

HMP Education



Oncology Learning Network

OPTIMIZING OUTCOMES IN RELAPSED/REFRACTORY MULTIPLE MYELOMA

Practical Strategies for Applying
Guidelines, Novel Therapies, and
Sequencing in Clinical Practice

Supported by an educational grant from Johnson & Johnson.

Faculty

Richa Parikh, MD

Assistant Professor

Department of Hematology and Medical Oncology

Emory University School of Medicine

Samantha Shenoy, MS, MSN, ACNP-BC

Nurse Practitioner

UCSF Medical Center

Faculty Disclosures

- **Richa Parikh, MD:** Consultant for Regeneron, Sanofi
- **Samantha Shenoy, MS, MSN, ACNP-BC:** Advisor for Johnson & Johnson

Disclosures

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Learning Objectives

- Assess current evidence-based clinical practice guidelines to characterize disease burden, standard-of-care treatment options, and sequencing considerations in R/R MM
- Evaluate recent clinical trial and real-world evidence supporting the use of novel and emerging therapies in the management of R/R MM
- Apply patient-centered, interdisciplinary care strategies to address treatment resistance, manage AEs and infection risk, and optimize outcomes for patients with R/R MM

R/R = relapsed/refractory; MM = multiple myeloma; AE = adverse event.

Program Information

- This program is provided by HMP Education, an HMP Global Company
- Supported by an educational grant from Johnson & Johnson

Polling

- Participate in polling at the beginning and end of the session to be entered to win a \$100 gift card!
- Scan this QR code to see the answer choices and submit your response



The winner will be announced at the conclusion of the Q&A. Winner must be present to claim their prize.

Introduction: Disease Burden and Unmet Needs

Richa Parikh, MD

Multiple Myeloma

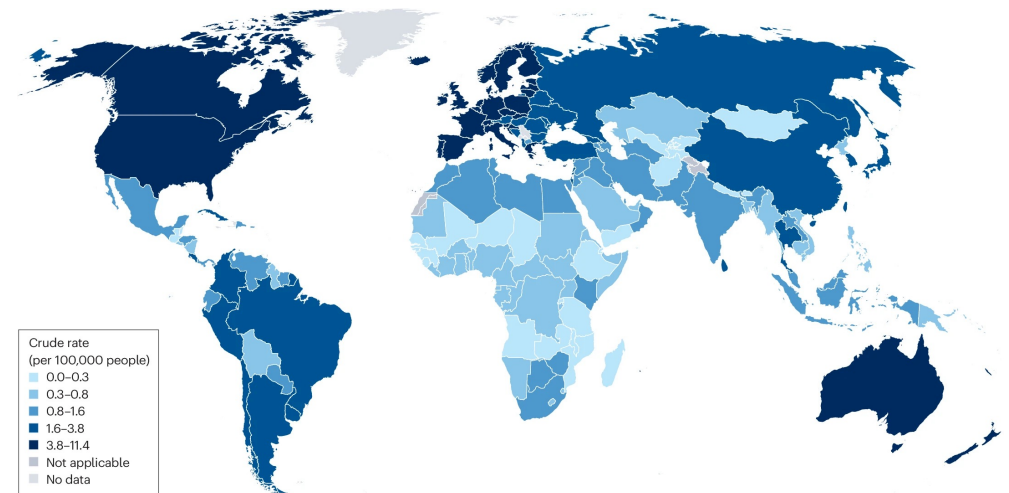
Epidemiology: Global Disease Burden

- Multiple myeloma (MM) is the **second most common hematologic malignancy** (~10% of blood cancers)
- The **absolute burden is large and growing** worldwide, driven by aging and population growth
- The **age-standardized burden is declining** in high-income countries such as the US, reflecting therapeutic advances
- MM remains **incurable**, with inevitable relapse and significant early mortality

Multiple Myeloma

Epidemiology: Global Disease Burden

Metric	GLOBOCAN 2022	GBD 2021
New cases	~188,000	~149,000
Deaths	~121,000	~116,000
Age-standardized incidence rate	—	~1.74 per 100,000
Age-standardized mortality rate	—	~1.37 per 100,000



Incidence of multiple myeloma across the globe, with higher incidence in high-income countries

GLOBOCAN = Global Cancer Observatory; GBD = Global Burden of Disease.

Mafrà A, et al. *J Natl Cancer Inst.* 2025;117(5):907-914. Qu F, et al. *Br J Haematol.* 2026;208(5):1641-1649. Malard F, et al. *Nat Rev Dis Primers.* 2024;10(1):45.

Multiple Myeloma

Epidemiology: US Disease Burden

- **~36,000 new cases** and **~10,850 deaths** annually
- Accounts for **~1.7%** of new cancers and **~1.7%** of cancer deaths
- **Incidence rising** (~23% increase in age-adjusted incidence over two decades, 1999–2020) while **mortality declines**

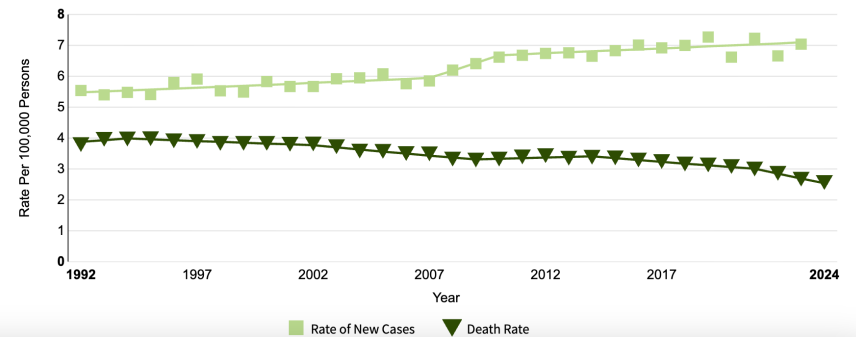
At a Glance

Estimated New Cases in 2026	36,000
% of All New Cancer Cases	1.7%
Estimated Deaths in 2026	10,850
% of All Cancer Deaths	1.7%

5-Year Relative Survival

63.7%

2016–2022



Zhu DT, et al. *Sci Rep.* 2024;14:14564. National Cancer Institute. Myeloma—Cancer Stat Facts. Surveillance, Epidemiology, and End Results Program. Accessed September 29, 2026. <https://seer.cancer.gov/statfacts/html/mulmy.html>.

Multiple Myeloma

Epidemiology: US Disease Burden

- US **5-year relative survival** rose from **~25%** (1975–1977) to **~60–62%** (2012–2021)
- Drivers: autologous transplant, proteasome inhibitors, immunomodulatory drugs, monoclonal antibodies
- Real-world median OS now **>10 years** in transplant-eligible patients; **~5 years** in those >75 years

Table 1: Long-term trends in U.S. age-adjusted mortality rates, 1975–2023 and key developments

Calendar years	Age adjusted U.S. myeloma mortality rate; APC % (95% CI)	P-value	Trend	Key developments
1975–1994	+1.43 (1.33–1.55)	<.01	Increasing	Pre-transplantation era; melphalan and corticosteroids were standard with limited efficacy and minimal survival improvement
1994–2002	–0.70 (–1.03 to –0.21)	0.02	Modestly decreasing	Introduction of ASCT following high-dose melphalan—first major advancement improving survival
2002–2009	–1.85 (–2.78 to –1.50)	<.01	Steep decline	Incorporation of IMiDs (thalidomide, lenalidomide) and PIs (bortezomib)—first therapies showing PFS and OS benefits
2009–2014	+0.52 (–0.10 to +1.69)	0.10	No significant change	Plateau phase; refinement of existing drug classes like carfilzomib and pomalidomide; no novel class approvals
2014–2021	–1.73 (–2.08 to –1.52)	<.01	Gradual decline	Approval of monoclonal antibodies (daratumumab, elotuzumab), SINES, and maintenance regimens; triplet combinations expand



OS = overall survival; APC = annual percentage change.

Kahlon N, et al. *Oncotarget*. 2026;17:216-225. National Cancer Institute. Myeloma—Cancer Stat Facts. Surveillance, Epidemiology, and End Results Program. Accessed September 29, 2026. <https://seer.cancer.gov/statfacts/html/mulmy.html>.

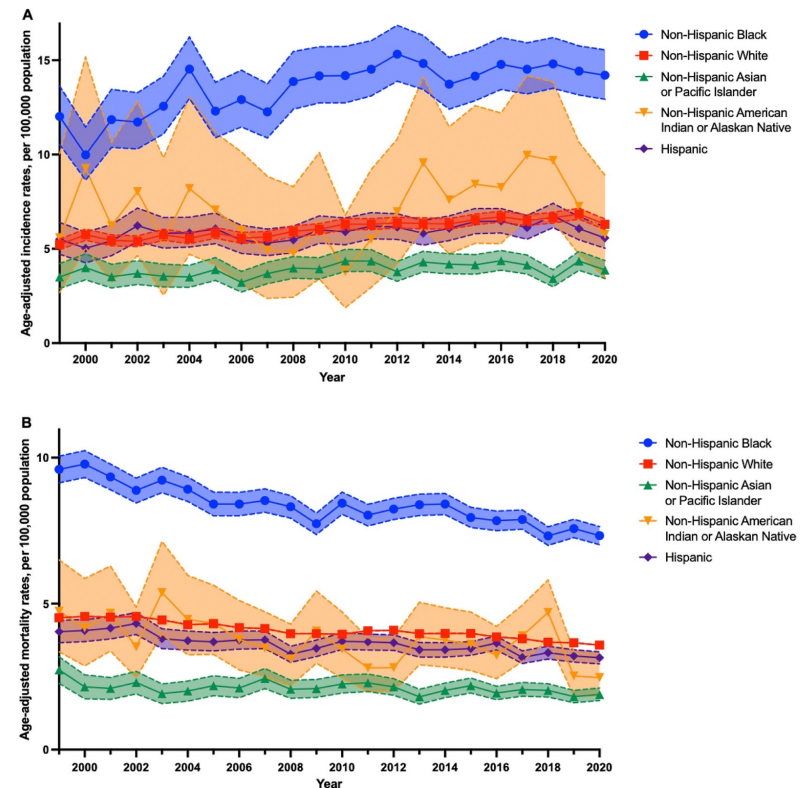
Multiple Myeloma

Epidemiology: US Disease Burden

Non-Hispanic Black individuals bear a disproportionate burden

- Highest incidence (~14 per 100,000, roughly double other groups)
- Younger age at diagnosis
- Highest mortality (~7.3 vs ~2.9 per 100,000 overall)

Asian/Pacific Islander and American Indian/Alaska Native populations have the lowest rates



Monitoring for Progression: IMWG Criteria

Any of the following

- New or ↑ in the size of existing plasmacytomas or bone lesions
- $\geq 25\%$ ↑ from the nadir of the following criteria
 - ↑ serum M-protein (w ≥ 0.5 g/dL absolute)
 - ↑ urine M-protein (w/ ≥ 200 mg/24 h absolute)
 - Difference between involved and uninvolved FLC levels* (w/absolute ↑ by > 10 mg/dL)
 - % BM PC* (w/absolute ↑ by > 10 mg/dL)
- $\geq 50\%$ increase in cPCs (≥ 200 cells/ μ L) if this is the only measure of disease

*If the above measures are unavailable.

IMWG = International Myeloma Working Group; FLC = free light chain; cPC = circulating plasma cell; FDG = fluorodeoxyglucose; M-protein = monoclonal protein; BM PC = bone marrow plasma cell; CBC = complete blood count; sCr = serum creatinine; MRD = minimal residual disease; CT = computed tomography; MRI = magnetic resonance imaging; PET = positron emission tomography.

International Myeloma Working Group. *Leukemia*. 2006;20(9):1467-1473.

Tests

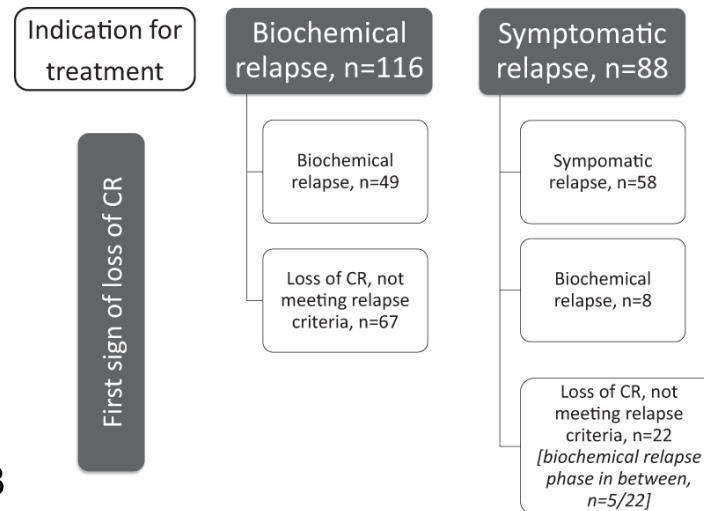
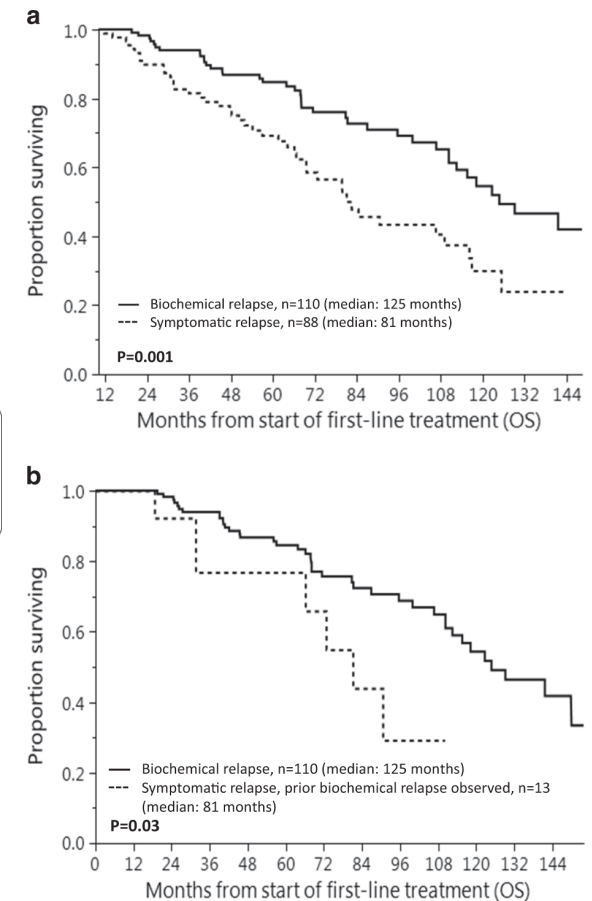
- CBC with differential; platelets
- Electrolytes; metabolic panel
- sCr & corrected serum Ca^{2+}
- M-proteins & immunoglobulins
- Serum FLC as clinically indicated
- Bone marrow aspiration & biopsy
- Assess MRD

Imaging as clinically indicated

- Consider using the same imaging modality during initial workup
- Whole body low-dose CT
- Skeletal MRI
- Whole-body FDG PET/CT

Patterns of Relapse and Refractoriness

- Single-center Mayo Clinic retrospective study of 351 NDMM patients (2004–2016) who achieved CR with first-line therapy and examined patterns of relapse from CR which were heterogeneous – biochemical relapse in 59 (25%); symptomatic relapse in 58 (24%); positive SIFE/M protein rise not meeting IMWG relapse criteria in 88 (37%) and abnormal FLC ratio in LC MM in 34 (14%) patients
- OS from start of first-line therapy was superior in patients starting second-line treatment for biochemical vs symptomatic relapse (125 vs 81 months, $p = 0.001$)

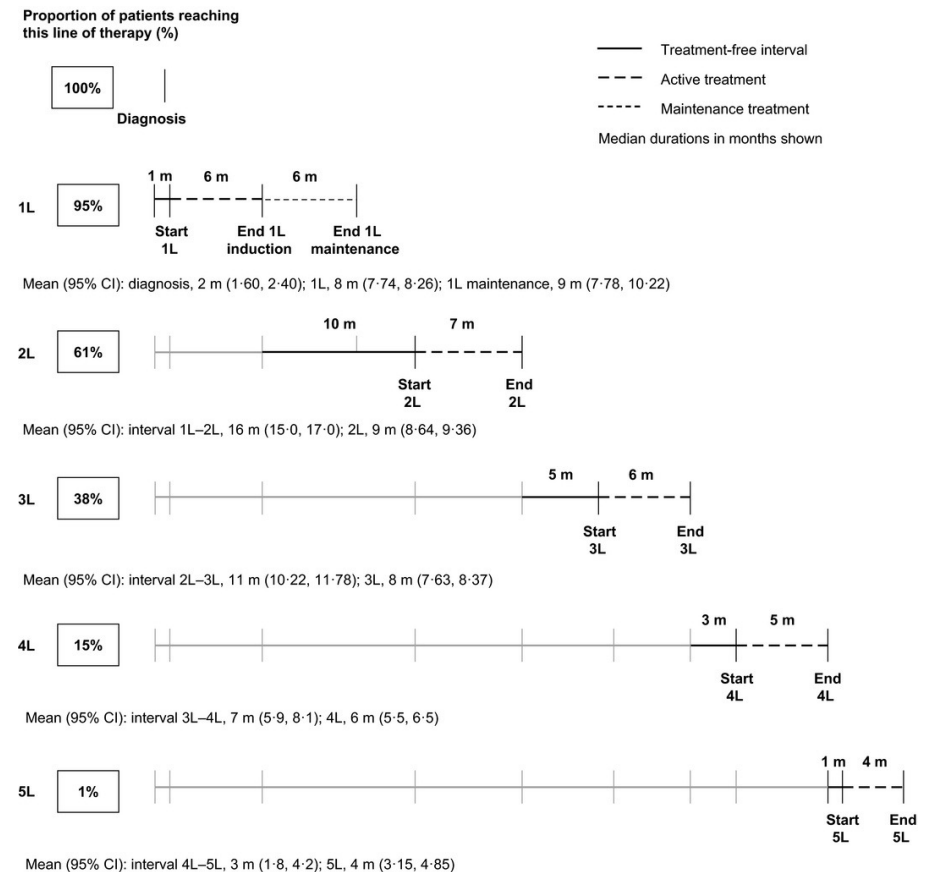


NDMM = newly diagnosed multiple myeloma; CR = complete response; SIFE = serum immunofixation electrophoresis; LC MM = light-chain multiple myeloma.
 Sidana S, et al. *Leukemia*. 2019;33(3):730-738.

Multiple Myeloma

Growing Prevalence of R/R Myeloma

- **Nearly all MM patients eventually relapse**
- RRMM accounts for large majority of the prevalent myeloma population – it is best expressed through attrition across lines of therapy and the rising proportion of patients who become class-refractory
- The Optum/attrition literature shows that only about two-thirds of diagnosed patients reach 2L, ~one-third reach 3L, and a small fraction reach 4L–5L

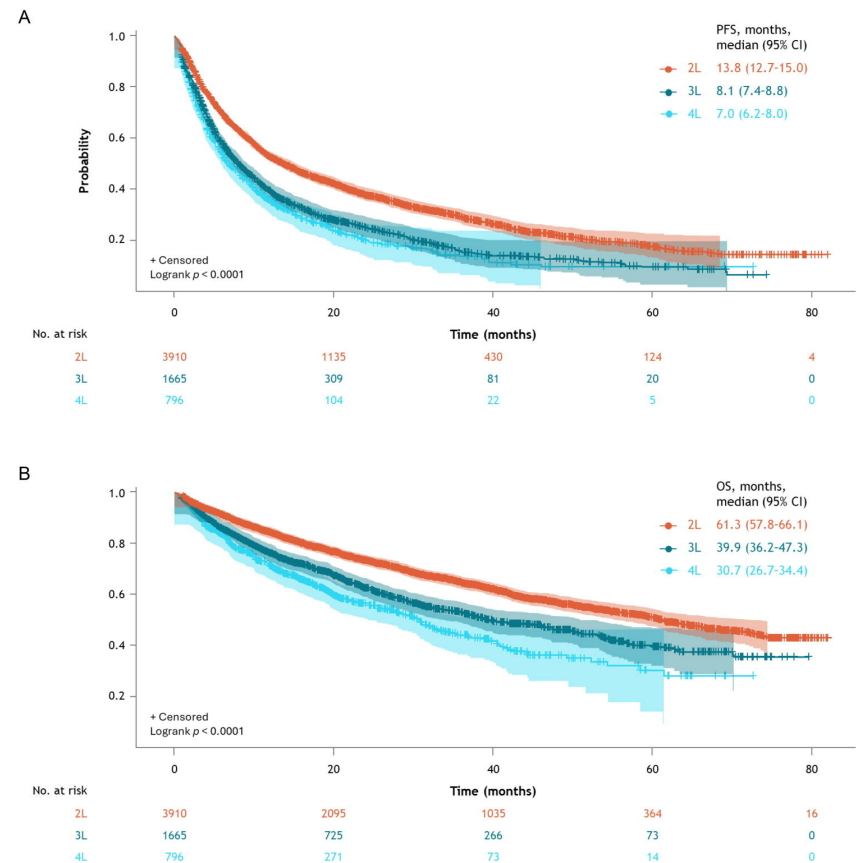


RRMM = relapsed/refractory multiple myeloma; 2L = second-line therapy; 3L = third-line therapy; 4L = fourth-line therapy; 5L = fifth-line therapy.
Yong K, et al. *Br J Haematol.* 2016;175(2):252-264.

