Platelet Disorder Support Association

Empowering ITP Patients

The Voice of the Patient: Immune Thrombocytopenia

A report on the Externally-Led Patient-Focused Drug Development Meeting

Externally-Led Public Meeting: July 26, 2019
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HOSTED BY:
Platelet Disorder Support Association

Platelet Disorder Support Association
Empowering ITP Patients

THE VOICE OF THE PATIENT: IMMUNE THROMBOCYTOPENIA

This report represents the summary report composed by the Platelet Disorder Support Association (PDSA) as a result of an Externally-Led Patient-Focused Drug Development meeting, a parallel effort to the FDA's Patient-Focused Drug Development Initiative. This report reflects the host organization's account of the perspectives of patients and caregivers who participated in the public meeting.

Submitted to:
Center for Drug Evaluation and Research (CDER) &
Center for Biologic Evaluation and Research (CBER)
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INTRODUCTION

On July 26, 2019, the Platelet Disorder Support Association (PDSA) hosted an Externally-Led Patient-Focused Drug Development (EL-PFDD) meeting to share with officials at U.S. Food and Drug Administration (FDA) and other key stakeholders a range of patient viewpoints on immune thrombocytopenia (ITP), covering the symptoms and impacts to daily life that are most important to patients and their perspectives on existing and future treatments.

EL-PFDD meetings meaningfully integrate patient insights, needs, and priorities into drug development and evaluation. ITP patients are *the* disease experts and the greatest burdens of living with ITP may not be factored into drug development and data collection plans. While the FDA has encouraged quality of life assessments, they do not go far enough. The EL-PFDD meeting gave the ITP community an opportunity to directly inform the FDA about the realities of living with ITP. Patient/caregiver input aids in conducting benefit-risk assessments for products under review and helps identify areas of unmet patient needs.

The meeting was conducted as a parallel effort with the agency's Patient-Focused Drug Development Initiative to more systematically gather patients' perspectives on their condition and available therapies to treat their condition. In addition, the recently passed 21st Century Cures Act has emphasized the importance of patient input in the regulatory process, mandating that regulators learn about which outcome measures matter to patients and to consider how patients weigh the balance of risks and benefits of a particular treatment. The patient perspective can inform the FDA's decisions and oversight of drug development and marketing application.

In an effort to maximize attendance, PDSA opted to host the EL-PFDD meeting as part of PDSA's ITP Conference 2019, which took place in Washington, D.C. Although much of the input gathered at the meeting aligns with current research on ITP and available treatments, the report content may not be representative of the entire population of people with ITP. There may be views on symptoms, impacts on daily life, treatments, and other experiences with ITP that are not reflected in this report.

More information on the FDA Patient-Focused Drug Development meetings can be found at: https://www.fda.gov/industry/prescription-drug-user-fee-amendments/fda-led-patient-focused-drug-development-pfdd-public-meetings.

Overview of ITP[1]

Immune thrombocytopenia (ITP) is an autoimmune bleeding disorder characterized by abnormally low levels of blood cells called platelets, a situation which is referred to as thrombocytopenia. Platelets are specialized blood cells that help maintain the integrity of the walls of our blood vessels and help prevent and stop bleeding by plugging holes in the vessel walls and by providing surfaces on which blood clotting takes place. A normal platelet count ranges from approximately 150,000 to 400,000 per microliter of blood depending on the laboratory. If someone has a platelet count lower than 100,000 per microliter of blood with no other reason for low platelets, the diagnosis of ITP must be considered.

There is currently no definitive laboratory test to diagnose ITP. Rather, ITP is considered a diagnosis of exclusion, meaning that other causes have either been eliminated or are thought unlikely. What tests to do to exclude other causes is not well-established and may differ among hematologists and patients.

While it may seem like ITP is a simple disease, there are many nuances to diagnosis, underlying mechanism, and management, in addition to the variability of outcomes between and among children and adults.

ITP can be discovered incidentally based on a blood count ordered for other reasons, e.g. a routine yearly checkup. However, as the platelet count falls, the risk of developing bleeding symptoms increases. Therefore, most patients with ITP present to their doctor with excessive bruising in the skin, also known as purpura, or tiny red dots on the skin called petechiae. Bleeding from mucous membranes may occur, usually from the nose or in the mouth and less commonly in the urine or stool. Heavy menses may also occur and cause anemia. More extensive internal bleeding is very uncommon at presentation.

ITP is generally called "newly-diagnosed" when it has been present for less than 3 months, "persistent" when present for 3-12 months, and "chronic" when present for longer. The clinical onset typically occurs over days to weeks or even months, but a more rapid onset may occur in some patients.

Eighty percent (80%) of children who present with ITP have a self-limited clinical course that resolves with or without treatment (i.e. spontaneously) within 12 months and often sooner. In contrast, the proportion of adults with ITP who have a chronic condition is much higher, exceeding 50% in most series. ITP that develops in older adolescents is more likely to follow the clinical course seen in adults rather than the more transient illness seen in younger children.

Mechanistically, the fundamental abnormality in ITP is that the patient's immune system recognizes their own platelets as "foreign," leading their B-lymphocytes to produce self-reactive anti-platelet antibodies that attach to platelet surfaces. A type of white blood cells in the spleen and in other organs, called macrophages (scavenger cells), recognize antibody-coated particles, in this case antibody-coated platelets, leading to their ingestion and destruction. The bone marrow attempts to compensate but is often unable to keep up with the destruction, especially in severe cases. Platelet production may also be impaired when anti-platelet antibodies bind to the cells in the bone marrow that produce platelets, called megakaryocytes.

[1] Unless otherwise cited, this section is largely derived from the report on Immune Thrombocytopenia prepared by the Platelet Disorder Support Association and PDSA Medical Advisors James Bussel, MD and Douglas Cines, MD. The full report can be found in the National Organization for Rare Disorder's (NORD) Rare Disease Database.

While it may seem like ITP is a simple disease, there are many nuances to diagnosis, underlying mechanism, and management, in addition to the variability of outcomes between and among children and adults. This includes variation in the severity of bleeding at any given platelet count as well as how individual patients respond to various forms of treatment.

Management depends on severity of symptoms, platelet count, age, lifestyle, response to therapy and its side effects, the presence of other medical issues that affect the risk of bleeding, quality of life, financial issues, and, of course, personal preferences of both the patient and the doctor.

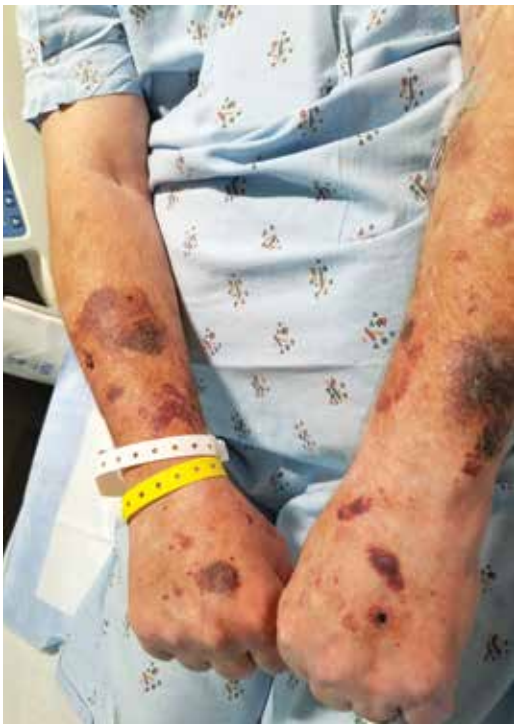
For most patients, however, living with ITP creates life-long challenges and impacts how they feel and function.

Burden of disease

Patients with ITP may exhibit symptoms of petechiae, purpura, and gastrointestinal and/or urinary mucosal tract bleeding.[2] The greatest concern with ITP is the risk of significant internal bleeding, such as intracranial hemorrhage. Other clinically significant concerns include complications from internal bleeding and an elevated risk of thrombosis and thromboembolism.[3] Some patients are fortunate and have their ITP controlled for long periods of time, even years, with observation or minimal treatment. For most patients, however, living with ITP creates lifelong challenges and impacts how they feel and function.[4]

Clinical manifestations

There is variation among individuals in their tendency to bruise and bleed when they have a low platelet count, i.e. some patients tolerate quite low platelet counts for long periods of time with minimal or no bruising and bleeding, while others may have substantial bleeding at the same counts. A child or adult with immune thrombocytopenia may display no symptoms (be asymptomatic) or the symptoms may appear when the platelet count is very low. Such symptoms may include:



- Skin that bruises very easily or even spontaneously
- A rash consisting of small red dots (petechiae) that represent small hemorrhages caused by broken blood vessels or leaks in a capillary wall
- Bleeding from the gums
- Frequent and long-lasting nose-bleeds that are hard to stop
- Blood blisters on the inside of cheeks
- Excessive and prolonged menstrual bleeding
- Less likely, signs of internal bleeding, e.g. in urine, vomit, or bowel movements
- In rare patients, bleeding in the brain called intracranial hemorrhage that is very much like a stroke
- Debilitating fatigue, anxiety, depression, low mental and physical energy

[2] Zufferey A, Kapur R, Semple J. Pathogenesis and therapeutic mechanisms in immune thrombocytopenia (ITP). *J. Clin. Med.* 6(2), 1-21 (2017).
[3] Nørgaard M, Cetin K, Maegbaek ML et al. Risk of arterial thrombotic and venous thromboembolic events in patients with primary chronic immune thrombocytopenia: a Scandinavian population-based cohort study. *Br. J. Haematol.* 174, 637-651 (2016).
[4] Salama A. Emerging drugs for immune thrombocytopenia (ITP). *Expert Opin Emerg Dr.* 2017;22(1).

In addition to serious physical bleeding-related manifestations of the disease, ITP is associated with debilitating fatigue (reported in up to ~40% of adults with ITP),[5] as well as impaired quality of life across domains of emotional, functional, and reproductive health, and work and social life. These symptoms that accompany the disease can interfere with daily activities and lead to anxiety, fear, depression, embarrassment of unexplained bruising, isolation, inadequacy, and frustration with a patient's ability to control their body and their health. Together, these multifaceted effects of ITP often take a significant toll on patients' quality of life. These problems can be exacerbated by the need to undergo frequent platelet counts and doctor visits and the side of effects of certain therapies used to treat ITP, such as corticosteroids.

These symptoms that accompany the disease can interfere with daily activities and lead to anxiety, fear, depression, embarrassment of unexplained bruising, isolation, inadequacy, and frustration with a patient's ability to control their body and their health. Together, these multifaceted effects of ITP often take a significant toll on patients' quality of life.

Immune thrombocytopenia etiology

Antibodies are normally produced by the body's immune system only in response to foreign substances, known as antigens, e.g. on bacteria, or blood cells, or tissue from unrelated people. ITP belongs to a group of disorders in which the body's natural immune defenses inappropriately act against its own cells or tissues (autoimmune disorders). In ITP, such an abnormal immune reaction leads to destruction of the individual's own platelets. For reasons that remain as of yet unknown, lymphocytes in the bone marrow, spleen, and elsewhere produce these antibodies that attach to platelet surfaces, i.e. the platelets are recognized as foreign by the immune system. In most individuals with ITP, the platelets are the only target of the misdirected immune response. In an estimated 20% of patients, ITP develops in the context of another disorder that predisposes to making additional types of autoantibodies. This is called secondary ITP.

The autoantibodies in ITP bind to otherwise normal platelets in the blood. The antibody-platelet complexes are recognized by tissue macrophages mainly in the spleen. Here, the macrophages ingest and destroy antibody-coated platelets as they would normally when they encounter any antibody-coated foreign particle. The bone marrow attempts to compensate by producing more platelets, but the rate of platelet destruction often exceeds the marrow capacity to generate new platelets, so thrombocytopenia develops. Platelet production by megakaryocytes in the bone marrow may also be impaired when the same autoantibodies that bind to the platelets attach to megakaryocytes, the platelet precursors in the bone marrow.

Therefore, the mechanisms underlying ITP and the resulting very low platelet counts can be characterized as including increased platelet destruction, reduced or inadequate platelet production, or both. It is not currently possible to define the relative importance of these two possibilities in a specific patient.

In children, ITP often appears within weeks after an acute viral infection. This suggests that antibodies produced to fight foreign viral substances (antigens) may "cross-react" with similarly-appearing antigens on platelets, which in turn lead to platelet destruction. This has been shown in the case of chicken pox. However, recall that it is not possible to identify the exact mechanism that leads to ITP in a given patient, nor is it possible to predict which child (or adult) will get better quickly and forever and which will not, nor who will bleed and who will not.

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[5] Kistangari G, McCrae KR. Immune thrombocytopenia. *Hematol. Oncol. Clin. North Am.* 27(3), 497-520 (2013).

It is quite rare for more than one family member or members of more than one generation to have ITP. When there is such a family history of thrombocytopenia, a genetic disorder involving platelets is much more likely. This is called hereditary thrombocytopenia and is generally not cause by platelet antibodies.

As mentioned, some people have secondary ITP, meaning that their ITP is part of another condition. Secondary ITP can be caused by systemic autoimmunity as occurs in systemic lupus (in which the immune system attacks other cells as well as platelets, including red blood cells leading to anemia), inherited immune disorders such as autoimmune lymphoproliferative syndrome (ALPS), common variable hypogammaglobulinemia which predisposes to recurrent infections, persistent infections (such as HIV, Hepatitis B or C, and the ulcer-causing stomach bacterium, Helicobacter pylori), and lymphoproliferative disorders such as chronic lymphocytic leukemia that impair the normal functioning of the immune system. Presentations resembling ITP may develop after an otherwise typical viral or bacterial infection, or in approximately 1 in 40,000 children after vaccination for measles-mumps-rubella (MMR). A number of drugs may suppress platelet production in the bone marrow or induce the formation of antibodies that attack platelets when the drug is present, leading to a clinical picture resembling ITPn. A good source of information on this subject is "Pathophysiology of secondary immune thrombocytopenia" (Cines et. al. 2009).

Affected populations

The incidence (how many people are diagnosed each year) of ITP among adults in the United States is estimated to be 3.3 per 100,000 adults/year. The prevalence (how many adults have ITP at any time) is 9.5 cases per 100,000. The annual prevalence is estimated at 5.3 per 100,000 among children; because children in ITP usually recover completely from the illness, the number of children who have ITP at any one time is almost equal to those diagnosed annually. Worldwide, it is estimated that there are well over 200,000 people affected by ITP.

ITP can occur at any age from 3 months of age to over 100 years of age. The incidence of ITP increases with age and is more common over the age of 60. Among younger adults (age 30-60) diagnosed with chronic

ITP, there are 2.6 cases among women for every case involving a male. In older adults, about the same number of men and women are diagnosed with ITP. Among children diagnosed with acute ITP, the male to female ratio is also almost equal, with 52% male to 48% female. About 40% of all patients diagnosed with one or another form of ITP are children younger than 10 years of age. Among children, the incidence is greatest between 2 and 4 years of age.

Diagnosis

The diagnosis of ITP is made by excluding other causes of thrombocytopenia, including certain medications or disorders that affect the bone marrow and reduce platelet production, such as acute leukemia and aplastic anemia. On occasion, a low platelet count may be detected incidentally by blood tests (CBC: complete blood count) ordered for other purposes and the individual is without apparent symptoms (asymptomatic). Inspection of the blood smear under the microscope will verify the platelets are truly reduced in number and not simply clumped (stuck together so they are too big to be counted by the machine as platelets and thus give a falsely low count), and that the platelets are not uniformly exceedingly small or exceedingly large (giant platelets approximating the size of red blood cells) which occurs in some hereditary thrombocytopenias. The red blood cells and white blood cells are normal in number and appear normal to the eye, which helps to exclude consideration of other causes of thrombocytopenia. The presence of unusual-appearing cells in the blood or additional abnormalities in the blood counts might indicate the need for a biopsy of the bone marrow to exclude other causes of impaired platelet production and/or consideration of secondary ITP.

In a patient who is otherwise in his/her usual state of good health, who has not recently taken a new medication, has thrombocytopenia but no other abnormality found by CBC or upon inspection of the blood smear, and has no family history of thrombocytopenia, the diagnosis of ITP is favored. There is no definitive test (e.g. measurement of platelet autoantibodies) to make the diagnosis or to exclude the diagnosis of ITP. A robust response to ITP-specific treatments such as IVIG (Intravenous Immunoglobulin) or glucocorticoids provides strong evidence in favor of the diagnosis.

Treatment

Overview: In some individuals, ITP goes into remission for an extended period of time, perhaps for the remainder of a person's life. For the rest, while there is no "cure" for ITP, fortunately almost all patients find their platelet count improves following treatment. What proves difficult for many ITP patients is finding the treatment that works for them without unwanted side effects. ITP can also recur, also at any time. There is currently no way to predict the course of the disease. Changes in diet or lifestyle may modify the sense of well-being.

Criteria for treatment: In many children and some adults, therapy may not be necessary at the time they first see the doctor and the disorder may resolve spontaneously. The decision to initiate treatment depends on the severity of bleeding, the severity of the thrombocytopenia, the age of the patient (increased risk of bleeding in adults and especially in the elderly), coincidental disorders that might predispose to bleeding (tendency to fall, concurrent anti-platelet or anticoagulants), lifestyle (e.g. youth and athletics), and risks and side effects of each intervention. These same factors also contribute to deciding which treatment to use.

The goal of therapy is to prevent bleeding, to stabilize and hopefully improve the platelet count, and help restore the patient's ability to have a normal lifestyle.

When treatment is deemed necessary, there are many options that have proven successful. Treatments differ in likelihood of benefit and risks and some are considered more toxic and are therefore generally deferred unless it is proven they are needed. Treatments also differ in their intended effect: short term platelet increase versus long-term maintenance of a stable platelet count. It is important to understand both the success rate and potential side effects before beginning any form of treatment. Hematologists may even recommend several treatments at once to increase their success rate and to lower doses in order minimize side effects.

