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Sustained Response After a Six-Week Course of Subcutaneous Daratumumab in Multi-Refractory Immune Thrombocytopenia

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To the editor.

A 6-week course of subcutaneous (SC) daratumumab produced a rapid, deep, and durable complete response in a woman with primary immune thrombocytopenia (ITP) refractory to corticosteroids, intravenous immunoglobulin (IVIG), rituximab, and two thrombopoietin receptor agonists (TPO-RAs). The response allowed her to avoid a splenectomy she had declined, and it has remained complete at six months of follow-up without any rescue therapy. This observation is consistent with, though it cannot prove, the hypothesis that CD38-positive long-lived plasma cells, rather than B cells alone, sustain autoantibody production in refractory ITP, and it raises a practical question: can a daratumumab course shorter than those used in published trials still achieve durable remission?

Case Presentation. A 54-year-old woman was diagnosed with primary ITP in December 2023. She presented to the emergency department with four to five intraoral hemorrhagic bullae and widespread petechiae and purpura (ITP Bleeding Assessment Tool [ITP-BAT] score, Grade 2). The platelet count was 4×10^9/L, confirmed on peripheral blood smear, which showed isolated thrombocytopenia without red-cell fragmentation or dysplastic features. Secondary causes were excluded: testing for human immunodeficiency virus, hepatitis B and C viruses, Helicobacter pylori, antinuclear antibodies, and antiphospholipid antibodies was negative; abdominal ultrasonography showed a normal-sized spleen (long axis 110 mm); and a bone-marrow biopsy excluded myelodysplastic syndrome and other primary marrow disorders. Throughout the disease course, the bleeding phenotype remained mucocutaneous (petechiae, purpura, and intermittent intraoral bullae); no World Health Organization grade 3–4 bleeding occurred, hemoglobin remained within the normal range, and neither red-cell transfusion nor bleeding-related hospitalization was required.

First-line therapy was intravenous methylprednisolone 1 mg/kg/day; because of the hemorrhagic bullae, IVIG 1 g/kg/day was given concurrently for two days. The platelet count peaked at 34×10^9/L in the first week but fell to 5×10^9/L by the third week. In the absence of active bleeding, the steroid was continued at 1 mg/kg/day through the fifth week, then tapered and stopped by the eighth week.

In February 2024, with a platelet count of 3×10^9/L, eltrombopag was started at 50 mg/day and escalated to 75 mg/day; over approximately four months the count remained persistently $<10\times10^9$/L (best value 9×10^9/L), and no meaningful response was achieved. In June 2024, at a platelet count of 3×10^9/L and with recurrent intraoral bullae, rituximab 375 mg/m²/week was given for four weeks. Response was assessed over the following six months (weekly, then biweekly monitoring); all values remained $<20\times10^9$/L, peaking at 18×10^9/L.

By December 2024 (six months after rituximab) the platelet count was 4×10^9/L, and splenectomy was recommended with planned perioperative support (IVIG and platelet transfusion). After being informed of the risks and the perioperative plan, the patient declined surgery; her refusal, not the platelet count, was the decisive reason it was not performed. Oral immunosuppressants such as azathioprine and mycophenolate mofetil were not used because they are not reimbursed for ITP in Türkiye, and fostamatinib and avatrombopag were not licensed or reimbursed for this indication and were therefore unavailable. Accordingly, in January 2025 the patient was switched to a second TPO-RA with a different structure, romiplostim, starting at 1 µg/kg/week and titrated weekly to the maximum 10 µg/kg/week by week 12. Romiplostim was continued at the maximum dose until December 2025; despite approximately one year of treatment the platelet count remained persistently $<10\times10^9$/L (often $<5\times10^9$/L; range $1–13\times10^9$/L), while the patient remained free of major

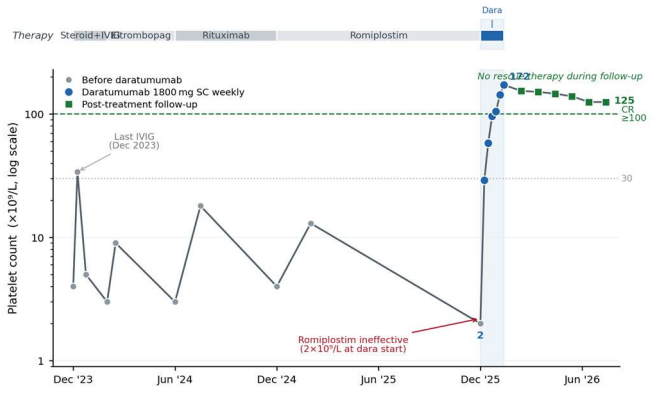

Figure 1. Platelet count over the full disease course (December 2023–June 2026; logarithmic scale). Counts remained persistently <20×10⁹/L through sequential corticosteroid/IVIG, eltrombopag, rituximab, and one year of maximal-dose romiplostim. Romiplostim was ineffective (2×10⁹/L at daratumumab initiation) and was stopped when subcutaneous daratumumab (1,800 mg weekly × 6; shaded band) began; the last IVIG dose had been given two years earlier, and no rescue therapy was used during follow-up. A complete response (≥100×10⁹/L) was reached during treatment and sustained through six months. IVIG, intravenous immunoglobulin; MP, methylprednisolone; SC, subcutaneous.

