Overall Survival, Progression, and Non-Relapse Mortality With Teclistamab Plus Daratumumab (Tec-Dara) vs Dara-Based Triplets in Relapsed/Refractory Multiple Myeloma (RRMM): MajesTEC-3 Post Hoc Analysis

Luciano J Costa,[1] Nizar J Bahlis,[2] Aurore Perrot,[3] Ajay K Nooka,[4] Jin Lu,[5] Charlotte Pawlyn,[6,7] Roberto Mina,[4,8] Meletios A Dimopoulos,[9,10] Elena Zamagni,[11,12] Surbhi Sidana,[13] Paula Rodriguez-Otero,[14] Robin Carson,[15] Weili Sun,[16] Kristen Lantz,[15] Anne Seifert,[17] Maria Rubin,[18] Huiling Pei,[19] Maria Victoria Mateos[20]

[1]Division of Hematology and Oncology, University of Alabama at Birmingham, Birmingham, AL, USA; [2]Arnie Charbonneau Cancer Institute, University of Calgary, Calgary, AB, Canada; [3]Universite de Toulouse, Centre Hospitalier Universitaire, Service d'Hematologie, Institut Universitaire du Cancer de Toulouse Oncopole, Cancer Research Center of Toulouse, Toulouse, France; [4]Emory University, Winship Cancer Institute, Atlanta, GA, USA; [5]Peking University People's Hospital, Peking University Institute of Hematology, National Clinical Research Center for Hematologic Disease, Beijing, China; [6]Royal Marsden NHS Foundation Trust, London, UK; [7]Institute of Cancer Research, London, UK; [8]Division of Hematology, Department of Molecular Biotechnology and Health Sciences, AOU Città della Salute e della Scienza di Torino, University of Turin, Turin, Italy; [9]Department of Clinical Therapeutics, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece; [10]Department of Medicine, Korea University, Seoul, South Korea; [11]IRCCS Azienda Ospedaliero Universitaria di Bologna, Istituto di Ematologia Seràgnoli, Bologna, Italy; [12]Dipartimento di Scienze Mediche e Chirurgiche, Università di Bologna, Bologna, Italy; [13]Stanford University School of Medicine, Palo Alto, CA, USA; [14]Cancer Center Clínica Universidad de Navarra, Pamplona, Spain; [15]Johnson & Johnson, Spring House, PA, USA; [16]Johnson & Johnson, Los Angeles, CA, USA; [17]Johnson & Johnson, High Wycombe, UK; [18]Johnson & Johnson, Raritan, NJ, USA; [19]Johnson & Johnson, Titusville, NJ, USA; [20]Hospital Universitario de Salamanca, Instituto de Investigación Biomédica de Salamanca, Instituto de Biología Molecular y Celular del Cáncer (Universidad de Salamanca–Consejo Superior de Investigaciones Científicas), Centro de Investigación Biomédica en Red de Cáncer, Salamanca, Spain.

Presented by LJ Costa at the 23rd International Myeloma Society (IMS) Annual Meeting and Exposition; September 23–26, 2026; Glasgow, Scotland

Disclosure Statement: Luciano J Costa, MD

- Serves as an advisory board member for AbbVie, Bristol Myers Squibb, Caribou, Genentech, Johnson & Johnson, Pfizer, and Sanofi
- Received honoraria from AbbVie, Adaptive Biotechnologies, Amgen, BeOne, Bristol Myers Squibb, Caribou, Johnson & Johnson, Pfizer, and Sanofi
- Works in an institution that has received research support from AbbVie, Bristol Myers Squibb, Caribou, Genentech, Johnson & Johnson, and Pfizer

Presented by LJ Costa at the 23rd International Myeloma Society (IMS) Annual Meeting and Exposition; September 23–26, 2026; Glasgow, Scotland

Background

- RRMM is characterized by successive relapses and progressive immune dysfunction,[1,2] with disease progression representing the leading cause of mortality in this setting[3]
- Tec-Dara significantly improved PFS and OS versus DPd/DVd in patients with RRMM and 1–3 prior LOTs in the phase 3 MajesTEC-3 study[4,5]
- With Tec-Dara, a PFS plateau emerged around 6 months and was sustained through 3 years of follow-up; progression events were rare
  - With rare progressions, Tec-Dara patients had longer exposure and more time at risk for non-relapse mortality (NRM)
- As patients live longer with Tec-Dara, understanding the contribution of NRM versus disease progression to mortality is increasingly important

We present a post hoc competing-risk analysis evaluating the contribution of disease progression and NRM to the observed OS in MajesTEC-3

DPd/DVd, daratumumab with dexamethasone and pomalidomide or bortezomib; LOT, line of therapy; OS, overall survival; PFS, progression-free survival; RRMM, relapsed/refractory multiple myeloma; Tec-Dara, teclistamab with daratumumab.