1. First line/emergency therapy

Treatment with corticosteroids (e.g. prednisone, dexamethasone, methyl prednisone) is usually the mainstay of initial therapy. These drugs function by suppressing the clearance of antibody-coated platelets and perhaps by increasing platelet production. They may also decrease the risk of bleeding by improving blood vessel lining cell function. Very high doses of dexamethasone have been reported in some studies to maintain a good platelet count after the drug is discontinued. However, other studies have thus far not affirmed the long-term benefit of such a "high-dose" approach. In general, as described in the 2019 ASH guidelines, the duration and dose of corticosteroids should be minimized because of their immediate and serious long-term side effects. Therefore, corticosteroids are used to control the disease until a transition can be made to other forms of treatment in patients who do not achieve a spontaneous remission.

If platelet counts do not improve immediately after initiating corticosteroid treatment, or for individuals who present with severe bleeding, treatment may include adding intravenous immunoglobulins (IVIG), usually by infusions given every 2-4 weeks as needed based on the count and bleeding,. IVIG is effective in about 85% of patients, but it does not lead to a cure. Platelet transfusions are reserved for emergent situations because they are destroyed by the autoantibodies in the same way as the individual's own platelets.

The orphan drug anti-D (WinRho SDF, Rhophylac), a hyperimmune form of gamma globulin, was approved by the Food and Drug Administration (FDA) to treat ITP in individuals who are red blood cell RhD antigen positive, do not already have antibodies on their red cells, and have not undergone splenectomy. The drug can be used repeatedly at 2-6-week intervals, including in children who have the acute or chronic form of ITP. However, use has decreased because concerns have been raised about a small number of individuals who had very severe side effects from brisk red cell destruction and its consequences soon after infusion.

2. Second line therapy

The criteria for determining whether second line therapy is needed are the same as those involving initiation of treatment plus patients with suboptimal responses to first line approaches, or those who continue to require a corticosteroid. As mentioned, corticosteroids should be used for the shortest duration possible to achieve these objectives and to provide a bridge to less toxic alternatives. Many adults and some children will require such long-term management because their platelet count will fall once the dose of corticosteroids is tapered. Current recommendations from ASH suggest that steroids not be used past the first 6 weeks after diagnosis of ITP.

One option in the second-line setting involves the use of thrombopoietin receptor agonists (TPO-RAs). TPO-RAs function by stimulating the body's production of platelets by megakaryocytes in the bone marrow, which release "proplatelets" that mature into platelets. By increasing the rate at which platelets are produced in the body, TPO-RAs may overcome the heightened rate of platelet destruction caused by antiplatelet antibodies and their ability to impair megakaryocyte function. Three TPO-RAs approved by the

FDA for use in ITP are avatrombopag (Doptelet®), eltrombopag (Promacta®) and romiplostim (Nplate®); one other is approved for low platelets in patients with liver disease and a fifth agent has been licensed for many years in China to treat ITP. In general, the goal of treatment is to obtain a stable platelet count above 50,000µL, not a normal platelet count. About 50-80% of individuals with ITP who receive treatment with platelet growth factors see an increase in their platelet count above 50,000/µL and many others see an increase to above 30,000/µL which can be clinically meaningful. In most patients the response is sustained while on treatment.[6]

Avatrombopag (Doptelet®), eltrombopag (Promacta®/Revolade®), and romiplostim (Nplate®), are approved by the U.S. Food and Drug Administration (FDA) for adults with ITP who have either responded poorly or not had a sustained off-treatment response to at least one other ITP medical therapy. Eltrombopag and romiplostim are also approved for use in children with ITP; romiplostim is approved for a patient with ITP at any time starting at or soon after diagnosis and who have failed one therapy, such as corticosteroids. As of November 2019, avatrombopag is not approved for use in children with ITP.

It is estimated that approximately 20-30% of individuals receiving a TPO-RA will eventually be able to discontinue treatment after 1-2 years while maintaining an acceptable platelet count, but there is no way to predict these outcomes in advance.[6,7]

The most common adverse reactions reported with all three TPO-RAs include headaches, joint and muscle pain, dizziness, gastrointestinal issues, rash, flu, and upper respiratory infections. Initial concern regarding bone marrow fibrosis (scarring) have been alleviated by years of experience with these agents. There is a potential for platelet counts to drop lower than it was before therapy was started if a TPO-RA is discontinued abruptly; therefore, small and slow changes in dose (tapering) are recommended when attempting to discontinue these agents.[6]

Patients with ITP are, seemingly paradoxically, at risk for thromboembolism (clotting) in addition to bleeding. Venous or arterial thromboembolism has been seen in 6-7% of patients using TPO-RAs in long-term studies; this has been seen in 6-7% of patients using TPO-RAs.[8] It is not clear if this risk is higher than in ITP patients treated successfully with splenectomy or corticosteroids. There is little evidence that the risk of clotting implies clotting in arteries is related to platelet count. Aspirin may be recommended to help reduce the risk of arterial clotting (heart attack, stroke) once the platelet counts exceed 50,000/µL, especially in the elderly or those with pre-existing conditions that might increase risk.

There is also a theoretical risk that TPO-RAs could stimulate the growth of abnormal clones (subpopulations) of "malignant" or "pre-malignant cells" in a patient with a bone marrow disorder such as myelodysplasia that was mistaken for ITP.[6]

Another option for second line therapy is anti-CD20 antibody, rituximab (Rituxan®) or several biosimilars which reduce production of anti-platelet antibodies. About half of the patients treated with rituximab respond initially, but only 20-30% maintain the response by 5 years. In one study, women of child-bearing age who were treated within 2 years of diagnoses had a "cure rate" above 50%, but similar success was not seen in any other subgroup. Rituximab is generally well-tolerated, but infusion reactions can occur.

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[6] Ghanima, W et al. "Thrombopoietin receptor agonists: ten years later." Haematologica. 2019 Jun; 104(6): 1112-1123. http://www.haematologica.org/content/haematol/104/6/1112.full.pdf

[7] Ghadaki B et al. "Sustained remissions of immune thrombocytopenia associated with the use of thrombopoietin receptor agonists." Transfusion. 2013 Mar 3. http://www.ncbi.nlm.nih.gov/pubmed/23451917

[8] Kuter, DJ et al. "Long-term treatment with romiplostim in patients with chronic immune thrombocytopenia: safety and efficacy." British Journal of Hematology. 2013 May; 161(3): 411-423.https://www.ncbi.nlm.nih.gov/pubmed/23432528

Administration may be repeated when a durable response is attained, but concern over repetitive administration of this immunosuppressant is warranted. Some hematologists add high doses of dexamethasone, given for four days per month for 1-3 cycles, to increase the response rate to rituximab.

A third option is splenectomy (typically laparoscopic), because the spleen plays a major role in destroying antibody-coated platelets and has some role in making antiplatelet antibodies. Splenectomy improves platelet counts in approximately 70-80% of patients initially and can induce a long-term remission in 60-70%. The high long-term success rate must be weighed against the small but real increased risk of thrombosis and serious infection both at the time of operation and life-long. Therefore, patients must receive and maintain appropriate vaccinations and receive urgent evaluation for serious febrile illnesses. Most guidelines recommend deferral of splenectomy for a year from diagnosis in order to determine if a patient will go into remission. However, splenectomy remains an option in patients who fail other forms of treatment or in resource-challenged areas where more expensive alternatives are not available.

Lastly, in 2018, Tavalisse® (fostamatinib disodium hexahydrate) was approved by the FDA for the treatment of thrombocytopenia in adults with ITP who have had insufficient response to a previous treatment. Approximately 20% of patients unresponsive to other forms of management responded based on pre-specified criteria but almost 40% did so using less stringent but clinically meaningful endpoints. It has a number of side effects (hypertension, diarrhea, headache, and increased liver tests) but potential advantages are that responses generally occur within weeks.

3. Third line therapy

A small percentage of patients fail to respond to or tolerate first- or second-line treatments. For those, options include dapsone, Imuran (azathioprine), Cytoxan (cyclophosphamide), Sandimmune (cyclosporine), Danocrine (danazol), Cellcept (mycophenolate mofetil), and Vincristine (vinca alkaloids) or combinations of previously described treatments. Several other novel forms of treatment are in clinical trials.

If the patient has antibodies or evidence of Helicobacter pylori infection, treatment with antibiotics and proton pump inhibitors may ameliorate the condition. Antibiotic-associated remission of ITP is much more common in Asia and in some parts of Europe than in patients who have lived their entire life in the U.S. or Canada.

Some patients report success with complementary therapies such as vitamins, supplements, diet changes, herbs, and energy work, such as Reiki. However, there are no controlled trials in ITP patients demonstrating utility or safety of any of these agents.

ITP treatments vary with the disease severity, age of the patient, experience of the hematologist, patient preference, and other factors. Therefore, it is important that a dialogue be maintained between the patient and his/her physician to ensure the patient's values, expectations and concerns are understood during sometimes difficult treatment decisions.

Meeting Design and Overview

PDSA hosted the EL-PFDD meeting to provide the international community affected by ITP (patients, caregivers, and other patient representatives) and specialists in the field an unprecedented opportunity to share with the FDA their stories about the burden of this rare disease and the shortcomings of existing management strategies. According to Caroline Kruse, President and CEO of PDSA, the greatest burdens of living with ITP are not always explicitly factored into drug development and data collection plans. The goal

of the EL-PFDD meeting was therefore "to increase awareness on the impact that ITP has on quality of life for affected individuals and families and convey these experiences to the FDA and other drug development stakeholders," she said.

The EL-PFDD meeting represented an important step for the ITP community in being the first of its kind to ever be held for Immune Thrombocytopenia and other platelet disorders. This groundbreaking event included 315 individuals from across the U.S. and Canada, 18 ITP patient association leaders from 12 countries representing the International ITP Alliance, FDA officials, as well as a broad cross-section of researchers, health care providers, and representatives from the pharmaceutical industry. Hundreds of additional patients, caregivers and others participated via the PDSA Facebook Livestream and the entire recording of each session can be viewed on PDSA's YouTube Channel:

Part 1: https://www.youtube.com/watch?v=KnEf3rRQSds
Part 2: https://www.youtube.com/watch?v=0oljnR0oOHg

Following the successful model the FDA developed to host similar meetings, the half-day event focused primarily on a range of patient viewpoints on ITP, covering the symptoms and impacts to daily life that are most important to patients, and their perspectives on existing and future treatments.

Four introductory presentations set the tone of the meeting. PDSA President & CEO Caroline Kruse and Joan Young, who founded PDSA in 1998, gave powerful speeches; both Kruse and Young had ITP and could therefore speak from both a personal and professional perspective. PDSA Medical Advisor and world-renowned ITP expert Dr. James Bussel provided a thorough medical explanation of ITP. Dr. Ann Farrell, Director of the Division of Hematology Products within the Office of Hematology and Oncology Products, then spoke about the importance of the patient perspective to the FDA's work, and affirmed that the FDA has learned a lot from these kinds of interactions. From there, the meeting had two primary focuses: (1) effects of ITP that matter most to patients and caregivers, and (2) patient perspectives on current approaches to treatments. For each of these topics, a panel of four patients and caregivers provided insights into the challenges patients and families face daily living in the world of ITP. After each panel, facilitated group discussion and live polling provided additional perspectives from patients and caregivers in the audience. Slideshows were used to supplement panelist presentations and facilitate polling. The meeting closed with PDSA Board Chair Peter Pruitt who shared thoughts as both a board member for over 10 years and caregiver to an ITP patient for more than 40 years.

Meeting Summary

Immune Thrombocytopenia (ITP) is an acquired disorder in which the body's immune system destroys healthy platelets and impairs platelet production, leaving the patient at risk for frequent, serious, and potentially life-threatening bleeds. An estimated 50,000 people in the U.S. are currently living with this rare autoimmune condition.

Patients with ITP face a complex set of challenges. ITP is a heterogeneous disease associated with significant morbidity not limited to bleeding. Due to variability in its underlying pathobiology and natural history, management of disease can be unpredictable despite the availability of several therapies with different mechanisms of action. Once diagnosed, ITP patients experience a range of physical and emotional challenges that may impose limits on their life activities as they seek to monitor their platelet counts, balance treatment side effects, and manage the fear and frequent reality of relapse.[9]

"Many things have changed since I was diagnosed in early 2000. It was two o'clock in the morning when I got the call that would change my life…'You need to get to the Emergency Room immediately. You have a platelet count of 2,000. You could bleed to death,'" Kruse opened.

Caroline Kruse, PDSA President & CEO

Caroline Kruse was diagnosed in April 2000 with a platelet count of 2,000. "Many things have changed since I was diagnosed in early 2000. It was two o'clock in the morning when I got the call that would change my life…'You need to get to the emergency room immediately. You have a platelet count of 2,000. You could bleed to death.'" Kruse opened. She has now been in remission for 16 years, but explicitly outlined her struggle to find effective treatments for ITP that did not also jeopardize her quality of life. Kruse first took prednisone to treat her ITP but experienced the most unwelcome side effects of the steroid, including weight gain and changes in mood. She also underwent a failed splenectomy, leaving her at a higher risk for infections, thrombosis and the potential for cardiovascular problems. She expressed that although she was concerned about complications from the ITP itself, her hematologist told her she ultimately had a greater risk of dying from the side effects of treatments if these were not carefully modulated. This demonstrates the difficulties ITP patients face when determining courses of treatment – it is not always a simple process to find a treatment that can effectively treat the ITP without causing other health issues or triggering negative side effects. Kruse is thankful for Joan Young and PDSA for the support during her patient journey and stressed to the audience ITP's significant burden on patients' and families' quality of life and its terrifying impact far beyond the platelet count.

[9] Cuker A, Prak E, Cines DB. Can Immune Thrombocytopenia Be Cured with Medical Therapy? *Semin Thromb Hemost.* 41 (4), (2015).

Joan Young, PDSA Founder

Joan Young was diagnosed with ITP on August 29, 1992. At the time, Young was a 46-year-old single mom with almost grown daughters, a house, and a mortgage. She explained that when she first noticed some bruises and felt fatigued, she was in denial. She eventually went to the doctor, and after almost two weeks and various blood tests, Young was diagnosed with ITP. With a platelet count of 7,000 at the time of diagnosis, she spent the next few years struggling to keep her count up. This meant that she subjected herself to a myriad of treatments in a desperate attempt to stabilize her platelet count at a normal level.

After sharing the story of her initial diagnosis, Young presented a detailed account of the crippling grip of treatment side effects, saying, "I could barely manage my life. I didn't recognize the person I had become…There is an incredible need. I'm glad the FDA is listening." Beginning with 60 mg daily of prednisone immediately following her diagnosis, Young did not experience a significant increase in her platelet count, but her blood pressure increased, her emotions seemed out of control, she developed a mouth fungus, and had trouble sleeping at night. She went on short-term disability at her job, citing an inability to concentrate or act sanely due to her condition caused by the side effects of her treatment.

Young recounted how her hematologist continually pressured her into having a splenectomy. After the prednisone failed to help her, Young began IVIG with little to no effect. After suffering a seizure and being put on seizure and heart medication in addition to the prednisone – and later colchicine – Young's platelet count remained below 10,000. On November 11, 1992, with an official platelet count of zero, Young agreed to a splenectomy. There was an immediate rise in platelets, but before her scar even healed, her platelets were back down to 5,000. She tried Danazol, but it affected her testosterone levels more than her platelet counts.

After her unsuccessful splenectomy, Young slipped deeper into the feeling that she was no longer in control of her own body, outlining her fears to the audience, "For months I was obsessed with my bruises.":

- "Were there more?"
- "Were they healing?"
- "Were there more blood blisters in my mouth than the day before?"
- "Where else was I bleeding that I couldn't see?"
- "Would I live long enough to see my grandchildren?"

In February 1993, Young fell sick with the flu. Desperate, her hematologist suggested a dose of Vincristine plus six Prosorba column treatments. "We were at the bottom of the treatment list," she explained. After receiving this treatment, Young's platelets went up to a high of 38,000 and she also:

- lost her hair
- came close to death during the fifth Prosorba column treatment
- was left a shell of the person she had once been

Young ended her story here and explained that although her platelet counts are no longer a problem, she still has longstanding consequences from the treatments. Her body and her life have been permanently changed by the treatments she underwent, and she says even seeing a bruise can bring back the trauma of her diagnosis.

Meeting Sessions

Additional information about the experience of living with ITP was captured in two live sessions that focused on (1) the effects of ITP that matter most to patients and caregivers, and (2) patient perspectives on current approaches to treatments. For each of these two themes, a panel of patients and caregivers presented moving summaries of their experiences and perspectives, offering a realistic glimpse into living life with ITP. Patients and caregivers who both attended the meeting in-person or participated via webcast then responded to a series of polling questions. Polling was followed by a facilitated discussion in which audience members were invited to further share their experiences and perspectives.

Panelist testimonies, remarks from audience participants at the meeting, and meeting polling question data yielded important information on the daily impacts of ITP and current treatments. To the extent possible, the terms used in this report to describe specific symptoms and treatment experiences reflect the words used by in-person participants and language used in submitted survey response. There may be symptoms, impacts, treatments, or other aspects of ITP that are not included in this report.

Key Themes

Topic 1: Health effects and daily impacts that matter most to patients

The first section focused on the health effects and daily impacts that matter most to patients. Several key themes emerged:

- Physical manifestations of ITP, such as bruising, petechiae, and bleeding, are often early indicators of something being wrong and prompt a visit to the doctor. However, these symptoms go beyond the physical discomfort they produce, usually not very much, and contribute to patients feeling "different" and isolated from their peers. Furthermore, severe bruising can arouse false accusations of abuse, and spontaneous bleeding and unexplained bruises can cause persistent anxiety in a patient and his or her family.
- "Invisible" symptoms can take just as severe a toll on an ITP patient. Fatigue, depression, and brain fog can make a patient feel like a shadow of him/herself; he or she feels weighed down and unable to complete daily tasks that were once easy. Although not always visible to others, these symptoms of ITP are all too real for the patients themselves, and take a toll on their emotional, mental, and physical well-being.

