Projecting Functional Cure in Patients With Relapsed/Refractory Multiple Myeloma (RRMM) in the MajesTEC-3 Study of Teclistamab-Daratumumab (Tec-Dara) Using a Mixture Cure Model

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- Serves as an advisory board member for Johnson & Johnson, Amgen, Celgene, Bristol Myers Squibb, Sanofi, Takeda, Roche, Novartis, Bayer, Adaptive Biotechnologies, Galapagos, Kite Pharma, Merck, Pfizer, AbbVie, and Servier

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Background and Objective

- Emerging immunotherapies that deliver unprecedented depth and durability of response are reshaping survival expectations in RRMM[1]
- Tec-Dara, a new SOC in 2L+ RRMM, significantly improved PFS (HR, 0.17) and OS (HR, 0.46) versus DPd/DVd in patients with RRMM and 1–3 prior LOTs in MajesTEC-3[2,3]
- Tec-Dara survival curves plateau from ~6 months, supporting potential for long-term disease control in a substantial proportion of patients[2]
  - 90% of patients who were alive and progression-free at 6 months remained so at ~3 years[2]
  - Sustained PFS benefit was observed regardless of cytogenetic or functional high-risk status[4]

We used a relative survival mixture cure model to estimate the proportion of patients on Tec-Dara with no excess long-term mortality risk on top of the general population

2L+, second-line or later; DPd/DVd, Dara plus dexamethasone with pomalidomide or bortezomib; HR, hazard ratio; LOT, line of therapy; OS, overall survival; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma; SOC, standard of care; Tec-Dara, teclistamab-daratumumab.

1. Kitundu JH. *Health Sci Rep*. 2025;8(12):e71581. 2. Costa LJ, et al. *N Engl J Med*. 2026;394(8):739–752. 3. TECVAYLI® (teclistamab-cqyv) [package insert]. Janssen Biotech, Inc. 2026. 4. Banerjee R, et al. Presented at: 31st EHA Annual Meeting; June 11–14, 2026; Stockholm, Sweden. Oral (S-198).

Phase 3 MajesTEC-3 Study Design

- Phase 3, multicenter, open-label trial conducted in 150 sites across 20 countries[1]

Key inclusion criteria

- RRMM
- 1–3 prior LOTs including a PI and lenalidomide
  - Patients with only 1 prior LOT must have been lenalidomide refractory per IMWG criteria
- ECOG PS score of 0–2

Key exclusion criteria

- Prior BCMA-directed therapy
- Refractory to anti-CD38 mAbs[a]

1:1 randomization N=587

22 Oct 2021 to 29 Sept 2023[b]

Tec-Dara
N=291
SC dosing following Dara schedule

DPd/DVd
N=296
by investigator's choice[c]

Primary endpoint
- PFS per IRC

Key secondary endpoints
- ≥CR[d] and ORR[d]
- MRD negativity (10^{-5})
- OS
- MySIm-Q Total Symptom score

Other secondary endpoints
- Safety
- PK and immunogenicity

Tec-Dara is a fully immunotherapy-based regimen with a steroid-sparing schedule after Cycle 1 Day 8[e] and monthly dosing after 6 cycles

[a]Prior exposure to anti-CD38 mAbs was permitted.
[b]During the COVID-19 pandemic.
[c]DPd/DVd were administered per the approved schedules.
[d]Response and disease progression were assessed by a blinded IRC per IMWG criteria.
[e]Dexamethasone, acetaminophen, and diphenhydramine pre-medication was required for the first 2 weeks; subsequent dexamethasone was not required thereafter.
BCMA, B-cell maturation antigen; CR, complete response; ECOG PS, Eastern Cooperative Oncology Group performance status; IMWG, International Myeloma Working Group; IRC, independent review committee; mAbs, monoclonal antibodies; MRD, minimal residual disease; MySIm-Q, Multiple Myeloma Symptom and Impact Questionnaire; ORR, overall response rate; PI, proteasome inhibitor; PK, pharmacokinetics; SC, subcutaneous.
1. Costa LJ, et al. *N Engl J Med.* 2026;394(8):739–752.

