THE REE WYNN FOUNDATION
Finding a Cure for TTP

Voice of the patient report

Externally-Led Patient-Focused Drug Development Meeting for Immune Thrombotic Thrombocytopenic Purpura (iTTP)

Meeting held virtually on January 26, 2024, 10 a.m. – 3 p.m. ET

Report date: February 10, 2025

Meeting Sponsor

Takeda

Immune Thrombotic Thrombocytopenic Purpura (iTTP) Voice of the Patient Report

The Ree Wynn Foundation provides education and promotes awareness of the rare blood disorder Thrombocytopenic Purpura to reduce the mortality rate and enhance the quality of life of those living with the disorder. This *Voice of the Patient* report was prepared on behalf of the Ree Wynn Foundation as a summary of the input shared by families and caregivers living with Immune Thrombotic Thrombocytopenic Purpura (iTTP) during an Externally-Led Patient Focused Drug Development (EL-PFDD) meeting, conducted virtually on January 26, 2024.

Authors and Collaborators: This report was prepared and submitted on behalf of the Ree Wynn Foundation by: James Wynn, President/Co-Founder, and Fonda Wynn, Chief Administrative Officer, the Ree Wynn Foundation, and by Chrystal Palaty, medical writer.

Consulting Partners include Larry Bauer, RN, MA, and James Valentine, JD, MHS from Hyman, Phelps & McNamara, P.C.

Disclosures: Ree Wynn Foundation is a 501(c)(3), 509 (a)(1) public charity. The Ree Wynn Foundation receives funding from pharmaceutical and life science companies in the form of unrestricted and restricted grants and sponsorship of programs and events.

James Valentine, JD, MHS and Larry Bauer, RN, MA are employed by Hyman, Phelps & McNamara, P.C., a law firm that represents patient advocacy organizations and companies that are developing therapeutics and technologies to advance health. The Ree Wynn Foundation contracted with Chrystal Palaty, PhD from Metaphase Health Research Consulting Inc. for assistance in writing this report.

Technical services: Provided by Dudley Digital Works.

Funding: Support for the ITTP EL-PFDD meeting was provided by the Ree Wynn Foundation and Takeda Pharmaceuticals. In return for financial support, Takeda Pharmaceuticals was acknowledged at the beginning of the meeting and their logo was displayed during the meeting break. Takeda did not provide input into design, planning, coordination, or execution of the meeting nor in the writing of the VOP report.

Report version date: February 10, 2025. **Revision statement**: This document was not revised and/or modified in any way after February 10, 2025.

Statement of use: The Ree Wynn Foundation has the necessary permissions to submit the *"iTTP Voice of the Patient Report"* to the FDA. Linking to this resource from the FDA website does not violate the proprietary rights of others. Permission to link from the FDA website is granted by the Ree Wynn Foundation (https://reewynn.org/).

Point of Contact: Please contact James Wynn, President and Co-Founder, the Ree Wynn Foundation, for questions related to this report admin@reewynn.org.

Dedication

This *Voice of the Patient* report is dedicated to the memory of **Reeshemah Wynn** who suddenly and unexpectedly lost her life from the complications of iTTP on January 4, 2012. Reeshemah dedicated her life to being a good mother, wife, sister and friend. She was incredibly strong and brave. I know that she appreciates the courage of all the TTP Warriors who have shared their stories for the benefit of others.

We also wish to dedicate this to the memory of **Vicki L. Nicolls** whose faith and courage led her to create the Ree Wynn Foundation to offer the hope of a better future for the TTP Community. It is incredibly humbling to carry the torch of such an unselfish and caring person. Our hope is to share the love and dedication that she exhibited in her life and to see her dream of finding a cure for TTP come to fruition.

Contents

Acknowledgements

The Ree Wynn Foundation wishes to thank the many individuals and organizations whose planning and hard work made our immune Thrombotic Thrombocytopenic Purpura (iTTP) EL-PFDD meeting and this *Voice of the Patient* report possible.

Thank you to the many FDA staff who attended our iTTP Externally Led Patient Focused Drug Development (EL-PFDD) meeting on January 26, 2024, and who are taking the time to read this report. Thank you to Karen Jackler, Ethan Gabbour, Lyna Merzoug, Will Lewallen, and all others from the FDA's Patient-Focused Drug Development Staff who skillfully guided us through this process, over many, many months of planning.

Thank you, Larry Bauer and James Valentine from Hyman, Phelps & McNamara, for their expert assistance in planning and moderating our EL-PFDD meeting. Thank you to the Dudley Digital Works media team for the production planning and behind the scenes work that made our meeting a success.

Thank you to our industry sponsor, Takeda Pharmaceuticals for their generous support of our EL-PFDD meeting. Without you, our meeting and this report would not have been possible.

Thank you to the Ree Wynn Foundation board members and volunteers who have given many hours to the planning of our EL-PFDD meeting including Justin Wynn, Chante Wynn, Travis Wynn, Christopher Collins II, Tamyra Bartley, Gary Holmes, and many others. We appreciate you all.

Thank you to all the representatives from advocacy and professional organizations, pharmaceutical companies, federal agencies, universities, and clinical and research centers from across the world for attending our meeting. Thank you to all of the researchers working in labs and clinics all around the world, striving towards a better understanding of TTP science to move us closer to future clinical trials. Our hope is that this meeting will encourage future research and successful new product development for people living with iTTP who urgently need treatments and options.

Finally, a huge thanks goes to our iTTP community, our iTTP warriors and caregivers. Thank you for so honestly sharing your experiences with iTTP. We couldn't have understood this disease or the unmet needs that exist without you. We are grateful for this opportunity to ensure that patient and family perspectives are considered in the drug development and regulatory processes.

iTTP EL-PFDD Meeting Insights

1. **Immune Thrombotic Thrombocytopenic Purpura (iTTP) is a rare, acute, and life-threatening disease, that usually presents as a medical emergency.** iTTP disproportionately impacts females and Black people. Many patients are hospitalized weeks and even months during their first episode.
2. **Most individuals living with iTTP experience a large number of disease-related health concerns.** The most difficult iTTP symptoms include blood clots, strokes, or pulmonary embolisms and many experience anxiety, depression, and PTSD. As iTTP can affect any organ, the presentation can be variable and can include confusion, difficulty speaking, headaches, fatigue, blood in urine, bruises, petechiae, bleeding from the nose and gums and chest and abdominal pain.
3. **iTTP has an enormous disease burden**. iTTP Warriors experience persistent symptoms even in remission. iTTP limits travel, sports and exercise, work, and social lives. Many iTTP Warriors experience a loss of who they were as a person, are unable to plan ahead for the future, have to watch what they wear and are unable to drive.
4. **Many iTTP Warriors experience multiple disease relapses, which are traumatic.** Relapses can be triggered by immunizations, pregnancy, infections, colds, and even stress. iTTP Warriors and their families worry about premature death. Many worry about their next relapse, about symptoms worsening, about impaired thinking and memory.
5. **Most iTTP Warriors have experienced extended hospitalizations. Despite receiving intensive amounts of medical treatments, none of these treatments address the underlying causes of iTTP nor do they cure the disease.** iTTP treatment includes life-saving blood transfusions, plasma exchange, and rituximab (Rituxan) as well as antidepressants or anti-anxiety medications, and many other medications including caplacizumab.
6. **iTTP Warriors undergo extensive monitoring to anticipate and prevent relapses.** Many receive preventative immunosuppressive treatments to stay in remission. Many rely on other approaches to reduce stress and help them manage, including counseling, psychotherapy, support groups, and mindfulness strategies.
7. **Side effects are the biggest drawback of current iTTP treatment approaches**. Treatments are ineffective at preventing relapse, emphasizing the enormous unmet need for better iTTP treatments. Plasma exchange is traumatic and invasive, and the process heightens PTSD. Other treatment drawbacks include high costs, enormous effort and time requirements, administration methods and limited availability and accessibility.
8. **Short of a complete cure, iTTP Warriors would like a treatment to prevent disease progression, to prevent the most serious iTTP symptoms, and to eliminate the need for transfusions.** They also identified many other needs including a need for steroid-sparing treatments, more iTTP information for patients, more attention on finding effective treatments for Black patients, and more research and clinical trial opportunities for all.

iTTP Clinical Summary[1]

What is immune thrombotic thrombocytopenic purpura or iTTP? iTTP is a systemic and potentially fatal autoimmune disorder. The condition was formerly referred to as *idiopathic* TTP, but is now more accurately referred to as *acquired* or *immune-mediated* thrombotic thrombocytopenic purpura. For consistency, this report refers to the disorder as *immune* thrombotic thrombocytopenic purpura.

Who is affected? The annual incidence in United States is about four to 11 cases per million, for an estimated 1,320 – 3,630 cases per year. Average onset ranges from 36 to 51 years of age. The disorder predominantly affects females and disproportionately affects Black individuals. Those who are already living with other autoimmune disorders are at higher risk of developing iTTP.

What causes this disease? There are two types of TTP. Hereditary TTP, also called congenital TTP (cTTP), is caused by an inherited gene variation in the gene encoding the ADAMTS13 protein, and accounts for less than 5% of all TTP cases. iTTP is much more common, accounting for 95% of all TTP cases. This meeting focuses on iTTP, the most common form.

iTTP is caused by auto-antibodies against ADAMTS13. ADAMTS13 is an enzyme that functions to cleave a protein called Von Willebrand Factor (VWF) into smaller pieces. VWF is an adhesion molecule that is released into circulation to stop bleeding at the site of an injury by initiating platelet adhesion. ADAMTS13 enzyme chops VWF into small pieces to prevent inappropriate clotting.

In iTTP, auto-antibodies directed against ADAMTS13 inactivate the protein, either by inhibiting ADAMTS13 activity and/or by enhancing the removal of ADAMTS13 from circulation. The inactivated ADAMTS13 enzyme is unable to cut these ultra-large, ultra-sticky VWF multimers, which then persist in circulation. These result in formation of large platelet-VWF aggregates, which block blood flow, particularly in small blood vessels and capillaries. Reasons for why auto-antibodies against ADAMTS13 develop are unknown, and genetic factors are yet to be identified.

How does iTTP present? iTTP presents as a medical emergency which will lead to death if left untreated. As iTTP can affect any organ in the body, the clinical presentation varies. A blood clot

---

[1] This clinical summary was extracted from the presentations made at the January 26, 2024 iTTP EL-PFDD meeting by **Dr. Long Zheng**, a Professor at the University of Kansas Medical Center and the first to identify a deficiency in the ADAMTS13 gene as the root cause of iTTP, and **Dr. Adam Cuker**, the Director of the Penn Comprehensive and Hemophilia Thrombosis Program and an Associate Professor of Medicine at the University of Pennsylvania.

in the brain can cause headaches, confusion, strokes, seizures, and coma. A blood clot in the heart can result in chest pain, arrhythmias, congestive heart failure, acute myocardial infarction, cardiac arrest, and death. Blood clots in the kidneys, pancreas or bowels leads to severe pain and damage to these organs. Individuals living with iTTP also experience hemolytic anemia, where red blood cells are broken down faster than they can be replaced, and low platelet levels, which can result in uncontrolled bleeding.

How is iTTP diagnosed? Diagnosis is based on clinical symptoms and laboratory findings. Treatment is started even before the ADAMTS13 results are obtained. A diagnosis confirmed by an ADAMTS13 enzyme activity of less than 10%. ADAMTS13 enzyme activity levels of 10-20% are ambiguous, whereas levels greater than 20% point to an alternate diagnosis.

How is TTP Treated? iTTP is fatal if not treated immediately. Treatments can be divided into rescue therapies, and immunosuppression. The initial rescue therapy and standard of care for iTTP is plasmapheresis or plasma exchange, which is administered immediately, while ADAMTS13 test results are pending. Plasma exchange removes anti-ADAMTS13 autoantibodies as well as the ultra-large, ultra-sticky VWF multimers from the patient's plasma. It also replenishes the ADAMTS13 enzyme from donor plasma. Caplacizumab, a newer FDA-approved rescue therapy, involves an antibody fragment that binds to VWF and blocks it from interacting with platelets. While both plasma exchange and caplacizumab can be lifesaving, they do not cure the disease and do nothing to prevent the formation of ADAMTS13 auto-antibodies.

Immunosuppression is typically achieved with corticosteroids and rituximab. Corticosteroids block the formation of the auto antibodies against ADAMTS13, leading to ADAMTS13 recovery and clinical improvement. Rituximab is a steroid-sparing immunosuppressive treatment that depletes B lymphocytes, reducing the production of auto-antibodies and the risk of relapse. Unfortunately, for reasons that are still unclear, rituximab is less efficacious in Black people than in other patient groups. The biological mechanisms responsible for this difference is a critical research question going forward and underscores the need for new disease treatments for all.

What barriers exist for developing new iTTP treatments? During the acute medical emergency of iTTP, health care providers, patients and family members may have a hard time considering clinical trial participation. iTTP is rare, so recruiting a meaningful number of subjects to a clinical trial can be a challenge. This is especially important as diversity and equity need to be considered in the design and enrollment of iTTP clinical trials.

EL-PFDD Meeting Summary

The immune Thrombocytopenic Purpura (iTTP) Externally-Led Patient Focused Drug Development (EL-PFDD) was held virtually on January 26, 2024. The meeting was an important opportunity for the iTTP patient community and the Ree Wynn Foundation to share patient perspectives regarding the symptoms and daily impact of this disease, as well as current and future approaches to iTTP therapies. The meeting was cohosted by **James Wynn**, the president and co-founder of the Ree Wynn Foundation, and **James Valentine**, JD, MHS from Hyman, Phelps & McNamara, P.C.

James Wynn opened the meeting by welcoming all meeting attendees including the members of the US Food and Drug Administration (FDA). He invited iTTP community members to participate through live online polls, telephone call-ins, and by providing written comments through an online portal. James Wynn introduced the first speaker, **Tanya Wroblewski,** MD, the Deputy Director of the Division of Non-Malignant Hematology at the Center of Drug Evaluation and Research at the FDA. In her opening remarks from the FDA, Dr. Wroblewski provided an overview of Patient-Focused Drug Development, described the role of the FDA, and emphasized the value that the patient and caregiver perspectives provide for the FDA. She encouraged patients and families to engage in this process and thanked the iTTP community for their participation.

Dr. Long Zheng, a Professor at the University of Kansas Medical Center presented a clinical overview of iTTP which served as a foundation for the first half of the meeting. **James Valentine** provided an overview of the meeting agenda which is shown in **Appendix 1**. The morning session was focused on *Living with iTTP: Symptoms and Daily Impacts,* and the afternoon session focused on *Perspectives on Current and Future Treatments for iTTP.* The morning session continued with a pre-recorded panel of individuals who shared patient and caregiver perspectives on the symptoms and daily impacts of the disorder. James Valentine moderated a discussion between individuals in a live Zoom panel as well as those who dialed in by phone, and James Wynn read out relevant comments entered through an online portal.

Dr. Adam Cuker, Director of the Penn Comprehensive and Hemophilia Thrombosis Program, as well as an Associate Professor of Medicine at the University of Pennsylvania Hospital, delivered a presentation about the current state of iTTP research and therapies. The afternoon continued with a pre-recorded panel of patients and caregivers who described the many medications and medical treatments as well as other approaches they have required to address iTTP manifestations. Again, meeting attendees had an opportunity to participate in online polling, to call in and submit written comments. To conclude, **Larry Bauer,** RN, MA**,** Hyman, Phelps, &

McNamara provided a summary of key points and **James Wynn** thanked all of the meeting attendees for their participation.

One-hundred and twenty-six viewers attended the livestream, including 30 iTTP Warriors, seven parents or caregivers, 25 other family members, six friends, 18 members from the FDA, five scientists/researchers, 29 from the healthcare industry, three healthcare providers, four from non-profit organizations, and two others.

EL-PFDD meeting attendees used online polling to indicate meeting demographics, shown in **Appendix 2**. The majority of online meeting attendees (56%) were iTTP Warriors, and the rest (44%) were caregivers of someone living with iTTP. All of the attendees were located in the continental United States, half from the US Eastern time zone, with representation from the US Central and Mountain time zones and from Canada. iTTP Warriors represented at the meeting were mostly female (93%), and all were over the age of 19 years of age. When asked about age of diagnoses, 9% were diagnosed between the ages of 13 and 18; almost half, or 48%, were diagnosed between the ages of 19-35 years; a quarter, or 26% were diagnosed between the ages of 36 and 50 years; 13% were diagnosed between the ages of 51 and 60; and 4% were diagnosed at the age of 61 years of age or older. As iTTP is a very severe disease, some of the iTTP Warriors represented at the meeting included those who had passed away.