- ITP significantly impacts patients' overall quality of life, making it a disease that is not restricted to the blood, but affects every aspect of a patient's life and well-being. Patients expressed how ITP has robbed them of a "normal" life and has left them feeling helpless or out of control of their own lives and bodies. The unpredictability of ITP and the inconsistent effectiveness and side effects of treatments often force patients to live with restrictions placed on their normal activities or cause the inability to pursue their passions and goals. This is above and beyond that depression, fatigue and brain fog described in the paragraph above.
- The panel and discussion demonstrated that many patients share similar symptoms of ITP or are impacted by the disease in similar ways, but there is still a substantial variation in how and when the disease manifests in a patient. The severity of symptoms can vary among the ITP community, but also within an individual patient; different symptoms may take priority at different times, or for different people. However, there was a general agreement on the fact that ITP can negatively – and severely – impact the daily life of patients and their loved ones and produces feelings of helplessness and having one's life uprooted.

Topic 2: Patient perspectives on current approaches to treatments

The second section of the meeting focused on ITP patient perspectives on current treatment options.

Several key themes emerged from this section of the meeting:

- A pattern of "standard" treatments emerged, but the wide variety of treatments that patients indicated having received both during the sessions and via the polling questions demonstrates how difficult it is to fully and effectively treat ITP.
- Although steroids are categorized as a first-line treatment and are therefore one of the, if not THE, initial treatments given to patients, patients and caregivers expressed a resistance to receiving prolonged steroid treatment because of the adverse side effects patients have experienced. More generally, patients struggle with whether to subject themselves to certain treatments because of the severity of side effects. The steroid side effects is one of the worst things about ITP according to patients.
- Patient response to treatments is inconsistent.
    - Treatments that work for one patient will not necessarily work for another, and an individual patient might begin losing their response to a familiar, previously effective treatment during the course of their illness. This uncertainty and lack of a guarantee in terms of both consistency and progress causes anxiety in patients and contributes to the lack of control they feel over their lives.
- Among the younger patients and caregivers of young patients, there was a call for ITP treatments that are designed specifically for children. Children are being treated with drugs that have been developed for adults, which affects the effectiveness of treatment among children. In particular a number of commonly used treatments have not been well-tested in children so appropriate dosage may not have ever been discovered.

Appendices

The appendices include the meeting agenda, polling questions and results.

TOPIC 1: HEALTH EFFECTS AND DAILY IMPACTS THAT MATTER MOST TO PATIENTS

The first discussion topic focused on the experiences of both patients with ITP and their caregivers, including the various symptoms and manifestations of the disease as well as the impact and burden of the disease on their daily lives. The session began with a panel of three patients and three parents. As mentioned, there is variation in how ITP manifests itself in individuals. Though they did not all share identical symptoms, treatments, etc., taken together, the panelists' experiences highlighted many of the same issues:

- **Panelist 1:** "I had a lieutenant ask me 'who had been beating me' because I had bruises all over my torso, arms, and legs," said the first panelist, who was diagnosed with ITP at age 17 while serving in the Marine Corps. For the past 37 years, he has endured various treatments and struggled to maintain his quality of life. In 2014, he went on long term disability because he was constantly sick from either the ITP itself or the medications he took to treat his ITP. At one point, his counts would not stabilize over 20,000 and his doctor informed him that his risk of bleeding – both internal and external – was very high if he even slightly injured himself. Between the constant fear of bleeding, not working, and the depression he developed over the course of his battle with ITP, the panelist explained that he did not leave the house except for doctors' appointments for almost 10 months. After attempting suicide, he began attending outpatient therapy groups. He explained to the audience that ITP has touched every part of his life, saying, "I want people to know that ITP does not just affect your blood, [but] that it [also] affects you physically and emotionally."

"I want people to know that ITP does not just affect your blood, [but] that it [also] affects you physically and emotionally."

- **Panelist 2:** The second panelist, the mother of a ten-year-old boy who has had ITP since age 2, said, "We had so many questions about [our son's] future. Will [our son] have a future, or can he bleed to death? Will he be able to live and play freely like other children? Will he be happy?" She explained how her son feels embarrassed by his medical condition and has not shared that he has ITP with his friends because he does not want to be seen as "different" from everyone else. She said that although he appears happy and healthy, his platelet count is always on her mind, as well as her husband's and her son's. "There is no other way to describe it other than being on an emotional roller coaster," she told the audience. She said she felt lost and helpless when her son was first diagnosed and attested to the common feeling of not being in control when it comes to chronic illness. The panelist also provided insight to the experiences of caregivers, explaining that "living with a child diagnosed with a chronic medical condition can have a profound impact on the entire family, not just the child," further demonstrating the effects of ITP that go far beyond platelet counts and the blood itself.

"There is no other way to describe it other than being on an emotional roller coaster."

- **Panelist 3:** "For us, not a minute goes by without thinking about how ITP affects your life," said the third panelist, a 62-year-old woman living with chronic refractory ITP. Diagnosed at age 4, she has only experienced remission for three months, immediately following her splenectomy when she was seven years old. Since 1961, she has tried every drug and treatment available, but none have been successful, leaving her platelet count in the single digits for the past 25 years and living with the four aspects of ITP that affect her the most: fear, guilt, fatigue and depression. "You wake up with fear every day," she said, continuing, "This fear cannot evade you, and for good reason. You wonder,

  Am I gonna' die today?

  Will I have an accident?

  What if I have to go to the hospital?

  Will the ER doctors know how to treat someone like me?

  What if I need surgery?

  Nothing works for me!!

  Maybe I should just stay home….

  The fear makes you worry about having a "normal" life….

  Will I be able to work?

  Should I get married?

  What about children?

  Will they get ITP?

  Will I see them grow up?

  Will I be around?

  Will I be a burden?

  What if I get a brain bleed? That is our biggest fear! I know only a small percentage of ITP patients get them, but we already beat the odds….only a small percentage of people get ITP!"

She explained that along with the fear of whether you can live "normally" is the guilt that comes from not being able to fulfill your role in life. A few of the questions the panelist posed were "Will I be able to work? Will I be a good wife and mother since I have so many limitations? Will my family be able to handle my disease? Will I be a burden to [my family]?" She then went on to explain how fatigue and depression severely limit your ability to complete daily tasks or even be able to plan a day ahead because "every day is reprioritized, depending on my energy levels. My "To-Do" list is constantly changing, and I feel guilty about not getting things done the way I want to." She also illustrated an exhaustive list on how ITP affects daily life. "Before I get up in the morning, I stretch," she said.

"I check to see if there is any blood on my pillowcase or sheets.

Did I cough or spit up any blood?

Is my urine smoky colored or are my stools black?

Do my gums bleed when I brush my teeth?

Do I have any blood blisters in my mouth or on my tongue?

When I shower, the water can't be too hot (vasodilation increases bleeding). I scan my body while showering to check for any new bruises or petechiae. Sometimes I count my bruises - usually 20 plus.

Moisturize: dry skin makes you itch, and itching makes you scratch which give you petechiae.

Should I wear support hose today?

Do I need to wear long sleeves today to cover my bruises?

Or long pants for the same reason?

Don't wear anything tight, it can bruise you.

Wear shoes that fit snugly and have traction.

No heavy handbags, they will bruise my shoulder.

Be careful going down the stairs, hold onto that handrail.

Should I just stay in bed today??

All this and I haven't even had breakfast yet!"

Her story demonstrated how an ITP patient's life is completely consumed by his or her disease, the demands it places on a patient's lifestyle, and as a mother herself, she directed attention to the agonizing burdens of raising a child with ITP. "You hold the keys to our future," she told the audience. "You hold the keys to the treatments that might put us in remission, or keep us in remission… You have heard our stories of life with ITP, and I assure you each one of us wants you to remember every word we have said, and that there are many more of us out there fighting to beat ITP. So many of us hang our hopes on the next treatment," she concluded.

"So many of us hang our hopes on the next treatment."

- **Panelist 4:** The fourth panelist of the morning session was a young man who was diagnosed with ITP in 2014, during his junior year of high school. He emphasized the "invisible" symptoms of ITP, saying, "Fatigue, depression, and brain fog were horrible symptoms of ITP. They plagued me every day. These symptoms worsened and became unmanageable. I had memory problems from depression dementia, which made my grades suffer, I even got an "F" for the first time in my life. I had to work hard to combat it, but I lived in a haze of confusion and slow thinking. Fatigue and depression were an invisible and unbearable weight. I had to sleep in my car between my college classes." He also found the uncertainty of ITP frustrating and scary, as there is no way to know what the next platelet count will be, or whether the new medication will work or have side effects. Equally as frustrating were the ways in which his lifestyle was restricted by ITP; after wrestling for eight years, he was planning to try out for his school's varsity team before his diagnosis prohibited him from doing so. "I was crushed to realize that all my hard work over the years was for naught… I gained 18 pounds from prednisone in one month. I started getting bullied by the people I had wrestled with all those years. I was devastated," he said. He felt robbed of his future and his ability to pursue what he loved, including a career in the military. Struggling to get out of bed most days, his fatigue was unbearable even with higher counts, and "it turned [him] into a shadow of [himself.]" After failed treatments, negative side effects of medications, and fighting the increasing weight of depression for a few years, the panelist underwent a splenectomy, which has succeeded in both raising his platelet count and giving him his life back. Although not having a spleen leaves him at risk for infection, and he continues to deal with the trauma of his battle with ITP, his life today is still a mark of progress – a life that has broken away from what once seemed "an endless cycle of misery, pain, and losing who I was."

- **Panelist 5:** "We want to create this environment and perhaps change protocol, guidelines, so hopefully another family doesn't have to go through this event," said the final panelists, the parents of a child who lost his battle with ITP at the age of 10. In their moving video testimonial, the couple explained that their son was diagnosed at age 7, and although he was not a bleeder in the first year, they still had to modify his daily activities – such as recess and his soccer schedule – "to protect him and keep him safe." His platelets ranged from below 10,000 to around 40,000, and he experienced more spontaneous bruising in his second year of diagnosis. "The third year is when things really changed for him," as the fluctuation in his platelets stopped and his levels were almost always below 10,000. In October of 2017, their son began getting frequent nosebleeds, and in November of that same year he had a severe nosebleed that would not stop. His parents recalled that he was swallowing

"We want to create this environment and perhaps change protocol, guidelines, so hopefully another family doesn't have to go through this event."

a lot of blood and then throwing up a lot of blood, and that clots were falling out of his nose. They took him to the emergency room, where they stopped the nosebleed and sent him home with prednisone. "But after a week, his levels didn't budge at all," his mother said, and after another severe nosebleed, they tried IVIG at the end of November. They explained that after this treatment, their son developed a severe migraine, was throwing up, and was unable to speak due to presumed aseptic meningitis. After another hospitalization where he had internal bleeding and hematuria, the goal was to initiate Rituxan, however the government of Ontario would not cover the cost, and the family was unable to access the treatment through alternative avenues. A few months later in May, their son developed a fluctuating mild headache responsive to Tylenol and symptoms suggestive of "a bug," and soon after he was found slurring his words and by the time they got him to the hospital, there was a lot of pressure on his brain. He underwent a total of two craniectomies but was not responsive after this last procedure and was put on life support for a few days. Ultimately, the life support was discontinued due to clinical brain death. He was 10 years and 3 months old.

Each panelist painstakingly described their individual experiences with ITP and the ways in which ITP has taken a toll on their lives, focusing on which symptoms preoccupied them the most. Some with ITP were more worried about bruising and risk of bleeding, while others were more afraid that their fatigue and brain fog would prevent them from fully living their lives. Others still were more focused on how ITP has made them feel helpless and like they do not have control over their lives or bodies. By the end of their testimony it was clear: Although ITP is a bleeding disorder, it affects so much more than the patient's blood. As one patient explained, "ITP was a life-changing diagnosis that left me with many scars, both visible and invisible." Every aspect of a patient's life is touched by ITP, and it has a profound impact on both patients and their caregivers.

These themes were reiterated during the facilitated discussion by other meeting participants. Their accounts of living with or caring for someone with a poorly understood and all-consuming chronic illness that inflicts physical, emotional, and psychosocial demands are summarized below.

It is worth mentioning that many hematologist-oncologists who take care of patients with ITP are much more focused on other diseases that they perceive as more serious, for example, cancer. Therefore, they may often not keep up to date on optimizing treatment of patients with ITP. This results in limited availability to patients of treatments, misuse of certain treatments, and either persisting with ineffective treatments or the patient being told that they cannot be successfully treated and left with a very low platelet count, bleeding, and the other mental and physical symptoms.

Pertinent insights about the burdens and symptoms of disease offered by members of the second panel are also integrated into the thematic analysis below.

Perspectives on symptoms that matter most to patients and their caregivers

Between the panel and the facilitated group discussion, a polling session systematically explored the issues raised by the panelists, including symptoms of ITP and their negative impacts, lifestyle restrictions caused by ITP, and their top concerns about living with ITP.

The polling responses were used as a starting point for the facilitated group discussion, and further demonstrated how the manifestations of ITP drastically impact patients' physical and emotional well-being.

The testimony of the individuals then provided insight to how the symptoms and manifestations of ITP are being experienced by patients and affecting their loved ones.

One polling question (Appendix 3, question 9) asked participants to identify up to three symptoms that currently have the most significant impact on the lives of patients, their caregivers, and family.

The symptoms that caregivers and patients were most worried about represented how ITP affects quality of life. Additionally, bruising/petechiae and frustration over the treatment "roller coaster" affected both patients' and their caregivers' lives in multiple ways.

Note: Full polling results can be found in Appendix 3.

A. Fatigue

"Fatigue and depression were an invisible and unbearable weight… It seemed like I was in a pit and couldn't get out."

"Fatigue and depression were an invisible and unbearable weight… It seemed like I was in a pit and couldn't get out."

It is worth noting that the symptom selected by the most polling participants was not a physical manifestation of ITP such as bruising, bleeding, or even platelet count, but a symptom that severely impacts patients' quality of life and daily living. The effects of ITP go beyond the blood and reaches into almost every aspect of patients' lives. Even if a patient's platelet counts are relatively higher or more stable or bleeding is controlled, fatigue can still plague him or her, inflicting paralyzing effects on day-to-day life. One panelist described how he decided to stop treatment due to negative side effects from medicines that were not significantly boosting his platelet count; although his platelet count was slightly higher than normal, "ITP took a significant toll on my daily life. I struggled to get out of bed and it only got worse from there. On my best days, I was barely able to get through the day. I could push ITP to the background, but it was exhausting. On my worst days, I laid in bed all day in a dark room. Fear had me stuck in the house for months while I had critical platelets. Anxiety and stress were always with me. I hated my life." Another panelist said that the severe fatigue he felt from ITP and ITP treatments "made once easy tasks such as showering extremely difficult."

B. Anxiety

"Fear had me stuck in the house for months while I had critical platelets. Anxiety and stress were always with me. I hated my life."

"Fear had me stuck in the house for months while I had critical platelets. Anxiety and stress were always with me. I hated my life."

Almost half of polling participants responded that anxiety is one of the top three symptoms that have a significant impact on their life, further demonstrating that ITP goes beyond the physical symptoms and can severely impact patients' emotional and mental well-being. Anxiety over platelet counts, restricted lifestyles, fear of the unknown, and treatment side effects can consume a patient's life. Polling participants also expressed developing anxiety over decreased energy levels, the effects of their disease on family, and in managing mental health effects. It is easy to feel lost and helpless when battling a chronic illness or caring for someone who is fighting a disease like ITP. One panelist explained, "I was robbed and started to withdraw from everything, even my friends. I was alone. Nobody understood what I was going through." This sense of loneliness and isolation can contribute to feelings of anxiety.

C. Bruising/Petechiae

"One morning I woke up with petechiae all over my arms and legs. It was even in my mouth."

While the "hidden" symptoms of ITP have profound effects on quality of life, the physical manifestations of ITP also play a significant role in patients' lives and should not be ignored. One panelist explained that bruising is what first indicated something was wrong with her son: "His body was covered in bruises – way too many to count." Bruises and petechiae also contribute to the isolation patients feel, as they are very visible markers of something being "wrong." They can also be a reminder for a patient that he or she is restricted from taking part in "normal" activities or pursuing what they love because of the risk to his or her physical health. One panelist said her exercise has been restricted to walking and aqua aerobics because of her bruising, that "even at the gym [she] get[s] bruised."

"His body was covered in bruises – way too many to count."

Nose bleeds can be socially isolating also, especially if it is difficult to stop them and there are drops of blood on clothes.

D. Frustration over treatment "roller coaster"

"ITP is described as a roller coaster. There is no way to know what the next platelet count will be, or if the phlebotomist will be able to successfully draw blood without leaving me in pain and bruised, or if the new medication will work of have side effects. The uncertainty of ITP is frustrating and scary."

"Due to all the medications and steroids that I have had to put into my body I have had cataracts in both eyes along with becoming insulin dependent."

One third of polling participants indicated frustration over the treatment "roller coaster" as one of their top concerns with ITP. The efficacy of treatment is not always consistent, or even guaranteed, and is a source of stress and anxiety for many ITP patients and their caregivers. Furthermore, the positive effects of treatments on a patient's ITP do not always outweigh the negative side effects that pose separate problems to the patient's health. One panelist explained, "Due to all the medications and steroids that I have had to put into my body, I have had cataracts in both eyes along with becoming insulin dependent." With other patients, splenectomies have been performed to address platelet counts, but this operation can cause other complications down the road due to leaving the immune system compromised. "I am still dealing with the trauma and negative thinking that I developed. Missing my spleen leaves me at risk of getting infections, which can be dangerous," remarked one panelist about his splenectomy. It also may not work.

Impact on daily life of patients and their caregivers

The panel and facilitated group discussion demonstrated how ITP is not merely about the platelet count, but a disease with the ability to invade every aspect of a patient's life. Meeting participants shared the consequences of ITP on their daily life and how having ITP has significantly changed their lifestyles.

One polling question (Appendix 3, question 10) asked participants to identify up to three activities their ITP limits or prevents them from doing.

