



Oncology Learning Network

Relapsed/Refractory Multiple Myeloma

**Evidence-Based
Guidelines and Essential
Strategies for Optimized
Treatment Selection
and Sequencing**

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Faculty Disclosures

- **Beth Faiman, PhD, MSN, APN-BC, AOCN[®], BMTCN[®], FAAN, FAPO:** Advisor – Janssen, Sanofi, GSK
- **Joshua Richter, MD, FACP:** Consultant – Janssen, BMS, Pfizer, Karyopharm, Sanofi, Takeda; Advisory Board – Janssen, BMS, Pfizer, Karyopharm, Sanofi, Takeda; Speakers Bureau – Janssen, BMS, Sanofi, Adaptive Biotechnologies, Pfizer

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Program Information

- Provided by HMP Education, LLC, an HMP Global Company
- Supported in part by an educational grant from Johnson & Johnson

Learning Objectives

- Evaluate the latest clinical trial data, safety and efficacy, and clinical rationale associated with novel and emerging monotherapies and combination strategies in R/R MM
- Describe the latest evidence-based guideline recommendations for treatment selection and sequencing, as well as strategies to mitigate potential toxicities associated with novel and emerging therapies for R/R MM
- Implement patient-centered interdisciplinary team strategies for precision medicine that address treatment resistance, care coordination, AE management, and overall outcomes

Pre-Event Survey

Please scan the QR code and submit your answers



Overview of MM and the Current Standard of Care in R/R MM: Clinical Practice Guidelines

Beth Faiman, PhD, MSN, APN-BC, AOCN[®], BMTCN[®], FAAN, FAPO

Pathobiology of Multiple Myeloma

Monoclonal gammopathies begin with uncontrolled division of a single plasma cell, leading to abnormal production of monoclonal (M) proteins, consisting of an antibody (immunoglobulin) or free light chain.

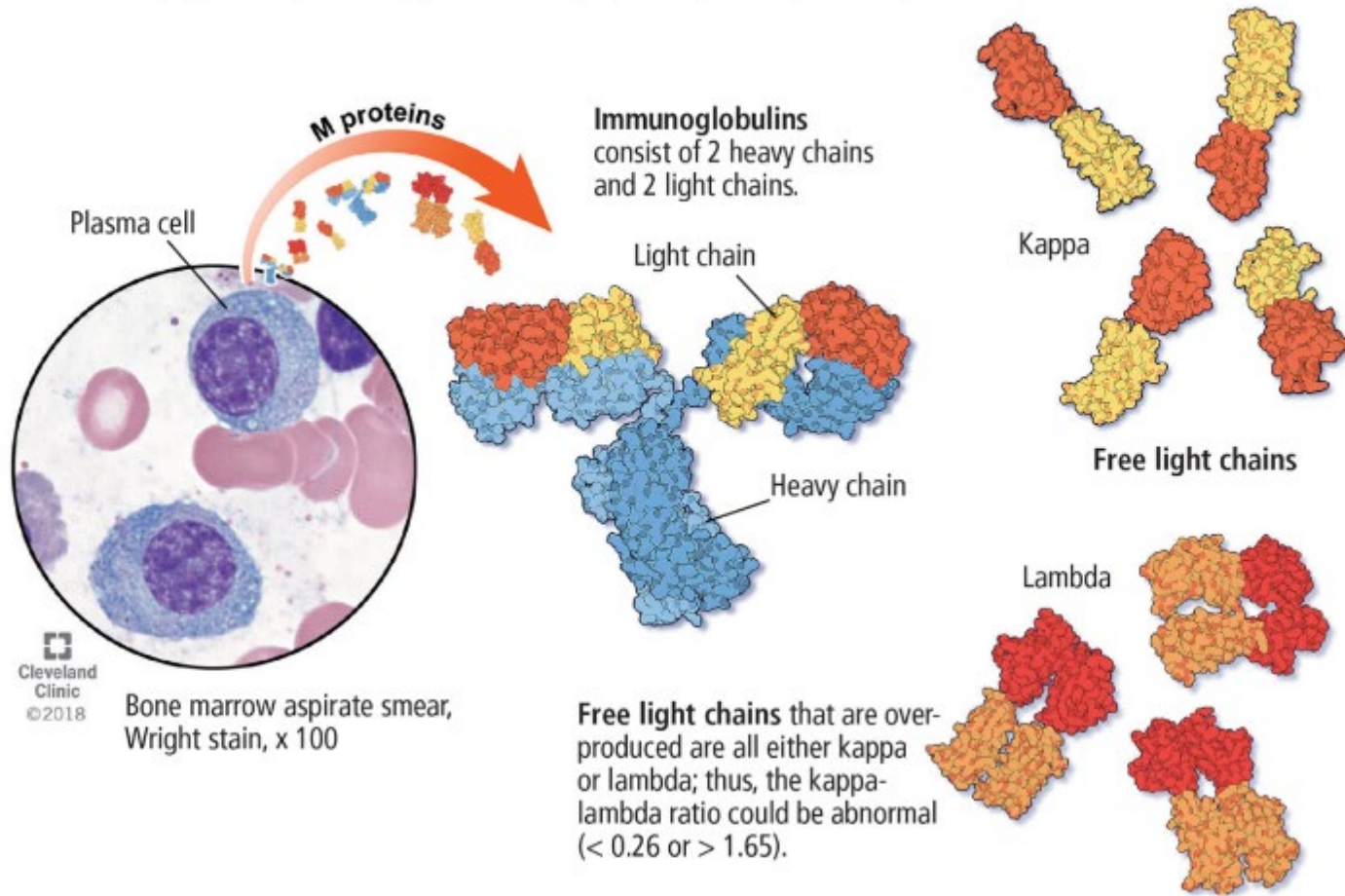
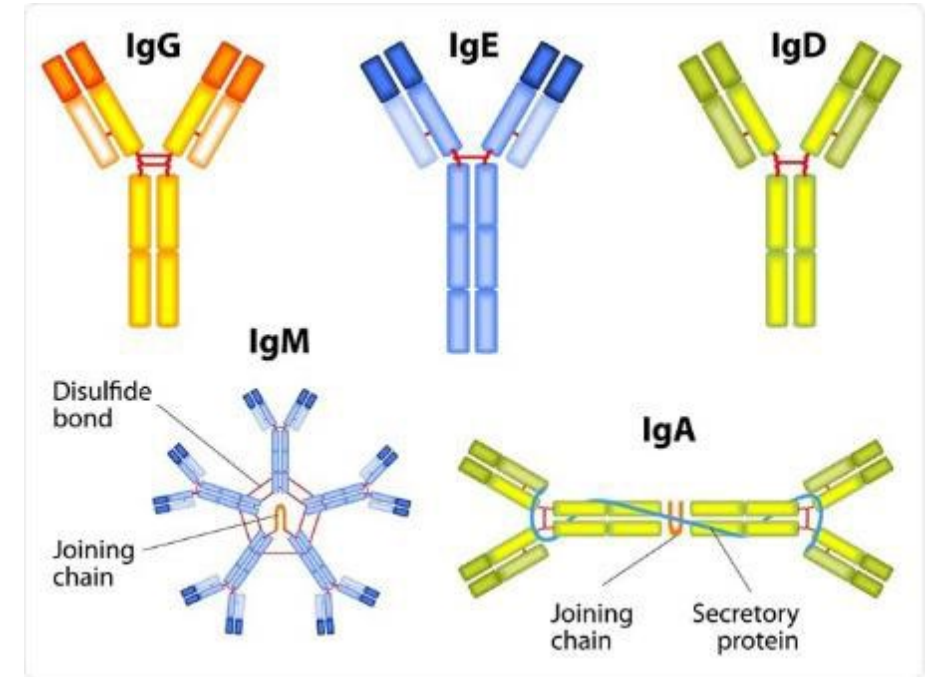


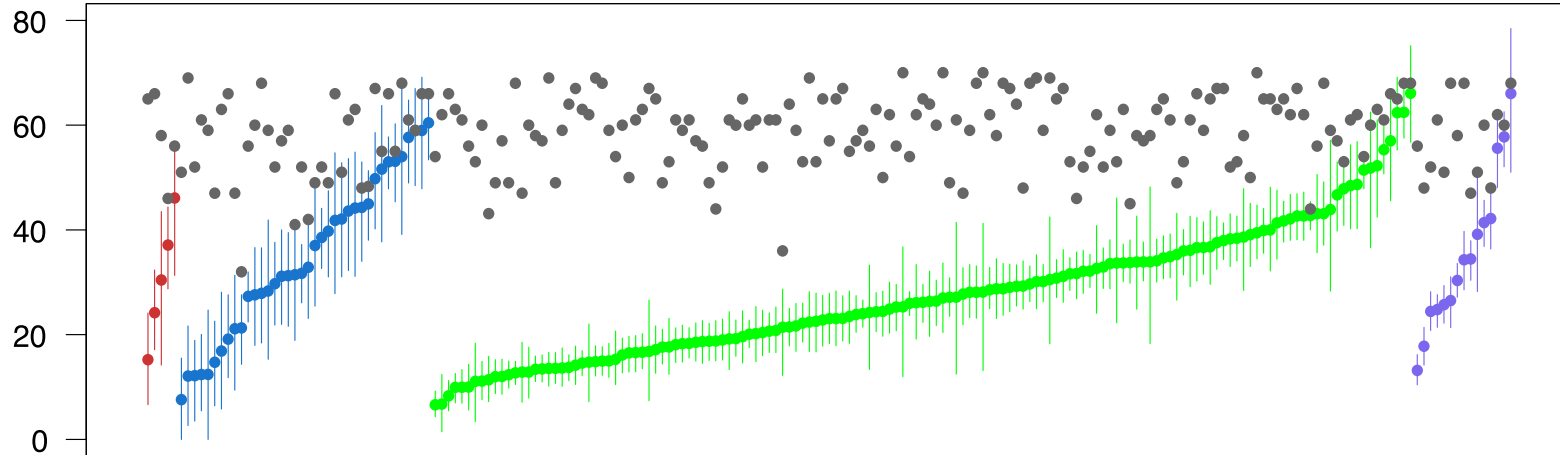
Figure 1.



Monoclonal gammopathies can lead to a number of conditions, clinically significant!

M = monoclonal.
Khouri J, et al. *Cleve Clin J Med.* 2019;86(1):39-46.

Timing of MM Initiation Is Earlier Than You May Think!



- Age at sample collection
- No IGH TRA; no HY
- IGH TRA
- HY
- IGH TRA and HY

Age of first chromosomal gain to age of sample collection was median 30 years.

Mayo Clinic



Baughn



Kumar



Rajkumar

Heidelberg



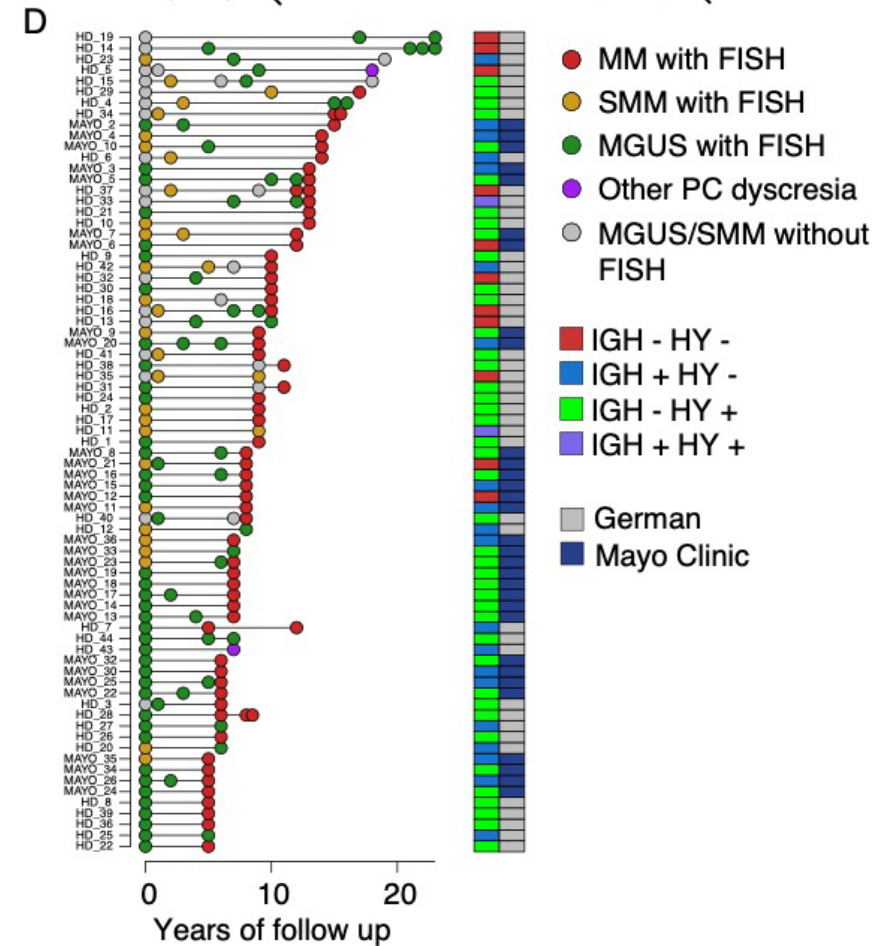
Weinhold



Raab



Poos



FISH = fluorescence in situ hybridization; HY = hyperdiploid; IGH = immunoglobulin heavy-chain; MGUS = monoclonal gammopathy of undetermined significance; SMM = smoldering myeloma; PC = plasma cell; TRA = chromosomal translocation.

Maura F, et al. *Nat Genet.* 2025;57(9):2203-2214. Rustad EH, et al. *Nat Commun.* 2020;11(1):1917. Oben B, et al. *Nat Commun.* 2021;12(1):1861. Maura F, et al. *Clin Cancer Res.* 2021;27(1):15-23. Samur MK, et al. *Blood.* 2025;145(5):520-525.

What Tests to Order to Diagnose, Monitor MM? How to Interpret?

Serum protein electrophoresis

How much monoclonal?

Serum immunofixation

What type of monoclonal?

Serum free light chains

Kappa and Lambda?

Serum immunoglobulins

IgG, IgA, IgM?

Urine studies, protein electrophoresis and immunofixation, light chains

Baseline 24-hr is the best, if proteinuria

*UA, renal dysfunction; **Ur Pro/Cr ratio***

Imaging

Bone Marrow Biopsy

Assess risk status t(4;14),14;16),
gain/amp 1q, del 17p

Test	Possible finding(s) with myeloma
CBC with differential counts	↓ Hgb, ↓ WBC, ↓ platelets
CMP and electrolytes	↑ Creat, ↑ Ca ⁺⁺ , ↑ uric acid, ↓ Alb
Serum electrophoresis with quantitative immunoglobulins (SPEP)	↑ M protein in serum, may have ↓ levels of normal antibodies
Immunofixation of serum	Identifies light/heavy chain types M protein
β ₂ m and LDH	↑ Levels (measure of tumor burden)
24-hour urine protein electrophoresis with immunofixation (UPEP)	↑ Monoclonal protein (<i>Bence Jones</i>)
BM aspirate and biopsy, FISH and cytogenetics	≥ 10% clonal plasma cells, prognosis (FISH and cytogenetics) Congo red BM stain if amyloid suspected Clonoseq ID through NGS
Low-dose whole-body CT, PET/CT or MRI	Osteolytic lesions, osteoporosis, EM disease

β₂m = β₂ microglobulin; BM = bone marrow; CBC = complete blood count; CMP = complete metabolic panel; CT = computed tomography; EM = extramedullary; Hgb = hemoglobin; LDH = lactate dehydrogenase; MRI = magnetic resonance imaging; PET = positron emission tomography; SPEP = serum protein electrophoresis; sFLV = serum free light chain; NGS = next generation sequencing; UA = urinalysis; UPEP = urine protein electrophoresis; WBC = white blood cell.

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. Faiman B. *Clin Lymphoma Myeloma Leuk*. 2014;14:436-440. Hillengass J, et al. *Lancet Oncol*. 2019;20(6):e302-e312. Terpos E, et al. *Leukemia*. 2023;37(6):1175-1185.