To include as many patient voices and perspectives as possible, patient comments were collected through an online comment submission portal before, during and for four weeks after the meeting. Meeting discussion questions are in **Appendix 3**, meeting panelists and callers are listed in **Appendix 4**, and online polling results from topics 1 and 2 are in **Appendix 5**. All submitted patient comments are included in **Appendix 6**, with selected comments included in the body of this report.

This *Voice of the Patient* report is provided to all iTTP community supporters including the US FDA, other government agencies, regulatory authorities, medical products developers, academics, clinicians, and any other interested individuals. The input received from the January 26, 2024, EL-PFDD meeting reflects a wide range of iTTP experiences, however not all symptoms and impacts may be captured in this report. The final report and the video of the of the EL-PFDD meeting are available on the Ree Wynn Foundation website at https://reewynn.org/.

Throughout the meeting and in the submitted patient comments, many referred to the disease simply as “TTP” and this was not changed or rewritten and is taken to mean “iTTP”. Individuals living with iTTP refer to themselves as “iTTP Warriors” because of the enormous strength and courage required to live with the disease. The term “iTTP Warriors” is used throughout this report interchangeably with “patients” and “individuals living with iTTP”.

Topic 1 - Living with iTTP: Symptoms and Daily Impacts

At the January 26, 2024 EL-PFDD meeting, iTTP Warriors and their family members shared their perspectives and experiences of living with iTTP through pre-recorded presentations, moderated discussion, online polling, and submitted comments. They described iTTP-related health effects, the impacts of the disease on activities of daily living, and their worries and fears for the future. Several important iTTP themes emerged during the EL-PFDD meeting that were not captured in online polling and are highlighted in **grey**.

Key iTTP Theme: iTTP is an acute and life-threatening disease that usually presents as a medical emergency.

Before experiencing a medically traumatic diagnosis, most patients had never heard of iTTP. Many experienced life-threatening symptoms such as strokes, heart attacks or uncontrolled pain. Others reported waking up in the hospital with no awareness of how or why they were there. Some were originally misdiagnosed with immune thrombocytopenia (ITP) or leukemia before receiving their diagnosis of iTTP.

> Berynes experienced the signs of a stroke. *“I was rushed to the hospital in an ambulance. I must have been in and out of consciousness because I don't remember most of the trip nor the arrival at the hospital. … I regained consciousness around midnight while hooked up to a plasma exchange machine and was briefly told what was happening. I was very confused and not fully aware of my situation.”* - Berynes, iTTP Warrior currently in remission
>
> *“My first incident came about due to four main symptoms, headache that would not go away, the bruising, the petechia rash, and extreme tiredness/fatigue. Those all came together. I ended up at the hospital and three days later I was in a coma. My body just shut down. … I spent six weeks in the hospital trying to get better.”* - Alisa, iTTP Warrior age 39

Key iTTP Theme: Many iTTP Warriors experience multiple disease relapses.

Relapses can be triggered by immunizations, pregnancy, infections, colds, or even stress. Most iTTP Warriors live in fear of their next relapse, and some can recognize when a relapse is about to happen, because of feelings of pain and tiredness or increased menstrual bleeding.

> Le Anne recognizes when she is getting close to relapse. *“I feel as if my inside starts burning up for some reason. ...At first, it was strange, but then it became a pattern. For me, that is one of the first things I noticed. And then, of course, tiredness. But I'm always*

> *tired. At this point, it's just extreme tiredness I experience. … Then of course, the normal joint pain and all that, it gets worse during that time."* - Le Anne, iTTP Warrior, age 69
>
> After Jimmy received an initial iTTP diagnosis and treatment, *"I started …having back-to-back relapses in 2011, 2012, 2013, until I had ultimately major relapse in 2014, which caused me to have to be put into an induced coma to get my body to relax and heal itself. During that time, I had to be put back on steroids, back on the regimen of plasmapheresis, in and out the hospital, receiving treatments and stay multiple stays in the hospital. ... The journey has not been easy living with thrombotic thrombocytopenia purpura."* – Jimmy, iTTP Warrior, diagnosed at 19 years of age

Key iTTP Theme: iTTP Warriors experience persistent symptoms, even in remission.

Both the symptoms and impacts of iTTP persist during remission.

> *"While I'm currently in remission with stable platelet levels in a normal ADAMTS13 range, my ongoing battle persists with headaches, cognitive issues, abdominal pain, and occasional bruising despite the stability in labs. …The frustrating reality lies in the struggle of doctors to explain or effectively treat these persistent symptoms. Referrals to different specialists often result in hesitation."* - Anise, 44-year-old iTTP Warrior
>
> Although Regina has been in remission for almost four years, *"I am always tired, always sleepy, very fatigued all the time. My body still aches. I still have joint pains."* - Regina, iTTP Warrior
>
> *"None of us asked for this. It's absolutely life changing in every way. Many of us are suffering from what I personally call the 'after affects'."* - Sharon, iTTP Warrior

Key iTTP Theme: Some groups – notably Black women – are more likely to be affected and impacted by iTTP.

> *"The existing health disparities in the US healthcare system are widely acknowledged, and iTTP is no exception. Notably, women of African-American descent are seven times more likely to develop iTTP than other demographics."* - Anise, 44-year-old iTTP Warrior

Poll Q1 & Q2

Most living with iTTP experience a large number of health concerns. Blood clots, stroke, pulmonary embolism followed by anxiety/depression, confusion and difficulty speaking are the most troublesome.

Meeting attendees first selected all of the iTTP-related health effects that they or their loved one had ever experienced; each individual selected an average of 8.4 different symptoms, an exceptionally high number. Meeting attendees then selected the top three most burdensome iTTP related health concerns. Poll question results are shown in **Appendix 5, Q1 and Q2**, and are listed below in the order of most burdensome and illustrated with selected patient quotes.

Blood clots/stroke/pulmonary embolism

Blood clots, stroke, and pulmonary embolism as their most burdensome health concern in the polls, and for many, these were their presenting symptom. Some experienced silent strokes as well as transient ischemic attacks (TIA), which are strokes that only last a few minutes.

> Lynda, an iTTP warrior, joined the EL-PFDD from the hospital, where she was being treated for a relapse. She described what her life was like before she experienced her initial stroke, *"I was a perfectly healthy and very active senior. … Suddenly on Easter Sunday, I had a stroke … The stroke was a complete surprise with no advanced symptoms. After the stroke my life drastically changed."* - Lynda, iTTP Warrior, diagnosed at 79 years
>
> Jennifer was preparing to be discharged from the hospital after her diagnosis and initial treatment. *"That day, I experienced a stroke, so I didn't leave and was unconscious for several days. I ended up staying in the hospital for five weeks altogether. I had two strokes and I was moved in and out of the ICU."* - Jennifer, iTTP Warrior
>
> Jimmy had a stroke while waiting in the doctor's office. *"I started having a small stroke, TIA, on my left side while my mother was sitting there talking to me. As we were getting orders to be transported to [the university hospital] for emergency treatment, I collapsed. I woke up three days later not knowing where I was."* – Jimmy, iTTP Warrior, diagnosed at 19 years of age

Anxiety/depression

In addition to ongoing anxiety and depression, many iTTP Warriors experience overwhelm, mood swings, lack of emotional control, post-traumatic stress disorder (PTSD) and panic attacks.

> *"I still struggle with memory issues, speech impediments, and a bad temper. Mood swings, come on without warning. …I am not the same person at all."* - Lynda, iTTP Warrior, diagnosed at 79 years
>
> *"The anxiety of experiencing all the symptoms and not knowing if it is just a headache or is this a 'TTP headache'. Living with this daily causes depression and PTSD. Even though there is treatment like plasma and steroids, just the thought of having to be admitted to the hospital to receive this treatment is traumatizing as well."* - T, iTTP Warrior
>
> *"I feel very alone with this disease. Even though I have friends, family, and support from Ree Wynn Foundation, I feel completely alone. … No one in my life understands how scared and traumatized I am from past episodes or can provide an ounce of solace aside from other patients who are few and far between. I developed panic attacks due to the fear that comes with this disease."*- Jeannette B, iTTP Warrior

Confusion, difficulty speaking

Many iTTP Warriors experience feelings of disorientation, "brain fog", memory impairment, cognitive challenges, attention deficits, and difficulties with speech and finding words. Many continue to experience these symptoms even during remission. During the EL-PFDD meeting, several panelists lost their train of thought or struggled to find words.

> Speech difficulties were part of Beth's iTTP presentation. *"The most disturbing thing was not being able to speak. They would ask me my name and date of birth - two things that should be easy to say. I was trying so hard, but I knew I wasn't saying it right. At one point I realized I was trying to say my maiden name (I have been married since 2006). I also was trying to hard to tell my husband I love him, and I couldn't."* - Beth, iTTP Warrior, age 40
>
> *"I definitely do not feel the same way I did before my diagnosis. I have become more paranoid and anxious about potential iTTP relapses and I have specially noticed persistent cognitive difficulties during my remission, including sudden confusion, mental fog, short-term memory loss, and difficulty finding words when speaking."* - Berynes, iTTP Warrior currently in remission

> *"I would go in Walmart and forget why I would go into Walmart, forget where my keys would be, they would be in my pocket or in my hand, get to a red light, stop, fall asleep not knowing why I would fall asleep."* – Jimmy, iTTP Warrior, diagnosed at 19 years of age

Headaches, distorted vision

Headaches are one of the most common iTTP symptoms selected in the poll and can be triggered by stress. In addition to vision distortion, some individuals see flashes, zig zags and floaters.

> Jimmy experienced excruciating headaches all night and day. *"About six to seven months prior to [diagnosis], I would have these excruciating headaches. … I thought that the headaches that I was experiencing were just [my] sinuses, or allergic reactions, but they were much more than that."* – Jimmy, iTTP Warrior, diagnosed at 19 years of age
>
> *"The headaches that come from the stress … are very real and very impactful. They can limit your ability to do things. … I have a stressful day at work or a stressful day at home with the kids or whatever, it can definitely make those things a lot more impactful to me and a lot more significant in the way they show."* - Rob, iTTP Warrior
>
> *"I began having headaches that were accompanied by flashes in my vision that looked like zigzags. Of course, what do I do? I go straight to Google and I self-diagnosed with an ocular migraine. I did not have a history of migraines before this."* - Beth, iTTP Warrior, age 40

Tiredness

iTTP Warriors experience fatigue; many feel tired all the time, and some require naps to get through their days. Fatigue has impacts on both cognition and memory.

> *"I was just driving home from the store and suddenly became very tired; so tired that although I was less than a mile from home, I thought I'd fall asleep instantly. I made it to the house and went straight to bed and woke up in the hospital six days later."* For Jennifer, the fatigue persists. *"While I felt I was generally improving, I noticed I never felt like I was getting enough sleep. Every time I sat down, I'd fall asleep."* - Jennifer, iTTP Warrior

> *"When I have long days, I am very much wiped out at the end of the day where I will have trouble remembering things. So [iTTP is] very impactful that way, as far as the headaches and the fatigue that come with it as well."* - Rob, iTTP Warrior
>
> *"One thing I struggle with is [that] if you are not in relapse, you can look and act pretty normal to others. But sometimes that normal everyone is seeing is taking a lot of effort on our part. So at the end of the day we can feel more exhausted than most - emotionally, mentally, and physically."* - Beth, iTTP Warrior, age 40

Blood in urine, discolored or dark urine, and stomach pains

Some iTTP Warriors experienced stomach pain followed by the distress of seeing blood in the urine.

> *"My first incident... What was it? Everything. Bleeding, blood in the urine, again, stomach pains."* - Le Anne, iTTP Warrior, age 69
>
> *"While I was sitting in class this particular day in June of 2004, I started having sharp stomach pains, and then I had to use the restroom and my urine was burnt orange."* – Jimmy, iTTP Warrior, diagnosed at 19 years of age

Purple bruises, red spots on skin

Bruises can be severe and frightening. Some experienced petechiae, which are small spots on the skin that look like a rash, but are the result bleeding capillaries.

> *"My first main symptoms were: (1) low grade headache that would NOT go away and lasted for a month or so; (2) lots of bruises on my extremities that came from nowhere; (3) petechial rash on my body; (4) constantly tired. I don't nap unless I'm sick, so that was out of the norm. Symptoms were benign on their own, but problematic together."* - Alisa, iTTP Warrior age 39
>
> Raquel described her aunt's bruises. *"Large in size, probably much bigger than a quarter, discoloration almost as if, and someone else is actually harming you*." She described how her aunt worries, "*Is [this bruise] something that happened because I'm participating in [an activity] or is this another sign of the TTP flaring up?"* - Raquel, niece and caregiver of an iTTP Warrior
>
> *"Some of the symptoms I have witnessed: bruising, small dots on her body and even cold or flu symptoms."* - Wanda, parent of an iTTP Warrior

Chest pain

For some iTTP Warriors, chest pain and difficulty breathing is a first symptom. Some have even experienced heart attacks.

> *"In December 2022, I had symptoms of a heart attack, sharp pains around my heart, tightness in my chest, pain between my shoulder blades and a weakness in my arms. After eight days in the hospital, tests proved that I had a healthy heart and it's just TTP acting up."* - Lynda, iTTP Warrior, diagnosed at 79 years
>
> *"But what really sent me to the hospital was that my heart began to... I felt as if I couldn't breathe. I also had a heart attack when I was 34 years old."* - Le Anne, iTTP Warrior, age 69

Bleeding from the nose or gums

This frightening symptom is often the first one that some patients experience.

> *Kenisha described her iTTP diagnosis as "The scariest thing that I have ever been through. I was sick for about a week and felt like I had the flu. I constantly kept waking up with different symptoms that kept progressing over time. … The biggest thing that made me go to the hospital was seeing blood just constantly coming from my gums and red dots all over my body."* - Kenisha, iTTP warrior, diagnosed at 18 years of age

Other iTTP health concerns

iTTP Warriors described experiencing many other iTTP-related symptoms that were not included in the poll responses. These include **dangerously low platelet counts**, **heavy menstrual bleeding**, **insomnia, sleep apnea**, **alopecia**, **susceptibility to infections** including longer colds and fevers, **vision loss**, **chronic pain**, **psoriasis**, **numbness and tingling**, **kidney and cardiac damage from blood clots**, **lupus** and **fibromyalgia**.

> *"Large patches of my hair started falling out. My doctor said it was from stress on the body and it would grow back, but I lost a huge amount of hair, like over 50%. My hair is still growing back, although it's a different texture now. It feels thicker it and it has a tighter corkscrew curl. It's been over two years with no haircut and it's half as long as it was before."* - Jennifer, iTTP Warrior
>
> *"I get mysterious symptoms that are possibly due to TTP. No one seems to know. In the spring I developed psoriasis all over my body. Severe hip, back and knee pain recurs*

> *without warning, and I have to go to the urgent care for relief. Once again, my ADAMTS13 score is only 9%, the critical level even though all of the other blood work is normal."* - Lynda, iTTP Warrior, diagnosed at 79 years
>
> *"Headaches, fatigue, and numbness in my hands and feet have been the most troublesome symptoms since my diagnosis that I still deal with today."* - T, iTTP Warrior

POLL Q3

iTTP has an enormous disease burden. Traveling, playing sports, exercise, work and attending social events are the activities of daily life that are most impacted.

Meeting attendees used online polling to select the top three activities that they or their loved one are not able to do or struggle with due to ITTP. Poll question results are shown in **Appendix 5, Q3** and are illustrated below with selected patient quotes.

Traveling

During the EL-PFDD meeting, traveling was selected in the polls as the activity most impacted by iTTP. Many are reluctant to travel and risk an injury or infection which may trigger a relapse. Some are afraid to travel to countries where treatment is unavailable. Some practice extreme caution and pack of all the additional medications required to treat a flare-up or relapse, know where the nearest hospital is located, and even carry detailed treatment instructions from their hematologists just in case.

> *"I went on a cruise. I got a cough while I was out there, and I still haven't got my voice back from it, but I was so scared on that cruise. I was like, 'Oh, my gosh, I'm not going to make it back.' It was so scary. I was sick for so long when I got back. It makes me sometimes scared to really live life. …I'm tired of being afraid."* - Regina, iTTP Warrior
>
> *"I cannot travel to countries that do not treat TTP. A flareup in a foreign country may lead to my demise."* - Le Anne, iTTP Warrior, age 69
>
> *"I love going to the beach. … It's hard because I don't want to risk getting any small cut. … I still go on vacation. I'll just get my blood counts checked before. … I try not to stress about it with the PTSD, the depression and all that because I don't want it to run my life, but unfortunately, it still does."* - Samantha, iTTP Warrior diagnosed at 18 years of age

Playing sports or exercising

Many living with iTTP are unable to play their favorite sports or even exercise because of the potential for injury, bruising and bleeding. For some, exercise now leads to very sore muscles, headaches, and very slow recovery times.