Multiple Myeloma

Growing Prevalence of R/R Myeloma

- In the US Flatiron cohort of **3,910 patients** starting second-line (2L) treatment, **42.6% went on to 3L** and **20.4% to 4L**
- Median age at 2L was 70 years
- At present, essentially every patient who survives initial therapy will eventually develop relapsed disease. With each successive line, the disease accumulates genomic and epigenetic alterations, producing progressively greater drug refractoriness and shorter remissions



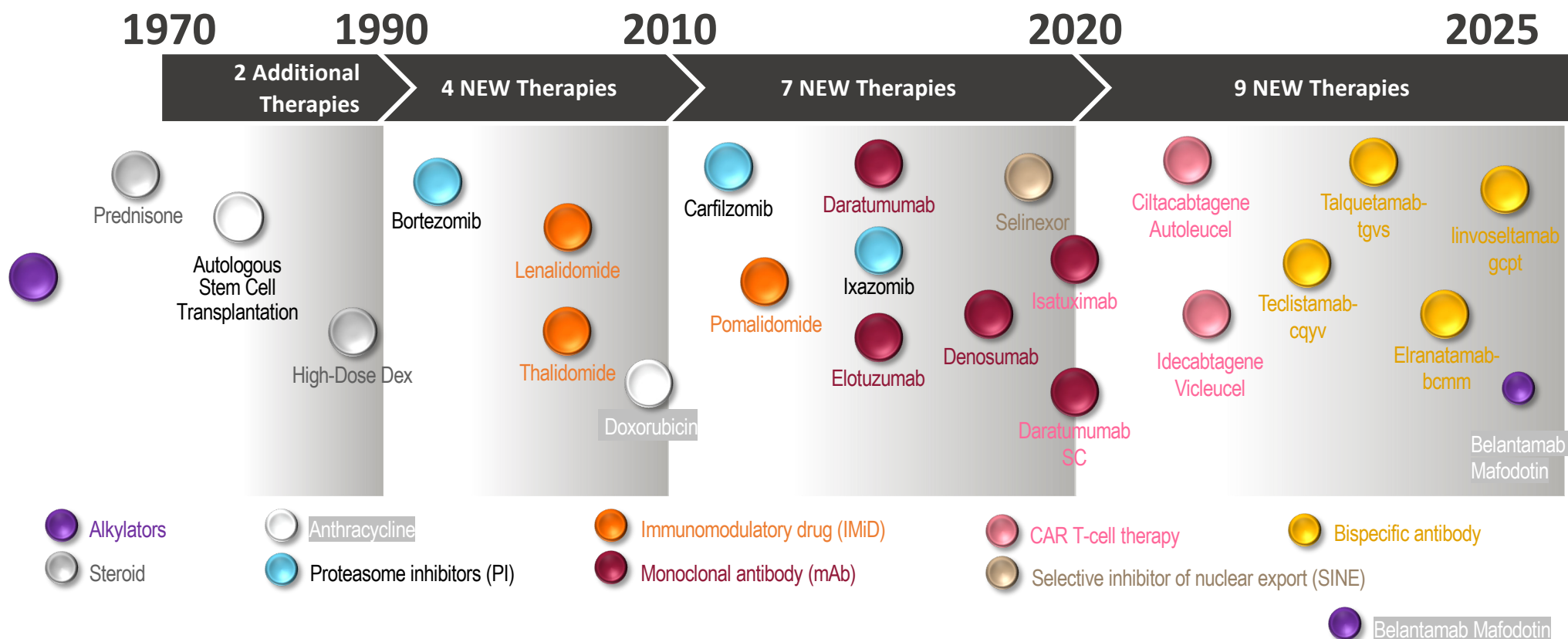
Key Learning Points

- MM incidence is rising, prevalence is rising, mortality is declining in high-income countries
- Remains incurable (but close to cure?)
- Shorter remissions with each relapse
- Relapse from CR can be biochemical or symptomatic
- Optimal timing of initiation of therapy at time of relapse?

Current Standard of Care and Evidence-Based Clinical Practice Guidelines in R/R MM

Richa Parikh, MD

A Buffet of Treatment Options for Multiple Myeloma at Diagnosis, Relapse



CAR = chimeric antigen receptor; Dex = dexamethasone; SINE = selective inhibitor of nuclear export; PI = proteasome inhibitor; mAb = monoclonal antibody; IMiD = immunomodulatory drug; FDA = Food and Drug Administration.
 Prescribing Information. Drugs@FDA: FDA-Approved Drugs. Accessed September 2025. <https://www.accessdata.fda.gov/scripts/cder/daf/>.

Factors in Treatment Selection at Relapse: Which Agents Are Approved, Balance Disease, and Patient Characteristics



T

Timing of relapse



R

Response to prior therapy



A

Aggressiveness of relapse



P

Performance status



P

Patient preference

- What worked, what didn't work, refractory status to LEN?
- Use at least 2 new drugs
 - CD38 mAbs (isatuximab and daratumumab) should not be used sequentially
- Salvage ASCT may be considered in eligible patients
- Clinical trials should always be considered

LEN = lenalidomide; ASCT = autologous stem cell transplantation.

Many Treatment Options at Early Relapse (1-3 Prior Therapies):

National
Comprehensive
Cancer
Network®
(NCCN®)

NCCN Guidelines® Version 2.2027
Multiple Myeloma

THERAPY FOR PREVIOUSLY TREATED MULTIPLE MYELOMA ^{a-d,m,p} Relapsed/Refractory ^q Disease After 1–3 Prior Therapies		
Preferred*		
Order of regimens does not indicate comparative efficacy		
T-cell Redirection Therapy ^s		
Anti-BCMA Therapy • Teclistamab-cqyv ± Daratumumab [†] (category 1)		
CAR T-cell Therapy[†] • Ciltacabtagene autoleucel (category 1)		
Anti-CD38 Refractory	Bortezomib-Refractory	Lenalidomide-Refractory
• Carfilzomib/Lenalidomide/Dexamethasone (category 1) • Carfilzomib/Pomalidomide/Dexamethasone	• Carfilzomib/Lenalidomide/Dexamethasone (category 1) • Carfilzomib/Dexamethasone + Daratumumab (category 1) • Carfilzomib/Dexamethasone + Isatuximab-irfc (category 1) • Lenalidomide/Dexamethasone + Daratumumab (category 1) • Lenalidomide/Dexamethasone + Isatuximab-irfc (category 1) • Pomalidomide/Dexamethasone + Daratumumab (category 1) • Pomalidomide/Dexamethasone + Isatuximab-irfc (category 1) • Carfilzomib/Pomalidomide/Dexamethasone	• Bortezomib/Dexamethasone + Belantamab mafodotin-blmf (category 1) ^s • Bortezomib/Dexamethasone + Daratumumab (category 1) • Carfilzomib/Dexamethasone + Daratumumab (category 1) • Carfilzomib/Dexamethasone + Isatuximab-irfc (category 1) • Pomalidomide/Dexamethasone + Daratumumab (category 1) • Pomalidomide/Dexamethasone + Isatuximab-irfc (category 1) • Carfilzomib/Pomalidomide/Dexamethasone

THERAPY FOR PREVIOUSLY TREATED MULTIPLE MYELOMA ^{a-d,m,p,s,u} Relapsed/Refractory Disease After 1–3 Prior Therapies	
Other Recommended	Useful in Certain Circumstances
• Bortezomib/Pomalidomide/Dexamethasone (category 1) • Bortezomib/Selinexor/Dexamethasone (category 1) • Cyclophosphamide/Pomalidomide/Dexamethasone (category 1) • Daratumumab + Talquetamab-tgvs/Dexamethasone [†] (category 1) • Idecabtagene vicleucel (category 1) • Ixazomib/Lenalidomide/Dexamethasone (category 1) • Lenalidomide/Dexamethasone + Elotuzumab (category 1) • Pomalidomide/Dexamethasone + Daratumumab + Talquetamab-tgvs [†] (category 1) • Bortezomib/Dexamethasone + Elotuzumab • Bortezomib/Cyclophosphamide/Dexamethasone • Bortezomib/Cyclophosphamide/Dexamethasone + Daratumumab • Bortezomib/Lenalidomide/Dexamethasone • Carfilzomib/Cyclophosphamide/Dexamethasone • Carfilzomib/Pomalidomide/Dexamethasone + Daratumumab • Cyclophosphamide/Lenalidomide/Dexamethasone • Ixazomib/Dexamethasone + Daratumumab • Ixazomib/Cyclophosphamide/Dexamethasone • Pomalidomide/Dexamethasone + Elotuzumab	• Bortezomib/Dexamethasone (category 1) • Carfilzomib/Dexamethasone (category 1) • Lenalidomide/Dexamethasone (category 1) • Pomalidomide/Dexamethasone (category 1) • Pomalidomide/Dexamethasone + Belantamab mafodotin-blmf (category 1) • Carfilzomib/Cyclophosphamide/Thalidomide/Dexamethasone • Carfilzomib/Selinexor/Dexamethasone • Carfilzomib/Dexamethasone + Belantamab mafodotin-blmf • Daratumumab • Pomalidomide/Selinexor/Dexamethasone • Selinexor/Dexamethasone + Daratumumab • Venetoclax/Dexamethasone ± Daratumumab or PI (only for patients with t(11;14)) For treatment of aggressive MM • Dexamethasone/Cyclophosphamide/Etoposide/Cisplatin (DCEP) • Dexamethasone/Thalidomide/Cisplatin/Doxorubicin/Cyclophosphamide/Etoposide (DT-PACE) ± Bortezomib (VTD-PACE) • Talquetamab-tgvs + Teclistamab-cqyv [†]
HCT as Indicated • Autologous HCT • Allogeneic HCT • Donor lymphocyte infusion can be considered in patients with disease relapse after allogeneic HCT	

NCCN = National Comprehensive Cancer Network; BCMA = B-cell maturation antigen; HCT = hematopoietic cell transplantation; DCEP = dexamethasone, cyclophosphamide, etoposide, and cisplatin; DT-PACE = dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, and etoposide; VTD-PACE = bortezomib, thalidomide, dexamethasone, cisplatin, doxorubicin, cyclophosphamide, and etoposide.

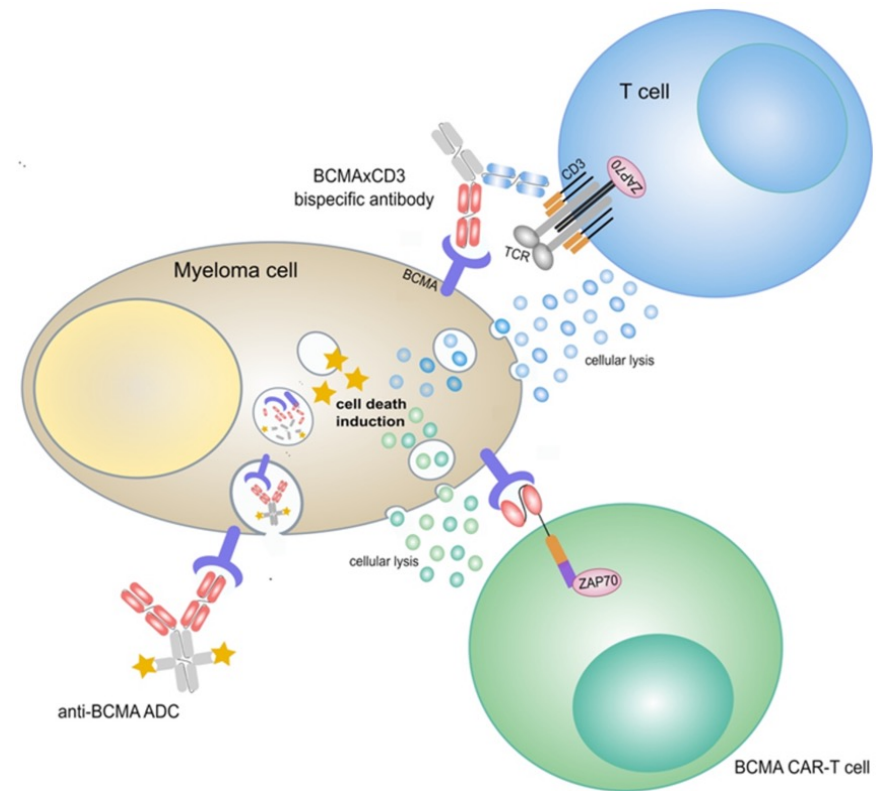
Reproduced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma V.2.2027. © 2026 National Comprehensive Cancer Network, Inc. All rights reserved. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. The NCCN Guidelines are a work in progress that may be refined as often as new significant data becomes available.

Novel and Emerging Therapeutic Strategies in R/R MM

Richa Parikh, MD

BCMA-Directed Immunotherapy Constructs

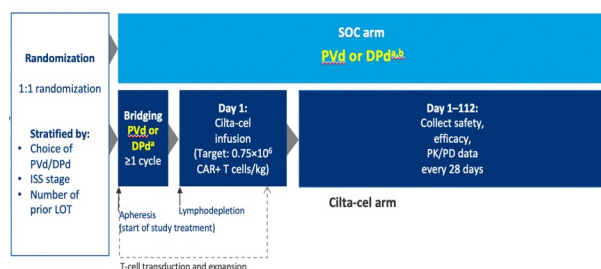
- BCMA (B-cell maturation antigen)
- Member of TNF receptor superfamily
- BCMA is expressed on late memory B cells committed to PC differentiation and PCs
- BCMA plays a role in survival of long-lived PCs
- BCMA is expressed more abundantly on malignant PCs than on normal ones



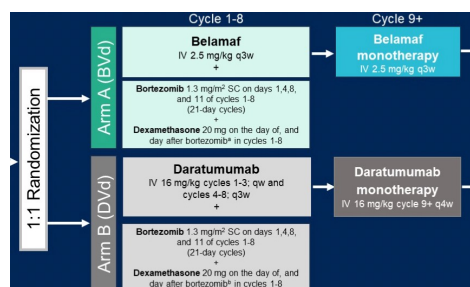
TNF = tumor necrosis factor; PC = plasma cell; ADC = antibody-drug conjugate.
Strassl I, et al. *Cancers (Basel)*. 2021;13(18):4701.

Treatment of triple-class–exposed patients in early lines in the BCMA era

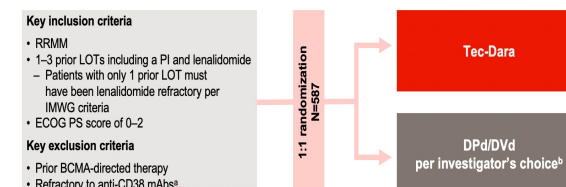
CARTITUDE-4



DREAMM-7

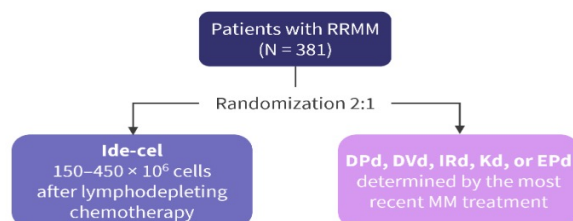


MajesTEC-3

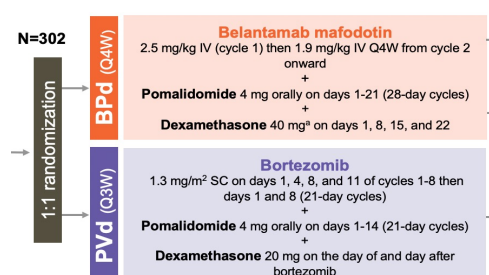


KarMMa-3

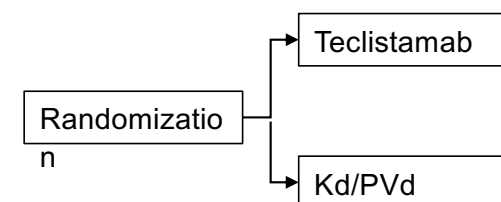
Phase III randomized, multicenter, open label study
Study period: April 2019 to September 2026 (planned end date)



DREAMM-8



MajesTEC-9



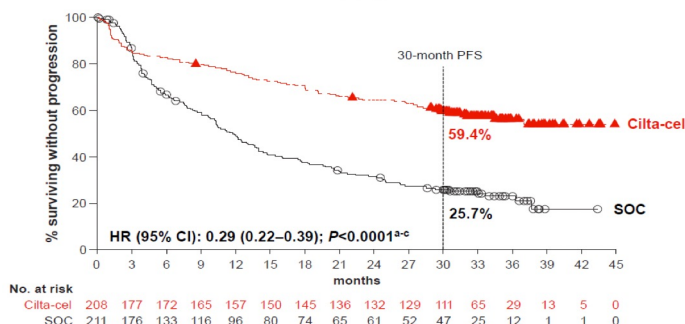
Kd = carfilzomib plus dexamethasone; PvD = pomalidomide, bortezomib, and dexamethasone; DPd = daratumumab, pomalidomide, and dexamethasone; BvD = belantamab mafodotin, bortezomib, and dexamethasone; DVd = daratumumab, bortezomib, and dexamethasone; ide-cel = idecabtagene vicleucel; belamaf = belantamab mafodotin; q3w = every 3 weeks; qw = once weekly; q4w = every 4 weeks; PK/PD = pharmacokinetics/pharmacodynamics; CAR⁺ = chimeric antigen receptor–positive; ISS = International Staging System; LOT = line(s) of therapy; ECOG PS = Eastern Cooperative Oncology Group performance status. ClinicalTrials.gov. CARTITUDE-4: NCT04181827. KarMMa-3: NCT03651128. DREAMM-7: NCT04246047. DREAMM-8: NCT04484623. MajesTEC-3: NCT05083169. MajesTEC-9: NCT05572515. Accessed September 2026. <https://clinicaltrials.gov/>.

CAR T-cell vs standard of care in early lines for patients with RRMM

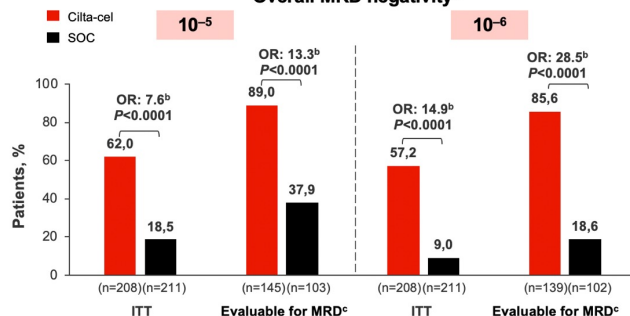
CARTITUDE-4

Median prior lines of therapy: 1 (1-3)
100% lenalidomide refractory

PFS

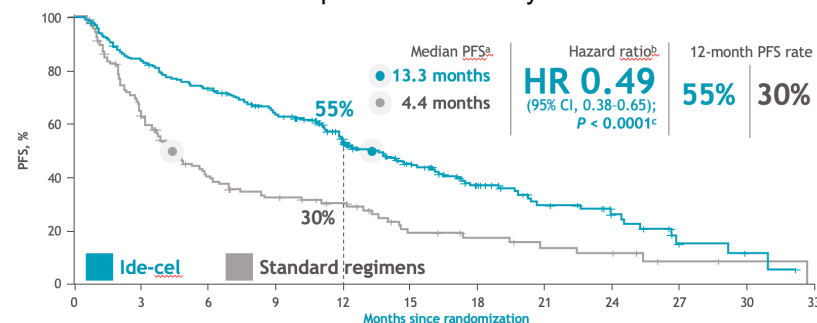
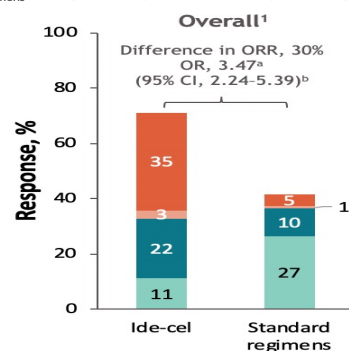


Overall MRD negativity^a



KarMMa-3

Median prior lines of therapy: 3 (2-4)
65-67% triple-class refractory



MRD negativity (10⁻⁵) in CR patients:
20% vs 1%

ASCO = American Society of Clinical Oncology; ORR = overall response rate; OR = odds ratio; PFS = progression-free survival; HR = hazard ratio; ITT = intention-to-treat; SOC = standard of care.
Dhakal B, et al. *J Clin Oncol*. 2023;41(suppl 17):LBA106.