Minimal/Measurable Residual Disease in MM

NCCN Guideline v2.2026 for Multiple Myeloma says “Consider MRD testing as indicated for prognostication after shared decision with patient” per follow-up/surveillance (MYEL-4) and have MRD response criteria (MYEL-E), including footnote a, which says, “...information on MRD after each treatment stage is recommended (eg, after induction, high-dose therapy/autologous stem cell transplants (ASCT), consolidation, maintenance). MRD tests should be initiated only at the time of suspected complete response.”

Residual Sequences Detected

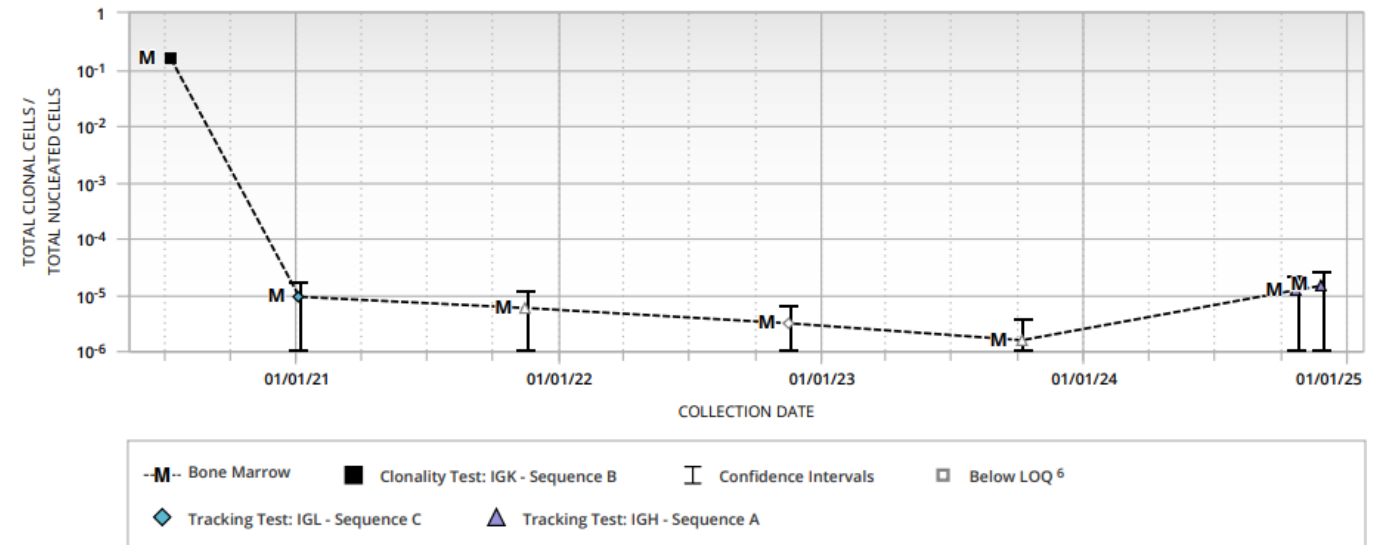
ESTIMATED MRD VALUE:
14 residual clonal cells per million nucleated cells (Range: >0 - 25)
Total nucleated cells evaluated from this sample: 1,155,745

The MRD range presented above represents the 95% confidence interval for the measured number of residual clonal sequences per million nucleated cells. Details for each identified dominant sequence from this sample are provided on subsequent pages of this report.

RESULTS SUMMARY

- Genomic DNA was extracted from a fresh bone marrow sample.
 - 3 of the 3 dominant sequences identified in a diagnostic sample from this patient were still present in this current sample.
 - 17 copies of the dominant sequence determining the MRD result (IGH Sequence A) were observed out of 1,155,745 total nucleated cells evaluated from this sample.
- ▶ **The results obtained from this assay should always be used in combination with the clinical examination, patient medical history, and other findings.**

SAMPLE-LEVEL MRD TRACKING *(shows only the sequence determining the MRD result for each time point)*



The number of clonal cells may vary by sample type. As such, changes in clonal cell values over time are best compared using the same sample type, indicated by connecting lines.

MRD = measurable residual disease; ASCT = autologous stem cell transplant.

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Multiple Myeloma Continuum: Active MM

ACTIVE MM

CRAB Criteria
Calcium elevation
Renal dysfunction
Anemia
Bone lesions

SMM

Low risk
Risk of progression: \approx 1% per year

High-risk: Likely to progress
to active MM within 2 years

M-spike \geq 2 g/dL
Serum Free Light Chain Assay
(kappa/lambda ratio \geq 20)
Bone marrow \geq 20% PCs

SLiM/MDEs

Bone marrow \geq 60% PC
Serum Free Light Chain Assay
(kappa/lambda ratio \geq 100)
MRI \geq 1 focal lesion \geq 5 mm

MGUS

Spike on SPEP/UPEP
Abnormal free light test
Bone marrow $<$ 10% PCs

MGCS

PREMALIGNANT CONDITIONS
MONITOR

CLINICAL TRIAL

TREAT

CRAB = calcium elevation, renal dysfunction, anemia, bone lesions; M-spike = monoclonal spike; MDE = myeloma-defining event; MGRS = monoclonal gammopathy of renal significance; SLiM = PC \geq sixty, light chain ratio, focal lesions by MRI.

Hillengass J, et al. *Lancet Oncol.* 2019;20(6):e302-e312. Ludwig H, et al. *eClinicalMedicine.* 2023;58:101910. 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.

Important to Risk Stratify: IMS/IMWG Consensus on High-Risk Myeloma Definition

Del17p

in more than 20% of sorted plasma cells

TP53 mut

(no threshold VAF)

**Biallelic
Del(1p32)**

2 among

t(4;14) or t(14;16) or t(14;20)

Gain/amp 1q

Monoallelic del(1p32)

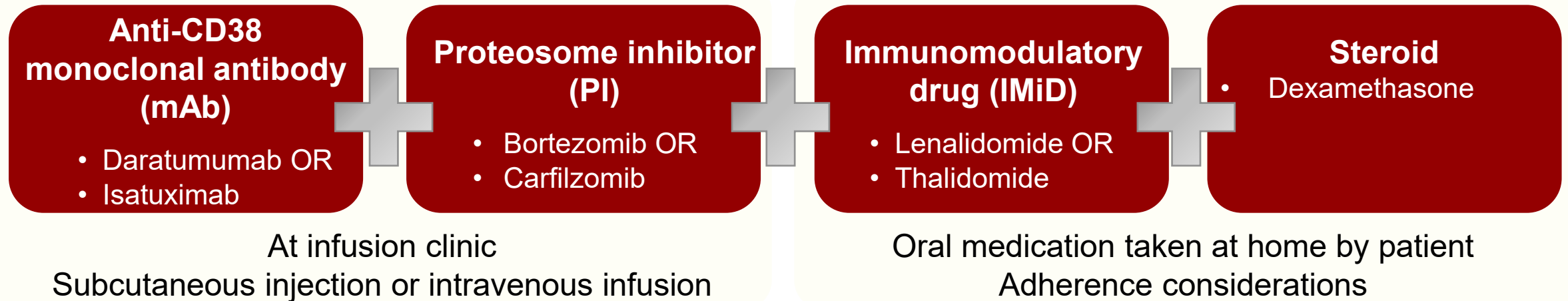
**β 2M \geq 5.5mg/L
(if creat $<$ 1.2mg/dL)**

IMS = International Myeloma Society; IMWG = International Myeloma Working Group; VAF = variant allele frequency.

Avet-Loiseau H, et al. *J Clin Oncol.* 2025;43(24):2739-2751.

Induction Standard of Care: Frontline Quadruplet

QUADRUPLET THERAPY is preferred for nearly all patients newly diagnosed with myeloma
HIGH MRD negative rates, deep and durable responses regardless of regimen (TE/TIE)



Supportive medication:

- **Antiviral prophylaxis** (eg, acyclovir or valacyclovir) to prevent viral infections, particularly shingles
- **Aspirin or other anticoagulant therapy** to reduce the risk of blood clots from IMiDs or carfilzomib
- **Bone-strengthening agents** (eg, zoledronic acid, denosumab) to strengthen bones and protect against fractures

TE = transplant eligible; TIE = transplant ineligible; mAb = monoclonal antibody; PI = proteasome inhibitor; IMiD = immunomodulatory drug. 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](https://www.nccn.org).

Don't Forget Important Supportive Considerations

Consideration	Intervention
Skeletal complications	Bone modifying agents PT exercises, RT for defined lesions, weightlifting restrictions?
Cardiac issues	Consider amyloidosis, hypertension with carfilzomib
VTE risk	ASA or anticoagulation Exercise, avoid immobility, hydration
Myelosuppression	Rule out vitamin deficiencies (B12, ferritin, iron + TIBC, B6), neutropenic prophylaxis and education
Gastrointestinal	Monitor diarrhea, constipation; Nausea prophylaxis (PIs, selinexor)
Renal	Avoid NSAIDs, Hydration, Monitor UPEP, 24-hour urine

VTE = venous thromboembolic event; ASA = aspirin; PT = physical therapy; RT = radiation therapy; TIBC = total iron binding capacity; NSAID = non-steroidal anti-inflammatory drug.

Faiman B, Tariman JD, eds. *Multiple Myeloma: A Textbook for Nurses*. 3rd ed. Oncology Nursing Society; 2021:352. Faiman B, et al. *Clin J Oncol Nurs*. 2017;21(5 Suppl):19-36. 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](https://www.nccn.org).

CASE DISCUSSION

CARLOS*

- 61-year-old w/ low back pain, ibuprofen, pain persisted
- Lumbar MRI – collapse L4, 10mm lesion; skeletal survey widespread lesions
- Bone marrow biopsy 70% kappa plasmacytosis
- Normal FISH, XY

CBC and CMP

CBC: Hgb (10.3 g/dL)
CMP calcium (11.1 mg/dL)
Cr 1.9 mg/dL and elevated globulin (6.9 g/dL)
PSA normal at 0.7 ng/mL

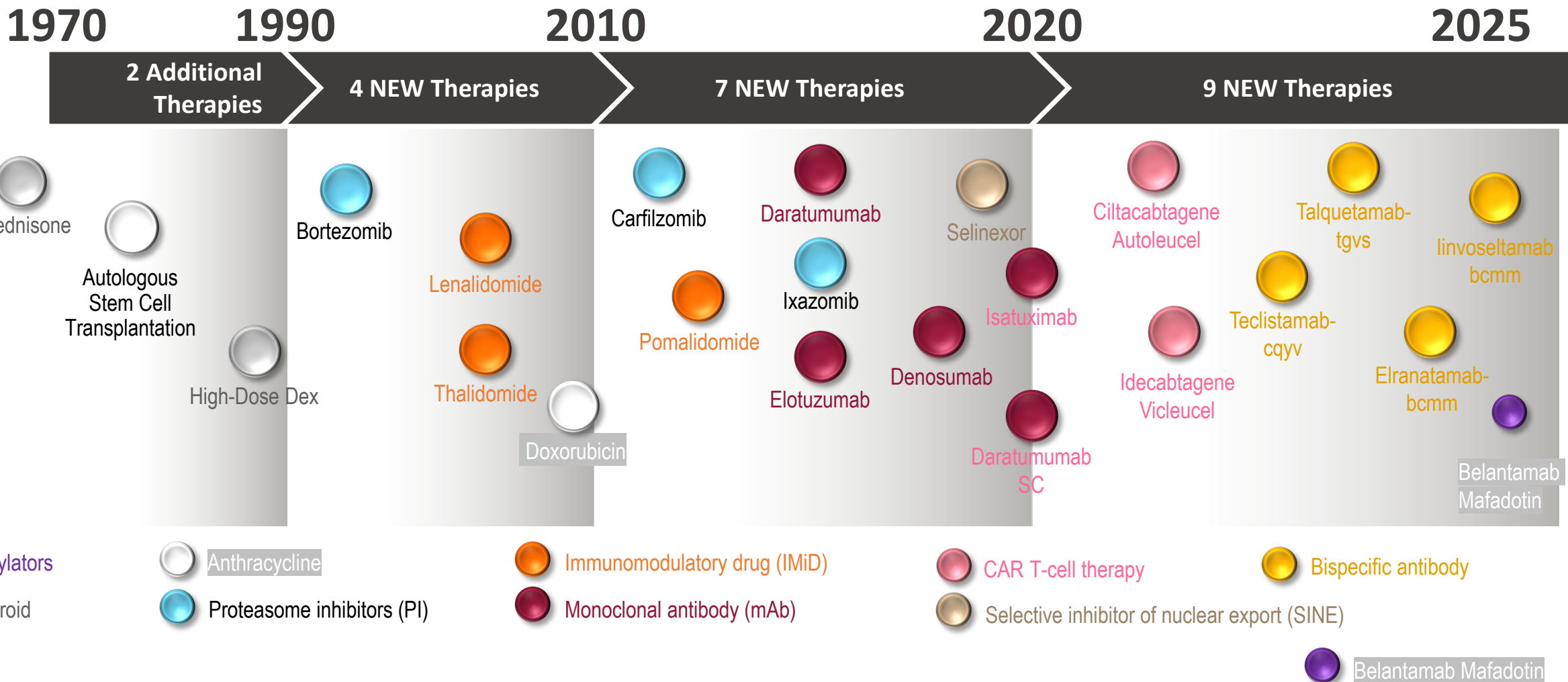
SPEP/sFLc

3.1 g/dL IgG kappa; kFS 2800



Treatment: Dara+VRd+ASCT
R (lenalidomide) maintenance
Declined clinical trial
Relapsed after 14 months

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



CAR = chimeric antigen receptor; Dex = dexamethasone; SINE = selective inhibitor of nuclear export.

Prescribing Information. Drugs@FDA: FDA-Approved Drugs. Accessed September 2025. www.accessdata.fda.gov/scripts/cder/daf/.

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

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

*If the above measures are unavailable.

FLC = free light chain; cPC = clonal plasma cells; FDG = fluorodeoxyglucose.

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

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

National Comprehensive Cancer Network® (NCCN®)

NCCN Guidelines Version 2.2026 Multiple Myeloma

Drug Class	FDA-Approved Myeloma Therapies	Common Combinations
PI	Bortezomib	VRd, Vd, VCd
	Carfilzomib	KRd, Kd, DKd, Isa-Kd
	Ixazomib	IRd
IMiD	Lenalidomide	VRd, Rd, KRd, DRd, ERd, IRd
	Pomalidomide ^a	Pd, ^a DPd, Epd, ^a PCd ^b
Anti-CD38	Daratumumab	DRd, DVd, DPd, DVMp, DKd
	Isatuximab	Isa-Pd, ^a Isa-Kd
Anti-SLAMF7	Elotuzumab	ERd, Epd ^a
XPO1 inhibitor	Selinexor	Xd, XVd, DXd, ^b XKd, ^b XPd ^b
CAR T	Idecabtagene vicleucel – 2 prior lines	
	Ciltacabtagene autoleucel – 1 prior line	
New agents or regimens in clinical trials are always an option		

THERAPY FOR PREVIOUSLY TREATED MULTIPLE MYELOMA Relapsed/Refractory Disease After 1–3 Prior Therapies	
Other Recommended	
Elotuzumab/Lenalidomide/Dexamethasone (category 1) Ixazomib/Lenalidomide/Dexamethasone (category 1) Selinexor/Bortezomib/Dexamethasone (category 1) Bortezomib/Cyclophosphamide/Dexamethasone Bortezomib/Lenalidomide/Dexamethasone Carfilzomib/Cyclophosphamide/Dexamethasone Daratumumab/Cyclophosphamide/Bortezomib/Dexamethasone Daratumumab/Carfilzomib/Pomalidomide/Dexamethasone Elotuzumab/Bortezomib/Dexamethasone Ixazomib/Cyclophosphamide/Dexamethasone Lenalidomide/Cyclophosphamide/Dexamethasone	After two prior therapies including an IMiD and a PI and disease progression on/within 60 days of completion of last therapy ▶ Pomalidomide/Cyclophosphamide/Dexamethasone (category 1)
Useful in Certain Circumstances	
Bortezomib/Dexamethasone (category 1) Bortezomib/Liposomal Doxorubicin/Dexamethasone (category 1) Lenalidomide/Dexamethasone (category 1) Carfilzomib/Cyclophosphamide/Thalidomide/Dexamethasone Carfilzomib/Dexamethasone (category 1) Selinexor/Carfilzomib/Dexamethasone Selinexor/Daratumumab/Dexamethasone Venetoclax/Dexamethasone ± Daratumumab or PI only (t[11;14])	After two prior therapies including an IMiD and a PI and with disease progression on/within 60 days of completion of last therapy ▶ Pomalidomide/Dexamethasone (category 1) ▶ Selinexor/Pomalidomide/Dexamethasone For treatment of aggressive MM ▶ Dexamethasone/Cyclophosphamide/Etoposide/Cisplatin (DCEP) ▶ Dexamethasone/Thalidomide/Cisplatin/Doxorubicin/Cyclophosphamide/Etoposide (DT-PACE) ± Bortezomib (VTD-PACE) After at least three prior therapies including a PI and an IMiD or are double-refractory to a PI and an IMiD ▶ Daratumumab

^a2 or more prior therapies; ^bOff-label, not currently FDA-approved.