> *"I stopped all strenuous exercises for the fear of falling or bleeding. …I really miss traveling and biking and kayaking."* - Lynda, iTTP Warrior, diagnosed at 79 years

> *"I have noticed a significant change in my body mentally and physically. For example, I am less active as I used to be. Before I got sick, I played basketball, ran track, and did dance."* - Kenisha, iTTP warrior, diagnosed at 18 years of age

> Rob still hikes but it now takes him longer to recover. *"It can take a good week before I'm able to even get over some of the fatigue that comes from doing that activity, getting more frequent headaches during that week following [hiking]."*- Rob, iTTP Warrior

Working or having a career

iTTP Warriors described a wide range of employment challenges that they face. Brain fog, cognitive fatigue and word-finding difficulties interfere with work, tasks take longer and headaches can be the result. Some iTTP Warriors consider changing to jobs that are less strenuous or have less contact with others to minimize infection.

> *"Working tasks that I used to be able to complete relatively simply and in a short timeframe, now can take two to four times longer just to complete. … My work is not very physically demanding, but it is mentally demanding. I deal with a lot of numbers. … I still do enjoy the work, but it is a lot more taxing on me now. …I often will get the headaches afterwards because of the stress it puts on my thinking."* - Rob, iTTP Warrior

> *"Due to my severe brain fog, I was out of work until late August. I returned on a part-time basis at that point, and in October I went back full-time. My job involves a lot of personal interactions, so it was really difficult because words just would not come to me and I would get worn out halfway through the workday."* - Jennifer, iTTP Warrior

> *"I was involved in a childcare program at a technical school and I couldn't do it anymore. … I did get sick because of all of the little children's germs and everything. It triggered a small relapse that they were able to catch, but it was a shame that I had to stop."* - Samantha, iTTP Warrior diagnosed at 18 years of age

Attending social events with family/friends including going to restaurants

Living with iTTP creates a double risk: individuals living with iTTP are immunosuppressed because of their treatments, and a cold or an infection can trigger an iTTP relapse. As a result, many iTTP Warriors only interact with very small numbers of people. The unpredictability of the disease can interfere with important family events such as vacations and narratives.

> *"I'm afraid to go out in the public because if my rituximab. … Cannot work full time, or travel internationally, or attend social events with large numbers of people. … So, [iTTP] stopped my husband from going places with me. I've accepted that life. I think my family has too."* - Mina, iTTP Warrior living with iTTP for over 30 years
>
> *"I limited contact with friends and dropped out of organizations. For example, I had to resign as chair of the 50th anniversary committee at my church because of my inability to plan and manage special events for a whole year. I felt angry and defeated."* - Lynda, iTTP Warrior, diagnosed at 79 years
>
> Juanita is excluded because of her immune issues. *"It made me feel like sometimes I was just more of a burden to my friends. … It just makes you feel that you don't really fit in that normal world. …I wasn't able to go to the movies with them or go to just friend plans or anything like that. Because it was like, 'well, it's a big place. There's going to be a lot of people. My immune system might not be able to handle the really small things.'"* - Juanita, iTTP Warrior, diagnosed at 13 years of age

Maintaining a home

Many living with iTTP lose independence as they begin to depend more on their family members for care and support, including help with maintaining a home.

> *"My husband's life has also changed as he must help me with housework and take me to multiple doctor appointments."* - Lynda, iTTP Warrior, diagnosed at 79 years
>
> *"[My husband] now has my entire medical file in memory, ready to go at a moments notice in case something happens to me. … I'm not sure I could live on my own and take care of bills and the money by myself if I were to lose my [husband]."* - Alisa, iTTP Warrior age 39

Attending school

Living with iTTP is particularly difficult for those individuals diagnosed at a younger age.

> Samantha was diagnosed when she was an 18-year-old senior in high school. *"I had to be really careful. I couldn't even go to my high school graduation. Back then, you didn't think about wearing a mask. I didn't really know anything of it, so I had to limit my social life."*- Samantha, iTTP Warrior diagnosed at 18 years of age 18
>
> Juanita was diagnosed in grade seven. *"I was out of school for two months. Then after, I only went to my classes. All the big school activities, I couldn't go because my immune system was very weak. … At lunchtime I couldn't eat at the cafeteria with all my friends. I ate at the teacher's lunchroom and I was only allowed to bring one friend. I was not living really your normal teenager life."* - Juanita, iTTP Warrior, diagnosed at 13 years of age
>
> Jimmy needed extra time to complete both his undergraduate and master's degrees. There was no outpatient plasmapheresis at the time, so he kept getting hospitalized. *"I was having so many setbacks and relapses with my iTTP that I was not able to attend school full time. With my undergrad, I graduated three years later. With my master's I graduated about three years later. For both, I had to … have more time to complete my assignments."* – Jimmy, iTTP Warrior, diagnosed at 19 years of age

Other iTTP impacts

ITTP Warriors described the many other ways that iTTP impacts daily life. These impacts range from losing the sense of who they were as a person, an inability to plan ahead for the future, inability to take risks, what they wear and their ability to drive.

Loss of who they were as a person. For many iTTP Warriors, living with iTTP has changed who they are as a person. Some felt that their independence has been compromised, or that they had to grow up too fast, many reported feeling different than they did before their diagnosis.

> *"I felt like an alien. Basically, everything that I knew about life before had changed, and the really meaning of life had really shifted. I felt that I was just not a 13-year-old anymore, ... I felt like I had grown and matured inside, like 20 years. Which in some ways, it was good, but at the same time, I just felt that I couldn't really relate to anyone that was there in my school."* - Juanita, iTTP Warrior, diagnosed at 13 years of age

> *"Despite putting in place strategies to help me navigate my life and work with these difficulties, I often struggle to hang on my sense of self as an independent woman."*- Berynes, iTTP Warrior currently in remission

> *"Having experienced my daughter go through a very traumatic experience of dealing with iTTP has changed her and our lives forever."* - Wanda, parent of an iTTP Warrior

Inability to plan for the future, take risks or make changes. iTTP warriors have challenges with planning vacations and weddings. Some are unable to relocate for jobs, relationships, or to be closer to loved ones because they needed to stay close to their physician or a familiar hospital.

> Kenisha is planning her wedding but is worried that she will have to delay if she has a relapse. *"One of my questions when I was booking my venue was, okay, 'what's the refund look like?' Or 'what if an emergency happens?' …I hope I don't get sick or end up in the hospital before my wedding day."* - Kenisha, iTTP warrior, diagnosed at 18 years of age

> *"I think about it from the perspective that we all want to be able to live the best version of what we consider our lives to be. TTP continues to be a hindrance to that. …Living with TTP, you feel very risk averse. … If you're wanting to relocate to be closer to family, that option goes out of the window because you're thinking, 'Hey, I need to be closer to this doctor because they understand my symptoms and TTP a little bit more.' There's that fear there to make any adjustments or changes in your life at all."* - Raquel, niece and caregiver of an iTTP Warrior

What they wear. Some have to dress to cover a port or bruises.

> *"What type of clothing do I wear today so that I can hide, whether it be a port or the bruises that you have in general. …It's like you're always living on edge. Is something new going to start displaying?"* - Raquel, niece and caregiver of an iTTP Warrior

Ability to drive. Many iTTP Warriors were instructed not to drive themselves to the hospital. Jennifer had to relearn to drive after her diagnosis.

> *"Before I left the hospital, I was told that while I presented as normal, I was not and should not be driving. …I started driving again … about six months, maybe a little more, after I first went to the hospital. I had to practice in parking lots, like teenagers learning to drive. At first, I only drove to doctor's appointments and I slowly built up to longer drives. I still can't multitask in the car like I used to. There's no change in the music station, talking on the phone while I'm driving."* - Jennifer, iTTP Warrior

Poll Q4

iTTP Warriors worry about premature death, followed by worries of relapse and fear of the next episode.

Meeting participants used online polling to select their top three worries about themselves or their loved one's condition in the future. Results are in **Appendix 5, Q4** and are illustrated below with patient quotes.

Dying prematurely

Premature death is the top worry selected by iTTP Warriors and their caregivers. If left untreated, iTTP results in death.

> *"My sister was in great health until January 12th, 2012. She developed a headache, chest pain and nausea. She went into the hospital and was diagnosed with TTP. She was being prepared for a plasma exchange treatment, but was unable to receive it due to developing complications. Sadly, she lost her life. The whole process just took 12 hours. Thankfully, she received a quick and accurate diagnosis so we know the true cause of her death. It was cardiac arrest caused by TTP."* – James Wynn, brother of an iTTP Warrior

> *"We talked about one of the things that patients experience is fear of premature dying. And I think that's something I can certainly say that I've experienced myself. After four relapses and issues with blood clots in all of my major organs, I just have concerns about what does this look like for me? I'm 37 years old and I have two children, I hope to have a long full life."* - Amanda, iTTP Warrior, age 37

> *"I try to continue working and live my life, and constantly it's things that I have to think about in my twenties, like the doctor asking, 'Do you have a will?', making sure my beneficiaries are in order, and things that people my age or my friends have never even thought about yet."* - Kenisha, iTTP warrior, diagnosed at 18 years of age

Worries about relapse and fear of the next episode

iTTP Warriors live with the worry of relapse. Some worry that any new symptom signals the approach of another iTTP episode.

> *"With iTTP, you hope that you don't have another recurrence. Some people have one recurrence, some people have many recurrences or relapses. I moved on with my life, but*

> *two years later, there it was again, another year later there it was again. And I think it's a really tough thing to have that kind of unknown hanging over your head while you're trying to bounce back, live your life."* - Amanda, iTTP Warrior, age 37

> *"My hope for the future is I stay in remission forever. ... I'm in fear each day that if the symptoms are there, my symptoms are still there. … Migraines, forgetting things, focusing, looking for bruises, looking for marks. I hope and wish this fear goes away."* - Joanna, iTTP Warrior, survived four episodes

> *"I continue to live my life even if it's a new normal for me. I do think of the uncertainty of relapse. I think that weighs heavy on me at times and I have to work hard at not letting it overwhelm my thoughts. I often check my skin for petechiae or bruising, but I know it is difficult to truly know when something is worrisome or not."* - Beth, iTTP Warrior, age 40

That symptoms will get worse

iTTP Warriors worry about organ damage from the blood clots as well as damage from long term treatments such as steroids.

> *"When I get a relapse, is my heart going to fail at that point? I think that's one of my biggest concerns moving forward in the future, is as each relapse that you have or each event that you have, how much more damage is being done to your organs, and how much more significant than those impacts are going to be moving forward after that?"* - Rob, iTTP Warrior

> Alisa experiences*, "Anxiety that any symptom is a symptom of TTP. Any headache, tummy ache, general tiredness, sinus issue, etc. EVERYTHING is suspect. It's exhausting knowing your body could turn on you at any moment."* - Alisa, iTTP Warrior, age 39

> *"I worry whenever my daughter contracts a cold or flu or even allergies because you don't know how serious it will be. ... Over time, my daughter has become more in tune with her own body and is able to recognize when things do not seem right to her. My daughter knows when it's time for her to get concerned or when it's to get her lab work done."* - Wanda, parent of an iTTP Warrior

Worsening impaired thinking/memory

> *"I'm worried about relapse and a lot of things, like memory issues. I know there's been some studies done that that's for real. .... Yeah, memory issues."* - Mina, iTTP Warrior living with iTTP for over 30 years

Blood clots leading to stroke or heart attack

> As Mina lives in Canada, she doesn't have access to Caplacizumab, a rescue therapy to prevent clotting. *"My worries: fear of next episode with no access to caplacizumab, dying prematurely, blood clots leading to stroke or heart attack."* - Mina, iTTP Warrior living with iTTP for over 30 years
>
> *"My symptom that had the most significant impact … it all started with a heart attack which they say was triggered by iTTP. Now they say odds are that will be my first symptom if I relapse."* - Karen, iTTP Warrior
>
> *"Some studies have shown that many iTTP survivors suffer from silent strokes. While additional research has demonstrated a higher-than-expected death rate in iTTP patients, often caused by cardiovascular disease or before our expected age of death."*- Berynes, iTTP Warrior currently in remission

Ability to start own family

Many iTTP Warriors worry about being able to start their own family, especially as a pregnancy can trigger a relapse.

> Joanna was told that her greatest risk of relapse was in the third trimester of her pregnancy or just after birth. *"At the beginning of the second trimester, I noticed I wasn't feeling well and [I experienced] petechiae, my biggest warning of them all. My hematology doctor took over and I recovered. I was an inpatient for six weeks."* Joanna's daughter was delivered at 30 weeks and three days, by emergency c-section. "*It makes me wonder if I could try and have another kid, but our bodies change each time we have an episode, let alone after pregnancy."* - Joanna, iTTP Warrior, survived four episodes
>
> *"One sour thought that creeps in my mind is the possible problems I could encounter if I wanted to start a family. I know many women with TTP have had successful pregnancies, but as rare as it is to have this disorder, the possibility still exists to have a high-risk pregnancy."* - Hazel, newly diagnosed iTTP Warrior

> *"As my daughter continues to get older and moving along with her life, I worry about her future. ... Will she be able to have children and if she does, will a pregnancy bring on a relapse?"* - Wanda, parent of an iTTP Warrior

Other iTTP-related worries

During the EL-PFDD meeting, respondents selected other worries in the polls including **needing to quit job**, **stomach problems**, **needing surgery**, and **fear of falling**. These reflect the many impacts that iTTP has on the activities of daily life described throughout this report.

During the meeting many iTTP Warriors and their caregivers expressed worries not included as poll responses including worries about **medications no longer working**, **low platelet levels** and **being too far from a hospital**.

> *"I still have nightmares, and I do have PTSD, I guess. ... What I'm worried about is what if rituximab stops working, and I'm admitted again, what are they going to do?"* - Mina, iTTP Warrior living with iTTP for over 30 years

> *"Unfortunately now, whenever my daughter not feeling well, I begin to worry and this has become a way of life for my family. Not knowing if a relapse is about to happen or taking precautions to make sure certain numbers do not continue to decrease, for instance, the platelet counts or the ADAMTS13. The first sight of bruising and small dots and even cold like symptoms we call the doctor and in most cases lab work is ordered."* - Wanda, parent of an iTTP Warrior

> "*I feel like a ticking time bomb since [TTP] puts me at greater risk for another stroke… I worry about my platelet count and being too far from a hospital."* - Lynda, iTTP Warrior, diagnosed at 79 years

Topic 2: Perspectives on Current and Future Treatments for iTTP

iTTP Warriors and their loved ones used online polling, moderated discussion and submitted comments to describe all the different medications, medical treatments as well as non-medical approaches used for iTTP-related symptom management. They described the most significant drawbacks associated with each approach and articulated their hopes for future ideal iTTP therapies. Several key insights emerged throughout the meeting that were not captured in the polls and are highlighted in **grey**.

Key iTTP insight: Most iTTP Warriors experience extended hospitalizations.

Many iTTP Warriors spent many weeks or months in the hospital when were initially diagnosed, and many spent additional time in the hospital for each relapse. During the EL-PFDD meeting, one iTTP Warrior even called from the hospital, where she was being treated for a relapse.

> Le Anne spent many weeks in the hospital after her initial diagnosis as well as for each of her relapses. *"I spent eight or nine weeks in the hospital, about six or seven weeks in ICU. …I did plasmapheresis, Rituxan, steroids and other normal cocktail of stuff. My numbers were beautiful, went home, and they wanted me to come back the Monday just to do routine blood work. I relapsed again. I had to spend another six weeks in the hospital and then they allowed me to go home."* - Le Anne, iTTP Warrior, age 69
>
> *"I spent almost the whole summer in the hospital … I was in and out the hospital for about a month. Then I returned back to work. Three days later I got readmitted. I stayed there until the end of August where I became an outpatient, which it kept an eye on me before releasing me again."* - Joanna, iTTP Warrior, survived four episodes

Key iTTP insight: Most iTTP Warriors receive extensive amounts of medical treatment, none of which addresses the underlying cause of iTTP.

