Congenital Cytomegalovirus (cCMV) Infection - FDA-Requested Listening Session

April 4, 2024, 1.5 hours

Objectives of Session

FDA would like to understand what factors impact parents' decision to start or decline antiviral treatment for their child with cCMV infection, and for those parents that do start, what factors impacted their decision to complete the 6-month treatment course. Additionally, FDA would like to understand their perceptions about their child participating in clinical trials for cCMV.

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 persons from the Congenital Cytomegalovirus (cCMV) community at the meeting. To the extent possible, the terms used in this summary describe the health needs, perspectives, preferences, and impacts reflect those of the individual participants. This report is not meant to be representative of the views and experiences of the entire Congenital Cytomegalovirus (cCMV) population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.

Participants Represented

- **Number of Caregiver Participants:** Six
- **Biological sex**: The caregiver participants represented their children. Four of the children represented were assigned male at birth. Two of the children represented were assigned female at birth.
- **Education level**: Caregiver participants' self-reported highest level of education ranged from trade school to Doctorate.
- **Geographic location**:
  - Two caregiver participants were from the Southeast, United States (U.S.).
  - One caregiver participant was from the Midwest, U.S.
  - One caregiver participant was from the West, U.S.
  - Two caregiver participants were from the Southwest, U.S.
- **Ages:** Caregiver participants represented their children, whose ages ranged from 3 months to 16 years of age.
- **Disease Severity**: Caregiver participants represented their children, whose caregiver-reported severity of cCMV ranged from mildly symptomatic to severely impacted.

Summary of Discussion by Question

<u>Round 1: Symptoms</u>

1. If your child was offered antiviral treatment, what factors did you consider when deciding whether or not to treat your child with antiviral medication?
   - All six participants indicated that their child received medication to treat cCMV.

- Three participants indicated their relationship with their child's physician was a factor.
- One participant shared that they did not want to have regrets about not treating their child.
- Three participants indicated that the data at the time were a factor that they considered.
- One participant considered reports of positive outcomes, side effects and toxicity profile, likelihood of benefit, and treatment burden.
- Four participants considered the severity of their child's symptoms.

a. Given what you know now, would you make the same decision today?
   - All six participants confirmed that they would make the same decision today to treat their child.

2. **Follow-up:** One participant indicated that their child was diagnosed at a time when the standard treatment duration was 6 weeks, but the doctor recommended 6 months of treatment. Did you do 6 months? What were your considerations when deciding how long to treat your child?
   - The participant responded that because their child was born at 32 weeks, the initial plan was to treat until their child was 40 weeks. After talking to their doctor, they decided to try and go to 6 months. However, due to medical reasons, the treatment was stopped early, and their child received about 3 months of treatment.

3. If your child was treated with antivirals:
   a. What was the hardest part of treatment?
      - Three participants indicated that the weekly blood draws to monitor for neutropenia were the hardest part of treatment.
      - One participant added that the blood draws were difficult due their baby's small size.
      - Two participants shared that the treatment was scary due to the precautions the medical providers used when administering the medication.
      - One participant mentioned that the hardest part of treatment was compliance due to twice daily treatment, traveling with the medication, maintaining the storage requirements of the medication, and finding a compounding pharmacy.
      - Two participants stated that one of the hardest parts of treatment was knowing their child was immunosuppressed during treatment.

   b. Do you think treatment was helpful?
      - Five participants believed the treatment helped or probably helped.
      - One participant did not know if treatment was helpful.

<u>Round 2: Perspectives about Clinical Trials</u>

4. If you were given the opportunity for your child to participate in a clinical trial for the treatment of cCMV, would you have permitted your child to participate?
   - All six participants would permit their child to participant in a clinical trial.

a. What if your child had an equal chance of receiving either the drug or a placebo?
    - Five participants indicated that they would not enroll their child in a clinical trial if their child had a chance of receiving the placebo, unless there was no other way to access the drug or no other available treatment.
    - One participant would enroll their child in a placebo-controlled clinical trial.

5. Would you consider committing to prolonged follow-up on the clinical trial. For example, clinical trial visits for 4 or more years?
    - All six participants stated that they would enroll their child in a clinical trial that had a prolonged follow-up.

6. Do you think it would be fair for a trial to only be available to newborns (first month of life)?
    - Five participants did not believe a clinical trial for cCMV should be available only to newborns.
        - Two of the five participants believed that clinical trials should not be available only to newborns because many infants are not tested at birth for cCMV.
        - One of the five participants recommended considering what primary and secondary outcomes might be beneficial to children outside of the first month of life and what treatments should be accessible outside of the first month. To clarify, a particular treatment may only be accessible through participation in a clinical trial. This participant would like families to have access to treatments that may show promise as it relates to the short term and/or long-term outcomes.
    - One participant indicated that the population you are studying should be based on the question you are asking. If the population being studied is newborns, then the study should be for newborns. The participant also indicated that a study on late term effects should be open to the general population.

7. **Follow-up:** Would the probability of a placebo make a difference to you? For example, 25% vs 50% chance of receiving placebo? Would it be more acceptable to receive a placebo if access to treatment was just delayed instead of not at all?
    - Four of the participants were not willing to have their child participate in a clinical trial in which their child may receive the placebo.
    - One participant shared that they were willing to have their child participate in a clinical trial in which their child may receive a placebo treatment to contribute to better understanding of the disease and care of the disease.
    - One participant shared that it would depend on the urgency to receive treatment. If it was an urgent matter, they would not take the risk of possibly receiving a placebo.