C = cyclophosphamide; D = daratumumab; d = dexamethasone; E = elotuzumab; I = ixazomib; Isa = isatuximab; K = carfilzomib; M = melphalan; P = pomalidomide; p = prednisone; R = lenalidomide; SLAMF7 = surface antigen CD319; SQ = subcutaneous; V = bortezomib; X = selinexor; XPO1 = export 1 receptor.

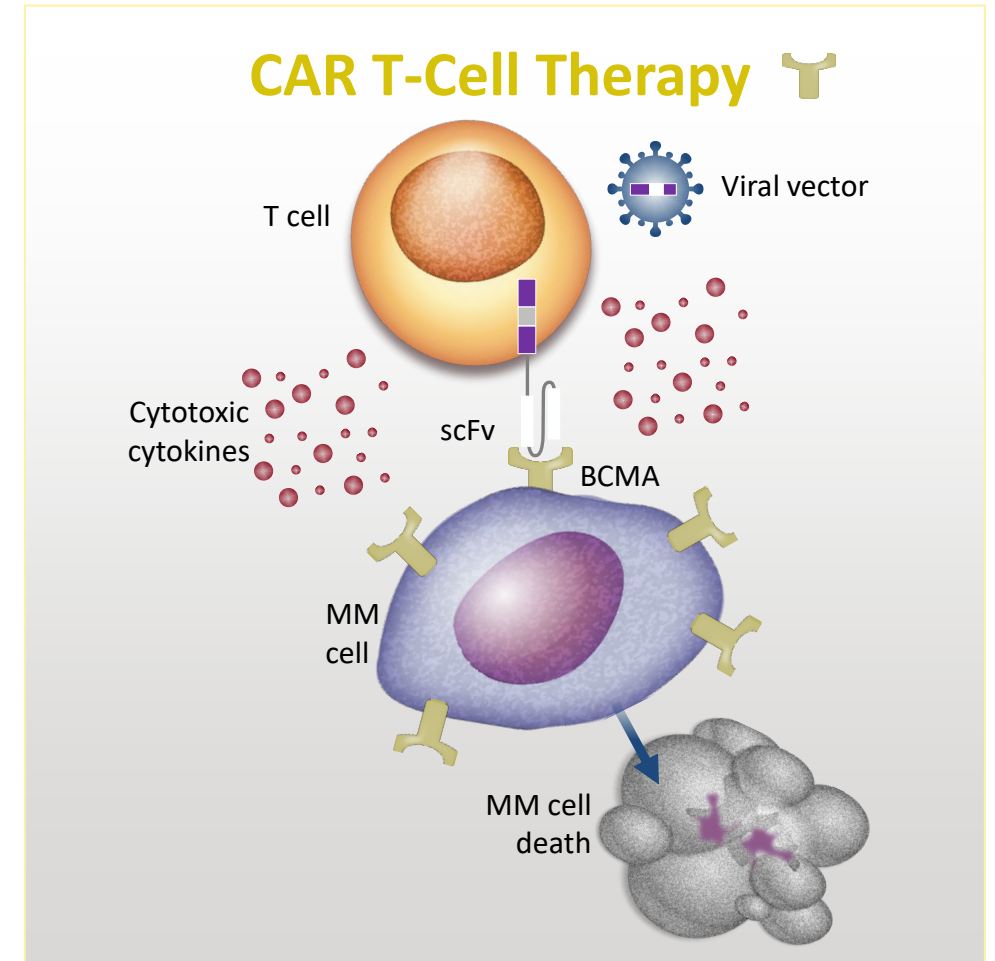
Rajkumar SV. 2024 Myeloma Algorithm. Clinical Care Options. December 27, 2023. Accessed April 4, 2025. <https://clinicaloptions.com/activities/oncology/2024-mm-algorithm/18440-26989/info>. Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma V.2.2026. © 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. Noonan K, et al. *J Adv Pract Oncol.* 2022;13(suppl 4):15-21. Steinbach M, et al. *J Adv Pract Oncol.* 2022;13(suppl 4):23-30. Moreau P, et al. *Lancet Oncol.* 2021;22(3):e105-e118. O'Donnell EK, et al. *Br J Haematol.* 2018;182(2):222-230. Mo CC, et al. *EJHaem.* 2023;4(3):792-810.

What Is Concerning about Carlos's Case?

- Earlier relapse than expected with standard risk disease
- What would you recommend, CART vs Clinical trial vs standard options?

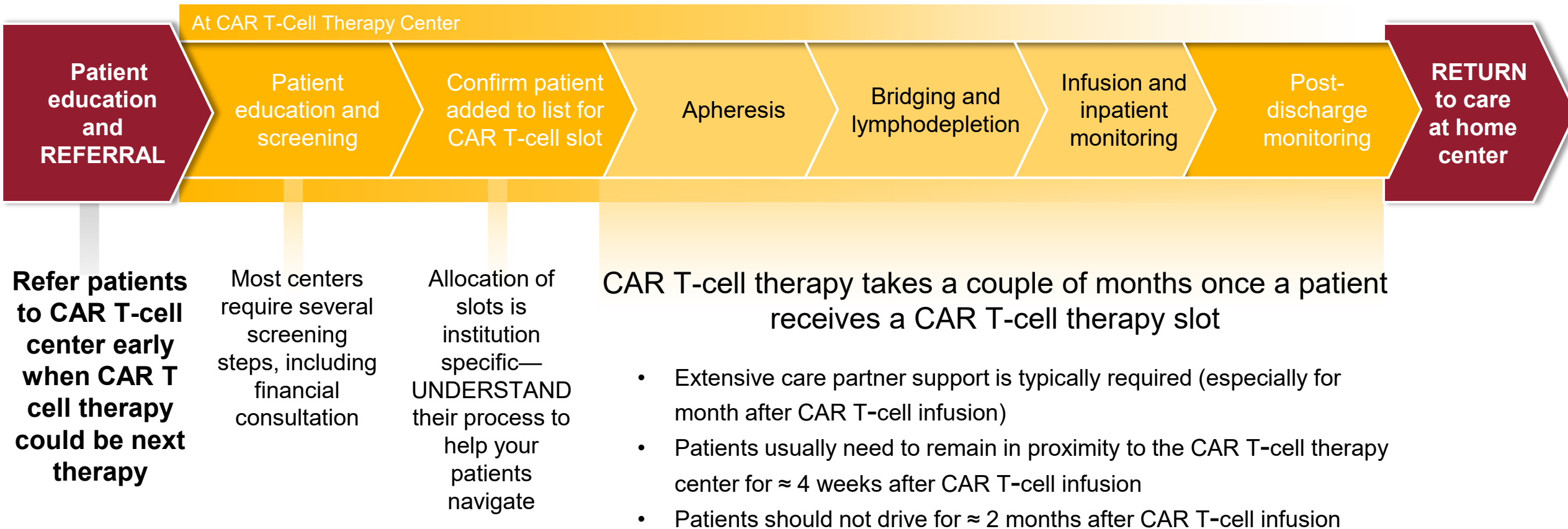
BCMA Is the Target for FDA-Approved CAR T-Cell Therapies

- 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



BCMA = B-cell maturation antigen; scFv = single chain fragment variable; TNF = tumor necrosis factor.
Shah N, et al. *Leukemia*. 2020;34(4):985-1005. Yu B, et al. *J Hematol Oncol*. 2020;13(1):125.

CAR T-Cell Therapy: A Process



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/
hypogammaglobulinemia



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!**

Emerging Role of BCMA in R/R MM

Joshua Richter, MD, FACP


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 kills and eliminates myeloma cells by a multi-targeted mechanism
- Mafodotin delivered to BCMA-expressing cells inhibits microtubule polymerization, inducing immune-independent apoptosis through 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

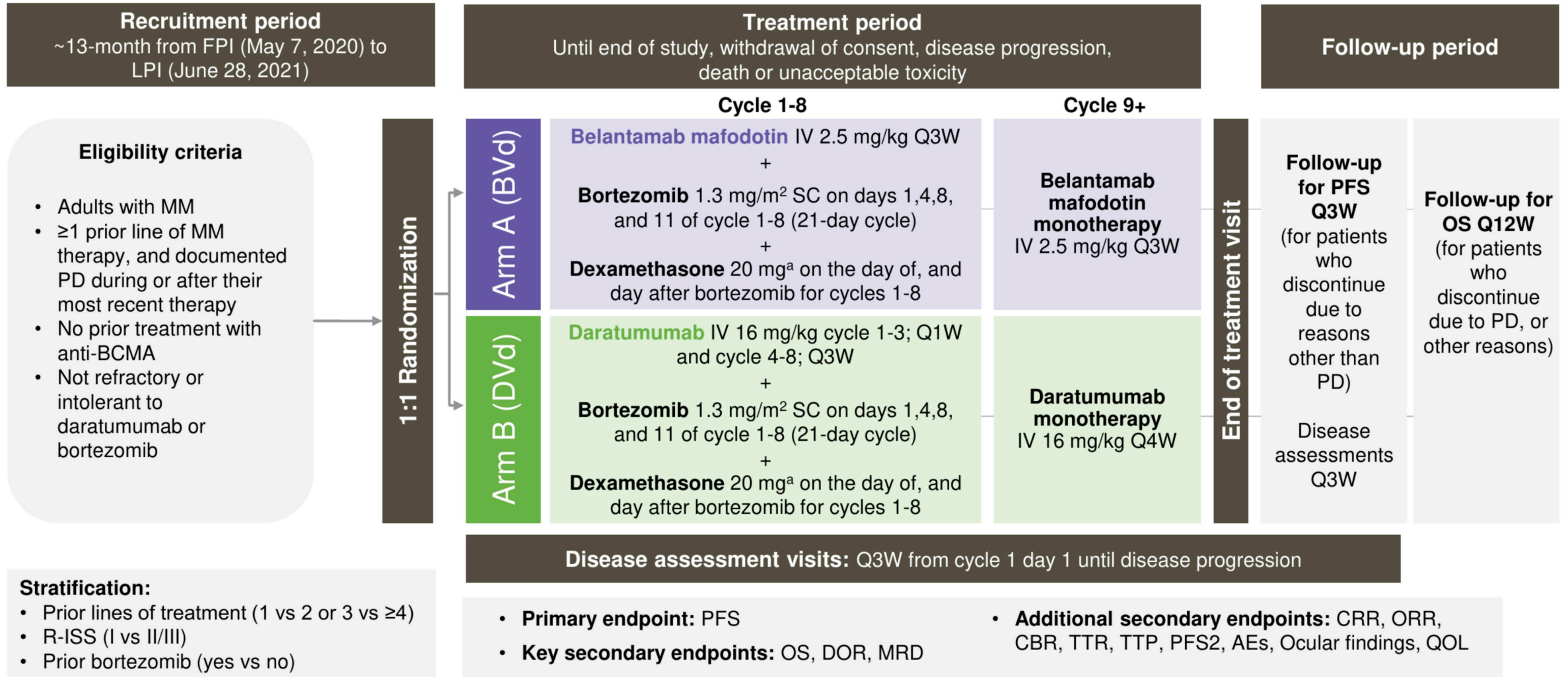
[Download \(PDF - 245.7KB\)](#) 

- 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

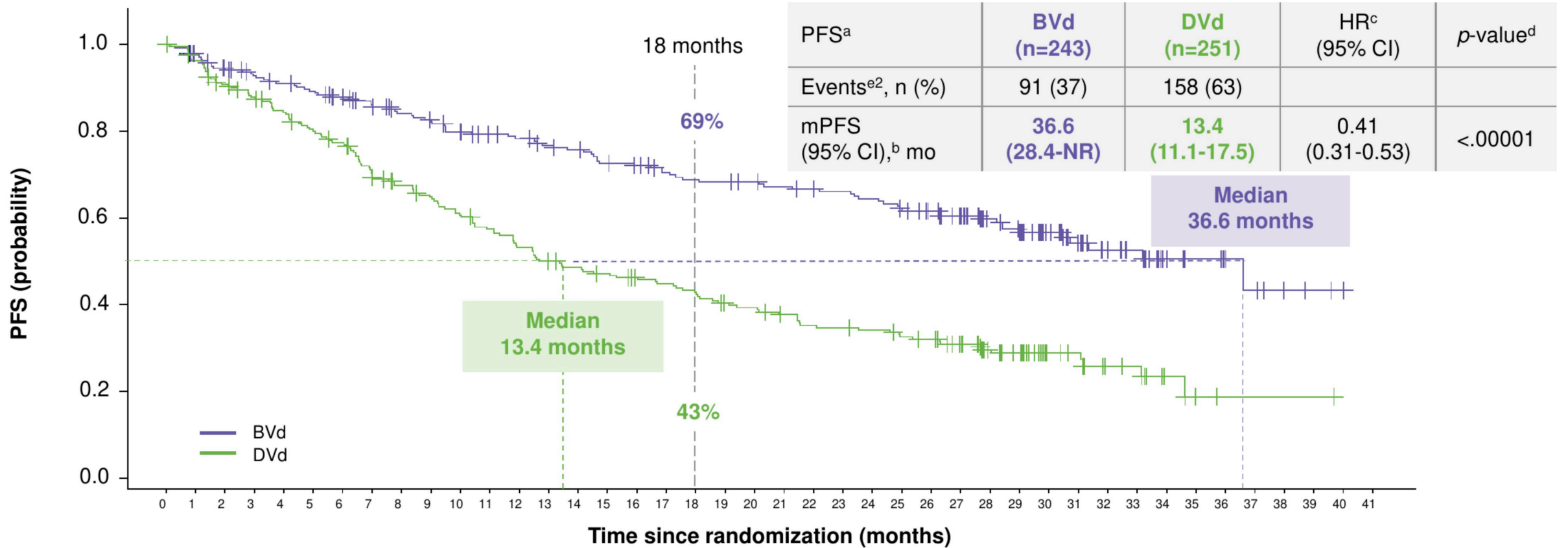
ADC = antibody-drug conjugate; ADCC/P = antibody-dependent cellular cytotoxicity and phagocytosis; APRIL = a proliferation-inducing ligand; ATP, = adenosine triphosphate; BAFF = B-cell activating factor; BCMA = B-cell maturation antigen; CRT = calreticulin; CTL = cytotoxic T-lymphocyte; Fc = fragment 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, 2024; Amsterdam, Netherlands. Cho SF, et al. *Front Immunol*. 2018;9:1821.