In CARTITUDE-4, as-treated cilta-cel population at 30-month median follow-up

CARTITUDE-4: Cilta-cel vs SOC in lenalidomide-refractory 2L–4L RRMM

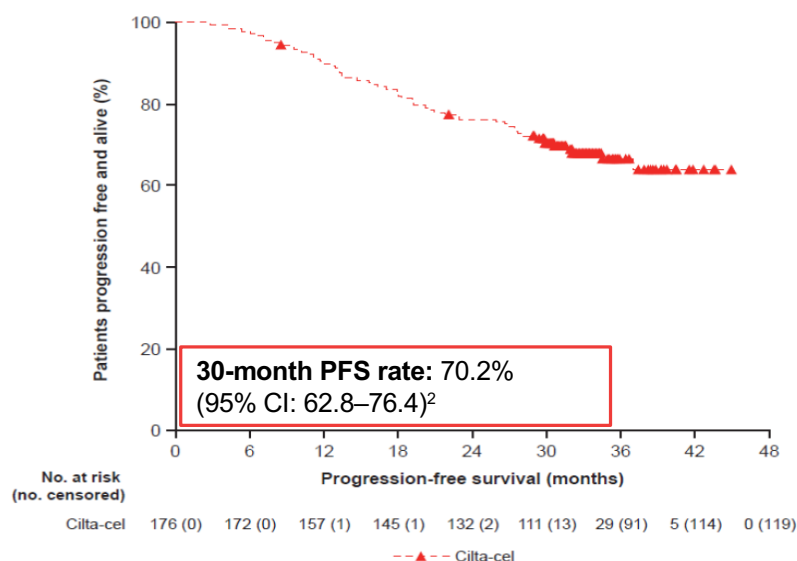
ITT: cilta-cel, n=208; SOC, n=211; Primary endpoint PFS, mFU 33.6 months

- Significant PFS and OS benefit with cilta-cel vs SOC
- mPFS not reached with cilta-cel vs 11.8 months with SOC

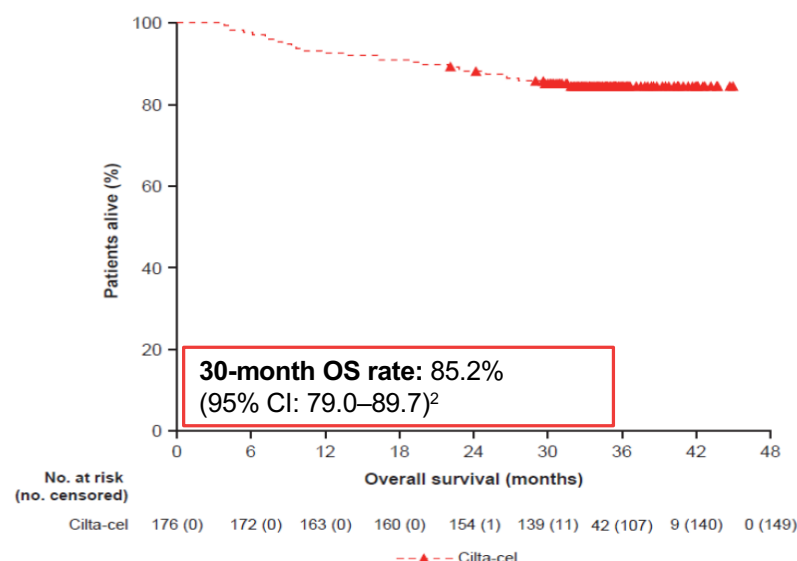
71% reduced risk of progression or death vs SOC (HR, 0.29; $p < 0.0001$)*

45% reduced risk of death vs SOC (HR, 0.55; $p = 0.0009$)†

PFS (as-treated cilta-cel population; n=176)



OS (as-treated cilta-cel population; n=176)



*A total of 242 PFS events (89 [43%] in 208 patients in the cilta-cel group and 153 [73%] in 211 patients in the SOC group) had occurred. There was a 30% absolute reduction in the risk of progression or death with cilta-cel vs SOC; †At data cut-off, 133 OS events had occurred (50 in the cilta-cel group [24%] and 83 in the SOC group [39%]). There was a 15% absolute reduction in the risk of death with cilta-cel vs SOC.

mFU = median follow-up; PFS = progression-free survival; mPFS = median PFS.

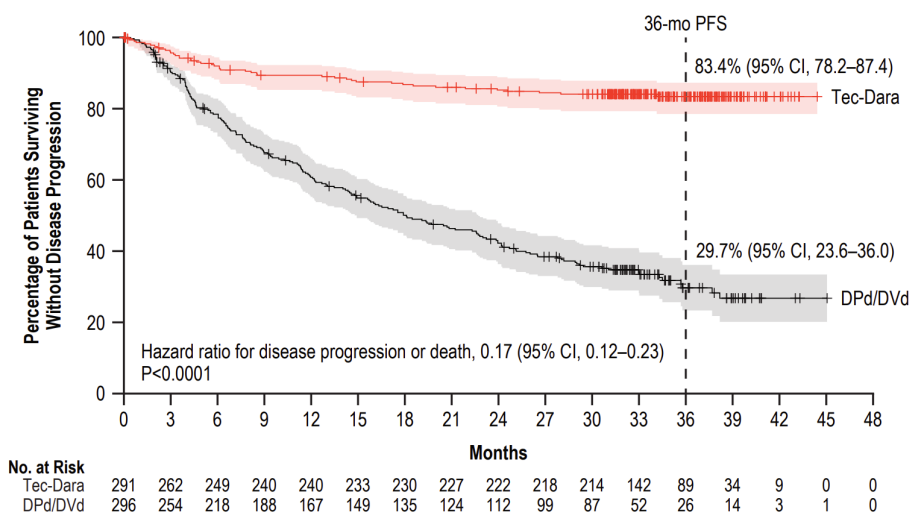
Einsele H, et al. *Lancet Oncol.* 2026;27(2):254-268. Einsele H, et al. *Lancet Oncol.* 2026;27(2):254-268 (Supplementary appendix to).

MajesTEC-3: Tec-Dara improved PFS and OS vs DPd/DVd

Median follow-up: 34.5 months

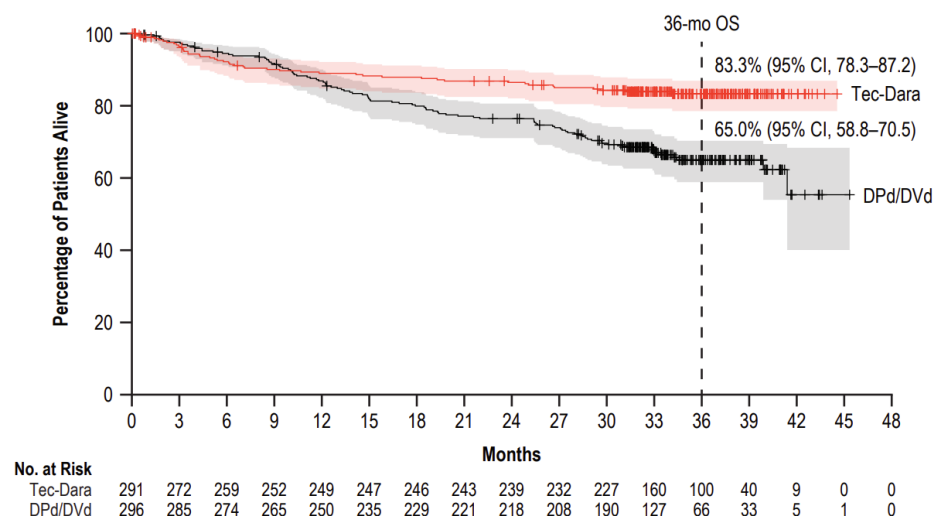
587 pts, 100% len exposed (83% refractory), 5% Anti-CD38 exposed

PFS



Median PFS was NR for Tec-Dara vs 18.1 months for DPd/DVd (HR, 0.17; 95% CI, 0.12-0.23; p<0.0001)

OS



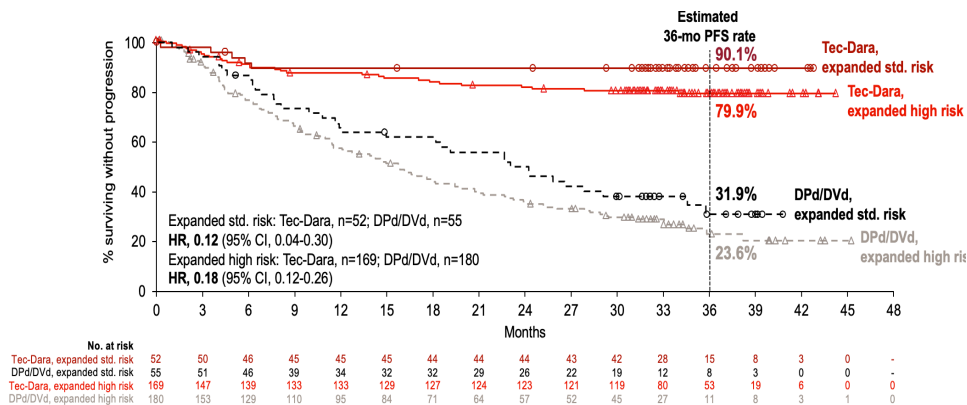
Median OS: NR in either treatment arm (HR, 0.46; 95% CI, 0.32-0.65; p<0.0001)

NR = not reached; D/Dara = daratumumab; d = dexamethasone; P = pomalidomide; Tec = teclistamab; V = bortezomib; Tec-Dara = teclistamab plus daratumumab; pts = patients; len = lenalidomide.

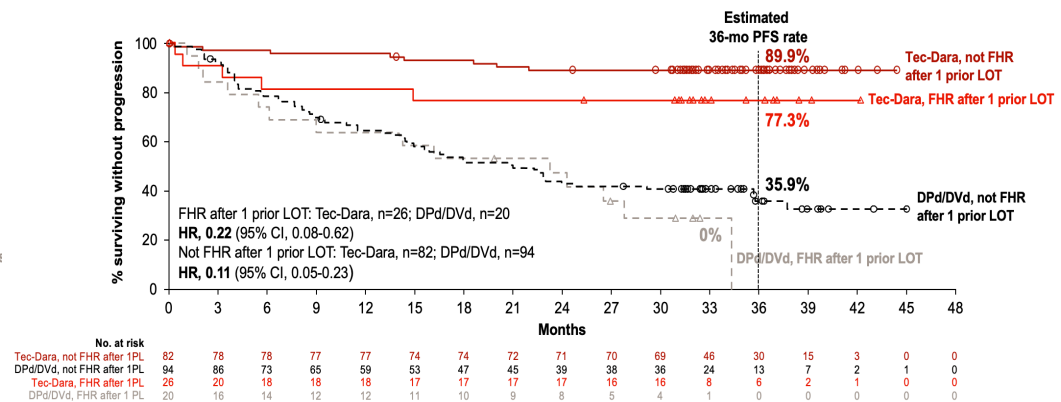
Costa LJ, et al. *N Engl J Med.* 2026;394:739-752. Costa LJ, et al. *N Engl J Med.* 2026;394:739-752 (supplementary appendix).

Tec-Dara for patients with high-risk MM: MajesTec-3 study

PFS by Expanded^a Cytogenetic Risk



PFS by Functional High-Risk

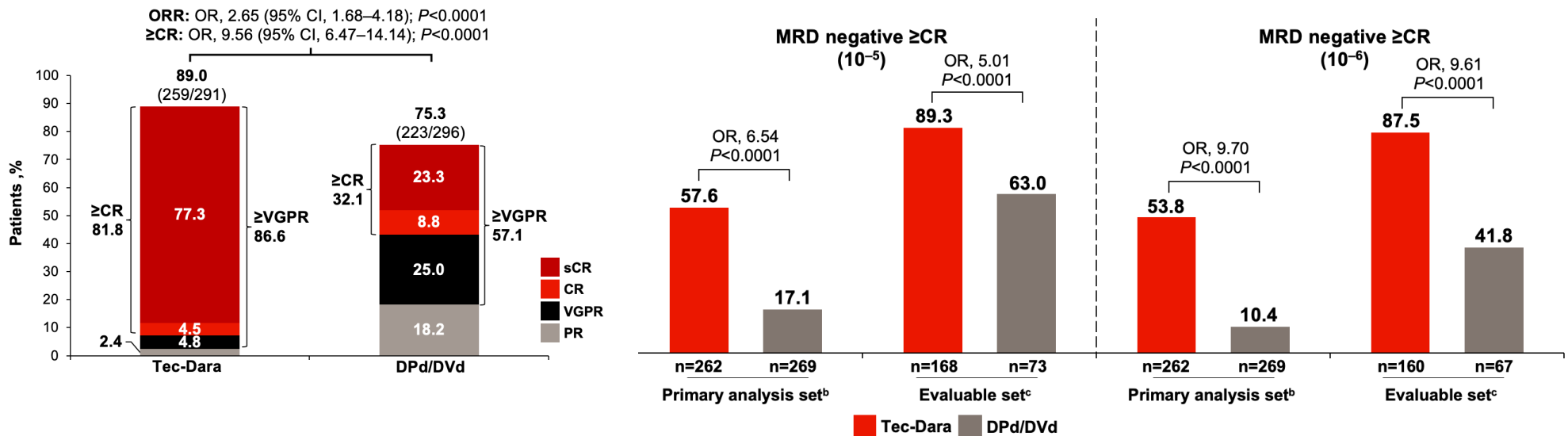


^aExpanded standard risk: none of del(17p), t(4;14), t(14;16), amp(1q21), or gain(1q21). Expanded high risk: ≥1 of del(17p), t(4;14), t(14;16), amp(1q21), or gain(1q21).

std = standard; FHR = functional high risk; 1PL = one prior line of therapy; EHA = European Hematology Association; del = deletion; t = translocation; amp = amplification; gain = copy-number gain.

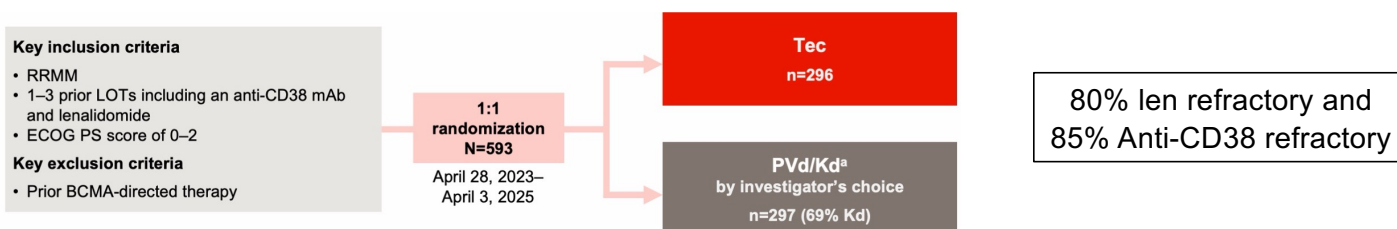
Banerjee R, et al. Teclistamab plus daratumumab in patients with relapsed/refractory multiple myeloma: analysis of MajesTEC-3 based on cytogenetic and functional risk. Presented at: European Hematology Association 2026 Congress; June 11-14, 2026; Stockholm, Sweden. Abstract EHA-2558.

MajesTEC-3: Tec-Dara improved CR and MRD rates vs DPd/DVd

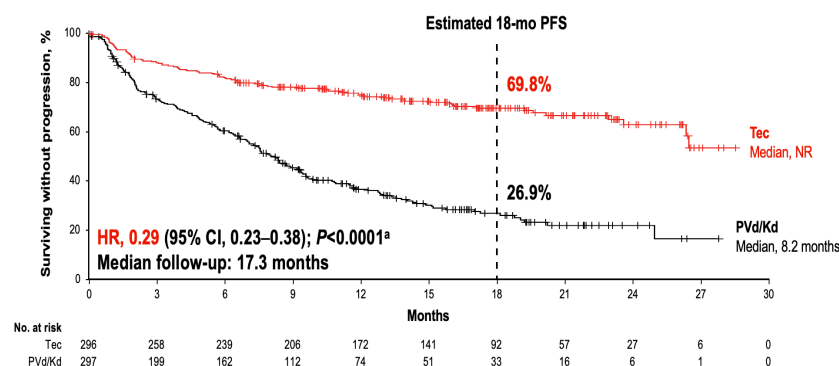


NEJM = New England Journal of Medicine; VGPR = very good partial response; $\geq$ CR = complete response or better.
 Costa LJ, et al. *N Engl J Med*. 2026;394(8):739-752.

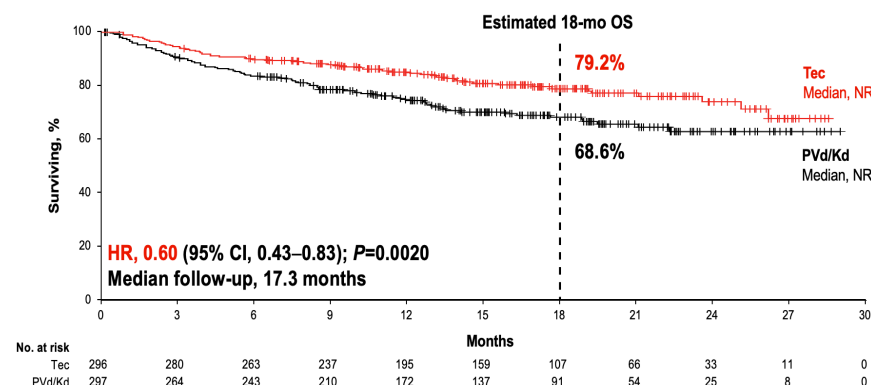
MajesTEC-9: teclistamab monotherapy improved PFS and OS vs SOC in RRMM exposed and refractory to lenalidomide and anti-CD38 Ab



Progression-free survival



Overall survival

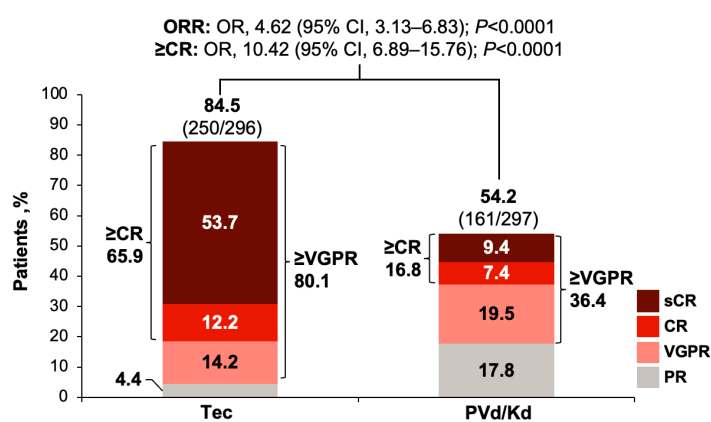
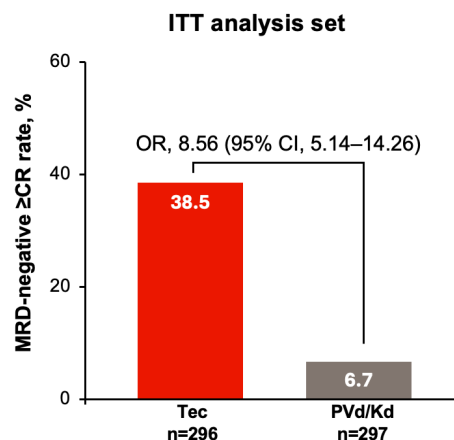
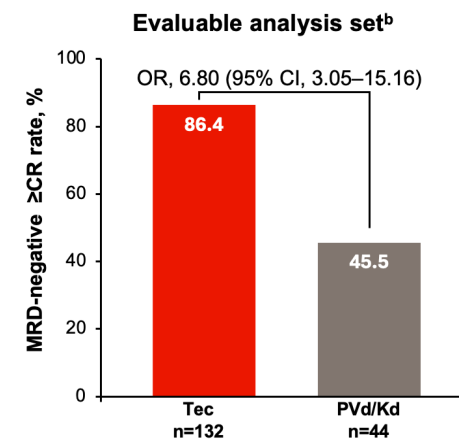


2/3 of pts received CART/bispecific antibodies in subsequent lines of therapy of the SOC arm

Ab = antibody.

Mina R, et al. *J Clin Oncol*. 2026;44(suppl 16):7507. Touzeau C, et al. *N Engl J Med*. 2026;395(5):440-453.

Teclistamab monotherapy improved responses and MRD negativity vs SOC in RRMM



Mina R, et al. *J Clin Oncol*. 2026;44(suppl 16):7507. Touzeau C, et al. *N Engl J Med*. 2026;395(5):440-453.

