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Efficacy and safety of vincristine as salvage therapy in refractory thrombotic thrombocytopenic purpura: a single center experience

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ABSTRACT

Aims: Thrombotic thrombocytopenic purpura (TTP) is a life-threatening thrombotic microangiopathy caused by severe ADAMTS13 deficiency, leading to widespread microvascular thrombosis and requiring urgent therapeutic plasma exchange (TPE) and immunosuppression. Although most patients achieve remission with first-line TPE and corticosteroids, approximately 10-40% develop refractory disease requiring additional therapies. In our center, rituximab is administered in cases of plasma exchange and steroid failure. In the event of rituximab failure, vincristine is given as a third-line treatment.

Methods: We conducted a retrospective single-center study of adult patients diagnosed with TTP between 2020 and 2025. All patients received first-line daily TPE plus corticosteroids. Refractoriness was defined as failure to achieve platelet recovery or biochemical improvement after 5-7 days of therapy. Patients laboratory results were obtained from the hospital's record system.

Results: A total of 25 patients were included. First-line therapy achieved remission in 48% of patients (12/25). Among 13 refractory patients, rituximab induced remission in 2 (15%). Eleven patients subsequently received vincristine salvage therapy, of whom 9 (81.8%) achieved complete remission, accompanied by rapid platelet recovery and normalization of lactate dehydrogenase levels. Two elderly patients with severe multisystem involvement died despite salvage therapy. Overall survival for the cohort was 92%.

Conclusion: Vincristine was highly effective and well tolerated as a salvage therapy in patients with refractory TTP who failed both TPE and rituximab, achieving remission in more than 80% of cases. These findings support vincristine as a valuable therapeutic option, particularly in settings where caplacizumab or other advanced biologics are unavailable. Larger prospective studies are warranted to better define its optimal timing and comparative efficacy among emerging salvage therapies.

Keywords: Thrombotic thrombocytopenic purpura, vincristine, refractory TTP, salvage therapy, plasma exchange, rituximab, ADAMTS13 deficiency

INTRODUCTION

Thrombotic thrombocytopenic purpura (TTP) is a life-threatening thrombotic microangiopathy characterized by microangiopathic hemolytic anemia and thrombocytopenia, frequently accompanied by ischemic organ involvement, most commonly affecting the brain and kidneys.[1] TTP may be congenital or acquired; however, both forms share a common pathogenic mechanism: severe deficiency of the von Willebrand factor (VWF)–cleaving protease A Disintegrin and Metalloprotease with ThromboSpondin type 1 motif, member 13 (ADAMTS13). Profound ADAMTS13 deficiency (<10%) leads to the accumulation of ultra-large VWF multimers, promoting spontaneous platelet aggregation and disseminated microvascular thrombosis.[1] If left untreated, acute TTP is associated with mortality rates approaching 90%, highlighting the need for rapid diagnosis and immediate treatment.[1]

The standard first-line treatment for acquired TTP consists of daily therapeutic plasma exchange (TPE) combined with immunosuppression, most commonly high-dose corticosteroids.[2,3] Plasma exchange removes circulating autoantibodies and replenishes functional ADAMTS13, resulting in a marked improvement in survival, with mortality decreasing to approximately 10-20% in the modern era.[1] Although the majority of patients respond to first-line therapy, an estimated 10-40% fail to achieve adequate platelet recovery and are classified as having refractory TTP, necessitating escalation of treatment to prevent fatal outcomes.[4,5]

Rituximab, an anti-CD20 monoclonal antibody that suppresses anti-ADAMTS13 autoantibody production through B-cell depletion, is the most widely used second-line therapy for refractory or relapsing TTP.[6] High remission rates have been reported, particularly when rituximab is administered early in the disease course.[6] Nevertheless, a subset of patients either does not respond to rituximab or cannot receive it due to contraindications. In such cases,

evidence guiding third-line or salvage therapies remains limited and is largely derived from small observational studies.[7]

Among traditional immunosuppressive agents, vincristine—a vinca alkaloid chemotherapeutic—has emerged as a potential salvage therapy in refractory TTP. In addition to its cytotoxic effects on rapidly dividing cells, vincristine appears to exert immunomodulatory and platelet-directed effects, including interference with platelet–VWF interactions. Small case series have reported remission rates ranging from 50% to 87% in refractory TTP, suggesting a possible therapeutic role despite the absence of randomized controlled trials.[8]

In this single-center observational study, we evaluated patients with TTP treated between 2020 and 2025, focusing on those who required vincristine as third-line salvage therapy after failure of plasma exchange, corticosteroids, and rituximab. Our aim was to assess the efficacy and safety of vincristine in refractory TTP and to contextualize its role within contemporary TTP management.