1. Kastritis E, et al. *Blood*. 2022;139(19):2904–2917. 2. Holthof LC, et al. *Cancers (Basel)*. 2020;12(4):988. 3. Tan CR, et al. *Blood Adv*. 2026;10(9):2937–2946. 4. Costa LJ, et al. *N Engl J Med*. 2026;394(8):739–752. 5. Mateos MV, et al. Presented at: 67th ASH Annual Meeting and Exposition; December 6–9, 2025; Orlando, FL. Oral LBA-6.

Presented by LJ Costa at the 23rd International Myeloma Society (IMS) Annual Meeting and Exposition; September 23–26, 2026; Glasgow, Scotland

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

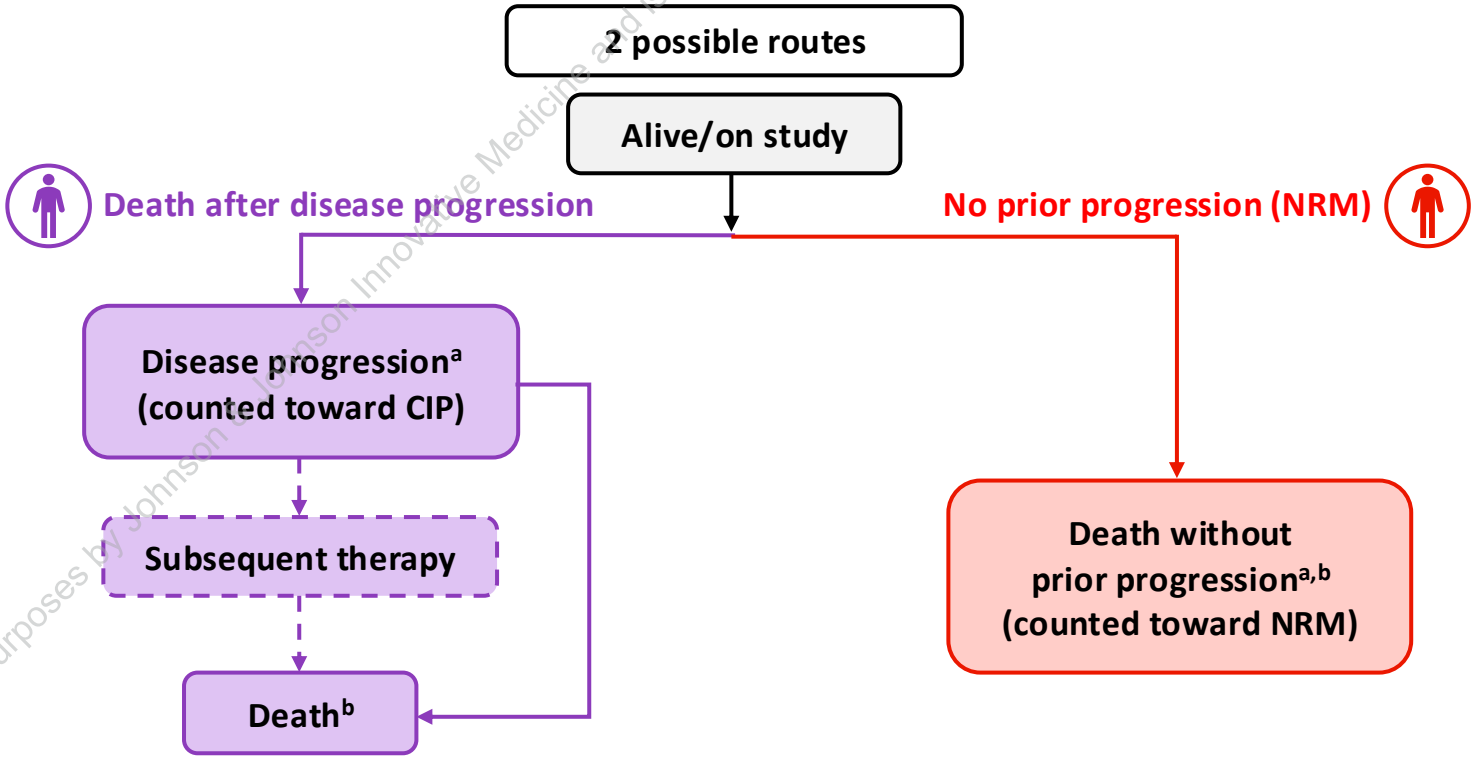
Fully immunotherapy-based Tec-Dara regimen with a steroid-sparing schedule after Cycle 1 Day 8[e] and monthly dosing after 6 cycles

[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.

Presented by LJ Costa at the 23rd International Myeloma Society (IMS) Annual Meeting and Exposition; September 23–26, 2026; Glasgow, Scotland

Why Competing-Risk Analyses Matter in MajesTEC-3

- **NRM** and **disease progression** are **mutually exclusive** components of PFS
  - NRM: Death without prior progression, irrespective of cause
- NRM and disease progression are also "competing events," requiring separation
  - A patient who experiences 1 event can no longer experience the other event
- Competing-risk analyses (cumulative incidence of progression [CIP] and NRM) are needed to accurately assess what is driving patient survival in MajesTEC-3



Competing-risk analyses help to separate "deaths after progression" from "deaths without prior progression"

[a]PFS event (defined as the time from the date of randomization to the date of first documented disease progression or death due to any cause, whichever comes first). PFS combines progression and death into a single endpoint but cannot distinguish between them.
[b]OS event (defined as the time from the date of randomization to the date of the patient's death due to any cause). OS captures all deaths but cannot distinguish deaths after progression from deaths without prior progression (NRM).

