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ORIGINAL ARTICLE

Evaluation of Treatment Responses in Patients with Immune Thrombocytopenic Purpura

ABSTRACT

Objectives: Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by immune-mediated platelet destruction and, in some cases, impaired platelet production. While conventional therapies, such as corticosteroids, IVIg, and splenectomy, are effective for most patients, refractory ITP remains a significant clinical challenge. This study aimed to evaluate the demographic characteristics, clinical features, treatment responses, and outcomes of hospitalized ITP patients in a real-world setting.

Methods: This retrospective study included 60 ITP patients treated in the Internal Medicine Clinics of Ankara Numune Training and Research Hospital between 2009 and 2013. Patients with platelet counts <30 × 10^9/L were analyzed for demographic data, clinical presentations, treatments received during hospitalization, and treatment responses. Statistical analyses were performed to identify factors associated with treatment outcomes.

Results: The cohort comprised 43 females (72.7%) and 17 males (27.3%), with a mean age of 47.6±16.9 years. First-line steroid therapy achieved a 65% response rate, with non-responders more likely to experience major bleeding (p = 0.039). Second-line therapies included IVIg (66.7% response rate) and splenectomy (53.8% response rate), with lower responses observed in refractory cases. Rituximab, vincristine, and eltrombopag response rates were 33.3%, 20%, and 33.3%, respectively. Two patients were resistant to all treatments; one died due to major bleeding, yielding a 1.6% mortality rate over four years.

Conclusion: Refractory ITP presents a significant treatment challenge, particularly in patients resistant to multiple therapies. While combination therapies and novel agents, such as TPO receptor agonists, hold promise, further randomized controlled trials are necessary to establish standardized treatment protocols and improve outcomes in refractory cases.

Keywords: Immune thrombocytopenic purpura, Thrombocytopenia, Treatment Responses

Immune thrombocytopenic purpura (ITP) develops as a result of shortened platelet lifespan caused by autoantibodies targeting platelets, leading to their premature destruction in the reticuloendothelial system, particularly in the spleen, in some cases with impaired platelet production. It is characterized by isolated thrombocytopenia after the exclusion of other known causes of thrombocytopenia, predominantly with a normal or increased number of megakaryocytes in the bone marrow (1).

The International Working Group defines primary ITP as a platelet count <100×10^9/L with the exclusion of other causes of thrombocytopenia (2). The disease is predominantly characterized by immune-mediated destruction of normal platelets in response to an unknown stimulus. Autoantibodies, primarily of the IgG type but occasionally IgA or IgM, bind to platelet membrane glycoprotein complexes (GpIb-IX, GpIIb-IIIa, Ia-IIa, PF IV, and PF V). The most recognized mechanism of ITP pathogenesis involves the recognition and phagocytosis of antibody-coated platelets by Fc receptors on reticuloendothelial system macrophages, leading to their clearance from circulation (3,4).

In ITP, peripheral platelet destruction is countered by an increased production of megakaryocytes in the bone marrow. However, anti-platelet antibodies may also impact megakaryopoiesis, resulting in reduced megakaryocyte numbers or impaired platelet production in the bone marrow (2,5,6).

Ebru Kılıç Güneş[1]
Engin Sennaroglu[2]

[1]*Department of Hematology, University of Health and Sciences, Gulhane Training and Research Hospital, Ankara, Türkiye*
[2]*Department of Internal Medicine, Girne University, Dr. Suat Günsel University of Kyrenia Hospital, Girne, Northern Cyprus.*

Corresponding author:
Ebru Kılıç Kılıç Güneş
✉ ebrukilic83@hotmail.com

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ITP in adults is typically treated when the platelet count falls below 30×10^9/L (7). Therapeutic strategies for ITP have been developed based on the disease's mechanisms. T lymphocytes lose immune tolerance to platelet antigens and activate B cells. Cyclosporine inhibits T cells, while azathioprine and mycophenolate mofetil inhibit lymphocyte proliferation. Cytotoxic agents also target this step, contributing a role in the treatment of ITP (8-10). CD20-positive B cells secrete anti-platelet antibodies, and rituximab inhibits this process. Steroids, which reduce antibody production, are the first-line agents used in treatment at this stage (11).