Dreamm-7

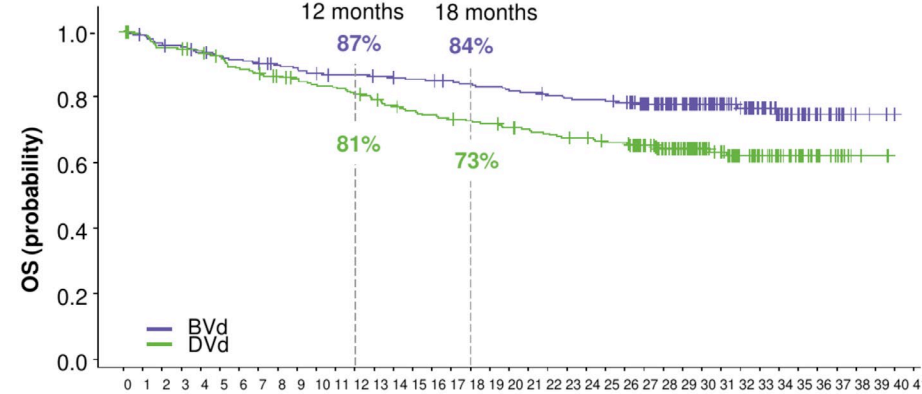
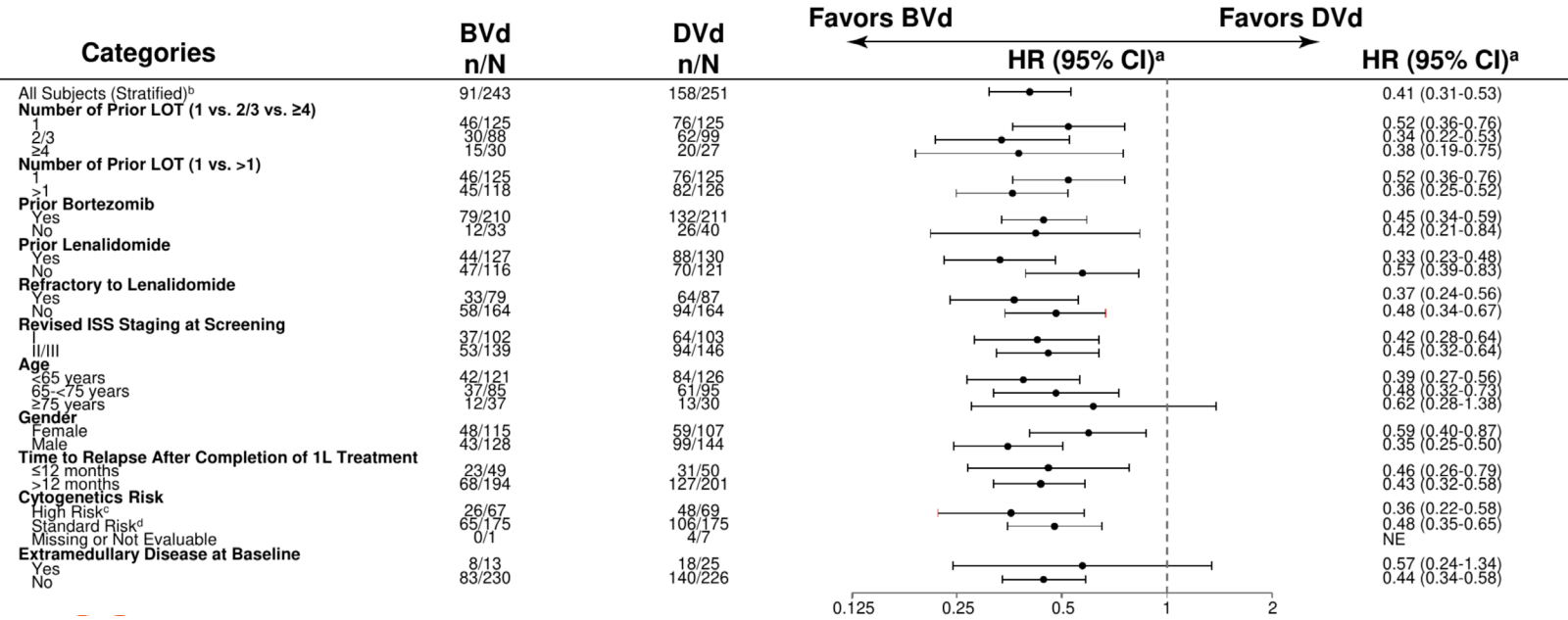


Dreamm-7

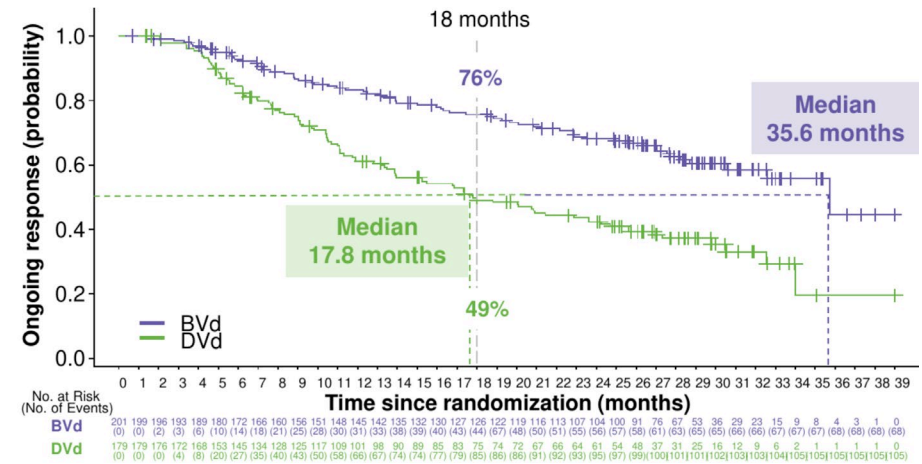


Dreamm-7

OS ^a	BVd (n=243)	DVd (n=251)	HR ^c (95% CI)	p-value ^d
Events, n (%)	54 (22)	87 (35)		
mOS (95% CI), ^b mo	NR	NR	0.57 (0.4-0.8)	.00049 ^e



DOR ^a	BVd (n=201)	DVd (n=179)
Events, n (%)	68 (34)	105 (59)
Patients with ongoing response	106 (53)	52 (29)
mDOR (95% CI), ^b mo	35.6 (30.5-NR)	17.8 (13.8-23.6)



DREAMM-8

Recruitment period

October 2020 to December 2022

Treatment period

Until PD, death, unacceptable toxicity, end of study, or withdrawal of consent

Eligibility criteria

- Adults with MM
- ≥ 1 prior line of MM therapy including LEN
- Documented PD during or after their most recent therapy
- No prior treatment with anti-BCMA or pomalidomide; not refractory/intolerant to bortezomib

N=302

1:1 randomization

BPd (Q4W)

PVd (Q3W)

Belantamab mafodotin

2.5 mg/kg IV (cycle 1) then 1.9 mg/kg IV Q4W from cycle 2 onward

+

Pomalidomide 4 mg orally on days 1-21 (28-day cycles)

+

Dexamethasone 40 mg^a on days 1, 8, 15, and 22

Bortezomib

1.3 mg/m² SC on days 1, 4, 8, and 11 of cycles 1-8 then days 1 and 8 (21-day cycles)

+

Pomalidomide 4 mg orally on days 1-14 (21-day cycles)

+

Dexamethasone 20 mg^a on the day of and day after bortezomib

End-of-treatment visit

Primary endpoint:

PFS (IRC assessed per IMWG)

Key secondary endpoints:

OS, MRD negativity, DOR

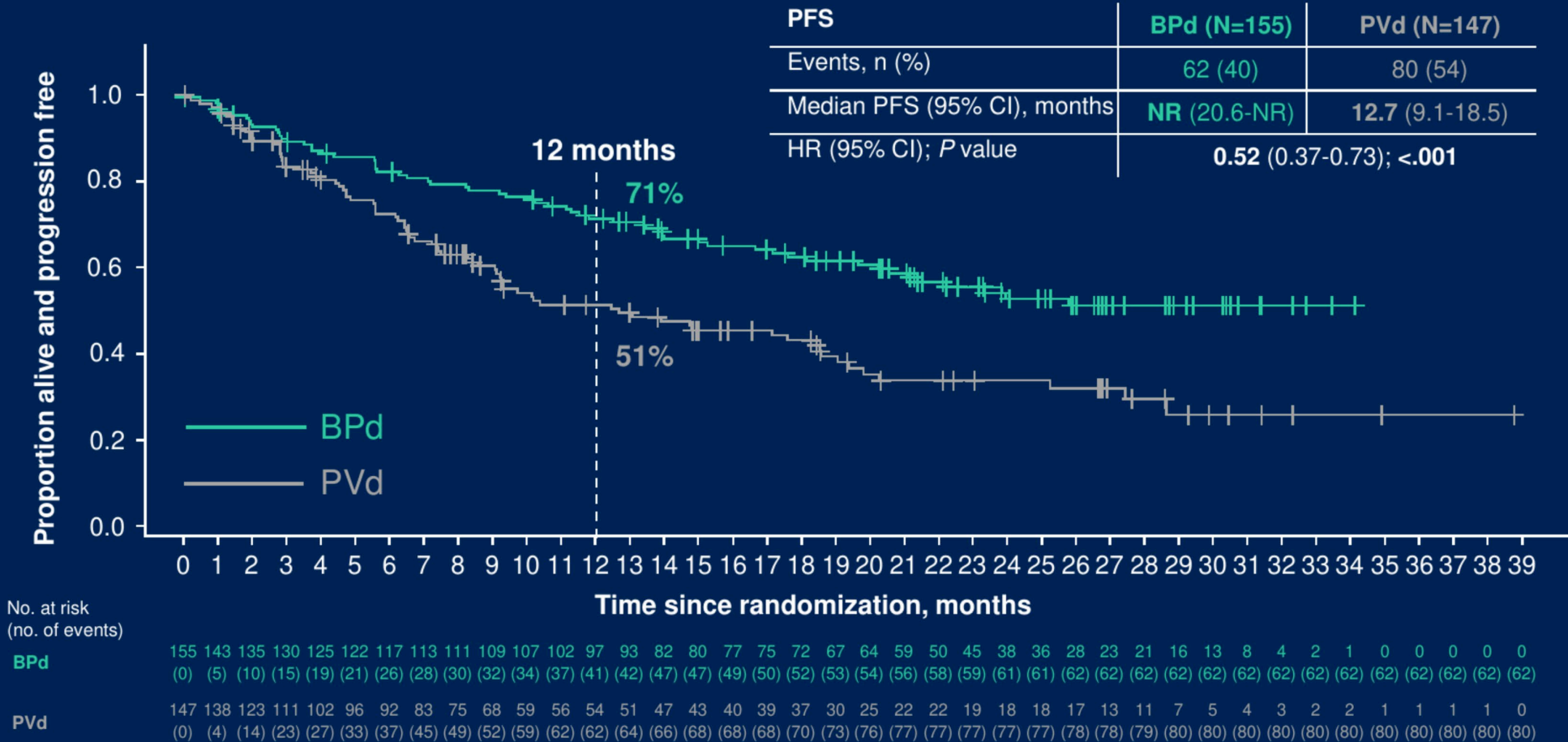
Additional secondary endpoints include:

ORR, CRR, \geq VGPR, TTBR, TTR, TTP, PFS2, AEs, ocular findings, HRQOL, and PROs

Stratification^b:

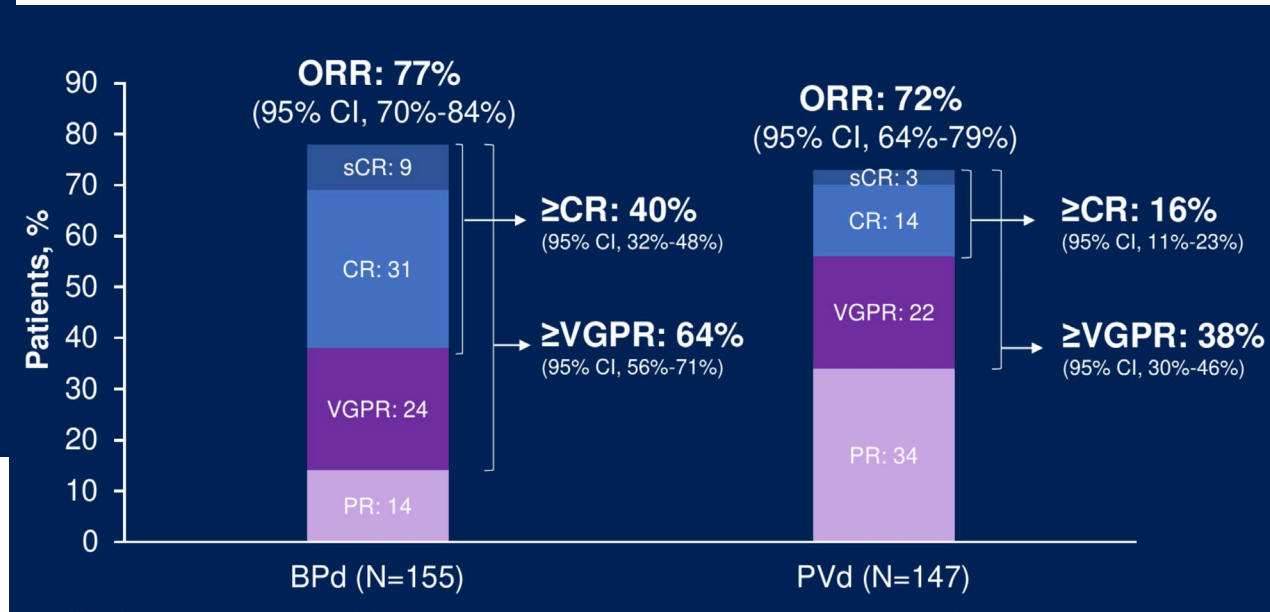
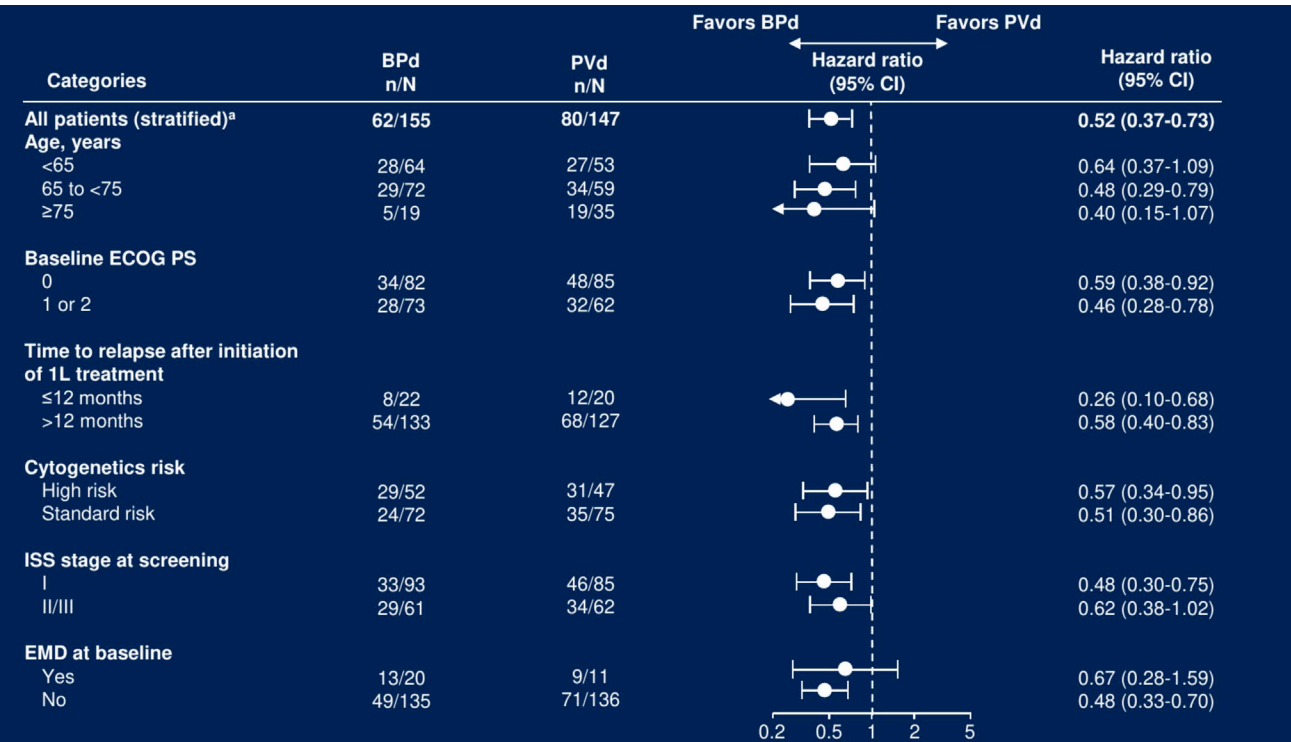
- Prior lines of treatment (1 vs 2 or 3 vs ≥ 4)
- Prior bortezomib (yes vs no)
- Prior anti-CD38 therapy (yes vs no)

