious or challenge rules or authority. For those of you who have teenagers with GSD, have you ever encountered a scenario where your teenager refused to take cornstarch?***

    - Of the four participants that responded, none of them indicated that their child(ren) had refused to take the cornstarch. However, three of the caregivers indicated that their children try to "push the limits" on timing, because they feel uncomfortable/self-conscious taking cornstarch in front of other people, like in the middle of a class or a test or with friends watching them.

4. ***As a caregiver to a child with GSD1a, what is the most concerning aspect of your child's condition now? What do you worry most about related to your child's future with GSD1a?***

    - Over half of the caregivers indicated that they worried about the future of their children. They shared that the most concerning aspects of their children's condition are their health problems, which included them getting the stomach bug, having to be hospitalized, and their child(ren)'s mental well-being including cognitive ability.

    - The other responses varied from being most concerned about the irreversible effects of low-blood sugar, fear of messing up the regimen/schedule and harming the children, living by the clock, finding the right daycare provider, maintaining the diet, insurance coverage, how the children will manage on their own when they grow up, and that the children will not have a normal life or be able to fit in with their peers.

5. ***What might your child say is the most challenging, frustrating, or scariest part of having GSD1a?***

    - Most caregivers responded that "living by the clock" was the most frustrating part for their children. Caregivers must constantly be aware of the time and how their children are feeling (as it relates to their blood glucose), and then stop what they are doing to make sure their child has taken cornstarch, if needed. This was accompanied by the fear of their child getting sick (stomach bug), aversion to hospitalization, fear of IVs and needles, and having to miss school due to health issues.

    - Two caregivers indicated that their children worried that they will not be able to live "normal" lives or be able to fit in with their peers who do not have GSD.

    - Two caregivers noted that their children struggle with the food restrictions.

    - One caregiver talked about how their child(ren) was concerned about not being able to pursue the job or career they are interested in. Another caregiver talked about their child(ren) worrying about their friends not understanding the disease. One caregiver mentioned how their child(ren) worried about being "on" all the time in terms of cornstarch intake and diet.

6. ***FDA recognizes that many patients take cornstarch and Glycosade to prevent hypoglycemia (low blood sugar). How do these treatments impact your child's and family's quality of life? Is it the amount of cornstarch/Glycosade or timing of when they take it that has a greater impact on your child's life?***

- A majority of caregivers indicated that both the amount and the timing of cornstarch impact their child's life. Too much cornstarch may lead to stomachache, constipation, or diarrhea, and too little cornstarch can lead to hypoglycemia and/or trips to the hospital. Finding the right amount is critical and finding the right doctor to help figure out the amount is extremely challenging. Timing is also critical and the children cannot take liberties with the timing of their doses of cornstarch.

- One caregiver shared that although both timing and the amount were important, timing was the bigger struggle. Having to stop what the child(ren) are doing and waking up in the middle of the night to take the cornstarch were constant challenges.

- One caregiver indicated that the amount was a bigger challenge. They had to switch between cornstarch and Glycosade and had to constantly change the amount of the feed. Finding the right amount was a constant struggle for them.

7. ***FDA recognizes that nutrition is important for your child's growth and to avoid hypoglycemia in patients with GSD1a. Have growth and nutrition been an issue for your child and if so, have you met with a nutritionist (or dietician) to modify your child's diet?*** **If YES - How frequently has your family met with a nutritionist or dietician?**

    - Three caregivers shared that their children didn't reach the target height, while the children of two other caregivers didn't experience growth/height issues.

    - Almost all of the participants had met with a nutritionist. The frequency of meeting with the nutritionist or dietician ranged from 1–4 times/year.

    - A majority of participants indicated that although the advice of the nutritionist was sound, it was often difficult to follow the nutritionist's recommendations in their daily routine.

8. ***Would you consider allowing your child to take part in a clinical trial that was testing whether gene therapy could decrease the severity of hypoglycemia (low blood sugar) and reduce the need for cornstarch/Glycosade, but didn't cure GDS1a? Why or why not?***

    - Almost all of the caregivers responded to this question in the affirmative, but one caregiver indicated that they would "strongly consider" a clinical trial after weighing the benefits and risks.

