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

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Program Information

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- 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

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

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.

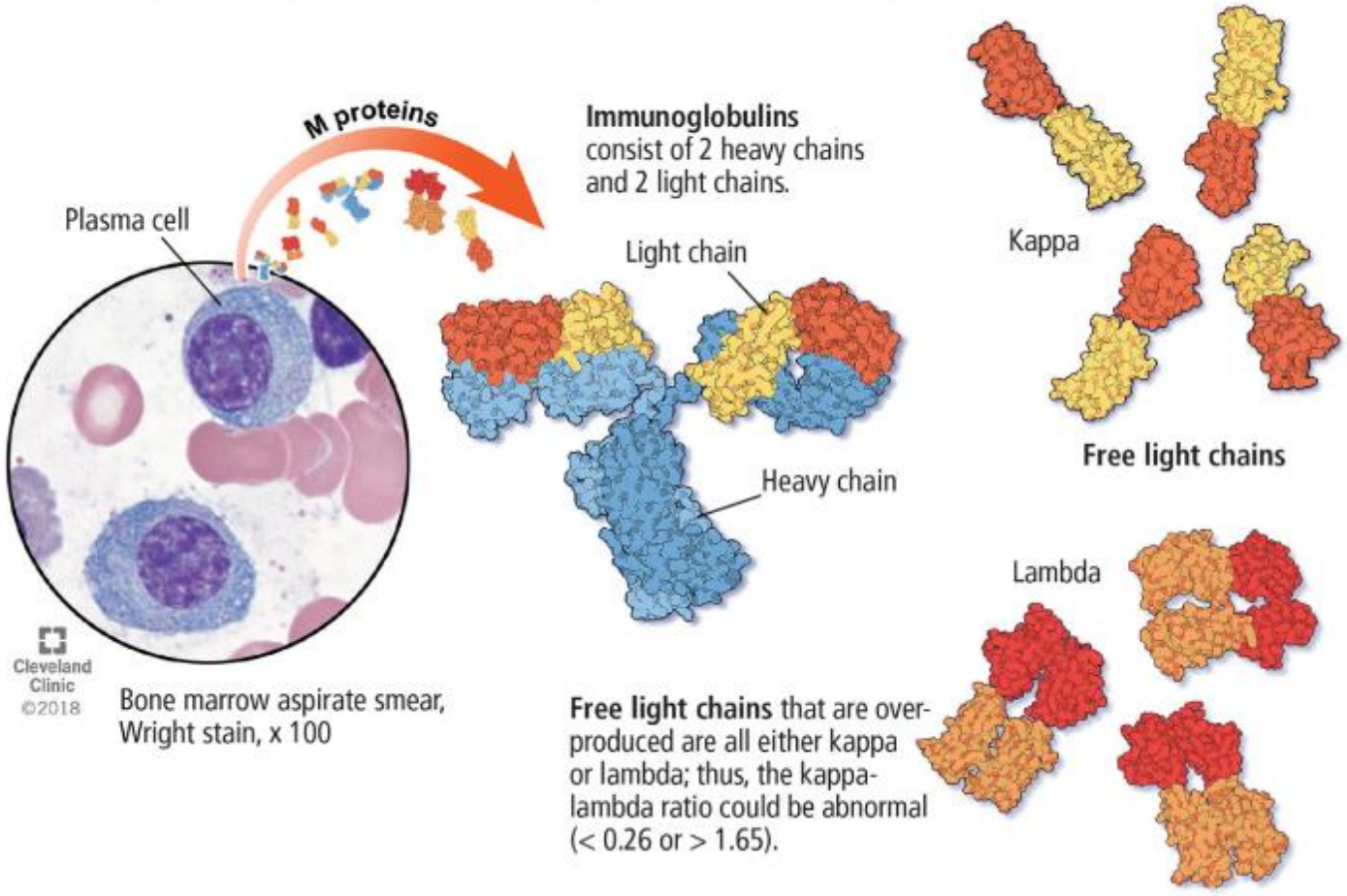
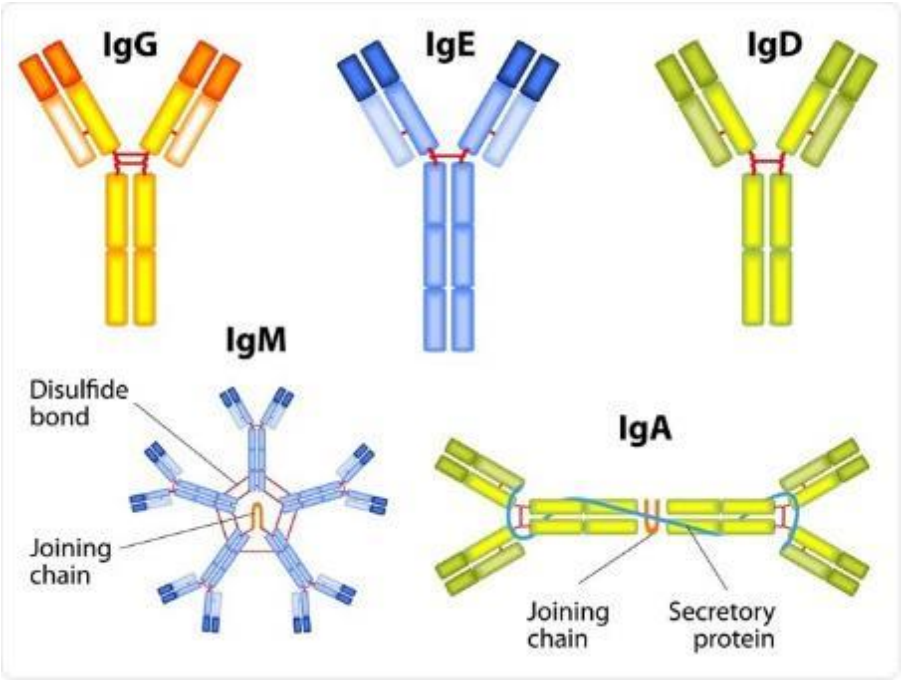


