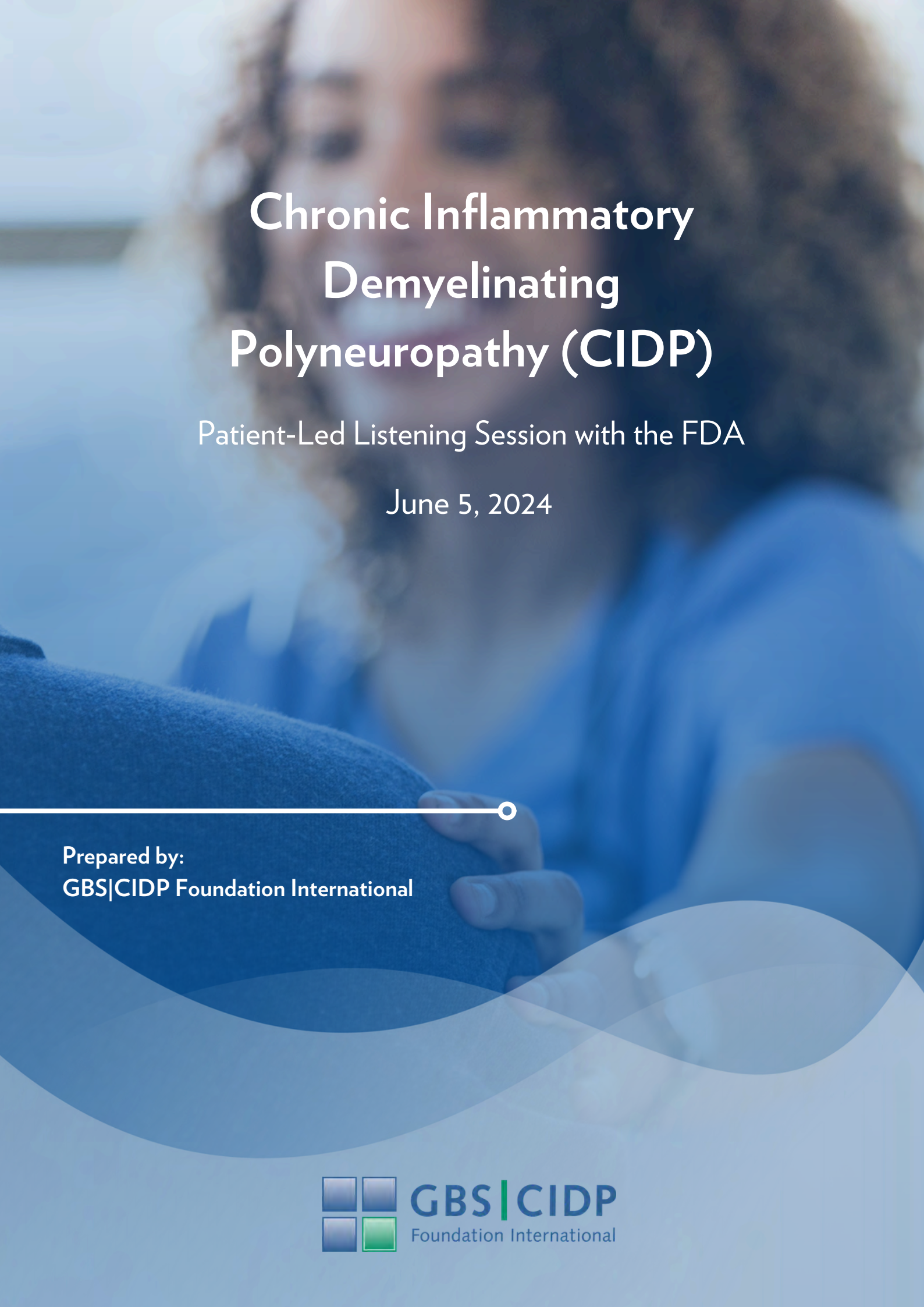

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

Patient-Led Listening Session with the FDA

June 5, 2024

Prepared by:
GBS|CIDP Foundation International

GBS | CIDP
Foundation International

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Objectives of the session
After this listening session, the GBS|CIDP Foundation International hopes the FDA recognizes the physical, mental, and emotional toll of relapsing CIDP symptoms. Furthermore, the Foundation hopes to inspire conversations about innovative clinical trial designs to reduce the risk of relapses of CIDP symptoms for patients while researchers work on finding improved therapies.

