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Response to Eltrombopag in Steroid Refractory and Steroid Dependent Immune Thrombocytopenia Real-world Experience

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Abstract

Objective: To evaluate Response to Eltrombopag in steroids refractory and steroids dependent immune thrombocytopenia.

Methodology: This prospective study was conducted at tertiary care bone marrow transplant center Rawalpindi from August 2024 to August 2025, Patients with ITP who had steroids-refractory or steroids-dependent immune thrombocytopenia, were treated with Eltrombopag, and responses were assessed.

Results: Immune thrombocytopenia (ITP) is characterized by decreased platelet count in the peripheral circulation. The first-line therapy is corticosteroids. Eltrombopag has been used as second-line therapy in ITP. 50 ITP patients who had failed or become dependent on first-line corticosteroid therapy were included in this study. The cohort had a mean age of 35.28 ± 19.31 years (range: 3-74 years) with a slight male predominance (54%). At the initiation of therapy, the median platelet count was 9 × 109/L (IQR: 7-15). The treatment yielded an overall response rate of 90%. Specifically, 72% of patients (36/50) achieved a complete response (CR), with a mean platelet count of 300.33 × 10/L. A further 18% of patients (9/50) attained a partial response (PR), with a mean platelet count of 76.33 × 10/L. Only 10% of patients (5/50) showed no response. The median time to achieve a response was 3 weeks (1-4 weeks) with no significant side effects observed, and responses were sustained for a mean duration of 7 months during follow-up. Statistical analysis confirmed a highly significant association between post-treatment platelet counts and the defined response categories (p=0.001).

Conclusion: Eltrombopag proves to be a second-line treatment with high efficacy and a favorable tolerability profile for a diverse demographic of steroid-refractory and steroid-dependent ITP patients. It facilitates a rapid and durable platelet response, achieving high rates of complete and partial response in a real-world clinical setting, thereby reducing the reliance on chronic steroid use.

Key words: Eltrombopag, immune thrombocytopenia, second line therapy, treatment.

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Introduction

Immune thrombocytopenia (ITP) is characterized by antibody-mediated platelet destruction characterized by low platelet counts (platelet count < 100 × 10^9/L) and an increased bleeding risk. For the diagnosis of ITP, alternative comorbid conditions that could lead to thrombocytopenia must be excluded. The phenotype of ITP is extremely heterogeneous, with clinical features includes mucosal bleeding or rarely as life-threatening bleeding. It is one of the most commonly encountered hematological emergencies.[1] Major advances have improved understanding of the immune mechanisms involved in ITP, as well as the role of endogenous thrombopoietin in its pathogenesis. These findings have clarified additional disease pathways and have supported the development of new therapeutic strategies. Refractory ITP is linked to a marked decline in quality of life and presents substantial challenges in clinical management.[2] Corticosteroids, remain the first-line treatment, yet up to 30–40% of patients become either refractory to steroids or dependent on chronic steroid use to maintain safe platelet counts.[3, 6] Corticosteroids prednisone (1 mg/kg/day) with gradual tapering or dexamethasone (40 mg/day for 4 days) are the commonly preferred glucocorticoids and , intravenous immunoglobulin (IVIG) can be used in emergency cases where immediate elevation of platelets count is desired, and anti-D immunoglobulin are recommended as initial therapy.[3,4] Selection of second-line treatments—such as rituximab, splenectomy, or thrombopoietin receptor agonists (TPO-RAs) was based on the duration of response to first-line therapy.[3,5] Eltrombopag is a medication that binds to the juxta membrane domain of the thrombopoietin receptor (TPO-RA and induces megakaryocyte proliferation, differentiation, and platelet production through the JAK/ STAT, AKT, and MAPK

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pathways.[6, 7] However, approximately 20–30% of patients develop steroid-refractory ITP (failure to respond to steroids) or steroid-dependent ITP (requiring prolonged steroids to maintain platelet counts), necessitating second-line therapies.[8,9] This article evaluates the real-world efficacy, safety, and long-term outcomes of eltrombopag in steroid-refractory and steroid-dependent ITP, synthesizing evidence from recent clinical studies and practice guidelines .[10,11]

Methodology

This study was prospectively performed at tertiary care bone marrow transplant center Rawalpindi from August 2024 to August 2025.The institutional ethics committee approved the study (Ref no: IRB-007/AFBMTC/Approval/2024). The patients' records were obtained from the outpatient department record room. Data were collected from files of patients, and information was later recorded in an excel sheet, while gaps in the data were addressed through follow-up phone calls to patients or their family members. Patients with ITP, diagnosed according to the American Society of Hematology guidelines[1,11] and managed with Eltrombopag, comprised the study population. All of these patients had undergone at least one or two previous treatment regimens before starting Eltrombopag. Patient's responses were classified according to platelet count.