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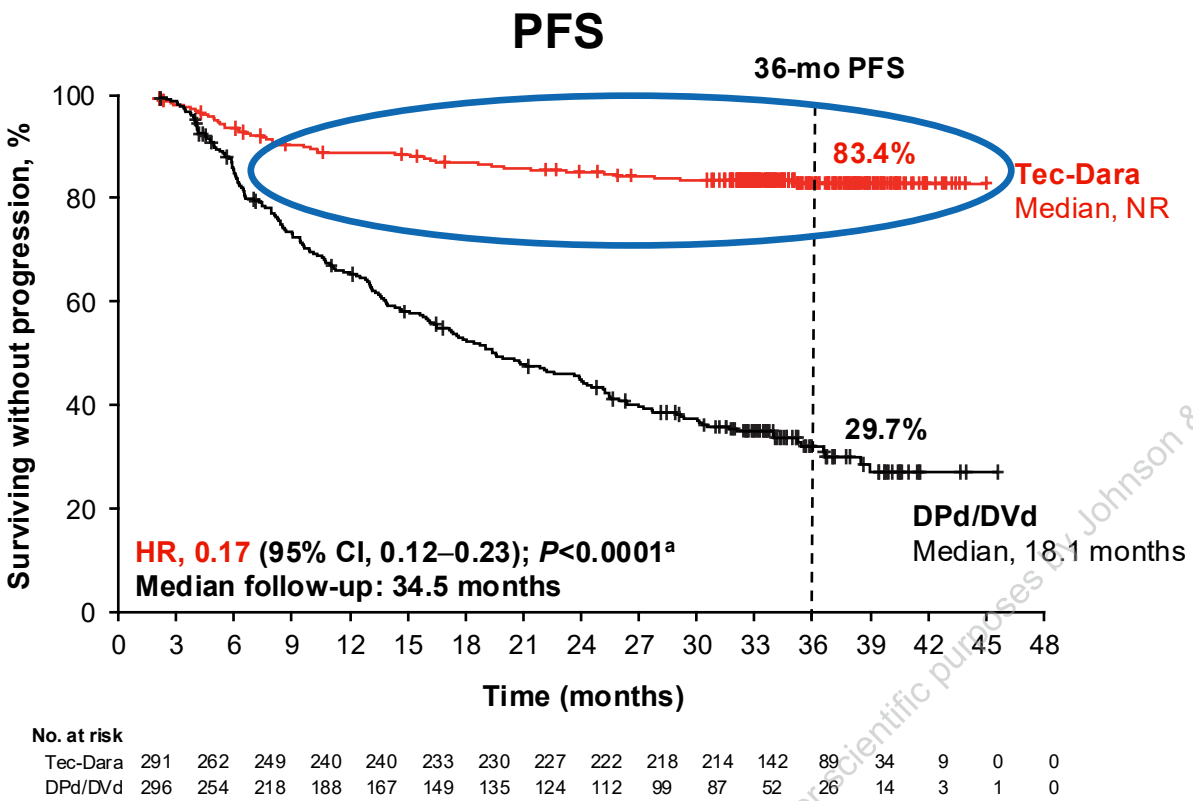
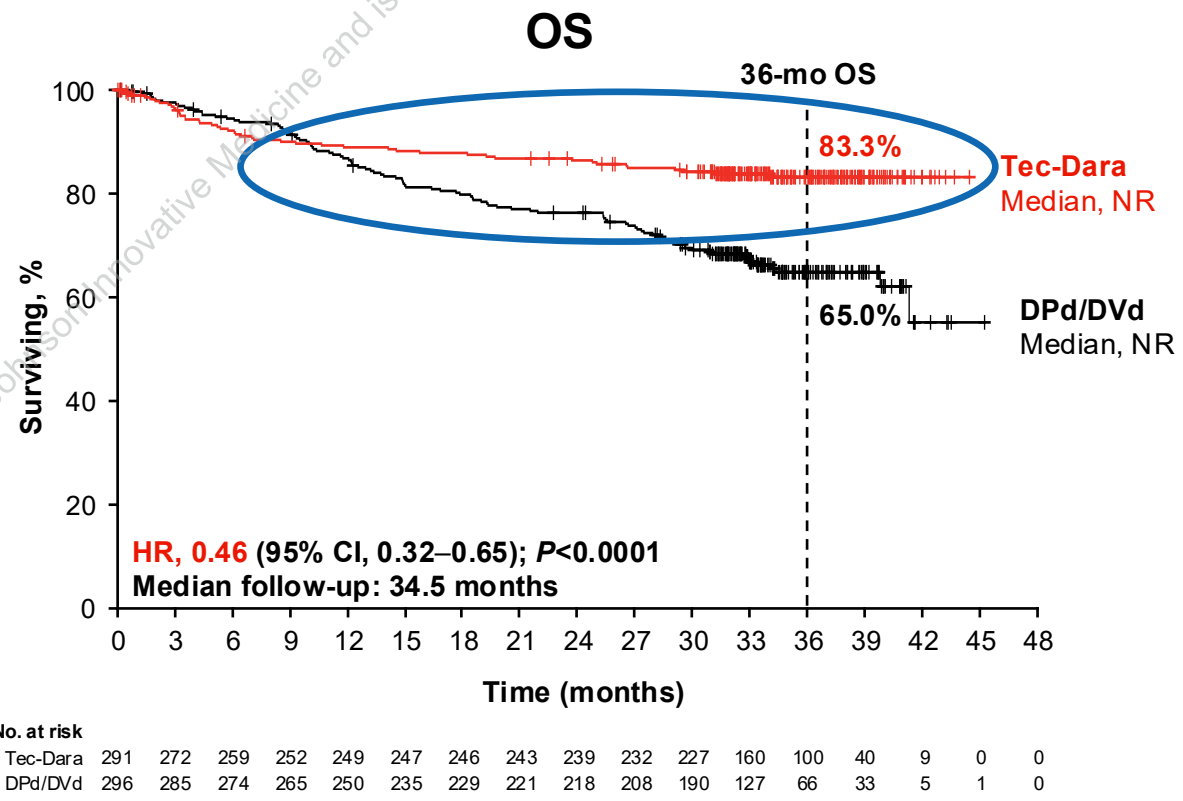
MajesTEC-3 PFS and OS[1,2]