Presented by LJ Costa at the 23rd International Myeloma Society (IMS) Annual Meeting and Exposition; September 23–26, 2026; Glasgow, Scotland

Statistical Analysis

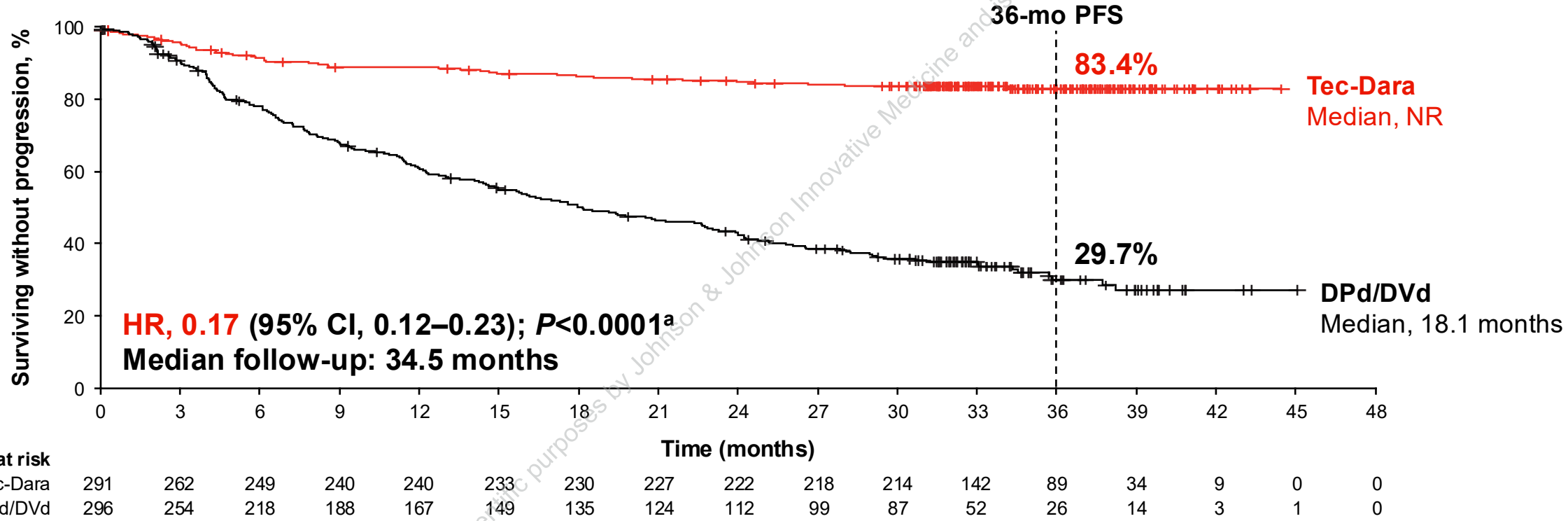
Primary analysis	Competing-risk analyses	Expanded analyses
PFS[a] and OS	CIP and NRM	OS
HR with 95% CIs from stratified Cox regression model **Stratified log-rank test**	**Cumulative incidence of progression (CIP)** Progression with NRM as competing risk **Non-relapse mortality (NRM)** Death with progression as competing risk **Fine-Gray sub-distribution HRs (sHR) and Gray's test**	**Restricted mean survival time** Applied when proportional hazards were not met, per SAP **Piecewise analysis** Time-stratified Cox analysis (≤10 months vs >10 months)

Complementary competing-risk analyses allow for a more accurate interpretation of long-term survival

[a]Per IRC.
CI, confidence interval; HR, hazard ratio; SAP, statistical analysis plan.

Presented by LJ Costa at the 23rd International Myeloma Society (IMS) Annual Meeting and Exposition; September 23–26, 2026; Glasgow, Scotland

MajesTEC-3: PFS (Primary Endpoint)[1,2]