DREAMM-8



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



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

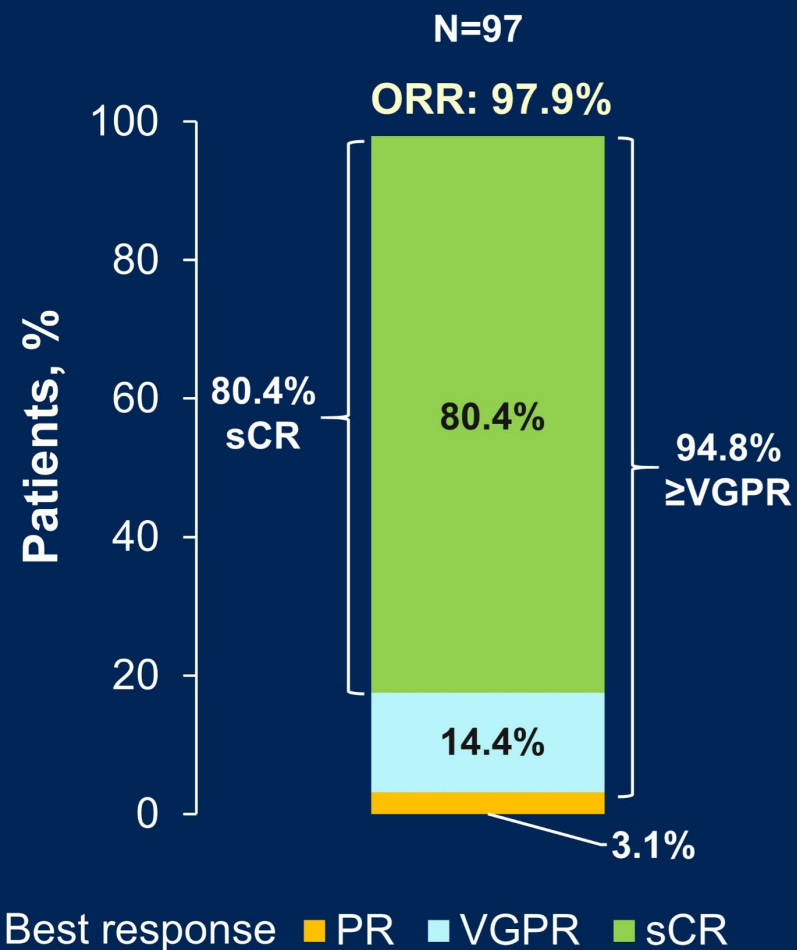
- Progressive MM per IMWG criteria
- ≥3 prior therapies or double refractory
- Prior PI, IMiD, anti-CD38 therapy
- Measurable disease
- ECOG PS ≤1

Median administered dose:
 0.71×10^6 ($0.51 - 0.95 \times 10^6$) 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.

CARTITUDE-1: Overall Response Rate

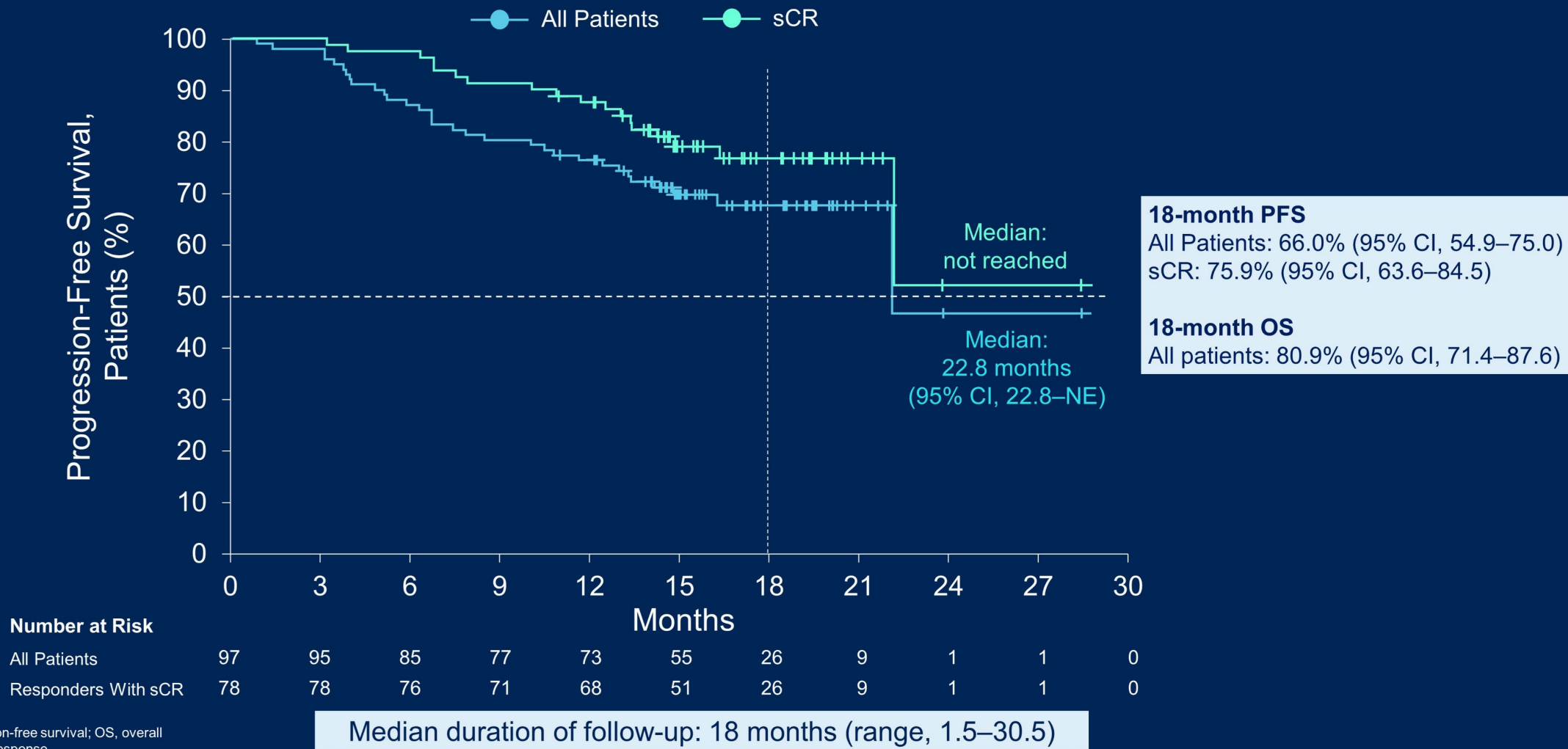


With longer follow-up, responses deepened with increasing rate of sCR

- 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 ≥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).

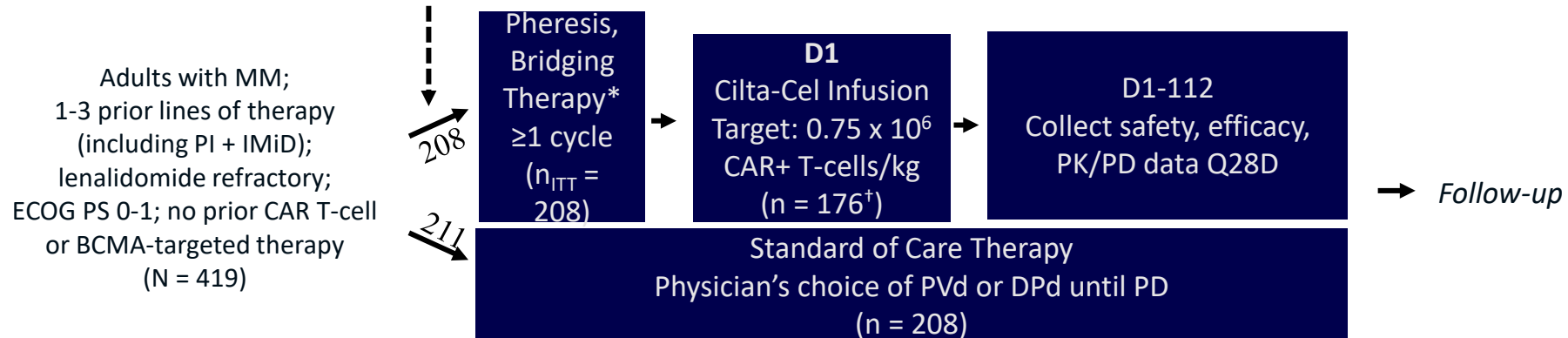
CARTITUDE-1: Progression-Free Survival



CARTITUDE-4: Phase III Trial of Cilta-Cel vs SoC in Lenalidomide-Refractory MM

- Randomized, open-label phase III trial

Stratified by choice of SoC (PVd/DPd), ISS stage, number previous lines of therapy



Primary endpoint: PFS

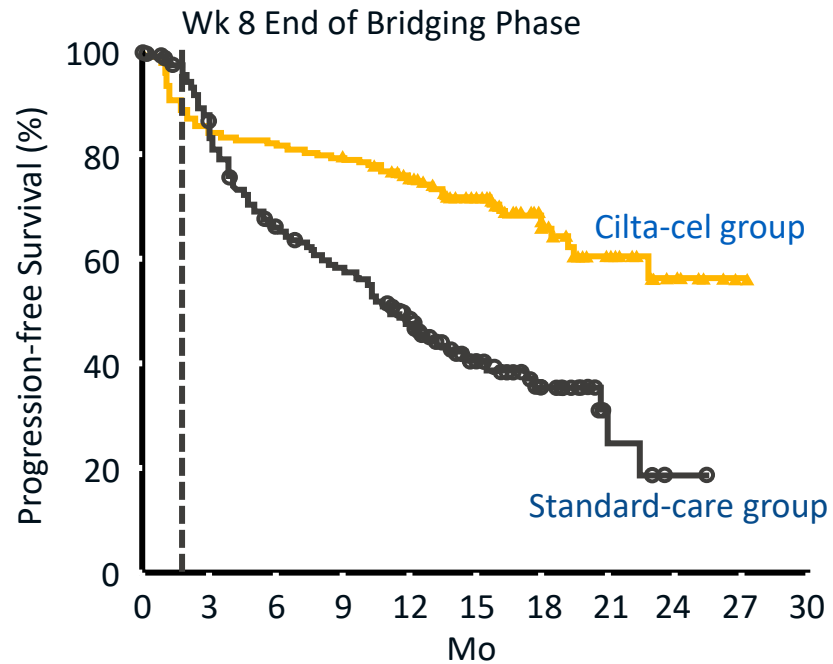
*Physician's choice of PVd or DPd. †As-treated population (n = 176): 32 patients did not receive cilta-cel as part of study due to PD (n = 30) or death (n = 2) during bridging therapy/lymphodepletion.

Secondary endpoints: ≥ CR, ORR, MRD negativity, OS, safety, PROs

Analysis after 15.9 mo median follow-up (range: 0.1-27 mo)

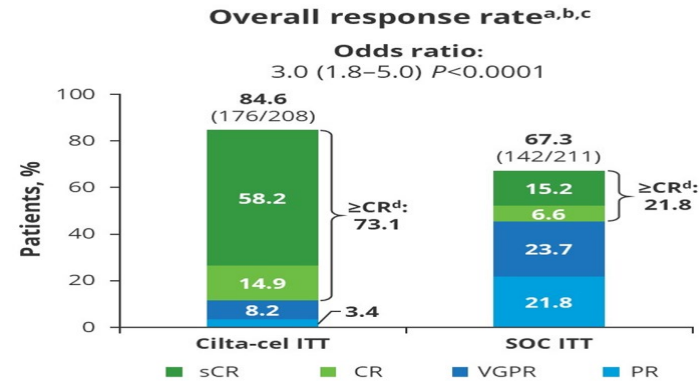
CARTITUDE-4: PFS and ORR (ITT Population)

Median F/U 15.9 mos



In subgroup analysis of PFS, all subgroups favored the Cilta-cel arm

	Cilta-Cel (n = 208)	SoC (n = 211)
mPFS, mo (95% CI)	NR (22.8-NE)	11.8 (9.7-13.8)
	HR: 0.26 (95% CI: 0.18-0.38; P <.0001)	
12-mo PFS, %	76	49

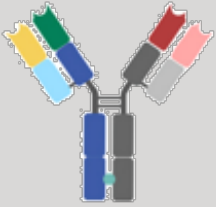
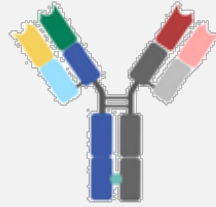
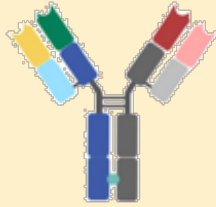



Cilta-Cel As-Treated Population

ORR 99.4%

≥ CR 86.4%

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 indicated for use in R/R MM with ≥ 4 prior lines of therapy, including

- Proteasome inhibitor
- Immunomodulatory agent
- Anti-CD38 monoclonal antibody

Teclistamab was approved 10/25/2022 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

Talquetamab was approved 8/9/2023 for adults with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody

Elranatamab was approved 8/14/2023 for use in adults with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody

Fab = fragment antigen binding; Fc = fragment crystallizable (region); FcRH5 = Fc receptor-homolog 5; FcRL5 = Fc receptor-like protein 5; 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

2 step-up doses of 0.05 mg/kg and 0.3 mg/kg; then 1.5 mg/kg SC weekly

ORR = 63.0%; 39.4% had CR or better

Median DoR = 18.4 months

Median PFS = 11.3 months

Separate study (n = 38) with prior BCMA-targeted treatment, ORR = 40%

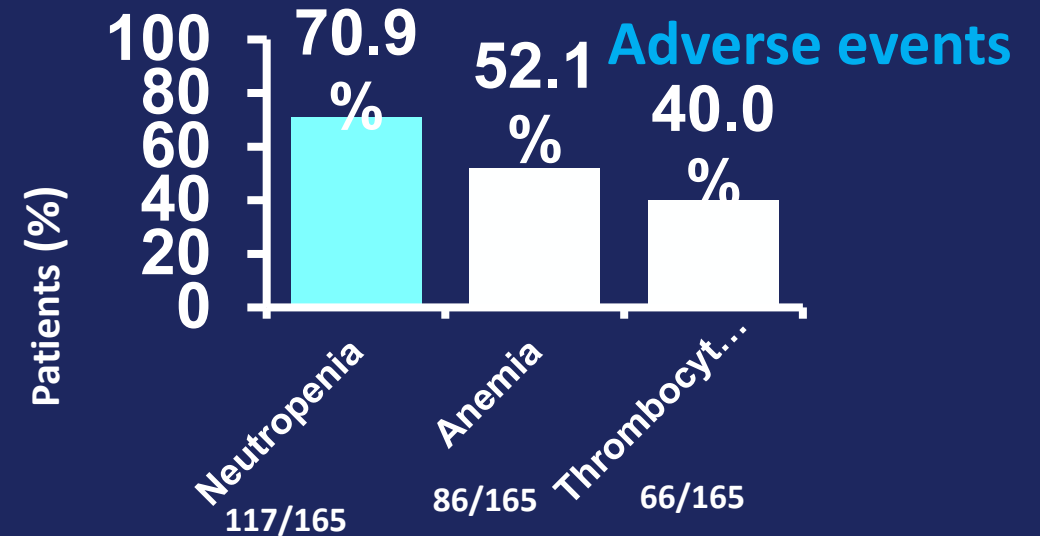
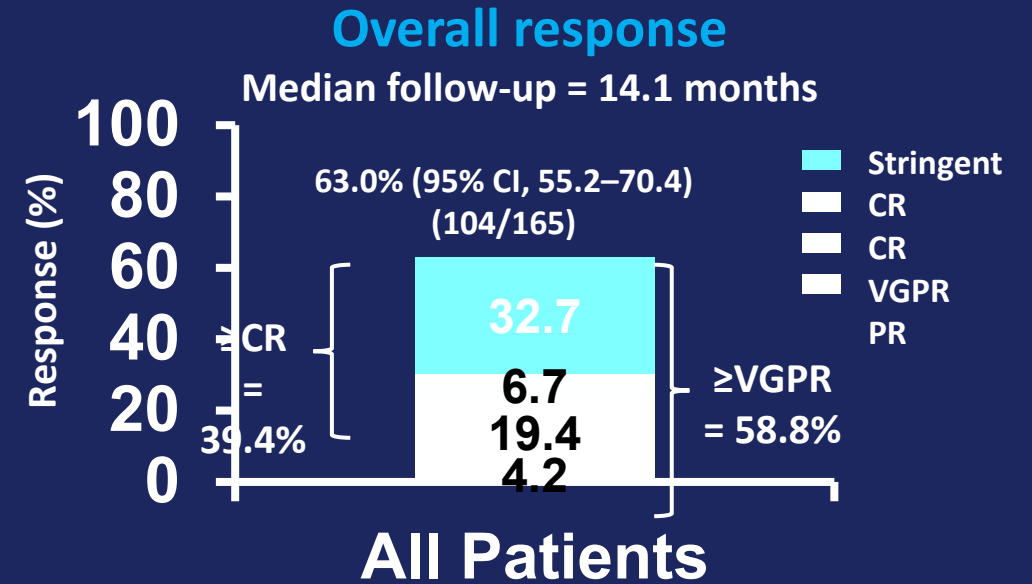
26% developed grade 3 to 4 infections