8. What information would you want to have included in the parental informed consent form?
    - All six participants believed that parental informed consent forms should contain the standard information.
    - One participant indicated that the informed consent document should emphasize that you can stop participating in the clinical trial at any time and a second participant agreed

with the concept that the right to stop participating in the clinical trial at any time should be emphasized and recommended that the person sharing or presenting the informed consent form should emphasize the right to discontinue participation at any time.

- Two participants thought that having an online community with other people doing the experimental treatment would be helpful. This community would provide encouragement, understanding and real-world experiences to other participants of the clinical trial.

Round 3: Impact of cCMV Infection

9. What aspects of cCMV have had the biggest impact on you and your child's day-to-day life?
    - One participant indicated that they were very lucky as their child is asymptomatic and is monitored every three months by an audiologist. They indicated that they feel very lucky that cCMV has not had a huge impact on their lives.
    - Another participant noted that their son is severely impacted by cCMV, and it impacts everything in the family's life. They indicated that there is an emotional burden of educating by just existing and that the lack of knowledge by medical providers is frustrating.
    - A participant shared that the impact has evolved from birth to now at 16 years old. The impact on their lives early on was related to their son's medical condition and now is more focused on advocating for their child. The parents advocate heavily to ensure their son is getting the education that he deserves. The thing that will have a lasting impact on their son is hearing loss. They worry how their son will live at college; what about fire alarms, fire detectors, how will he take over that safety responsibility.
    - One participant mentioned that there is a large variety of impacts that affect lives of cCMV families, such as time, appointments, everything. Simplicity does not exist. They said that it's a sacrifice they all give to their children. They are new to this and doing all the organ scans with two to three appointments per week. They noted being afraid of losing their job because of all the time spent. They also mentioned fire alarms and the worry that the children will get in trouble because they can't hear if someone is talking to them.
    - Another participant shared that because their son is severely impacted that every single part of their lives has been affected. There are so many little things. They do not have a social life and had to quit their job. When they visit family members, the car is loaded with all of their son's supplies.
    - A participant shared that their daughter is non-verbal and has intellectual and physical disability. They shared that every single thing they do every single day is impacted by cCMV; including where they live, where they work and what they do. It is difficult to plan family activities. The hardest thing is the lack of awareness and knowing that they were not given the opportunity to prevent this. They believed they were robbed of the ability to try to reduce the risk of cCMV during pregnancy.

FDA Offices & Divisions in Attendance

- Office of the Commissioner (OC) – *4 offices*
    - OC/OCPP/PAS – Office of Clinical Policy and Programs/Patient Affairs Staff *(organizer)*
    - OC/OCPP/OOPD – Office of Clinical Policy and Programs/Office of Orphan Products Development
    - OC/OCPP/OPT – Office of Clinical Policy and Programs/Office of Pediatric Therapeutics *(requestor)*
    - OC/OMHHE – Office of Minority Health and Health Equity

- Center for Biologics Evaluation and Research (CBER) – *6 offices/divisions*
    - CBER/OCD – Office of the Center Director
    - CBER/OCD/PS – Office of the Center Director/Policy Staff
    - CBER/OTP/OCE/DCEGM/GMB3 – Office of Therapeutic Products/Office of Clinical Evaluation/Division of Clinical Evaluation General Medicine/General Medicine Branch 3
    - CBER/OVRR/DCTR/CRB1 – Office of Vaccines Research and Review/ Division of Clinical and Toxicology Review/ Clinical Review Branch 1
    - CBER/OVRR/DCTR/CRB2 – Office of Vaccines Research and Review/ Division of Clinical and Toxicology Review/ Clinical Review Branch 2
    - CBER/OVRR/DCTR/CRB3 – Office of Vaccines Research and Review/ Division of Clinical and Toxicology Review/ Clinical Review Branch 3

- Center for Devices and Radiological Health (CDRH) – *5 offices/divisions*
    - CDRH/OCD – Office of the Center Director
    - CDRH/OPEQ/OHTI/DHTIC – Office of Product Evaluation and Quality/Office of Health Technology I/Division of Health Technology IC
    - CDRH/OPEQ/OHTIII -- Office of Product Evaluation and Quality/Office of Health Technology III
    - CDRH/OPEQ/OHTIII/DHTIIIB -- Office of Product Evaluation and Quality/Office of Health Technology III/Division of Health Technology IIIB
    - CDRH/OSPTI/OIED/DPCD - Office of Strategic Partnerships and Technology Innovation/Office of Equity and Innovative Development/Division of Patient-Centered Outcomes

- Center for Drug Evaluation and Research (CDER) – *6 offices/divisions*
    - CDER/OND/OID – Office of New Drugs/Office of Infectious Diseases
    - CDER/OND/OID/DAV - Office of New Drugs/Office of Infectious Diseases/Division of Antivirals (*requestor*)
    - CDER/OND/OII/DPTII – Office of New Drugs/Office of Immunology and Inflammation/ Division of Pharm/Tox for Immunology and Inflammation

- CDER/OND/ORDPURM/DRDMG – Office of New Drugs/Office of Rare Diseases, Pediatrics, Urology and Reproductive Medicine/Division of Rare Diseases and Medical Genetics
- CDER/OTS/OB/DBII – Office of Translational Sciences/Office of Biostatistics/Division of Biometrics II
- CDER/OTS/OCP – Office of Clinical Pharmacology

Non-FDA Attendees

- Reagan-Udall Foundation for the FDA
- National Institute for Health/National Center for Advancing Translational Sciences
- National Institute for Health/ National Institute of Allergy and Infectious Diseases/Division of Microbiology and Infectious Diseases

Financial Interest

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