No. at risk

Tec-Dara	291	262	249	240	240	233	230	227	222	218	214	142	89	34	9	0	0
DPd/DVd	296	254	218	188	167	149	135	124	112	99	87	52	26	14	3	1	0



No. at risk

Tec-Dara	291	272	259	252	249	247	246	243	239	232	227	160	100	40	9	0	0
DPd/DVd	296	285	274	265	250	235	229	221	218	208	190	127	66	33	5	1	0

Tec-Dara PFS and OS curves plateau from ~6 months, suggesting a substantial proportion of patients may achieve long-term disease control and potentially a functional cure

[a]The *P* value crossed the prespecified stopping boundary for superiority for the first interim analysis (*P*=0.0139).
CI, confidence interval; NR, not reached.

1. Costa LJ, et al. *N Engl J Med.* 2026;394(8):739–752. 2. Mateos MV, et al. Presented at: 67th ASH Annual Meeting and Exposition; December 6–9, 2025; Orlando, FL. Oral LBA-6.

The Relative Survival Mixture Cure Model (MCM) Estimates the Proportion of Patients With No Excess RRMM-Related Mortality Risk

What proportion of patients may achieve long-term disease control?

- A relative survival MCM estimates the proportion of patients whose mortality risk is no greater than the general population mortality because of RRMM or treatment (**"statistical cure fraction"**)[1]

How does the MCM work?

1	2	3	4
Start with a model fit to the observed RRMM patient survival from a given trial	Account for expected survival in a similar matched population[a]	Isolate mortality risk specific to RRMM or treatment	Estimate proportion of patients with no excess mortality risk from RRMM or treatment
All-cause survival in RRMM patients	**Survival in general population**	**Relative survival**	**Statistical cure fraction**

[a]Matched by age, gender, and country.

