CHILDREN'S TUMOR FOUNDATION
ENDING NF THROUGH RESEARCH

Patient Listening Session

Cutaneous Neurofibromas in NF1

MAY 21, 2024

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Statement of Purpose

The objective of this Listening Session was to inform the FDA about a rare disease called neurofibromatosis type 1 (NF1) and the burden for a specific manifestation known as cutaneous neurofibromas (cNF). While **our previous PLS** highlighted the experience of NF patients broadly and a had particular focus on plexiform neurofibromas, this meeting's aim was to shed light on the experiences of patients with cNFs, an often under-appreciated manifestation that is present in 95% of NF1 patients. Whereas cNFs have been historically considered a "cosmetic" issue, recent studies have brought to light the fact that cNFs strongly impact quality of life (causing pain, itching, and significant social distress) and remain a top priority for the NF1 community.

About CTF

The Children's Tumor Foundation (CTF) is the world's leading nonprofit dedicated to funding and driving innovative research that will result in effective treatments for the millions of people worldwide living with NF, a group of genetic conditions that causes tumors to grow on nerves throughout the body. The Children's Tumor Foundation's mission of driving research, expanding knowledge, and advancing care for the NF community fosters its vision of one day ending NF for all NF patients. For more information, visit **ctf.org**

About NF

NF refers to all types of neurofibromatosis and schwannomatosis, genetic conditions that cause tumors to grow on nerves throughout the body. One in every 2,000 people is born with some type of neurofibromatosis or schwannomatosis, which may lead to blindness, deafness, bone abnormalities, disfigurement, learning disabilities, disabling pain, or cancer. NF continues to be under or misdiagnosed and affects all races, ethnic groups, and genders equally. Even when benign, these tumors can cause significant morbidity and mortality because of their continuous growth and surgical inaccessibility. To date, there is only one safe, effective FDA-approved treatment for NF, directed to NF1-specific plexiform neurofibromas.

About Cutaneous Neurofibromas (cNFs)

Cutaneous neurofibromas are the most common type of tumor related to neurofibromatosis type 1 (NF1), affecting 95% of those with the condition. They are benign tumors that develop along a nerve on or under the skin. They may look like small lumps, bumps, or nodules. Cutaneous neurofibromas may develop at any time of life, but also seem to increase in number during times of hormone changes, such as during puberty or, for women, during pregnancy. Typically, adults with NF1 will develop more tumors as they age,

but there is no way to determine when, where, or how many neurofibromas will develop over the lifetime, as it varies greatly from person to person.

Executive Summary

During the Listening Session, six adult patients and/or caregivers of NF1 children described their experiences living with cNF directly with members of the FDA. Collectively, they represented much of the diversity of the NF1 community in terms of age, background, disease severity, and outlook on their condition. Through heartfelt testimony and an extensive question and answer section, these patient representatives relayed the significant burden of this particular manifestation, the community's tolerance for risk, and their preferences for treatment.

Remarks and Briefings

Patient Affairs Staff began the meeting with opening remarks. Dr. Annette Bakker, CEO of the Children's Tumor Foundation, detailed CTF's role in advancing treatments for NF. Dr. Jaishri Blakeley MD of Johns Hopkins University then gave a brief overview of the disease state, recounting for the FDA the clinical characteristics of cNF in NF1 and what we know about the natural history of the condition.

We then moved to the reason we were all gathered for this session: the patient and care advocate testimonies. Below we include a brief synopsis of the powerful stories that were shared with the FDA.

Patient Testimonies

William G.

The first speaker, William from Michigan, began by thanking the FDA for the opportunity to speak to them. He defined his experience as someone living with NF1 and very affected by cNFs including being denied employment opportunities, being harassed for his appearance by strangers, and an overall struggle to help others understand that he is more than his diagnosis.

Mercedes C.

Next, Mercedes from Idaho recounted her story with NF. As a *de novo* case who was diagnosed later in life, Mercedes developed many cNF tumors on her face and body as an adult. She cannot work due to chronic pain related to cNFs, and she has been denied customer service jobs in the past due to her appearance.