Safety

Cytokine release syndrome = 72.1%; grade 1 (50.3%), grade 2 (21.2%)

33% of patients had ≥2 CRS events

36.4% of patients with CRS required tocilizumab



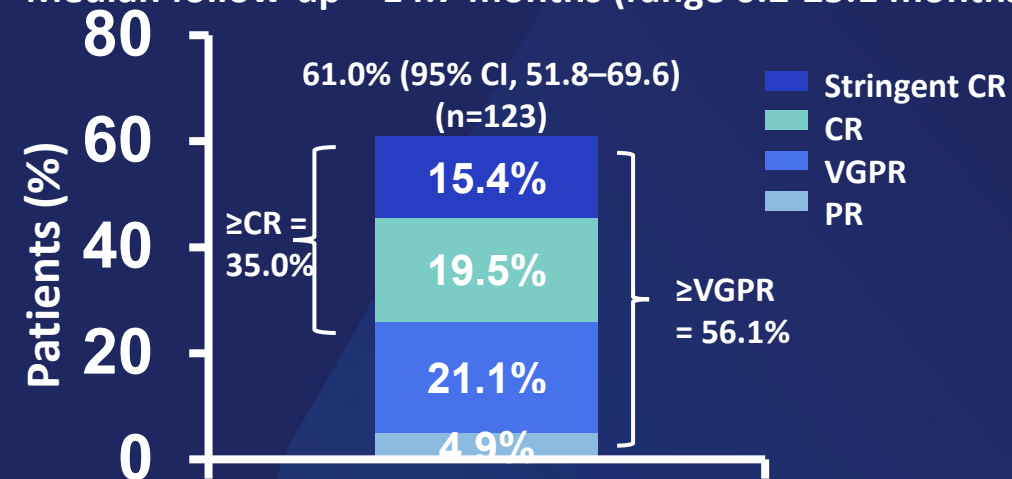
CI = confidence interval; PR = partial response; SC = subcutaneous(ly); VGPR = very good partial response.

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

Overall response

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



- Among responders, median TTR = 1.2 mo (0.9–7.4)
 - Median DOT= 5.6 mo (0.03–19.8)
 - Median DOR NE (12 mo–NE)
 - Probability of maintaining response at 6 mo was 90.4% (95% CI, 79.8–95.6)
- **Safety**
 - TEAEs occurring in ≥20% of patients
 - CRS events all grade 1 (42.0%) or grade 2 (14.3%)
 - 98.8% with first 3 doses, and 90.6% with step-up dose
 - ≥ 1 CRS event in 18 patients (15.1%)
 - Treated with tocilizumab (22.7%) and corticosteroids (8.4%)
 - ICANS in 4 of 119 (3.4%) patients, all events of grade 1/2
 - Supportive treatment with corticosteroids (1.7%), tocilizumab (1.7%), and levetiracetam–seizure prophylaxis (0.8%)
 - No permanently discontinuation due to CRS or ICANS

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	33 (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.

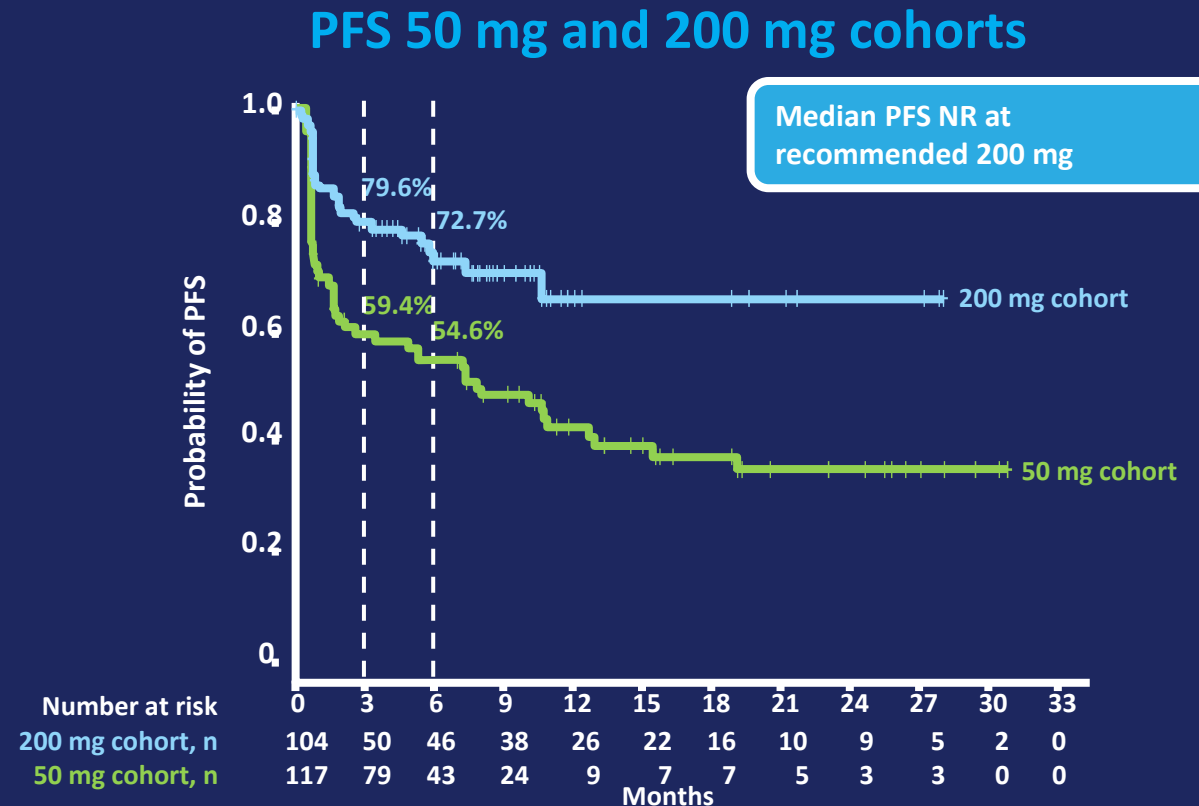
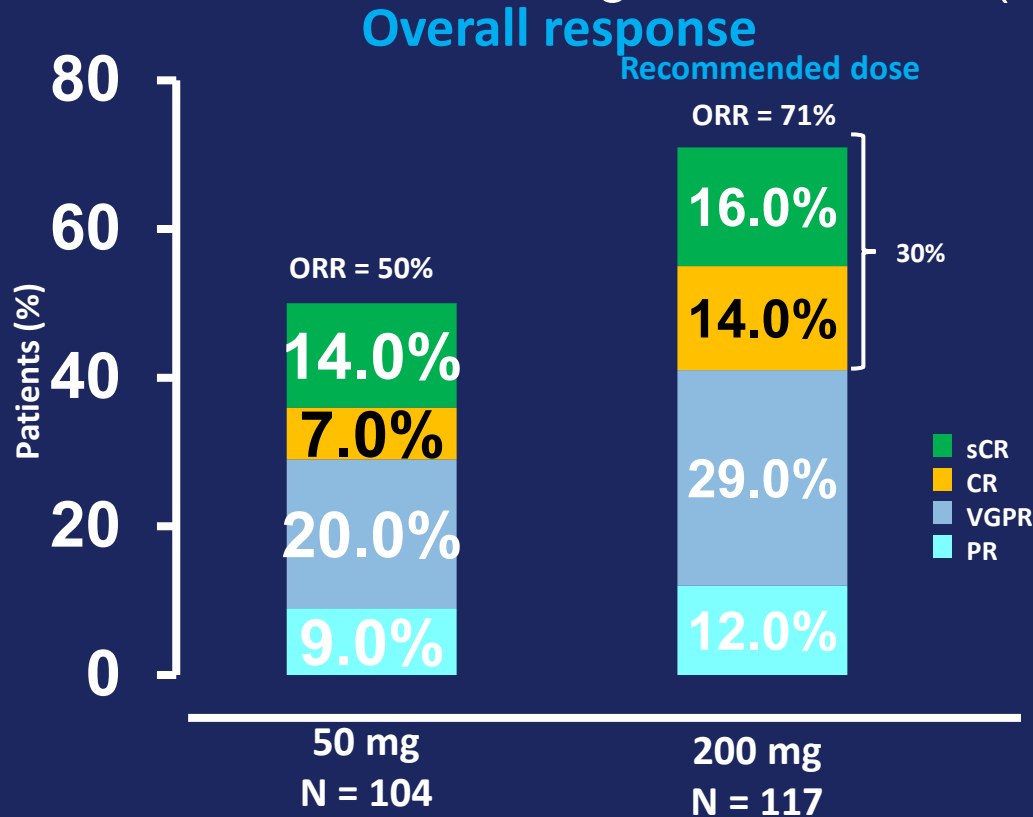
TTR = time to objective response; DOT = duration of treatment; NE = not evaluable/estimable; TEAE = treatment-emergent adverse event.

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

Phase 2 ORR and PFS at 50 mg and **200 mg dose regimens; BCMA x CD3**

- Median age 65 years (50 mg, n = 104) and 70 years (200 mg, n = 117)
- ≥3 prior lines including anti-CD38 Ab, PI, and IMiD or ≥ triple class refractory
- Median DoR at 50 mg = 7.7 months (0.3–31.3) and at 200 mg = 5.6 months (0.2–28.2)



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: Novel Binding Domains Targeting CD3, BCMA, and GPRC5D

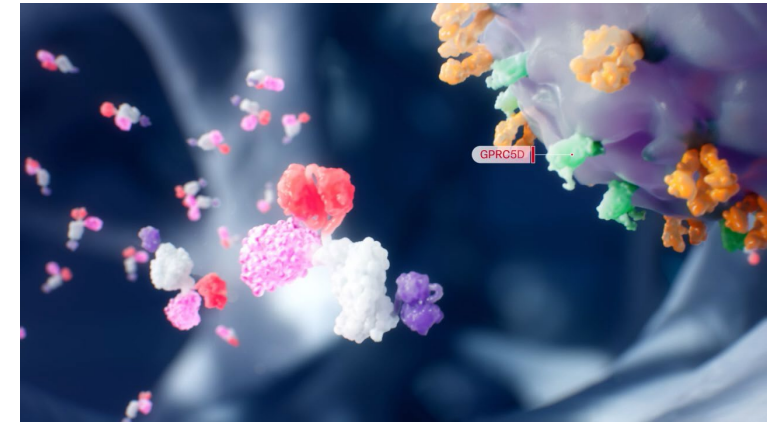
Molecule

Dual-Targeted Molecule to Bind Both BCMA and GPRC5D

Novel CD3, BCMA, and GPRC5D Binding Domains

Implications

- Enhanced myeloma cell targeting due to “**double lock-down**” effect of binding 2 myeloma antigens
- **More comprehensive targeting of myeloma cells**
 - BCMA-/GPRC5D+, BCMA+/GPRC5D-, and dual BCMA+/GPRC5D+
- **Prevention of antigen escape**
- **Potential to improve GPRC5D-related safety profile**
- **Manageable CRS profile with only 1 step-up dose needed**



RESEARCH ARTICLE | OCTOBER 16, 2025

Ramantamig (JNJ-79635322), a novel T-cell-engaging trispecific antibody targeting BCMA, GPRC5D, and CD3, in multiple myeloma models

Kodandaram Pillarisetti, Danlin Yang, Leopoldo Luistro, Jianhong Yao, Melissa Smith, Peter Vulfson, James Testa, Jr, Randolph Ponticiello, Scott R Brodeur, Bradley Heidrich, Kathryn Packman, Sanjaya Singh, Ricardo M Attar, Yusri A Elsayed, Ulrike Philippart

Check for updates

Blood blood.2025030027.

<https://doi.org/10.1182/blood.2025030027>

Article history

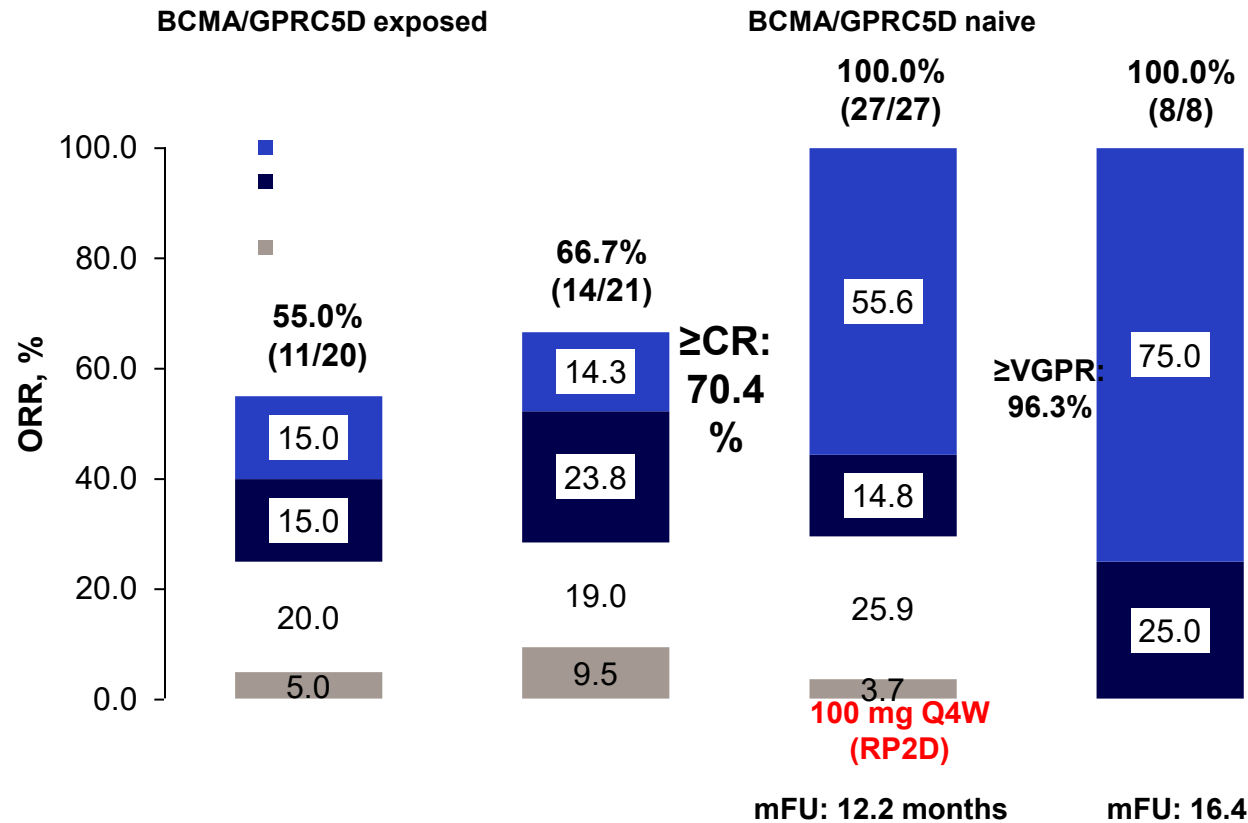
Split-Screen Share Tools PDF

Key Points

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

CRS = cytokine release syndrome.