Disclaimer
Discussions in FDA Patient Listening Sessions are informal. All opinions, recommendations, and proposals are unofficial and nonbinding on FDA and all other participants. This report reflects the GBS|CIDP Foundation International's account of the perspectives of patients and care partners 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 CIDP, health effects and impacts, and treatment experiences, reflect those of the participants. This report is not meant to be representative of the views and experiences of the entire CIDP patient population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.

Glossary
Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
A neurological disorder characterized by inflammation and damage to myelin surrounding nerves, leading to weakness, numbness, and impaired motor function.

Intravenous Immunoglobulin therapy (IVIg)
A therapy that involves a concentrated solution of immunoglobulin, antibodies, administered through intravenous infusion to treat various autoimmune and inflammatory conditions.

Subcutaneous Immunoglobulin therapy (SCIg)
A form of immunoglobulin therapy administered through injection into the fatty tissue under the skin, used to treat various immune deficiencies and autoimmune disorders.

Plasmapheresis or Plasma-Exchange
A therapeutic procedure that involves the removal, treatment, and return of blood plasma to the body, often used to remove harmful antibodies or toxins in conditions such as autoimmune diseases or certain neurological disorders.

Summary of Discussion, arranged by Speaker

Dr. Jeffrey Allen, Chair of GBC|CIDP Foundation Global Medical Advisory Board

Topic Presented: Brief Overview of CIDP

- Presented the clinical characteristics of CIDP
- Patients often present with weakness and numbness, clinical examination typically will find reduced reflexes and motor and sensory deficits.
- Noted that severity of CIDP is a spectrum, but nearly half of CIDP patients experience a level of disability that impedes their independence.
- Though the cause of weakness and numbness is the result of inflammation around the nerves and/or myelin damage, what triggers the immune system to cause this damage is unknown and an area for further research.
- There are a few proven effective treatments for CIDP, including immunoglobulin (Ig), plasma exchange, and corticosteroids, but some patients either do not respond to treatment or partially respond; there are a few evidence-based pathways to take for treating CIDP patients.
- The current goal for treatment is to reduce symptoms for patients and encourage a new sense of normal for patients.
- Despite some proven effective treatment options, there are still many unmet needs for patients; the lack of a biomarker for disease activity and diagnostic guidance, the prevalence of disability for patients despite adhering to treatment, and the substantial burden of current treatment options.

Patient Panelist: Jon

Topic Presented: Frequent Relapses while Managing Other Health Issues Despite Continuous CIDP Treatment

- Diagnosed in 2015 after experiencing symptoms of muscle spasms and weakness that accumulated over the years
- Was treated with steroids which did not help his condition and left him with no reflex ability from the waist down
- Changed treatment to intravenous immunoglobin (IVIg) where infusions started at 6 hours/day for 4 days in a row and then maintenance infusions twice a week for 6-8 hours/day
- Improvements were not immediate, but eventually saw gradual improvement after 5 months
- Eventually experienced a relapse of CIDP with different symptoms, which included poor breathing and difficulty walking
- Described the experience as walking with a 75-pound backpack
- The schedule of infusions changed from every 8 weeks to every 4 weeks to improve the impact of IVIg.
- Mentioned that he prefers infusions in a center versus home-infusion
- Was diagnosed with lung cancer and was forced to allocate time to take treatments for his lung cancer and CIDP