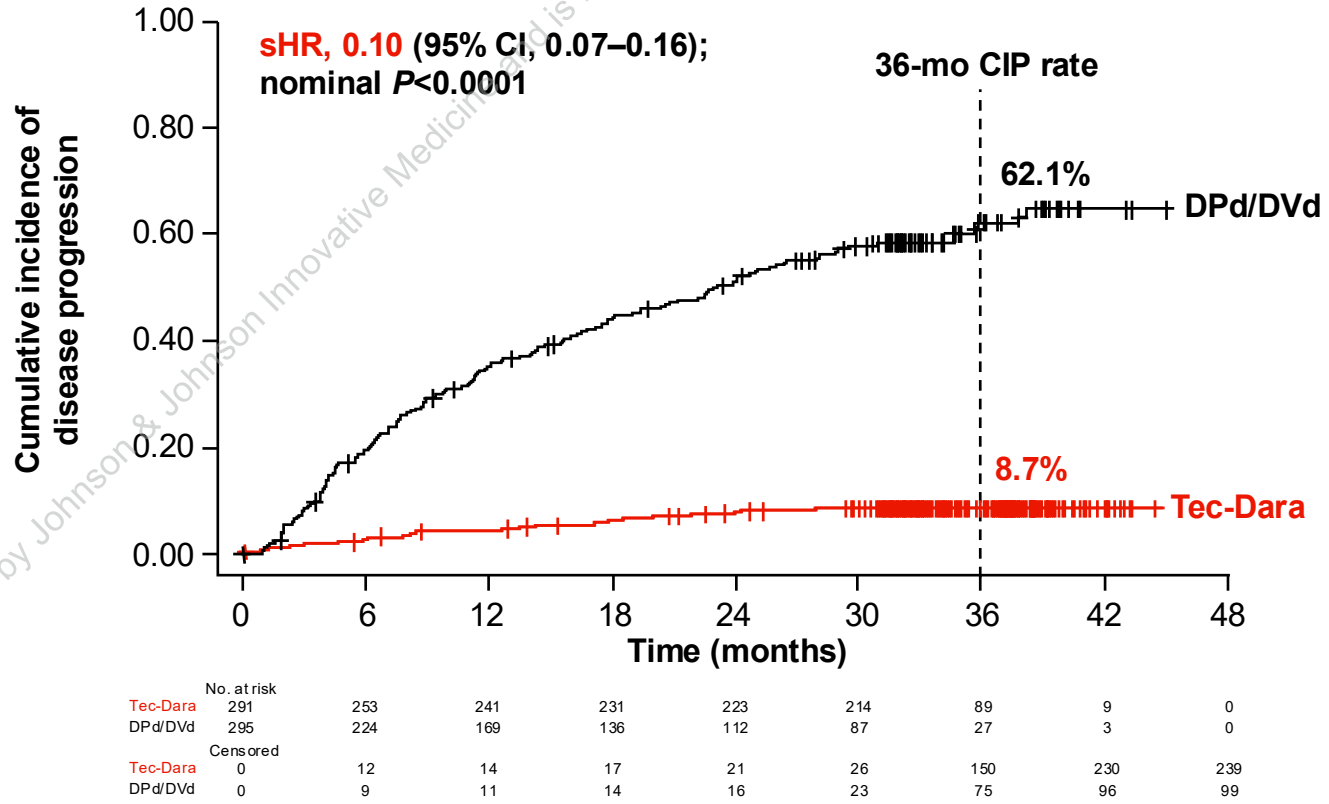
Tec-Dara led to a PFS plateau around 6 months, with >90% of patients at 6 months estimated to sustain such a benefit at 3 years

[a]The *P* value crossed the prespecified stopping boundary for superiority for the first interim analysis (*P*=0.0139).
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.
From: *N Engl J Med*. Costa LJ, et al. Teclistamab plus Daratumumab in Relapsed or Refractory Multiple Myeloma. 394(8):739–752. Copyright © 2026 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

MajesTEC-3: Cumulative Incidence of Progression

With NRM as a competing risk,[a] CIP was substantially lower with Tec-Dara

- Progression:
  - Tec-Dara: 24/291; 18 with subsequent death
  - DPd/DVd: 171/296; 72 with subsequent death



Tec-Dara substantially reduced CIP versus DPd/DVd; progression is uncommon with 90% reduction[b] versus DPd/DVd

[a]Rate of disease progression when accounting for the fact that patients who die prior to progression cannot go on to experience disease progression.
[b]Based on sHR.

Presented by LJ Costa at the 23rd International Myeloma Society (IMS) Annual Meeting and Exposition; September 23–26, 2026; Glasgow, Scotland

MajesTEC-3: Causes of Non-Relapse Mortality

NRM was primarily due to AEs in both treatment groups

- AEs were primarily infections and infestations, occurring most commonly within 6 months of treatment initiation
  - Tec-Dara: 12; 11 ≤6 months[a]
  - DPd/DVd: 4; 2 ≤6 months
- Infection prophylaxis was recommended per protocol,[1] with IgRT and antimicrobial use reinforced as experience and guidelines evolved
- Supportive RWE and IMWG guidelines recommend IgRT prophylaxis for the reduction of high-grade infections with BCMA-targeting BsAbs[2–5]

NRM, n	Tec-Dara (n=28)	DPd/DVd (n=26)
AE-related[b]	19	16
Infections and infestations	12	4
General disorders and administration-site conditions	2	4
Respiratory, thoracic, and mediastinal disorders	2	3
Nervous system disorders	1	2
Hepatobiliary disorders	1	1
Cardiac disorders	1	0
Immune system disorders	1	0
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	0	1
Gastrointestinal disorders	0	1
PD without IRC-determined progression	2	8
Other	7	2

Infection-related NRM may be reduced through diligent use of established IgRT and antimicrobial prophylaxis protocols

