REDEFINING THE HORIZON: A DEEP SURVIVAL MIXTURE META-ANALYSIS QUANTIFYING THE STATISTICAL CURE FRACTION OF CELLULAR THERAPIES IN RELAPSED MULTIPLE MYELOMA

Authors: H.Alamy[1], F.Khalid[2], L.Manzoor[3], S.Maryam[4], R.Chennuri[5], I.Khan[6], H.Kommu[7], S.Bhavanam[8] and A.Das[9]

Affiliations: 1. Desert Regional Medical Center, Palm Springs, California, US 2. Sheikh Zayed Medical College, Rahim Yar Khan, Pak 3. Dow University of Health Sciences, Karachi, Pak 4. Shifa International Hospital, Islamabad, Pak 5. New York Medical College / St. Clare's and St. Mary's Hospital, Denville, USA 6. Ziauddin Medical University, Karachi, Pak 7. JIPMER, Puducherry, India 8. Brookdale University Hospital and Medical Center, Brooklyn, USA 9. Mayo Clinic, Rochester, US

DESERT CARE NETWORK | DESERT REGIONAL MEDICAL CENTER

INTRODUCTION

Standard Cox proportional hazards models assume indefinite hazard continuation, precluding identification of cured subpopulations. In relapsed/refractory multiple myeloma (RRMM), CAR-T therapies demonstrate survival plateaus inconsistent with traditional survival modeling — conflating functional cure with prolonged remission and obscuring critical distinctions between cellular therapy classes.

METHOD

Study design

- Reconstructed pseudo-individual patient data from six pivotal trials (N=1,053) using Guyot et al. digitization methodology
- Weibull mixture cure model S(t) = π + (1−π)·S_susceptible(t) fitted via maximum likelihood (L-BFGS-B optimizer, eight random starts)
- Bootstrap 95% confidence intervals derived from 200 resamplings
- Trials: cilta-cel (CARTITUDE-4, N=208), ide-cel (KarMMa-3, N=254), teclistamab (MajesTEC-1, N=165), elranatamab (MagnetisMM-3, N=123), talquetamab (MonumenTAL-1, N=143), cevostamab (Phase I/II, N=160)

AIM

To apply deep survival mixture modeling to six pivotal RRMM trials, quantifying the statistical cure fraction (π) of CAR-T versus bispecific antibody therapies and resolving clinical treatment-sequencing questions.

CONCLUSIONS

Deep survival mixture modeling provides mathematically verifiable cure-fraction estimates. CAR-T therapies possess a statistically significant cure fraction, while bispecific antibodies show almost no cure probability despite similar initial response rates. This quantitative distinction resolves clinical sequencing debates: prioritize curative-intent CAR-T therapy first in eligible RRMM patients.

RESULT

CAR-T therapies: statistically significant cure fractions

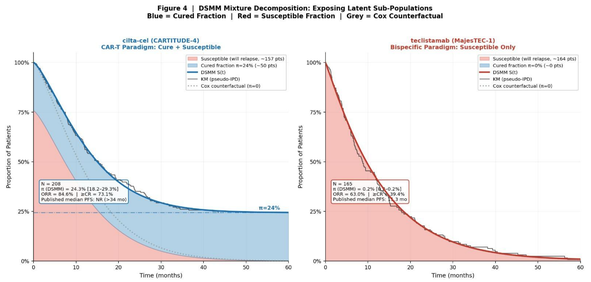
cilta-cel π=24.3% (95% CI 18.2–29.3%; ORR 84.6%, ≥CR 73.1%; median PFS not reached at >34 months) and ide-cel π=20.4% (95% CI 15.4–24.4%; ORR 71.0%, ≥CR 39.0%; median PFS 13.3 months). Pooled CAR-T cure fraction: 22.4%.

Bispecific antibodies: cure fractions near zero

teclistamab, elranatamab, talquetamab and cevostamab each showed π≈0.2%, statistically indistinguishable from zero. Pooled bispecific cure fraction: 0.2%, despite comparable short-term overall response rates.

CAR-T hazard functions converged to zero by month 40; bispecific hazards persisted indefinitely.