The activities that caregivers and patients find most difficult to accomplish represented how ITP takes a significant toll on daily life. Top concerns included sports or the capacity to exercise, hobbies or social activities, and completing daily tasks. These results show the far-reaching effects of ITP beyond physical and emotional symptoms, as it places severe restrictions on the day-to-day lifestyles of many patients.

Note: Full polling results can be found in Appendix 3.

A. Sports or the capacity to exercise

"No more biking, roller skating, scuba diving, contact sports, skiing… Even at the gym I get bruised. Walking and aqua aerobics are the only exercises I can safely do."

Seventy-five percent of participants responded that ITP prevents them from participating in sports or limits their capacity to exercise.

Seventy-five percent of participants responded that ITP prevents them from participating in sports or limits their capacity to exercise. Many patients and caregivers expressed that they or their loved ones have been "robbed" of the ability to participate in activities they love or pursue things they are passionate about. It is often the case that a patient was once active, but after being diagnosed with ITP, had to make a significant change to their lifestyle and routine. This sudden altering of a person's life can take a toll on their emotional well-being, as they are being deprived of something that once brought them joy. One panelist's dreams of wrestling was taken from him with his diagnosis, making his years of training feel like it was for nothing. A mother in the audience spoke on behalf of her son, saying that ITP "took him away from wrestling and football," and she urged the FDA to approve drugs and treatments for children because "children's lives matter too." Furthermore, the limitations on exercise for ITP patients can deprive them of the benefits exercise can have on someone's mental and physical health, thus ultimately contributing to the way ITP affects quality of life and mental health in patients.

From the audience, a twelve-year-old diagnosed last October spoke up and said, "The biggest and hardest thing for me is not being able to do things with my friends."

B. Hobbies or social activities

"All of this with being alone and not working, along with the depression, kept me from leaving the house except to go to doctors' appointments for close to 10 months."

Over half of polling participants indicated that ITP places strict limits on a patient's ability to take part in hobbies or social activities, which, like the limits on sports and exercise, can severely affect a patient's quality of life. ITP can restrict a person's hobbies and social activities for various reasons; someone might not be able to partake in the activities he or she prefers because of risk of injury, a low platelet count and the complications that arise from it, or fatigue and depression. Whatever the cause, the inability to engage in hobbies and social activities has

negative consequences on an ITP patient's emotional and mental well-being. Withdrawal and isolation are a natural consequence of someone feeling that they can no longer participate in the things they enjoy, or that they have been robbed of their life. Because ITP restricts a patient's lifestyle through both physical and emotional limitations, it can create feelings of loneliness and helplessness. Patient participants described the feelings of isolation and loneliness they felt, and how they would often withdraw from people because others simply could not understand what they were going through. From the audience, a twelve-year-old diagnosed last October spoke up and said, "The biggest and hardest thing for me is not being able to do things with my friends." "ITP is more than a bleeding disorder, isn't it," said another audience member. "It really has an impact on so many aspects of a person's life and on a family's life."

"Predicting platelet levels is a risky business. There have been many times that I planned a vacation thinking my counts were safe and have wound up hemorrhaging out on an airplane due to the combination of my low platelets and the cabin pressure."

C. Traveling or spending time away from home

"Predicting platelet levels is a risky business. There have been many times that I planned a vacation thinking my counts were safe and have wound up hemorrhaging out on an airplane due to the combination of my low platelets and the cabin pressure."

Over fifty percent of polling participants responded that their ITP restricts their ability to travel or spend time away from home. ITP is unpredictable and patients have expressed how it makes them feel out of control of their own lives. This feeling of not being in control, and the anxiety surrounding platelet counts, uncertain responses to treatment, and the effects of fatigue and depression severely limit ITP patients' ability to move freely when and where they want. One participant told the audience that her platelets drop to zero almost every other month. "I spent most of October in the hospital," she said, a testament to the unpredictability of the disease and the way it causes someone to feel like they have lost control. Various stories of restricted mobility due to ITP demonstrate how ITP touches all aspects of life and influences the extent to which they can live their lives.

D. Completing school or work activities and daily tasks

"The fatigue is overwhelming, and it limits your ability to do daily chores and activities…then there is the guilt about not being able to fulfill your role in life."

"The fatigue is overwhelming, and it limits your ability to do daily chores and activities…then there is the guilt about not being able to fulfill your role in life."

ITP does not only affect individuals' ability to complete strenuous tasks, but even the activities that constitute daily life. Participants spoke of having trouble getting out of bed, showering, tackling a to-do list, attending school, or maintaining the ability to go to work. "I was so sick I had to stop working in 2014. I then went on long-term disability on the advice of management. Now I was home all day alone," explained one panelist, and he was not alone in his experience. Several other participants said they also were on disability from work because ITP prevented them from being able to fully execute their jobs. One woman in the audience spoke about the "anxiety of regular life problems" that ITP provokes. "You can't even make an appointment without having all of these checks in place," she said, explaining that she has to get her platelets checked before even going to the dentist. The high percentage of individuals who struggle to complete daily tasks and activities due to their ITP reveals just how debilitating the disease is, and how no aspect of life is free from its reach.

TOPIC 2: PATIENTS' PERSPECTIVES ON CURRENT APPROACHES TO TREATMENT

The second topic focused on current and future approaches to treatment, as well as supportive care and medical devices used to help manage ITP. The session began with a panel of three patients and one parent discussing their current forms of treatment, the downsides to their regimens, what an ideal treatment looks like to them, and what factors they take into account when selecting a course of treatment. Panelists described the various treatment regimens they or their loved ones undergo to manage the symptoms of ITP, and their testimonies provided insight to the shortcomings and unmet needs of ITP patients regarding treatment and management for ITP symptoms:

- **Panelist 1:** "There's nothing out there for me now," said the first panelist, a 62-year-old woman who was diagnosed with ITP at age 30. Within six months of her diagnosis, she had been on high dose prednisone, 125 mg daily for five months, and underwent a splenectomy, leaving her immune system compromised. She explained that while the surgery helped, it was not a permanent fix and she began having lasting problems around 2006. "My energy was zero, I was literally spending 12-14 hours a night in bed but not sleeping, I was covered in bruises and routinely had a mouth full of blood blisters. Mostly though, I was fatigued… and scared," she told the audience. The panelist then had her first brain bleed in 2008, found PDSA, and began treatments again. She took Nplate and it was an effective treatment for about eight years, when it suddenly stopped working and she once again experienced crippling fatigue, bruising, bleeding, and fear of another brain bleed. And so, began an endless journey of trying different treatments and medicines without experiencing any lasting success. In 2018, the panelist said she spent four consecutive weeks hospitalized with ITP: "I was treated with Rituximab, Promacta, Atarax for anxiety, more Rituxan, higher dose Promacta,

"There's nothing out there for me now."

Tylenol, Dexamethasone. None of it worked. None of it. None." She received one of the first bottles of Tavalisse distributed with FDA approval which also proved ineffective. Eventually, she was put on Nplate again, and it worked, demonstrating the unpredictability of ITP treatments and their effectiveness. She continued by saying that although the Nplate is working again, "the efficacy of the medication is very random – sometimes I need a shot a week, sometimes it's three weeks between shots at the same dose," further demonstrating the variability in effectiveness of ITP treatments and that ITP is truly an individual disease.

- **Panelist 2:** The second panelist, a thirteen-year-old boy who has had ITP since age 8, said, "So many drugs get approved for adults but not kids, making it harder for kids to get the treatment that they truly need to help them." Although his platelet counts are relatively stable on Nplate, he pointed out that not only is it one of the few drugs specifically created to treat ITP, but that when he started taking it, it was only approved for adults and not kids, which made insurance coverage difficult to obtain. He also explained that he struggles with the way ITP restricts his lifestyle, saying he misses a lot of school and activities because of his fatigue. He said that it is easy to feel isolated, especially because kids his age don't understand his illness or the limitations it places on him. "When I was first diagnosed, some friends avoided me for fear of catching my disease and even told me that I wasn't invited to their birthday parties because their parents worried I would get hurt… This made me feel left out, sad, and alone," he explained. His story demonstrates the urgency for kid-specific treatments, so that young ITP patients can live a "normal" life, like this panelist has been since starting Nplate.

"When I was first diagnosed, some friends avoided me for fear of catching my disease and even told me that I wasn't invited to their birthday parties because their parents worried I would get hurt… This made me feel left out, sad, and alone."

- **Panelist 3:** "I often feel like I am playing Russian roulette with my life," said the third panelist, a 55-year-old woman living with chronic refractory ITP since her diagnosis at age 21. Currently on Promacta, she said that her platelets are in a safe range only part of the time – "most of my counts are either critically low, between 1,000 and 5,000, or critically high, over 1 million at times." During the periods of low counts, the panelist experiences severe fatigue that leaves her bedridden with blood blisters, bloody noses, vaginal hemorrhaging, and spontaneous bruises/petechiae. She told the audience that her ITP is debilitating, but that because she does not "look sick," people do not understand the trials she has had to endure. With only 2 years of remission in the last 34 years, she has adopted a strict immune power diet, been treated with numerous rounds of steroids, received IVIG, took Rituxan, eltrombopag, alternative medicines, and had a splenectomy. The steroids triggered negative side effects such as weight gain and mood shifts, and IVIG once caused her to get aseptic meningitis, and she eventually became immune to both treatments. This panelist's story is a testament to the inconsistency in ITP treatments; she demonstrates that the efficacy of ITP treatments can vary within an individual, and that while a certain treatment might work for some, that does not guarantee universal success.

The steroids triggered negative side effects such as weight gain and mood shifts, and IVIG once caused her to get aseptic meningitis, and she eventually became immune to both treatments.

- **Panelist 4:** The fourth panelist of the afternoon session was a young woman who was diagnosed at age 16. Now nineteen years old, she has tried several ITP treatments with varying success, saying, "My hematologist had labelled me his 'conundrum' as my ITP was not responding to treatments as he had hoped." She told the audience that she has received several rounds of steroid treatment, but "hated how the steroids made [her] feel and look." Eventually, she began to refuse steroids even though her bleeding was worsening. "My parents were also worried about not only the immediate effects of the steroids, but the long-term effects of the high doses that were needed." The panelist began taking Nplate, but her platelet counts continued to fluctuate, going between 70,000 and 11,000 within the course of a week. She has now been on Revolade since October 2017, and her platelets are stabilized at 120,000. However, her hematologist has told her that they need to start considering future options. "I am fearful of the effects of being on this medication long term, and at such a young age. I am fearful that it will stop working for me," she said. Although she has found a treatment that is successful for now, she knows that there are other risks that come with ITP treatments that could ultimately prohibit any further use of that medicine.

"I am fearful of the effects of being on this medication long term, and at such a young age. I am fearful that it will stop working for me."

Participants at the meeting and online were then asked to respond to polling questions about current treatments and multidisciplinary care for ITP, as well as questions about future treatments and what they considered to be a meaningful improvement that a treatment could provide. The polling responses were used as a starting point for the facilitated group discussion and revealed patients' and caregivers' perspectives on the management of ITP. The opinions of patients and caregivers on the options for and experiences with treatment are explored in the thematic analysis below.

Perspectives on treatments and considerations in decisions regarding treatment

Between the panel and the facilitated group discussion, a polling session systematically explored the issues raised by the panelists, including the efficacy of ITP treatments, any issues with treatments, and factors patients consider when making a decision about treatment.

The polling responses were used as a starting point for the facilitated group discussion, and further demonstrated the shortcomings in available ITP treatments and the difficulties patients have in finding a treatment that works and will not have negative effects when used long-term. The testimony of the individuals then provided insight to how patients access – or struggle to access – treatments for ITP and how they experience the effects of various treatments.

39% had tried 3-5 different treatments and 25% had tried 6-8 different treatments.

Polling results from a question (Appendix 3, question 14) that asked participants how many conventional ITP treatments they have tried indicated that 39% had tried 3-5 different treatments and 25% had tried 6-8 different treatments, and polling results from the following question (Appendix 3, question 15) that asked participants how many complementary treatments they have tried indicated that 40% had tried complementary therapeutic disciplines. This set of questions demonstrated the extent to which patients must undergo multiple treatments before finding one that works – assuming they do eventually find an effective course of treatment.

Another polling question (Appendix 3, question 18) asked participants to identify the issues they experience on their current treatment, while a later set of questions (Appendix 3, question 19 and 20) asked participants to prioritize what they most want out of a treatment for ITP in terms of what aspect of ITP the treatment address and how the treatment will affect the patient's daily life.

Most patients expressed that an ideal treatment would improve platelet count and increase energy levels, have few side effects that would negatively impact their quality of life and would increase the possibility of going into remission. Participants also indicated the need for therapies with a route of administration that better aligns with lifestyles, and voiced concerns around those with the capacity to induce an impaired immune system. The audience discussion revealed the extent to which the medical needs of ITP patients go unmet and brought attention to the work that still needs to be done in order to better serve the needs of the ITP community.

Note: Full polling results can be found in Appendix 3.

A. Effectiveness of treatment(s)

"In November of '17 the Nplate stopped working. Again, with the absolutely crippling fatigue, bruising, bleeding, and mostly the fear."

Seventy-four percent of polling participants responded that they have tried at least three different conventional ITP treatments, demonstrating the difficulty ITP patients experience trying to find a treatment that works for them. Many ITP patients also turn to complementary treatments to find something that helps them cope, with another 73% of polling participants indicating that they have tried at least one form of complementary treatment for their ITP. The extent of treatments tried by ITP patients startlingly shows that there are medical needs of the ITP community that remain unmet. Many ITP patients have undergone multiple forms of treatment in an attempt to raise their platelet counts and ease the symptoms of ITP, and it is difficult to predict which treatment will be the one to successfully treat a patient's ITP without also having side effects that negatively affecting his or her quality of life. According to the polling results, the participants have tried over twenty types of treatments, with varying efficacy across the group as well as individually. One audience member said, "The amount of medications [I've tried] has blown my mind," and that there is no guarantee how long a treatment will remain effective – "I might get three months, I might get a year." Another participant explained that her daughter was refractory to five treatments before finding Promacta. The unpredictability of treatments in consistently and effectively managing ITP has a profound effect on an ITP patient's quality of life. Patient testimonies clearly demonstrated the need for a better understanding from the FDA and scientific community of the burdens that ITP presents for patients and caregivers in living life with the disease.

Seventy-four percent of polling participants responded that they have tried at least three different conventional ITP treatments.

B. Issues with current treatment(s)

"Then they tried Rhogam, which made me really sick and also didn't increase my platelets."

Almost 90% of polling participants responded that a primary factor they consider when deciding on a course of treatment is few side effects. Although treatment is a desired course of action, many ITP patients also experience negative side effects that can overshadow the benefits of a treatment. One panelist

Almost 90% of polling participants responded that a primary factor they consider when deciding on a course of treatment is few side effects.

explained that some treatments have caused headaches, moodiness, difficulty focusing, and bone pain. "Those [effects] have been bad enough sometimes to cause me to miss school and extracurricular activities. Sometimes it can be so bad that all I want to do is sleep," he said. As indicated, quality of life is a large concern for ITP patients, and although some treatments might successfully treat the physical symptoms of ITP, they could also be detrimental to the patient's quality of life, which effectively negates a significant purpose of receiving treatment. Participants' responses to the polling questions, as well as their contributions to the panel presentation and group discussion, show that treating ITP symptoms can come at a cost to other aspects of a patient's well-being. To successfully treat ITP, patients often sacrifice other elements of their health or quality of life. This clearly demonstrates a severe shortcoming in available ITP treatment that must be addressed. Furthermore, side effects of pain and/or headache are more difficult to treat because so-called non-steroidal anti-inflammatories often cannot be used because of their inhibition of platelet function.

C. Factors to consider when deciding a course of treatment

"I am looking for a treatment that would provide me with a CONSISTENT, safe platelet count. I often feel like I am playing Russian roulette with my life."

"I am looking for a treatment that would provide me with a CONSISTENT, safe platelet count. I often feel like I am playing Russian roulette with my life."

When deciding a course of treatment, ITP patients must consider multiple factors, such as the long-term response, side effects and finances. As one audience member said, "ITP is a snowflake disease," due to the fluctuating symptoms experienced from one person to another, and just as different people can manifest symptoms of the disease differently, certain people respond to treatments differently than others, or a patient might even have varying responses over the course of a treatment. One participant explained that first line treatments didn't really work for her, and that on Nplate, her platelet counts can go from 90 to 740 within one week. Her story demonstrated the difficulties ITP patients face trying to find a treatment with consistent results. Furthermore, patients struggle to find treatments that effectively relieve their ITP symptoms of their ITP without negatively affecting other aspects of their health. One panelist expressed that at one point she refused to take steroids again, even though her bleeding was worsening. She said that her parents were worried about the long-term effects of the high dosage that would be needed. Other audience members agreed that patients are hesitant to explore treatment options because their negative effects often outweigh the benefits – they need stability and a better chance of success. Finally, finances play a significant role in patients' decisions to pursue a course of treatment. One participant asked, "How can you get the prescription your doctor wants you to have if it's not financially feasible? How do you demystify the insurance world to find out what companies cover what drugs?" A panelist also spoke to the financial obstacles that may prevent access to treatment, particularly for children because many drugs are approved for adults but not children, thus limiting their options even further.

"How can you get the prescription your doctor wants you to have if it's not financially feasible?"

BENEFIT-RISK ASSESSMENT FRAMEWORK

Incorporating the patient voice into a benefit-risk assessment framework for Immune Thrombocytopenia (ITP).

There are five key decision factors analyzed within the structured benefit-risk assessment framework as part of the developmental process in regulatory decision-making for drugs and biologics specific for human use. These key factors include: Analysis of Condition, Current Treatment Options, Benefit, Risk, and Risk Management. This approach allows for transparency for how decisions are made by the FDA in terms of what's approved and what isn't by providing a succinct summary of each decision factor. In order to provide a clear overview of the severity of a condition and the dire need for better treatment, "Analysis of Condition" and "Current Treatment Options" sections are essential in the decision-making process for drug regulation. The "Benefit", "Risk", and "Risk Management" sections are used to provide an overview of the efficacy and safety of a particular drug. Ultimately the benefits of a particular treatment need to outweigh the risks in order for approval to be granted.