METHODS

Ethics

This study was approved by the Dicle University Ethics Committee for Non-interventional Clinical Researches (Date: 26.11.2025, Decision No: 74). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Design and Patient Population

We conducted a retrospective, single-center analysis of adult patients diagnosed with TTP between 2020 and 2025 at Dicle University Educational Hospital. All patients fulfilled established clinical criteria for TTP, including severe thrombocytopenia (typically $<30\times10^9$/L), microangiopathic hemolytic anemia with schistocytes on peripheral blood smear, and absence of an alternative cause of thrombotic microangiopathy. Given the life-threatening nature of TTP, treatment was initiated immediately upon clinical suspicion without awaiting ADAMTS13 assay results.

Treatment Strategy

All patients received first-line therapy consisting of daily TPE with fresh frozen plasma replacement combined with high-dose corticosteroids. Plasma exchange was performed once daily, exchanging approximately 1-1.5 plasma volumes, and continued until remission criteria were met. Remission was defined as a sustained platelet count $>150\times10^9$/L for at least two consecutive days, accompanied by clinical stabilization and improvement in hemolysis parameters. Corticosteroids were administered concurrently (prednisone 1 mg/kg/day or equivalent methylprednisolone) to suppress autoantibody production. Refractory TTP is a type of thrombotic microangiopathy that does not result in clinical improvement despite first-line treatments such as plasma exchange and steroid therapy.[1]

Patients who failed to demonstrate platelet recovery or biochemical improvement after 5-7 days of daily TPE and corticosteroids were considered refractory to first-line therapy. These patients received second-line treatment with rituximab (375 mg/m² intravenously once weekly, up to four doses), while daily plasma exchange was continued. Refractoriness was defined as failure to achieve platelet recovery or evidence of clinical deterioration despite approximately one week of therapy. Patients who initially responded but experienced an early exacerbation within 30 days of discontinuing plasma exchange were also classified as refractory.

Patients who remained refractory after rituximab therapy, or whose exacerbation was not controlled by rituximab, received vincristine as third-line salvage therapy. Due to clinical deterioration in our patients, four doses of rituximab therapy were not awaited, and treatment was switched to vincristine. Vincristine was administered intravenously at a dose of 2 mg (approximately 1.4 mg/m², capped at 2 mg) once weekly for up to three doses, depending on clinical response. Plasma exchange was continued concomitantly until remission was achieved. No additional immunosuppressive agents were introduced during this salvage phase. Unfortunately, given the retrospective nature of this study and the limitations of our dataset, we were unable to consistently collect data on these parameters across all patients. Nonetheless, we have made efforts to include available data related to the number of TPE sessions and treatment outcomes such as platelet recovery.

Data Collection and Outcomes

Data collected included patient demographics, baseline laboratory values (platelet count, lactate dehydrogenase [LDH], creatinine), number of plasma exchange sessions, and details of administered therapies. The primary outcome was clinical remission, defined as normalization of platelet count ($>150\times10^9$/L) with discontinuation of plasma exchange for at least 30 days. Secondary outcomes included time to remission, treatment failure, and overall survival. Treatment response was defined by platelet recovery and LDH normalization, whereas treatment failure was defined as persistent thrombocytopenia or hemolysis despite therapy, or TTP-related death.

Statistical Analysis

Given the observational nature of the study, analyses were descriptive. Continuous variables were summarized using medians and ranges, and categorical variables were reported as frequencies and percentages.

RESULTS

A total of 25 patients with TTP were included in the analysis. The median age was 41 years (range, 21-85), and 14 patients (56%) were male. At presentation, all patients exhibited severe thrombocytopenia and microangiopathic hemolysis. The median platelet count at admission was 24×10^9/L, and the median LDH level was 900 IU/L. All patients had severely reduced ADAMTS13 activity (<10%) with detectable inhibitors, confirming the diagnosis of acquired immune TTP.

Treatment Response and Outcomes

All patients received first-line therapy with daily TPE and corticosteroids (**Table**). Twelve patients (48%) achieved remission with first-line therapy alone, with platelet recovery above 150×10^9/L and normalization of LDH after a median of

seven plasma exchange sessions (range, 5-14). These patients required no additional therapy.