1. Felizzi F, et al. *Pharmacoecon Open*. 2021;5(2):143-155.

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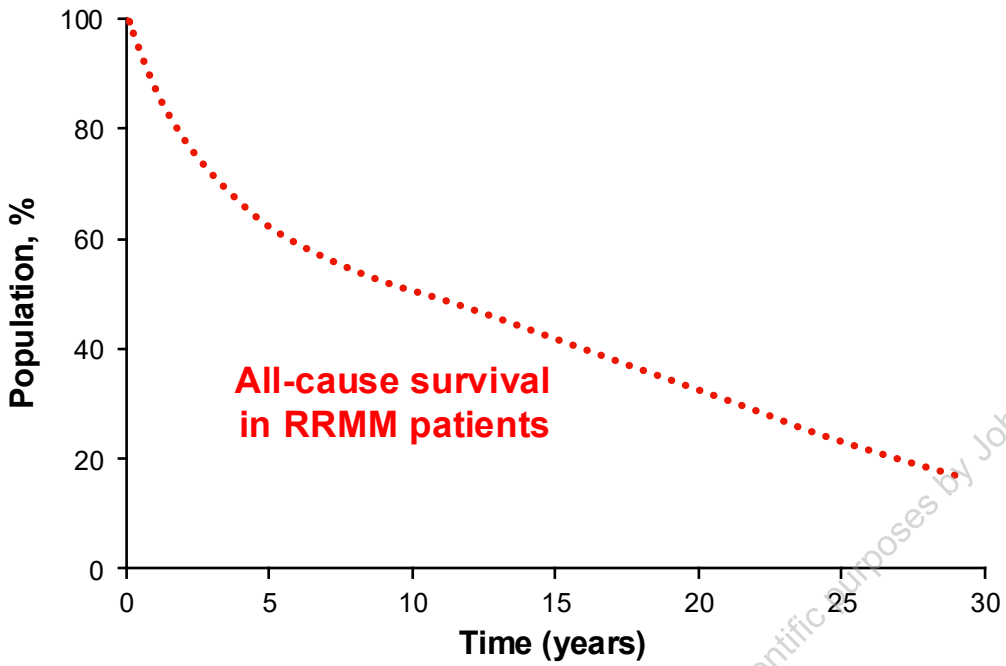
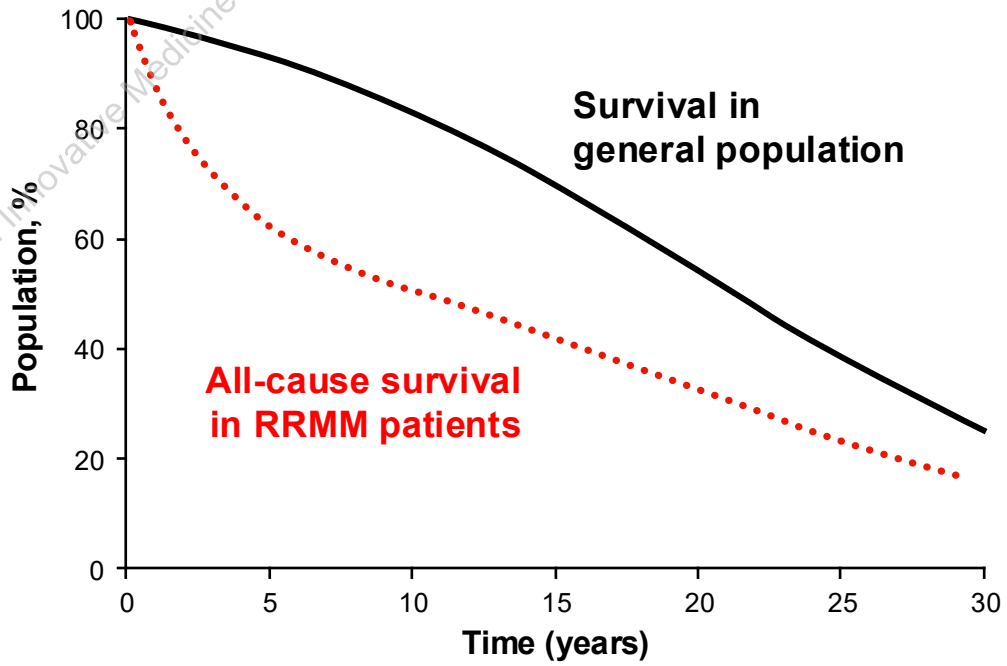
Illustrative Example: Relative Survival MCM

1



All-cause survival in RRMM patients: Model is fit to the observed RRMM patient survival data from a given trial

2



Survival in general population: Mortality risk derived from life tables, matched by age, gender, and country[a]

[a]United Nations 2023 life tables.