Safety profile of teclistamab and teclistamab-daratumumab

MajesTEC-9

TEAE, n (%) ^c	Tec (n=291)		PVd/Kd (n=283)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any TEAE	290 (99.7)	247 (84.9)	277 (97.9)	216 (76.3)
Hematologic				
Neutropenia	182 (62.5)	158 (54.3)	81 (28.6)	63 (22.3)
Anemia	110 (37.8)	52 (17.9)	119 (42.0)	46 (16.3)
Thrombocytopenia	80 (27.5)	31 (10.7)	110 (38.9)	60 (21.2)
Nonhematologic ^d				
CRS	192 (66.0)	2 (0.7)	0	0
Diarrhea	124 (42.6)	15 (5.2)	72 (25.4)	4 (1.4)
Hypertension	20 (6.9)	13 (4.5)	51 (18.0)	32 (11.3)
Any infection	241 (82.8)	121 (41.6)	193 (68.2)	82 (29.0)
URTI	77 (26.5)	7 (2.4)	58 (20.5)	6 (2.1)
Pneumonia	64 (22.0)	42 (14.4)	43 (15.2)	30 (10.6)

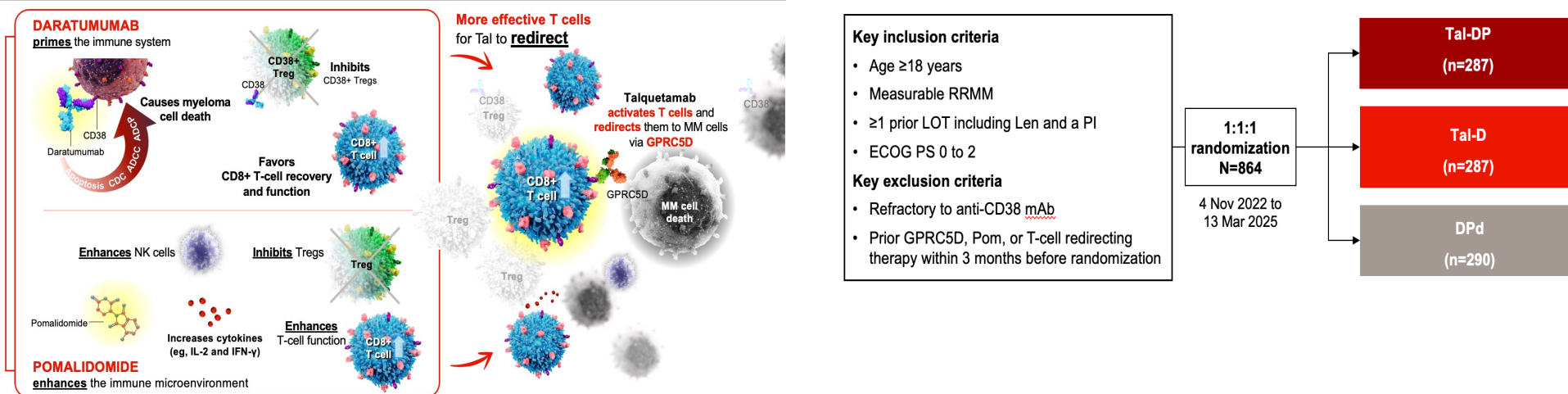
MajesTEC-3

TEAE, n (%) [‡]	Tec-Dara (n=283)		DPd/DVd (n=290)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Any TEAE	283 (100)	269 (95.1)	290 (100)	280 (96.6)
Hematologic				
Neutropenia	222 (78.4)	214 (75.6)	240 (82.8)	228 (78.6)
Anemia	111 (39.2)	58 (20.5)	103 (35.5)	50 (17.2)
Thrombocytopenia	103 (36.4)	55 (19.4)	126 (43.4)	68 (23.4)
Nonhematologic [§]				
Any infection	273 (96.5)	153 (54.1)	244 (84.1)	126 (43.4)
COVID-19	124 (43.8)	17 (6.0)	97 (33.4)	6 (2.1)
URTI	115 (40.6)	12 (4.2)	88 (30.3)	7 (2.4)
Pneumonia	65 (23.0)	47 (16.6)	53 (18.3)	43 (14.8)
CRS [¶]	170 (60.1)	0	-	-
Diarrhea	147 (51.9)	10 (3.5)	89 (30.7)	7 (2.4)

TEAE = treatment-emergent adverse event; URTI = upper respiratory tract infection; CRS = cytokine release syndrome.

Mina R, et al. *J Clin Oncol*. 2026;44(suppl 16):7507. Touzeau C, et al. *N Engl J Med*. 2026;395(5):440-453. Costa LJ, et al. *N Engl J Med*. 2026;394(8):739-752.

MonumenTAL-3: Tal-D +/- Pom vs DPd in RRMM for patients with ≥ 1 prior line

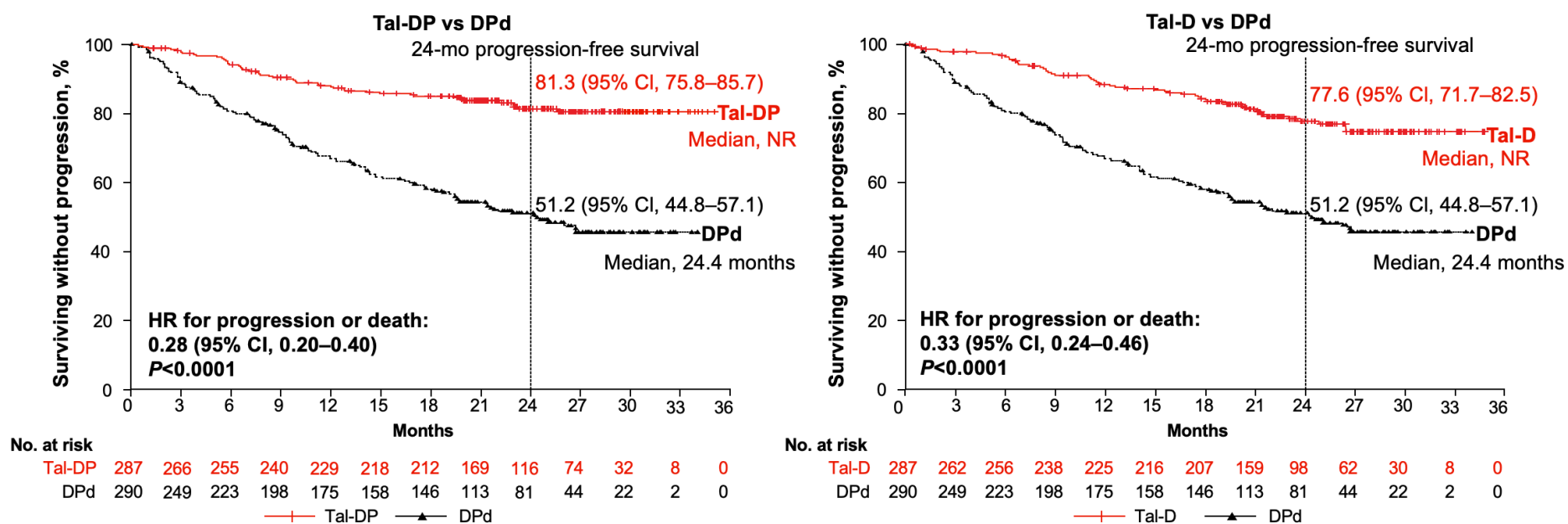


864 pts, 2 prior lines (median), 85% len refractory, 11% dara exposed

Tal-D = talquetamab plus daratumumab; Pom = pomalidomide; dara = daratumumab; Treg = regulatory T cell; NK = natural killer; IL-2 = interleukin 2; IFN- γ = interferon gamma.

Mina R, et al. *N Engl J Med.* 2026;395:671-683.

Tal-dara and Tal-dara-poma improved PFS compared to DPd in RRMM

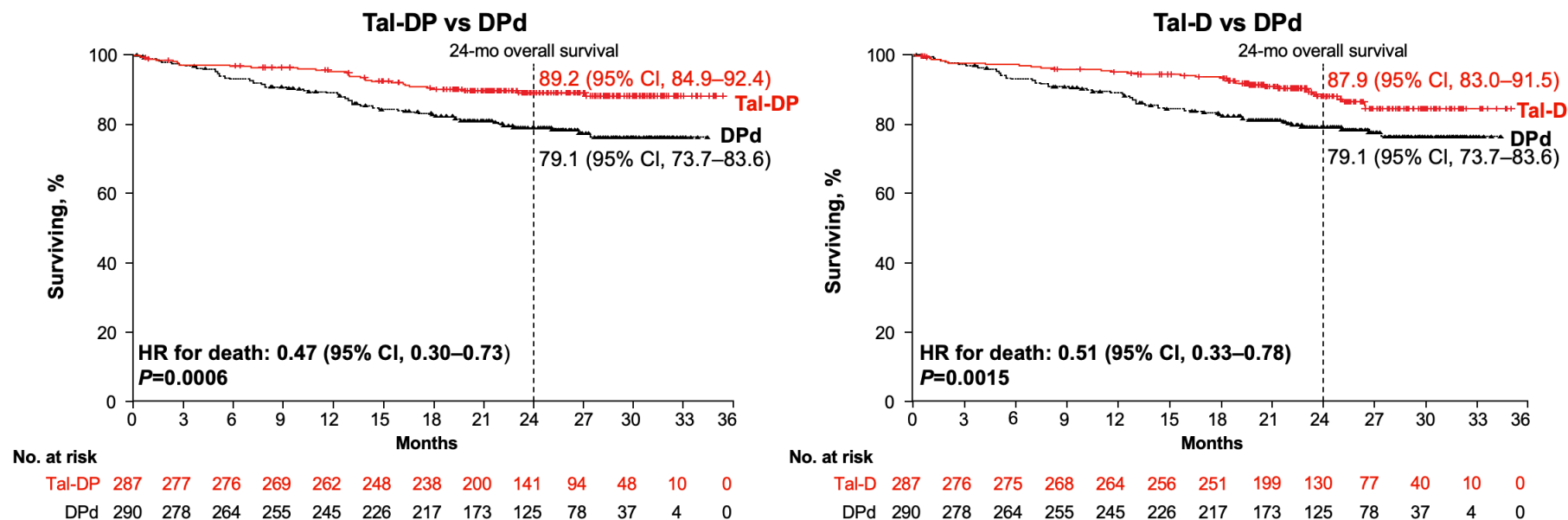


Tal-DP and Tal-D significantly improved PFS vs DPd

Tal-DP = talquetamab, daratumumab, and pomalidomide

Voorhees PM, et al. *HemaSphere*. 2026;10(suppl 1):S100. Mina R, et al. *N Engl J Med*. 2026;395:671-683.

Tal-dara and Tal-dara-poma improved OS compared to SoC in RRMM



Tal-DP and Tal-D resulted in clinically meaningful OS improvement vs DPd, with >87% of patients alive at 2 years; P -values did not cross the prespecified boundary for superiority (0.0001)

Safety profile of Talquetamab combinations in the MonumenTAL-3 trial

	TEAE, n (%)	Tal-DP (n=276)		Tal-D (n=274)		DPd (n=283)	
		Any Grade	Grade 3/4	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Hematologic	Neutropenia	232 (84.1)	211 (76.4)	112 (40.9)	80 (29.2)	255 (90.1)	244 (86.2)
	Anemia	136 (49.3)	66 (23.9)	107 (39.1)	41 (15.0)	117 (41.3)	45 (15.9)
	Thrombocytopenia	136 (49.3)	66 (23.9)	93 (33.9)	36 (13.1)	108 (38.2)	39 (13.8)
	Infections	241 (87.3)	104 (37.7)	231 (84.3)	80 (29.2)	235 (83.0)	120 (42.2)
	Taste changes ^b	201 (72.8)	–	205 (74.8)	–	11 (3.9)	–
Non-hematologic	Non-rash skin AE ^c	191 (69.2)	6 (2.2)	177 (64.6)	7 (2.6)	24 (8.5)	0
	CRS	187 (67.8)	2 (0.7)	160 (58.4)	2 (0.8)	–	–
	Nail-related AE ^d	155 (56.2)	1 (0.4)	157 (57.3)	1 (0.4)	1 (0.4)	0
	Decreased weight	126 (45.7)	21 (7.6)	105 (38.3)	13 (4.7)	21 (7.4)	1 (0.4)
	Fatigue	83 (30.1)	14 (5.1)	60 (21.9)	8 (2.9)	69 (24.4)	9 (3.2)

AE, n (%)	Tal-DP (n=276)	Tal-D (n=274)
Taste changes^a	201 (72.8)	205 (74.8)
Grade 3 or 4	–	–
Leading to discontinuation of Tal	11 (4.0)	6 (2.2)
Non-rash skin^b	191 (69.2)	177 (64.6)
Grade 3	6 (2.2)	7 (2.6)
Leading to discontinuation of Tal	5 (1.8)	2 (0.7)
Nail related^c	155 (56.2)	157 (57.3)
Grade 3	1 (0.4)	1 (0.4)
Leading to discontinuation of Tal	3 (1.1)	0
Rash-related^d	105 (38.0)	107 (39.1)
Grade 3	5 (1.8)	7 (2.6)
Leading to discontinuation of Tal	1 (0.4)	2 (0.7)
Ataxia/balance disorders^e	40 (14.5)	34 (12.4)
Grade 3	8 (2.9)	6 (2.2)
Leading to discontinuation of Tal	13 (4.7)	6 (2.2)
Weight decreased	126 (45.7)	105 (38.3)
Grade 3	21 (7.6)	13 (4.7)
Leading to discontinuation of Tal	6 (2.2)	5 (1.8)

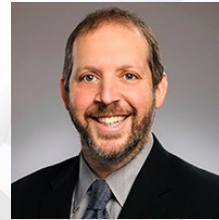
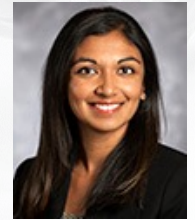
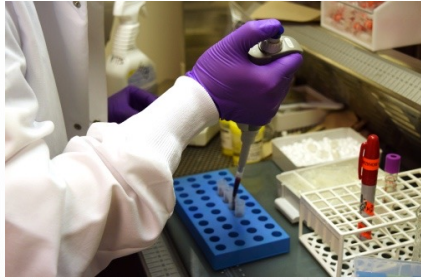
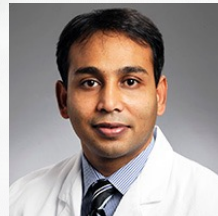
Voorhees PM, et al. *HemaSphere*. 2026;10(suppl 1):S100. Mina R, et al. *N Engl J Med*. 2026;395:671-683.

Key Learning Points

- Many treatment options for early relapse
 - BCMA-directed CAR T-cell therapy
 - BCMA-directed bispecific Abs (monotherapy or in combination)
 - GPRC5D-directed bispecific Abs (monotherapy or in combination)
 - Belantamab mafodotin combinations
 - CD38, PI, IMiD combinations
- Sequencing?

GPRC5D = G protein–coupled receptor class C group 5 member D.

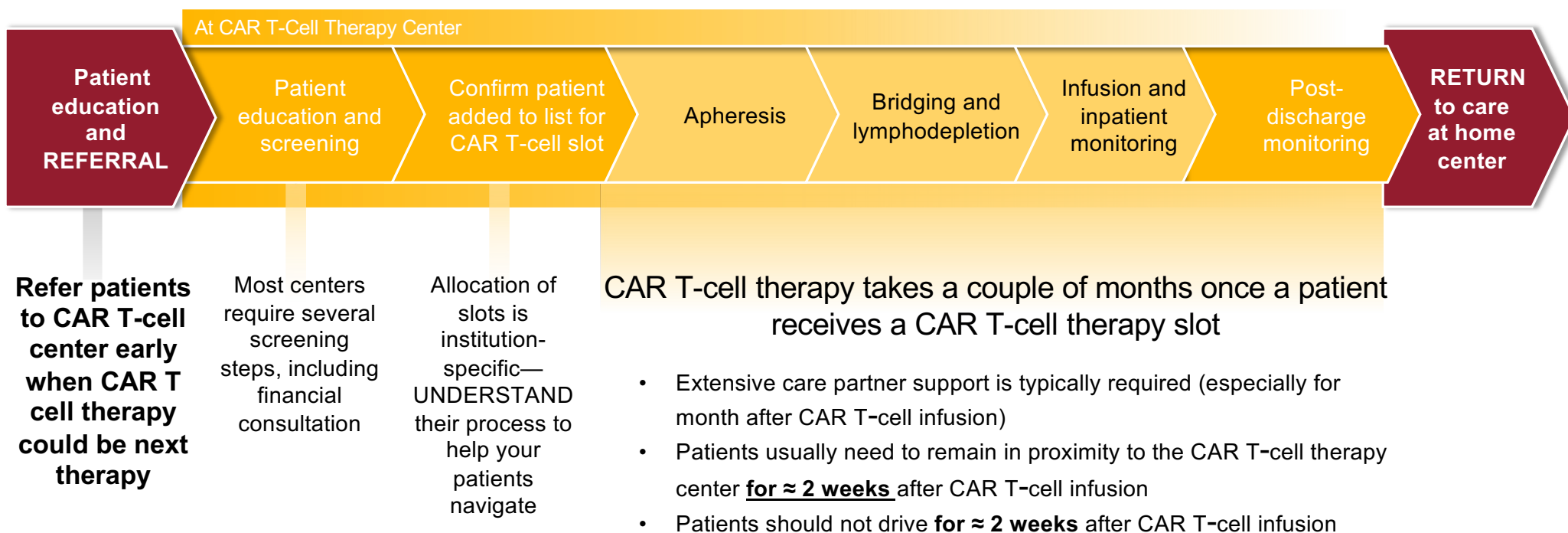
Myeloma Group at Emory Winship



Novel and Emerging Therapeutic Strategies in R/R MM (cont.)

Samantha Shenoy, MS, MSN, ACNP-BC

CAR T-Cell Therapy: A Process



Catamero D, et al. *J Adv Pract Oncol*. 2022;13(suppl 4):31-43. Teoh PJ, Chng WJ. *Blood Cancer J*. 2021;11(4):84. Shah UA, Mailankody S. *BMJ*. 2020;370:m3176.

Acute AEs

- Cytokine-release syndrome
- Immune effector cell–associated neurotoxicity syndrome
- Cytopenias
- Hemophagocytic lymphohistiocytosis/macrophage activation syndrome

**TYPICALLY MANAGED BY
CAR T-CELL THERAPY CENTER**

Delayed AEs



B-cell aplasia/
hypogammaglob
ulinemia



Prolonged
cytopenias



Long-term
neurologic
events/
movement and
neurocognitive
treatment-
emergent AEs



Transient
cardiac toxicities



Atypical
infections

**TYPICALLY MANAGED BY
PRIMARY ONCOLOGY TEAM**

**APs are critical
for coordination of care
between CAR T center
and community
center!**

AP = advanced practitioner.

Maus MV, et al. *J Immunother Cancer*. 2020;8(2):e001511. Cohen AD, et al. *Blood Cancer J*. 2022;12(2):32. Chakraborty R, et al. *Transplant Cell Ther*. 2021;27(3):222-229.