Patient Panelist: Lynn

Topic Presented: Difficultly with CIDP Treatments

- Described herself as previously an athlete until she began experiencing a sudden onset of severe weakness and numbness.
- Originally misdiagnosed with Guillain-Barre Syndrome (GBS) after experiencing tingling in her fingers, feet, and tongue until it started to paralyze her
- Was hospitalized for four months, given five courses of IVIg (which did not stop or reverse symptoms), and waited for doctors to see results
- Went to rehab where her physical therapists and occupational therapists advocated that she did not have GBS but rather that she had a chronic condition; this turned out to be true, and she eventually confirmed the CIDP diagnosis.
- Found that typical CIDP treatment was not improving her symptoms
- Eventually received seven courses of plasmapheresis over four months, which was the only treatment protocol that stopped the progression of her symptoms.
- Described her dependence on plasmapheresis, noting that between plasmapheresis sessions, she starts to feel her symptoms returning
- Mentioned that she believed that her rapid case of CIDP symptoms was helpful in accelerating the diagnosis process unlike the typical presentation of CIDP which is slow and gradual
- She noted the emotional burden, saying that every time she tries a new treatment option she is at risk of paralysis.
- Described a time where a new treatment protocol was attempted, she experienced a relapse of symptoms, and it took 3 months to return to her previous level of functioning

Patient Panelist: Diana

Topic Presented: Complications from CIDP and Medication Brand Dependence

- Diagnosed at 4 and ½, Diana experienced the symptoms of CIDP for over 40 years.
- Relapsed at age 6 and was treated with Prednisone and Physical Therapy
- Relapsed again at 27 after her legs gave out walking down a hallway at work; she then progressed to feeling numbness and weakness with an obscure feeling of pins and needles.
- Experienced a cycle of doctor's denying and reconfirming her CIDP diagnosis during her relapse
- Received IVIg regularly and then switched to SCIg until her preferred Ig brand was discontinued
- Experienced an allergic reaction to an agent in the new Ig brand she was given, which resulted in aseptic meningitis
- Went for a few years without Ig treatment due to fear of the allergen. Instead, she treated relapses with steroids until eventually gaining enough confidence to try Ig therapy again, finally using SCIg. SCIg helped to control her CIDP symptoms without any allergic reaction.
- Described a chronic migraine disorder, which she feels may be related her aseptic meningitis
- Mentioned that she currently believes she is in remission after being stabilized, but still has fatigue and weakness persist in her day to day

Patient Panelist: Crystal
Topic Presented: The Emotional Toll of CIDP Relapses

- Diagnosed 10 years ago and received IVIg every three weeks
- Experienced a relapse that was very severe, and it made her doctor want to try other treatments like plasmapheresis, chemotherapy, and steroids. These alternative options did not stop the progression of CIDP symptoms and left her with paralysis and depression.
- Begged her doctor to be put back on IVIg and had to see 3 doctors to finally be heard
- Had a hard time learning how to walk again at 55 with IVIg infusions every week
- Still experiences PTSD when going to the hospital for visits or treatment, especially when she gets the identification bracelet put on
- Because of insurance issues out of her control, she went without infusions for 2 months and this resulted in another severe relapse and exacerbation of her symptoms
- This experience led to a "downward spiral" where her base line of functionality dropped, and she was left with permanent axonal damage to her calves.
- Was put on anti-depressants and sees a therapist for anxiety
- Cut her hair short because of her persistent muscle weakness and to feel more control
- Described her belief that her experiences and relapses caused her husband to have a heart attack from stress

Patient Panelist: Corbin
Topic Presented: Frequent Relapses and Progressive Disability Despite CIDP Treatment

- Diagnosed in 2015 with the classic presentation of CIDP where he lost strength and tactile function while enduring a heart condition
- Received a nerve biopsy as part of the diagnosis process
- Received IVIg and started to recover some functionality but still had numbness in his feet and hands
- In 2018, he had to switch insurance providers and through a long process of approvals and reapprovals he did not receive IVIg for months that delay resulted in a relapse of symptoms.
- He describes this relapse as pain "creeping" back with spasms, feet burning at night, failed hand coordination, and being forced to use a cane.
- It was difficult to get an appointment with the neuromuscular doctor and he had to have many diagnostic tests to verify his relapse of CIDP. By the time he received IVIG, he was using a rollator to get around. To reverse all of that was a challenge because he had to be on higher dose of IVIG.
- He switched to SCIg after experiencing more cardiovascular symptoms from taking IVIg.
- He relapsed again this year when there was an insurance change leaving him without Ig for several weeks.