Definition: Complete response (CR) is defined as a platelet count ≥ 100 × 10^9/L. Partial Response (PR) is defined as a platelet count ≥ 30 but < 100 × 10^9/L and a doubling from baseline. Treatment with Eltrombopag Initiated at 50 mg once daily in the morning, on an empty stomach

The data were entered into a Microsoft Excel spreadsheet and subsequently analyzed using SPSS version 25. Percentage and frequency were mentioned with categorical variables, and median (IQR) or mean (min-max) were calculated with continuous variables. A one-way ANOVA test was applied to assess the association of responses with post platelets accounts.

Results

A total of 50 ITP patients were treated at our institute between 2023 and 2025. All patients fulfilling the inclusion criteria received Eltrombopag during this period. We analyzed the treatment results of 50 patients. The study cohort had a mean age of 35.28 ± 19.31 years (min-max: 3-74). Of the 50 patients, 27 (54%) were male and 23 (46%) were female. The main presentations in patients with ITP were easy bruising in 20/50 (40%), epistaxis in 4/50 (8%), gum bleeding in 8/50 (16%), hematuria in 3/50 (6%), and 8/50 (16%) of the females presented with menorrhagia, and the remaining patient had no bleeding problem.

Table I: Demographic characteristics of patients.

Age n (%)	
Pead's	9(18)
Adults	41(82)
Gender n (%)	
Male	27(54)
Female	23(46)
Indications n (%)	
Steroid Refractory	33(66)
Steroid Dependent	17(34)

This study evaluated individuals with newly diagnosed (acute), persistent, and chronic ITP who were either refractory to steroids or dependent on them. The median time from diagnosis to the start of Eltrombopag therapy was 139 days (IQR: 58- 398). The patients included in the study had a platelet count of 9 (IQR: 7-15) at the time of initiation of Eltrombopag. The baseline median values were 11.3 g/dL for hemoglobin, 10.5 × 10^9/L for WBC, and 18 × 10^9/L for platelets. 90% of patients were given a dose of 50mg and 10% were given 25 mg as a starting dose. The median duration to achieve a response was 3 weeks (1-4 weeks) with no significant side effects observed. There were a significant association of post treatment platelets counts with responses (P=0.001). The treatment yielded an overall response rate of 90%.

Table II: Treatment Regimen and Response outcomes.

Steroids Treatment n (%)	
50mg/kg	45(90)
25mg/kg	5(10)
Response n (%)	
Complete Response (CR)	36(72)
Partial Response (PR)	9(18)
No Response	5(10)

Patients who showed complete response with mean platelets count of 300.33 (95%CI: 230.06-370.60) were 36/50 (72%), partial response with mean platelet count of 76.33 (95%CI: 58.28-94.38) was shown by 9/50 (18%) patient and 5 (10%) patients showed no response having mean platelets count 21.20 (95%CI: 7.41-34.98) (figure

1). The maximum mean platelets count was 232 x 109/l. post-Eltrombopag follow-up showed a mean response duration of 7 months.

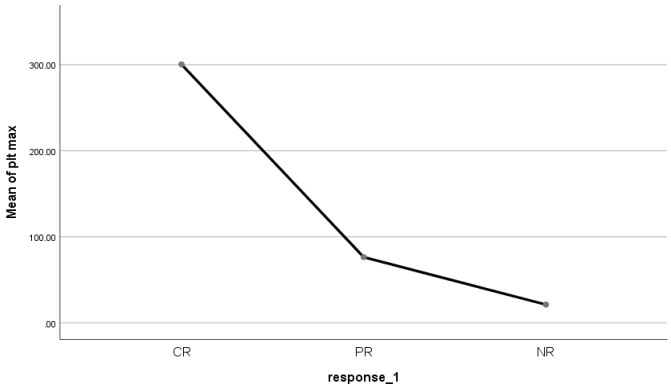

Figure 1. Association of post treatment platelets counts with responses.