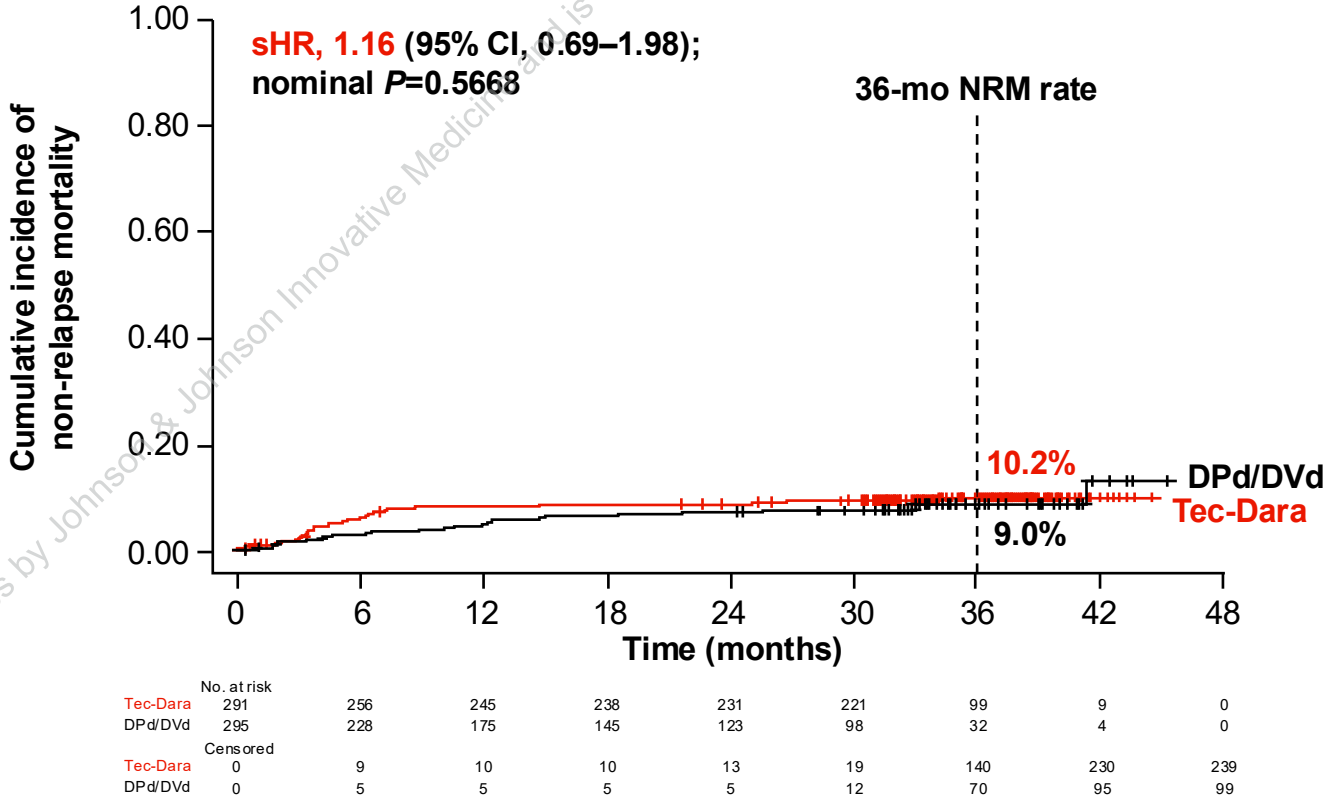
[a]Only 3 out of 11 Tec-Dara patients received ≥1 dose of IgRT.
[b]Listed per System Organ Class. Of note, patients may have been listed as having more than 1 cause of death, which may have been due to 1 or more system organ class.
AE, adverse event; BsAb, bispecific antibody; IgRT, immunoglobulin replacement therapy; PD, progressive disease; RWE, real-world evidence.
1. Costa LJ, et al. *N Engl J Med.* 2026;394(8):739–752. 2. Smits F, et al. *Blood Cancer J.* 2026;16(1):26. 3. Lancman G, et al. *Blood Cancer Discov.* 2023;4(6):440–451. 4. Cheruvalath H, et al. *Blood*. 2024;144(Supp 1):256. 5. Rodriguez-Otero P, et al. *Lancet Oncol.* 2024;25(5):e205–e216.