> *"I was rushed to the hospital on the brink of death. The on-call hematologist recognized iTTP symptoms, prompting immediate plasmapheresis in high doses and steroids to save my life. Rituximab was added later because my TTP was refractory. However, this lifesaving moment did not conclude my journey."* - Anise, iTTP Warrior, age 44
>
> *"My treatment included 20 plasma exchange transfusions, four rituximab infusions, high doses of steroids along with a mountain of other medications. Once discharged from the hospital, I learned how to self-administer complete injections into my stomach and gave myself 30 of them at home. Once finally released from the hospital I still had to go for labs, outpatient treatments and appointments with my hematologist, initially every*

other day, and as time went by less and less frequently." - Berynes, iTTP Warrior currently in remission

Key iTTP insight: iTTP Warriors require extensive ongoing monitoring to try to anticipate and prevent relapses.

Many take a preventative approach to avoiding relapses. Some can feel when a relapse is imminent.

> *"I am able to manage my TTP, by monitoring my blood work."* - Samantha, iTTP Warrior diagnosed at 18 years of age
>
> Le Anne regards monitoring as preventative care. *"Every two weeks I do routine blood work to monitor ... everything. I have come close to relapsing, but the goal of my doctors is to make me stay out of the hospital. … I was only doing the Rituxan every four months and then [my doctor] decided recently to do it every three months, because it's like a pattern: after three months, my [ADAMTS13] numbers begin to really go down."* - Le Anne, iTTP Warrior, age 69
>
> *"I go in for blood work quarterly. I get the full blood panel done. ... I'm able to have some large amount of control over my treatment and my course of action. … With testing, we have been able to catch my flare-ups quicker each time. My last [treatment]was preventative treatment instead of reactive. We managed to avoid a full-blown lapse."* - Alisa, iTTP Warrior, age 39

Poll Q5

iTTP treatment is intensive and includes life-saving blood transfusions, plasma exchange, and rituximab (Rituxan) as well as antidepressants or anti-anxiety medications, and many other medications to address iTTP symptoms.

Meeting attendees used online polling to select all the medications or medical treatments have you or your loved one used (currently or previously) to treat symptoms associated with iTTP. Each respondent selected an average of 3.9 options. Poll results are shown in **Appendix 5, Q6** and illustrated below with patient quotes.

Blood transfusions, plasma exchange

Plasma exchange removes the ultra-large, ultra sticky VWF multimers and anti-ADAMTS13 autoantibodies from the patient's plasma and replenishes the ADAMTS13 protein from donor plasma and is necessary as a life-saving treatment. All iTTP Warriors reported that they had received blood transfusions or plasma exchange as a lifesaving treatment. Most continue to receive plasmapheresis or blood transfusions until their ADAMTS13 levels stabilized.

> *"When I got rushed to the hospital, I was barely responsive and my platelet count was at 14 [x10^6/L], 13%. The doctor realized and recognized that it was TTP, and he basically told my parents that I was going to die in 12 hours if I didn't get the plasmapheresis. He wanted more testing done, but before the test would come back, I would be dead. So he needed to go ahead and put the access in and start plasmapheresis." – Stella, iTTP Warrior*
>
> Berynes was hospitalized for bruising, low platelets and symptoms of stroke. "*Treatment for TTP started right away. An emergency central line was placed and my first plasma exchange transfusion started. I regained consciousness around midnight while hooked up to a plasma exchange machine, and was briefly told what was happening. I was very confused and not fully aware of my situation."* - Berynes, iTTP Warrior currently in remission
>
> *"They had a very hard time inserting the catheter because they couldn't get the bleeding to stop. I was then transported to another hospital for the rest of my one-week hospital stay, where I underwent four plasmapheresis treatments, one blood transfusion, daily caplacizumab injections and rituximab treatments. I do not remember the night of February 17th at all, but my husband has told me the very difficult time that I had during the first plasmapheresis."* - Beth, iTTP Warrior, age 40

Downsides: Plasmapheresis is lifesaving but does not cure iTTP. Both the intrusive catheter installation and the plasmapheresis itself are traumatic for many and some experience allergic reactions to the plasma. The plasmapheresis is often co-administered with steroids.

> *"I had an emergency procedure to place a catheter in my jugular vein so that I could receive lifesaving plasma exchange treatment. Once the ICU physicians initiated the plasma exchange, my body went into anaphylaxis. ... Not only was I in critical condition due to my newly diagnosed TTP, but I also needed emergency treatment to combat the anaphylactic shock. I still have flashes of these memories, but I have learned to compartmentalize the trauma."* - Amanda, iTTP Warrior, age 37
>
> *"I hated every moment of it, because the plasma felt very cold running through my body and I would have an allergic reactions until the doctors decided to run the treatment very slow. When I was transferred to the new hospital, I was very lucky because they had apheresis center inside the hospital. Even though I would still have allergic reactions, I felt a little bit better because the plasma was now warm. The doctors also came up with*

> *a plan to premedicate me before the treatments to prepare my body while receiving the plasma treatments."* - Kenisha, iTTP warrior, diagnosed at 18 years of age

Rituximab (Rituxan)

Rituximab is a steroid-sparing immunosuppressive treatment that reduces the production of auto-antibodies by eliminating B lymphocytes. Rituximab administered during relapses and also preventatively when ADAMTS13 levels are low.

> *"I'm in remission right now, and my hematologist monitors my platelets and ADAMTS13 every three months. If my ADAMTS13 goes to a certain percentage level, treatments are involved, which are … four rituximab infusions, or one dose of rituximab every eight weeks to raise my ADAMS levels back up and prevent them from further decline."* - Anise, iTTP Warrior, age 44

> *Le Anne now recognizes when she is approaching a relapse and receives a preventative rituximab treatment about every three months. "I begin to feel some kind of familiarity, so I do look into that. So far, Rituxan has worked."* - Le Anne, iTTP Warrior, age 69

> *"I'm very blessed. Since 2011, I've been given rituximab every 18 months. It's keeping me alive. … My ADAMSTS13 seems to fluctuate. I could go down to 20, I could be 40. It's all over. When it starts going downhill is when they decide to treat me with rituximab."* - Mina, iTTP Warrior living with iTTP for over 30 years

Downsides: Rituximab needs to be regularly readministered as benefits last for only a few months. A major side effect of rituximab is immunosuppression, which leaves iTTP Warriors immunocompromised and susceptible to an infection which may lead to another relapse. For reasons that are still unknown, rituximab is less efficacious in Black patients, a group disproportionately affected with iTTP. Those who have experienced bad reactions or allergies to rituximab require special administration procedures including in-patient administration, pre-medication, slow infusion drips, close medical supervision.

> *"Rituximab is keeping me alive but compromises my immune system."* - Mina, iTTP Warrior living with iTTP for over 30 years

> *"After receiving rituximab three different times in my life, my doctors no longer recommended the treatment for me, because of the way my body reacts to it."* - Kenisha, iTTP warrior, diagnosed at 18 years of age

> After her diagnosis, *"I received plasma exchanges every day, as well as other medications. I was started on rituximab, but on my second dose I had a very violent reaction, so that medication was stopped."* - Jennifer, iTTP Warrior

Antidepressants or anti-anxiety medications

More than half of iTTP Warriors selected this poll response option, however there were very few comments made during the meeting.

> *"My GP prescribed Pristiq to help with my anxiety. I eventually only had to get blood work done every three months."* - Beth, iTTP Warrior, age 40

Caplacizumab-ydhp (Cablivi)

Caplacizumab (Cablivi) is a newer FDA-approved drug that binds and prevents Von Willebrand factor from interacting with platelets. Cablivi is usually administered in combination with plasma exchange and steroids. Downsides include an increased risk of bleeding as a side effect. iTTP Warriors also mentioned site-related reactions, allergies, and the large number of treatments required.

> *"I went through physical therapy, I tried different medications to help my blood pressure and my heart rate, and I did about 75 days of the daily caplacizumab injections before my ADAMTS13 returned to normal range."* - Beth, iTTP Warrior, age 40
>
> *"Once I was home, I continued on self-administered Cablivi shots for 30 days. This was to reduce the chance of blood clots and help keep the platelet count steady.* - Jennifer, iTTP Warrior

Other medications and medical treatments

Individuals with iTTP selected many other medications in the polls including **blood thinners** such as aspirin or dipyridamole, **blood pressure medications**, **recombinant ADAMTS13**, and **statins**.

> After her diagnosis, Lynda said that she, *"Was forced to take prescription drugs, which included heavy doses of aspirin, statin, and blood pressure pills."* - Lynda, iTTP Warrior, diagnosed at 79 years

Not one of the poll respondents indicated that they had not used any medications or medical treatments.

> Regina is in remission, and is currently not receiving any treatments. Her physician retired, and she is unable to find a new hematologist to treat her iTTP, so she worries about the next relapse. *"I haven't had treatment in four years now, but it's scary because I don't know when the next day is going to come where I might relapse again. They've got all these statistics and being an African-American woman, it's scary."* - Regina, iTTP Warrior

iTTP Warriors described other medical approaches in the meeting that were not included as poll responses. These include **immunosuppressive treatments**, **migraine medications, and chemotherapy drugs** including bortezomib.

Immunosuppressive treatments. Many patients are co-administered corticosteroids to block the ADAMTS13 auto-antibodies. A downside is that they need to be slowly tapered and have both short- and long-term side effects.

> Kenisha's doctor abruptly discontinued her steroids which led to vision loss, an extreme side effect. *"[Steroids] affected my life the most. ... Even though the steroids can make you feel good when you are first on them, they have so many risks and you have to be careful. That's why I make sure to stay on top of my blood work and keep a close relationship with all of my doctors."* - Kenisha, iTTP warrior, diagnosed at 18 years of age
>
> *"In conjunction with plasma exchange, my treatment for TTP includes high-dose steroids, which I like to call the best-worst miracle drug on the planet. High-dose steroids are used to achieve rapid immunosuppression. While steroids work fantastically well at their job, they also wreak havoc on my body due to short-term and long-term side effects."* - Amanda, iTTP Warrior, age 37

Migraine medications. Headache medications don't always work.

> *"My neurologist prescribed newer migraine medication, Ubrelvy and Aimovig, which unfortunately proved ineffective and resulted in side effects, and we discontinued it… we're still trying to figure out effective migraine treatments."*- Anise, iTTP Warrior, age 44
>
> Before her diagnosis, *"I was initially treated for migraine with what they called a migraine cocktail in an IV, while they waited for my blood work to come back."* - Beth, iTTP Warrior, age 40

Poll Q 6

Counseling or psychotherapy as well as other supportive approaches are used to manage iTTP symptoms.

Meeting attendees used online polling to select all the approaches, besides medications and treatments that they were using currently or previously to help manage symptoms of ITTP. Each respondent selected an average of 2.8 options. Poll results are shown in **Appendix 5, Q6** and illustrated below with patient quotes.

Counseling or psychotherapy

Many iTTP Warriors rely on counseling or psychotherapy to deal with iTTP-related anxiety and trauma. Many participate in support groups to connect with others who have experienced difficulties.

> As few children are diagnosed with iTTP, Juanita found support from others who had life-changing experiences. *"I kind of feel like a rare bug. Finding people that had gone through maybe similar life-changing experience, even though TTP was not their life-changing experience, but just relating on that deeper level helped me, even though these were adults. I think sharing that was like, 'okay, I'm actually not that rare'."* - Juanita, iTTP Warrior, diagnosed at 13 years of age
>
> *"I often wonder if I would have the will to follow through with treatment of a third episode. The psychological outfall is extremely hard to cope with. I've been to therapy/EMDR to address this, but it has not been very helpful."* - Jeannette B, iTTP Warrior

Mindfulness/meditation

Many iTTP Warriors rely on mindfulness and meditation as well as prayer, yoga, community support and maintaining a positive attitude to reduce stress and find comfort.

> *"I just keep praying and keep moving forward every day. That's all you can do."* - Regina, iTTP Warrior
>
> *"My doctors and I are vigilant and keeping up-to-date on blood work and keeping stress levels at a minimum to keep relapse at bay. ... I owe my support system so much for helping maintain a positive attitude throughout this journey. My doctors, my family,*

> *friends, coworkers, the Ree Wynn Foundation... they all have given me a new outlook on our chaotic world. They remind me every day that there still are amazing people in the world who care."* - Hazel, newly diagnosed iTTP Warrior

Other non-medical approaches

In the poll, iTTP Warriors selected **physical/occupational therapy, dietary supplements**, like folic acid, **acupuncture**, and **CBD** as approaches used to address and manage iTTP symptoms. Some indicated that they had **not used any non-medical approaches to manage symptoms**. No one selected **genetic counseling** as an approach that they had tried.

> *"I had home-based physical therapy for a few months to work on my memory issues and I was given worksheets and several website activities to complete each day. The brain fog continued. I was extremely tired."* - Jennifer, iTTP Warrior

In addition, during the EL-PFDD meeting, several iTTP Warriors described how they used **sleep machines** for sleep apnea.

> *"I noticed I never felt like I was getting enough sleep. Every time I sat down, I'd fall asleep. I went for a sleep study and they found I needed a CPAP machine. I was told that the TTP likely reset me and now I required this machine to sleep. It took some time to catch up on sleep, but I feel way better now."* - Jennifer, iTTP Warrior
>
> Lynda was first alerted about her sleep apnea by her Apple watch. *"After two sleep studies and months of waiting, I was diagnosed with central sleep apnea, so I sleep with the nocturnal oxygen machine every night. My doctor believes the stroke caused this problem."* - Lynda, iTTP Warrior, diagnosed at 79 years

Polls Q7 & 8

Side effects are the biggest drawback of current iTTP treatment approaches. Treatments are not very effective for preventing relapse, emphasizing the enormous unmet need for more effective iTTP treatments.

Meeting attendees used online polling to first indicate how well their current treatment regimen treats the most significant iTTP symptoms, and then to select the top three biggest drawbacks of their or their loved one's current treatment approaches. The results of both polls are shown in **Appendix 5, Q7 & Q8** and the top responses are described below with patient quotes.

Side effects

Side effects were the top treatment downside selected during the polls and mentioned throughout the meeting. iTTP Warriors described anaphylactic reactions and allergies to plasma exchange and rituximab, immune suppression from rituximab and steroids, as well as side effects from short- and longer-term steroid use, including bone issues, joint damage and vision issues.

> *"I am currently on, every 12 weeks, maintenance infusion of rituximab and every other day steroids usage. … Treatments have had major side effects, [including] weight gain. The treatment has caused just self-esteem issues. … Each day presents a different feel from living with the illness itself, and the side effects of the medication and treatment itself. Some days I don't feel like getting out of bed. Some nights I stay up late from being on steroids since I was 19 years old."* – Jimmy, iTTP Warrior, diagnosed at 19 years of age
>
> Jeannette's side effects persisted even after discontinuing Rituxan: leg pain, heartburn, itchiness due to an antifungal allergy, a cold and stomach bug. *"All of this happened within less than two months after my fourth infusion. This became so stressful I choose to discontinue treatments."* - Jeannette B, iTTP Warrior
>
> Amanda experienced side effects from high dose steroids. *"Side effects I experience include mood changes, difficulty with sleep, excessive hunger and thirst, weight gain, and hair loss. Even now, these symptoms persist in my day-to-day life. I have long-term joint pain and joint damage at 37 years old."* - Amanda, iTTP Warrior, age 37

Treatments are not very effective at preventing relapse

Current treatments are not very effective at treating relapse, and iTTP Warriors have endured multiple relapses. In addition, iTTP warriors selected **not very effective at treating target symptoms** and **only treats some, not all, symptom(s)** in the polls. This is consistent with the results of poll question 7, where most meeting participants indicated that their current treatment regimen treats the most significant symptoms of iTTP only **somewhat**. Some mentioned the unpredictable responses to treatments.

> *"When consuming all these different treatments, you never know how your body may react the next time. You're literally sitting and waiting every day to see if the medication is working or if you went through all of that pain for nothing."* - Kenisha, iTTP warrior, diagnosed at 18 years of age

> *"Then having those relapses going in the hospital and staying six weeks at a time or eight weeks at a time when there was no outpatient plasmapheresis."* – Jimmy, iTTP Warrior, diagnosed at 19 years of age
>
> *"I've had TTP for seven years and it is a constant in my life that shows up without warning and wreaks havoc physically and emotionally for myself and my family. … Over the last seven years, I've experienced four relapses, each presenting their own unique challenges."* - Amanda, iTTP Warrior, age 37

High cost or co-pay, not covered by insurance

Some iTTP Warriors had to deal with insurance companies while they were experiencing a relapse. Others were not able to obtain an injectable Rituxan formulation (injectable versus infusion).