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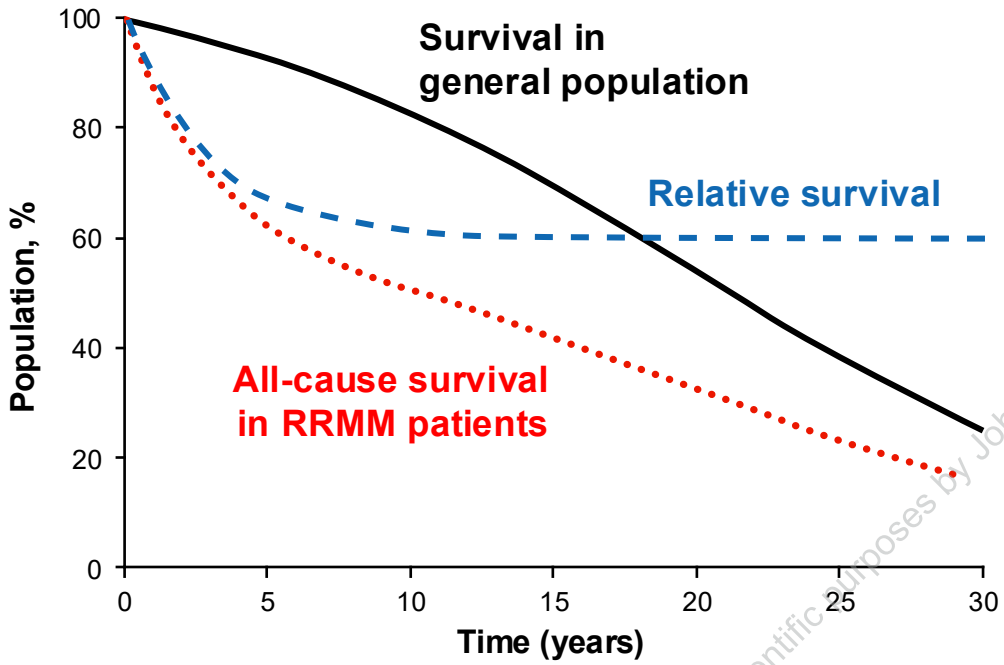
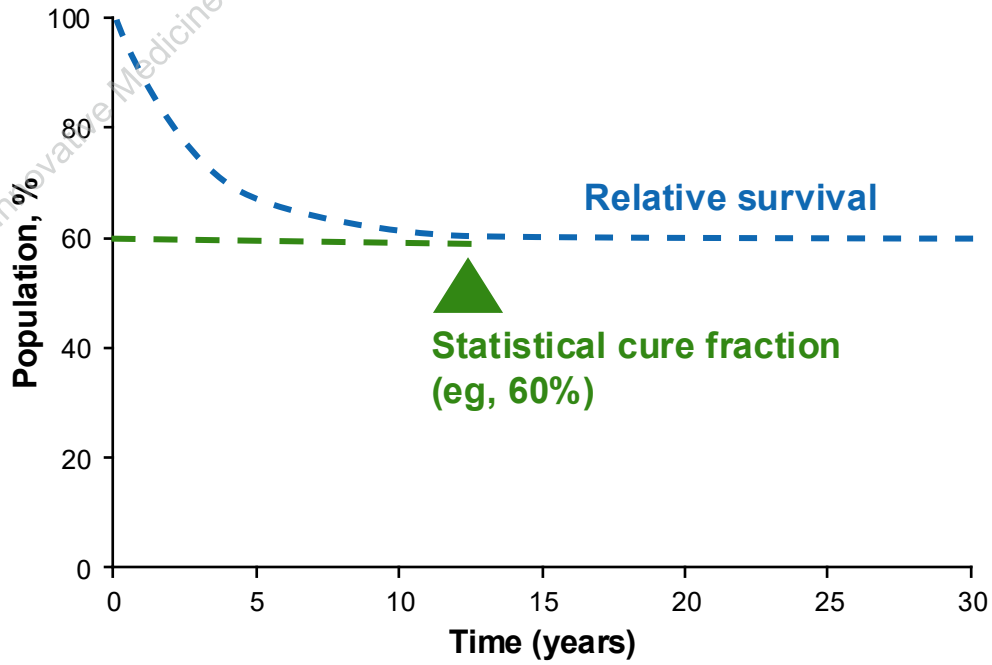
Illustrative Example: Relative Survival MCM (*cont.*)