Belantamab Mafodotin: Mechanisms of Action

Mechanisms of action: S

- Belantamab mafodotin has multimodal immune-independent ADC-mediated and immune-dependent mechanisms such as ADCC/ADCP^{1,2}
- Belantamab mafodotin, a humanized afucosylated, anti-BCMA monoclonal antibody conjugated to the microtubule inhibitor, mafodotin, is the first off-the-shelf BCMA-targeted ADC^{1,2}
- Belantamab mafodotin specifically eliminates myeloma cells by a multi-targeted mechanism
- Mafodotin delivered to BCMA-expressing cells inhibits microtubule polymerization, which inhibits immune-independent apoptosis that leads to the release of markers of ICD, which modulates the adaptive immune response. The antibody component of belantamab mafodotin enhances ADCC/P^{1,2}

Blenrep[®] approved by US FDA for use in treatment of relapsed/refractory multiple myeloma

CC/P

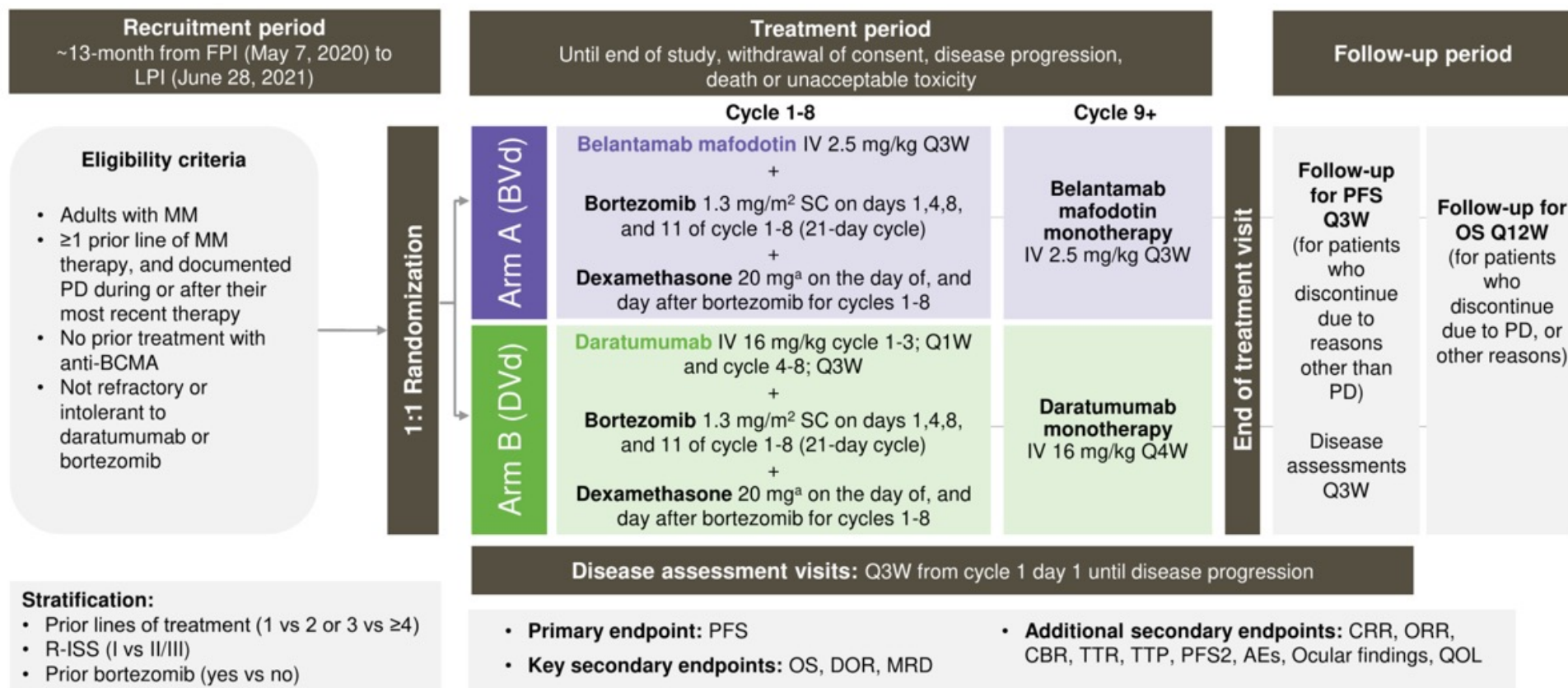
[Download \(PDF - 245.7KB\)](#) 

- Significant unmet need for patients requires new and novel treatments¹
- DREAMM-7 showed a 51% reduction in the risk of death and tripled median progression-free survival in 3L+ indicated population versus a daratumumab-based triplet²
- *Blenrep* is the only anti-BCMA accessible in the community setting where 70% of patients receive care, and with a new streamlined REMS programme³
- Robust clinical development is ongoing to advance *Blenrep* in earlier lines of treatment, including newly diagnosed patients⁴

ADCC/P = antibody-dependent cellular cytotoxicity and phagocytosis; APRIL = a proliferation-inducing ligand; ATP = adenosine triphosphate; BAFF = B-cell activating factor; CRT = calreticulin; CTL = cytotoxic T-lymphocyte; Fc = fragment crystallizable; HMGB1 = high mobility group box 1; ICD = immunogenic cell death.

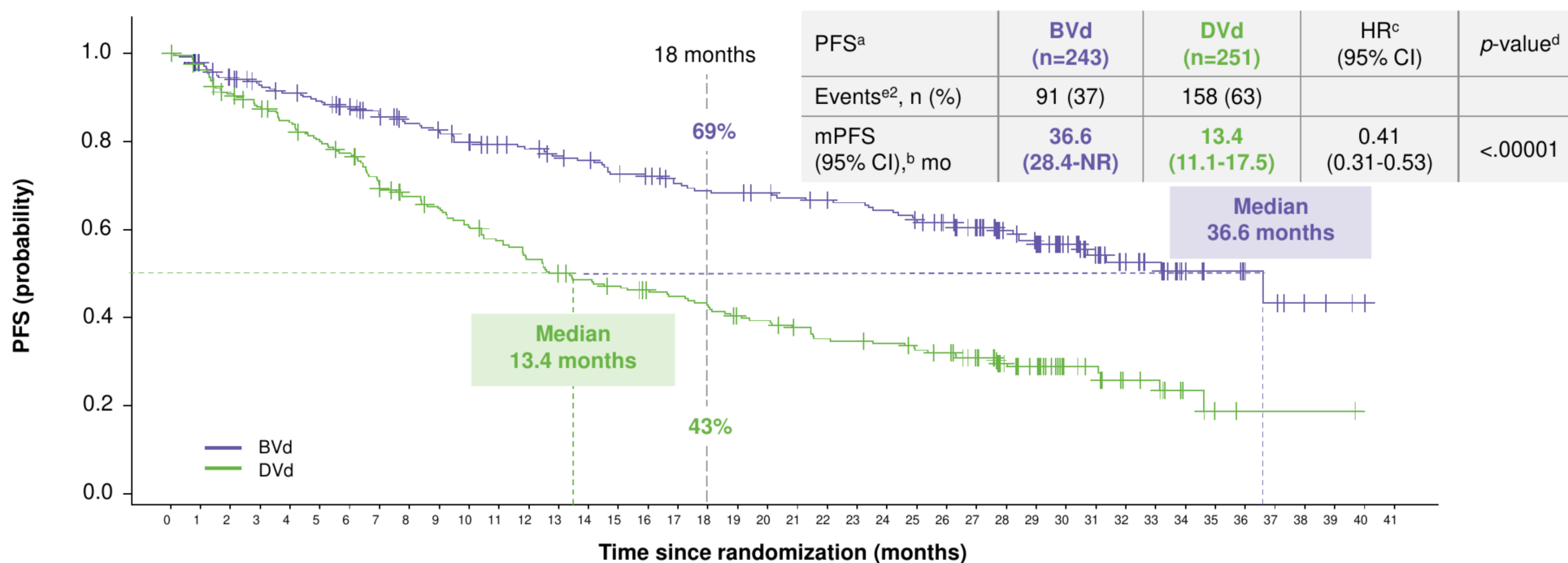
Tai YT, et al. *Blood*. 2014;123(20):3128-3138. Montes de Oca R, et al. Poster PF558. Presented at: EHA 2019; June 13-16, 2019; Amsterdam, Netherlands. Cho SF, et al. *Front Immunol*. 2018;9:1821.

Dreamm-7



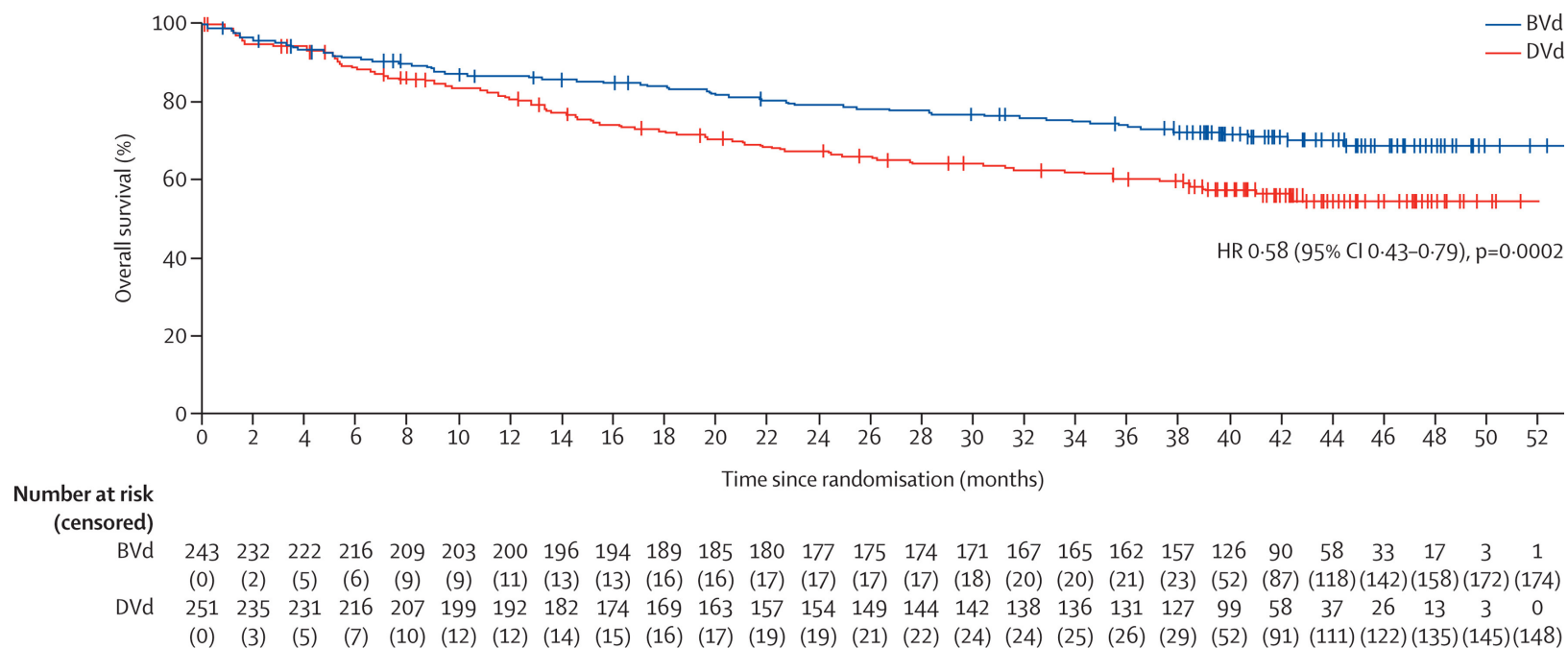
Mateos MVM, et al. Abstract 439572. Presented at: ASCO Plenary Series: February 2024 Session; 2024.

Dreamm-7



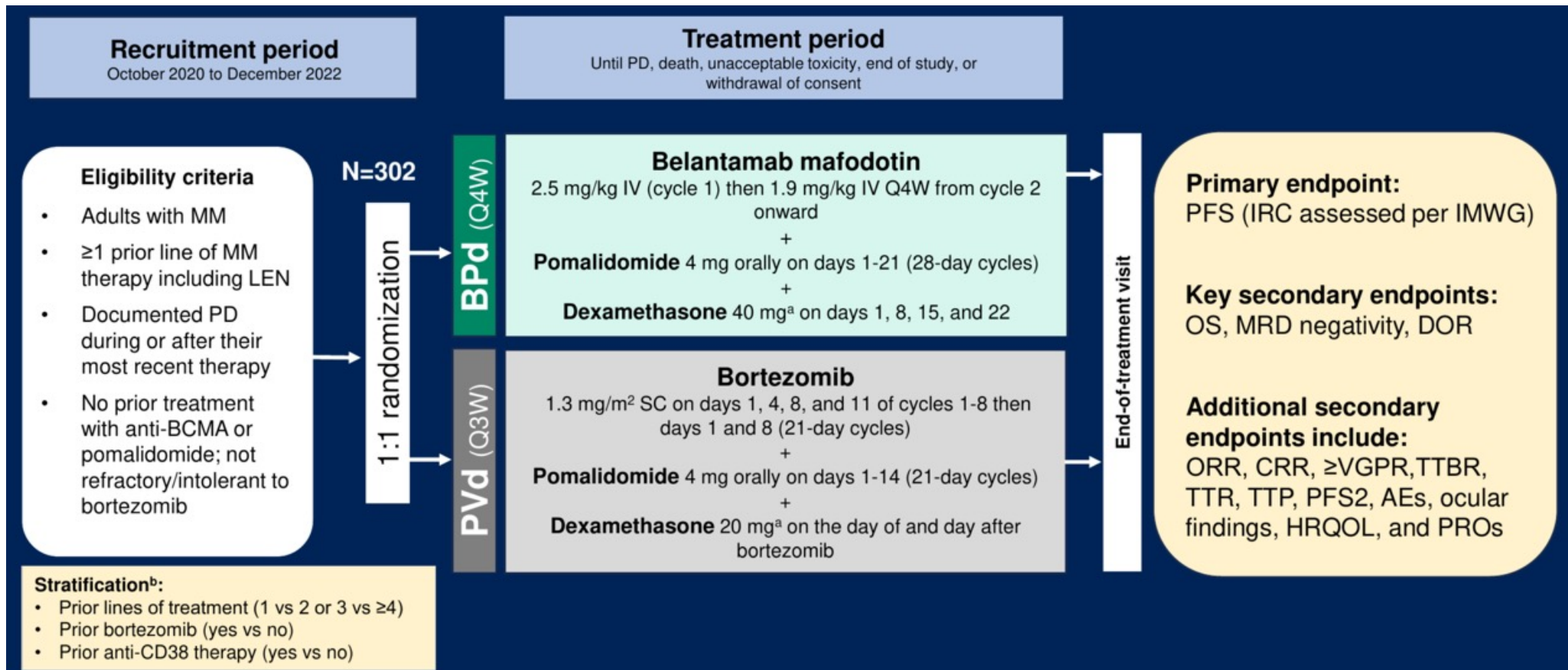
Mateos MVM, et al. Abstract 439572. Presented at: ASCO Plenary Series: February 2024 Session; 2024.

Dreamm-7



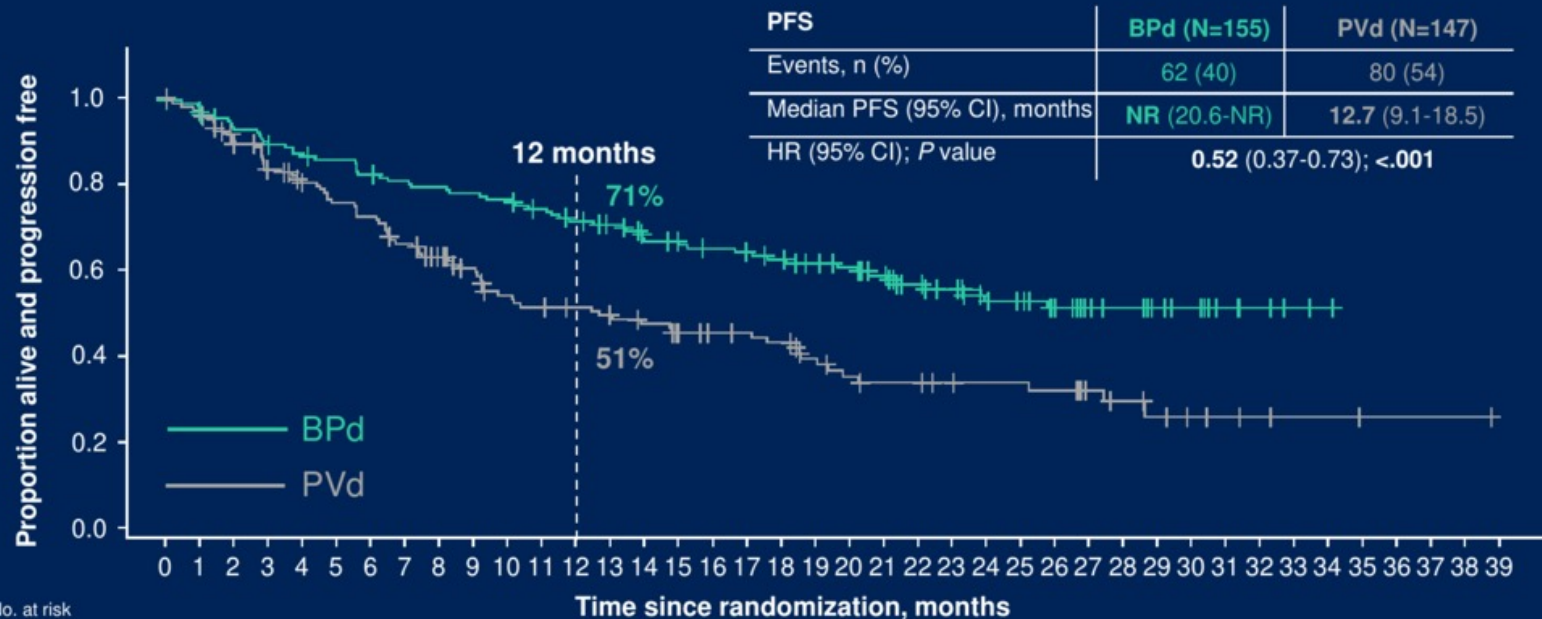
Hungria V, et al. *Lancet Oncol.* 2025;26(8):1067-1080.

DREAMM-8



Trudel S, et al. 2024 ASCO Annual Meeting; May 31-June 4, 2024; Chicago, IL.

DREAMM-8



No. at risk
(no. of events)

BPd

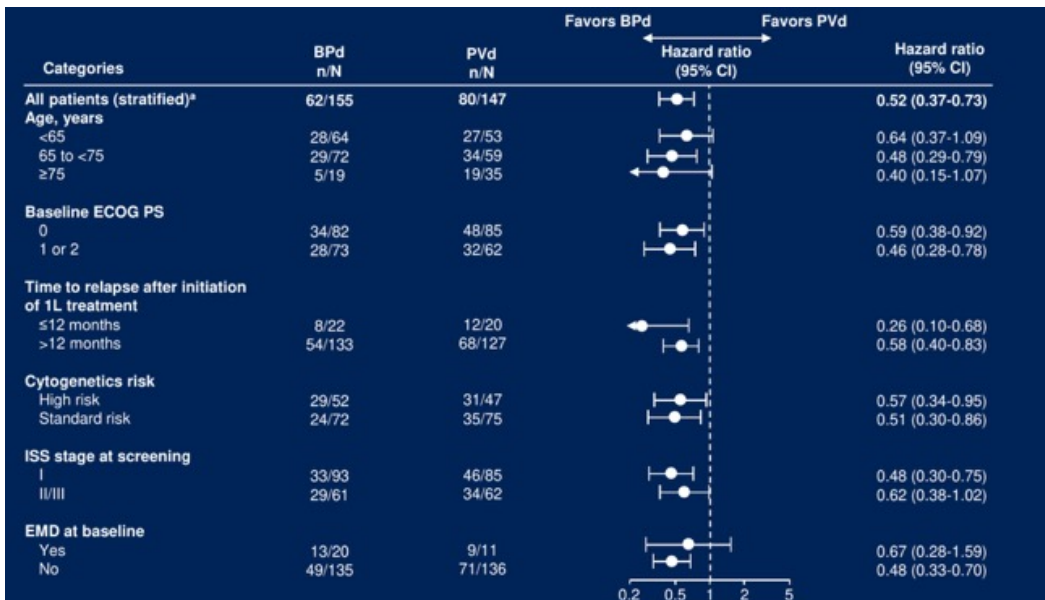
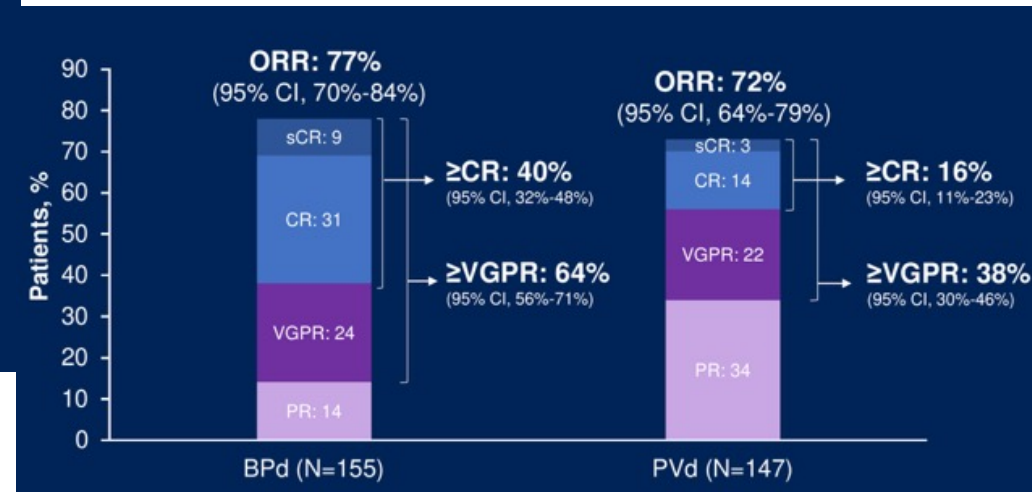
155 143 135 130 125 122 117 113 111 109 107 102 97 93 82 80 77 75 72 67 64 59 50 45 38 36 28 23 21 16 13 8 4 2 1 0 0 0 0 0
(0) (5) (10) (15) (19) (21) (26) (28) (30) (32) (34) (37) (41) (42) (47) (47) (49) (50) (52) (53) (54) (56) (58) (59) (61) (61) (62) (62) (62) (62) (62) (62) (62) (62) (62) (62)

PVd

147 138 123 111 102 96 92 83 75 68 59 56 54 51 47 43 40 39 37 30 25 22 22 19 18 18 17 13 11 7 5 4 3 2 2 1 1 1 1 0
(0) (4) (14) (23) (27) (33) (37) (45) (49) (52) (59) (62) (62) (64) (66) (68) (68) (68) (70) (73) (76) (77) (77) (77) (77) (77) (78) (78) (79) (80) (80) (80) (80) (80) (80) (80) (80) (80) (80)

BPd led to a statistically significant and clinically meaningful reduction in risk of disease progression or death vs PVd (HR, 0.52; 95% CI, 0.37-0.73; $P < .001$)

DREAMM-8



Dimopoulos MA, et al. *N Engl J Med*. 2024;391(5):408-421.

