Non-Relapse Mortality across Anito-cel and other BCMA-Targeted Therapies in Relapsed/Refractory Multiple Myeloma (RRMM): A Systematic Review and Meta-Analysis

Poster MM - 744

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Objective

- To estimate and compare non-relapse mortality (NRM) associated with BCMA-targeted therapies among patients with relapsed/refractory multiple myeloma (RRMM), using evidence from clinical trials and real-world studies.

Conclusions

- Anito-cel, a BCMA-targeted CAR T-cell therapy, was associated with lower observed NRM after adjustment for available study-level characteristics, relative to both other BCMA-targeting CAR T-cell and bispecific therapies.
- Differences are most pronounced versus bispecific antibodies, likely driven by higher infection-related mortality in this class.
- Lower observed NRM with anito-cel is consistent with a reduced infection burden, supporting a differentiated safety profile.
- **Limitations**: These findings should be interpreted in light of the non-comparative nature of the included studies, study heterogeneity, and limited follow-up. Longer-term follow-up and real-world evidence are needed to determine whether the observed NRM advantage persists as the evidence base matures.

Plain Language Summary

Non-relapse mortality (NRM) measures deaths that were not caused by multiple myeloma, a type of blood cancer, getting worse. Researchers use it to help assess treatment safety.

We reviewed published research studies and studies of everyday medical practice of anito-cel and other treatments that target B-cell maturation antigen (BCMA), a protein found on myeloma cells.

Based on the available evidence, anito-cel was linked to a lower risk of NRM than the other therapies evaluated.

Overall, these findings suggest that anito-cel may be linked to fewer treatment-related deaths than similar BCMA-targeted therapies.

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Base case dataset for meta-analysis

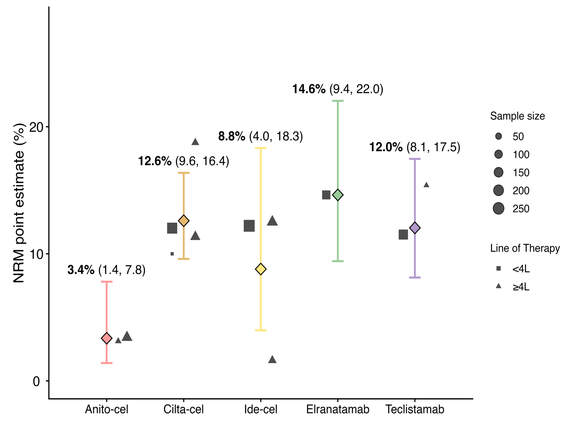
Table 1: Input Data for the Meta-analysis

Study	Source	Treatment	Study Setting	Median Follow-Up (months)	LOT	Total Patients	NRM Events	NRM %
ARC-101	Individual patient data	Anito-cel	Trial	32.3*	≥4L	32	1	3.1
iMMagine-1	Individual patient data	Anito-cel	Trial	15.9	≥4L	117	4	3.4
CARTITUDE-2 Cohort A	Cohen et al. IMS 2022[4]	Cilta-cel	Trial	17.1	<4L	20	2	10.0
CARTITUDE-1	Martin et al. ASH 2021[5]	Cilta-cel	Trial	18	≥4L	97	11	11.3
CARTITUDE-4	San Miguel et al. NEJM 2023[6]	Cilta-cel	Trial	15.9	<4L	208	25	12.0
CARTIFAN-1	Mi et al. J Clin Oncol 2023[7]	Cilta-cel	Trial	18	≥4L	48	9	18.8
CRB-401	Lin et al. Nat Med 2023[8]	Ide-cel	Trial	18.1	≥4L	62	1	1.6
KarMMa-3	Rodriguez et al. NEJM 2023[9]	Ide-cel	Trial	18.6	<4L	254	31	12.2
KarMMa	Munshi et al. NEJM 2021[10]	Ide-cel	Trial	13.3	≥4L	128	16	12.5
MagnetisMM-3 Cohort A	Lesokhin et al. Nat Med 2023[11]	Elranatamab	Trial	14.6	<4L	123	18	14.6
MajesTEC-1	Moreau et al. NEJM 2022[12]	Teclistamab	Trial	14.1	<4L	165	19	11.5
MajesTEC-1 China cohort	Cai et al. Cancer 2024[13]	Teclistamab	Trial	15	≥4L	26	4	15.4

*Indicates median follow-up time of the data cutoff for anito-cel phase 1 study. The single NRM event happened at an earlier follow-up time which was within the study inclusion criteria of 15.9 ±3 months