Fc receptor-mediated phagocytosis leads to the clearance of IgG-sensitized platelets by the reticuloendothelial system. Splenectomy eliminates the primary site of platelet clearance (7,12). Intravenous immunoglobulin (IVIg) and anti-D immunoglobulin block reticuloendothelial system cells, while corticosteroids reduce phagocytosis (13,14). Vinca alkaloids inhibit macrophage activity (15). Thrombopoietin (TPO) levels are unexpectedly low relative to the degree of thrombocytopenia in ITP, and TPO receptor agonists exert their effects by addressing this deficit (16,17).

In patients with refractory ITP exhibiting bleeding symptoms and resistance to multiple drugs, treatments such as combined chemotherapy (cyclophosphamide, prednisone, vincristine, azathioprine, or etoposide), alemtuzumab, and hematopoietic stem cell transplantation (both autologous and allogeneic) have been reported. However, these treatments are highly toxic and costly, and their long-term side effects remain unknown (18).

In this study, we retrospectively analyzed the demographic characteristics, clinical courses, administered treatments, and treatment responses of 60 adult ITP patients diagnosed and treated at the Internal Medicine Services of Ankara Numune Training and Research Hospital between 2009 and 2013.

MATERIALS AND METHODS

The study adhered to the principles of the Declaration of Helsinki and good clinical practice guidelines during its design, data collection, and analysis. Ethics committee approval was granted by the Ankara Numune Training and Research Hospital (17.08.2011; 2011-225).

In this thesis study, 60 patients who were hospitalized and treated for Immune Thrombocytopenic Purpura (ITP) in the General Internal Medicine Clinics and Emergency Internal Medicine Clinic of Ankara Numune Training and Research Hospital between January 2009 and January 2013 were retrospectively analyzed. The diagnosis of ITP was established in patients with normal physical examination findings, aside from bleeding symptoms, after excluding secondary causes of thrombocytopenia.

According to national and international guidelines, bone marrow aspiration and biopsy were performed for patients with findings suggestive of other hematological diseases, those over 60 years old, cases unresponsive to first-line treatment, or patients scheduled for splenectomy.

The following data were collected during hospitalization in the Internal Medicine Clinics: age, gender, comorbidities, medication use, presenting symptoms, major bleeding, newly diagnosed or relapsed ITP, prior treatments, duration of ITP diagnosis, platelet, white blood cell, and hemoglobin levels at presentation, administration of platelet transfusion, presence of bone marrow biopsy, and the accompanying iron deficiency anemia. All patients included in the study were part of the treatment-indicated group defined as Plt<30×10^9/L.

First-line treatment involved systemic corticosteroids (0.5–2 mg/kg). Non-responders were treated with pulse steroids (1 g/day for 3 days) or/and IVIg (400 mg/kg/day for 5 days), splenectomy, rituximab (375 mg/m^2 weekly for 4 doses), eltrombopag (25–75 mg/day), or vincristine (1 mg/day). Only treatments administered during hospitalization in the Internal Medicine Department were analyzed; outpatient treatments and therapies given in other departments were excluded.

Treatment response was evaluated based on the International Working Group and Turkish Hematology Association Guidelines. Non-responders were defined as patients with a platelet count <30 × 10^9/L or without a twofold increase from baseline. Responders were those achieving a post-treatment platelet count >30 × 10^9/L. Relapse was defined as a platelet count dropping below 30 × 10^9/L or the presence of bleeding. Patients maintaining platelet counts >30 × 10^9/L without bleeding were considered in remission.

Statistical Analysis

The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) for Windows 20 (IBM SPSS Inc., Chicago, IL) and MedCalc 11.4.2 (MedCalc Software, Mariakerke, Belgium). The normal distribution of the data was evaluated with the Kolmogorov-Smirnov test. Numerical variables with a normal distribution were presented as mean ± standard deviation, while those without a normal distribution were expressed as median. Categorical variables were reported as numbers and percentages.