Mercedes is passionate about advocacy in the NF space and raising awareness. She also emphasized a frustration over the lack of access to healthcare in her area and that, though she would love to participate in clinical trials, they are often not available to her.

Lilly S.

Lilly from New York then spoke with the group about how the time and money required to manage her tumors has caused her to put aspects of her life on hold. She reported that she deferred education, career, and family to focus on treating her cNFs, either through demanding clinical trials or extensive surgical sessions.

> *"I chose a life as close to what I wanted as possible. I wanted to be a journalist, I wanted to be a lawyer, I wanted to travel, I wanted to be an American Gladiator, I wanted to be a mom. One way or another, NF has kept me from doing it. NF has made me feel guilty for even wanting it."*

Lilly explained that this is all because of her experiences with the stigma of having cNF tumors. She characterized how this fear of being out in public weighs on her.

> *"Even the times I was lucky enough to do what I wanted to do, people seeing my tumors and being disgusted made it nearly impossible to exist in certain spaces."*

Lastly, Lilly laid out her hopes for the future of NF treatments: more options and the ability for people with NF to live the lives they want.

Whitney S.

Whitney from Kentucky shared her perspective on how cNFs affect her mental health. She described how the fear of progression weighs on her like a dark cloud. In a heart-wrenching moment, she recounted her fears of cNF progression during pregnancy — something that causes here much anguish about becoming a mother.

> *"Beyond this, I carry the weight of shattered dreams. My desire to have a big family with three or four children has been crushed by the fear of NF1 progression. The hormonal changes associated with pregnancy can exacerbate cNF growth, presenting an unbearable risk to both my physical and emotional well-being. This risk has compelled me to reassess my dreams, as the potential consequences are ones I am unwilling to accept."*

Like many living with NF1, Whitney wanted the FDA to understand that cNFs are not a manifestation of NF that can be ignored.

> *"Cutaneous Neurofibromas can significantly impact an individual's physical and emotional well-being, and it's offensive to dismiss them as merely cosmetic concerns. Dismissing these concerns fails to recognize the profound impact it has on individuals."*

Ellie K.

Ellie from Montana spoke on behalf of herself and her 6-year-old daughter, both of whom have NF1. According to Ellie, although she has a mild form of NF with only a handful of cNF tumors, the tumors can cause a lot of itching and, if they get bumped just right, a zing of pain. Ellie also talked about two particularly bothersome tumors on her foot which cause significant pain when she walks.

Though her daughter has no tumors as of now, she told the group she knows the future for her is still unknown.

> *"I know NF is a progressive disease, and so I know that my cNFs will continue to grow, and new ones will grow too. However, it is our children with NF and my [daughter] Charlie that I fear for. She is so strong, brave, and confident but her future is unknown. Yes, I may have a very mild case, but that does not mean her case will be the same. I pray that her case will be even more mild than mine, but that is the unknown."*

Ellie has participated in past clinical trials and conveyed to the group that if her daughter ever had any symptoms, she would be interested in enrolling her in trials.

Sally G.

Lastly, Sally from New York shared her perspective on behalf of her 17-year-old daughter Alice who lives with NF1. Alice has hundreds of small tumors on her body that cause her significant itching and discomfort. Sally stated to the group that what she's looking for isn't a therapy that makes skin perfect, but something that can help treat a bump when it begins to appear and stop its growth.

Sally expressed her tendency to downplay the effects of cNF tumors on her child – something she believes is common for parents of children with NF1.

> *"I'd equate it to our own mortality... We know we are mortal but don't live each moment with this awareness because it would be overwhelming.*

Similarly, I know Alice's cNFs will grow… but I don't live each moment with this awareness because, quite frankly, it would be unbearable."

Sally said that she has made cNFs a priority as an advocate for NF1 research because they impact nearly everyone with NF1 and, as others had already depicted in the session, affect how others perceive you; most often in a negative way.

Q&A Session

After the patient testimonies, the meeting moved into a question-and-answer session. One representative from the FDA asked about the helpfulness of a clinical trial for a topical treatment that could only be used in a limited area and whether that clinical trial would be of interest to the group. One participant remarked that in the case of particularly bothersome tumors, treatment of a smaller area is very helpful—such as the tumor on the bottom of her foot. Others with much more tumor burden said that, while treating small areas was better than nothing, they would love to have something more extensive.