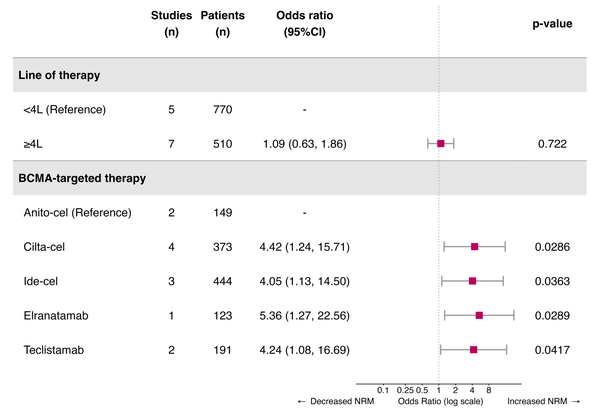
Pooled NRM rates from meta-analysis

Figure 1: NRM Rates Across BCMA-targeted Therapies



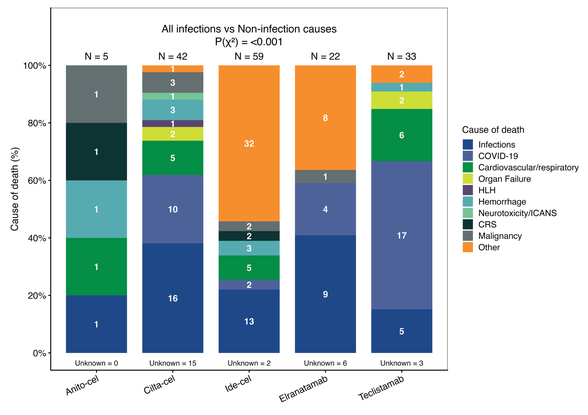
Multivariate Analysis

Figure 2: Results of the Multivariate Meta-analysis of NRM Across Trials



Proportion of known causes of deaths in trials

Figure 3: Specific Causes of Death Across BCMA-targeted Therapies



Infections shown separately from COVID-19 in cause of death counts; the χ^2 test for infections combines both categories; Other causes of death include: **Cilta-cel:** ascites (n=1); **Ide-cel**: Other causes (n=25), general AE (n=5), amyotrophic lateral sclerosis (n=1), shock (n=1); **Elranatamab**: general AE (n=6), sudden death (n=1), treatment toxicity (n=1); **Teclistamab**: hypovolemic shock (n=1), sudden death (n=1)

BACKGROUND

- Anitocabtagene autoleucel (anito-cel) is an investigational BCMA-targeted CAR T-cell therapy that has shown promising results in patients with 4L+ RRMM in the phase 2 iMMagine-1 trial.[1]
- NRM captures deaths not attributable to disease progression. Although anito-cel demonstrated a favorable safety profile in iMMagine-1, its NRM has yet to be compared with other BCMA-targeted therapies.
- To address this evidence gap, we conducted a systematic review and meta-analysis of clinical trials and real-world studies reporting NRM for BCMA-targeted therapies.

METHODS

- We systematically searched databases and conferences for studies of BCMA-targeted therapies in RRMM. Eligible studies were randomized/non-randomized trials or observational studies of patients with ≥2 prior lines of therapy published from 2012–2025.
- Pooled NRM proportions were estimated using random-effects meta-analysis, adjusting for covariates. Informed by previous literature[2,3], 9 covariates were identified: treatment type, LOT, treatment era, follow-up time, study setting, prior BCMA exposure, bridging therapy, age and progression-free survival. Univariate analyses identified significant covariates for selection in the multivariate analyses.
- The base case analysis was restricted to clinical trials with follow-up within ±3 months of the iMMagine-1 trial's median follow-up of 15.9 months, which accounts for the confounding relationship between follow-up time and NRM (longer follow-up time allows for more events). Deaths occurring after salvage therapy or of unknown cause were also excluded.
- Causes of death were compared across all trials by Pearson chi-squared test, excluding unknown causes and using categories previously cited by Dos Santos et al., 2024.[2]
- Sensitivity analyses were also conducted relaxing the follow-up restriction and incorporating real-world studies.

RESULTS

- Fifty-three records reporting on 30 studies were identified, including 14 clinical trials and 16 real-world studies.
- The base case analysis was limited to 12 clinical trials as seen in **Table 1** (n=1,280 patients) with pooled NRM rates ranging from 3.4% (anito-cel) to 14.6% (elranatamab) (**Figure 1**).
- Multivariate meta-regression showed that NRM was significantly associated with treatment type but not with LOT (<4L vs ≥4L) (p=0.722; **Figure 2**).
- Cause of death distributions differed significantly across treatments in clinical trials, with most of the difference attributed to infections rather than other causes (p<0.001) (**Figure 3**).
- NRM estimates varied widely and were strongly influenced by follow-up duration, which was longer in trials than in real-world cohorts; median follow-up time was 18.1 vs. 9.6 months, respectively.
- Treatment-related differences remained consistent across sensitivity analyses relaxing follow-up restrictions and incorporating real-world studies, although follow-up time and study setting were both significant predictors of NRM (data not shown).

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Abbreviations

Non-relapse mortality (NRM)
Relapsed/Refractory Multiple Myeloma (RRMM)
Line of therapy (LOT)
B-cell maturation antigen (BCMA)
Cytokine release syndrome (CRS)
Hemophagocytic lymphohistiocytosis (HLH)
Immune effector cell-associated neurotoxicity syndrome (ICANS)

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