3



Relative survival: Isolated mortality risk specific to RRMM or treatment

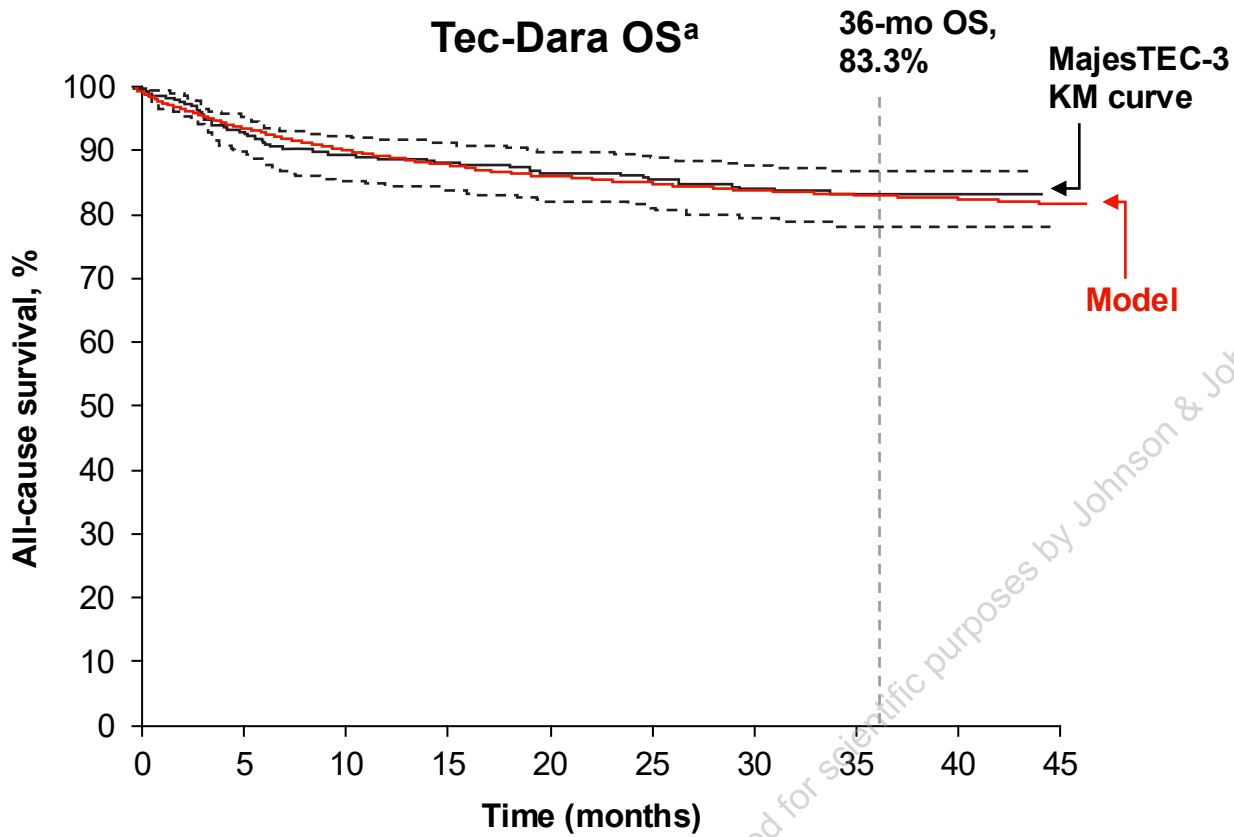
4

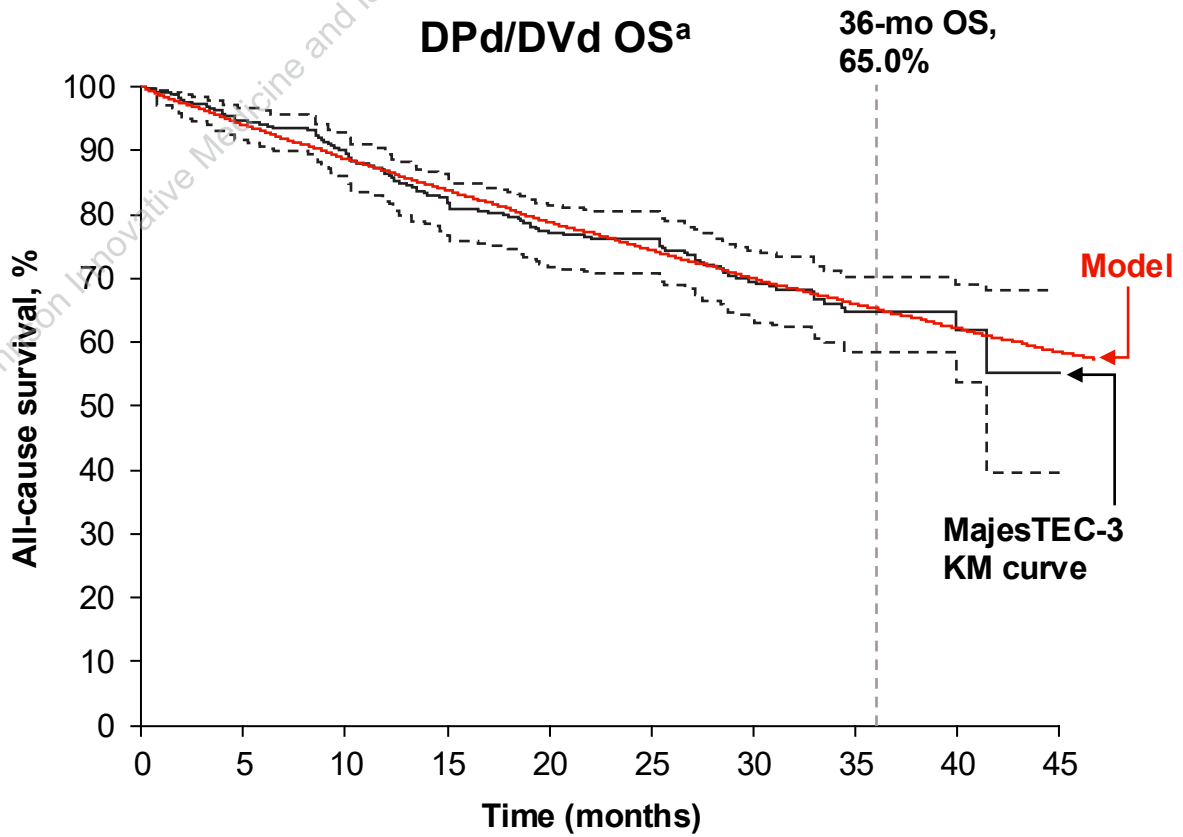


Statistical cure fraction: Proportion of patients with no excess mortality risk from RRMM or treatment[a]

[a]Statistical cure fraction is a population-level model estimate, not confirmation of cure for an individual patient.

MajesTEC-3 OS by Best-Fit Models





The OS best-fit models closely reproduce the OS observed in MajesTEC-3

[a]KM curve (black solid) and its 95% CI (black dashed) for OS in the MajesTEC-3 study.
