Glycogen Storage Disease Type 1 Adults—FDA-Requested Listening Session

March 18, 2021

Objectives of Session

- To gain a better understanding of GSD Type 1a patient & 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 GSD1a and its symptoms changed over time? Was it easier or harder to manage during childhood, puberty, and/or other times?***

- A majority of the participants indicated that it was harder and more stressful to manage GSD1a during childhood. The reasons included: interfering with social life/activities, not feeling normal, frequent hospitalizations because of stomach viruses and low blood sugar, and having a gastrostomy tube (G-tube).

- Two participants indicated that it was easier to manage their GSD1a during childhood as their parents took care of everything. They noted that it got harder to manage GSD1a as they got older. The reasons included: weight gain, interfering with sleep, not having a "normal" life, frequent hospitalizations, not being symptomatic with hypoglycemia, and not having a social life.

- One participant described how even though she and her sibling both have GSD1a, their experience differed. GSD1a was more challenging for her as an adult, but was more challenging for her sibling as a child due to illnesses.

- Three participants indicated that they had a G-tube during childhood, and it was very hard. Once they started cornstarch therapy, life got easier.

- One participant felt symptomatic only if their blood sugar was "very low" during their 20s and 30s. But in their 40s, their blood sugar is more regulated, and they feel symptomatic when they are approaching low blood glucose.

- One participan indicated that the symptoms have mostly been the same over time. The main problem specific to childhood was poor growth. The main problem now is hypoglycemia.

- Many participants commented that the frequency/intensity of monitoring of their blood glucose for hypoglycemia has varied over time.

2. What is the most concerning or frustrating aspect of your condition now (over the last few years)?

- A majority of the participants indicated that two of the most frustrating aspects of their condition are not having a normal social life and gaining weight. Social life examples included: making friends, going out with friends, going to school or college, and dating. Three of the five participants who said this added that frequent hospitalizations are also very frustrating because they lead to missing school or having to be on an IV. One of the five participants noted that GSD1a seems to have taken over their life and controls it.

- Two participants mentioned that their condition affects their mental health because it is a constant problem that affects every aspect of their life.

- One participant indicated that the most frustrating part is inconsistent and unpredictable blood glucose levels. The patient would get two different blood sugar numbers with the same routine.

3. FDA recognizes that many patients take cornstarch and Glycosade to prevent hypoglycemia (low blood sugar). Please describe how the need to take these medicines impacts your quality of life. Is it the amount of cornstarch/glycoside or timing of when you take it that has a greater impact?

- A majority of the participants indicated that both timing and amount of cornstarch/Glycosade impacted their quality of life. Three out of four participants noted that the timing was harder when they were younger, especially in school and college, at work, while going out with friends, or traveling, and the amount is harder because of weight gain.

- One caregiver indicated that the amount is not challenging for their child, but the timing has a great impact on the child's life, especially when at school, work, or out with friends. The caregiver noted that the hard part is that cornstarch and water cannot be mixed ahead of time but need to be mixed at the time it is taken.

- One participant indicated that the need of cornstarch has impacted their willingness to exercise because if they lose weight from exercising, they have to eat more cornstarch to prevent their blood sugar from going low.

- A majority of the participants said that the timing of taking cornstarch has impacted their night sleep because they have to wake up in the middle of night to take cornstarch/Glycosade and they cannot get a full night's sleep.

- One patient indicated that having less cornstarch in a day would help financially by saving money. In addition, it would help to control calorie intake.

- One participant currently not on cornstarch/Glycosade explained that they were on cornstarch for most of their life and switched to complex carbohydrates with very low sugar, such as bread and pasta last year. The patient noted that managing with diet still challenging because of the amount of attention it required as needed to avoid many food. This participant still considered fear of hypoglycemia to be one of the most troubling aspects of the disease.

4. As you may know, some clinical trials involve different types of medical products, for example some involve an experimental drug and others involve gene therapy. If you were thinking about

taking part in a clinical trial, would it make a difference to you if the clinical trial involves an experimental drug or gene therapy? Please explain why.

- Four participants said they would want to participate in a clinical trial as long as it has the potential to improve their quality of life. They noted that it would not make any difference whether the clinical trial involves an experimental drug or gene therapy: preventing kidney stones, reducing the amount of cornstarch, and improving quality of life.
- One participant would not want to participate in a clinical trial that involves an experimental drug. However, the patient would want to participate in a gene therapy.
- One participant participated in a Glycosade study before and it was crucial because cornstarch had stopped working for the patient.
- One participant would not want to participate in any kind of clinical trials. The patient noted that the gene therapy involves taking steroids and was opposed to taking steroids because he thought that they may cause/worsen liver problem. This participant was very concerned about exchanging one problem for another problem.