Presented by LJ Costa at the 23rd International Myeloma Society (IMS) Annual Meeting and Exposition; September 23–26, 2026; Glasgow, Scotland

MajesTEC-3: Non-Relapse Mortality

With CIP as a competing risk,[a] NRM was similar between treatments

- Deaths without progression
  - Tec-Dara: 28/291; 19 due to AEs[b]
  - DPd/DVd: 26/296; 16 due to AEs[b]
- NRM was similar between groups regardless of early AE-related deaths

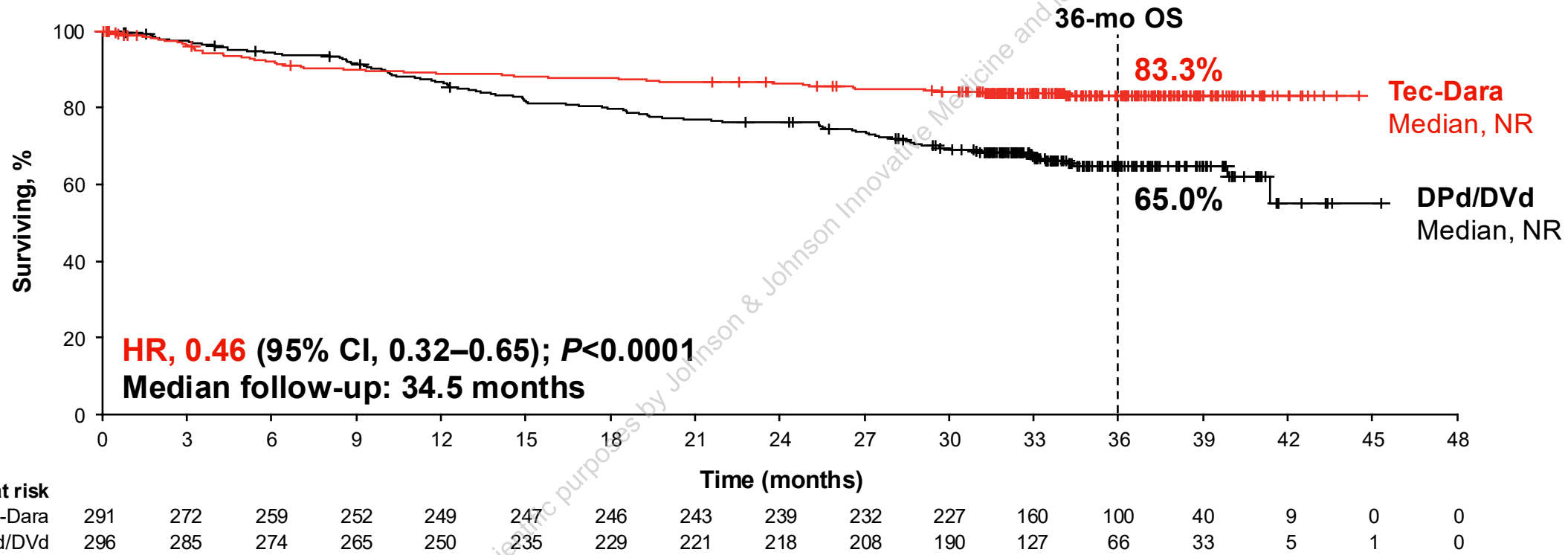


No meaningful difference between Tec-Dara and DPd/DVd in NRM

[a]Rate of dying from non-relapse causes when taking into consideration that patients who experience disease progression first are no longer "at risk" of NRM.
[b]In the Tec-Dara group, 12 out of 19 AEs were infections; in the DPd/DVd group, 4 out of 16 were infections. Other NRM deaths included deaths attributed to progressive disease without IRC-determined progression (Tec-Dara, n=2; DPd/DVd, n=8) and "Other" (Tec-Dara, n=7; DPd/DVd, n=2).

Presented by LJ Costa at the 23rd International Myeloma Society (IMS) Annual Meeting and Exposition; September 23–26, 2026; Glasgow, Scotland

MajesTEC-3: OS[1,2]



Tec-Dara significantly improved OS versus DPd/DVd, with an estimated 83% of patients alive at 3 years