The benefit-risk assessment framework was completed using information from various places. Some of the information came directly from the ITP EL-PFDD meeting held on July 26, 2019. Other sources included evidence based published literature. This framework provides a sample of what could be included in a benefit-risk assessment completed for a drug under review for ITP. Over time, with new research developments and knowledge growth in the field, the information within the framework can be updated.

This EL-PFDD meeting has highlighted the importance and urgency in finding medical interventions for ITP that are long lasting and have minimal side effects and are safe for all age groups to use. Improved access to medical therapies was also expressed. The EL-PFDD meeting showcased the importance of increased awareness, early diagnosis and management, and better treatment options for individuals with ITP.

Decision Factor	Evidence and Uncertainties	Conclusion and Reasons
Analysis of Condition	Immune Thrombocytopenia (ITP) is a rare autoimmune bleeding disorder that affects men and women of all ages. The hallmark of ITP is a low platelet count due to immune system dysfunction. Platelets are essential for normal clotting. This results in an increased propensity to bleed excessively with little to no injury. Bleeding risks range from mild cutaneous bleeding to dangerous life-threatening mucosal bleeding. Life-threatening intracranial hemorrhage is another specific lethal risk with this condition. The clinical consequences of ITP and current treatment options are heterogeneous but can be debilitating, profound, and for some, lethal. Not all individuals with ITP will experience the same clinical symptoms. The disease shows variable expressivity. The degree to which these symptoms impact a person living with ITP may change over time living with the disorder. Overall, individuals with ITP have an up to 20-year reduced lifespan. *See the Voice of the Patient report for a more detailed narrative.*	Immune Thrombocytopenia (ITP) is a rare autoimmune bleeding disorder affecting any age group and gender with wide-ranging complications that vary from person to person and in the individual over time. Bleeding consequences range from mild to life-threatening. ITP related Intracranial hemorrhages (ICH) are often fatal or cause debilitating neurological sequelae. Individuals with ITP endure multi-systemic complications related to unpredictable bleeding, mental health issues, reduced health-related quality of life including often debilitating chronic fatigue. These effects profoundly compromise the enjoyment of life and being able to work or attend school with frequent hospitalizations for blood work and/or treatment. For parents with children who have ITP, their lives and finances are compromised as well. ITP is a heterogenous condition that can change in severity over time. *Individuals with severe and refractory type ITP may have a reduced overall life expectancy.*
Current Treatment Options	***There is currently no long-term cure for ITP.*** Corticosteroids, Anti-D, and IVIG are often used as a first-line therapy. They provide a temporary boost in platelet count stabilizing the disorder, if the patient responds, lasting for only days to weeks. Thrombopoietin receptor agonists and Rituxan are common second-line therapies. They can require a hospital admission and/or many follow-up visits to measure how platelet counts are responding. Frequent appointments are expensive and time consuming. Not all ITP patients respond to the same treatment options. All treatment options come with potential serious side effects, and access may be limited due to their high cost or governmental regulations. *See the Voice of the Patient report for a more detailed narrative.*	There IS an unmet need for effective and tolerable FDA-approved therapies to treat ITP, particularly ones that increase and sustain individual platelet counts to minimize bleeding risks, reduce exercise intolerance and chronic fatigue – providing gains in function and the ability to live a normal, full life absent of strict activity restrictions and unpredictable bleeding. There is also an unmet need for improved treatments that are affordable and available worldwide.

CONCLUSION

The PFDD meeting emphasized the critical and ongoing need for increased awareness and understanding around the multifaceted impact of ITP on a patient's overall health, mental well-being and quality of life; and its far-reaching effect on caregivers, family members and the general community at large. Also highlighted was the vast need to develop targeted therapies for more consistent outcomes with fewer side effects, better access to and more affordable treatment options, and a more well-rounded, clearly defined guideline that would help physicians and patients to develop an individualized care plan for ITP. A leading clinical expert provided insight into the complex issues faced by clinicians and researchers in diagnosing, treating and developing better therapies for this disease. Furthermore, FDA was provided with a unique opportunity to hear detailed accounts from patients and caregivers, at a variety of positions in their journeys and living on different continents, at this PFDD meeting and to more intimately and thoroughly understand the physical, emotional and far-reaching burdens of living with ITP.

Unmet needs of ITP patients and what can be done

Patients with ITP are experts on what it's like to live with their condition; they are best able to identify and articulate the impact of ITP. The patient voice offers principal perspectives into quality of life issues and the advantages and adverse effects of each treatment, yet at times their chief complaints and fundamental needs may not be factored explicitly into drug development. The ITP community was honored and very pleased to have been given the opportunity to advance the science of patient input and to provide guidance to the FDA about the needs of patients with ITP. PDSA remains committed to clearly communicating the significant medical needs of our patient population.

Patients want more efficient diagnostic tests: Patients describe the unpredictability and frustration of living with ITP, feeling limited in their life choices and worn out or depressed by the many ups and downs that accompany the condition. These challenges begin with the difficulty in confirming the initial diagnosis. Because there is no test for ITP, diagnosis is made as a process of elimination.[10]

Patients want treatments that last and better quality of life: Ideally, therapies should have fewer side effects and should address the fatigue and depression that play major roles in their lives. Greater durability of the effect of therapies and long-term surveillance for risk factors and complications can minimize the anxiety that comes with the ongoing fear of relapse. They don't want to feel forced into splenectomy or continued steroids and they don't want to run out of treatment choices. Patients want studies to address the burden of their disease beyond the platelet count.[11]

Patients want increased awareness in public and professional health communities and comprehensive treatment centers to improve care and outcomes: Stories of physicians who over-treat or incorrectly treat ITP patients due to their minimal knowledge about this rare disease are all too common. Raising awareness for ITP in the clinical sphere is crucial in better informing medical professionals, and raising public awareness for ITP is vital in empowering patients to take control of their disease. Comprehensive treatment centers for ITP and other bleeding disorders would mitigate the risk posed by non-specialists treating ITP patients, thus improving a patient's treatment options, therapy experience, and quality of life.

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[10] Rodeghiero F, Ruggeri M. ITP and international guidelines: What do we know, what do we need? *La Press Medicale.* 43 (4), (2014).
[11] Rodeghiero

Research and federal funding opportunities: Ongoing research, clinical studies, and therapy development are vital to improving the treatment landscape, giving patients more choices with which to live their lives fully, with fewer side effects and long-term control of their ITP.[12] These opportunities would not only provide access to more affordable treatments but also minimize recurrent emergency treatment and hospitalization, lessening the financial burden of disease on families affected by ITP.

At the conclusion of the meeting, PDSA Board Chair Peter T. Pruitt Jr. shared reflections from the perspective of both an organizational leader and caregiver. "Putting on this [annual] conference is a bit of a herculean task," he began, "…and to add this [PFDD meeting] on to it on Friday makes it an over-the-top task….I've been to a lot of conferences and this has maybe been one of the most powerful and impactful sessions we've had," he said. He thanked the FDA, industry partners, and clinicians for their willingness to hear patient/caregiver voices and for their commitment in dismantling barriers that hinder brighter futures for people with ITP. As the caregiver to his 62-year-old wife diagnosed with ITP at age four, he continued to outline the significance of the patient/caregiver voice and the interminable need for education, advocacy and support to generate increased awareness about the crippling effects of and need for better outcomes for people with ITP. "I have to thank the caregivers, right?" he asked. "Being one of them [myself]; for the strength and support you provide, and the love you provide those of your families and members who are suffering from ITP, but most importantly, I want to thank the patient panelists and those of you [in the audience] who spoke. It takes a tremendous amount of courage to get up and talk about such personal challenges. Here at the PDSA, we're here to support, we're here to help you and your physician receive the information you need to manage your ITP, to advocate for you, to inform you, and this is just the beginning…whether you're a caregiver of or sufferer with ITP, hearing that you're not crazy, that the things you are feeling are not, and are what others are feeling. This session was really important from that standpoint," he concluded.

Ongoing research, clinical studies, and therapy development are vital to improving the treatment landscape, giving patients more choices with which to live their lives fully, with fewer side effects and long-term control of their ITP.

"I've been to a lot of conferences and this has maybe been one of the most powerful and impactful sessions we've had …whether you're a caregiver of or sufferer with ITP, hearing that you're not crazy, that the things you are feeling are not, and are what others are feeling. This session was really important from that standpoint."

The Platelet Disorder Support Association is grateful to the patients and caregivers who bore the unseen bruises of ITP, to the physicians and scientific experts who participated and listened with interest, and to the FDA for its support, participation and dedication in upholding this vital initiative in the unification and affirmation of the global ITP community. It is with great optimism that we anticipate this information will be used to establish patient-centric standards and guide approvals of much needed therapies and better outcomes for immune thrombocytopenia.

[12] Izak M, Bussel JB. Management of thrombocytopenia. F1000prime Reports. 6, (2014).

APPENDIX 1: MEETING AGENDA, PANELIST/SPEAKER BIOS, AND TOPIC QUESTIONS

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AGENDA

9:00 – 11:00 AM	Registration
11:00 – 11:30 AM	Welcome, Introductions, & Opening Remarks *PDSA President & CEO Caroline Kruse, PDSA Founder Joan Young, FDA Representative Ann Farrell, MD*
11:30 AM – 12:00 PM	Background on Immune Thrombocytopenia (ITP) *James Bussel, MD*
12:00 – 12:30 PM	Panel Discussion Topic 1: Effects of ITP that Matter Most to Patients and Caregivers *A panel of patients and caregivers will provide comments*
12:30 – 1:30 PM	Facilitated Group Discussion by Patients on Topic 1: Effects of ITP that Matter Most to Patients and Caregivers *Patient representatives from the audience will be invited to contribute to discussion*
1:30 – 2:15 PM	Lunch
2:15 – 2:45 PM	Panel Discussion on Topic 2: Patient Perspectives on Current Approaches to Treatments *A panel of patients and caregivers will provide comments*
2:45 – 3:45 PM	Facilitated Group Discussion by Patients on Topic 2: Patient Perspectives on Current Approaches to Treatments *Patient representatives from the audience will be invited to contribute to the discussion*
3:45 – 4:00 PM	Open Public Comments and Closing Remarks

ABOUT THIS EXTERNALLY-LED PATIENT-FOCUSED DRUG DEVELOPMENT MEETING

The Platelet Disorder Support Association (PDSA), a patient support an advocacy organization serving those who suffer from and care for individuals with immune thrombocytopenia (ITP) and other rare platelet disorders, is holding the EL-PFDD meeting between the ITP community and the U.S. Food and Drug Administration (FDA) during ITP Conference 2019. The EL-PFDD meeting will advance PDSA's mission: to enhance the lives of people with immune thrombocytopenia (ITP) and other platelet disorders through education, advocacy, research, and support.

PDSA is one of several organizations serving the 7,000+ known rare diseases to ever host an externally-led PFDD meeting, and our PFDD meeting is the first of its kind to ever be held for ITP and other platelet disorders. PFDD meetings meaningfully integrate patient insights, needs, and priorities into drug development and evaluation. Following the successful model that the FDA developed to host similar meetings, the half-day event will focus primarily on a range of patient viewpoints on immune thrombocytopenia (ITP), covering the symptoms and impacts to daily life that are most important to patients

and their perspectives on existing and future treatments.

The goal of this meeting is to increase awareness of the FDA and other drug development stakeholders on the impact that ITP and rare platelet disorders have on quality of life for affected individuals and their families. The PFDD meeting provides the ITP community an opportunity to inform the FDA about the realities of living with ITP. Patient/caregiver input may encourage the approval of new therapies, impact clinical trial design, inform FDA's decisions and oversight, and improve outcomes for patients living with the disease.

Instructions for Polling Questions

Each session in today's meeting will include a series of polling questions on immune thrombocytopenia (ITP) and its impact on your family's life. In-person attendees are encouraged to use their mobile phones or computer to participate in these polling questions. **Note: Responses should be cast by the patient OR caregiver – NOT BOTH. No more than ONE vote should be cast for each individual with ITP.**

Visit PollEv.com/beatITP prior to the meeting and create your account.

During polling, respond at PollEv.com/beatITP or text BEATITP to 22333 once to join, then A, B, C, D, E…

Standard message and data rates apply.

PANELIST BIOS

Haley Agius

Haley is 19 years old and lives in St. Thomas, Ontario, Canada with her parents, Julie and Paul, and older brother, Brennan. She was diagnosed with ITP at the age of 16. Haley attends Wilfrid Laurier University in Waterloo, Ontario where she studies Kinesiology, concentrating on Health and Rehabilitation. She enjoys all sports, especially hockey and soccer, working out, and spending time with friends.

John Colgan

John lives in Phoenix, AZ with his wife, Rebecca. He was diagnosed with ITP in 1982 at the age of 17 and has been on Social Security Disability since 2014. John has made it his purpose to educate the public on how ITP has changed his life, but not taken it over and spends as much time as possible with his grandchildren.

Leilani De Castro | Parent to Joey Fitzgerald

Leilani lives in Santa Ana, California with her fiancé, Joey Sr., and their son, Joey Jr. Joey Jr. was diagnosed with Immune Thrombocytopenia (ITP) at the age of two. Leilani works in the Office of Research at Cal State Fullerton. She loves to travel and enjoys spending time with her family and friends.

Lib Elder

Lib is a 62-year-old woman living in rural Virginia. She was diagnosed with ITP at age 30, although earlier surgical records and anecdotal evidence would suggest she's had ITP from childhood. Lib has drawn disability since surviving her first brain bleed in 2008. She has been described as having "chronic brain bleeds" by two neurologists. She is an artist by nature and continues to create, often incorporating health and social issues into the themes of her work. She is an animal activist and often works on political

campaigns of particular interest to her. The zoonosis concerns raised by her failed splenectomy have impacted her ability to safely advocate for animals, and the bleeding issues have dramatically changed her approach to art, which used to be primarily in the medium of cut glass but is less so every day.

Jennifer MacWhirter DiRaimo | Parent to Luca DiRaimo

Jennifer is 42 years of age, married with two amazing boys and a new baby on the way. She currently lives in London, Ontario, Canada, although she was born and raised in Toronto (Ontario, Canada). Jennifer is a certified Genetic Counselor with a Master's degree from Brandeis University in Genetic Counseling and has worked as a Genetic Counselor for over fourteen years. Jennifer is currently on a child loss leave of absence due to the death of her oldest son, Luca, who developed a brain bleed at the age of ten last May (2018). Luca was diagnosed with ITP just after his seventh birthday, but he was only an active spontaneous bleeder for the last eight months of his life. Jennifer's hobbies include crafting, running, reading, learning new things, spending time with family/friends and her two dogs.

Linda McGuirl

Linda is 55 years of age and lives in Point Pleasant, New Jersey with her husband, Michael. She has three grown children and has had ITP since the age of 21. Linda retired from being a Financial Advisor in 2018 due to her chronic refractory ITP and is currently on disability. She is an active Board member of PDSA and has been a Facilitator of the PDSA ITP Support Group of Northern/Central New Jersey since 2008. Linda is also an active Patient Advocate for people with ITP. Her hobbies include horseback riding, skiing, and dancing when her platelet counts are at safe levels. When her counts are low and she is bedridden, Linda enjoys listening to books via Audible.

John Phillips

John is 22 years old, lives in Elk Grove, California and was diagnosed with ITP at age 17. He currently attends college, frequently volunteers at blood drives and is the chairperson for blood drives at his college. He co-facilitates the ITP Support Group in Sacramento, California with his mother, Dawn, and is grateful for his amazing and supportive family that helps him through the hard times and celebrates the good times. In his free time, John enjoys meditation, camping, and playing the didgeridoo.

Barbara Pruitt

Diagnosed at 4 years old, Barbara is a 62-year-old mother of two grown children and lives in Coral Gables, Florida with her husband, Peter. A retired nurse, Barbara enjoys painting, golf, cloisonné and jewelry work. In addition to her most recent position as grandma, Barbara has become a passionate advocate for people suffering with ITP. As a chronic, refractory patient for 58 years with only three months of remission and platelet count of 5,000 who has participated in several clinical trials, Barbara offers a unique perspective on the patient journey. As both a patient and parent, Barbara feels deeply connected to the newly diagnosed and parents of children with ITP as they manage the fears and uncertainties inherent in living with this rare bleeding disorder.

Logan Resch

Logan is 14 years old. He lives in Milton, Georgia with his mom, Jana, dad, Mike, and brother, Liam. A young patient advocate and mentor, Logan is a regular contributor to the Platelet Disorder Support Association's support and advocacy programs counseling both parents and children affected by the disease. He likes to swim, play basketball, and video games. Logan aspires to attend college and become a nurse when he's older.

SPEAKER BIOS

James Bussel, MD | Weill Medical College of Cornell University

James Bussel is a Professor of Pediatrics, Medicine, and Obstetrics at the Weill Medical College of Cornell University in New York City. His training was initiated at Yale, continued at Columbia College of Physicians and Surgeons, then he completed a Pediatric Residency at Cincinnati Children's Hospital, and a Fellowship in Pediatric Hematology/Oncology at the combined Cornell/Memorial Sloan Kettering program. Dr. Bussel's publications are centered around diagnosis and especially management of patients with ITP, including children with ITP, adults with ITP, pregnant women with ITP, HIV-infected patients with thrombocytopenia, and fetuses affected by autoimmune and alloimmune thrombocytopenia. He has worked with IVIG, IV anti-D, rituximab, and most recently the thrombopoietic agents.

Ann Farrell, MD | Director, Division of Hematology Products, Office of Hematology and Oncology Products, U.S. Federal Drug Administration

Dr. Ann Farrell graduated from Rush Medical College and completed her residency at New Haven Hospital, Yale University. A staff member of the U.S. Food and Drug Administration, Dr. Farrell is the Director of the Division of Hematology Products, within the Office of Hematology and Oncology Products. She researches drug treatment, development, and approval, with a focus on hematological disorders.