Another FDA representative asked the group how they defined "meaningful" treatment. The patient representatives had all sorts of answers, including treatments that could halt progression and those that would work for patients in the long term. One participant also identified that success for her would be something that could lessen the itching and pain of her cNFs.

Someone else from the FDA asked if any of the participants used currently available treatments for cNFs. Two participants identified using the nutritional supplement turmeric, and others reported using prescription antihistamines to help with itching.

Lastly, someone from the FDA asked the patients about their willingness to participate in long-term clinical trials. Several patients said that they definitely would, and some went on to remark that access to current trials – either geographically or financially – has been difficult for them in the past.

Conclusion

The meeting ended with an exchange of appreciation between the patient representatives and members of the FDA for participating in the session.

The patient representatives who told their stories left audience members with the following take-home points:

- cNF is a significant and serious manifestation of NF1 with a high amount of unmet need

- Patients are eager for more treatment options and are willing to accept risk
- The NF community is not a monolith and a diverse group of patients should be consulted about upcoming treatments

On behalf of the NF community, the Children's Tumor Foundation would like to thank the FDA for helping us elevate the patient voice for such an important issue.

Attendees

Six representatives of the NF community were joined by Dr. Annette Bakker, CEO of the Children's Tumor Foundation, and Dr. Jaishri Blakeley of Johns Hopkins University to relay an important message to the FDA.

In addition, over 40 FDA staff from 14 different offices/divisions from 4 different Centers attended this PLS.

Office of the Commissioner (OC) – *3 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 Product Development
- OC/OCPP/OPT - Office of Clinical Policy and Programs/Office of Pediatric Therapeutics

Center for Biologics Evaluation and Research (CBER) – *2 offices*

- CBER/OCD – Office of the Center Director
- CBER/OCD/PS – Office of the Center Director/Policy Staff

Center for Drug Evaluation and Research (CDER) – *8 offices*

- CDER/OND/ODES/DCOA – Office of New Drugs/Office of Drug Evaluation Science/Division of Clinical Outcome Assessment
- CDER/OND/OII/DDD – Office of New Drugs/Office of Immunology and Inflammation/Division of Dermatology and Dentistry
- CDER/OND/OOD/DOII – Office of New Drugs/Office of Oncologic Diseases/Division of Oncology II
- 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/DBIII – Office of Translational Science/Office of Biostatistics/Division of Biostatistics III

- CDER/OTS/OCP – Office of Translational Science/Office of Clinical Pharmacology
- CDER/OTS/OCP/DCEP – Office of Translational Science/Office of Clinical Pharmacology/Division of Cardiometabolic and Endocrine Pharmacology
- CDER/OTS/OCP/DCPI – Office of Translational Science/Office of Clinical Pharmacology/Division of Cancer Pharmacology I

Center for Devices and Radiological Health (CDRH) – *1 office*

- CDRH/OPEQ/OHTIII – Office of Product Evaluation and Quality/Office of Health Technology III

Non-FDA Attendees
National Institutes of Health (NIH)

- NIH/NCATS – National Center for Advancing Translational Sciences

Disclosures

The Children's Tumor Foundation is a financial investor in NFlection Therapeutics Inc, the sponsor of NFX-179 (NCT05005845). For more information on this investment, please visit: **https://www.ctf.org/news/childrens-tumor-foundation-expands-into-a-new-strategic-chapter-as-impact-investor-in-nf-research**

Disclaimer

Discussions in FDA Patient Listening Sessions are informal. All opinions, recommendations, and proposals are unofficial and nonbinding by FDA and all other participants. This report reflects CTF's account of the perspectives of patients and caregivers who participated in the Patient Listening Session with the FDA. To the extent possible, the terms used in this summary to describe specific manifestations of NF1/cNF effects and impacts, and treatment experiences, reflect those of the participants. This meeting summary is not meant to be representative of the views and experiences of the entire NF1 patient population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.