CARTITUDE-1: Phase 1b/2 Study Design

Primary Objectives

- Phase 1b: Characterize cilta-cel safety and confirm the recommended phase 2 dose
- Phase 2: Evaluate cilta-cel efficacy

Key Eligibility Criteria

- Progressive MM per IMWG criteria
- ≥3 prior therapies or double refractory
- Prior PI, IMiD, anti-CD38 therapy
- Measurable disease
- ECOG PS ≤1

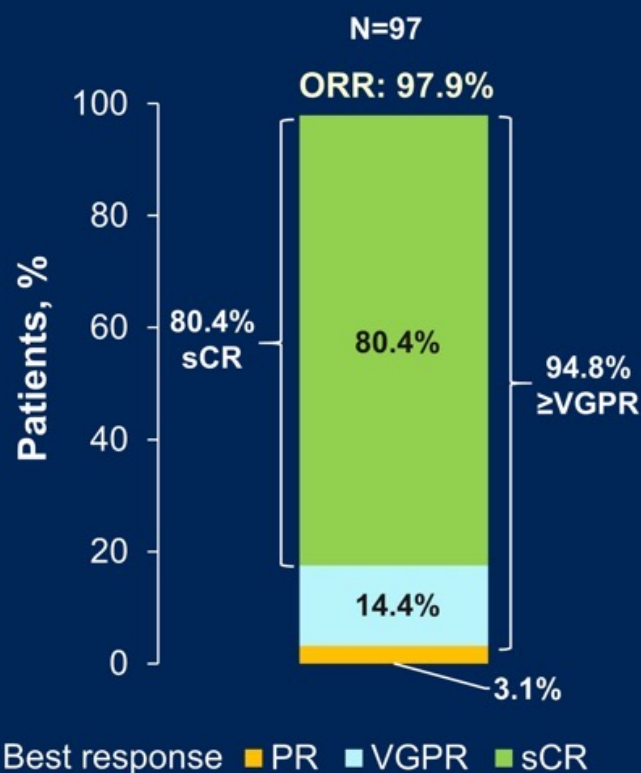
Median administered dose:
 0.71×10^6 (0.51 – 0.95×10^6) CAR+ viable T cells/kg



CAR, chimeric antigen receptor; Cy, cyclophosphamide; ECOG PS, Eastern Cooperative Oncology Group performance status; Flu, fludarabine; IMiD, immunomodulatory drug; IMWG, International Myeloma Working Group; MM, multiple myeloma; PD, pharmacodynamics; PI, proteasome inhibitor; PK, pharmacokinetics. Feb 11, 2021 data cut-off. ^aTreatment with previously used agent resulting in at least stable disease.

Usmani SZ, et al. Presented at: 2021 ASCO Annual Meeting; June 4-8, 2021; Virtual.

CARTITUDE-1: Overall Response Rate



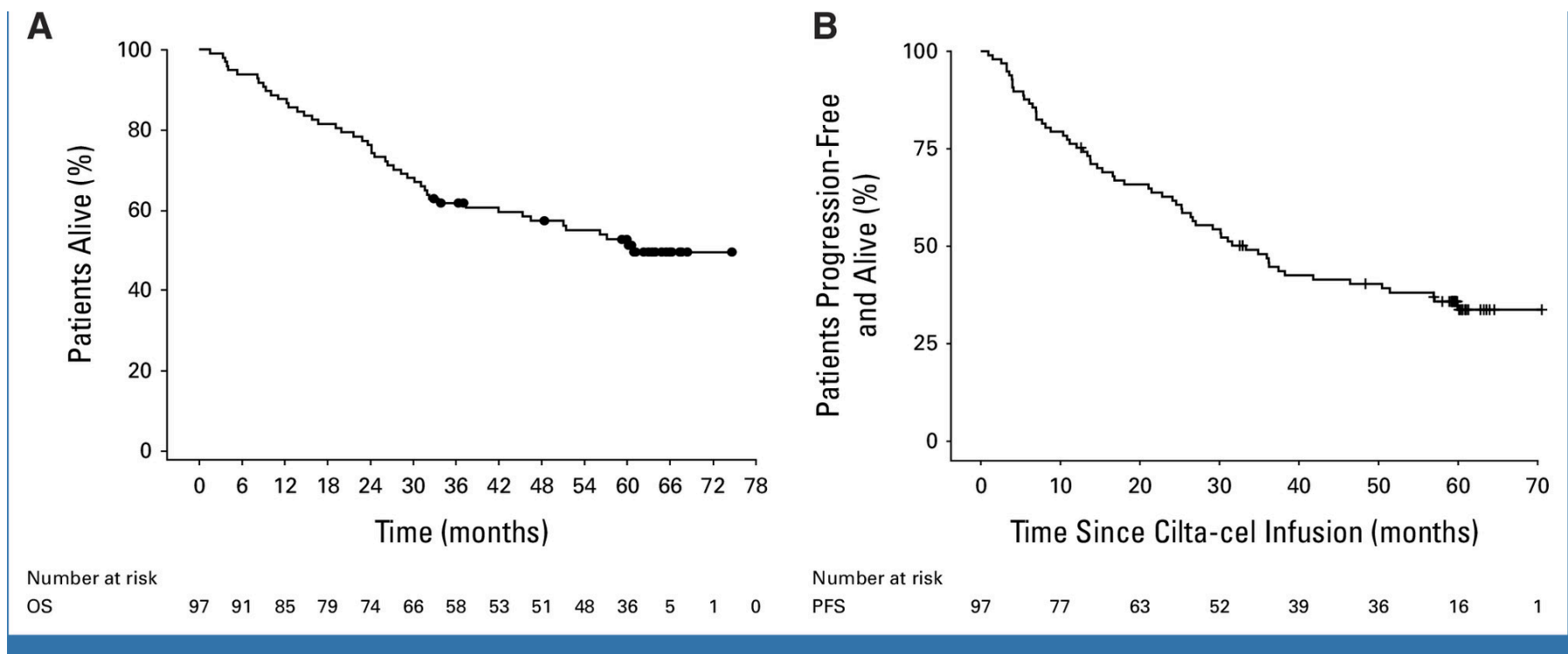
With longer follow-up, responses deepened with increasing rate of sCR

- Median time to first response: 1 month (range, 0.9–10.7)
- Median time to best response: 2.6 months (range, 0.9–15.2)
- Median time to $\geq$ CR: 2.6 months (range, 0.9–15.2)
- Median duration of response: 21.8 months (95% CI, 21.8–NE)
 - Estimated 73% of responders have not progressed or died at 12 months
 - Median duration of response not reached in patients with sCR
- Response rates were comparable (range, 95–100%) across different subgroups (eg, number of prior lines of therapy, refractoriness, extramedullary plasmacytomas, and cytogenetic risk)^a

CR, complete response; ORR, overall response rate; sCR, stringent complete response; VGPR, very good partial response. ORR assessed by independent review committee. ^aSubgroups by number of prior lines of therapy (≤ 4 , >4), refractoriness (triple-class, penta-drug), cytogenetic risk (high risk, standard risk), baseline bone marrow plasma cells ($\leq 30\%$, >30 to $<60\%$, $\geq 60\%$), baseline tumor BCMA expression ($\geq$ median, $<$ median), and baseline plasmacytomas (including extramedullary and bone-based).

Usmani SZ, et al. Presented at: 2021 ASCO Annual Meeting; June 4-8, 2021; Virtual.

Long-Term (≥ 5 -Year) Remission and Survival After Treatment With Ciltacabtagene Autoleucel in CARTITUDE-1 Patients With Relapsed/Refractory Multiple Myeloma



Jagannath S, et al. *J Clin Oncol*. 2025;43(25):2766-2771.

Overview of Approved Bispecific Antibodies in Multiple Myeloma

Teclistamab (anti-BCMA)	Talquetamab (anti-GPRC5D)	Elranatamab (anti-BCMA)	Linvoseltamab (anti-BCMA)
IgG1 Fc	IgG1 Fc	IgG2a Fc	IgG4 Fc
			

Approved: 10/25/2022 8/9/2023 8/14/2023 7/2/2025

All approved for use in adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody

Fc = fragment crystallizable (region); IgG = immunoglobulin G.

Cho SF, et al. *Front Oncol.* 2022;12:1032775. FDA. October 25, 2022. Accessed November 4, 2023. www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-teclistamab-cqyv-relapsed-or-refractory-multiple-myeloma. FDA. August 14, 2023. Accessed November 4, 2023. <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-elranatamab-bcmm-multiple-myeloma>. FDA. August 9, 2023. Accessed November 4, 2023 <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-talquetamab-tgvs-relapsed-or-refractory-multiple-myeloma>.

Teclistamab: MajesTEC-1 Trial Efficacy Results

MajesTEC-1

Efficacy:

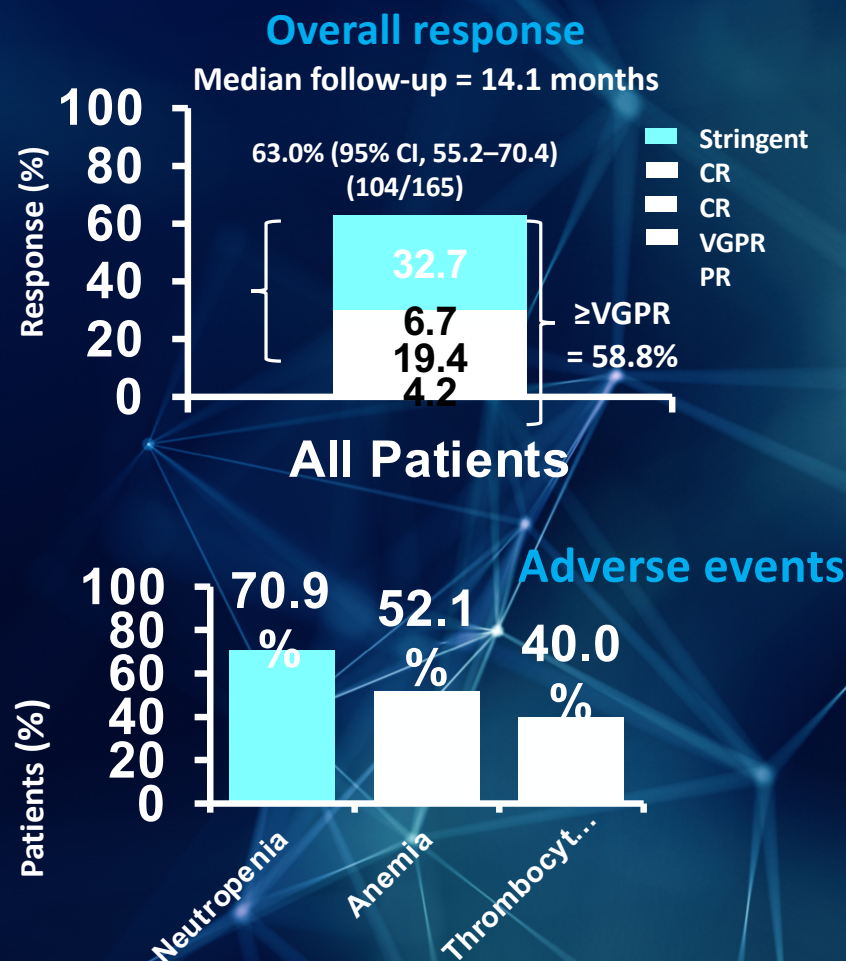
- ORR = 63.0%; 46% had CR or better
- Median DoR = 24 months
- Median PFS = 11.3 months
- Separate study (n = 38) with prior BCMA-targeted treatment, ORR = 40%

Safety:

- Cytokine release syndrome = 72.1%; grade 1 (50.3%), grade 2 (21.2%)
- 26% developed grade 3 to 4 infections
- 33% of patients had ≥ 2 CRS events

DoR = duration of response; PR = partial response; VGPR = very good partial response.

Moreau P, et al. *N Engl J Med*. 2022;387:495-505. Touzeau C, et al. *J Clin Oncol*. 2022;40(16 suppl); Abstract 8013. FDA. October 25, 2022. Accessed November 4, 2023. www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-teclistamab-cqyv-relapsed-or-refractory-multiple-myeloma. Teclistamab [Package Insert]. <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=54e0f974-ccee-44ea-9254-40e9883cee1e>. Teclistamab Prescribing Info. Drugs@FDA: FDA-Approved Drugs. Accessed October 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761291s013lbl.pdf.



Elranatamab: MagnetisMM-3 Update

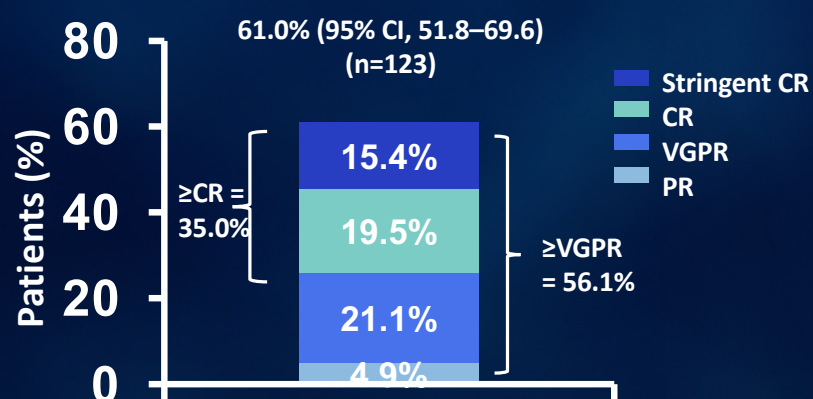
HMP Education

Oncology Learning Network

Median DOR NE (12 mo–NE)
PFS 17.2 months

Overall response

Median follow-up = 14.7 months (range 0.2–25.1 months)



TEAEs, n (%)	Any grade	Grade 3/4
Any TEAE	123 (100)	87 (70.7)
Hematologic^a		
Anemia	60 (48.8)	46 (37.4)
Neutropenia	60 (48.8)	60 (48.8)
Thrombocytopenia	38 (30.9)	29 (23.6)
Lymphopenia	38 (26.8)	31 (25.2)
Nonhematologic		
Cytokine release syndrome	71 (57.7)	0
Diarrhea	52 (42.3)	2 (1.6)
Fatigue	45 (36.6)	4 (3.3)
Decreased appetite	41 (33.3)	1 (0.8)
Hypokalemia	32 (26.0)	13 (10.6)

^aPreferred terms included in hematologic TEAEs are provided in Supplementary Table 2 of Lesokhin AM, et al.

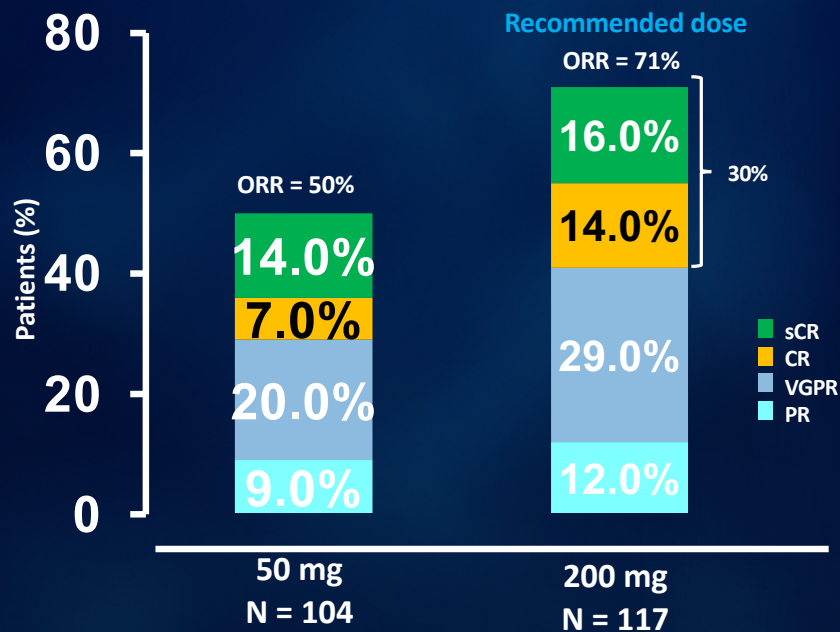
TTR = time to objective response; DOT = duration of treatment; NE = not evaluable/estimable.

Bahlis NJ, et al. Abstract 159. ASH 2022; December 10-13, 2022; New Orleans, LA. Lesokhin AM, et al. *Nat Med.* 2023;29(9):2259-2267.

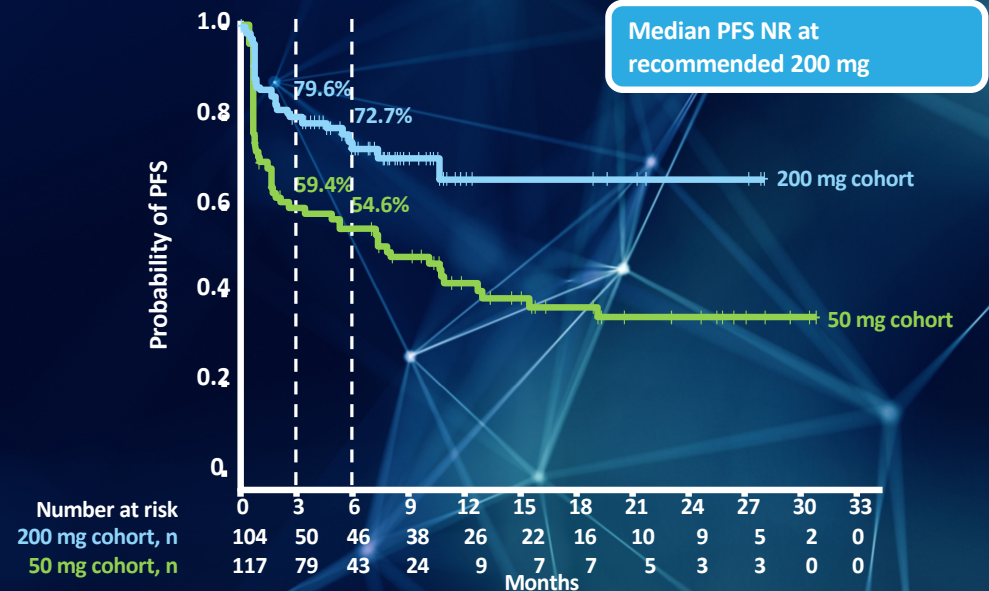
Linvoseltamab (REGN5458): LINKER-MM1

- Median DoR = 29.4 months

Overall response



PFS 50 mg and 200 mg cohorts



Richter J, et al. Poster P-04. Presented at: 2023 International Myeloma Society (IMS) Annual Meeting and Exhibition; September 27-30, 2023; Athens, Greece. IMS Annual 2023. Accessed November 4, 2023.
<https://imsannual2023.eventscribe.net/fsPopup.asp?efp=T0dKRktCQkMxMzg1OA&PosterID=604868&rnd=0.27828&mode=posterInfo>.

JNJ-5322 Trispecific Ramantamig

Ramantamig, a Novel T Cell Engaging Trispecific Antibody Targeting BCMA, GPRC5D, and CD3, in Multiple Myeloma Models

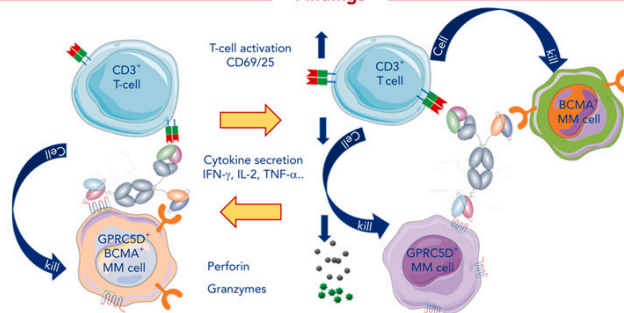
Context of Research

In multiple myeloma, cell-specific antigens are important for developing effective T-cell-engaging therapeutics, and may improve immune responses leading to cancer cell cytotoxicity and long-lasting clinical response

Aim of This Study

To evaluate ramantamig, a trispecific antibody targeting BCMA, GPRC5D and CD3 through *in vitro*, *ex vivo*, and *in vivo* models

Findings



(This image was previously presented by Pillarisetti et al in abstract form at the 65th annual meeting of the American Society of Hematology, San Diego, CA, 10 December 2023.)