Factors associated with two categorical risk groups were analyzed using the independent samples T-test for normally distributed numerical variables and the Mann-Whitney U-test for non-normally distributed numerical variables. For the comparison of categorical variables, the Chi-Square Test and Fisher's Exact Chi-Square Test were employed. To determine independent predictors of steroid non-response in first-line therapy, a stepwise multivariable logistic regression analysis was conducted. A p-value of <0.05 was considered statistically significant in all analyses.

RESULTS

A total of 60 patients, including 17 males and 43 females, were enrolled in the study. The mean age of the patients was 47.6±16.9 years (range: 16–85 years). Analysis of clinical admission reasons revealed that 16.7% (n=10) were asymptomatic, 50% (n=30) presented with petechiae, purpura, or ecchymosis, 21.7% (n=13) had gum bleeding, 18.3% (n=11) presented with vaginal bleeding, 15% (n=9) with epistaxis, 5% (n=3) with hematuria, and 3.3% (n=2) presented with gastrointestinal bleeding. Major or life-threatening bleeding was observed in 3.3% (n=2) of the patients.

60% (n=36) of patients, presenting to the emergency department with bleeding complaints received platelet transfusion. Bone marrow biopsy was performed as a diagnostic method in 48.3% (n=29) of the patients. Among these 29 patients, bone marrow aspiration findings were normal in 41.7% (n=25), while decreased megakaryocytes were observed in 6.7% (n=4).

Seventy-five percent (n=45) of the patients were newly diagnosed

with ITP, while 25% (n=15) had a relapsed/refractory disease. The median duration of ITP, among relapsed/refractory patients was 4 years. Of these, 53.3% had received corticosteroids, 13.3% had been treated with IVIg, 13.3% had undergone a combination of IVIg and splenectomy, and 13.3% had received Eltrombopag. The demographic, clinical, and other characteristics of the study population are summarized in Table 1.

Table 1. Demographics, Clinical Characteristics, and Treatments of Hospitalized ITP Patients

	(n=60)
Age	47.6±16.9
Gender (male)	17 (28.3%)
Gender (female)	43 (72.7%)
Comorbidities	
Hypertension	9 (15.0%)
Diabetes Mellitus (DM)	7 (11.7%)
Coronary Artery Disease (CAD)	3 (5.0%)
Other	5 (8.5%)
Clinical Presentation	
Petechiae-Purpura-Ecchymosis	30 (50.0%)
Gum bleeding	13 (21.7%)
Menorrhagia	11 (18.3%)
Asymptomatic	10 (16.7%)
Nasal bleeding	9 (15.0%)
Hematuria	3 (5.0%)
Gastrointestinal bleeding (GI bleeding)	2 (3.3%)
Major bleeding	3 (5.0%)
Initial Laboratory Findings	
Platelets ($x10^9$/L)	5 (1-25)
WBC ($x10^9$/L)	7.4 (2.7-21.0)
Hemoglobin (g/dl)	12.1±2.6
Vitamin B12 (pg/ml)	233 (3.4-2000)
Folate (ng/mL)	6.2 (2.7-227.0)
Platelet Transfusion	36 (60.0%)
Bone Marrow Biopsy	
Not performed	31 (51.7%)
Normal	25 (41.7%)
Reduced megakaryocytes	4 (6.6%)
ITP Diagnosis Status	
Newly Diagnosed	45 (75.0%)
Relapse/Refractory ITP	15 (25.0%)
Duration of ITP (median - years)	4 (1-30)
Prior ITP Treatment (n=15)	
Steroids	8 (53.3%)
Steroids + IVIg	2 (13.3%)
Splenectomy	2 (13.3%)
TPO agonist	3 (20%)

ITP: Immune thrombocytopenic purpura; IVIg: Intravenous immunoglob.