Median follow-up: 34.5 months.
KM, Kaplan-Meier.

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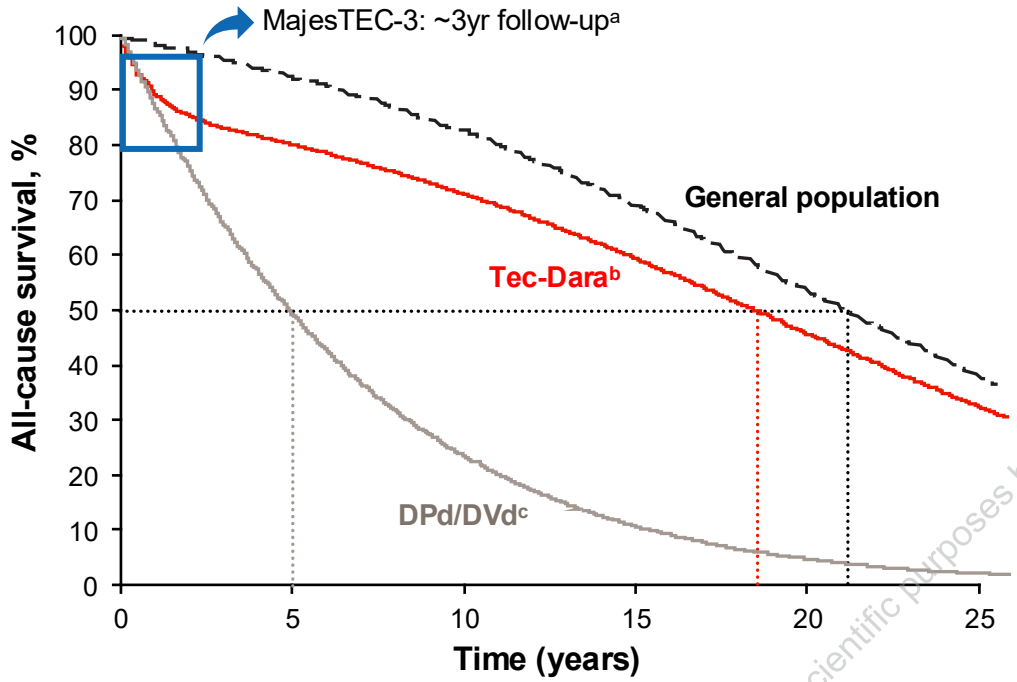
Model Estimates of Median OS for Tec-Dara

Estimated all-cause survival



Estimated median survival

The model projects substantially longer median OS with Tec-Dara, approaching the matched general-population estimate

[a]Median follow-up: 34.5 months.
[b]Determined using the best-fit relative survival MCM.
[c]Determined using the best-fit relative survival model without cure.

