Emapalumab as Precision Salvage Therapy for Post-HCT HLH/MAS-Like Hyperinflammation with Severe Graft Dysfunction

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Background

Severe post-HCT HLH/MAS-like hyperinflammation is life-threatening and often overlaps with other endothelial, infectious, and alloimmune complications.

Standard escalation with etoposide may be prohibitive when marrow reserve is poor and graft recovery must be preserved.

IFN-γ is a central macrophage-activating cytokine in HLH biology, supporting Emapalumab as a rational precision-salvage option.

Objective: describe a severe post-HCT case in which targeted IFN-γ neutralization was selected because conventional cytotoxic escalation was considered unsafe.

Case Summary

Severe secondary HLH/MAS-like hyperinflammation after allogeneic HCT with profound graft dysfunction

20-year-old male with relapsed pre-B ALL in CR2.

10/10 MUD PBSC HCT on 10/29/2025 after TBI/cyclophosphamide/thiotepa.

Day +180: no evidence of ALL, ClonoSEQ negative, 100% donor chimerism, marrow cellularity ~10%.

Phenotype: fever, multilineage cytopenias, hypertriglyceridemia, marrow hemophagocytosis, ferritin 28,000 ng/mL, neopterin >500, CXCL9 884, sIL-2R 1,238, liver inflammation.

Competing risks: TA-TMA, platelet transfusion dependence, WBC 0.4 × 10^9/L, BK viremia/viruria, HHV-6/HSV gut infection, resolved EBV-PTLD and adenoviremia, thrombosis, prior GVHD concerns.

Why Emapalumab?

Profound marrow hypocellularity and severe cytopenias made etoposide high risk.

Active infectious vulnerability and liver injury increased the danger of broader cytotoxic immunosuppression.

A precision approach was needed to control macrophage-driven hyperinflammation while preserving graft recovery.

Emapalumab 3 mg/kg was administered from 5/20/2026 through 6/3/2026.

Conclusion

This case supports biologic feasibility of targeted IFN-γ blockade as precision salvage in severe post-HCT HLH/MAS-like hyperinflammation with graft dysfunction.

The benefit signal was accompanied by improvement in ferritin, liver inflammation, and hematopoietic recovery trajectory.

This remains a single-patient experience; concurrent corticosteroids, anakinra, tofacitinib, and TMA-directed therapies limit causal attribution.

Prospective study is needed to define optimal timing, patient selection, and integration with other post-HCT inflammatory syndromes.

Figure 1. Clinical course, therapeutic rationale, and response to emapalumab

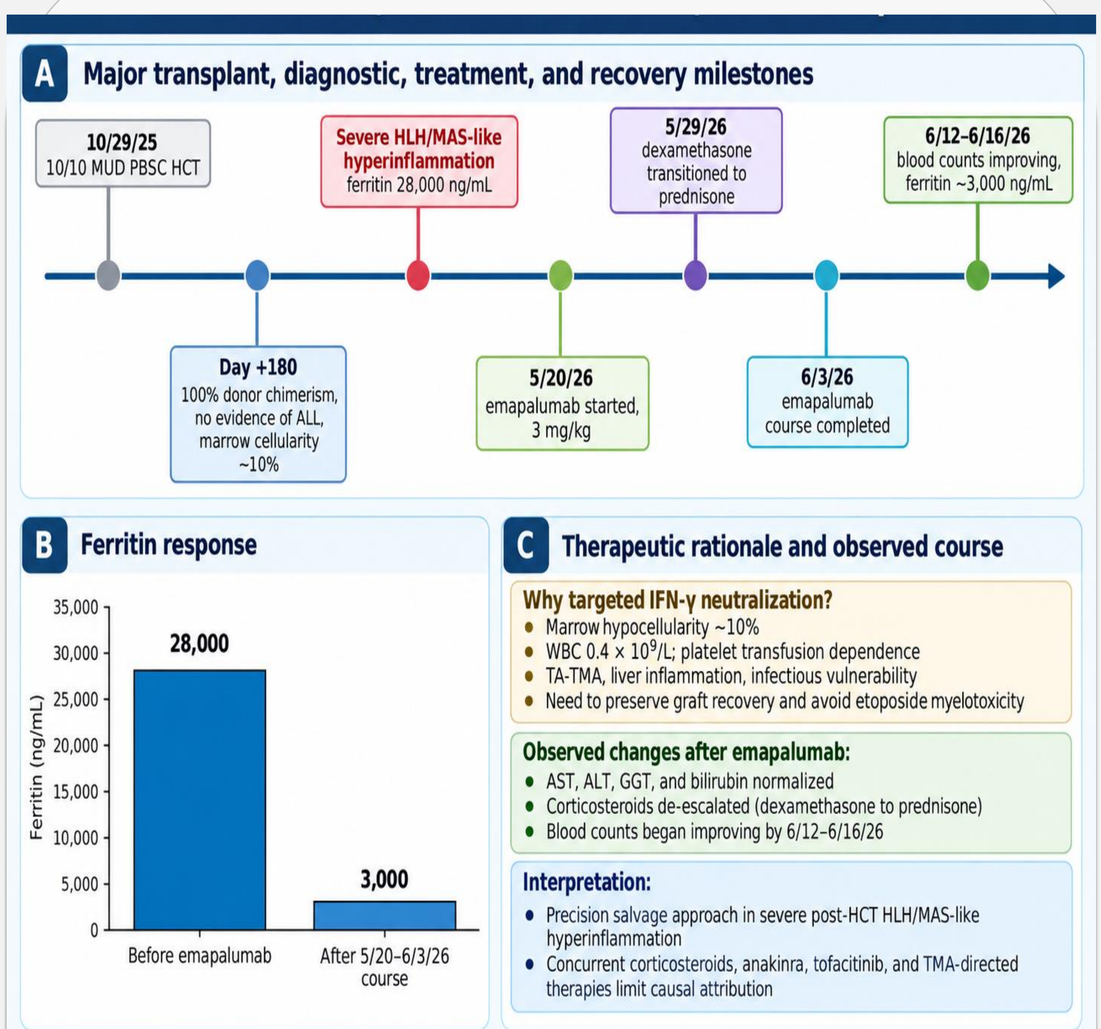

Figure summary: targeted IFN-γ neutralization was selected because severe marrow hypocellularity, WBC 0.4 × 10^9/L, platelet transfusion dependence, infectious vulnerability, and liver injury.

Key Outcomes

- Ferritin declined from 28,000 to approximately 3,000 ng/mL.
- AST, ALT, GGT, and bilirubin normalized.
- Dexamethasone transitioned to prednisone
- Blood counts began improving by 6/12–6/16/2026.
- Clinical course allowed steroid de-escalation and reassessment of the need for CD34-selected stem-cell boost.