All 60 patients received first-line steroid therapy (1 mg/kg/day), with an overall response rate of 65%. Non-responders (n=21) were older than responders, but the difference was not statistically significant (p=0.174). Major bleeding occurred more frequently in non-responders (14.3%) compared to responders (0%; p=0.039), and platelet transfusion rates were also higher in non-responders (81.0% vs. 48.7%; p=0.026). Additionally, a significant association was observed between decreased megakaryocytes and non-response to steroid therapy (p=0.031). No significant association was found between having a prior ITP diagnosis and the response to steroids (p=0.757). First-line steroid therapy response rates are shown in Figure 1.

Among 21 patients unresponsive to first-line steroid therapy, 3 responded to pulse steroid therapy, and 18 received second-line IVIg (400 mg/kg/day for 5 days or 1 g/kg/day for 2 days), achieving a 66.7% response rate (n=12). No significant age difference was observed between IVIg responders and non-responders (p=0.814). Major bleeding and platelet transfusion rates were identical in both groups.

Among the 13 patients who underwent splenectomy, 7 responded to the treatment, yielding an overall response rate of 53.8%. Ten patients underwent splenectomy following IVIg therapy, while 3 underwent the procedure after rituximab. Of these, 1 responded to rituximab before surgery, while 2 proceeded with splenectomy without responding to steroids, IVIg, or rituximab. No significant differences were found in terms of age, gender, clinical presentation, or laboratory findings were observed between splenectomy responders and non-responders. Response rates to second-line therapies (IVIg and splenectomy) are shown in Figure 2.

Among 6 patients treated with fourth-line rituximab therapy, 2 responded, while 4 did not, resulting in a rituximab response rate of 33.3%. Of the 2 responders, 1 subsequently underwent splenectomy, while the other patient remained under follow-up. Of the 5 patients treated with vincristine, 1 responded to the treatment, while 4 did not, yielding a vincristine response rate of 20%.

Of the three patients treated with eltrombopag, one responded to the therapy, while two did not, resulting in an eltrombopag response

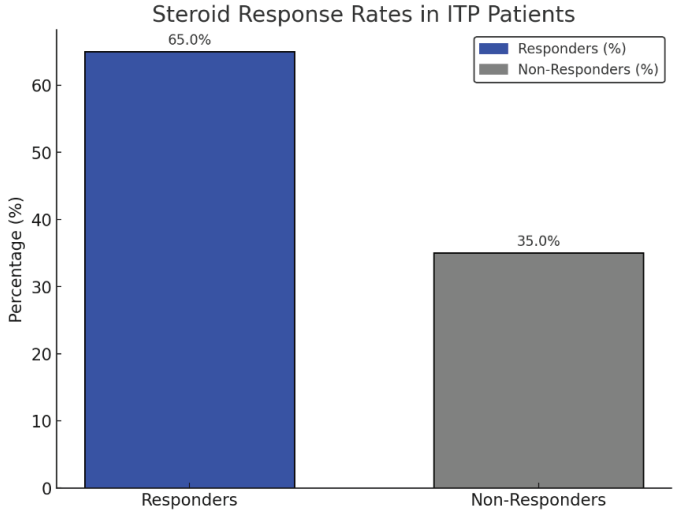

Figure 1. First-line steroid therapy response rates.

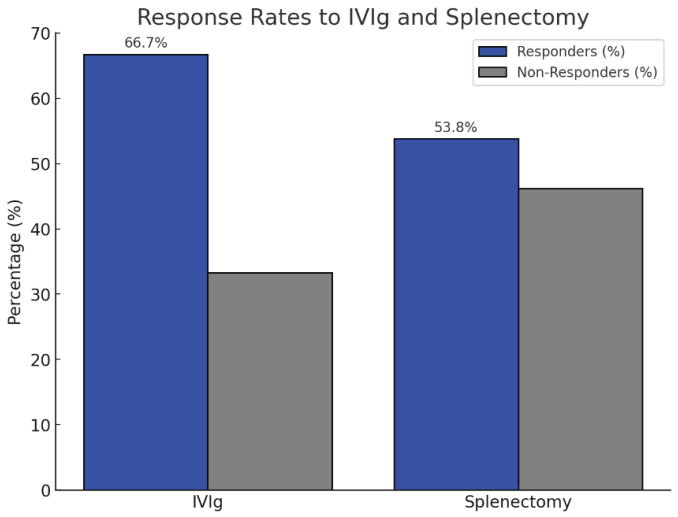

Figure 2. Response rates to second-line therapies (IVIg and splenectomy).

rate of 33.3%. All three patients treated with eltrombopag had previously refractory to steroid, IVIg, and splenectomy. Additionally, two of these patients were also refractory to vincristine.