Conclusions: Ramantamig binds CD3 on T cells, and BCMA and GPRC5D on myeloma cells, enhancing tumor binding due to avidity. Ramantamig induced potent T-cell mediated cytotoxicity against single and dual target-expressing myeloma cells and *in vivo* xenografts.

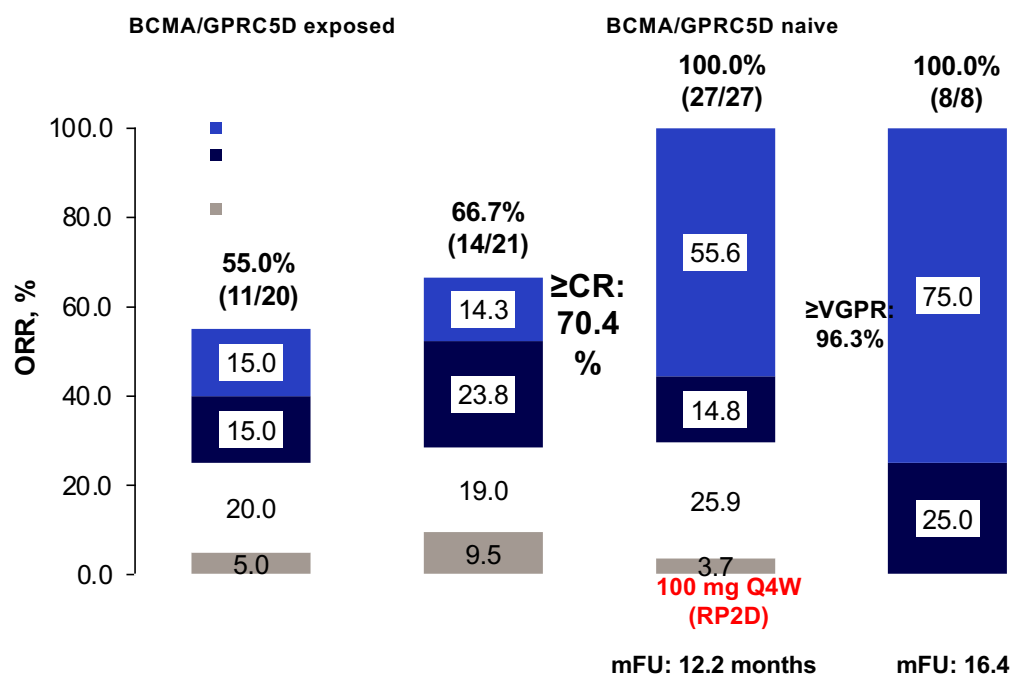
Pillarisetti et al. DOI: 10.1182/*blood*.2025030027



- Enhanced myeloma cell targeting due to “**double lock-down**” effect of binding 2 myeloma antigens
- Prevention of antigen escape
- Potential to improve GPRC5D-related safety profile
- Manageable CRS profile with only 1 step-up dose needed
- Q 4 week dosing
- CD3 portion: low-affinity binder → outpatient dosing with a lower CRS profile

CD3 = cluster of differentiation 3; Q4W = every four weeks.
Pillarisetti K, et al. *Blood*. 2026;147(8):834-847.

JNJ-5322 Trispecific: ORR in Patients Naive or Exposed to BCMA/GPRC5D Therapies



Data cut-off date: April 15, 2025. RP2D selected as 100 mg Q4W with one 5 mg SUD.

SUD = step-up dose; RP2D = recommended phase 2 dose.

van de Donk NWCJ, et al. First-in-Human Study of JNJ-79635322 (JNJ-5322)...Initial Phase 1 Results. Presented at: 2025 ASCO Annual Meeting; May 30–June 3, 2025; Chicago, IL.

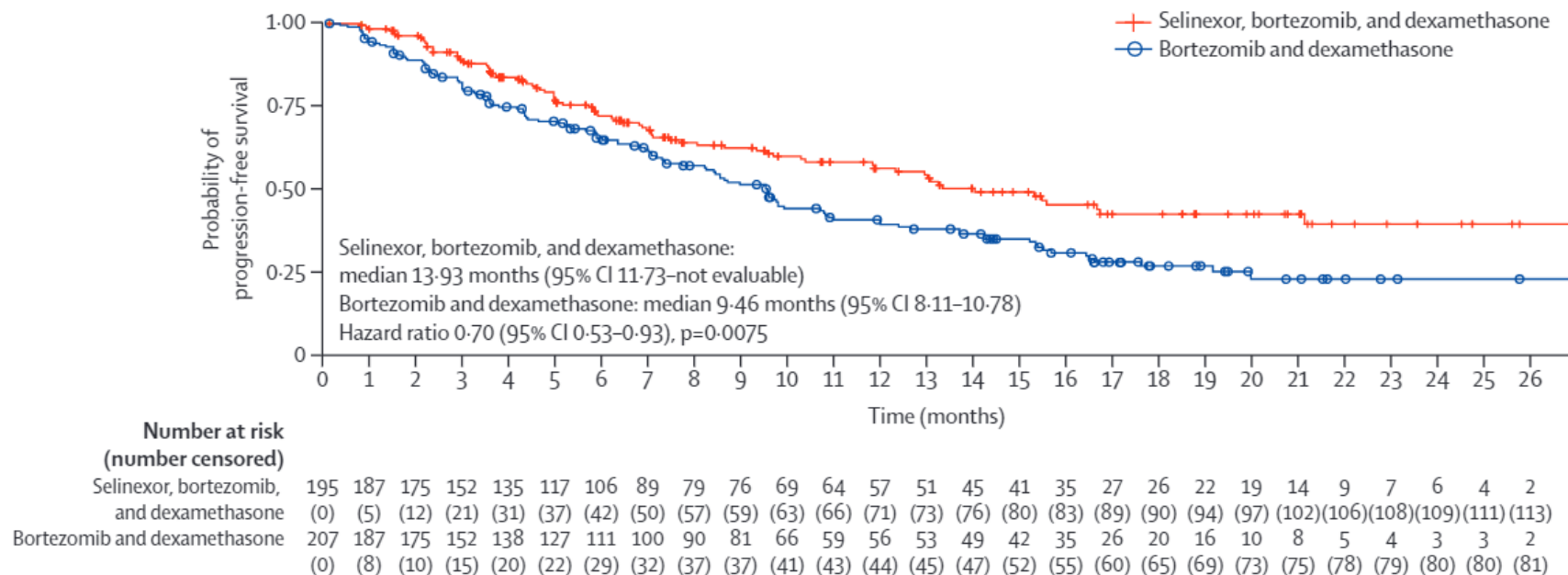
Other Novel and Emerging Therapies in R/R MM

Samantha Shenoy, MS, MSN, ACNP-BC

BOSTON Study: Prolonged PFS with SVd vs Vd

	SVd (n=195)	Vd (n=207)
Median PFS, months (95% CI)	13.93 (11.73–NE)	9.46 (8.11–10.78)
HR 0.70 (95% CI: 0.53–0.93) P=0.0075		

- Early PFS benefit observed with SVd vs Vd
- There was a 30% decrease in the risk of relapse with SVd vs Vd

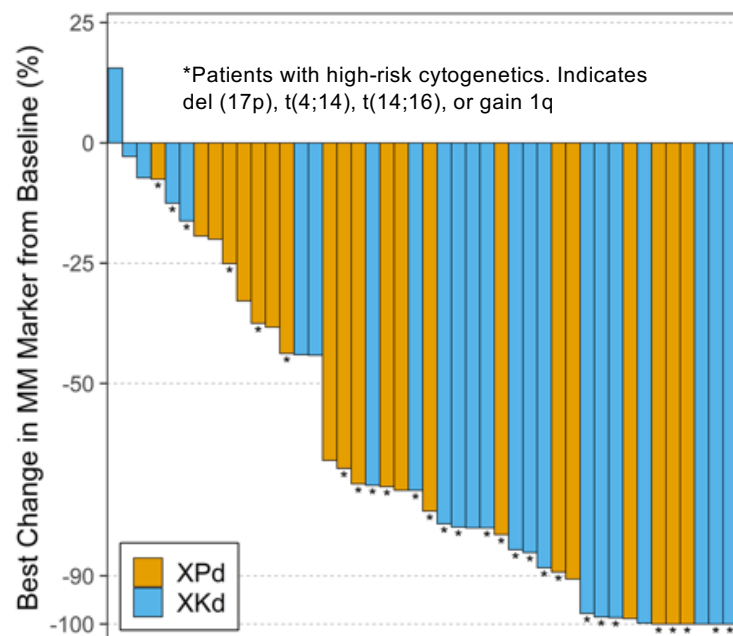


CI = confidence interval; HR = hazard ratio; NE = not evaluable; PFS = progression-free survival; SVd = selinexor/bortezomib/dexamethasone; Vd = bortezomib/dexamethasone.

Grosicki S, et al. *Lancet*. 2020;396(10262):1563-1573.

Data Demonstrated Clinical Activity of XPd and XKd in Patients Receiving Prior Anti-CD38 Therapy

Best Percentage Change in MM Marker From Baseline (N=44)



Overall Response Rate Amongst Subgroups (As of June 15, 2021)

	Subgroup	XPd	XKd
ORR, n/N (%)	All evaluable patients	12/21 (57.1)*	15/23 (65.2) [†]
	Patients with αCD38 mAb in most recent prior line	6/10 (60.0)	10/17 (58.8) [†]
	Patients naive or nonrefractory to third drug in Xd-based triplet	7/11 (63.6)*	14/22 (63.6) [†]
CBR, n/N (%)	All evaluable patients	16/21 (76.2)	17/23 (73.9)
	Patients with αCD38 mAb in most recent prior line	7/10 (70.0)	11/17 (64.7)
	Patients naive or nonrefractory to third drug in Xd-based triplet	9/11 (81.8)	16/22 (72.7)

Responses with selinexor-based triplet regimens

- 66% (29/44) of patients saw a reduction of ≥ 50% in M-protein levels
- 63% (28/44) of patients had high-risk cytogenetics
 - ❖ 63% (22/28) of these patients had reductions ≥ 50%

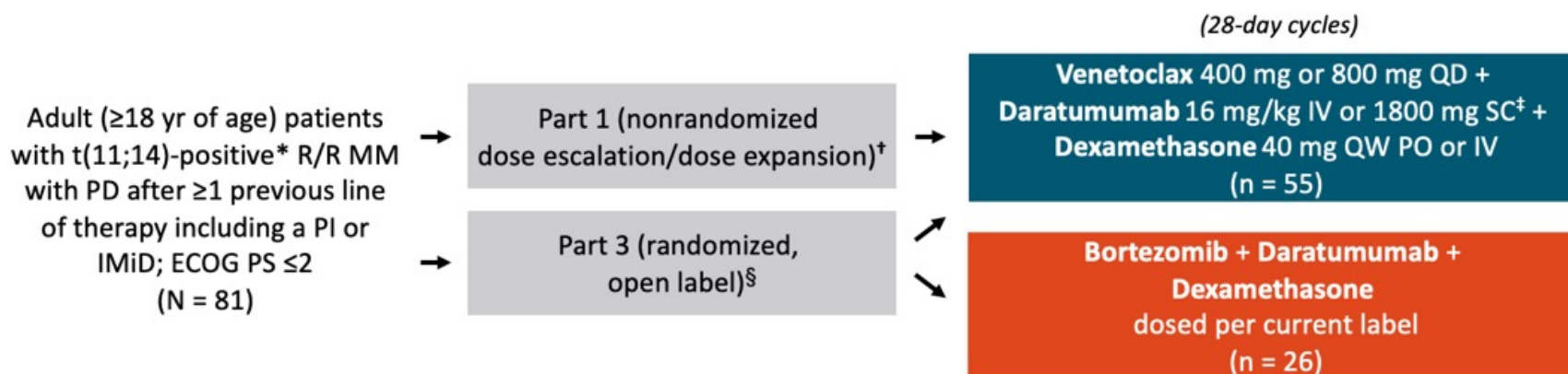
*The ORR in the XPd cohort was 11/19 (57.9%) as of 1 March 2021. The current data extract includes 2 additional patients who were enrolled on or after 24 March 2021. One additional patient in the XPd cohort responded to therapy as of 6 July 2021; [†]The ORR in the XKd cohort was 12/18 (66.7%) as of 1 March 2021. The current data extract includes 5 additional patients, who were enrolled on or after 20 January 2021. 3 of the 5 patients responded to therapy.

CBR = clinical benefit rate; mAb = monoclonal antibody; ORR = overall response rate; XKd = selinexor, carfilzomib, dexamethasone; XPd = selinexor, pomalidomide, and dexamethasone.

Lentzsch S, et al. Abstract 1651. Presented at: 63rd American Society of Hematology Annual Meeting; December 10-14, 2021; Atlanta, GA.

Update of VenDd Vs DVd in t(11;14) R/R MM: Study Design

- Multicenter dose-escalation/dose-expansion phase I/II study (data cutoff: April 25, 2023)



- **Primary endpoint:** PFS, response rates (ORR, ≥ VGPR, ≥ CR)
- **Secondary endpoints:** MRD negativity[¶]
- **Other endpoints:** safety

*As determined by central laboratory plasma cell-enriched FISH; [†]Patients from part 1 who received 400 mg or 800 mg of venetoclax were included in analysis of part 3; [‡]Cycles 1–2: D1, 8, 15, 22; cycles 3–6: D1, 15; cycle 7+: D1; [§]Patients stratified 4:2:5 to receive Ven400Dd, Ven800Dd, or DVd; [¶]At time of suspected sCR/CR, MRD negativity (<10⁻⁵ and <10⁻⁶) determined in BM aspirates by NGS and assessed again at 6 and 12 mo post confirmation.

FISH = fluorescence in situ hybridization; NGS = next-generation sequencing; sCR = stringent complete response.

Bahlis NJ, et al. Abstr 338. Presented at: ASH 2023; December 9-12, 2023; San Diego, CA. ClinicalTrials.gov. ID: NCT03314181. Accessed October 2025. <https://clinicaltrials.gov/study/NCT03314181>.

Update of VenDd Vs DVd in t(11;14) R/R MM: Response (Primary Endpoints)

Response, %	VenDd (n = 55)	DVd (n = 26)
ORR	96.4	65.4
sCR	40.0	11.5
CR	27.3	7.7
VGPR	25.5	19.2
PR	3.6	26.9
≥ CR	67.3	19.2

- Median f/u for survivors was longer with VenDd (30.0 mo; range: 1.0-57.6) vs DVd (17.8 mo; range: 0.0-36.0)

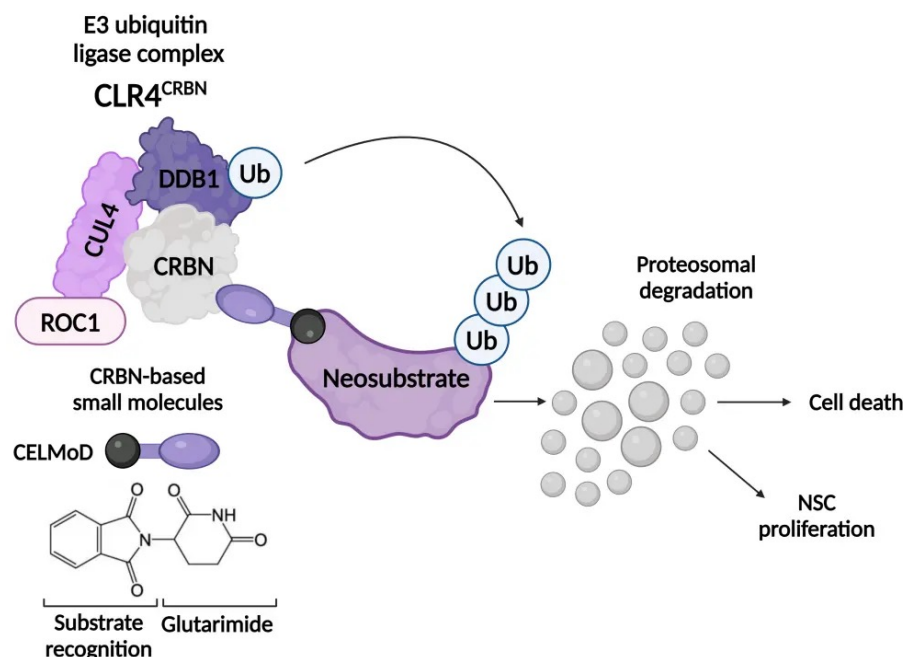
Update of VenDd Vs DVd in t(11;14) R/R MM: PFS (Primary Endpoint)

Outcome	VenDd (n = 55)	DVd (n = 26)
Median PFS, mo (95% CI)	46.1 (40.6-NE)	15.5 (7.5-NE)
12-mo PFS rate, % (95% CI)	94.2 (83.1-98.1)	59.9 (35.5-77.6)
18-mo PFS rate, % (95% CI)	87.9 (74.4-94.4)	47.6 (24.1-68.0)
24-mo PFS rate, % (95% CI)	77.7 (62.1-87.4)	39.7 (17.0-61.8)
33-mo PFS rate, % (95% CI)	74.3 (57.8-85.1)	39.7 (17.0-61.8)
Events, n	16	11

- Median PFS was longer in VenDd arm (46.1 mo) compared with DVd arm (15.5 mo)
- 33-mo PFS rate was higher in VenDd arm (74.3%) compared with DVd arm (39.7%)

CELMoD Agents: Iberdomide and Mezigdomide

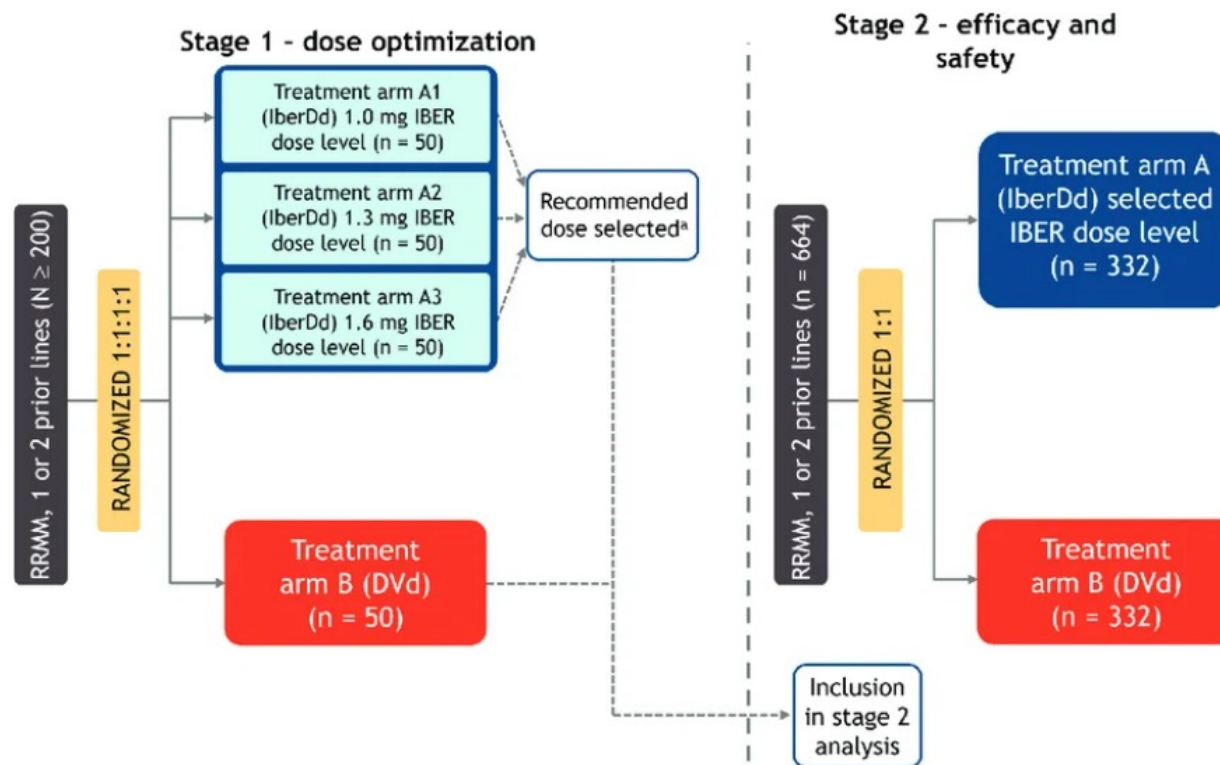
- Greater tumoricidal and immune-stimulatory effects than immunomodulatory drugs (IMiDs)
- Can overcome IMiD resistance and has synergy with standard-of-care agents in MM
- AEs: **Neutropenia**, Anemia, Thrombocytopenia, Infection, Fatigue
- DVT ppx



CELMoD = cereblon E3 ligase modulator; DVT = deep vein thrombosis; ppx = prophylaxis

Richardson PG, et al. *N Engl J Med.* 2023;389(11):1009-1022. Lonial S, et al. *Future Oncol.* 2025;21(14):1761-1769.

