CT – 1508 Extramedullary Disease and Prolonged Hematotoxicity After Real-World Ide-Cel for Relapsed/Refractory Multiple Myeloma

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INTRODUCTION

- Idecabtagene vicleucel (ide-cel) provides meaningful clinical activity in relapsed/refractory multiple myeloma (RRMM), yet real-world effectiveness remains heterogeneous across clinical subgroups.
- Extramedullary disease (EMD) represents an aggressive disease phenotype, while prolonged post–CAR T cytopenias impair marrow recovery and complicate post-relapse therapy.
- Transatlantic evidence synthesis of major registries provides robust characterization of the EMD-associated survival penalty and persistent hematotoxicity under standard-of-care (SOC) conditions.

AIM

- **Primary Aim:** Quantify the real-world prevalence and progression-free survival (PFS) impact of EMD among RRMM patients receiving commercial ide-cel across independent US and European registries.
- **Secondary Aim:** Characterize rates, time course, and predictive risk factors for prolonged grade ≥3 hematotoxicity (Day 30 and Day 90 post-infusion).

METHOD

Data Sources: Synthesized non-overlapping, EMD-stratified real-world ide-cel cohorts from the **US Myeloma CAR T Consortium**, **CIBMTR registry**, and the French **DESCAR-T / FENIX registry**.

Endpoints:
Efficacy: Overall response rate (ORR), day-90 response, and median PFS stratified by EMD status.
Safety: Persistent grade ≥ 3 cytopenias at day 30 and day 90, severe thrombocytopenia, and hematopoietic rescue interventions.
Synthesis: Descriptive sample-size–weighted pooling and hazard ratio estimation across mutually exclusive cohorts to prevent double counting.

CONCLUSIONS

- Real-world transatlantic evidence confirms **EMD as an adverse biomarker**, resulting in substantially lower response durability and roughly halved median PFS duration following commercial ide-cel.
- Prolonged grade ≥3 cytopenias represent a major post–ide-cel challenge affecting 40% of patients at 3 months, heavily driven by baseline marrow tumor burden.
- Findings advocate for standardized pre-infusion EMD staging, optimized bridging to cytoreduce marrow bulk, and dedicated post-CAR T hematopoietic support protocols.

RESULTS

Cohort (N=510): Real-world EMD prevalence was **21.8%** (n=111/510) across US and French cohorts.

Survival Penalty: Median PFS was halved in EMD vs. non-EMD (**5.5 vs. 12.3 months**; ~55% reduction); EMD independently predicted inferior PFS (HR **1.5**, 95% CI 1.1–2.2, *p* = 0.02).

Response Disparity: Day-90 ORR was significantly lower with EMD (**52% vs. 82%**).

Persistent Cytopenias: Grade ≥3 cytopenias persisted in **65% at Day 30** and **40% at Day 90**; baseline marrow burden ≥50% predicted Day-90 cytopenia (OR **6.40**, 95% CI 1.40–33.60).

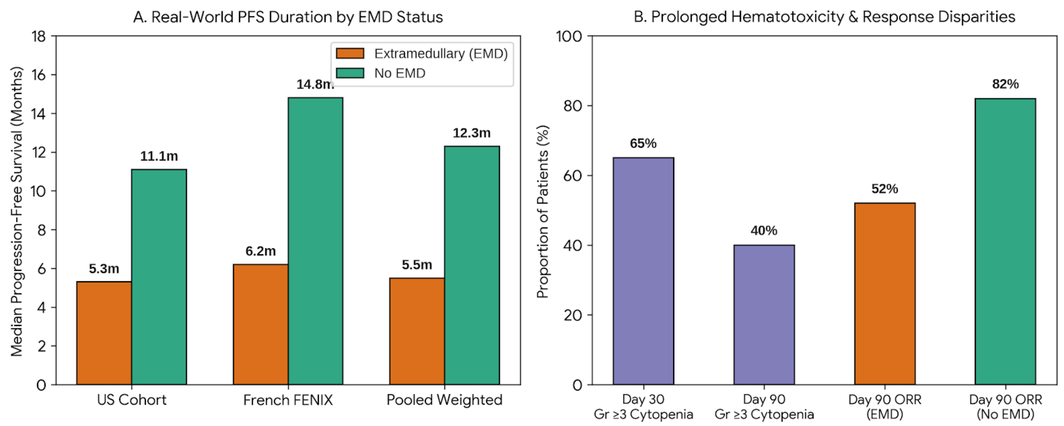

Figure 1. Real-World Efficacy by EMD Status and Prolonged Hematotoxicity Profile Following Ide-Cel. (**A**) Median progression-free survival (months) among RRMM patients with versus without extramedullary disease across US, French DESCAR-T, and pooled weighted cohorts, showing an approximate 55% reduction in PFS duration. (**B**) Incidence of persistent grade ≥ 3 cytopenias at day 30 and day 90 alongside day-90 overall response rate (ORR) disparities by EMD status.

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