> *"My biggest problem is dealing with the insurance company and getting everything approved in a timely fashion. If my doctor says I need to start treatment on Friday and it's Tuesday, I need this done now. I don't need to fool around with the insurance company, then the pharmacy making sure I get it in the format I want, et cetera. So using a drug like Rituxan for an off-label use like we are for TTP, that is very frustrating."* - Alisa, iTTP Warrior, age 39
>
> *"Most difficult for me is having the insurance to cover my needs when I do have an episode."* - Regina, iTTP Warrior

Requires too much effort and/or time commitment

iTTP Warriors described the extensive amounts of effort and time required for treatment including long hospitalizations, frequent and ongoing plasmapheresis treatments, and lengthy rituximab infusions. They also described the substantial amount of monitoring required.

> *"I've only had one TTP crisis, but the continuation of the plasmapheresis went on for six months."* – Stella, iTTP Warrior
>
> *"I went to the outpatient clinic to have blood work done three times a week. … It's been just over three years since the onset of my TTP at this point. My abilities are still changing and improving. My sense of taste recently returned. And in just the last few weeks, I was told that I can get blood work drawn just twice a year. [Except] of course, prior to a trip out of town or if I'm feeling unwell."* - Jennifer, iTTP Warrior

Route of administration

iTTP Warriors described how plasmapheresis catheters were installed in their neck or legs, which many found upsetting. Some were horrified by the feeling of cold plasma running through their body, others described issues with the saline used for rituximab infusions and some experienced injection site reactions.

> Stella had plasmapheresis for six months and during that time had three different access changes. *"The [first] access that I got was an archaic, big metal piece, put in my leg. … it was very traumatizing and very uncomfortable to have that access put in."* The first catheter in Stella's neck became infected due to her low platelet numbers. *"They had to take that access out and put another access in the other side of my neck for me to have plasmapheresis."* – Stella, iTTP Warrior
>
> *"It has been a journey adapting to many different treatments because most of them are not as simple as just taking a pill orally. They involve medication through IVs and even catheters put in your neck. Being 20 years old and experiencing all of these things is very traumatizing. … I even had to go home from the hospital with a catheter in my neck for three weeks so that I can continue my treatments out of the hospital."* - Kenisha, iTTP warrior, diagnosed at 18 years of age
>
> *"If I have the Rituxan administered in a drip bag with D50 [dextrose] or sugar water, instead of saline, that helps me drastically through the actual infusion process. Saline gives me this dragon breath thing, … you're constantly tasting it, and it's like it comes through the pores of my throat, and it's awful. It causes sinus drainage, which gives you nausea."* - Alisa, iTTP Warrior, age 39

Limited availability or accessibility

Those living with iTTP have a lot of anxiety about obtaining treatment for their condition. Not all hospitals have plasmapheresis units, so many iTTP Warriors are transferred to larger centers for treatment. iTTP Warriors felt that health providers lack knowledge about how to best treat iTTP, and some have been unable to find a doctor who will agree to treat them, which is a very common situation for many in the iTTP community. Others require specialized treatments which are hard to find.

> *"I struggle with treatment due to the providers available. I don't feel they know how to properly treat me, how to troubleshoot issues, signs to watch out for, the effects from Rituxan, etc. It's like being led by the blind."* - Jeannette W, iTTP Warrior

> *"Many local doctors depend on us--the patient--to educate them on how to treat us... that absolutely has to change. It's a rare blood disorder, but in my case, the information and support after being diagnosed, was just as rare. ... In 2021, I had only one hospital option for treatment in the state, for plasma exchange... that has to change."* - Sharon, iTTP Warrior

> *"A team of physicians met and confirmed that in order to continue treatment, they needed a specialized type of plasma called Octaplas. This is not always readily available in hospitals. Octaplas is a solvent-treated pooled plasma that can minimize severe transfusion-related reactions in patients that are allergic to regular donor plasma."* - Amanda, iTTP Warrior, age 37

Other drawbacks of iTTP treatment

In the polls, iTTP warriors also selected **other drawbacks** and **not applicable because not using any treatments**, but there were no relevant patient quotes on these topics.

Poll Q 9

Short of a complete cure, those living with iTTP want a treatment to prevent disease progression/worsening, strokes, bleeds and blood clots, and to eliminate the need for transfusions.

Meeting attendees used online polling to select the top three specific things that they would look for in an ideal treatment, short of a complete cure. The results of both polls are shown in **Appendix 5 Q9**, and the top responses are described below with patient quotes.

Prevent disease progression/worsening

> *"If they could prevent the disease from progressing, that means there'll be less blood clots, less visits to the hospital, less infusions and all that."* - Le Anne, iTTP Warrior, age 69

> *"One of the things I'd like to see is minimizing long-term disease progression. … When I think about long-term outcomes, I think about living a full life. I think about being able to function as a person who can go to work and participate in activities with your family.*

> *And do it in a full way where you're not feeling like you have to proactively manage all of your symptoms at all times and have this fear or worry about your disease consistently relapsing."* - Amanda, iTTP Warrior, age 37

Prevent stroke or bleeds and blood clots

> *"While I am immensely grateful for the research, blood donors and treatments already in place, I deeply wish for additional studies that can help determine what causes such a high risk of early cardiovascular disease death in iTTP survivors, as well as ways to treat and repair the many cognitive impairments associated with this disease that have so radically diminished my quality of life."* - Berynes, iTTP Warrior currently in remission

Eliminate need for transfusion

Many would like a medication that eliminated the need for transfusions. Others hope that their medication can be administered in a pill format or that they

> *"The doctor states my body doesn't produce plasma, so I get it through the IV. I wish there was a daily pill."* - Sandrea, iTTP Warrior

> *"Cablivi … reduces plasma exchange… I know that that group is working really hard at hopefully one day we won't need transfusions. …I would love to have more drugs available for us. I know there's another one coming in the pipe, recombinant ADAMTS13, and I've got my fingers crossed that that's going to be another drug for us."* - Mina, iTTP Warrior, had TTP for 30 years

Other treatment needs

In the online polls, iTTP Warriors selected all of the things they would look for in an ideal treatment including **reduce brain fog**, **help with fatigue**, **restore memory,** and **reduce pain**.

> *"If we had something that would help us with the short-term memory, because I feel like that's seen in everyone. And for a long time I thought I was all by myself. …And I would say memory loss, memory, brain fog. I could be going somewhere and be like, 'Where was I was supposed to be going there? What did I come to the store to get?" I wish they had a magic pill for that."* - Regina, iTTP Warrior

> *"I aspire to see an increase in clinical trials for iTTP patients, exploring drugs that effectively tackle daily symptoms such as migraines and cognitive issues."* - Anise, iTTP Warrior, age 44

> *“My earnest plea is for enhanced quality of care, to less invasive and traumatizing treatments, and treatments to address the daily symptoms and side effects associated with iTTP. … Let us work together towards bridging the gaps in awareness and treatments for iTTP.”* - Anise, iTTP Warrior, age 44

Throughout the meeting, iTTP Warriors identified other important things that need to be addressed for their community. Some of these include a **cure for iTTP**, need for **treatments with less side-effects**, **more effective and steroid-sparing treatments**, **more iTTP information for patients**, **more attention on finding effective treatments for Black patients**, and **more research and clinical trial opportunities**.

Cure for iTTP

This is a wish of all iTTP Warriors and their loved ones.

> *"As the sister of a TTP warrior, it is my hope that priority is given to finding a cure or at very least a sustainable treatment for those suffering with the physical, mental and emotional anguish of this traumatizing and unpredictable disease."* - Cassie, sister of an iTTP Warrior

More iTTP information for patients. Prior to their iTTP diagnosis, most had never heard about iTTP. This meeting emphasized the need for both patient and provider information and education including more reliable disease information, treatment options, and information for recognizing and addressing relapse. Many articulated the need for iTTP treatment guidelines and standards for the medical community.

> *“If there was a care plan in place for us when we do relapse, that would be great*.” - Regina, iTTP Warrior

> *“My hopes for a new treatment for TTP would be more information regarding triggering the onset and possible relapses. We're told there's nothing you can do but monitor your blood work and it's very stressful not knowing when or what might trigger an episode. It would also be helpful to have more consistency and treatment among providers. A universally accepted standard course of treatment would be helpful, so patients know their doctors are taking the most up-to-date actions. Lastly, I would like to see doctors around the country be familiar with serving TTP patients. The limited geographic options for treatment facilities is really disconcerting.“* - Jennifer, iTTP Warrior

> *“We don't have those standards as far as this is how you diagnose it, this is how you treat it, this is how you care for someone with this. A lot of people seem to have these cognitive impairments. There is no real understanding as to, well, ‘you need to make sure*

> *you're going to see a neurologist for some of these things, these are the tests that you need to look at that can measure the impacts of some of these damages to your brain.'"* – Rob, iTTP Warrior

The Black iTTP community is particularly underserved. More awareness is needed about the risk of this disease, particularly in Black women. As well, more research is needed to find better iTTP treatments for Black patients as rituximab, a mainstay of iTTP treatment, is less efficacious in Black people.

> *"Women of African-American descent are seven times more likely to develop iTTP than other demographics. By collaborating with the Ree Wynn Foundation and through social media outreach, I connected with numerous women who, much like me, share both my complexion and struggle. Together we have faced common challenges, including dismissive attitudes from doctors, a dearth of information about the disease, limited treatment beyond the initial iTTP crisis and recurrence of the illness. My hope is anchored in the prospect of rebuilding the trust among the FDA, healthcare providers, pharmaceutical companies, and nonprofit organizations, and the Black community in matters of health."* - Anise, iTTP Warrior, age 44

More research and clinical trial opportunities. During the meeting, iTTP Warriors identified many areas where research and clinical trial opportunities are required. Many Warriors feel that more trials will help with finding a cure. They are extremely interested in reducing the use of plasma exchange as a treatment option.

> *"A concern for me is the lack of research and effective treatments for iTTP symptoms. iTTP is predominantly managed as a hospital condition. … There is an urgent need for more research, particularly clinical trials for BIPOC ITT patients, enhanced provider education, improved access to care, and prioritizing of treatments. Throughout my journey from one specialist to another, I encountered the reluctance in prescribing medications due to uncertainties of the effects on individuals with iTTP. This hesitancy resulting in my prolonged suffering and diminished quality of life."* - Anise, iTTP Warrior, age 44

> *"My journey with TTP has not been easy, and for me participating in research is one of the ways that I find meaning on my path of living with an incurable rare disease. …My big ask and something I look for is continued opportunities for patients with TTP to be able to have research opportunities. Funding for research is so extremely important. We need better treatment options and we need to be able to access the treatment across all spaces in the US and across the globe."* - Amanda, iTTP Warrior, age 37

INCORPORATING PATIENT INPUT INTO A BENEFIT RISK ASSESSMENT FRAMEWORK

The immune Thrombocytopenic Purpura (iTTP) EL-PFDD meeting helped to increase the understanding of how this disease impacts patients and their loved ones and also reinforced the urgent need for effective therapeutics for this disease and related symptoms. **Table 1** speaks to the disease burden that patients living with iTTP endure. It serves as the proposed introductory framework for the Analysis of Condition and Current Treatment Option to be adapted and incorporated in the FDA's Benefit-Risk Assessment. This may enable a more comprehensive understanding of these disorders for key reviewers in the FDA Centers and Divisions who would be evaluating new treatments for iTTP. The data resulting from this meeting may help inform the development of iTTP-specific, clinically meaningful endpoints for current and future clinical trials, as well as encourage researchers and industry to investigate better treatment. Note that the information in this sample framework is likely to evolve over time.

The information presented captures the perspectives of patients and families living with iTTP presented at the January 26, 2024, EL-PFDD. The collective hope of iTTP Warriors and their loved ones, is that this meeting will encourage future research and successful new product development for people living with iTTP who urgently need treatment options.

> *"We hope that you will remember what you hear today and understand the urgent need for new treatments for iTTP."* – James, brother of an iTTP Warrior who lost her life to complications of iTTP

TABLE 1: Benefit-Risk Table for immune Thrombocytopenic Purpura (iTTP)

	EVIDENCE AND UNCERTAINTIES	CONCLUSIONS AND REASONS
ANALYSIS OF CONDITION/ IMPACTS ON ACTIVITIES OF DAILY LIVING	**Immune Thrombotic Thrombocytopenic Purpura (iTTP) is a rare, acute, and life-threatening disease, that usually presents as a medical emergency.** iTTP disproportionately impacts females and Black people. Many patients are hospitalized weeks and even months during their first episode. **Most individuals living with iTTP experience a large number of disease-related health concerns.** The most difficult iTTP symptoms include blood clots, strokes, or pulmonary embolisms and many experience anxiety, depression, and PTSD. As iTTP can affect any organ, the presentation can be variable and can include confusion, difficulty speaking, headaches, fatigue, blood in urine, bruises, petechiae, bleeding from the nose and gums and chest and abdominal pain.	**iTTP has an enormous disease burden**. iTTP Warriors experience persistent symptoms even in remission. iTTP limits travel, sports and exercise, work, and social lives. Many iTTP Warriors experience a loss of who they were as a person, are unable to plan ahead for the future, have to watch what they wear and are unable to drive. **Many iTTP Warriors experience multiple disease relapses, which are traumatic.** Relapses can be triggered by immunizations, pregnancy, infections, colds, and even stress. iTTP Warriors and their families worry about premature death. Many worry about their next relapse and about symptoms worsening, about impaired thinking and memory.
CURRENT TREATMENT OPTIONS/ PROSPECTS FOR FUTURE TREATMENTS	**Most iTTP Warriors have experienced extended hospitalizations. Despite receiving intensive amounts of medical treatments, none of these treatments address the underlying causes of iTTP nor do they cure the disease.** iTTP treatment includes life-saving blood transfusions, plasma exchange, and rituximab (Rituxan) as well as antidepressants or anti-anxiety medications, and many other medications including caplacizumab. **iTTP Warriors undergo extensive monitoring to anticipate and prevent relapses.** Many receive preventative immunosuppressive treatments to stay in remission. Many rely on other approaches to reduce stress and help them manage, including counseling, psychotherapy, support groups, and mindfulness strategies.	**Side effects are the biggest drawback of current iTTP treatment approaches**. Treatments are ineffective at preventing relapse, emphasizing the enormous unmet need for better iTTP treatments. Plasma exchange is traumatic and invasive, and the process heightens PTSD. Other treatment drawbacks include high costs, enormous effort and time requirements, administration methods and limited availability and accessibility. **Short of a complete cure, iTTP Warriors would like a treatment to prevent disease progression, to prevent the most serious iTTP symptoms, and to eliminate the need for transfusions.** They also identified a need for steroid-sparing treatments, more iTTP information for patients, more attention on finding effective treatments for Black patients, and more research and clinical trial opportunities towards a cure.
	See the Voice of the Patient report for a more detailed narrative.	