Figure 1.

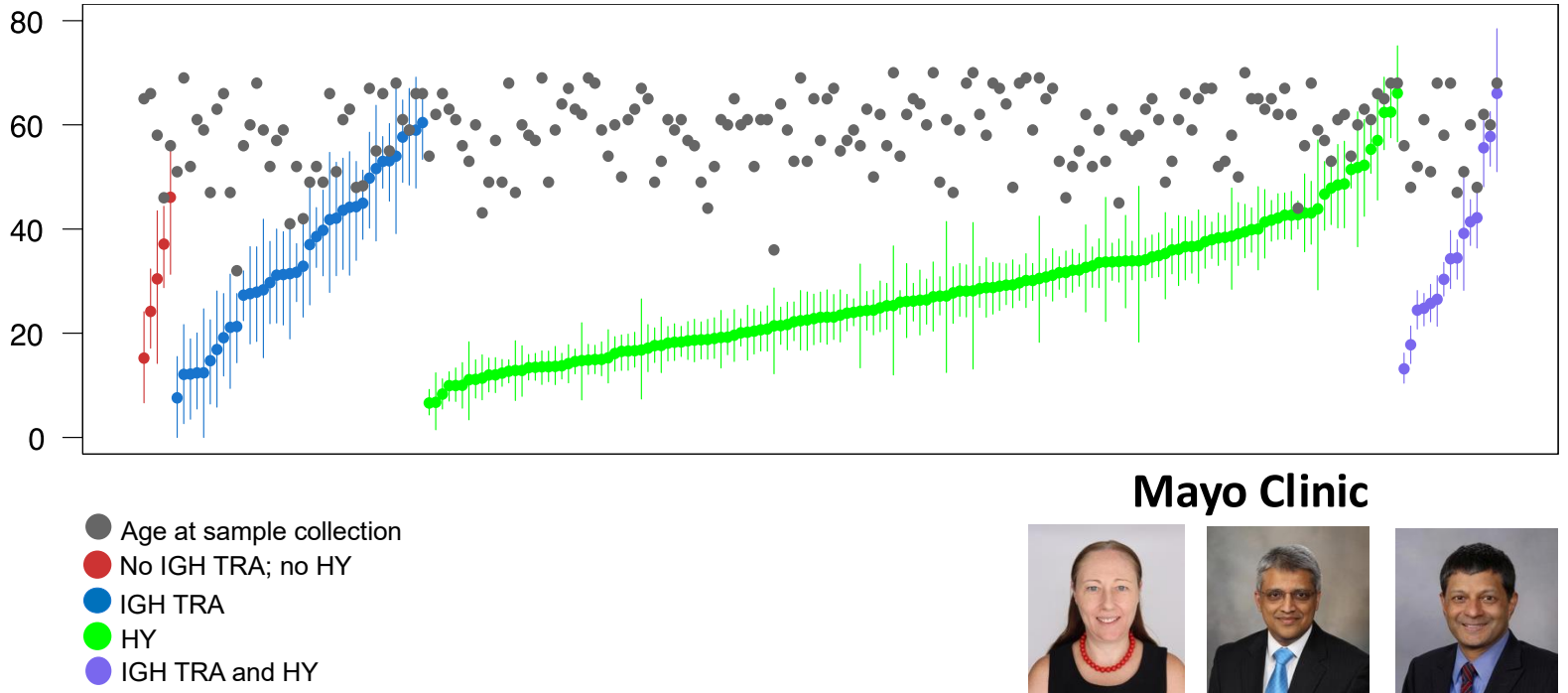


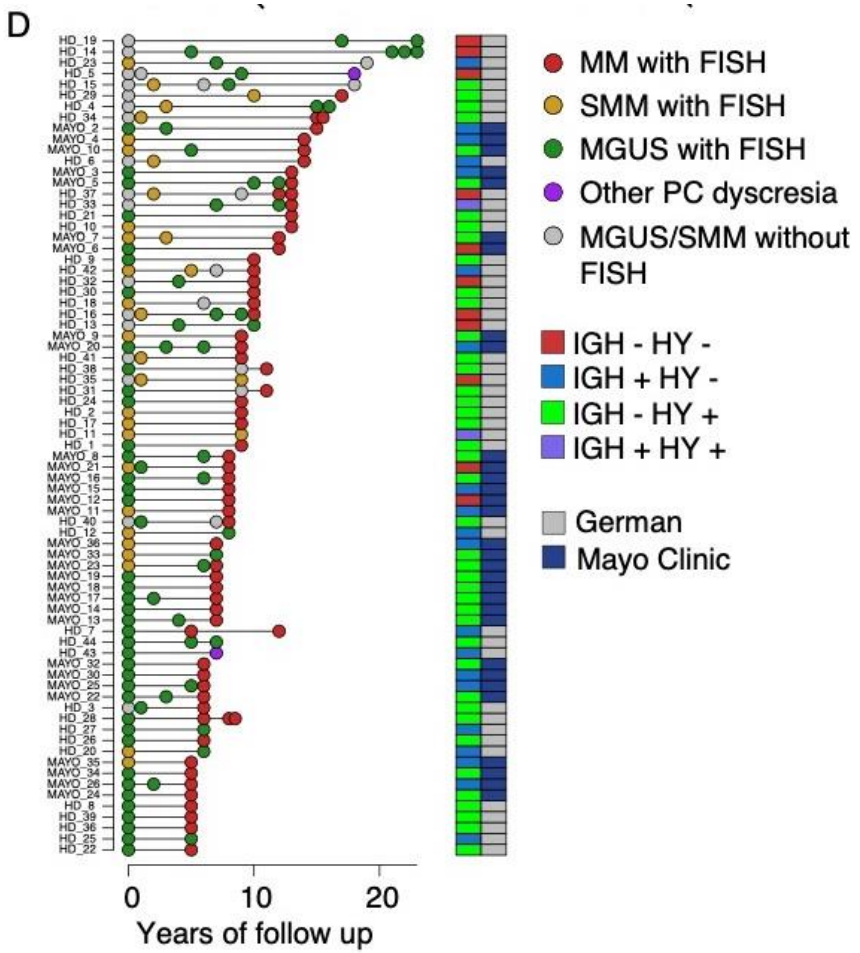
Monoclonal gammopathies can lead to a number of conditions, clinically significant!