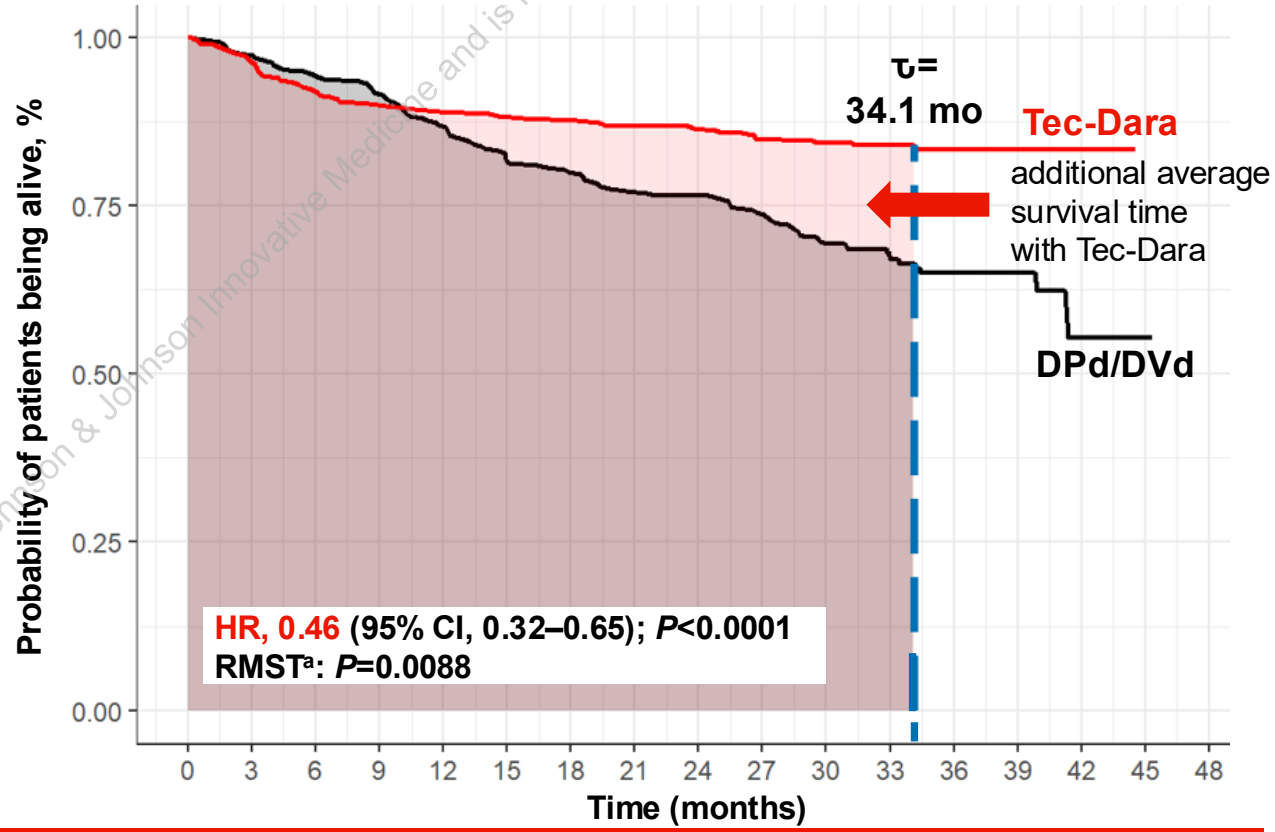
1. Costa LJ, et al. *N Engl J Med*. 2026;394(8):739–752. 2. Mateos MV, et al. Presented at: 67th ASH Annual Meeting and Exposition; December 6–9, 2025; Orlando, FL. Oral LBA-6.
From: *N Engl J Med*. Costa LJ, et al. Teclistamab plus Daratumumab in Relapsed or Refractory Multiple Myeloma. 394(8):739–752.

MajesTEC-3: Restricted Mean Survival Time (RMST) OS[1,2]

Pre-planned RMST analysis supported an OS benefit with Tec-Dara versus DPd/DVd

- Tec-Dara increased average survival time through 34.1 months post-randomization (nominal *P*=0.0088)[a]

- RMST is an alternative, clinically interpretable measure of treatment effect, particularly when proportional hazards are not met
- Calculated as area under the KM curve up to a prespecified time point (τ)