Caroline Kruse | President and CEO, the Platelet Disorder Support Association

Caroline Kruse is the President and CEO of the Platelet Disorder Support Association (PDSA), the global leader in empowering patients with immune thrombocytopenia (ITP) and other platelet disorders through education, advocacy, research, and support. Caroline's focus on mission has resulted in growing PDSA's local ITP support groups, launching education and awareness initiatives, the designation of National ITP Awareness Month, the co-founding of the International ITP Alliance, and a greater emphasis on research resulting in the establishment of the ITP Natural History Study Registry through a cooperative agreement with NORD and the FDA, and funding patient-centered research that will make a difference in the lives of patients with ITP and other platelet disorders.

Prior to her appointment in January 2009 by the PDSA Board of Directors, Caroline served as a PDSA board member and PDSA's first Director of Public Relations and founded the first local ITP support group in the country, in Cleveland, Ohio, in 2003, and continues to serve as its facilitator. She brings a personal perspective to PDSA as a patient with two rare diseases, including ITP, so she knows firsthand the physical and emotional struggles ITP patients face on a daily basis.

Joan Young | Founder, the Platelet Disorder Support Association

Joan Young founded the Platelet Disorder Support Association in 1998, after struggling through an eighteen-month battle with ITP that took a significant toll on her physical and emotional well-being. Since retiring from PDSA in 2008, Joan continues to educate and inspire others through her contributions to healthcare-focused publications, lectures, and memoir, *Wish by Spirit*.

ITP PATIENT-FOCUSED DRUG DEVELOPMENT – DISCUSSION TOPIC QUESTIONS

Topic 1: Effects of ITP that Matter Most to Patients and Caregivers

1. Of all the symptoms or disease manifestations that you experience because of your condition, which 1-3 symptoms or manifestations have the most significant impact on your life? (Examples may include fatigue, bleeding [e.g. bleeding from nose, mouth, blood blisters, heavy menses, bruising], anxiety, depression)
2. Are there specific activities that are important to you but that you cannot do at all or as fully as you would like because of your condition? (Examples of activities may include engagement in personal relationships, participation in sports or social activities, completion of school or work activities, etc.)
3. How do your symptoms and their negative impacts affect your daily life on the best days? On the worst days?
4. How has your condition changed over time? Would you define your condition today as being well-managed?
5 What worries you most about your condition?

Topic 2: Patient Perspectives on Current Approaches to Treatments

1. What are you currently doing to help treat your condition or its symptoms? (Examples may include prescription medicines, over-the-counter products, and non-drug therapies such as diet modification)
   a. How has your treatment regimen changed over time, and why?
2. How well does your current treatment regimen control your condition?
   a. How well have these treatments worked for you as your condition has changed over time?
3. What are the most significant downsides to your current treatments, and how do they affect your daily life? (Examples of downsides may include going to the clinic for treatment, time devoted to treatment, side effects of treatment, route of administration, etc.)
4. What specific things would you look for in an ideal treatment for your condition?
   a. What would you consider to be a meaningful improvement in your condition that a treatment could provide?
5. What factors do you take into account when making decisions about selecting a course of treatment?

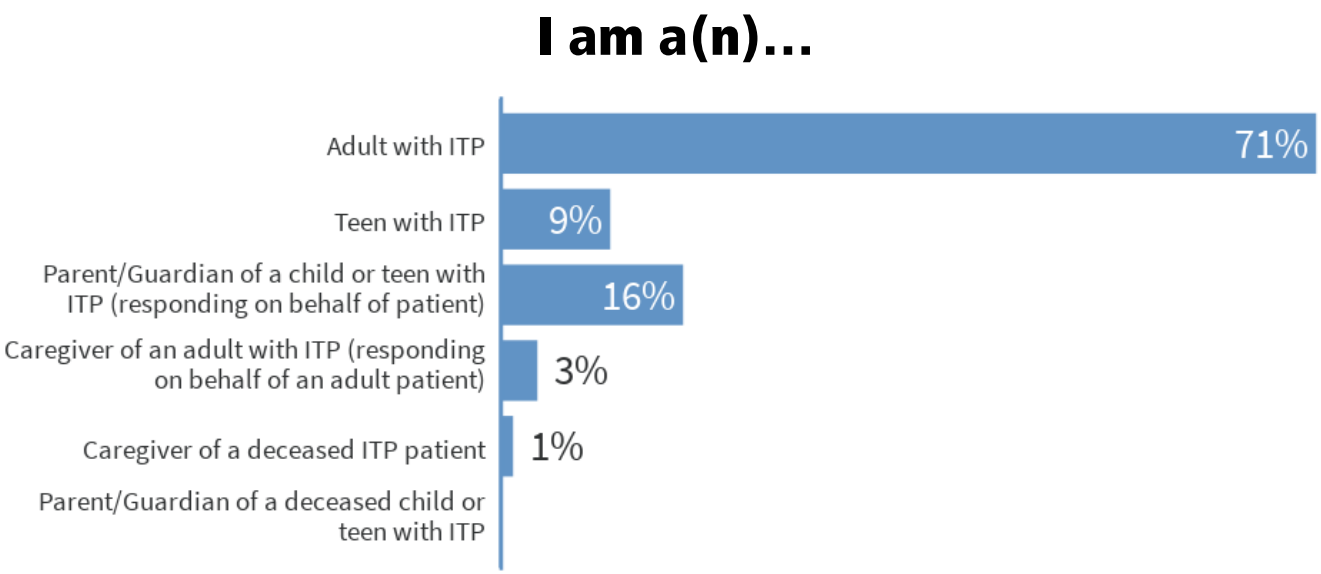
APPENDIX 2: MEETING PARTICIPANTS

Patients	105
Caregivers	94
Industry professionals	64
Researchers	3
Other	17
Government	7
Healthcare professionals	11
TOTAL MEETING PARTICIPANTS	**301**

APPENDIX 3: POLLING QUESTIONS AND RESULTS

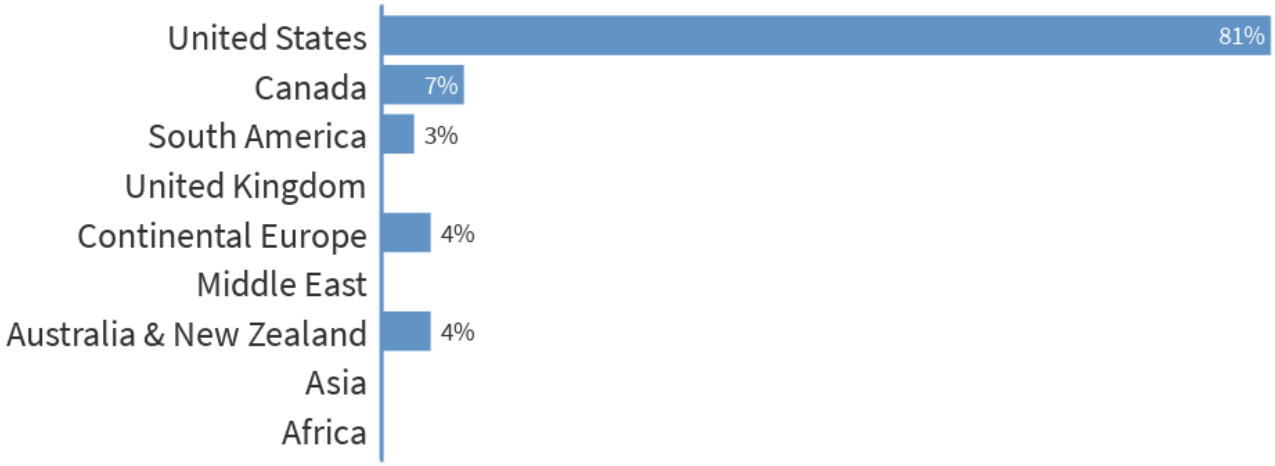
DEMOGRAPHICS

PARTICIPANT PROFILES



1. I am a(n)...	# of responses	% of responses
Adult with ITP	67	71%
Teen with ITP	9	9%
Parent/Guardian of a child or teen with ITP (responding on behalf of patient)	15	16%
Caregiver of an adult with ITP (responding on behalf of an adult patient)	3	3%
Caregiver of a deceased ITP patient	1	1%
Parent/Guardian of a deceased child or teen with ITP	0	0%
Total	**95**	

Where do you currently live?

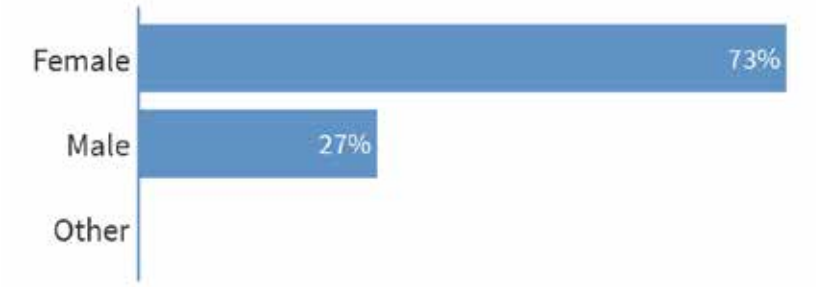


2. Where do you currently live?	# of responses	% of responses
United States	54	81%
Canada	5	7%
South America	2	3%
United Kingdom	0	0%
Continental Europe	3	4%
Middle East	0	0%
Australia and New Zealand	3	4%
Asia	0	0%
Africa	0	0%
Total	**67**	

Are you aware of any family history of low platelets?

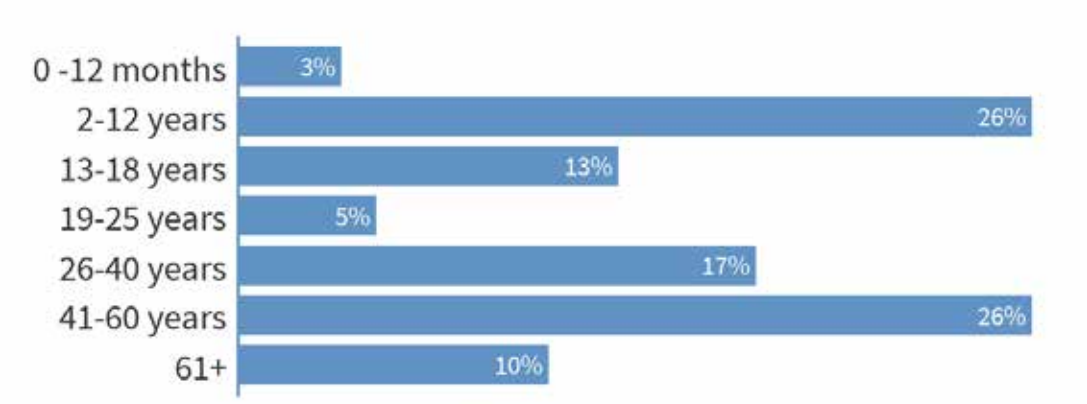
3. Are you aware of any family history of low platelets?	# of responses	% of responses
No	66	86%
Unsure	1	1%
Yes	10	13%
Total	**77**	

Select patient's sex



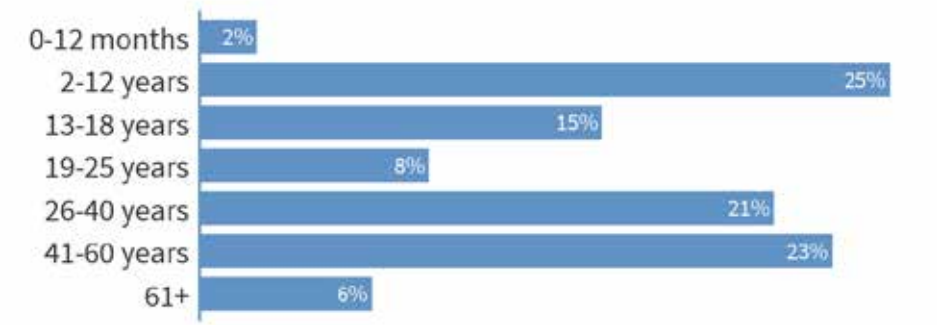
1. Select patient's sex	# of responses	% of responses
Female	68	73%
Male	25	27%
Other	0	0%
Total	**93**	

Select patient's age (indicate at death if deceased)



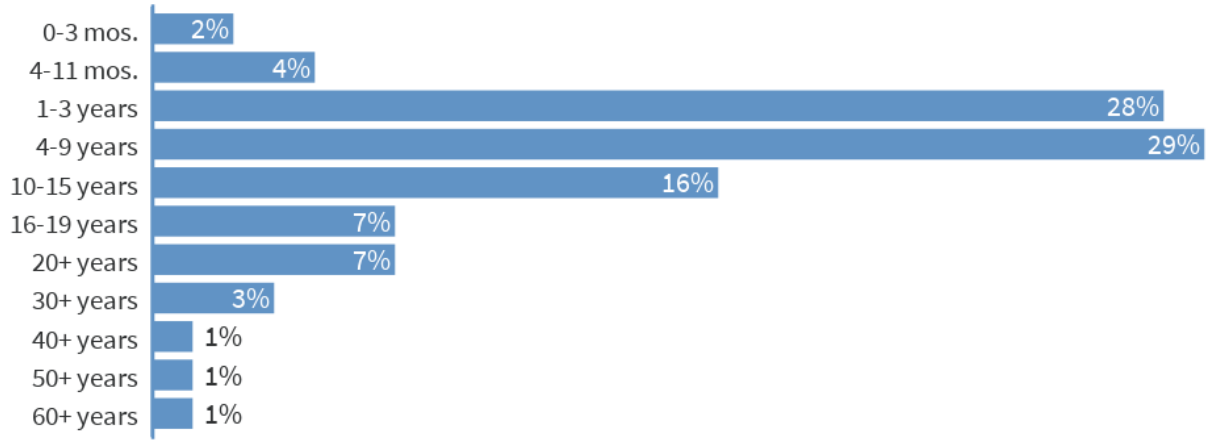
1. Select patient's age (indicate at death if deceased)	# of responses	% of responses
0-12 months	3	3%
2-12 years	23	26%
13-18 years	11	13%
19-25 years	4	5%
26-40 years	15	17%
41-60 years	23	26%
61+	9	10%
Total	**88**	

Select patient's age at confirmed diagnosis



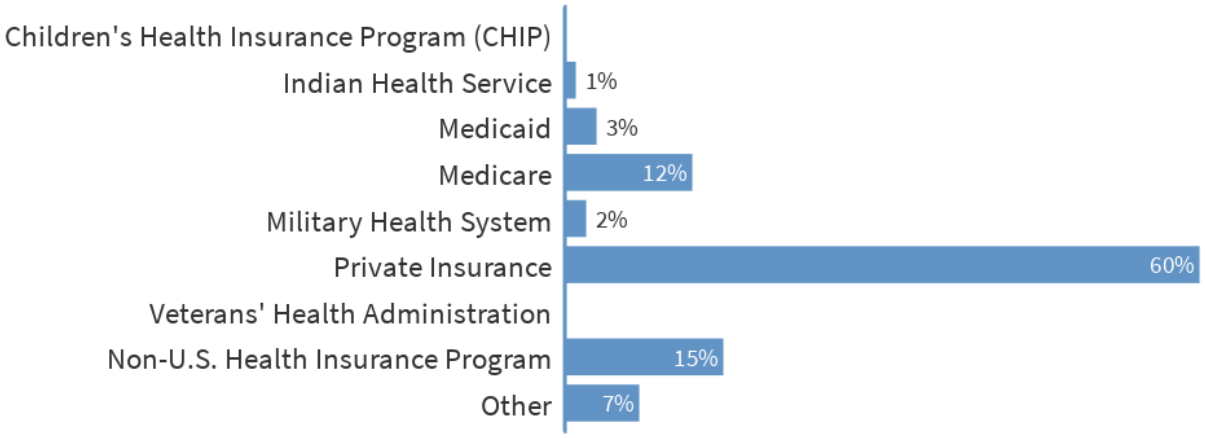
6. Select patient's age at confirmed diagnosis	# of responses	% of responses
0-12 months	1	2%
2-12 years	12	25%
13-18 years	7	15%
19-25 years	4	8%
26-40	10	21%
41-60	11	23%
61+	3	6%
Total	**48**	

Select number of years living with ITP



7. Select number of years living with ITP	# of responses	% of responses
0-3 months	2	2%
4-11 months	4	4%
1-3 years	25	28%
4-9 years	26	29%
10-15 years	14	16%
16-19 years	6	7%
20+ years	6	7%
30+ years	3	3%
40+ years	1	1%
50+ years	1	1%
60+ years	1	1%
Total	**89**	