EXCALIBER-RRMM: a phase III trial of iberdomide, daratumumab, and dexamethasone in relapsed/refractory multiple myeloma



Mezigdomide, carfilzomib, and dexamethasone versus carfilzomib and dexamethasone in patients with relapsed or refractory multiple myeloma (SUCCESSOR-2): a phase 3, open-label, randomised controlled trial

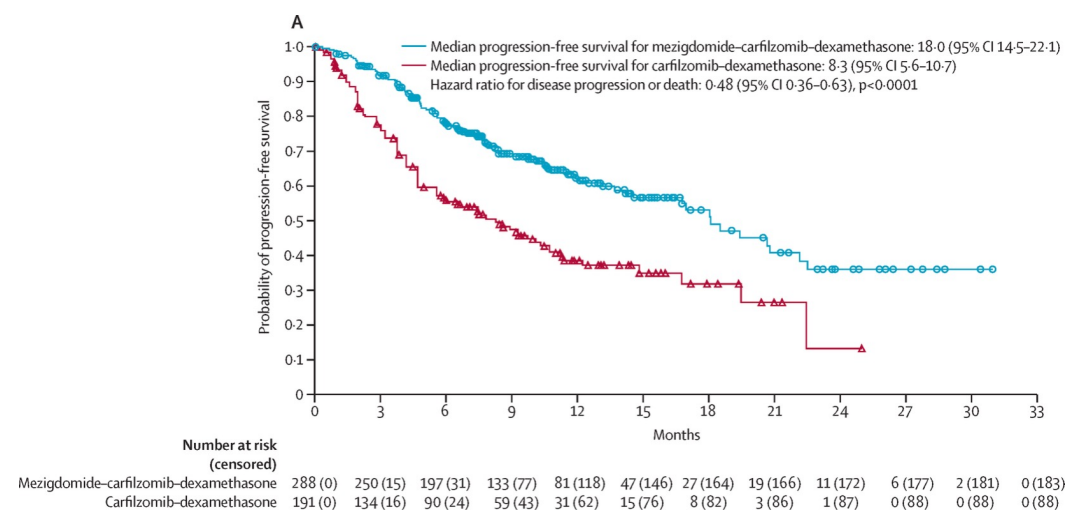


Table 3. Most common adverse events and serious adverse events

	Mezigdomide-carfilzomib-dexamethasone (n=288)		Carfilzomib-dexamethasone (n=186)	
	Any grade	Grade 3 or 4	Any grade	Grade 3
Patients with an adverse event	286 (99%)	241 (84%)	178 (96%)	105 (56%)
Haematological				
Neutropenia*	199 (69%)	176 (61%)	32 (17%)	17 (9%)
Thrombocytopenia†	174 (60%)	113 (39%)	77 (41%)	42 (23%)
Anaemia	149 (52%)	75 (26%)	66 (35%)	28 (15%)
White blood cell count decrease	67 (23%)	54 (19%)	23 (12%)	7 (4%)
Non-haematological				
Diarrhoea	112 (39%)	10 (3%)	33 (18%)	1 (1%)
Upper respiratory tract infection	79 (27%)	13 (5%)	31 (17%)	3 (2%)
Fatigue	67 (23%)	9 (3%)	39 (21%)	7 (4%)

Key Learning Points

- Although T-cell redirection therapy has become an integral part of myeloma therapy, novel agents are still needed in lines prior to and subsequent to TCR
- T(11;14) myeloma mandates the need to assess the timing and role of BCL-2 inhibition (venetoclax)
- Selinexor has improved tolerability when given once weekly as opposed to twice weekly. Early data shows improvement of T-cell fitness with Selinexor
- Utilization of non-TCR approaches can be delivered in any clinical setting and avoid the TCR-specific toxicities (ICANS, CRS, increased risk of infection)
- CELMoDs have shown efficacy in combo with known MM agents in RRMM patients, can overcome IMiD resistance and have a tolerable safety profile

Clinical Challenges and Practical Management Strategies

Samantha Shenoy, MS, MSN, ACNP-BC

SHARE Approach to Shared Decision-Making Reduces Decisional Regret, Improves Adherence



Benefits to Healthcare Professionals

- Improved quality of care delivered
- Increased patient satisfaction
- So many treatments available!

Benefits to Patients

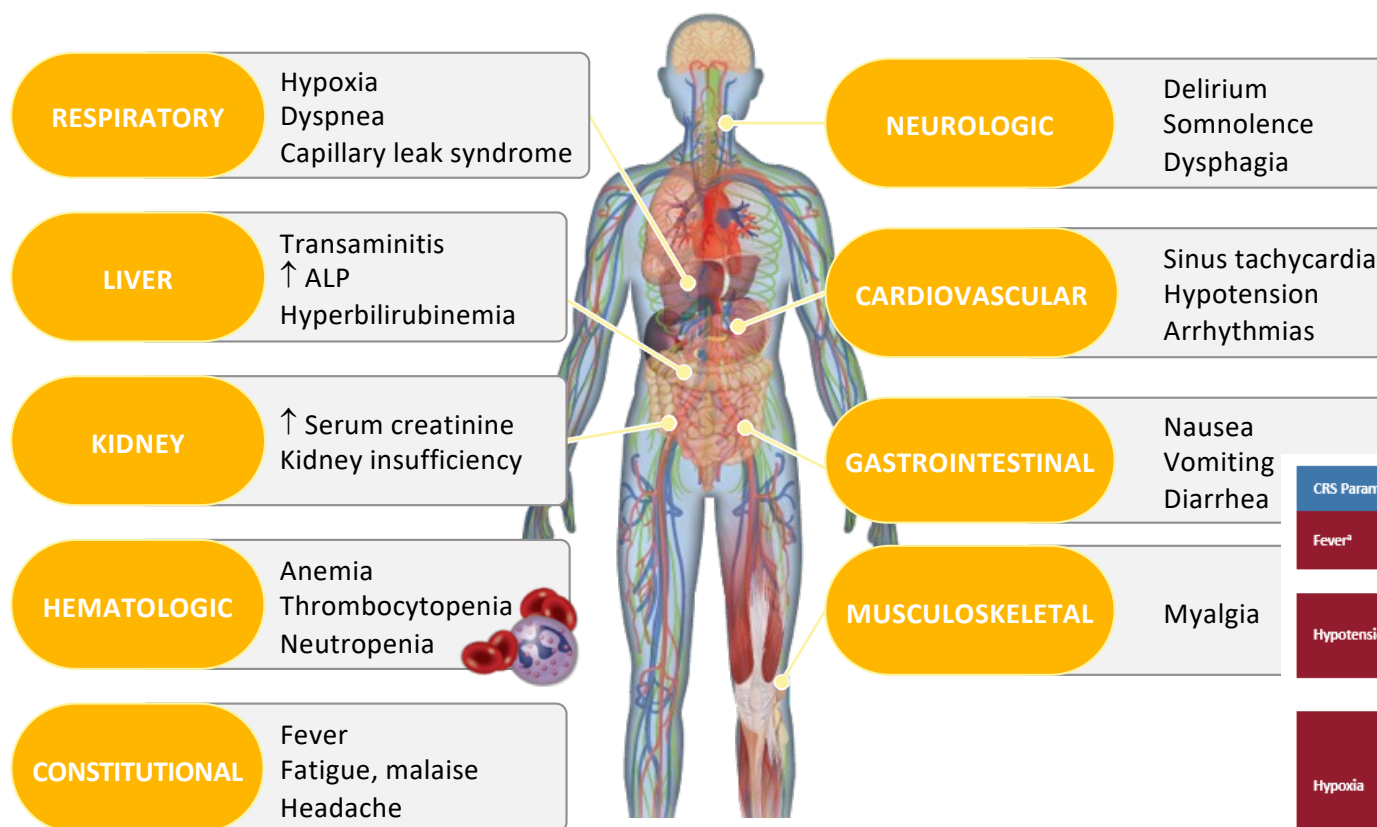
- Improved patient experience of care
- Improved patient adherence to treatment recommendations using the SHARE Approach builds a trusting and lasting relationship between healthcare professionals and patients



FREE Professional Education and Training

<https://www.ahrq.gov/health-literacy/professional-training/index.html>

ASTCT CRS Monitoring, Grading (BsAb and CART)



Monitoring for CRS

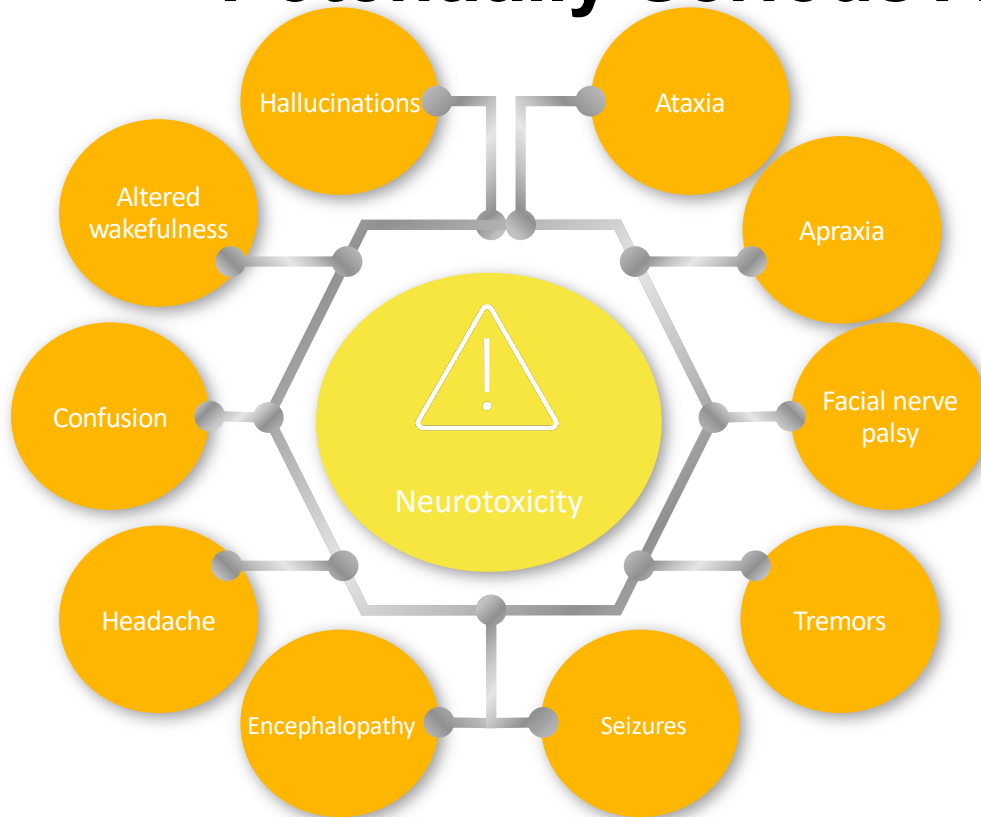
- **Vital signs (temperature, O₂ saturation, etc.)**
- **Fever is hallmark – treat**
- **Review of systems and physical exam**
- **Laboratory monitoring**
 - CRP, Ferritin, LDH

CRS Parameter	Grade 1	Grade 2	Grade 3	Grade 4
Fever^a	Temperature ≥ 38° C	Temperature ≥ 38° C	Temperature ≥ 38° C	Temperature ≥ 38° C
Hypotension	None	Not requiring vasopressors	Requiring a vasopressor with or without vasopressin	Requiring multiple vasopressors (excluding vasopressin)
Hypoxia	None	Requiring low-flow nasal cannula ^a or blow-by	Requiring high-flow nasal cannula ^a , face mask, nonrebreather mask, or Venturi mask	Requiring positive pressure (eg, CPAP, BiPAP, intubation and mechanical ventilation)

ASTCT = American Society for Transplantation and Cellular Therapy; BsAb = bispecific antibody; ALP = alkaline phosphatase; CPK = creatine phosphokinase; CRP = C-reactive protein; LDH = lactate dehydrogenase.

Oluwole OO, Davila ML. *J Leukoc Biol.* 2016;100(6):1265-1272. June CH, et al. *Science.* 2018;359(6382):1361-1365. Brudno JN, Kochenderfer JN. *Blood.* 2016;127(26):3321-3330. Brudno JN, Kochenderfer JN. *Blood Rev.* 2019;34:45-55. Shimabukuro-Vornhagen A, et al. *J Immunother Cancer.* 2018;6(1):56. Lee DW, et al. *Biol Blood Marrow Transplant.* 2019;25(4):625-638.

Immune Effector (IE-Neurotoxicity): Rare but Potentially Serious AE (BsAb and CART)



Monitoring for ICANS

- ICE screening tool 0-10, 10 no impairment
- Review of systems and physical exam
 - Focus on neurologic system
- Rule out infection
- If ICANS suspected
 - Neuroimaging (ideally MRI)
 - Diagnostic lumbar puncture for opening pressure and infection tests
- Corticosteroids are typically indicated for ICANS $\geq$ grade 2
- Patient and care partner information
- Late effects (MNT) were reported in 3% of patients, and cranial nerve palsy (CNP) events in 7% (CART-1, 4 studies).

MNT= movement and neurocognitive treatment-emergent adverse events; CNP = cranial nerve palsy; IE = immune effector; ICANS = immune effector cell-associated neurotoxicity syndrome; ICE = immune effector cell encephalopathy.

Brudno JN, Kochenderfer JN. *Blood*. 2016;127(26):3321-3330. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25(4):625-638.

Medications Can Reduce Infection Risk

Type of Infection Risk	Medication Recommendation(s)
Viral: herpes simplex (HSV/VZV); CMV	Acyclovir prophylaxis
Viral: influenza, COVID-19	Consider antiviral therapy if exposed or positive for influenza or COVID-19, per institution recommendations
Hepatitis B virus (HBV) reactivation	Entecavir prophylaxis in patients positive for chronic HBV infection (defined as serologically positive for hepatitis B surface antigen [HBsAg]) if treated with CAR T-cell therapy , bispecific antibodies, or daratumumab
Bacterial: blood, pneumonia, and urinary tract infection	Consider prophylaxis with levofloxacin
Pneumococcal infection	The Centers for Disease Control and Prevention recommends pneumococcal vaccination (1 dose of PCV20 or 1 dose of PCV15 followed by 1 dose of PPSV23 at least 1 year later); CAR T-cell therapy or ASCT: revaccinate 3 to 6 months after treatment ; bispecific: update vaccination status prior to starting therapy
<i>Pneumocystis jirovecii</i> pneumonia (PJP)	Consider prophylaxis with trimethoprim-sulfamethoxazole
Fungal infections	Consider prophylaxis with fluconazole
IgG < 400 mg/dL (general infection risk)	IVIG replacement (400 mg/kg once every 4 weeks) is indicated; IVIG replacement during CAR T-cell therapy and bispecific antibody therapy is not guided by the presence of infections^a CAR T-cell therapy: day +30 through 1 year. After 1 year continue until serum IgG > 400 mg/dL Bispecific: start at the second cycle of therapy and continue until the end of therapy or serum IgG > 400 mg/dL
Absolute neutrophil count (ANC) < 1000 cells/ μ L (general infection risk)	Consider GCSF 2 or 3 times/week (or as frequently as needed) to maintain ANC > 1000 cells/ μ L and treatment dose intensity; CAR T-cell therapy: start oral levofloxacin at 500 mg daily^b or per clinician discretion and continue through neutrophil recovery ; bispecific: consider starting with therapy and administer throughout the first cycle

^aIVIG is indicated in all patients with MM with IgG < 400 mg/dL and recurrent life-threatening infections; ^bAlternatives: cefdinir 300 mg by mouth twice a day or amoxicillin/clavulanate 875 mg by mouth twice a day.

ANC = absolute neutrophil count; BCMA = B-cell maturation antigen; CMV = cytomegalovirus; GCSF = granulocyte colony-stimulating factor; HSV = herpes simplex virus; HBV = hepatitis B virus; HBsAg = hepatitis B surface antigen; IgG = immunoglobulin G; IVIG = intravenous immunoglobulin; PCV = pneumococcal conjugate vaccine; PJP = *Pneumocystis jirovecii* pneumonia; PPSV = pneumococcal polysaccharide vaccine; VZV = varicella zoster virus. Raje NS, et al. *Lancet Haematol*. 2022;9(2):e143-e161. Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma V.2.2026. © National Comprehensive Cancer Network, Inc. 2026. All rights reserved. Accessed October 15, 2025. To view the most recent and complete version of the guideline, go online to NCCN.org. Cao W, et al. *Blood*. 2020;136(4):516-519.

Team Approach to Care Is Critical!

Assessment &

Monitoring

- Baseline & serial assessments
- Side-effect surveillance

Care Coordination

- MDs, APPs, pharmacists, labs, infusion suites

Symptom & Toxicity

Mgmt

- Peripheral neuropathy, CRS, cytopenias, infections

APP = advanced practice providers.

Patient Education

- Treatment expectations
- Self-care training

Care Navigation

- Transitions (eg, CAR-T)
- Insurance / financial

Primary Care

- Secondary Cancer Monitoring, health maintenance

Psychosocial Support

- Listening & guidance
- Family/caregiver support

Dosing Strategies for Adherence

Daratumumab

Consider reduced frequency (eg, monthly) after initial cycles in very frail/elderly patients

Isatuximab

For elderly/frail patients, consider slowing infusion rate for early doses or extending infusion to >3-4 hours if needed

Carfilzomib

Cardiac monitoring,
Once v twice weekly
Echo, EKG, NT-pro-BNP

Lenalidomide

Use a lower dose (10-15 mg/day) and/or shortened schedule in older patients, those with renal dysfunction

Selinexor

Watch for hyponatremia, thrombocytopenia, once weekly dosing with another agent

Bortezomib

Use SC over IV to reduce neuropathy; switch to weekly dosing; limit total cycles (eg, 4-6)

Dexamethasone

Reduce to 20 mg/week or lower; split dosing across 2 days if needed

Bispecific Ab

Dose reduce frequency if responders, infection, and GPRC5D skin-related toxicities

EKG = electrocardiogram; NT-pro-BNP = N-terminal pro-B-type natriuretic peptide.

Survivorship Care Plans Are Important and Recommended for Each Survivor



A Survivorship Care Plan for Each Survivor

- **Record of care**
 - Diagnosis, including diagnostic tests and results
 - Treatments received, total dosage, responses, toxicities
 - Other supportive services (psychosocial, etc)
 - Contact information for key providers
 - Point of contact for continuing care
- **Follow-up plan**
 - Ongoing health maintenance therapy/testing
 - Recommended screenings
 - Late/Long-term effects of treatments
 - Recommendations/Resources for healthy behaviors, support, etc

Institute of Medicine. Cancer Survivorship Care Planning. Fact Sheet; November 2005. Accessed April 4, 2025. <https://apos-society.org/wp-content/uploads/2016/06/factsheetcareplanning.pdf>. Salz T, et al. *Cancer*. 2014;120(5):722-730. Bilotti E, et al. *Clin J Oncol Nurs*. 2011;15 Suppl:25-40. Kurtin S. In: Tariman JD, Faiman B, eds. *Multiple Myeloma: A Textbook for Nurses*. 2nd ed. Oncology Nursing Society; 2015.

Key Learning Points

- Rapidly changing novel treatment landscape for myeloma!
- **Bispecific antibodies** act as a bridge between T cells and cancer cells to use a patient's immune system to target myeloma
- Patients receiving these agents may present with treatment-related AEs, including infections, CRS, neurotoxicity, and tumor flare
- **CRS, neurotoxicity, cytopenias, and infection** are AEs associated with Bispecific Antibodies and CAR T-cell therapy, with acute and delayed toxicities to be recognized
- Awareness of the symptoms and AEs associated with these treatments, and competence in selecting the appropriate pharmacologic management, is essential for the resolution and optimal recovery of patients
- Patient adherence, ongoing education, survivorship, and support are critical

Polling

- Participate in polling at the beginning and end of the session to be entered to win a \$100 gift card!
- Scan this QR code to see the answer choices and submit your response



The winner will be announced at the conclusion of the Q&A. Winner must be present to claim their prize.

Discussion and Live Q&A

The background is a dark blue gradient. On the right side, there is a complex network of thin, glowing blue lines connecting various points, resembling a molecular structure or a data network. The lines and points have a slight glow, giving the background a technological or scientific feel.

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- Scan this QR code to claim credit after the session
- Participants who complete the evaluation online within 30 days of the event will receive documentation of credit