Patient Panelist: Julie

Topic Presented: Dependence on Treatment and Personal Experience with a Clinical Trial

- Diagnosed at 28, Julie has been dealing with CIDP for 29 years
- She has tried every treatment from prednisone to plasmapheresis, yet IVIg is the only thing that works.
- For the last 29 years she receives IVIg at home every two weeks for 5 hours /day.
- Her initial infusion time was 8-9 hours/day.
- She had two kids when she was diagnosed, her husband had pancreatic cancer and passed, and was forced to work to provide for her kids and get insurance.
- She cannot go more than a week past her scheduled infusions before feeling the symptoms of CIDP take over.
- She has permanent nerve damage that leaves her hands curled and unable to straighten.
- She showed in the session that if she can't move her fingers, she knows she is reverting to paralysis.
- She has no strength to snap her fingers, but even the ability to simulate a snapping motion is a blessing to her.
- She uses Ankle-Foot Orthosis devices (AFOs) to move around in her home but needs a motorized wheelchair to go longer distances.
- Once when she was switching insurance providers, she was waiting to get approval for IVIg, she got so desperate that she considered self-infusion with an older vile of IG and self-accessing her port.
- Julie participated in a clinical trial once and did so with the optimism of finding a treatment option other than IVIg. The trial required a washout period, which initially was scary, and she began to feel the CIDP symptoms (weakness) return by the 4th day of the washout.
- During the trial, she was getting a shot every week, and the medication did not reduce her CIDP symptoms.
- By the third week of the trial she experienced hand tremors, an inability to feed herself, and deteriorating motor skills; this was 17 days beyond her typical treatment schedule.
- A loading dose of IVIg helped her recover from the setbacks she experienced during the trial, yet it took 6 months to get back to her previous level of functioning.

Commonality Among Panelists

When a new treatment is tried or there is a shift in their typical treatment schedule, symptoms may reappear or worsen, and it will often take them months to recover or return to their previous quality of life.

Questions Posed to Panelists:

1.Does your interest in participating in a clinical trial depend on whether a placebo group is included in the trial design?

- The first patient responder, Julie, said she was willing to try another trial if there was rescue medicine. She emphasized that she would be hesitant but is committed to altruism and helping the community and finds the risk to be worth the overall benefit for the community.
- The second responder, Lynn, noted that her willingness to try a trial is dependent on being able to cross over to the treatment arm or have immediate access to, in her case, plasmapheresis and that she would have to look at the calendar to determine if worsening symptoms from a washout or placebo fits into her schedule. It can take months and months to come back, but her baseline wouldn't be the same. She would have to look at what is going on with her family to see if she could help move things forward for other patients. She also remarked that she would be worried about her base line functionality decreasing.

2.What concerns you most about the risk of CIDP symptoms relapsing? (i.e. feeling the symptoms, progressive disability, not getting the symptoms under control)

- The first patient to respond was Corbin, and he discussed the unpredictability of recovery time and rest from CIDP relapses. He also discussed the difficulty of accepting a new normal after a relapse and the worry that he might not get back to the level of functionality he had before the relapse started. Corbin explained that when he relapses, everything falls off and it can be discouraging, mentally draining, and physically exhausting. As a result, he has an inability to get proper rest when his CIDP symptoms relapse or flare up.