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!





Mayo Clinic

Baughn

Kumar

Rajkumar

Heidelberg


Weinhold


Raab


Poos

Age of first chromosomal gain to age of sample collection was median <u>30 years.</u>

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_2m and LDH	↑ Levels (measure of tumor burden)
24-hour urine protein electrophoresis with immunofixation (UPEP)	↑ Monoclonal protein (*Bence Jones*)
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)

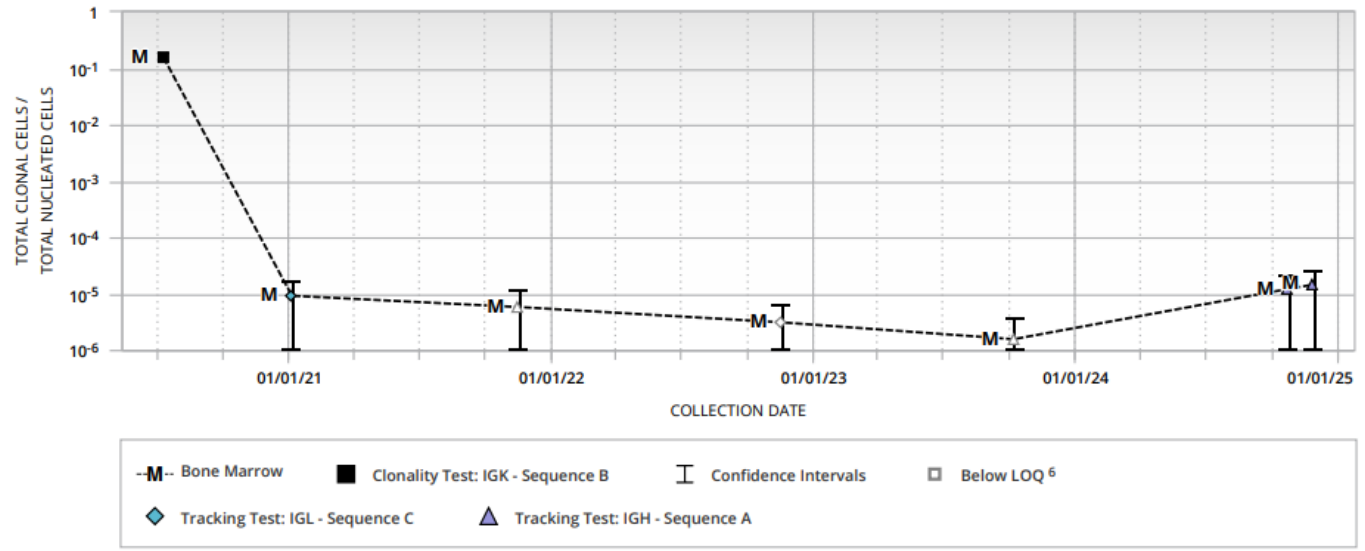
Total nucleated cells evaluated from this sample: 1,155,745