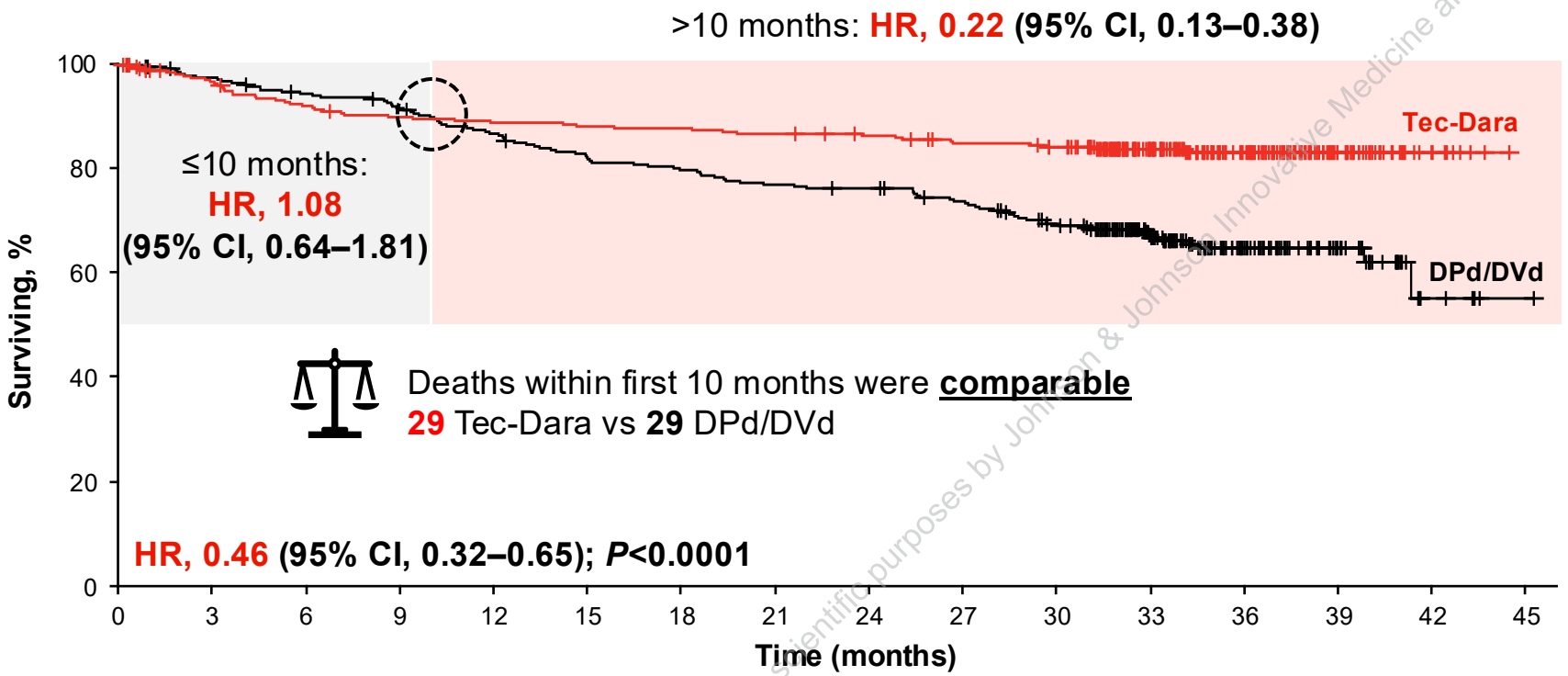


RMST demonstrated consistent OS benefit with Tec-Dara versus DPd/DVd[1,2]

[a]34.1 months represents the smaller value of the longest OS event time observed from either arm at the time of clinical cut-off (Tec-Dara, 34.1 months; DPd/DVd, 41.4 months). The estimated average survival time through 34.1 months was 30.3 months for Tec-Dara and 28.2 months for DPd/DVd; RMST difference was 2.15 months, thus favoring Tec-Dara.
KM, Kaplan-Meier.

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.

MajesTEC-3: Time-Stratified Cox Analysis of OS



Cause of death within first 10 months (curve cross):

- Tec-Dara: AEs (n=18),[a] PD (n=5), "Other" (n=6)[b]
- DPd/DVd: AEs (n=8), PD (n=20), "Other" (n=1)[c]

Tec-Dara substantially reduced the risk of death by 78% versus DPd/DVd after 10 months

[a]Of 18 AE deaths, 12 were infections.
[b]3 patients died due to unknown reasons; 3 occurred outside the TEAE reporting window (n=1, unrelated to study treatment [COVID-19 occurring >30 days after last dose]; n=1, death occurred after initiation of subsequent therapy [septic shock]; n=1, death following diagnosis of secondary amyloidosis).
[c]1 patient died due to unknown reasons.
TEAE, treatment-emergent adverse event.

Presented by LJ Costa at the 23rd International Myeloma Society (IMS) Annual Meeting and Exposition; September 23–26, 2026; Glasgow, Scotland

Conclusions

- Tec-Dara significantly improved PFS (HR, 0.17) and OS (HR, 0.46) over DPd/DVd in patients with RRMM and 1–3 prior LOTs,[1,2] with a sustained plateau in survival curves
- With Tec-Dara, progressions became uncommon after 6 months, with an unparalleled reduction in disease progression (sHR, 0.10), which is the leading cause of mortality in RRMM[3]
- There was no meaningful difference in NRM between treatments over time; infection-related NRM occurred with both treatments
  - Infections can be better managed now with guideline-based IgRT and antimicrobial prophylaxis[4]
- OS benefit with Tec-Dara versus DPd/DVd was driven by durable disease control without an increase in NRM
  - Superior OS with Tec-Dara was supported by RMST[1] and time-stratified Cox analysis (>10 months)

Tec-Dara's OS benefit is driven by profound suppression of disease progression, while NRM remains comparable over time

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. 3. Tan CR, et al. *Blood Adv.* 2026;10(9):2937–2946.
4. Rodriguez-Otero P, et al. *Lancet Oncol.* 2024;25(5):e205–e216.

Presented by LJ Costa at the 23rd International Myeloma Society (IMS) Annual Meeting and Exposition; September 23–26, 2026; Glasgow, Scotland

Acknowledgments

- The patients who participated in the MajesTEC-3 study and their families and caregivers
- The physicians, nurses, and staff members at each site
- The members of the Study Safety Committee
- Caren Minadeo and Arpan Patel, who assisted with data management and programming, respectively, of the primary MajesTEC-3 trial data
- Additional members who were involved in data collection and analysis
- This study was sponsored by Johnson & Johnson

Medical writing and editorial support were provided by Holly Clarke, PhD, CMPP™, and Bethany Reinecke, PhD, CMPP™ of Lumanity Communications Inc., and funded by Johnson & Johnson.

Presented by LJ Costa at the 23rd International Myeloma Society (IMS) Annual Meeting and Exposition; September 23–26, 2026; Glasgow, Scotland

https://www.congresshub.com/Oncology/IMS2026/Teclistamab/Costa-Overall

The QR code is intended to provide scientific information for individual reference, and the information should not be altered or reproduced in any way.