GRAPHS & ILLUSTRATIONS



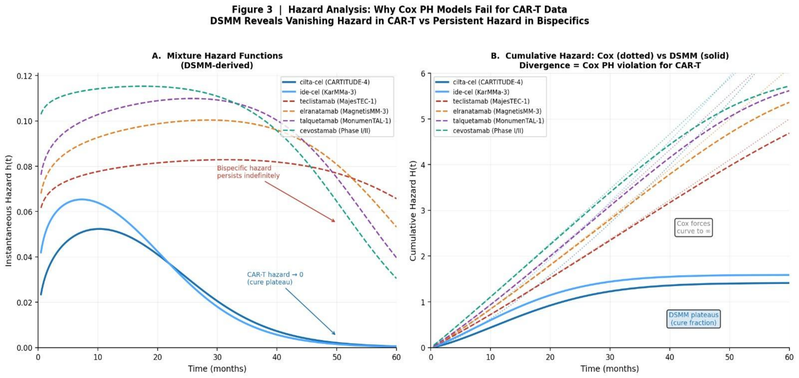
22.4%

Pooled CAR-T cure fraction

0.2%

Pooled bispecific-antibody cure fraction

Figure 4. Cure-fraction decomposition: cilta-cel (CAR-T) vs teclistamab (bispecific).



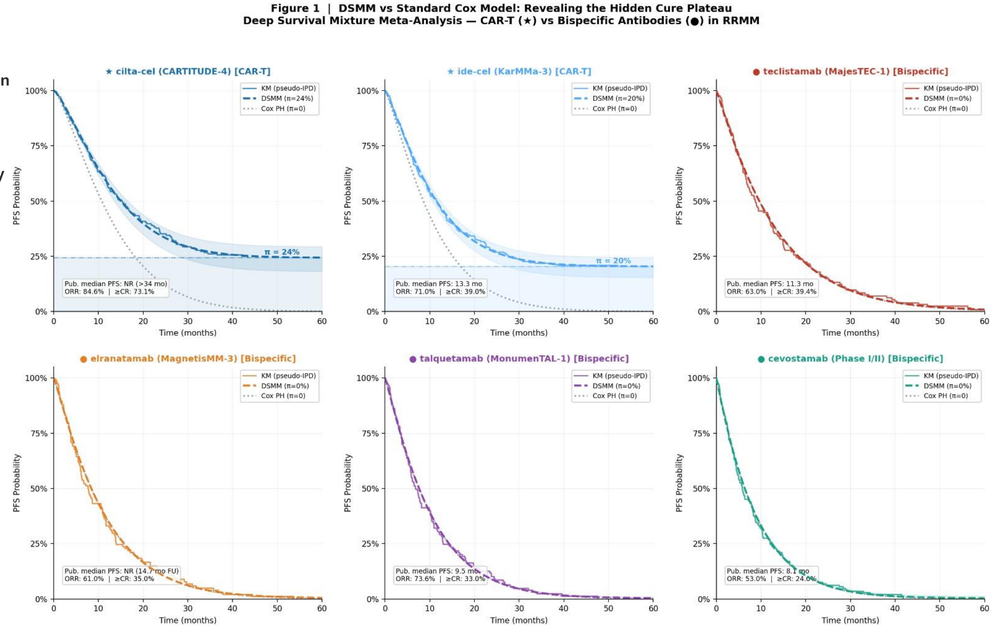


Figure 1. DSMM vs standard Cox model across six pivotal RRMM trials — CAR-T (cilta-cel, ide-cel) reveal a cure plateau; bispecific antibodies do not.

ACKNOWLEDGEMENTS

The authors thank the investigators and patients of the CAR-T and bispecific antibody trials included in this analysis (CARTITUDE-4, KarMMa-3, MajesTEC-1, MagnetisMM-3, MonumenTAL-1, and the cevostamab Phase I/II trial) for their published data, as well as Desert Regional Medical Center Internal Medicine Residency Program for support. No funding was received for this work.

CONTACT INFORMATION

Haroon Alamy MD, PGY-2 IM Resident

Haroon_Alamy@outlook.com

Desert Regional Medical Centre, Palm Springs, CA

REFERENCES

Trial data sources: CARTITUDE-4 (cilta-cel), KarMMa-3 (ide-cel), MajesTEC-1 (teclistamab), MagnetisMM-3 (elranatamab), MonumenTAL-1 (talquetamab), and a Phase I/II study of cevostamab.