The Calculus of Relapse: A Neural Ordinary Differential Equation Model of Continuous Disease Acceleration Following CAR-T versus Bispecific Therapy in Multiple Myeloma

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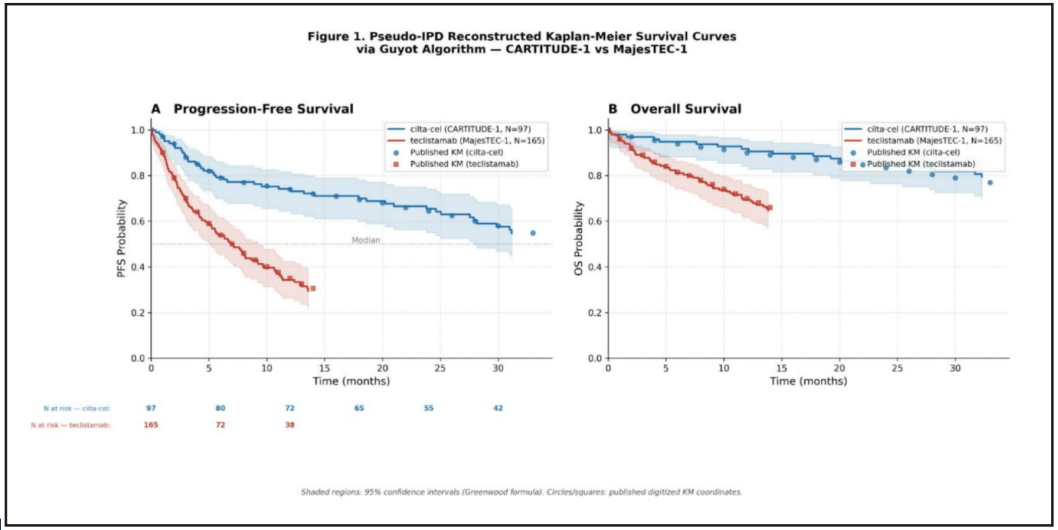
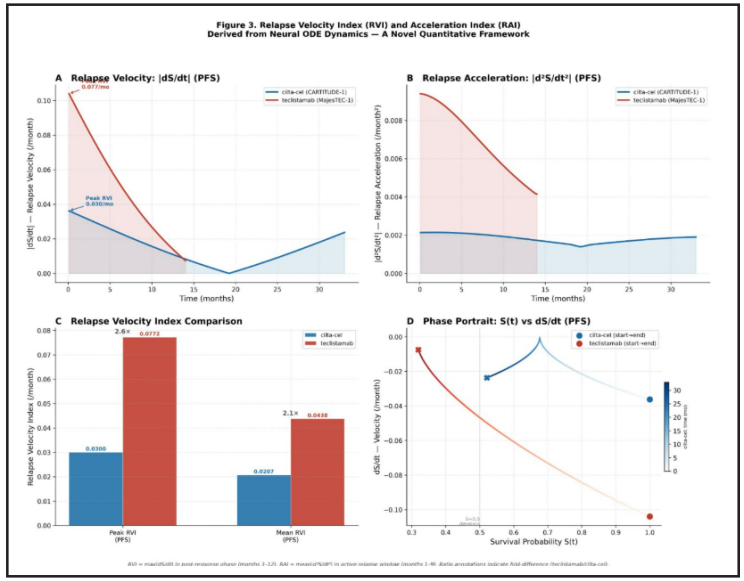
Introduction

Relapsed/refractory multiple myeloma (RRMM) treatment has been transformed by CAR-T cell therapies and bispecific antibodies , yet comparative analyses of disease kinetics following treatment failure remain limited. Traditional survival analysis provides discrete time-to-event estimates but cannot characterize continuous relapse velocity or acceleration. We introduce Synthetic Longitudinal Trajectory Meta-Analysis (SLT-MA) using neural ordinary differential equations (Neural ODEs) to quantify differential disease progression dynamics.

Methods

We reconstructed pseudo-individual patient data from published Kaplan-Meier curves of CARTITUDE-1 (cilta-cel, N=97, median follow-up 33.4 months) and MajesTEC-1 (teclistamab, N=165, median follow-up 14.1 months) using the Guyot algorithm. Neural ODE models were trained with architecture $dS/dt = h\_param(S,t) + f_\theta(S,t)$, combining generalized Weibull warm start with neural correction layers optimized via L-BFGS-B (training MSE 0.00032 and 0.00021, respectively). We derived novel metrics: Relapse Velocity Index (RVI, instantaneous progression rate), Relapse Acceleration Index (RAI, rate of velocity change), and Area Under Velocity Curve (AUVC, cumulative progression burden).





Results

1)PFS: Neural ODE modeling estimated longer progression-free survival with cilta-cel (33months) vs teclistamab (7months).
2)Relapse velocity: The peak relapse velocity was 3.1-fold higher with teclistamab (0.0704/ month vs 0.0230/month), indicating faster disease progression/relapse.
3)Disease acceleration: The RAI was 2.7-fold higher with teclistamab (9.089×10^{-3} vs 3.385×10^{-3}/month²), indicating greater acceleration of disease progression after failure.
4)Cumulative progression burden: AUVC was 1.52-fold higher with teclistamab (0.725 vs 0.477), indicating a greater overall cumulative progression burden.

Conclusion

Bispecific antibody failure is characterized by significantly more aggressive disease acceleration than CAR-T failure, consistent with immune exhaustion-driven explosive relapse. The 3.1-fold differential in relapse velocity has critical implications for therapy sequencing in RRMM, suggesting CAR-T may provide more durable disease control with less aggressive post-relapse kinetics. SLT-MA represents a novel framework for comparative effectiveness research in hematologic malignancies.