Select patient's health insurance program

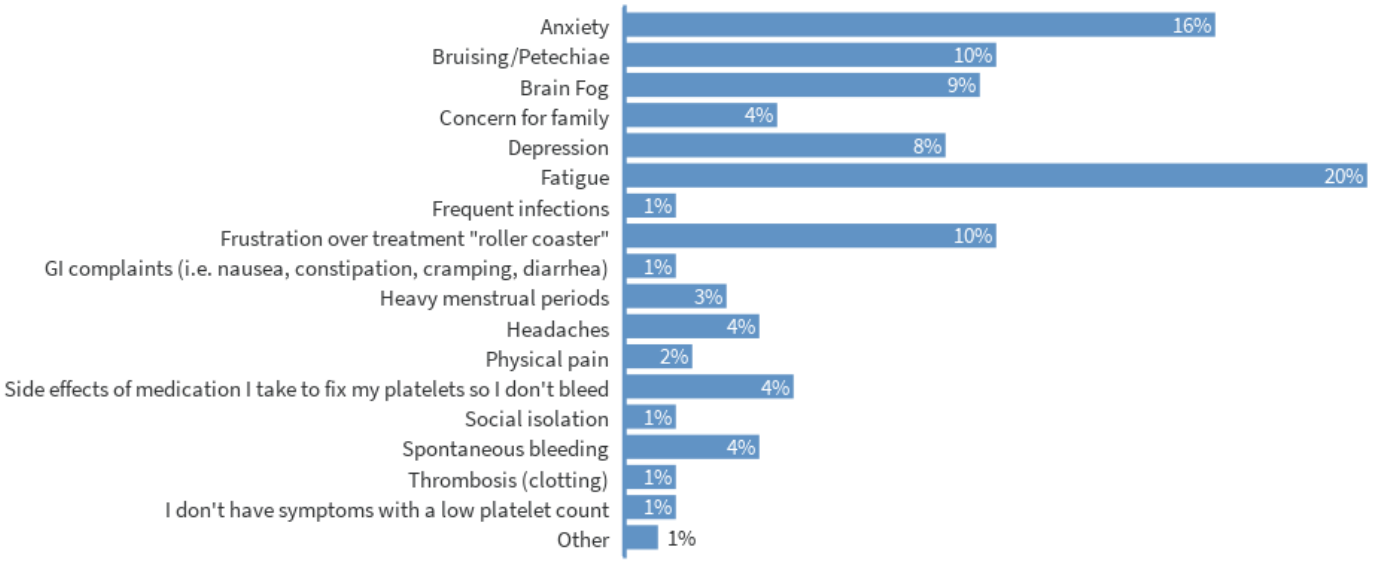


8. Select patient's health insurance program	# of responses	% of responses
Children's Health Insurance Program (CHIP)	0	0%
Indian Health Insurance	1	1%
Medicaid	3	3%
Medicare	12	12%
Military Health System	2	2%
Private Insurance	60	60%
Veterans' Health Administration	0	0%
Non-U.S. Health Insurance Program	15	15%
Other	7	7%
Total	**100**	

TOPIC 1

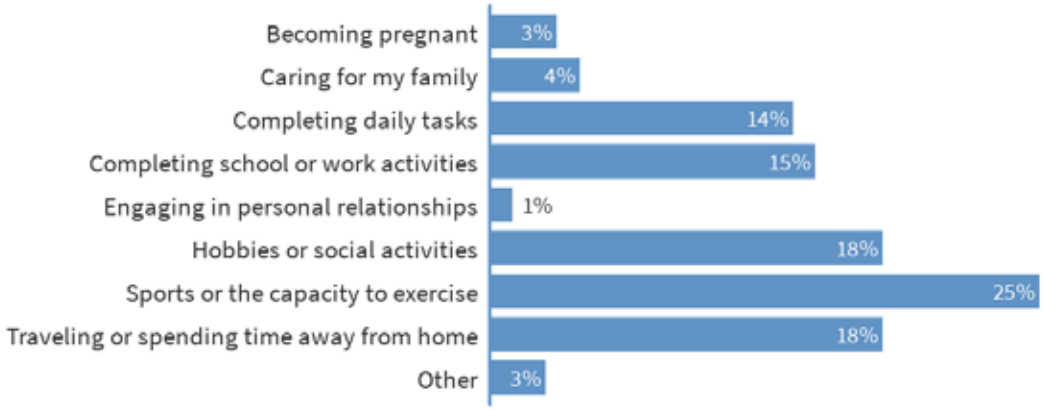
HEALTH EFFECTS AND DAILY IMPACTS THAT MATTER MOST TO PATIENTS

Which symptom(s) from ITP has the most significant impact on your life? (select top 3)



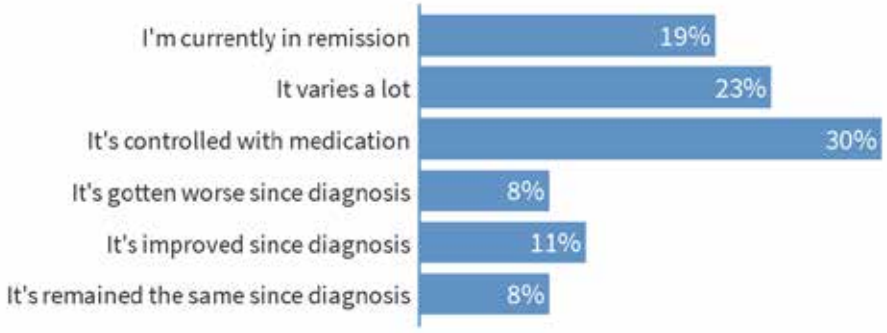
9. Which symptom(s) from ITP has the most significant impact on your life? (select top 3)	# of responses	% of responses
Anxiety	35	16%
Bruising/Petechiae	22	10%
Brain Fog	21	9%
Concern for family	9	4%
Depression	19	8%
Fatigue	44	20%
Frequent infections	3	1%
Frustration over treatment “roller coaster”	22	10%
GI complaints (i.e. nausea, constipation, cramping, diarrhea)	3	1%
Heavy menstrual periods	6	3%
Headaches	8	4%
Physical pain	4	2%
Side effects of medications I take to fix my platelets, so I don’t bleed	10	4%
Social isolation	3	1%
Spontaneous bleeding	8	4%
Thrombosis (clotting)	3	1%
I don’t have symptoms with a low platelet count	3	1%
Other	2	1%
Total	**225**	

What activities does your ITP limit or prevent you from doing?



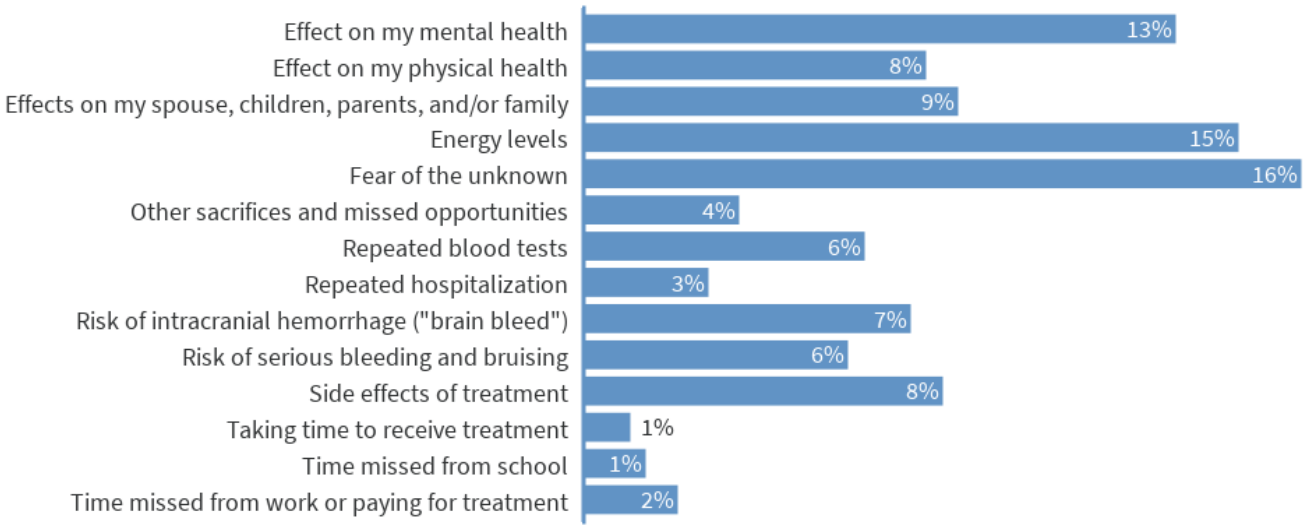
10. What activities does your ITP limit or prevent you from doing?	# of responses	% of responses
Becoming pregnant	6	3%
Caring for my family	8	4%
Completing daily tasks	27	14%
Completing school or work activities	29	15%
Engaging in personal relationships	2	1%
Hobbies or social activities	35	18%
Sports or the capacity to exercise	49	25%
Traveling or spending time away from home	35	18%
Other	5	3%
Total	**196**	

How has your condition changed over time?



11. How has your condition changed over time?	# of responses	% of responses
I'm currently in remission	16	19%
It varies a lot	19	23%
It's controlled with medication	25	30%
It's gotten worse since diagnosis	7	8%
It's improved since diagnosis	9	11%
It's remained the same since diagnosis	7	8%
Total	**83**	

What aspects of your condition cause the greatest anxiety? (select top 3)

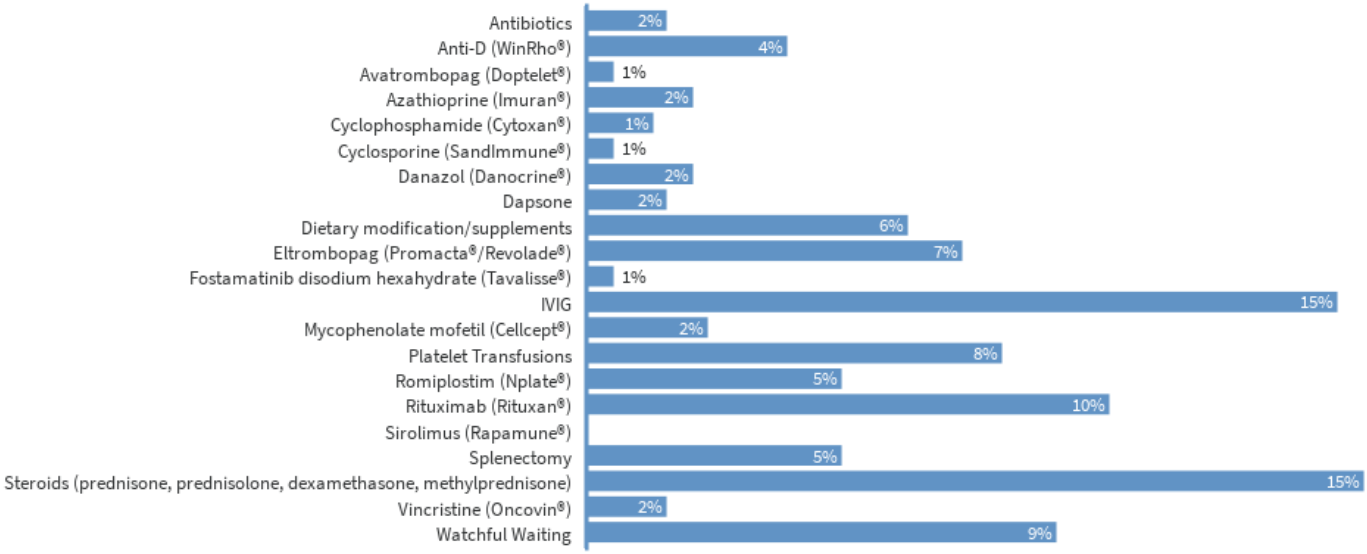


12. What aspects of your condition cause the greatest anxiety? (select top 3)	# of responses	% of responses
Effect on my mental health	38	13%
Effect on my physical health	22	8%
Effects on my spouse, children, parents, and/or family	24	9%
Energy levels	42	15%
Fear of the unknown	46	16%
Other sacrifices and missed opportunities	10	4%
Repeated blood tests	18	6%
Repeated hospitalization	8	3%
Risk of intracranial hemorrhage (“brain bleed”)	21	7%
Risk of serious bleeding and bruising	17	6%
Side effects of treatment	23	8%
Taking time to receive treatment	3	1%
Time missed from school	4	1%
Time missed from work or paying for treatment	6	2%
Total	**282**	

TOPIC 2

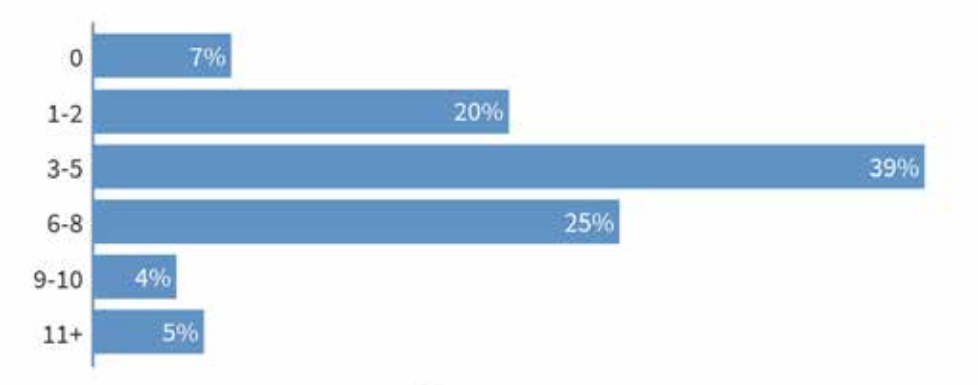
PATIENTS' PERSPECTIVES ON CURRENT APPROACHES TO TREATMENT

What treatments have you taken for your ITP? (select all that apply)



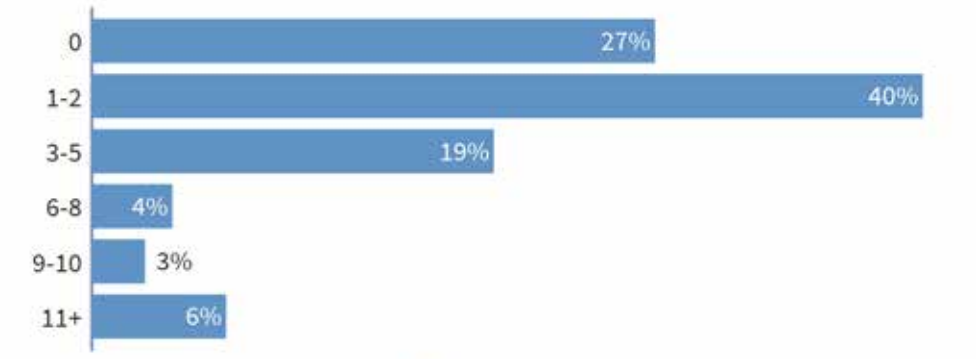
13. What treatments have you taken for your ITP? (select all that apply)	# of responses	% of responses
Antibiotics	6	2%
Anti-D (WinRho®)	15	4%
Avatrombopag (Doptelet®)	2	1%
Azathioprine (Imuran®)	8	2%
Cyclophosphamide (Cytoxan®)	5	1%
Cyclosporine (SandImmune®)	2	1%
Danazol (Dancrine®)	8	2%
Dapsone	6	2%
Dietary modification/supplements	24	6%
Eltrombopag (Promacta®/Revolade®)	28	7%
Fostamatinib disodium hexahydrate (Tavalisse®)	2	1%
IVIG	56	15%
Mycophenolate mofetil (Cellcept®)	9	2%
Platelet Transfusions	31	8%
Romiplostim (Nplate®)	19	5%
Rituximab (Rituxan®)	39	10%
Sirolimus (Rapamune®)	0	0%
Splenectomy	19	5%
Steroids (prednisone, prednisolone, dexamethasone, methylprednisone)	58	15%
Vincristine (Oncovin®)	6	2%
Watchful Waiting	35	9%
Total	**378**	

How many conventional ITP treatments have you tried?



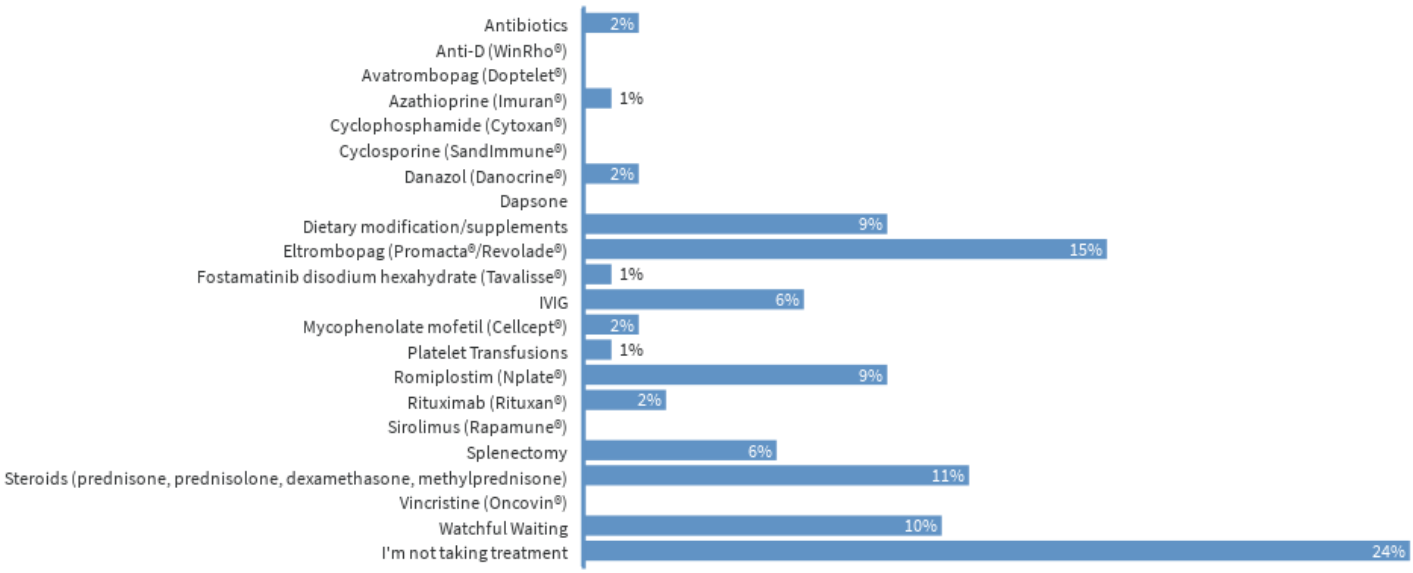
14. How many conventional ITP treatments have you tried?	# of responses	% of responses
0	5	7%
1-2	15	20%
3-5	30	39%
6-8	19	25%
9-10	3	4%
11+	4	5%
Total	**76**	

How many complementary treatments have you tried?