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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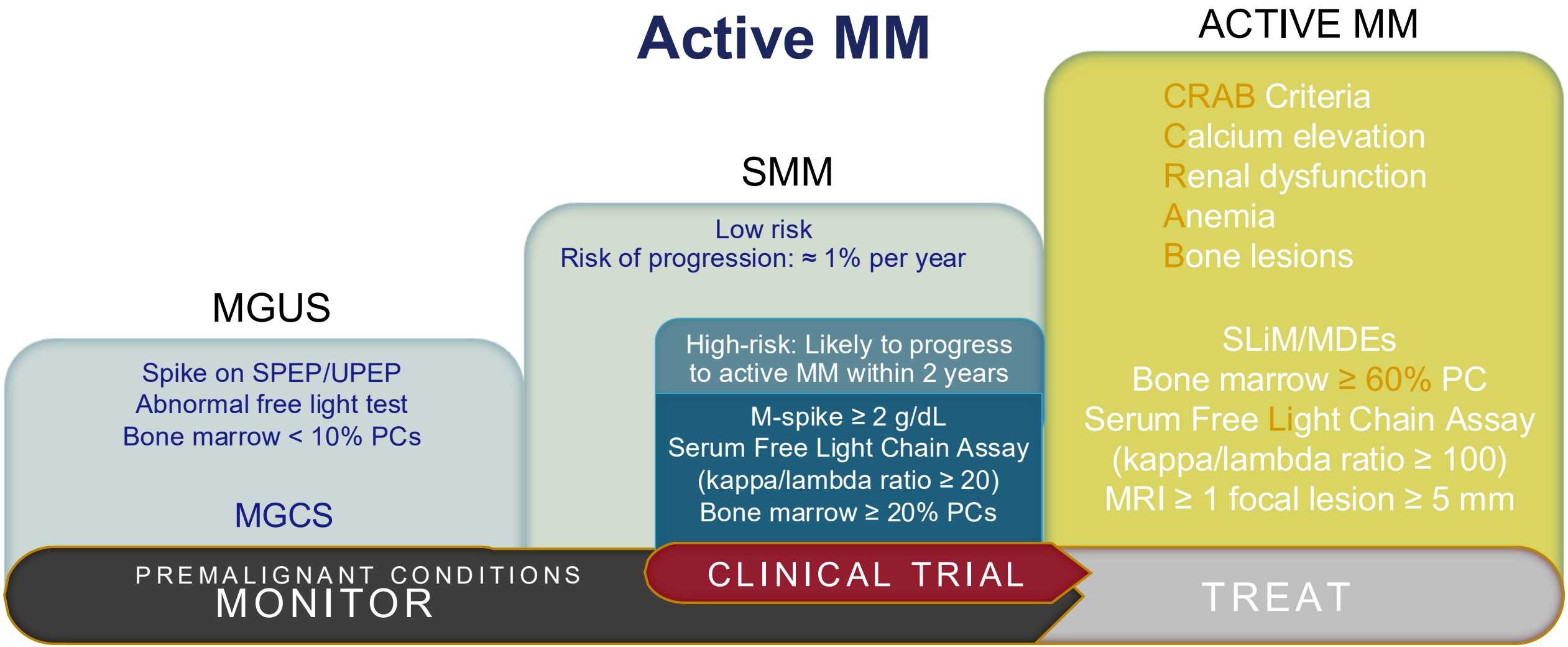
Multiple Myeloma Continuum: Active MM



CRAB = calcium elevation, renal dysfunction, anemia, bone lesions; M-spike = monoclonal spike; MDE = myeloma-defining event; MGRS = monoclonal gammopathy of renal significance; SLiM = PC ≥ 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)**

β2M ≥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)

Anti-CD38 monoclonal antibody (mAb)
- Daratumumab OR
- Isatuximab

+

Proteosome inhibitor (PI)
- Bortezomib OR
- Carfilzomib

+

Immunomodulatory drug (IMiD)
- Lenalidomide OR
- Thalidomide

+

Steroid
- Dexamethasone

At infusion clinic
Subcutaneous injection or intravenous infusion

Oral medication taken at home by patient
Adherence considerations

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 = proteosome inhibitor; IMiD = immunomodulatory drug.
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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.**