    - While the primary motivation for having their children participate in clinical trials included a reduction in the frequency of cornstarch for four caregivers, the other reasons ranged from reducing hypoglycemia for three caregivers, increasing the quality of life of their children for two caregivers, and having their children feel "normal" for one caregiver.

9. ***Would you be willing to treat your child's GSD1a with gene therapy if you knew there could be severe or life-threatening risks? Please explain why or why not. If yes - What if the benefits of gene therapy don't last throughout your child's life, but the risks from the therapy do?***

    - Most caregivers found this question difficult to answer. While three caregivers indicated a strong yes, one caregiver was not in favor at this time, and the remaining three caregivers would weigh the risks first before making a decision.

- Some caregivers indicated they would be able to decide to treat their child(ren) with gene therapy depending on how long the benefits lasted. One caregiver wanted to weigh the impact on the quality of life of their child(ren). Another caregiver wanted to give their child(ren) a chance at feeling "normal", even if it was for a short duration.

- Two caregivers wanted to have conversations with their children before making a decision. One caregiver added wanting their children to understand what it meant to participate in clinical trials, so they were in favor of allowing their older child to participate in clinical trials, but would wait for their younger child to grow older before talking to them about participating in clinical trials.

- One caregiver recognized the potential risks, but still wanted their child(ren) to participate with the hope for better therapies in the future that would mitigate the risk.

Partner Organization

- Reagan-Udall Foundation for the FDA assisted with producing the summary of this meeting.
- National Organization for Rare Disorders (NORD) helped identify and prepare patient community participants.
- OPA contractor support assisted with producing the summary of this meeting.

FDA Divisions Represented

- Office of the Commissioner, Office of Patient Affairs (*organizer*); Office of Orphan Products Development; Office of Combination Products; Office of Clinical Policy & Programs; Office of Pediatric Therapeutics
- Center for Biologics Evaluation and Research (CBER), Office of the Director; Office of Tissues and Advanced Therapies (OTAT); Office of Tissues and Advanced Therapies/Division of Clinical Evaluation & Pharmacology/Toxicology (DCEPT); Office of Tissues and Advanced Therapies/General Medicine Branch I (GMBI); Office of Tissues and Advanced Therapies/General Medicine Branch II (GMBII); Office of Biostatistics & Epidemiology (OBE)
- Center for Drug Evaluation and Research (CDER), Office of the Center Director; Office of the Center Director/Professional Affairs and Stakeholders Engagement; Office of New Drugs/Office of Cardiology, Hematology, Endocrinology & Nephrology/Division of Diabetes, Lipid Disorders and Obesity; Office of New Drugs/Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine/ Division of Rare Diseases and Medical Genetics (DRDMG); Office of New Drugs/Office of Rare Diseases, Pediatrics, Urologic, and Reproductive Medicine/Division of Pharm/Tox for Office of Rare Diseases, Pediatrics, Urologic, and Reproductive Medicine (DPT-ORPURM); Office of New Drugs/Office of Neuroscience/Division of Psychiatry; Office of New Drugs/Clinical Assessment Staff; Office of Translational Sciences/Office of Clinical Pharmacology/Division of Translational & Precision Medicine; Office of Regulatory Policy/Division of Regulatory Policy III; Office of Translational Sciences/Office of Biostatistics/Division of Biometrics III; Office of Translational Sciences/Office of Biostatistics/ Division of Biometrics IV
- Center for Devices and Radiological Health (CDRH), Office of Strategic Partnerships and Technology Innovation/ Division of All Hazards Response, Science and Strategic Partnerships (DAHRSSP); Office of Product Evaluation and Quality/Division of Health Technology III A (DHTIIIA)

Patients and Caregivers Represented

Seven caregivers participated in the listening session representing children with GSD1a:

- All caregivers described the severity of their children's GSD1a: Four caregivers described their children's GSD1a as moderately severe, two caregivers described GSD1a as moderate, and one caregiver described GSD1a as mild.
- Patient ages ranged from 4 years old to 19 years old.

Prior to the Listening Session, Caregivers Shared

- All of the patients have been hospitalized before due to GSD1a.
- The hypoglycemic episodes of the patients ranged from 2–20 per month.
- All of the patients use cornstarch or Glycosade more than four times in a day to treat or manage their hypoglycemia.

Financial Interest

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