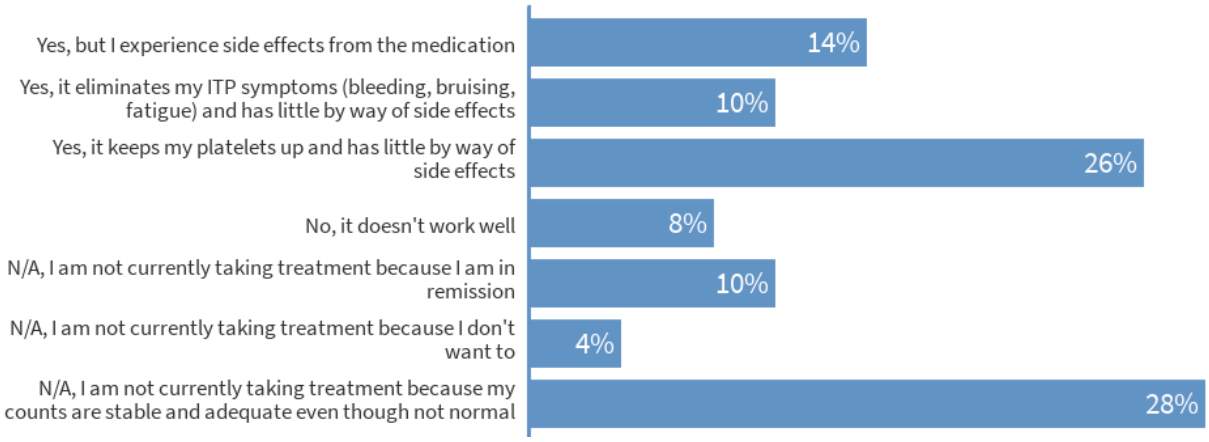
15. How many complementary treatments have you tried?	# of responses	% of responses
0	21	27%
1-2	31	40%
3-5	15	19%
6-8	3	4%
9-10	2	3%
11+	5	6%
Total	**77**	

What treatment(s) are you currently taking for your ITP? (select all that apply)



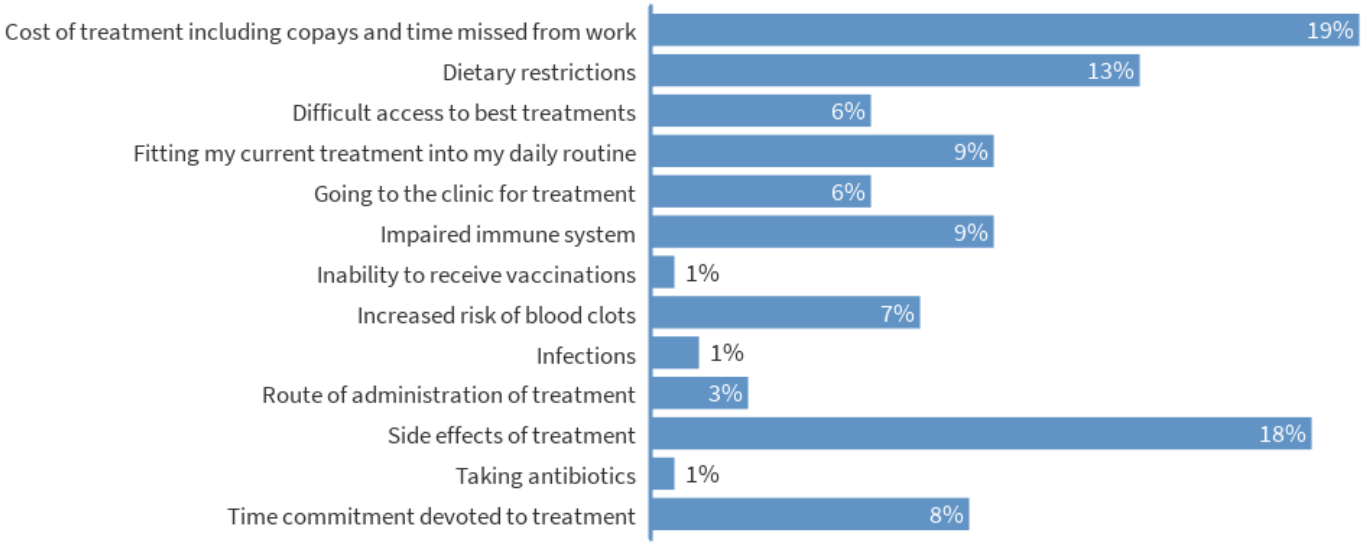
16. What treatment(s) are you currently taking for your ITP? (select all that apply)	# of responses	% of responses
Antibiotics	2	2%
Anti-D (WinRho®)	0	0%
Avatrombopag (Doptelet®)	0	0%
Azathioprine (Imuran®)	1	1%
Cyclophosphamide (Cytoxan®)	0	0%
Cyclosporine (SandImmune®)	0	0%
Danazol (Danocrine®)	2	2%
Dapsone	0	0%
Dietary modification/supplements	11	9%
Eltrombopag (Promacta®/Revolade®)	19	15%
Fostamatinib disodium hexahydrate (Tavalisse®)	1	1%
IVIG	8	6%
Mycophenolate mofetil (Cellcept®)	2	2%
Platelet Transfusions	1	1%
Romiplostim (Nplate®)	11	9%
Rituximab (Rituxan®)	3	2%
Sirolimus (Rapamune®)	0	0%
Splenectomy	7	6%
Steroids (prednisone, prednisolone, dexamethasone, methylprednisone)	14	11%
Vincristine (Oncovin®)	0	0%
Watchful Waiting	13	10%
I'm not taking treatment	30	24%
Total	**125**	

Does your current ITP treatment "work" for you?



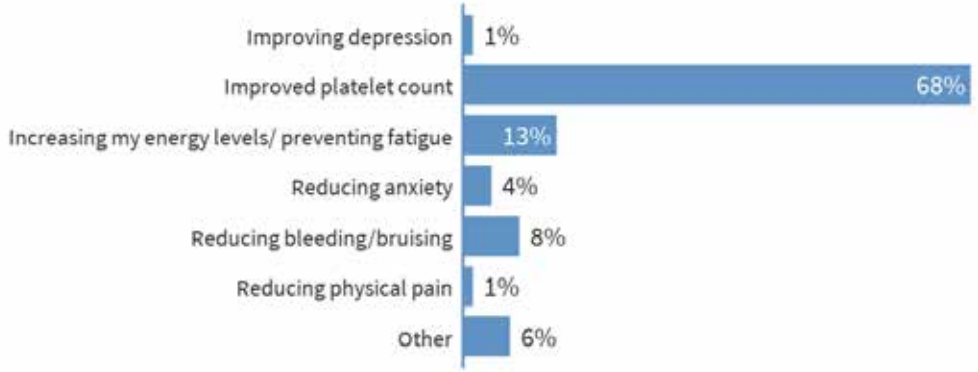
17. Does your current ITP treatment "work" for you?	# of responses	% of responses
Yes, but I experience side effects from the medication	11	14%
Yes, it eliminates my ITP symptoms (bleeding, bruising, fatigue) and has little by way of side effects	8	10%
Yes, it keeps my platelets up and has little by way of side effects	20	26%
No, it doesn't work well	6	8%
N/A, I am not currently taking treatment because I am in remission	8	10%
N/A, I am not currently taking treatment because I don't want to	3	4%
N/A, I am not currently taking treatment because my counts are stable and adequate even though not normal	22	28%

What are issues you deal with your current treatment (select top 3)



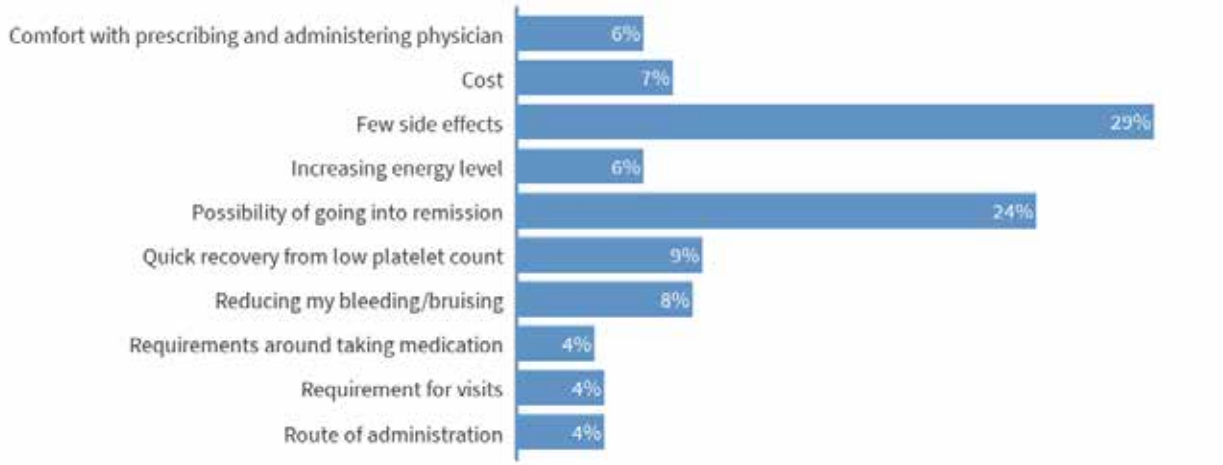
18. What are issues you deal with your current treatment (select top 3)	# of responses	% of responses
Cost of treatment including copays and time missed from work	29	19%
Dietary restrictions	20	13%
Difficult access to best treatments	9	6%
Fitting my current treatment into my daily routine	14	9%
Going to the clinic for treatment	9	6%
Impaired immune system	14	9%
Inability to receive vaccinations	1	1%
Increased risk of blood clots	11	7%
Infections	2	1%
Route of administration of treatment	4	3%
Side effects of treatment	27	18%
Taking antibiotics	1	1%
Time commitment devoted to treatment	13	8%
Total	**154**	

Which symptoms would an ideal treatment improve?



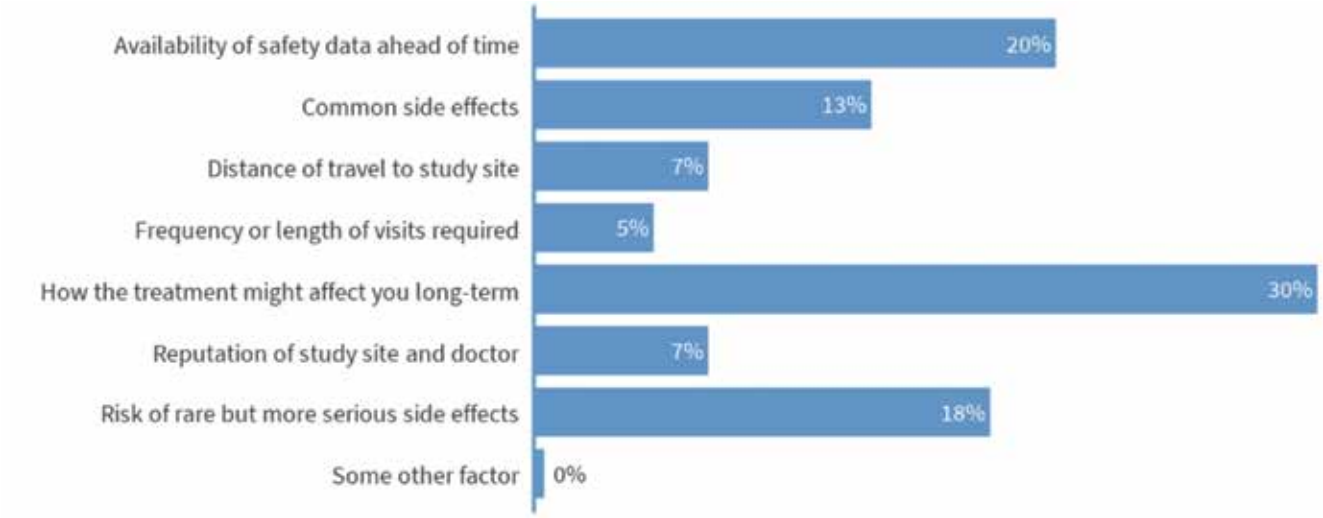
19. Which symptoms would an ideal treatment improve?	# of responses	% of responses
Improving depression	1	1%
Improved platelet count	54	68%
Increasing my energy levels/preventing fatigue	10	13%
Reducing anxiety	3	4%
Reducing bleeding/bruising	6	8%
Reducing physical pain	1	1%
Other	5	6%
Total	**80**	

Which factors would you consider when deciding on a course of treatment? (select top 3)

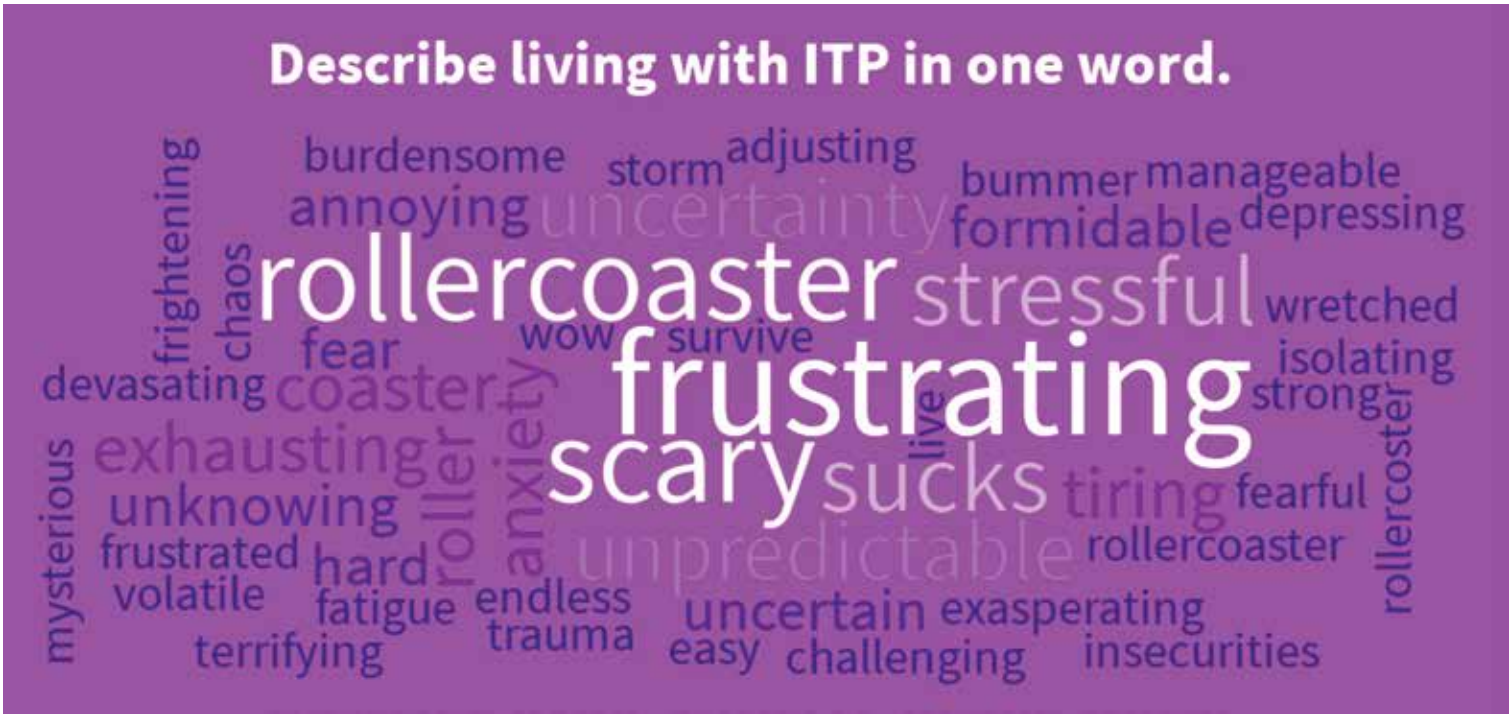


20. Which factors would you consider when deciding on a course of treatment? (select top 3)	# of responses	% of responses
Comfort with prescribing and administering physician	13	6%
Cost	16	7%
Few side effects	65	29%
Increasing energy level	13	6%
Possibility of going into remission	53	24%
Quick recovery from low platelet count	19	9%
Reducing my bleeding/bruising	18	8%
Requirements around taking medication	8	4%
Requirement for visits	9	4%
Route of administration	9	4%
Total	**223**	

Which factors are most important to you when considering participating in a clinical trial? (select top 3)



21. Which factors are most important to you when considering participating in a clinical trial? (select top 3)	# of responses	% of responses
Availability of safety data ahead of time	48	20%
Common side effects	31	13%
Distance of travel to study site	16	7%
Frequency or length of visits required	11	5%
How the treatment might affect you long-term	72	30%
Reputation of study site and doctor	16	7%
Risk of rare but more serious side effects	42	18%
Some other factor	1	0%
Total	**237**	



22. Describe living with ITP in one word	# of responses
Hard	2
Fear/Fearful	3
Rollercoaster	12
Stressful	5
Tiring/Fatigue/Exhausting	7
Endless	1
Frustrating	10
Devastating	1
Strong	1
Chaos	1
Formidable	2
Unknowing	2
Uncertainty/Uncertain	6
Isolating	1
Bummer	1
Frightening/Scary/Terrifying	9
Storm	1
Anxiety	3
Trauma	1

	# of responses
Exasperating	1
Sucks	5
Why	1
Challenging	1
Survive	1
Annoying	2
Burdensome	1
Unpredictable	4
Adjusting	1
Depressing	1
Insecurities	1
WOW	1
Easy	1
Manageable	1
Volatile	1
Mysterious	1
Live	1
Wretched	1

Platelet Disorder Support Association

Empowering ITP Patients

Our Mission: The Platelet Disorder Support Association is dedicated to enhancing the lives of people with immune thrombocytopenia (ITP) and other platelet disorders through education, advocacy, research and support.

Patient-founded in 1998 to educate and empower those impacted by ITP and other rare platelet and bleeding disorders, PDSA is now a powerful force serving and unifying the global community of patients, practitioners, caregivers, advocates and key disease stakeholders. PDSA is committed to building awareness, educating the global community, and providing critical connections and resources that empower patients to take charge of their disease and encourage practitioners to exercise patient-centered medical care.

PDSA receives no federal funding. It never has. Charitable gifts from our individual and corporate donors, membership contributions, and inspiring awareness and philanthropic events coordinated by committed volunteers energize, uphold and preserve our mission.

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