bleeding

In December 2025, citing financial constraints and difficulty attending weekly visits, the patient consented to an off-label 6-week course of SC daratumumab after a review of the literature in refractory ITP; because daratumumab is not reimbursed for ITP in Türkiye, an off-label application was submitted and approved. At this point, the disease met criteria for chronic ITP (>12 months' duration). Daratumumab was given subcutaneously at 1,800 mg once weekly for six weeks. Before the first dose, complete blood typing with subgroup analysis was performed to pre-empt daratumumab interference with pretransfusion testing; hepatitis serologies were rechecked and negative, and the baseline IgG was normal (9.46 g/L). Standard premedication was used. Antiviral prophylaxis (acyclovir 400 mg) and *Pneumocystis jirovecii* prophylaxis (trimethoprim-sulfamethoxazole, three days per week) were given from the first dose until three months after treatment; no vaccinations were administered during treatment. Safety was assessed clinically and with a complete blood count at every weekly and subsequent monthly visit; no injection-site reactions, infections, or other adverse events were recorded.

Romiplostim, which had been ineffective (platelet count 2×10⁹/L at daratumumab initiation), was stopped when daratumumab began; no IVIG had been given since first-line treatment two years earlier, and no platelet transfusion or other rescue therapy was administered during the daratumumab course or the six-month follow-up. From a baseline of 2×10⁹/L, weekly platelet counts during the six-week course rose to 29, 58, 96, 105, and 143×10⁹/L, reaching 172×10⁹/L at the end of week 6 (**Figure 1**). Complete response, defined per International Working Group criteria as a platelet count ≥100×10⁹/L in the absence of bleeding, was thus achieved. Follow-up then moved to a monthly schedule, with counts of 154, 151, 146, 139, and 125×10⁹/L; at the sixth month after treatment (June 2026) the count was stable at 125×10⁹/L without any further ITP-directed therapy. The full treatment sequence is summarized in **Table 1**.

Several aspects of this case warrant discussion. Our observation aligns with other recent reports of daratumumab activity in multi-refractory ITP: an open-label intravenous phase 2 trial in adults,[1] a case series of CD38-targeted rescue after multiple prior agents,[2] and a pediatric series with rapid platelet recovery and immune-reconstitution data.[3] These reports are consistent with the hypothesis that long-lived, CD38-positive plasma cells, largely resistant to anti-CD20 depletion, contribute to autoantibody production in refractory ITP,[4] and in our patient daratumumab restored sustained remission after rituximab and two TPO-RAs had failed. We emphasize, however, that no patient-specific immunological data, serial immunoglobulins beyond a baseline IgG, lymphocyte or plasma-cell subsets, CD38+ cell dynamics, or platelet autoantibodies, were obtained, so this mechanistic interpretation remains inferential.

The SC schedule we used delivered the same weekly dose of 1,800 mg as evaluated in the DART study, the largest dedicated ITP experience to date. That nonrandomized phase 2 study assigned 21 patients with a median of four prior therapies to sequential dose-increasing cohorts receiving 8 or 10 weekly SC injections of 1,800 mg and reported a sustained response (two consecutive platelet counts ≥50×10⁹/L at week 24) in 38%.[5] Our patient reached a platelet count >120×10⁹/L after six weekly doses. This is descriptively in line with the DART investigators' own observation that two of three patients in their safety run-in responded after only four injections, prompting their suggestion that four doses might be as effective as eight or ten.[5] Together, these observations raise, but cannot, from a single case, establish, the possibility that the treatment duration extrapolated from myeloma schedules may not be strictly necessary in ITP.

This report has clear limitations. It describes a single patient with only six months of follow-up, so durability is uncertain, and longer observation is needed. As a single favorable case, it is subject to selection and publication bias, and, as noted, no patient-specific immunological characterization was performed to support the proposed mechanism. Within these constraints, the case suggests that SC daratumumab, given for as few as six weekly doses, may be a rescue option worth evaluating in multi-refractory ITP, including in patients who decline splenectomy, a hypothesis that should be tested prospectively.

Table 1. Sequence of ITP-directed therapies and platelet response (platelet counts in $\times 10^9$/L).

Therapy	Dates	Dose & schedule	Plt before	Best plt	Outcome / reason stopped
Methylprednisolone + IVIG	Dec 2023	MP 1 mg/kg/day (tapered, stopped wk 8) + IVIG 1 g/kg/day × 2 days	4	34	Relapse; <10 by week 3
Eltrombopag	Feb–Jun 2024	50 → 75 mg/day	3	9	Insufficient; persistently <10
Rituximab	Jun–Dec 2024	375 mg/m²/week × 4; 6-month assessment	3	18	Insufficient; 4 at 6 months
Splenectomy	Dec 2024	Recommended with perioperative IVIG + platelet support	4	—	Declined by patient
Romiplostim	Jan–Dec 2025	1 → 10 µg/kg/week (max from wk 12), ~1 year	4	13	Insufficient; persistently <10 (often <5)
Daratumumab (SC)	Dec 2025–Jan 2026	1,800 mg SC weekly × 6	2	172	Complete response; 125 at 6 months, ongoing

At diagnosis (December 2023): platelet count 4×10^9/L; ITP-BAT bleeding score Grade 2; normal-sized spleen; secondary causes excluded. IVIG, intravenous immunoglobulin; MP, methylprednisolone; SC, subcutaneous.

Informed consent. Informed consent for publication of clinical data was obtained from the patient.

Author contributions. T.G.K. conceptualized the report, reviewed the literature, and wrote the manuscript. A.M.Y. contributed to patient care and clinical data collection and reviewed and approved the final manuscript. Both authors read and approved the final version.

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Competing interests: The authors declare no competing interest.

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