Discussion

In this single-center study of 50 patients with immune thrombocytopenia treated with Eltrombopag, yielded a high overall response rate (ORR 90%), with Complete response in 72 percent, partial response in 18 percent, and no response in 10 percent. The median time to response was 3 weeks, and the mean response duration was 7 months. These findings are in line with both randomized trials and real-world studies of response to TPO-RA.[1–4]

When we compare our results with large clinical trials such as the RAISE trial and the EXTEND trial, our response rates fall within or slightly above the reported ranges. In the EXTEND study, the overall response rate was around 86 percent, confirming durable platelet responses over prolonged follow up. Our overall response of 90 percent and complete response of 72 percent compare favorably with these landmark trials.[14,17]

The study population had a median age of 35 years with a broad range (3–74 years) due to the inclusion of pediatric patients. Similar studies reported median ages of 35–52 years, with both adult and pediatric cases represented.[5, 6, 21]

In our cohort, the most common presentation was easy bruising in 40 percent of patients. Gum bleeding was seen in 16 percent, menorrhagia in 16 percent of female patients, epistaxis in 8 percent, and hematuria in 6 percent. A small proportion of patients had no bleeding symptoms at presentation.

These findings are consistent with the classical bleeding pattern described in immune thrombocytopenia. According to the International Consensus Report on ITP management by[3] mucocutaneous bleeding is the hallmark feature of ITP. This includes petechiae, purpura, easy bruising, epistaxis, and gum bleeding. Major internal bleeding is less common and usually occurs at very low platelet counts.

In the RAISE trial, the majority of patients had grade 1 or 2 bleeding at baseline. Cutaneous bleeding such as bruising and petechiae was the most frequent presentation. This supports our finding that easy bruising was the leading symptom in 40 percent of cases.

Real world registries have reported mucosal bleeding rates between 20 and 40 percent in newly diagnosed ITP patients. Epistaxis is commonly reported in 10 to 20 percent of patients in observational cohorts. Our rate of 8 percent is slightly lower but still within the expected range. Gum bleeding reported in 16 percent of our patients is also comparable to published data where oral cavity bleeding ranges from 10 to 25%.[3,10,12,16]

Menorrhagia is a well-recognized manifestation in women with ITP. Studies indicate that up to 20 to 30 percent of reproductive age females with ITP experience heavy menstrual bleeding. Our rate of 16 percent is slightly lower but remains consistent with the reported spectrum. This variation may reflect differences in age distribution and reporting practices.[10,16]

Hematuria is less common in ITP and is usually seen in severe thrombocytopenia. Published literature reports urinary tract bleeding in fewer than 10 percent of patients. Our finding of 6 percent aligns with these observations.

Importantly, some patients with very low platelet counts may have minimal or no bleeding symptoms. Several studies, including large cohort analyses summarized in the International Consensus guidelines, confirm that bleeding severity does not always correlate directly with platelet count. In our cohort, the presence of asymptomatic patients despite thrombocytopenia reflects this well documented clinical variability.

Overall, the bleeding profile observed in our patients closely matches the pattern described in major trials and real-world studies. The predominance of mild mucocutaneous bleeding, the moderate frequency of

menorrhagia in females, and the low rate of serious internal bleeding are all consistent with established clinical data. These similarities further confirm that our patient population represents a typical ITP cohort as described in international literature.

In our cohort, the baseline median hemoglobin was 11.3 g/dl, white blood cell count was 10.5 × 10⁹/L, and platelet count was 18 × 10⁹ per liter. These values reflect typical laboratory findings in immune thrombocytopenia, where isolated thrombocytopenia is the key feature and other cell lines are usually preserved.

The median hemoglobin of 11.3 g per dL in our patients is slightly lower than the normal adult reference range. In large trials such as the RAISE trial, baseline hemoglobin values were generally within or near normal limits because ITP primarily affects platelets and not red blood cells. Mild reductions in hemoglobin, as seen in our study, may result from chronic bleeding, nutritional deficiencies, or prior therapy exposure. The baseline white blood cell counts of 10.5 × 10⁹ per liter in our cohort is within the upper normal range. In both the RAISE trial and long-term data from the EXTEND trial, total leukocyte counts were typically normal at baseline, consistent with the diagnosis of primary ITP. An elevated or markedly abnormal white blood cell count would usually suggest an infection or low dose steroids. Therefore, our findings support the typical pattern of isolated thrombocytopenia.

Real world observational studies have reported similar mild anemia in patients with prolonged disease duration. These comparisons indicate that our patient population is broadly similar to those included in pivotal trials and real-world analyses. The presence of isolated thrombocytopenia with relatively preserved hemoglobin and white blood cell counts supports the diagnosis of primary immune thrombocytopenia. The similarity in baseline platelet levels also strengthens the validity of comparing our response outcomes with previously published data. [3,9,14]

Overall, our baseline hematological parameters align well with established clinical trial populations and observational studies, confirming that our cohort represents a typical ITP population eligible for thrombopoietin receptor agonist therapy.