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



At the RP2D in patients naive to BCMA/GPRC5D (n=27)

Median follow-up, months (range)	12.2 (7.4–18.6)
Median time to first response, months (range)	1.2 (0.3–5.2)
Median time to best response, months (range)	5.9 (0.3–11.1)

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

Key Take-Aways

- BCMA has established itself as a key target in late relapsed myeloma as well as early relapse. Ongoing studies evaluating the role in frontline therapy
- Sequencing is still a big question. Current data suggests more optimal outcomes sequencing CART before bisab
- Other targets are emerging beyond BCMA
 - GPRC5d, FcRH5, CD38, CD19
 - Dual target CAR-T, trispecific antibodies

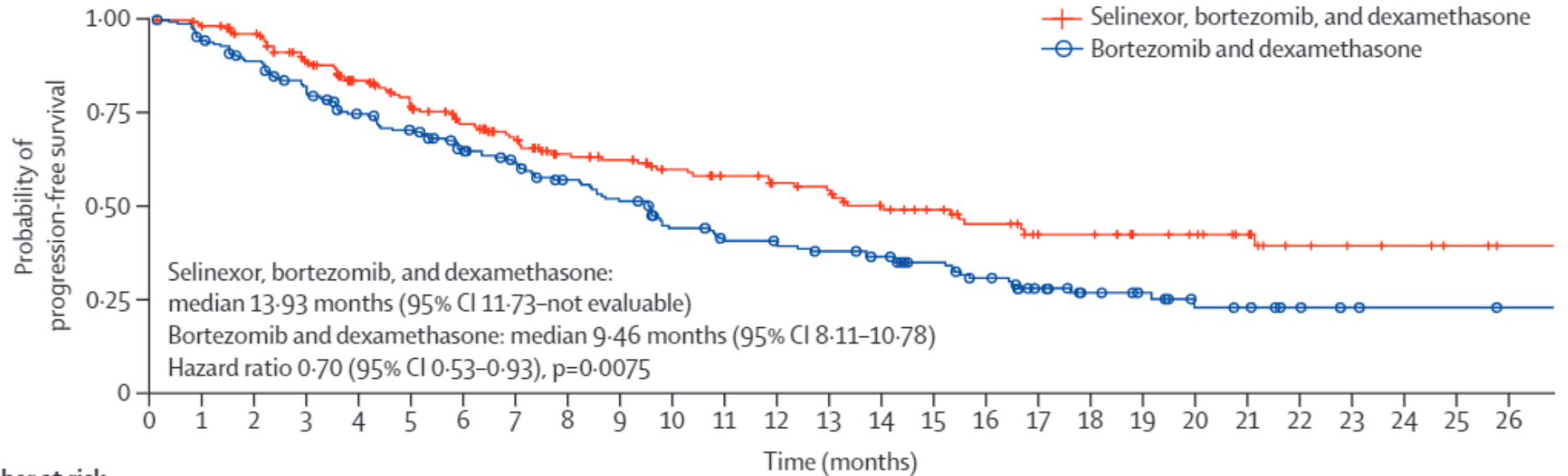
Other Novel and Emerging Therapies in R/R MM

Joshua Richter, MD, FACP

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

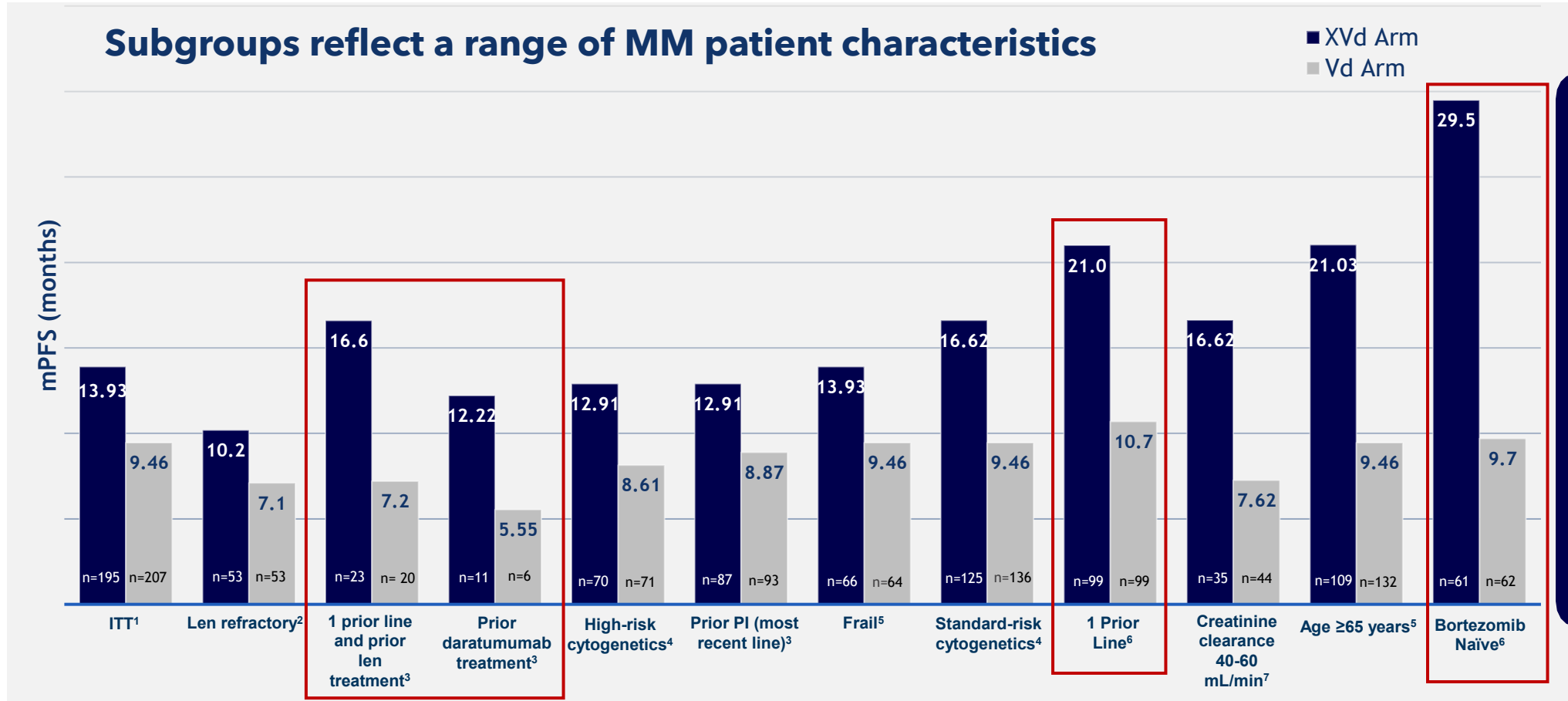


	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26
Number at risk	195	187	175	152	135	117	106	89	79	76	69	64	57	51	45	41	35	27	26	22	19	14	9	7	6	4	2
(number censored)	(0)	(5)	(12)	(21)	(31)	(37)	(42)	(50)	(57)	(59)	(63)	(66)	(71)	(73)	(76)	(80)	(83)	(89)	(90)	(94)	(97)	(102)	(106)	(108)	(109)	(111)	(113)
Bortezomib and dexamethasone	207	187	175	152	138	127	111	100	90	81	66	59	56	53	49	42	35	26	20	16	10	8	5	4	3	3	2
(number censored)	(0)	(8)	(10)	(15)	(20)	(22)	(29)	(32)	(37)	(37)	(41)	(43)	(44)	(45)	(47)	(52)	(55)	(60)	(65)	(69)	(73)	(75)	(78)	(79)	(80)	(80)	(81)

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.

BOSTON – Consistent PFS Benefit Across Subgroups



Limitations of subgroup analyses:

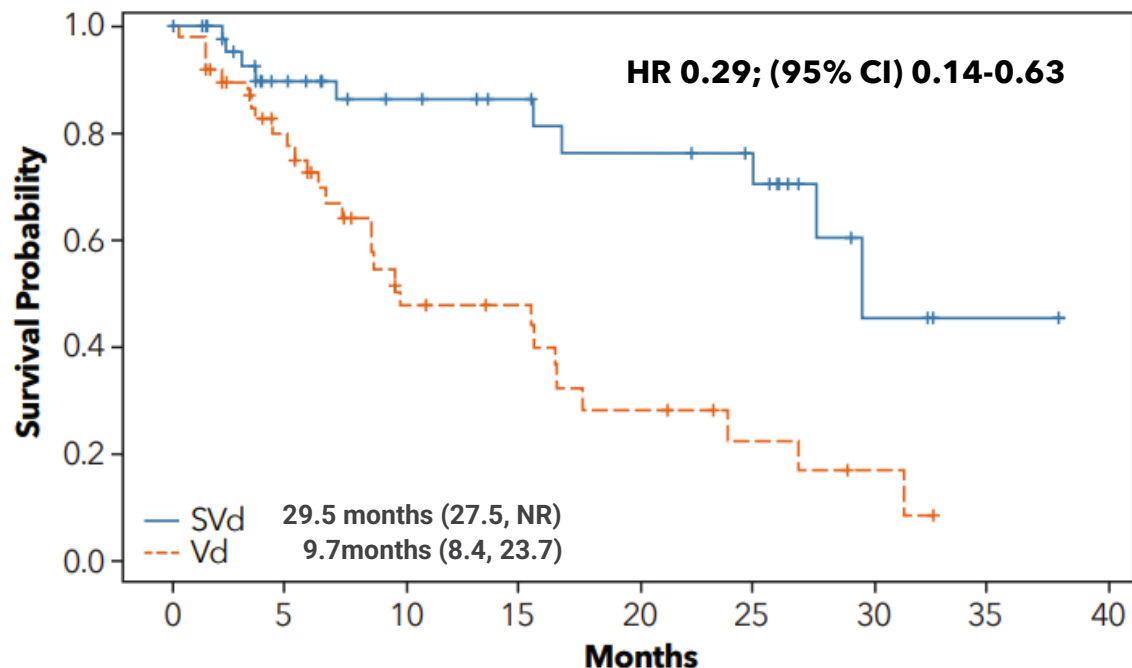
These subgroup analyses were exploratory in nature, not included in the study objectives, and do not control for type 1 error

These subgroup analyses were not powered or adjusted for multiplicity to assess PFS across these prespecified subgroups

Grosicki S, et al. *Lancet*. 2020;396(10262):1563-1573. Mateos MV, et al. Poster #P886. Presented at: EHA Hybrid Congress 2023; June 8-11, 2023. Karyopharm Therapeutics. Accessed October 2025. <https://investors.karyopharm.com/2020-05-28-Karyopharm-Reports-Positive-Phase-3-BOSTON-Data-in-Oral-Presentation-at-the-American-Society-of-Clinical-Oncology-2020-Virtual-Scientific-Program>. Richard S, et al. *Am J Hematol*. 2021;96(9): 1120-1130. Auner HW, et al. *Am J Hematol*. 2021;96(6):708-718. Mateos, MV et al. Presented at: EHA Hybrid Congress 2023; June 8-11, 2023. Poster #P917. Delimpasi S, et al. *American Journal of Hematology*. 2021;1-4.

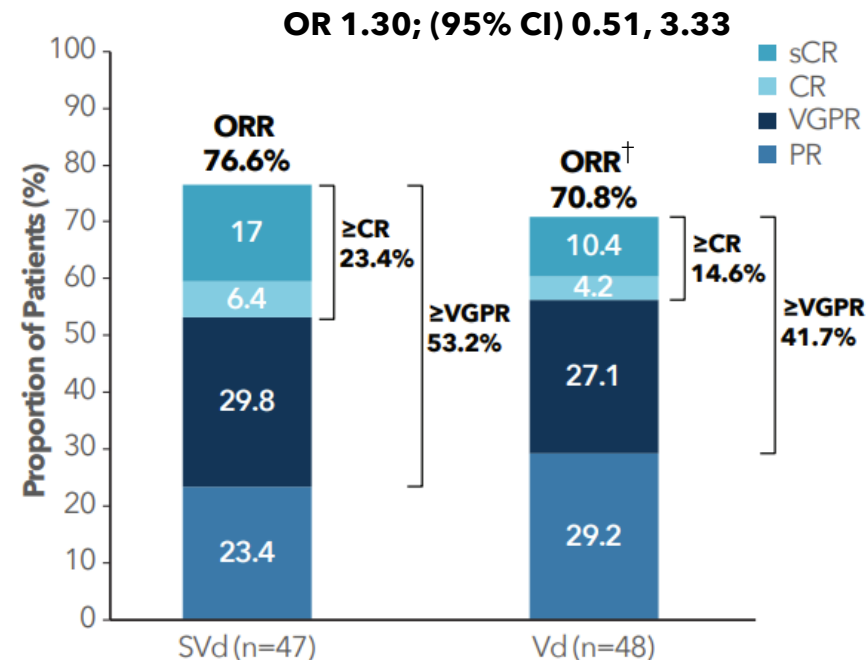
Median PFS and Responses in PI-Naïve Patients

Median PFS



SVd	47	28	22	18	15	12	3	1	0
Vd	48	31	14	12	7	4	2	0	

Response Rates



†The sum of the individual % values of each category, may not add up to the total value due to rounding.

Efficacy analyses were based on 15 Feb 2021 data cut and safety analyses on 15 Jun 2022 data extract.

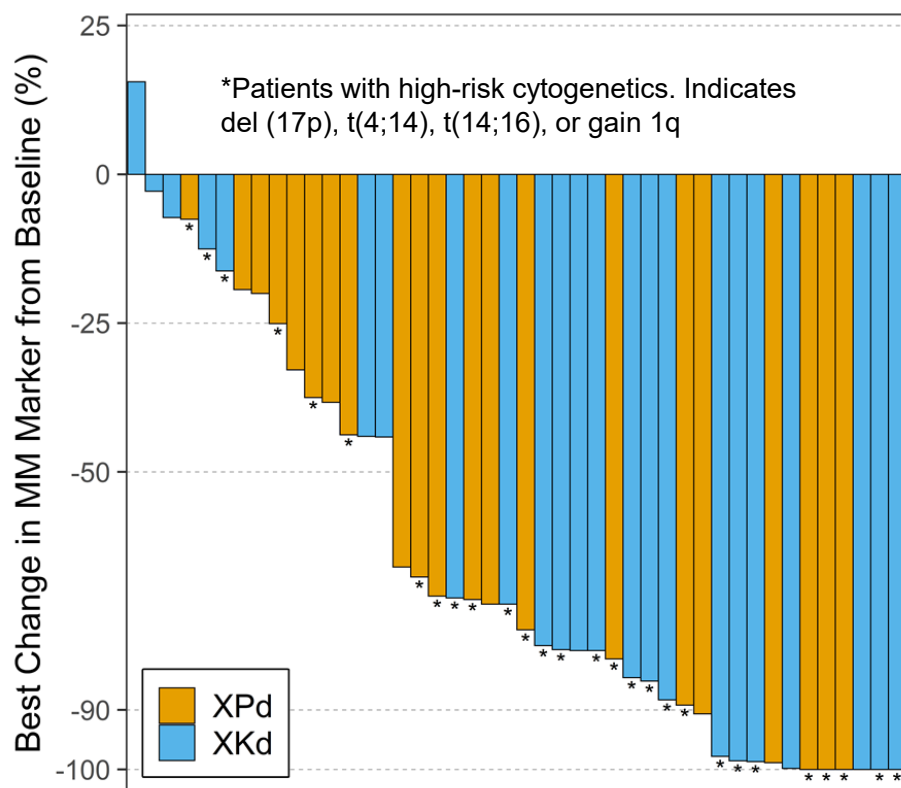
These subgroup analyses were exploratory in nature, not included in the study objectives and do not control for type 1 error. The analyses were not powered or adjusted for multiplicity to assess efficacy outcomes across these subgroups.