DISCUSSION

In this thesis study, 60 patients treated for ITP in the Internal Medicine Clinics of Ankara Numune Training and Research Hospital were included. Thrombocytopenia was confirmed with peripheral blood smear analysis, and secondary causes of thrombocytopenia were excluded. Only hospitalized patients from the Internal Medicine Clinics were included, and the treatments they received during their hospitalization were analyzed.

In ITP, bleeding symptoms are typically confined to the skin and mucosa. In our cohort, 16.7% were asymptomatic, while 83.3% had bleeding symptoms, including 2 patients (3.3%) with life-threatening major bleeding. Comparable rates of bleeding symptoms were reported by Portielje et al. (81%) (19), Ben-Yahuda et al. (82%) (20), and Neylon et al. (72%), with skin manifestations as the primary bleeding site in 57% of cases (21). The rate of bleeding symptoms observed in our study was relatively higher compared to the literature. This discrepancy can be attributed to the fact that only patients with a treatment indication and those hospitalized were included in our study.

In the literature, the response rates for standard-dose steroid therapy are generally reported to be between 53% and 75%. The response rates to standard-dose steroid therapy in our study are consistent with the literature. While previous studies suggest that steroid response decreases with age and that patients with a shorter duration of symptoms respond better to steroids, our study did not find a significant association between age and steroid response (7,22).

The IVIg response rate in our study was 66.7%, consistent with the reported range of 65–80% in the literature (23). No significant association was observed between IVIg response and age, gender, comorbidities, presenting complaints, major bleeding, or platelet counts at admission. Of the 13 patients who underwent splenectomy, 7 responded, yielding a response rate of 53%. This is slightly lower than the literature-reported rates of 58–71% (24). All splenectomy cases in our series were steroid-refractory, with 3 also IVIg-refractory, which may explain the lower response rate. Studies suggest that splenectomy response rates are reduced in steroid- and IVIg-refractory cases, though responses in steroid- or IVIg-responsive patients remain variable (11,25).

In our study, 6 patients received rituximab therapy (375 mg/m²/week for 4 weeks), and the rituximab overall response rate was found to be 33.3%. The rituximab response rates reported in the literature range between 40–60%. In the R-ITP 1000 study published in 2014, rituximab was used at a dose of 1000 mg/m² on days 1–15 in ITP patients resistant to conventional treatments, and the overall response rate was found to be 43.1% (26). Publications suggested that patients who had previously responded to splenectomy but relapsed had better responses to rituximab (27). Five of our cases were resistant to splenectomy, which may explain the lower rituximab response rate compared to the literature.

In our study, 5 patients received vincristine therapy (1 mg/week for 2 doses). A response was achieved in 1 patient, yielding a response rate of 20%. All patients receiving vincristine therapy were resistant to steroids and IVIg, 4 were resistant to splenectomy, and 3 were resistant to rituximab. Vinca alkaloids are a potential option for ITP treatment in refractory cases and emergencies due to their ability to rapidly increase platelet levels, particularly when TPO agonists are not accessible.

Eltrombopag therapy (25–75 mg/day) was administered to 3 patients, of whom 1 responded, resulting in a response rate of 33.3%. All patients receiving eltrombopag were refractory to steroids, IVIg, and splenectomy. In the EXTEND study conducted, eltrombopag response rates were reported at 70–80% (16). The lower response rates observed in our study likely reflect the small number of treated cases and the highly refractory nature of the patients.