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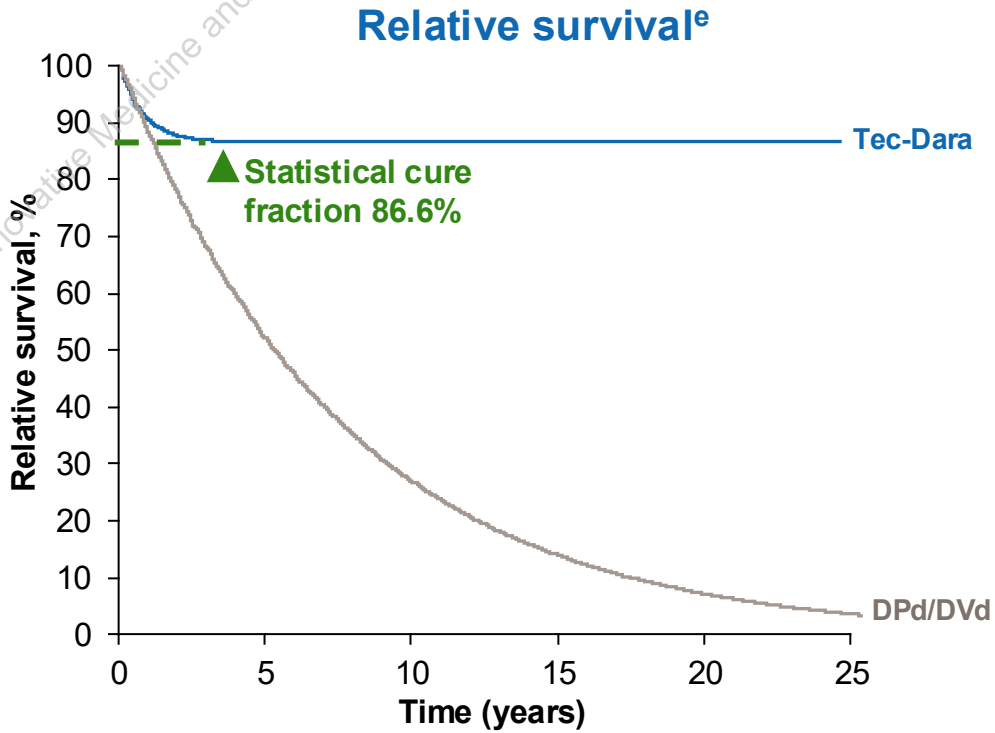
Model Estimates of Mortality Risk With Tec-Dara

- Across tested models,[a] estimated statistical cure fractions were consistently high with Tec-Dara,[b] and low with DPd/DVd

Statistical cure fraction, %	Tec-Dara	DPd/DVd
Best-fit model (95% CI)[c,d]	86.6 (81–91)	0 (0–53)
Range across tested models	84.4 to 86.8	0 to 51.3



~87% of patients treated with Tec-Dara are estimated to have no excess long-term mortality risk on top of the general population by best-fit models

[a]Tested models analyzed survival related to excess risk in the uncured fraction using 7 classical parametric models including exponential, Weibull, lognormal, loglogistic, Gompertz, gamma, and generalized gamma.
[b]Results from the Gompertz function were excluded for Tec-Dara because it resulted in a non-zero ceiling in excess mortality due to the shape parameter being negative.
[c]Best-fit models were selected according to statistical goodness of fit criteria; MCMs applied the exponential function for Tec-Dara OS and DPd/DVd OS.
[d]Profile-likelihood 95% CIs shown here; these replace the Wald CIs reported in the abstract and typically provide more accurate coverage.
[e]From best-fit model.

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Conclusions

- Tec-Dara demonstrated OS and PFS plateaus from ~6 months through 3 years in MajesTEC-3, supporting potential for long-term disease control[1]
- Best-fit MCM models estimated that the fraction of patients with no excess mortality risk on top of the general population was 86.6% for Tec-Dara versus 0% for DPd/DVd[a]
- Tec-Dara estimated median OS was comparable to the general population and ~4× longer versus DPd/DVd (18.5 vs 4.9 years)
- Modeling suggests a substantial proportion of Tec-Dara patients may achieve long-term disease control consistent with emerging concepts of functional cure in cancer
- MajesTEC-3 is ongoing; model-based estimations will be supported with continued follow-up

Tec-Dara may redefine long-term survival expectations for a substantial proportion of patients with RRMM based on early modeling results

[a]Tec-Dara 95% CI: 81%–91%; DPd/DVd 95% CI: 0%–53%.

1. Costa LJ, et al. *N Engl J Med*. 2026;394(8):739–752.

Acknowledgments

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