Table. Distribution of remission, refractoriness, and mortality in treated patients

Therapy line	Patients treated (n)	Remission achieved (n, %)	Refractory (needed next-line) (n)	Mortality (n)
First-line (TPE + steroids)	25	12 (48%)	13	0
Second-line (rituximab)	13 (52%)	2 (15%)	11	0
Third-line (vincristine)	11 (44%)	9 (81.8%)	–	2

TPE: Therapeutic plasma exchange

Thirteen patients (52%) were refractory to first-line treatment and received second-line rituximab. Among these patients, only two (15%) achieved remission following rituximab therapy, allowing discontinuation of plasma exchange by days 10-12 of hospitalization. The remaining 11 patients showed persistent thrombocytopenia and ongoing hemolysis despite continued plasma exchange and rituximab and were therefore escalated to third-line therapy with vincristine.

Response to Vincristine Salvage Therapy

Eleven patients received vincristine as third-line salvage therapy. Of these, nine patients (81.8%) achieved complete remission. Platelet counts increased rapidly following vincristine initiation, reaching normal levels (>250×10^9/L) within 1-2 weeks in most responders. This was accompanied by parallel normalization of LDH levels and resolution of clinical manifestations. Plasma exchange was successfully tapered and discontinued in all responders, and remission was sustained for at least 30 days after cessation of therapy.

Two patients (18.2%) did not respond to vincristine and died from TTP-related complications. Both were elderly patients with severe multisystem involvement at presentation. One patient died from intracerebral hemorrhage in the setting of persistent severe thrombocytopenia, and the other from presumed TTP-related myocardial ischemia. No further salvage therapies were pursued due to rapid clinical deterioration. Overall survival for the cohort was 92% (23 of 25 patients) (**Table**).

Safety

Vincristine was generally well tolerated. Mild peripheral neuropathy occurred in two patients and transient leukopenia in two patients; both resolved without intervention. No cases of severe neurotoxicity, clinically significant myelosuppression, or treatment-limiting adverse events were observed, and vincristine was not discontinued in any patient due to toxicity.

DISCUSSION

In this single-center study, we evaluated vincristine as third-line salvage therapy in patients with refractory TTP. Our findings demonstrate that vincristine induced remission in the majority of patients who failed to respond to both first-line plasma exchange with corticosteroids and second-line rituximab, with an overall remission rate of 81.8%. This result is clinically meaningful, as these patients had ongoing, life-threatening disease despite standard therapies.

The remission rate observed in our cohort is consistent with previously reported outcomes for vincristine in refractory or relapsed TTP, which range from 50% to 87%.[8] Our results corroborate earlier small case series, including those by Ferrari et al.[8] and Öngören et al.,[9] and further support the role of vincristine as an effective salvage option in this setting. Together, these findings reinforce existing evidence that vincristine remains a viable therapeutic strategy when conventional approaches fail.

The mechanisms underlying vincristine's efficacy in TTP are likely multifactorial. In addition to its cytotoxic effects on rapidly dividing cells, vincristine may suppress autoantibody-producing immune cells, thereby facilitating recovery of ADAMTS13 activity. Experimental and clinical data also suggest a direct platelet-directed effect, with reduced platelet–VWF interactions, potentially leading to a more rapid interruption of microvascular thrombosis.[10] Importantly, vincristine causes minimal bone marrow suppression at the doses used in TTP, preserving megakaryocyte function and allowing platelet recovery—an advantage over other cytotoxic agents in patients with severe thrombocytopenia.[7,10]

In our cohort, the apparent response to rituximab was lower than that reported in other series, with remission achieved in only 15% of patients treated with rituximab as second-line therapy. This finding likely reflects the timing of rituximab administration in our practice, where it was introduced after failure of first-line therapy in patients with advanced and rapidly progressive disease. Given the delayed onset of rituximab's immunologic effects, many patients required a more rapidly acting intervention. In contrast, studies reporting higher rituximab response rates often employed early or upfront rituximab administration. Our results therefore do not diminish the role of rituximab but highlight the continued need for additional salvage strategies in severe or rapidly refractory TTP.[1,5]

Vincristine was particularly effective in patients who had already failed rituximab, suggesting a complementary or distinct mechanism of action.[9] The high overall survival rate of 92% in our cohort underscores the clinical impact of successful salvage therapy in this population. While some patients might eventually respond to prolonged immunosuppression, the acute and fulminant nature of TTP often precludes a "wait-and-see" approach, making timely escalation of therapy essential.[5]

Compared with other salvage options—such as cyclophosphamide, cyclosporine, splenectomy, or bortezomib—vincristine offers a favorable balance between efficacy and toxicity.[2] Newer agents, including caplacizumab, have demonstrated efficacy in accelerating platelet recovery and reducing exacerbations; however, access may be limited in some settings due to cost or availability.[5] In this context, vincristine remains a practical and widely accessible option, particularly in resource-limited environments. In patients who received vincristine, clinical and laboratory improvements were observed on average after the fourth day.