5. ***Would you consider taking a gene therapy that decreased the severity of hypoglycemia (low blood sugar) and reduced your need for cornstarch/Glycosade, but didn't completely cure your GSD1a? Why or why not?***

- Four participants said they would consider taking gene therapy even if it will not cure their GSD1a completely but reduce their need for cornstarch/Glycosade. The reasons included: reducing the amount of cornstarch, improving quality of life, fewer hospitalizations, and not living by the clock.
- One participant wanted to know how much gene therapy would cure the GSD1a and the decision would depend on what "decrease" would mean regarding the severity of low blood sugar.
- One participant would not be willing to participate in a gene therapy because of possible side effects, such as liver problems.

6. ***Would you be willing to treat your 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 the gene therapy don't last throughout your life, but the risks from the therapy do?***

- Two participants were willing to participate in gene therapy even if it has serious risks. The reasons included: GSD1a controls their life and they are willing to take risks to regain their independence, they believe that they would have fewer hospitalizations, and decreasing the amount of cornstarch would be a great lifestyle improvement and allow them to have better control over their weight. One of them would want to know specific risks associated with gene therapy if the benefits do not last long, but the risks do.
- Three participants indicated they would not be willing to participate in gene therapy if there could be severe or life-threating risks. They would want to know the possible risks and whether there were any long-term side effects, such as kidney or heart issues. One of them would consider gene therapy if there were not too many long-term side effects. One of the participants expressed concern about duration of effect, as this individual thought it would not want to have to adapt to current lifestyle after having a period of "normality."

- One caregiver indicated that their decision to participate in gene therapy would depend on the risks. The caregiver noted that if the benefits of the gene therapy last 5–10 years, then it would be worth the risk.

7. Do you have any other thoughts about what scientists and researchers should consider when planning clinical trials that study potential treatments for GSD1a?

- Some participants emphasized that they hope scientists will continue their research to find a long-term treatment to improve the quality of life by avoiding hypoglycemia and hospitalization. Two of the participants indicated that researchers should consider that the same therapy may not work for every patient and asked them to keep working on different ways to find treatments for different patients.
- One participant asked the scientists to research potential long-term side effects of clinical trials, such as kidney issues.
- One participant asked the scientists to research the risks for women of childbearing potential after participating in the gene therapy.
- One participant indicated the mental health problems with having GSD1a and asked scientists to focus on addressing the mental health issues that occur along with GSD1a.
- One participant suggested that the scientists research stem cell therapy to minimize the side effects compared to gene therapy.

8. Additional Comments

- All participants emphasized the need of more awareness for GSD1a by people.
- Most participants indicated issues with insurance companies to cover their GSD1a treatments and noted the lack of awareness of this disease by insurance companies and medical professionals.
- A majority of the participants indicated that most of the time GSD1a is compared with diabetes, but GSD1a should be recognized as a separate disease.
- One participant would like to know how gene therapy would work in the United Kingdom (UK)/internationally.
- Some shared that they are willing to help the FDA, medical product developers, and researchers in any way they can.

9. Follow-up Question from Office of Tissues and Advanced Therapies (OTAT), Center for Biologics Evaluation and Research (CBER): When we do a clinical trial in gene therapy, we usually do a 5-year follow-up with patients, but it's difficult because patients tend to drop out of the clinical trial. Long-term data is very critical for us, especially in this condition where there is long-term impact. Would you be willing to participate in a clinical trial long-term and if so, for how long?

- All three participants who answered this question indicated that they would stay in a trial as long as it takes. The reasons included: benefit to future research, help other people with GSD1a, and to help make gene therapy better.

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.
- DRT Strategies, Inc. assisted with producing the summary of this meeting.

FDA Divisions Represented

- Office of the Commissioner, Patient Affairs Staff (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

Five patients and one caregiver participated in the listening session representing GSD1a adult patients:

- All patients and the caregiver described the severity of their or their child's GSD1a: Four of them described their GSD1a moderately severe and one patient described it very severe.
- Patient ages ranged from 18 years old to 47 years old.

Prior to the Listening Session, Patients and Caregivers Shared

- A majority of the participants have been hospitalized before due to GSD1a.
- A majority of the participants 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.