CR = complete response; ORR = overall response rate; PR = partial response; sCR = stringent complete response; SVd = selinexor + bortezomib + dexamethasone; Vd = bortezomib + selinexor; VGPR = very good partial response.

Mateos MV, et al. Poster #P917. Presented at: EHA Hybrid Congress 2023; June 8-11, 2023.

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.

STOMP: Study Overview & Objectives

Selinexor and backbone Treatments Of multiple Myeloma Patients (**STOMP**): multi-center, multi-arm, open-label, randomized dose escalation (Phase 1) and expansion (Phase 2) study evaluating selinexor in various triplet and quadruplet combinations in patients with NDMM and RRMM.

Select Study Endpoints

Primary: Phase 1: MTD, RP2D. Phase 2: ORR, DOR, CBR.

Secondary: Phase 1 & 2: safety and tolerability per CTCAE. Phase 2: PFS, OS.

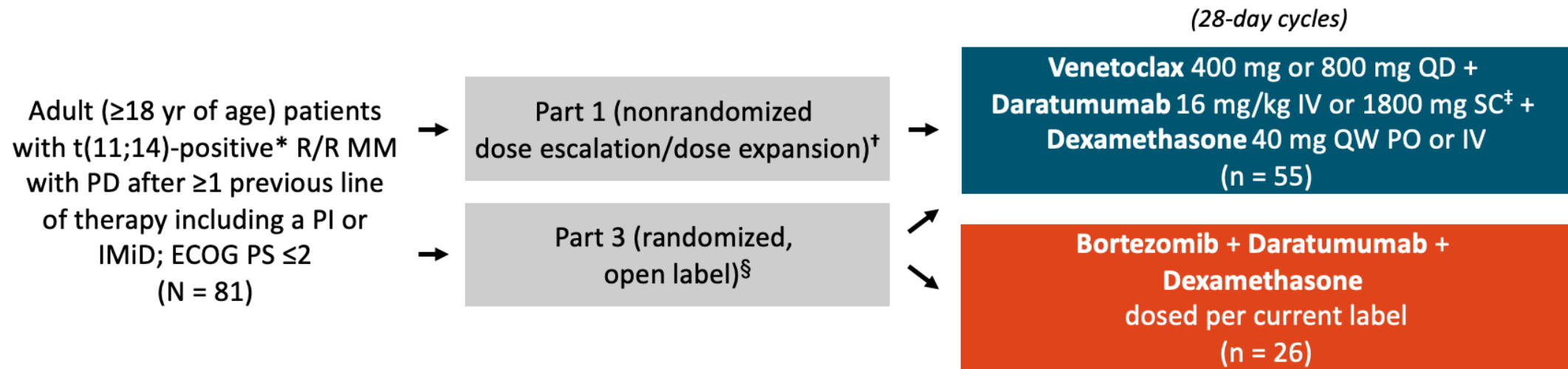
XPd Pomalidomide + Dexamethasone	XVd Bortezomib + Dexamethasone	XKd Cohort 1 & 2 Carfilzomib + Dexamethasone	XNd Ixazomib + Dexamethasone	XBd Belantamab mafodotin + Dexamethasone
XRd RRMM and NDMM Lenalidomide + Dexamethasone	XDd Daratumumab + Dexamethasone	XPVd Pomalidomide + Bortezomib + Dexamethasone	XPEd Pomalidomide + Elotuzumab + Dexamethasone	XDPd Daratumumab + Pomalidomide + Dexamethasone

CBR = clinical benefit rate; CTCAE = common terminology criteria for adverse events; DOR = duration of response; MM = multiple myeloma; MTD = maximum tolerated dose; RP2D = recommended phase 2 dose; NDMM = newly diagnosed multiple myeloma; ORR = overall response rate; OS = overall survival; PFS = progression-free survival; RRMM = relapsed/refractory multiple myeloma.

ClinicalTrials.gov. Accessed January 6, 2022. <https://clinicaltrials.gov/ct2/show/NCT02343042>.

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.

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%)

Key Take-Aways

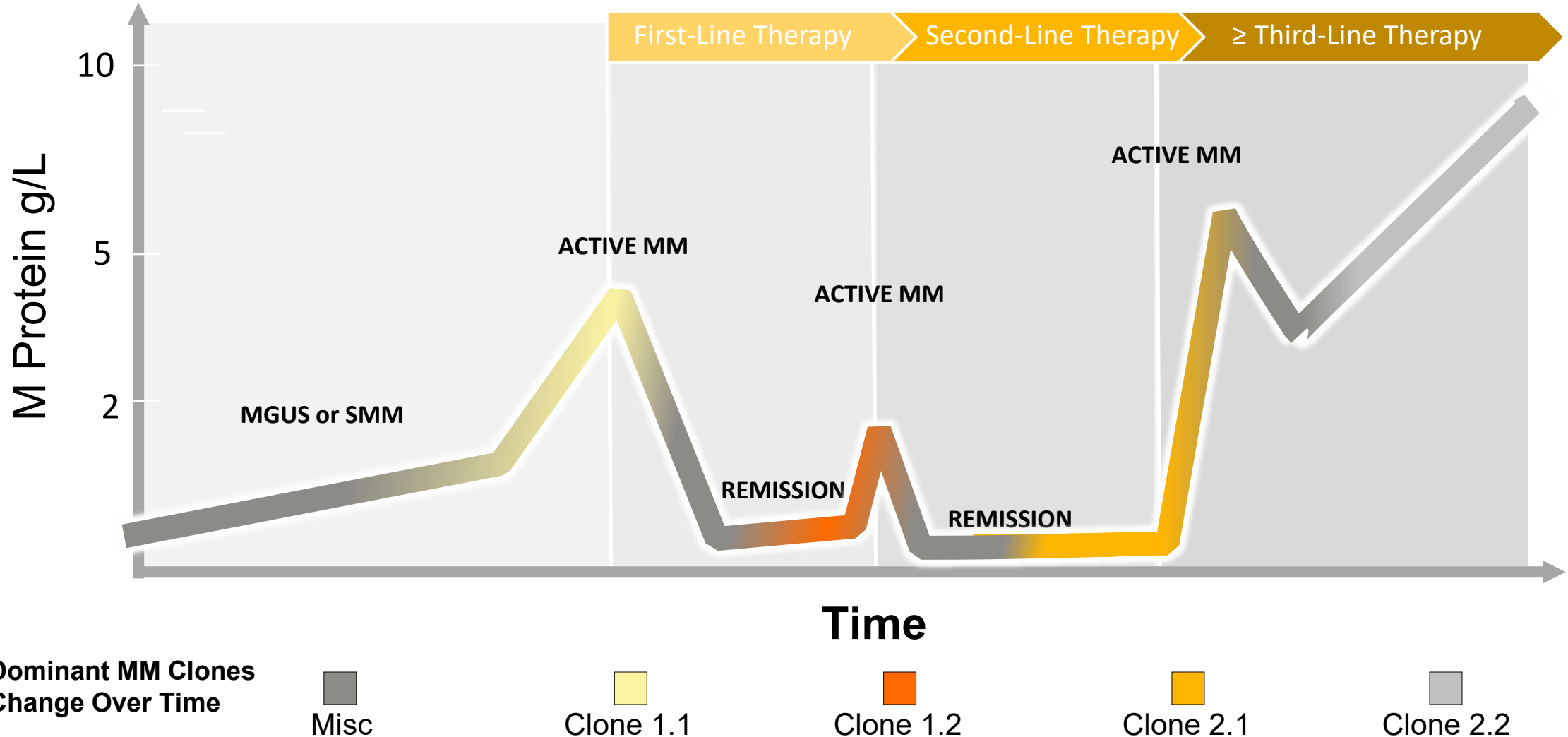
- Although T-cell redirection therapy has become an integral part of myeloma therapy, novel agents are still needed in lines prior to and subsequent to TCR
- T(11;14) myeloma mandates the need to assess the timing and role of BCL-2 inhibition (venetoclax)
- Selinexor has improved tolerability when given 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)

R/R MM Clinical Challenges and Barriers

Beth Faiman, PhD, MSN, APN-BC, AOCN[®], BMTCN[®], FAAN, FAPO

Clonal Evolution: The Relapsing Nature of MM

Dominant Clones Change Over Time



M protein = monoclonal protein; misc = miscellaneous (no dominant clone).
 Adapted from Durie B, Keats JJ, et al. *Blood*. 2012;120(5):1067-1076.

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)

RESPIRATORY

Hypoxia
Dyspnea
Capillary leak syndrome

NEUROLOGIC

Delirium
Somnolence
Dysphagia

LIVER

Transaminitis
↑ ALP
Hyperbilirubinemia

CARDIOVASCULAR

Sinus tachycardia
Hypotension
Arrhythmias

KIDNEY

↑ Serum creatinine
Kidney insufficiency

GASTROINTESTINAL

Nausea
Vomiting
Diarrhea

HEMATOLOGIC

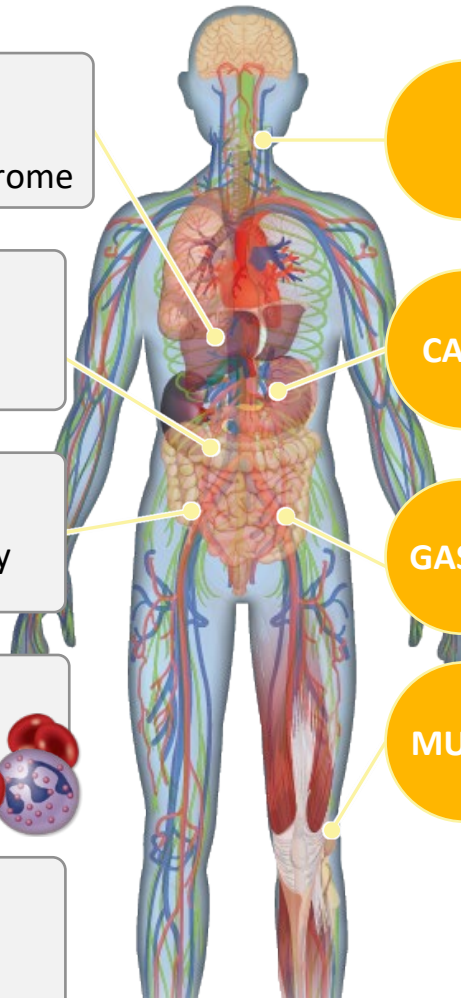
Anemia
Thrombocytopenia
Neutropenia

MUSCULOSKELETAL

Myalgia

CONSTITUTIONAL

Fever
Fatigue, malaise
Headache



Monitoring for CRS

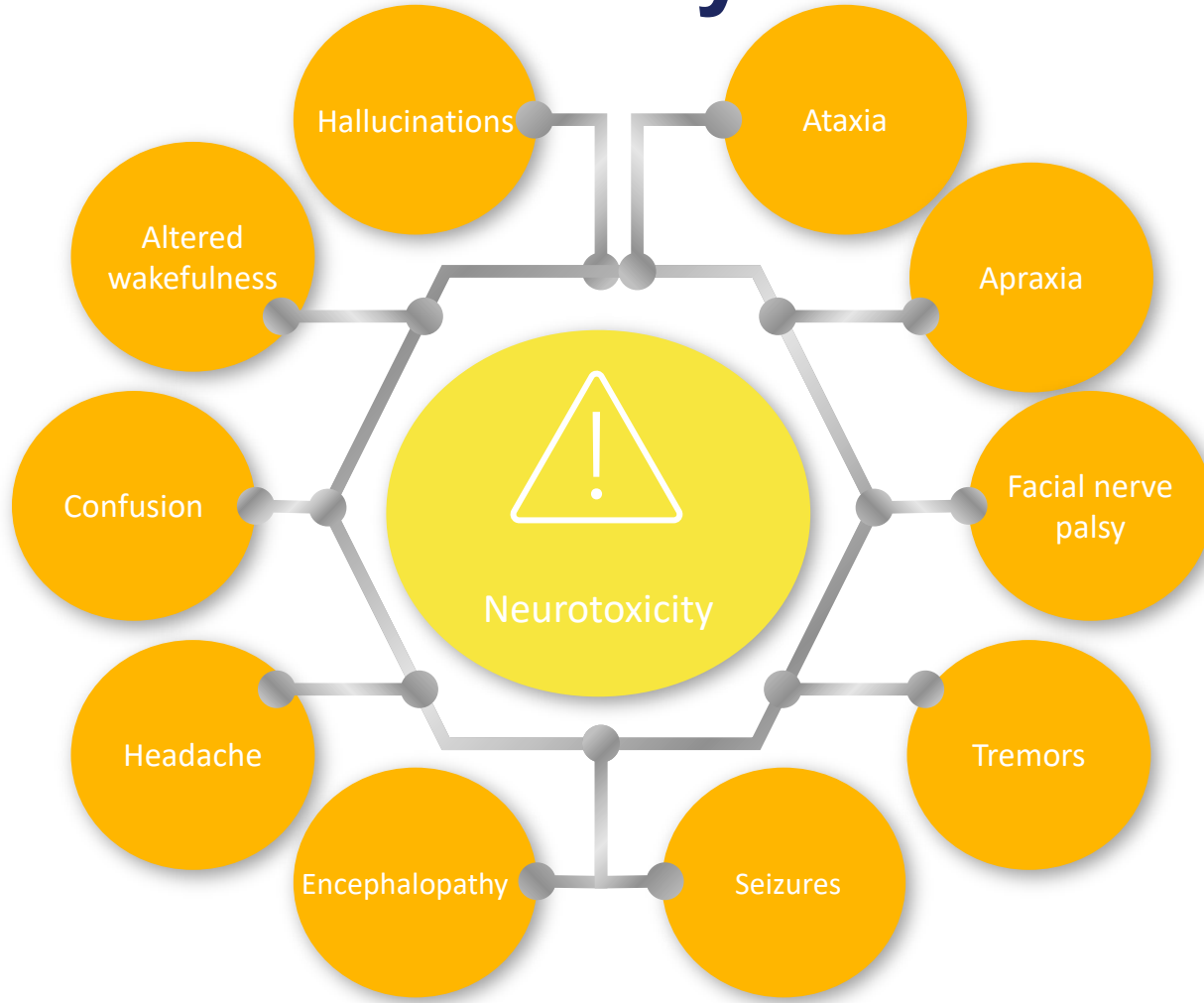
- **Vital signs (temperature, O₂ saturation, etc.)**
- **Fever is hallmark – treat**
- Review of systems and physical exam
- Laboratory monitoring – CRP, Ferritin, LDH

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 ^c or blow-by	Requiring high-flow nasal cannula, ^c face mask, nonbreather mask, or Venturi mask	Requiring positive pressure (eg, CPAP, BiPAP, intubation and mechanical ventilation)

Note: Fever, Hypotension, and Hypoxia are graded with and/or^b other parameters.

ALP = alkaline phosphatase; CPK = creatine phosphokinase; CRP = C-reactive protein; CRS = cytokine release syndrome. 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 of CART (Parkinson's, movement disorders now reported)

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; IgG = immunoglobulin G; IVIG = intravenous immunoglobulin; PCV = pneumococcal conjugate vaccine; 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

Patient Education

- Treatment expectations
- Self-care training

Care Navigation

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

Psychosocial Support

- Listening & guidance
- Family/caregiver support

Primary Care

- Secondary Cancer Monitoring, health maintenance

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

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://apoc-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 Take-Aways

- 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

Post- Event Survey

Post-Event Survey and you'll be entered to win a \$100 gift card!



Thank You