Among all patients included in our study, 2 of 60 were identified as resistant to all treatments, including steroids, IVIg, splenectomy, rituximab, vincristine, and eltrombopag. One of these patients died due to major bleeding, while the other was lost to follow-up. The mortality rate among ITP patients hospitalized in internal medicine clinics over the 4-year study period was 1.6%, with major bleeding being the leading cause of death. In a study by Portielje et al. (19), which investigated mortality rates in ITP, 129 patients were followed for 2 years, and the 2-year mortality rate was reported as 3.3%.

The primary strength of our study is the comprehensive analysis of treatment responses in a well-defined cohort of hospitalized ITP patients, providing valuable real-world insights; however, its limitations include the relatively small sample size, retrospective design, and the lack of long-term follow-up to assess sustained responses and outcomes.

CONCLUSION

Refractory ITP remains a challenging condition to manage in clinical practice due to its resistance to conventional therapies and the associated risk of severe complications, such as major bleeding. There is an urgent need for randomized controlled trials to estab-

lish standardized treatment protocols for refractory cases. Combination therapies involving immunosuppressive drugs, monoclonal antibodies, and TPO receptor agonists show potential as effective strategies, but robust evidence from well-designed clinical studies is required to guide their implementation. Advancing our understanding of refractory ITP through such trials will help optimize patient outcomes and improve the quality of care.

Ethics Committee Approval: Ethics committee approval was granted by the Ankara Numune Training and Research Hospital (No: 2011-225, Date: 17.08.2011).

Informed Consent: Informed consent was obtained from all individual participants included in the study.

