Successful Platelet Engraftment Following Avatrombopag After Gene Therapy for Transfusion-Dependent β-Thalassemia

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Background

Delayed platelet recovery is a recognized complication after betibeglogene autotemcel and busulfan-based myeloablation for transfusion-dependent β-thalassemia.

Persistent thrombocytopenia prolongs transfusion dependence and may increase bleeding risk during recovery.

Evidence guiding thrombopoietin receptor agonist use after autologous gene therapy remains limited.

Objective: describe a single-patient experience of delayed platelet recovery followed by platelet engraftment after avatrombopag.

Case Summary

Adult male with transfusion-dependent β-thalassemia undergoing gene therapy

Busulfan conditioning on days −6 to −3 (2/17/26–2/20/26).
Betibeglogene autotemcel (ZYNTEGLO) infused on 2/23/26 (day 0).
Infused dose: 10.0 × 10^6 CD34+ cells/kg; vector copy number: 6.0 vc/dg.
WBC engraftment occurred on day +17 (3/12/26).
Course notable for pancytopenia with delayed platelet recovery requiring transfusion support.
Pre-gene-therapy HLA class I antibodies were present, a possible contributor to delayed platelet engraftment.

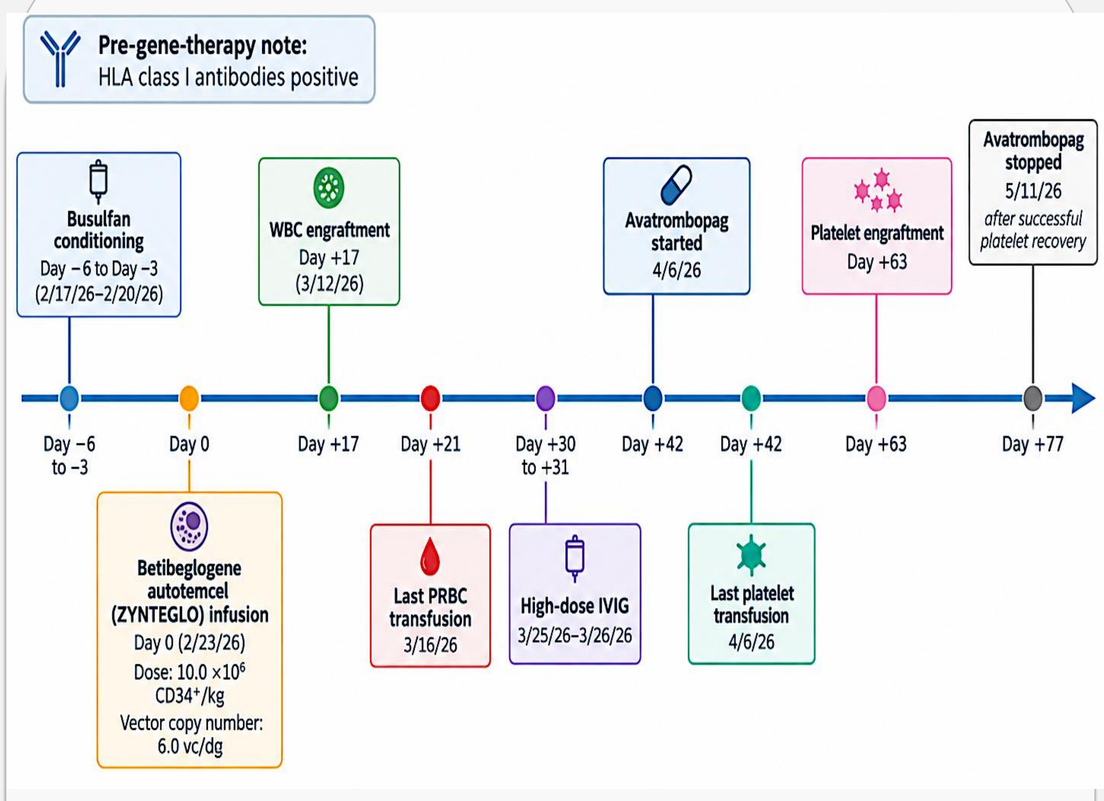
Recovery Milestones

- Last PRBC transfusion: 3/16/26
- High-dose IVIG: 3/25/26–3/26/26
- Last platelet transfusion: 4/6/26
- Avatrombopag started: 4/6/26
- Platelet engraftment achieved on day +63
- Avatrombopag stopped: 5/11/26 after successful recovery

Key Takeaways

- Avatrombopag use was followed by successful platelet engraftment in prolonged post-beti-cel thrombocytopenia.
- Recovery may also reflect natural marrow recovery and the cumulative effect of other supportive measures.
- Prospective multicenter experience is needed to define patient selection, timing, dosing, and duration of therapy.

Clinical Timeline



Timeline highlights the sequence from busulfan conditioning and betibeglogene autotemcel infusion to avatrombopag initiation, platelet engraftment, and drug discontinuation after recovery.

Discussion

Neutrophil recovery was timely, whereas platelet recovery was delayed to day +63.

This case highlights a management gap when thrombocytopenia persists after gene therapy despite supportive care.

Avatrombopag was chosen as an oral thrombopoietin receptor agonist after ongoing platelet transfusion needs.

The temporal association with platelet recovery supports feasibility and hypothesis generation, but it does not establish efficacy.

Conclusion

In TDT gene therapy experience, avatrombopag was followed by successful platelet engraftment after prolonged thrombocytopenia.

- TPO receptor agonists may merit formal study as supportive care after autologous gene therapy for selected patients with delayed platelet recovery.