Appendix 1: iTTP EL-PFDD Meeting Agenda

January 26, 2024, 10 am – 3 pm EST

10:00 – 10:05 am	Opening Remarks and Welcome *James Wynn, CEO and President of the Ree Wynn Foundation*
10:05 – 10:15 am	FDA Opening Remarks *Tanya Wroblewski, MD, Deputy Director of the Division of Non-Malignant Hematology at the Center of Drug Evaluation and Research at the FDA*
10:15-10:30 am	Clinical overview of iTTP *Dr. Long Zheng, University of Kansas Medical Center*
10:30 – 10:35 am	Introduction and Meeting Overview *James Valentine, JD, MHS, Hyman, Phelps & McNamara, P.C.*
10:35-10:45 am	Demographic polling

Topic 1 - Living with iTTP: Symptoms and Daily Impacts

10:45 – 11:10 am	Patient/caregiver panel
11:10 am -12:30 pm	Audience polling and moderated discussion *Moderator: James Valentine, JD, MHS, Hyman, Phelps & McNamara, P.C.*
12:30-1:00 pm	Lunch break
1:00 pm – 1:10 pm	Treatment overview *Dr. Adam Cuker, Director, Penn Comprehensive and Hemophilia Thrombosis Program, Associate Professor of Medicine at the University of Pennsylvania Hospital*

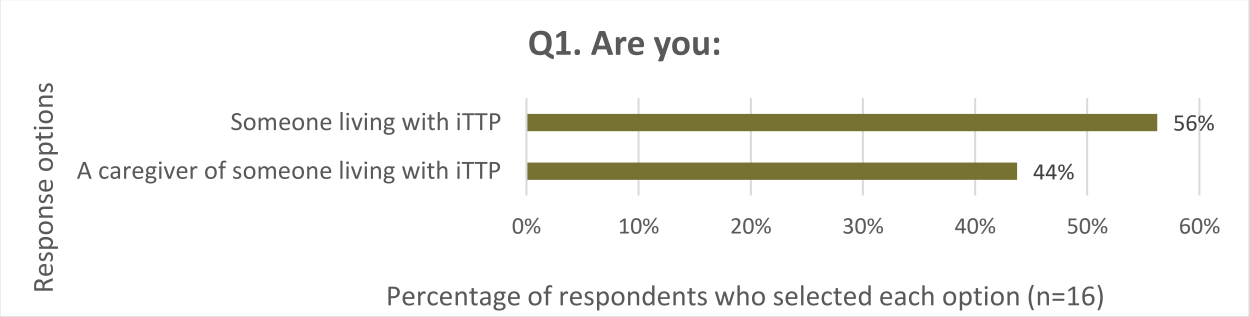
Topic 2: Perspectives on Current and Future Treatments for iTTP

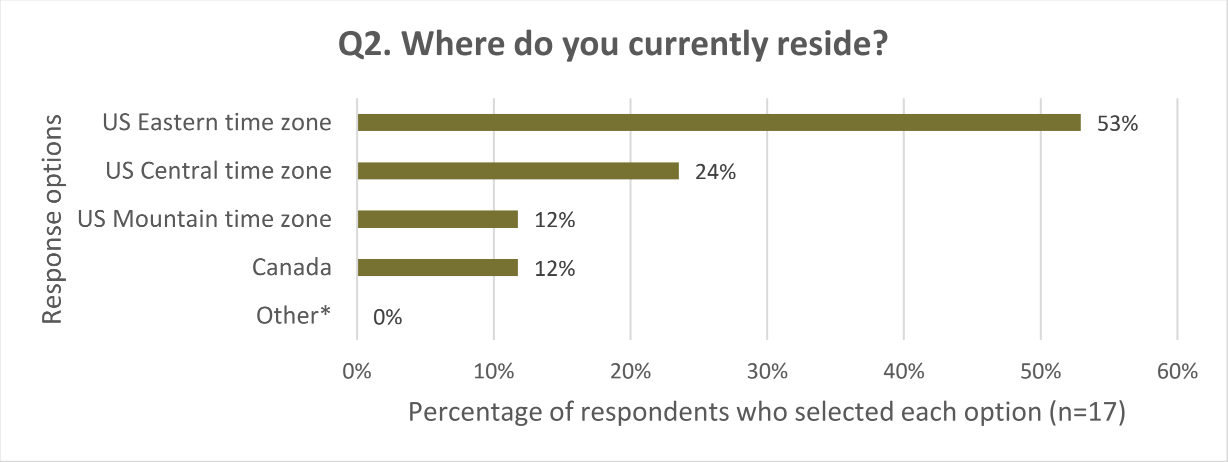
1:10 – 1:35 pm	Patient/caregiver panel
1:35 – 2:45 pm	Audience polling and moderated discussion *Moderator: James Valentine, JD, MHS, Hyman, Phelps & McNamara, P.C.*
2:45 – 2:55 pm	Meeting Summary *Larry Bauer, RN, MA Hyman, Phelps & McNamara, P.C.*
2:55 – 3:00 pm	Closing Remarks James Wynn, co-moderator and CEO and President of the Ree Wynn Foundation

Appendix 2: Demographic questions

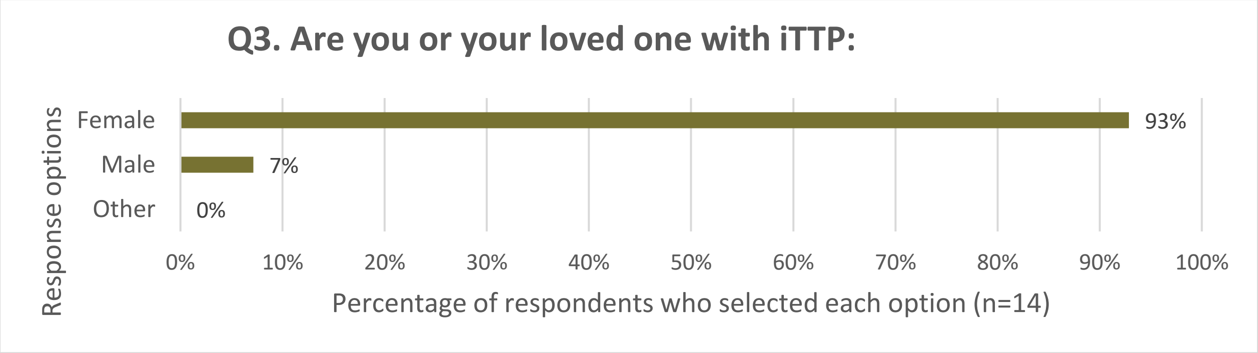
The graphs below include patients, parents and caregivers who chose to participate in online polling at the January 26, 2024, meeting. The number of individuals who responded to each polling question is shown below the X axis (n=x).

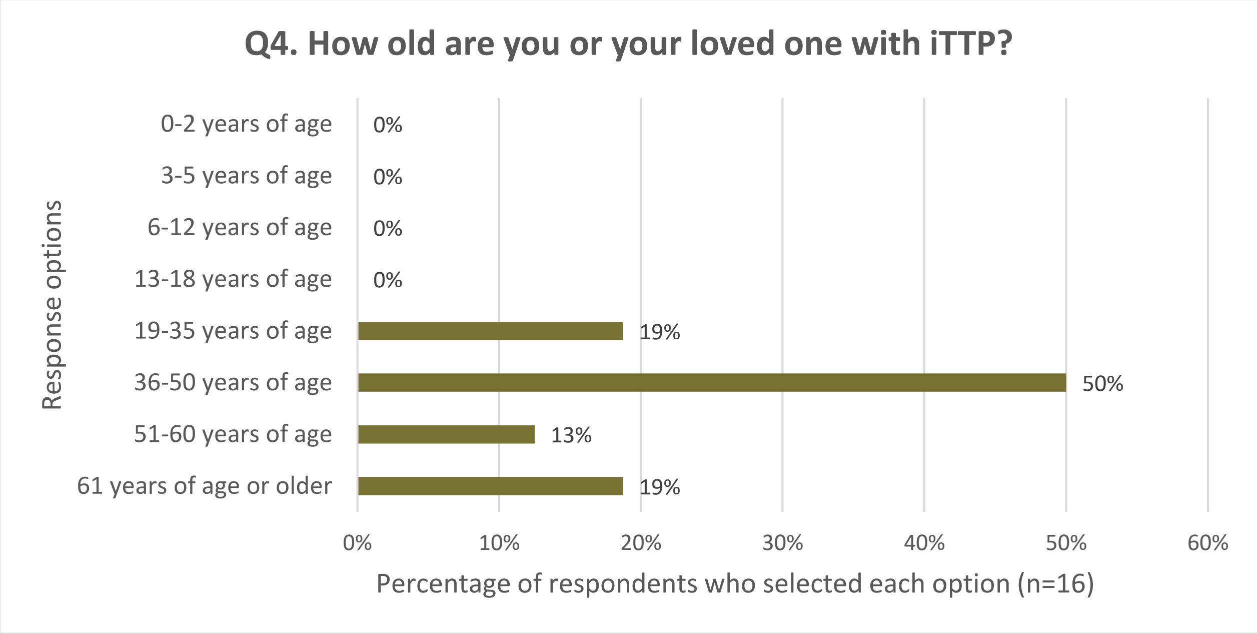
While the response rates for these polling questions is not considered scientific data, it provides a snapshot of those who participated in the ITTP EL-PFDD meeting. Note that meeting demographics are dynamic and may have changed as more individuals joined the meeting.

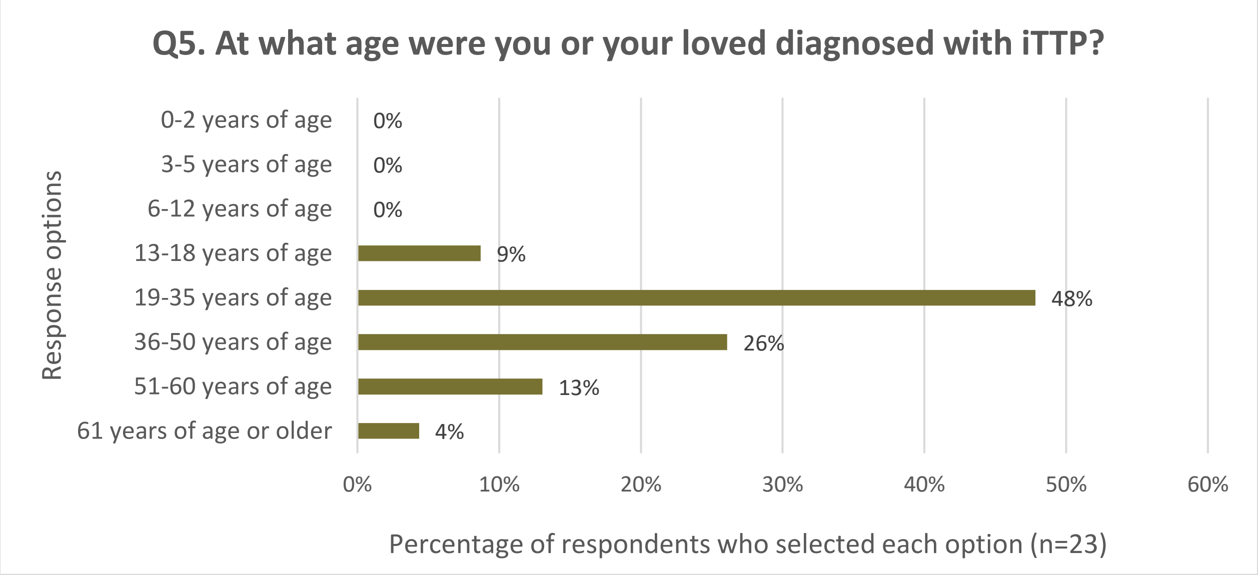




*Includes: US Pacific time zone, US Alaska time zone, US Hawaii time zone, Mexico, Asia, Middle East, and Europe.




Q4. How old are you or your loved one with iTTP?
Response options
0-2 years of age
3-5 years of age
6-12 years of age
13-18 years of age
19-35 years of age
36-50 years of age
51-60 years of age
61 years of age or older
0%
0%
0%
0%
19%
50%
13%
19%
0%
10%
20%
30%
40%
50%
60%
Percentage of respondents who selected each option (n=16)


Q5. At what age were you or your loved diagnosed with iTTP?
Response options
0-2 years of age
3-5 years of age
6-12 years of age
13-18 years of age
19-35 years of age
36-50 years of age
51-60 years of age
61 years of age or older
0%
0%
0%
9%
48%
26%
13%
4%
0%
10%
20%
30%
40%
50%
60%
Percentage of respondents who selected each option (n=23)

Appendix 3: Meeting Discussion Questions

TOPIC 1 – Living with iTTP: Symptoms and Daily Impacts

1. Of all the symptoms and health effects of iTTP, which 1-3 symptoms have the most significant impact on you or your loved one's life?
2. How does iTTP affect you or your loved one on best and on worst days?
3. How have your or your loved one's symptoms changed over time? How has the ability to cope with the symptoms changed over time?
4. Are there specific activities that are important to you or your loved one that you cannot do at all or as fully because of iTTP?
5. What do you fear the most as you or your loved one gets older? What worries you most about you or your loved one's condition?

TOPIC 2 – Perspectives on Current and Future Treatments for iTTP

1. What are you currently doing to manage you or your loved one's iTTP symptoms?
2. How well do these treatments treat the most significant symptoms and health effects of iTTP?
3. What are the most significant downsides to your or your loved one's current treatments and how do they affect daily life?
4. Short of a complete cure, what specific things would you look for in an ideal treatment for iTTP? What factors would be important in deciding whether to participate in a new research trial?

Appendix 4: ITTP EL-PFDD Panelist and Callers

Session 1: Pre-Recorded Panelists
Berynes, iTTP Warrior currently in remission
Joanna, iTTP Warrior, survived four episodes
Lynda, iTTP Warrior, diagnosed at 79 years
Beth, iTTP Warrior, age 40
Wanda, parent of an iTTP Warrior

Session 1: Zoom Panel
Juanita, iTTP Warrior, diagnosed at 13 years of age
Jimmy, iTTP Warrior, diagnosed at 19 years of age
Rob, iTTP Warrior
Raquel, niece and caregiver of an iTTP Warrior

Session 1: Callers
Kenisha, iTTP warrior, diagnosed at 18 years of age
Amanda, iTTP Warrior, age 37
Samantha, iTTP Warrior, diagnosed at 18 years of age

Session 2: Pre-Recorded Panelists
Anise, iTTP Warrior, age 44
Jennifer, iTTP Warrior
Kenisha, iTTP warrior, diagnosed at 18 years of age
Jimmy, iTTP Warrior, diagnosed at 19 years of age
Amanda, iTTP Warrior, age 37

Session 2: Zoom Panel
Alisa, iTTP Warrior, age 39
Le Anne, iTTP Warrior, age 69
Regina, iTTP Warrior
Mina, iTTP Warrior living with iTTP for over 30 years

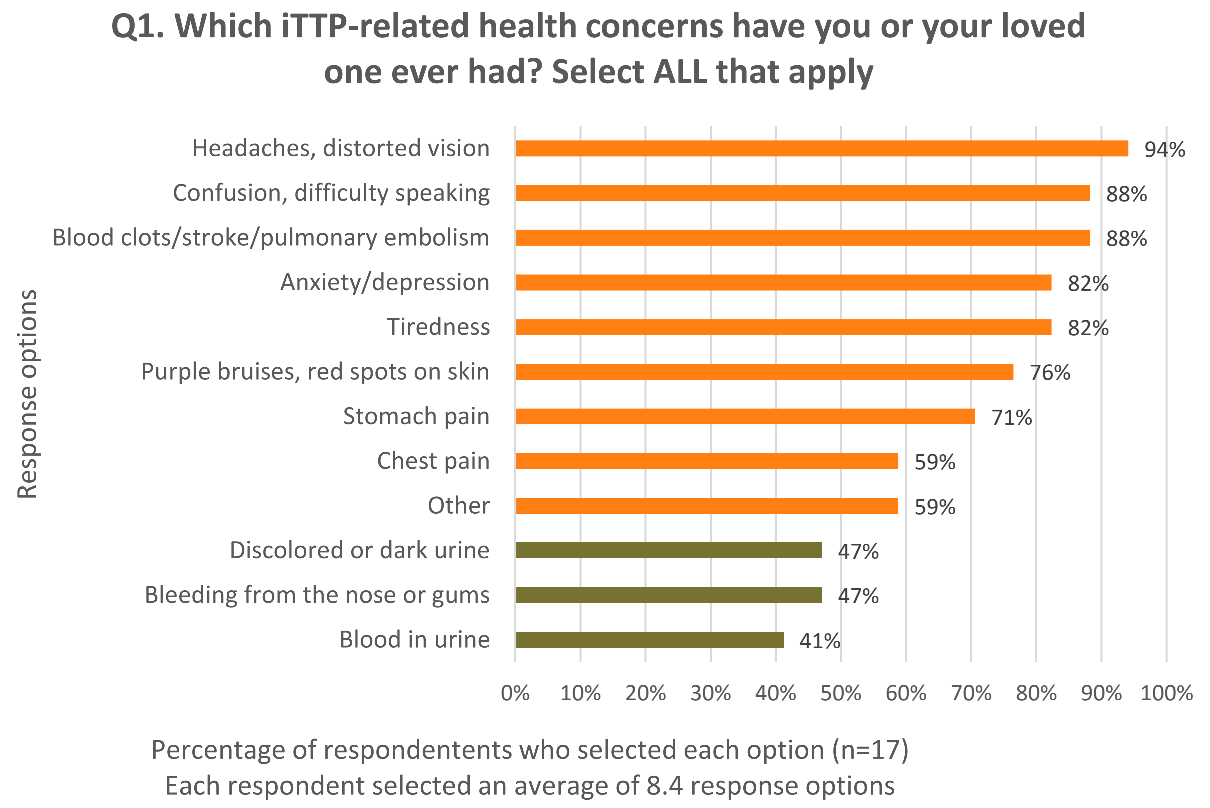
Session 2: Callers
Stella, iTTP Warrior
Lynda, iTTP Warrior, diagnosed at 79 years
Amanda, iTTP Warrior, age 37