Our baseline platelet count was 9 × 10⁹/L (IQR: 7-15) matching thresholds in clinical trials (<30 × 10⁹/L) and real-world studies (median 15–30 × 10⁹/L).[8,13] The median time to start eltrombopag in our cohort was 139 days, which reflects real-world delays. However, newer studies suggest that earlier initiation of TPO-RAs may improve outcomes and reduce prolonged steroid exposure.[6, 8] Low platelets count at the time of initiation of therapy showed that many patients had severe thrombocytopenia at treatment initiation, yet they still demonstrated strong response rates.

Most of patients about 90% were given a dose of 50mg and 10% were given 25 mg as a starting dose. In study reported a response rate of 22% at three weeks when 12.5 mg of eltrombopag was used.[23] In study from Korea reported a response rate of 72.2% when 25 mg to 50 mg of eltrombopag was used which shows that in referred study when low dose of 12.5mg explain a longer time to respond as compared to 50mg used in our patient.

The median time from diagnosis to the start of eltrombopag therapy was 139 days (IQR: 58- 398). he median time from diagnosis to initiation of eltrombopag therapy was 139 days. This reflects real world practice, where second line therapies are often started after failure of corticosteroids or other first line treatments. In several observational studies, the median time to initiation has ranged from a few months to more than two years, depending on access, physician preference, and patient characteristics. Increasing evidence now suggests that earlier introduction of thrombopoietin receptor agonists may reduce prolonged steroid exposure and associated complications such as weight gain, hypertension, diabetes, and osteoporosis. [1,24]

The median time to response (3 weeks) was consistent with other real-world reports.[1,14] However, in one study the median number of days required to achieve a platelet count of was 14 (range: 3-210)[13,22] which is slightly less than our results. Other reported platelets count of 17.5 – 152.5 at the end of 4 weeks that is more than our study. (21) Our mean platelet counts during CR (~300 × 10⁹/L) fall within the therapeutic target range of 50–400 × 10⁹/L established in RCTs [13, 16]

Dose distribution in our cohort showed that 90 percent of patients started at 50 mg and 10 percent at 25 mg. Studies using lower starting doses, such as 12.5 mg, reported slower and lower early response rates. In

contrast, cohorts using 25 to 50 mg reported response rates above 70 percent. This suggests that adequate dosing plays a critical role in achieving rapid platelet recovery. [2,9,19]

In our patients, 72 percent achieved complete response, 18 percent achieved partial response, and 10 percent showed no response. In comparison, among chronic ITP patients treated with eltrombopag in other reports, 182 patients, which is 63.8%, achieved complete response, 65 patients, which is 22.8 percent, achieved partial response, and 38 patients, which is 13.4 percent, showed no response.[13] These findings show that our complete response rate is good and compares favorably with previously published data.

Eltrombopag has also been associated with reduced need for rescue therapy and fewer bleeding events in both clinical trials and real-world studies. By maintaining stable platelet counts, it decreases hospital admissions and improves daily functioning. The TAPER trial further demonstrated that selected patients can achieve durable treatment free remission after gradual dose reduction, suggesting a potential disease modifying effect in some individuals.[16]

Likewise, several studies have reported platelet response rates ranging from 50 to 90 percent, depending on the response criteria applied, with favorable safety and tolerability profiles. None of our patient showed significant side effects in terms of bleeding and thrombosis. In contrast studies indicate, that TPO-RA may increase the risk of venous thromboembolism.[4] Thrombopoietin receptor agonists have also demonstrated effectiveness in decreasing bleeding events and reducing the requirement for additional or rescue therapies. [4, 13]

The EXTEND trial confirmed long-term durability, showing an ORR of 86% with more than half of patients for years. [10, 11, 18, 19] Similarly, the TAPER trial highlighted that selected patients achieved durable treatment-free remissions after tapering eltrombopag.[15] Pediatric studies (PETIT and PETIT2) also demonstrated high efficacy and tolerability of eltrombopag, supporting its role across age groups.[21]

Taken together, our study supports eltrombopag as an effective and well-tolerated second-line therapy, producing rapid and durable platelet responses in both adults and children, consistent with clinical trial and real-world evidence.

Conclusion

Eltrombopag proves to be a second-line treatment with high efficacy and a favorable tolerability profile for a diverse demographic of steroid-refractory and steroid-dependent ITP patients. It facilitates a rapid and durable platelet response, achieving high rates of complete and partial response in a real-world clinical setting, thereby reducing the reliance on chronic steroid use.

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