- The second patient to respond was Diana, who expressed her anxiety when undergoing another relapse and restarting IVIg. After her first diagnosis, she gained permanent nerve and motor damage that she never recovered from because of a delayed IVIg treatment. She has a permanent foot drop and missing calf muscles due to nerve loss, so the experience of going through the diagnostic process again and restarting IVIg was both mentally and physically taxing. Even though some nerve damage can be reversed over a long period of time, she is concerned with the possibility of experiencing lesser functional ability with more weakness, fatigue, and sensory deficits. In her experience, fatigue can be the most overwhelming during a relapse. Lastly, Diana worries about losing her quality of life when treatment is delayed or withheld because it can mean the difference between walking independently and needing assistive devices like walkers and wheelchairs. Her new normal is not as good as it was.

3. If you could have one symptom of CIDP "cured", which symptom would it be, and how much of a risk would you be willing to take? (A lot of risk, some risk, minimal risk)?

- The first patient to respond was Crystal, who emphatically responded that fatigue was the one symptom she wishes she could have cured because she felt like it would help her cope better with the other CIDP symptoms. She described a constant feeling of walking through Jello and that the energy she had at the beginning of the day had to be carefully prioritized. She would accept "some risk" to have this symptom cured.
- The second patient to respond was Jon, who discussed the symptoms of unrelenting muscle spasms and how debilitating that could be in his life. He would accept "minimal risk" to have this symptom cured. Jon explained that his IVIg works well but would be concerned about coming off of it.
- Panelist Lynn pointed out that the responders to this question discussed symptoms not thought of as typical CIDP symptoms, fatigue, muscle spasms. These are not usually symptoms targeted or measured during clinical trials; instead, weakness and numbness are usually the symptoms being evaluated during clinical trials.
- The third patient to respond was Corbin, who explained that out of all his symptoms he would want his strength back. Spinal stenosis and significant arthritis have been adding to his pain and overall disability, and having some strength and energy back would make these other things more manageable.

The following questions were asked of the panelists by FDA attendees in the audience:

1.My original question was posed about the most impactful symptom. I heard someone mentioned fatigue. Could some of the other panelists share what other symptoms are outside the typical?

- Crystal expanded on her original answer of fatigue to explain that she would also consider the brain fog and spams as the most impactful symptoms. However, she felt the fatigue was most important to highlight in this scenario because it limits her ability to handle the other CIDP symptoms and is the most disruptive in her life, forcing her to take breaks and getting less done.
- Lynn weighed in and noted that aside from the frequent paralysis, she experiences regular vestibular headaches that affect her blood pressure and make it hard for her to get out of bed for days. She believes that most doctors see it skeptically and do not treat the headaches accurately as they relate to her CIDP.
- Julie experienced horrible pain in her feet which would feel as though they were on fire, prickly. She stated that if she could cut her feet off, she would feel better. She said people with CIDP must work twice as hard to do basic things. More specifically, her brain must work double time to lift a foot up. When things should be done automatically, it requires twice as much energy.
- Corbin described his symptom impact, noting that he experiences brain fog and mental fatigue in addition to pain. He remarked that treating the pain can increase the brain fog, so that he is constantly weighing whether to push through the pain for more mental acuity or to treat his pain. He noted that constant decision-making on this matter is difficult and draining.

- Diana noted that, like Crystal, fatigue and low endurance are her hardest struggles. She described the emotional roller coaster of feeling good at the start of an activity, and then feeling negative as fatigue sets in. Jon described the impact of weakness, which impacts his ability to walk, especially in airports. He noted that the more weakness he has, the more difficult recovery is on a day-to-day basis.

2.Are there any issues related to access to treatment that impacted your condition?

- Corbin responded by sharing that all of his relapses occurred when his scheduled infusions and subcutaneous medication were disrupted by insurance's administrative issues, such being forced to switch to other brands of IG and having approval difficulties. When people with CIDP do not receive their treatment on time, they relapse. This can be difficult to bounce back from and can be detrimental to the body and mind.
- Crystal shared the burden placed on her to go through every tier of medication established by her insurance before being put on IVIg, the only treatment that works. Crystal described the increasing disability that she is left with because of the tiered system of trying less expensive medications.
- Julie explained that when an IVIg product was recalled, she was glad she had to switch because she was then on the same product for a long time. Initially, it was scary when she received a notification from her insurance. Luckily, it was a quick change, unlike many others she's heard of doing a brand switch.
- Lynn shares that she experienced hardships with insurance rejections and forced peer to peer consults just to try a medication. She described a scenario where she was at the hospital for a medication dose, but the infusion was halted because of an insurance administrative protocol or error. Had the infusion not been halted, her hospital bill would have been crippling. She shared a similar experience when a new insurance did not get through the plasmapheresis approval quickly enough and now has an extremely high medical bill.