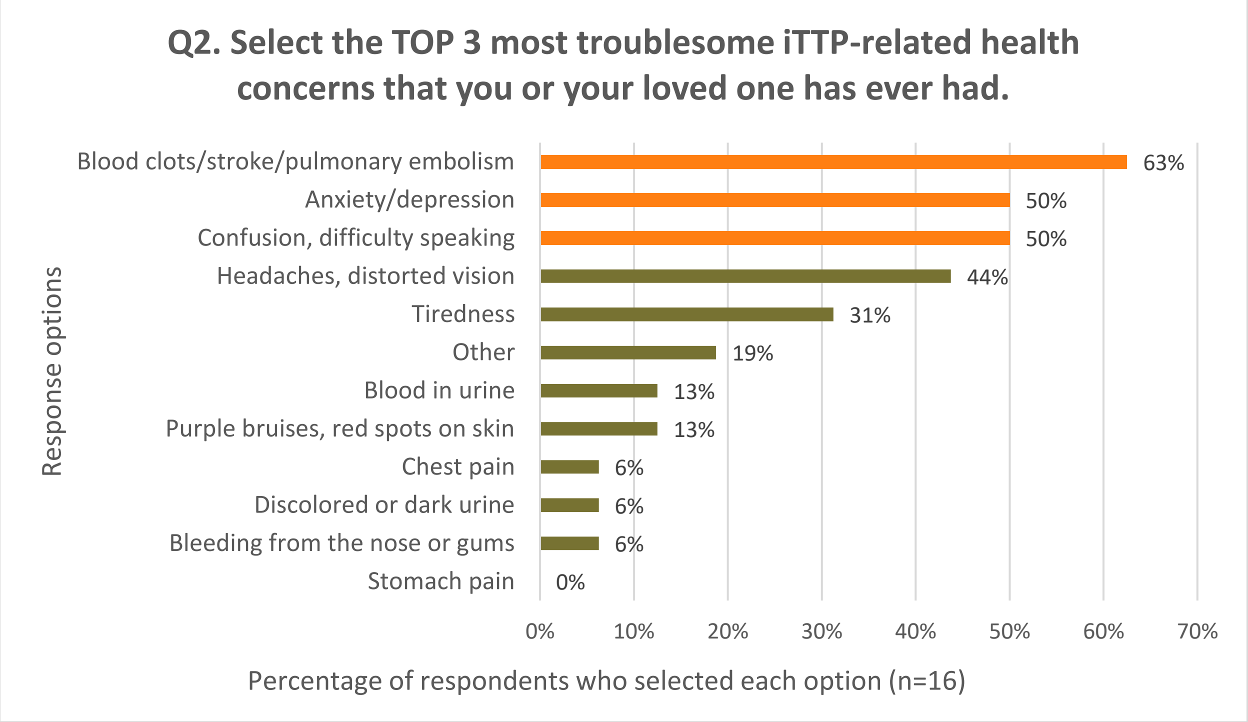
Appendix 5: Meeting Poll Results

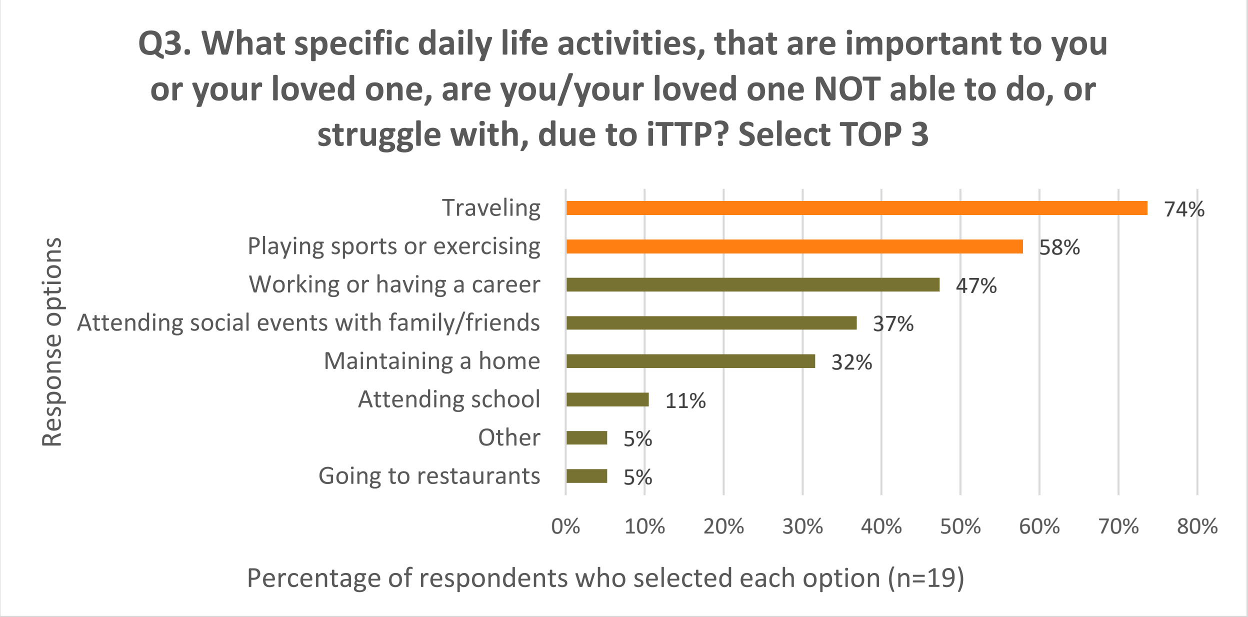
The graphs below include patients and caregivers who chose to participate in online polling during sessions 1 and 2. The number of individuals who responded to each polling question is shown below the X axis (n=x).

Please note that for most questions, poll respondents could select more than one option. The responses for these polling questions are not considered scientific data. These are intended to complement the patient comments made during and after the meeting.

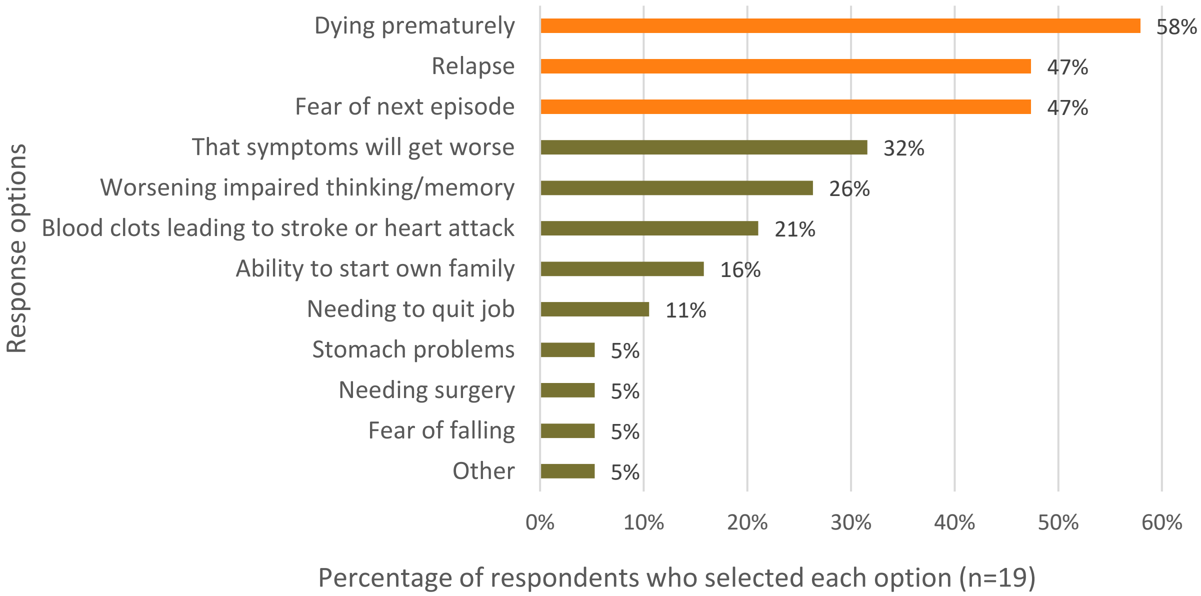
Response options selected by more than 50% of poll respondents are shown in **orange.**



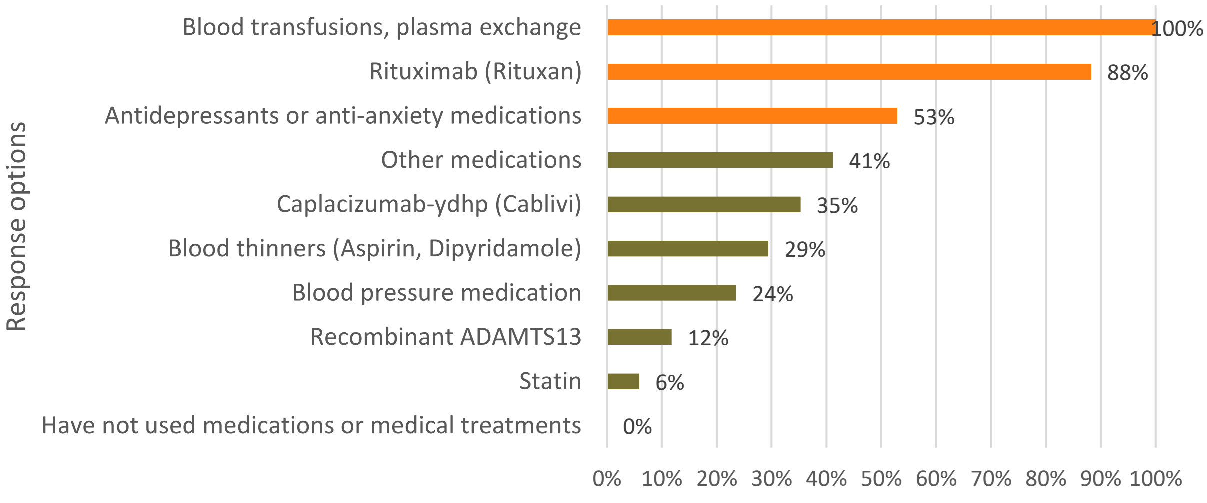

Q2. Select the TOP 3 most troublesome iTTP-related health concerns that you or your loved one has ever had.
Response options
Blood clots/stroke/pulmonary embolism
63%
Anxiety/depression
50%
Confusion, difficulty speaking
50%
Headaches, distorted vision
44%
Tiredness
31%
Other
19%
Blood in urine
13%
Purple bruises, red spots on skin
13%
Chest pain
6%
Discolored or dark urine
6%
Bleeding from the nose or gums
6%
Stomach pain
0%
0%
10%
20%
30%
40%
50%
60%
70%
Percentage of respondents who selected each option (n=16)


Q3. What specific daily life activities, that are important to you or your loved one, are you/your loved one NOT able to do, or struggle with, due to iTTP? Select TOP 3
Response options
Traveling
74%
Playing sports or exercising
58%
Working or having a career
47%
Attending social events with family/friends
37%
Maintaining a home
32%
Attending school
11%
Other
5%
Going to restaurants
5%
0%
10%
20%
30%
40%
50%
60%
70%
80%
Percentage of respondents who selected each option (n=19)

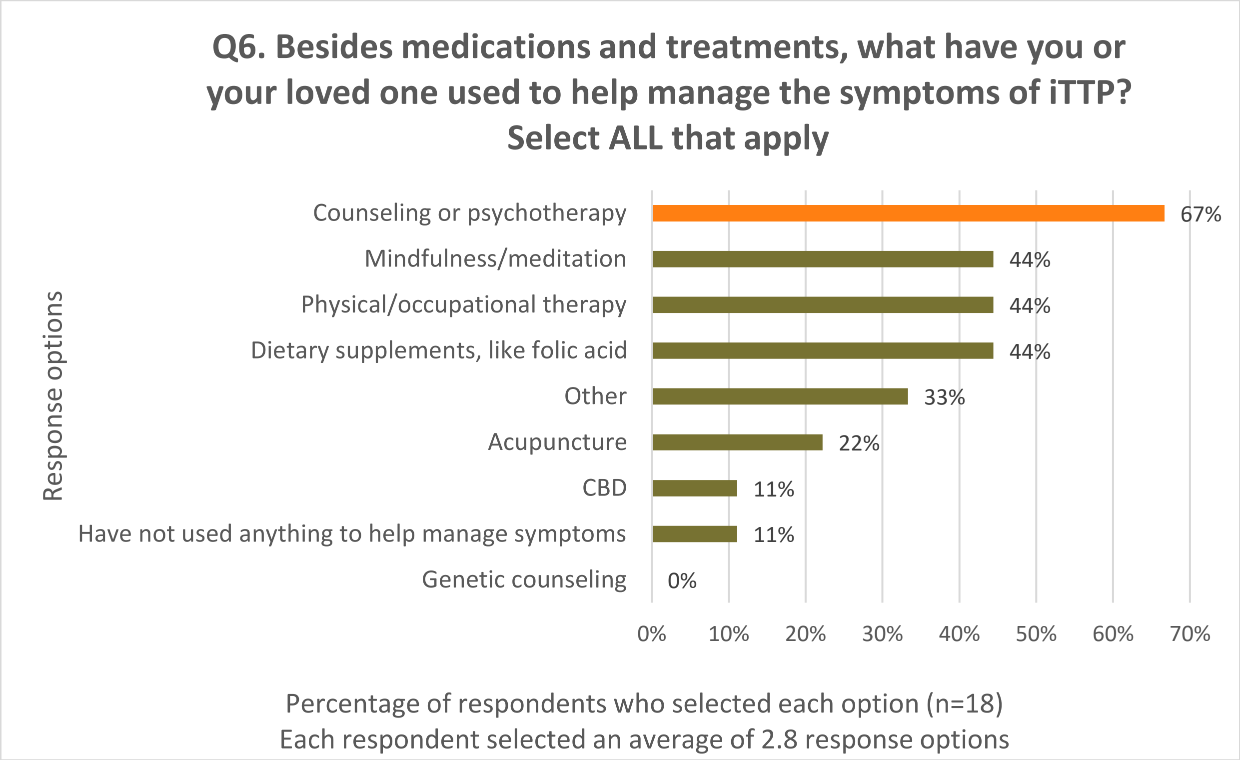
Q4. What worries you most about you or your loved one's condition in the future? Select TOP 3



Q5. What medications or medical treatments have you or your loved one used (currently or previously) to treat symptoms associated with iTTP? Select ALL that apply

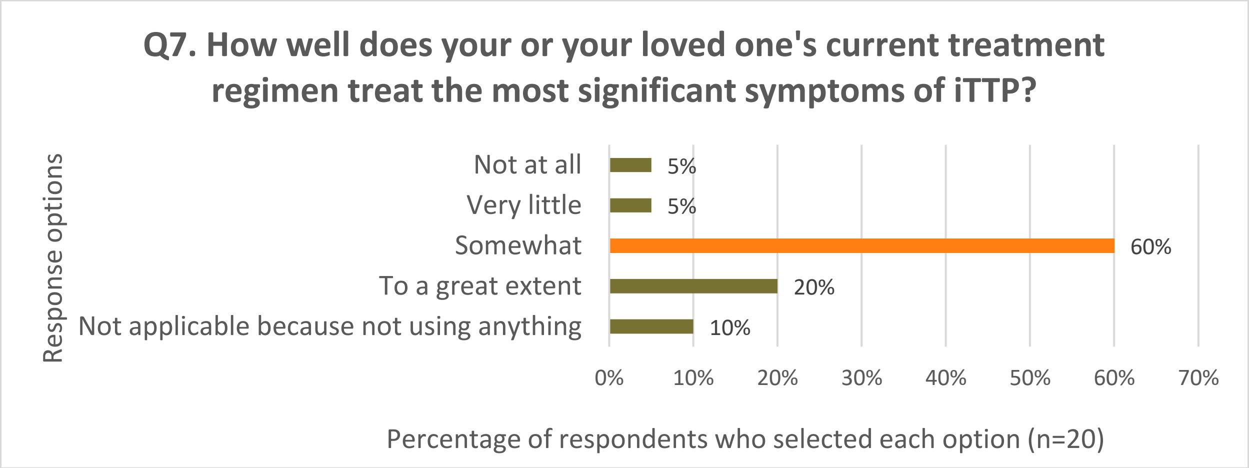


Percentage of respondents who selected each option (n=17)
Each respondent selected an average of 3.9 response options