The treatment was completed with three doses of vincristine, administered weekly. We observed a good response rate in our patients, but larger cohorts are needed to draw broader conclusions.

Limitations

Several limitations of this study should be acknowledged. Its retrospective design and relatively small sample size limit definitive conclusions regarding causality. In addition, serial ADAMTS13 measurements were not routinely available to correlate biochemical recovery with clinical response. Despite these limitations, the consistent and rapid responses observed after vincristine initiation in a highly refractory population support a meaningful therapeutic effect.

In conclusion, our findings suggest that vincristine is an effective and well-tolerated salvage therapy for refractory TTP, particularly in patients who fail to respond to rituximab. Vincristine continues to represent a valuable component of the therapeutic armamentarium for severe TTP, and further prospective, multi-center studies are warranted to define its optimal timing and comparative role alongside emerging therapies.

CONCLUSION

TTP remains a life-threatening condition requiring prompt and aggressive therapy. Although most patients achieve remission with plasma exchange and corticosteroids, a substantial subset develops refractory disease. In this single-center study, vincristine was appeared to be effective as third-line salvage therapy, inducing remission in more than 80% of patients who failed both plasma exchange and rituximab, and was associated with an overall survival rate of 92%. Vincristine was well tolerated, with no serious treatment-limiting toxicities observed.

These findings support vincristine as a valuable rescue therapy for refractory TTP, particularly in settings where access to newer agents may be limited. Prospective, multi-center studies are needed to better define the optimal timing of vincristine and its comparative role alongside emerging therapies in the management of refractory TTP.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was approved by the Dicle University Ethics Committee for Non-interventional Clinical Researches (Date: 26.11.2025, Decision No: 74).

Informed Consent

This retrospective study used pre-existing anonymized patient data. No additional intervention was performed, and there was no direct patient contact. The study was approved by the Ethics Committee, and the requirement for written informed consent was waived by the ethics committee.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

Concept: VD, AK, MOA; Design: VD, AK, MOA; Data Collection and/or Processing: VD, AK, MOA; Analysis and/or Interpretation: VD, AK, MOA; Literature Review: VD, AK, MOA; Writing the Article: VD; Critical Review: VD, AK, MOA.

REFERENCES

1. Scully M, Thomas M, Underwood M, et al. Thrombotic thrombocytopenic purpura and pregnancy: presentation, management, and subsequent pregnancy outcomes. *Blood*. 2014;124(2):211-219. doi: 10.1182/blood-2014-02-553131
2. Subhan M, Scully M. Advances in the management of TTP. *Blood Rev.* 2022;55:100945. doi:10.1016/j.blre.2022.100945
3. Coppo P, Cuker A, George JN. Thrombotic thrombocytopenic purpura: toward targeted therapy and precision medicine. *Res Pract Thromb Haemost*. 201816;3(1):26-37. doi:10.1002/rth2.12160
4. Sayani FA, Abrams CS. How I treat refractory thrombotic thrombocytopenic purpura. *Blood*. 2017;130(14):1684. doi:10.1182/blood-2017-08-803171
5. Zheng XL, Vesely SK, Cataland SR, et al. ISTH guidelines for treatment of thrombotic thrombocytopenic purpura. *J Thromb Haemost*. 2020; 18(10):2496-2502. doi:10.1111/jth.15010
6. Cuker A, Cataland SR, Coppo P, et al. Redefining outcomes in immune TTP: an international working group consensus report. *Blood*. 2021; 137(14):1855-1861. doi:10.1182/blood.2020009150
7. Lemiale V, Valade S, Mariotte E. Unresponsive thrombotic thrombocytopenic purpura (TTP): challenges and solutions. *Ther Clin Risk Manag*. 2021;17:577-587. doi:10.2147/TCRM.S205632
8. Ferrari B, Peyvandi, F. How I treat thrombotic thrombocytopenic purpura in pregnancy. *Blood*. 2020;136(19):2125-2132. doi:10.1182/blood.2019000962
9. Öngören S, Salihoğlu A, Apaydın T, et al. Vincristine as an adjunct to therapeutic plasma exchange for thrombotic thrombocytopenic purpura: a single-ınstitution experience. *Balkan Med J*. 2018;35(6):417-421. doi:10.4274/balkanmedj.2017.1215
10. Gutterman LA, Stevenson TD. Treatment of thrombotic thrombocytopenic purpura with vincristine. *JAMA*. 1982;247(10):1433–1436. doi:10.1001/jama.1982.03320350037025