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REFERENCES

1. Stasi R, Evangelista ML, Stipa E, Buccisano F, Venditti A, Amadori S. Idiopathic thrombocytopenic purpura: Current concepts in pathophysiology and management. Thromb Haemost 2008;99(1):4-13. [CrossRef]
2. Rodeghiero F, Stasi R, Gernsheimer T, Michel M, Provan D, Arnold DM, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: Report from an international working group. Blood 2009;113(11):2386-93. [CrossRef]
3. Cines DB, Blanchette VS. Immune thrombocytopenic purpura. N Engl J Med 2002;346(13):995-1008. [CrossRef]
4. Kuwana M, Okazaki Y, Ikeda Y. Splenic macrophages maintain the anti-platelet autoimmune response via uptake of opsonized platelets in patients with immune thrombocytopenic purpura. J Thromb Haemost 2009;7(2):322-9. [CrossRef]
5. British Committee for Standards in Haematology General Haematology Task Force. Guidelines for the investigation and management of idiopathic thrombocytopenic purpura in adults, children and in pregnancy. Br J Haematol 2003;120(4):574-96. [CrossRef]
6. Stasi R, Provan D. Management of immune thrombocytopenic purpura in adults. Mayo Clin Proc 2004;79(4):504-22. [CrossRef]
7. Neunert C, Terrell DR, Arnold DM, Buchanan G, Cines DB, Cooper N, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv 2019;3(23):3829-66. Erratum in: Blood Adv 2020;4(2):252. [CrossRef]
8. Quiquandon I, Fenaux P, Caulier MT, Pagniez D, Huart JJ, Bauters F. Re-evaluation of the role of azathioprine in the treatment of adult chronic idiopathic thrombocytopenic purpura: A report on 53 cases. Br J Haematol 1990;74(2):223-8. [CrossRef]
9. Emilia G, Morselli M, Luppi M, Longo G, Marasca R, Gandini G, et al. Long-term salvage therapy with cyclosporin A in refractory idiopathic thrombocytopenic purpura. Blood 2002;99(4):1482-5. [CrossRef]
10. Provan D, Moss AJ, Newland AC, Bussel JB. Efficacy of mycophenolate mofetil as single-agent therapy for refractory immune thrombocytopenic purpura. Am J Hematol 2006;81(1):19-25. [CrossRef]
11. Neunert CE, Arnold DM, Grace RF, Kuhne T, McCrae KR, Terrell DR. The 2022 review of the 2019 American Society of Hematology guidelines on immune thrombocytopenia. Blood Adv 2024;8(13):3578-82. [CrossRef]
12. Cines DB, Bussel JB. How I treat idiopathic thrombocytopenic purpura (ITP). Blood 2005;106(7):2244-51. [CrossRef]
13. Cheung E, Liebman HA. Anti-RhD immunoglobulin in the treatment of immune thrombocytopenia. Biologics 2009;3:57-62. [CrossRef]
14. Lazarus AH, Crow AR. Mechanism of action of IVIG and anti-D in ITP. Transfus Apher Sci 2003;28(3):249-55. [CrossRef]
15. Sikorska A, Słomkowski M, Marlanka K, Konopka L, Górski T. The use of vinca alkaloids in adult patients with refractory chronic idiopathic thrombocytopenia. Clin Lab Haematol 2004;26(6):407-11. [CrossRef]
16. Wong RSM, Saleh MN, Khelif A, Salama A, Portella MSO, Burgess P, et al. Safety and efficacy of long-term treatment of chronic/persistent ITP with eltrombopag: Final results of the EXTEND study. Blood 2017;130(23):2527-36. Erratum in: Blood 2018;131(6):709. [CrossRef]
17. Bussel JB, Cheng G, Saleh MN, Psaila B, Kovaleva L, Meddeb B, et al. Eltrombopag for the treatment of chronic idiopathic thrombocytopenic purpura. N Engl J Med 2007;357(22):2237-47. [CrossRef]
18. Passweg JR, Rabusin M. Hematopoetic stem cell transplantation for immune thrombocytopenia and other refractory autoimmune cytopenias. Autoimmunity 2008;41(8):660-5. [CrossRef]
19. Portielje JE, Westendorp RG, Kluin-Nelemans HC, Brand A. Morbidity and mortality in adults with idiopathic thrombocytopenic purpura. Blood 2001;97(9):2549-54. [CrossRef]
20. Ben-Yehuda D, Gillis S, Eldor A. Clinical and therapeutic experience in 712 Israeli patients with idiopathic thrombocytopenic purpura. Israeli ITP Study Group. Acta Haematol 1994;91(1):1-6. [CrossRef]
21. Neylon AJ, Saunders PW, Howard MR, Proctor SJ, Taylor PR; Northern Region Haematology Group. Clinically significant newly presenting autoimmune thrombocytopenic purpura in adults: A prospective study of a population-based cohort of 245 patients. Br J Haematol 2003;122(6):966-74. [CrossRef]
22. Schiavotto C, Rodeghiero F. Twenty years experience with treatment of idiopathic thrombocytopenic purpura in a single department: Results in 490 cases. Haematologica 1993;78(6 Suppl 2):22-8.
23. Liebman HA, Pullarkat V. Diagnosis and management of immune thrombocytopenia in the era of thrombopoietin mimetics. Hematology Am Soc Hematol Educ Program 2011;2011:384-90. [CrossRef]
24. Rodeghiero F. A critical appraisal of the evidence for the role of splenectomy in adults and children with ITP. Br J Haematol 2018;181(2):183-95. [CrossRef]
25. Law C, Marcaccio M, Tam P, Heddle N, Kelton JG. High-dose intravenous immune globulin and the response to splenectomy in patients with idiopathic thrombocytopenic purpura. N Engl J Med 1997;336(21):1494-8. [CrossRef]
26. Tran H, Brighton T, Grigg A, McRae S, Dixon J, Thurley D, et al. A multi-centre, single-arm, open-label study evaluating the safety and efficacy of fixed dose rituximab in patients with refractory, relapsed or chronic idiopathic thrombocytopenic purpura (R-ITP1000 study). Br J Haematol 2014;167(2):243-51. [CrossRef]
27. Arnold DM, Dentali F, Crowther MA, Meyer RM, Cook RJ, Sigouin C, et al. Systematic review: Efficacy and safety of rituximab for adults with idiopathic thrombocytopenic purpura. Ann Intern Med 2007;146(1):25-33. [CrossRef]