- Corbin expressed his concern that his preferred brand of IVIg will eventually stop working and he advocates for research in understanding why. His only current options are to switch brands that may or may not work. This change is very scary and if he had more options, he would not be fearful of going back into paralysis.

Patients Represented

- **Ages**: Participant ages ranged from 50-80 years of age
- **Experience**: Participants have experienced CIDP ranging from 7 to 46 years
- **Disease Severity**: All participants have some variation of debilitating nerve damage and range from needing to use a cane to needing a wheelchair to move around.
- **Remission**: Only one of the participants is in remission, defined as not currently receiving medical treatment for CIDP, but still living with physical limitations/disabilities. All other participants are on a scheduled cycle of treatment to maintain their condition; these include IVIg, SCIg, or Plasmapheresis

FDA Offices & Divisions in Attendance

Office of the Commissioner (OC) – 3 offices

- OC/OCPP/PAS - Office of Clinical Policy and Programs/Patient Affairs Staff (organizer)
- OC/OCPP - Office of Clinical Policy and Programs
- OC/OCPP/OOPD - Office of Clinical Policy and Programs/Office of Orphan Product Development

Center for Biologics Evaluation and Research (CBER) – 3 offices

- CBER/OCBQ/DIS/PSB - Office of Compliance and Biologics Quality/Division of Inspections and Surveillance/Program Surveillance Branch
- CBER/OCD – Office of the Center Director
- CBER/OTP/OCE/DCEGM/GMB2 – Office of Therapeutic Products/Office of Clinical Evaluation/Division of Clinical Evaluation General Medicine/General Medicine Branch 2

Center for Devices and Radiological Health (CDRH) – 7 offices

- CDRH/OCD – Office of the Center Director
- CDRH/OPEQ/OHTII/DHTIIC – Office of Product Evaluation and Quality/Office of Health Technology II/Division of Health Technology II C
- 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 III B
- CDRH/OPEQ/OHTIII/DHTIIIC – Office of Product Evaluation and Quality/Office of Health Technology III/Division of Health Technology III C
- CDRH/OPEQ/OHTIV/DHTIVB – Office of Product Evaluation and Quality/Office of Health Technology IV/Division of Health Technology IV B

- CDRH/OPEQ/OHTVIII/DHTVIIIC – Office of Product Evaluation and Quality/Office of Health Technology VIII/Division of Health Technology VIII C

Center for Drug Evaluation and Research (CDER) – 10 offices

- CDER/OCD/PFDD – Office of the Commissioner/Patient Focused Drug Development
- CDER/OCOMM/PASES – Office of Communications/Professional Affairs and Stakeholder Engagement Staff
- CDER/OND/ODES/DCOA – Office of New Drugs/Office of Drug Evaluation Science/Division of Clinical Outcome Assessment
- CDER/OND/ON – Office of New Drugs/Office of Neuroscience
- CDER/OND/ON/DNI – Office of New Drugs/Office of Neuroscience/Division of Neuroscience I
- 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 I
- 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

Non-FDA Attendees

National Institutes of Health (NIH)

- NIH/NINDS – National Institute of Neurological Disorders and Stroke

Financial Interests

- Dr. Allen provided the following financial disclosures: Honoraria, consultation fees, advisory board: Alnylam, Annexon, Argenx, Alexion, Astra Zeneca, Immunovant, Immunopharma, CSL Behring, Grifols, Johnson & Johnson, Pfizer, Takeda.
- All other participants did not identify financial interests relevant to this meeting and are not receiving compensation for participation in this listening session.