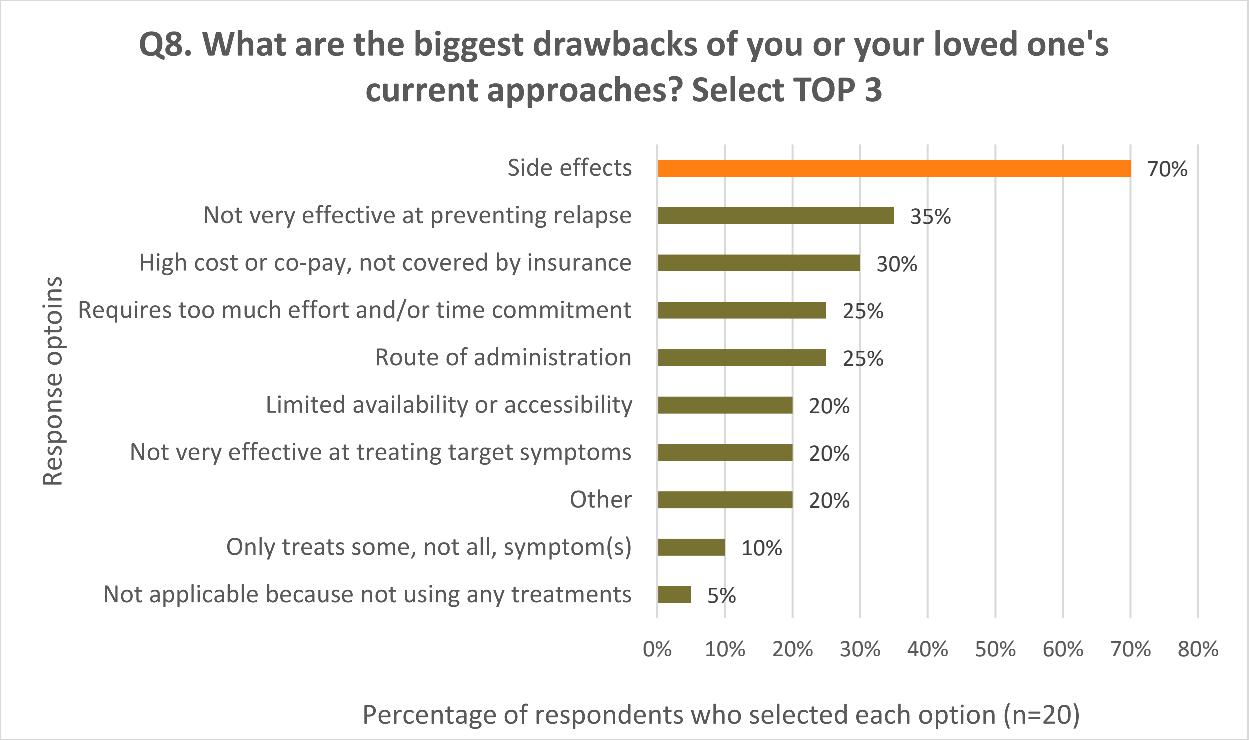
Q6. Besides medications and treatments, what have you or your loved one used to help manage the symptoms of iTTP? Select ALL that apply

Percentage of respondents who selected each option (n=18)
Each respondent selected an average of 2.8 response options

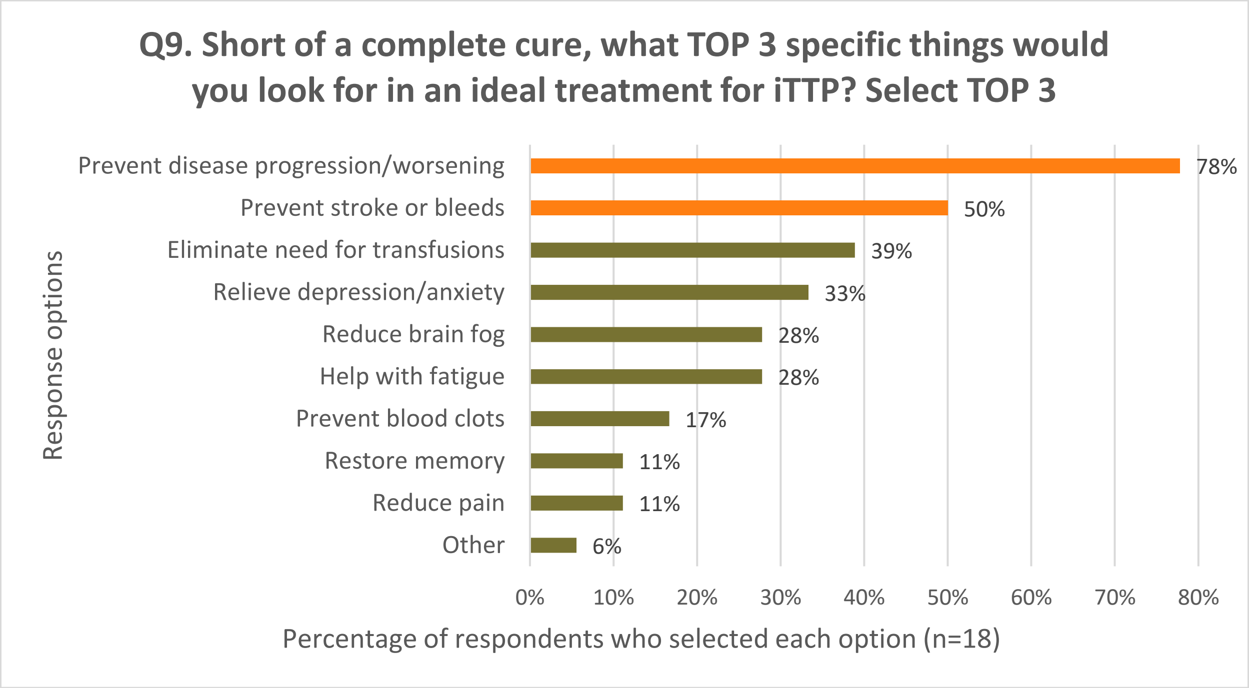


Q7. How well does your or your loved one's current treatment regimen treat the most significant symptoms of iTTP?

Percentage of respondents who selected each option (n=20)



Q8. What are the biggest drawbacks of you or your loved one's current approaches? Select TOP 3



Q9. Short of a complete cure, what TOP 3 specific things would you look for in an ideal treatment for iTTP? Select TOP 3

Appendix 6: Submitted Patient Comments

The immune Thrombotic Thrombocytopenic Purpura (ITTP) Externally-Led Patient Focused Drug Development (EL-PFDD) was held virtually on January 26, 2024. To include as many patient voices and perspectives as possible, patient comments were collected through an online comment submission portal during and for one month after the meeting. All submitted patient comments are compiled in this appendix, with selected comments included in the main body of the *Voice of the Patient* report.

The comments are presented in the order that they were submitted, and all the comments submitted by each patient are grouped together. In order to maintain the patient voice, comments were not extensively edited except for minor spelling and grammar changes. Patients are described with their first name, and if there were two patients with the same first name, a second initial was used. Some minor points were redacted in order to protect the identity. When those who submitted comments responded to the meeting discussion questions (**Appendix 3**), they are included in italics.

Lorraine, iTTP Warrior
Which iTTP symptoms have the most significant impact on your life? Short term memory loss and general fatigue
Will feedback from patients outside the USA be considered as well for the feedback you are looking for?

Sandrea, iTTP Warrior
For TTP, I've been getting plasma treatments going on 6 years. My labs are tested and my ADAMTS13 activity is always low. The doctor states my body doesn't produce plasma so I get it through an IV infusion. I wish there was a daily pill I could take to treat this instead.

Sharon, iTTP Warrior
My response is: none of us asked for this. It's absolutely life changing in every way. Many of us are suffering from what I personally call the after affects. Many local doctors depend on us--the patient--to educate them on how to treat us... that absolutely has to change. It's a rare blood disorder, but in my case, the information and support after being diagnosed, was just as rare. Education, early detection, protocol is desperately needed. In 2021, I had only one hospital option for treatment in the state, for plasma exchange... that has to change.

Samantha, iTTP Warrior diagnosed at 18 years of age
My life has changed over time since this happened when I was a young adult. I am able to manage my TTP, my monitoring, my blood work.

Mina, iTTP Warrior living with iTTP for over 30 years
iTTP symptoms - memory issues, fatigue and PTSD

Activities - cannot work full time or travel internationally. Attending social events with large number of people.

Symptoms have not changed but I am able to cope better.

My worries: fear of next episode with no access to caplacizumab, dying prematurely, blood clots leading to stroke or heart attack

Currently on rituximab and doing yoga to keep my stress level low.

Rituximab is keeping me alive but compromises my immune system.

Hazel, newly diagnosed iTTP Warrior
Although I am new to the TTP Warrior group, four months under my belt, but I am optimistic about my future. My doctors and I are vigilant and keeping up-to-date on blood work and keeping stress levels at a minimum to keep relapse at bay. Honestly, hearing others horror stories of their experience with TTP made me realize how lucky I am to have had mild after-effects. One sour thought that creeps in my mind is the possible problems I could encounter if I wanted to start a family. I know many women with TTP have had successful pregnancies, but as rare as it is to have this disorder, the possibility still exists to have a high-risk pregnancy. My doctors remind me to take things a step at a time and TOGETHER, we will cross that bridge when it's time. I owe my support system so much for helping maintain a positive attitude throughout this journey. My doctors, my family, friends, coworkers, the Ree Wynn Foundation... they all have given me a new outlook on our chaotic world. They remind me every day that there still are amazing people in the world who care.

Jeannette B, iTTP Warrior
I feel very alone with this disease. Even though I have friends, family, and support from Ree Wynn Foundation, I feel completely alone. Even doctors give me the same textbook talk when I try to ask questions to educate myself. No one in my life understands how scared and traumatized I am from past episodes or can provide an ounce of solace aside from other patients who are few and far between. I developed panic attacks due to the fear that comes with this disease.

My hematologist recommended Rituxan treatments which I discontinued after the initial four within the first month. The side effects hit me hard and my doctors will not acknowledge them. My left inner leg has felt as if is bruised since starting infusions four months ago and has been completely dismissed by doctors. I have read side effects can occur at any time after treatments and docs have insisted they would only occur at the time of infusions. These include heartburn and itchiness to name a few. The itchiness was so bad I thought I had a yeast infection, which is how I learned I have an allergy to some antifungals. I became ill with the common cold and then a stomach bug shortly after. All of this happened within less than two months after my 4th infusion. This became so stressful I choose to discontinue treatments. High stress is a common factor in all episodes and low ADAMTS13 labs. I am even considering changing careers to one with very little/no stress.

I often wonder if I would have the will to follow through with treatment of a third episode. The psychological outfall is extremely hard to cope with. I've been to therapy/EMDR to address this but it has not been very helpful. Recovery has always involved having to learn to walk again because my legs become atrophied. Steroids are difficult when tapering off and discontinuing. With the two episodes I've had, my sciatica severely flares up and now I think I may be relapsing any time I have sciatic pain. When I had a reaction to the antifungal medication, I developed petechia and thought I was relapsing. It is difficult to find a balance of remaining vigilant and advocating for myself but not live in constant fear of relapsing or believing I have gone mad.

Thank you for this opportunity to voice my experience and apologies if this should've been parsed into multiple comments.

Cassie, sister of an iTTP Warrior
As the sister of a TTP warrior, it is my hope that priority is given to finding a cure, or at very least, a sustainable treatment for those suffering the physical, mental, and emotional anguish of this traumatizing and unpredictable disease.

Karen, iTTP Warrior
My symptom that had the most significant impact was it all started with a heart attack which they say was triggered by iTTP. Now they say odds are that will be my first symptom if I relapse.

Beth, iTTP Warrior, age 40
The most disturbing thing was not being able to speak. They would ask me my name and date of birth - two things that should be easy to say. I was trying so hard but I knew I wasn't saying it right. At one point I realized I was trying to say my maiden name (I have been married since 2006).
I also was trying to hard to tell my husband I love him, and I couldn't.
I struggle with controlling emotions. There can be times when I feel totally normal, but then there are other times when I feel very irritable/impatient/nervous. Prior to TTP I was not this way. It effects my blood pressure and my face even gets extremely flush. This can affect my personal and professional life.
One thing I struggle with is if you are not in relapse, you can look and act pretty normal to others. But sometimes that normal everyone is seeing is taking a lot of effort on our part. So at the end of the day we can feel more exhausted than most - emotionally, mentally, and physically.

Alisa, iTTP Warrior, age 39
Which symptoms most affect you or your loved one now? Memory/mental issues. Memory of a goldfish. Very much like ADD/ADHD now.
What were the first symptoms that you detected (where you suspected something was not right, or when looking back after diagnosis you now believe to be related to iTTP)? My first main symptoms were: (1) low grade headache that would NOT go away and lasted for a month or so; (2) lots of bruises on my extremities that came from nowhere; (3) petechial rash on my body;

(4) constantly tired. I don't nap unless I'm sick, so that was out of the norm. Symptoms were benign on their own, but problematic together.

How does iTTP affect you or your loved one on best and on worst days? Describe your best days and your worst days. Anxiety that any symptom is a symptom of TTP. Any headache, tummy ache, general tiredness, sinus issue, etc. EVERYTHING is suspect. It's exhausting knowing your body could turn on you at any moment.

How have your or your loved one's symptoms changed over time? How has the ability to cope with the symptoms changed over time? Symptoms haven't changed, but we know what to look for, and get regular testing so we are able to watch out for relapses.

How does iTTP affect you or your loved one? What are the challenges you face? [My husband] now has my entire medical file in memory, ready to go at a moments notice in case something happens to me.

How does iTTP affect life activities (school/work, learning abilities, self-sufficiency, living situation, activities, etc.)? I now have hypertension (brought on sooner than expected with genetics), I have plantar fasciitis in both feet. Memory is my biggest problem now.

If you or your loved one could do one activity that you are currently unable to, what would it be? Travel with less anxiety.

What capabilities are you most concerned about you or your loved one potentially losing while growing older? I'm not sure I could live on my own and take care of bills and the money by myself if I were to lose my [husband].

What frustrates you or your loved one most about this condition? My memory. I have to set reminders for everything, and even then, it's 50/50 whether it'll get done on time or not.

What are you currently doing to manage you or your loved one's iTTP symptoms? Frequent testing and monitoring.

Which specific iTTP symptoms do the treatments address? All of them as far as I know.

How has this treatment regimen changed over time and why? With testing, we have been able to catch my flare-ups quicker each time. My last one was preventative treatment instead of reactive. We managed to avoid a full-blown lapse.

How well do these treatments improve the ability to do specific activities that are important in daily life? -Rituxan works for me fortunately. So my bounce back is good as long as I get the meds soon enough.

What are the most significant downsides to your or your loved one's current treatments and how do they affect daily life? (Examples of downsides may include bothersome side effects, going to the hospital for treatment, etc.) Minimized immune system is my biggest problem. I'm afraid to get sick with ANYTHING, because I know it will lead to a relapse.

Short of a complete cure, what specific things would you look for in an ideal treatment for iTTP? What factors would be important in deciding whether to participate in a new research trial?
Less fighting from the insurance/FDA when getting approval to use drugs that could help. If the insurance company wouldn't tell me I needed an entire dog and pony show to get basic Rituxan infusions. Bonus points if I could get the shot instead of the slow drip.

T, iTTP Warrior
Headaches, fatigue, and numbness in my hands and feet have been the most troublesome symptoms since my diagnosis that I still deal with today. The anxiety of experiencing all the symptoms and not knowing if it is just a headache or is this a "TTP headache". Living with this daily causes depression and PTSD. Even though there is treatment like plasma and steroids, just the thought of having to be admitted to the hospital to receive this treatment is traumatizing as well.

Le Anne, iTTP Warrior, age 69
I cannot travel to countries that do not treat TTP. A flare up in a foreign country may lead to my demise!

I forgot to say thank you to the hematology group who have kept me alive. Special thanks to my medical angels! I forgot to say thank you to the hematology group at RWJ who have kept me alive. Special thanks to Dr. Kaveney. Dr. Guo, Nurse Barbara Maffei, and Dr. Harrison (no longer at RWJ) who are my medical angels! Thank you for the outstanding care you continue to provide me.

Jeannette W, iTTP Warrior
I am considering relocating to another state because of the lack of care in New Mexico. For example, there is only one hospital in NM that provides plasma exchange and I live, thankfully only, an hour away.
I struggle with treatment due to the providers available. I don't feel they know how to properly treat me, how to troubleshoot issues, signs to watch out for, the effects from Rituxan, etc. It's like being led by the blind.

Wanda, parent of an iTTP Warrior
So delighted to be a part of this session and so proud of the Ree Wynn Foundation for the work they continue to do.
James your mother and sister would be so proud much love! 👏🏾👏🏾👏🏾

Eric, husband of an iTTP Warrior
Thank you so much for this wonderful meeting, it was very professional, enlightening, and invaluable. My wife has TTP and this has really helped open my eyes to better understand what she is going through. Thank you so much for all you do to help fight TTP.