CASE DISCUSSION

CARLOS*

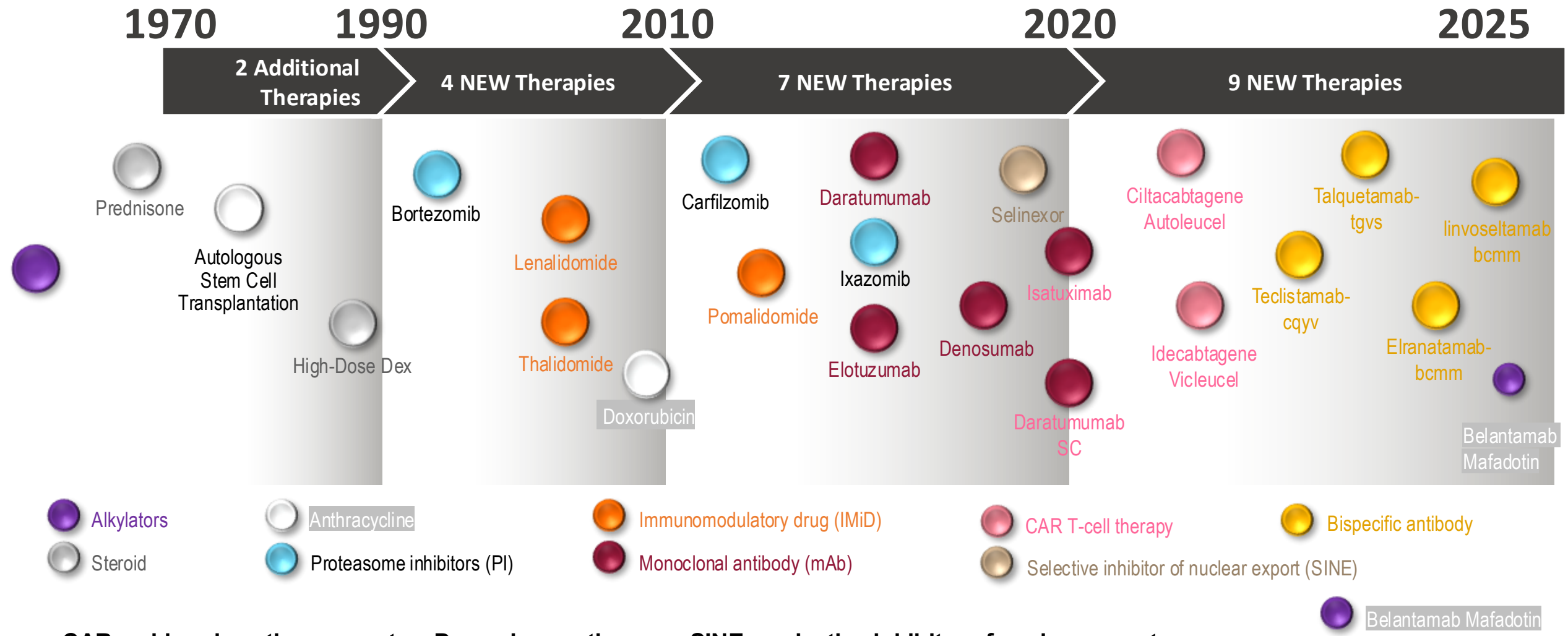
- 61-year-old w/ low back pain, ibuprofen, pain persisted
- Lumbar MRI – collapse L4, 10mm lesion; skeletal survey widespread lesions
- Bone marrow biopsy 70% kappa plasmacytosis
- Normal FISH, XY

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

***HIPAA-compliant, not actual patient name, stock photo.**
PSA = prostate-specific antigen.

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
- ≥ 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)
- ≥ 50% increase in cPCs (≥ 200 cells/μL) if this is the only measure of disease

Tests

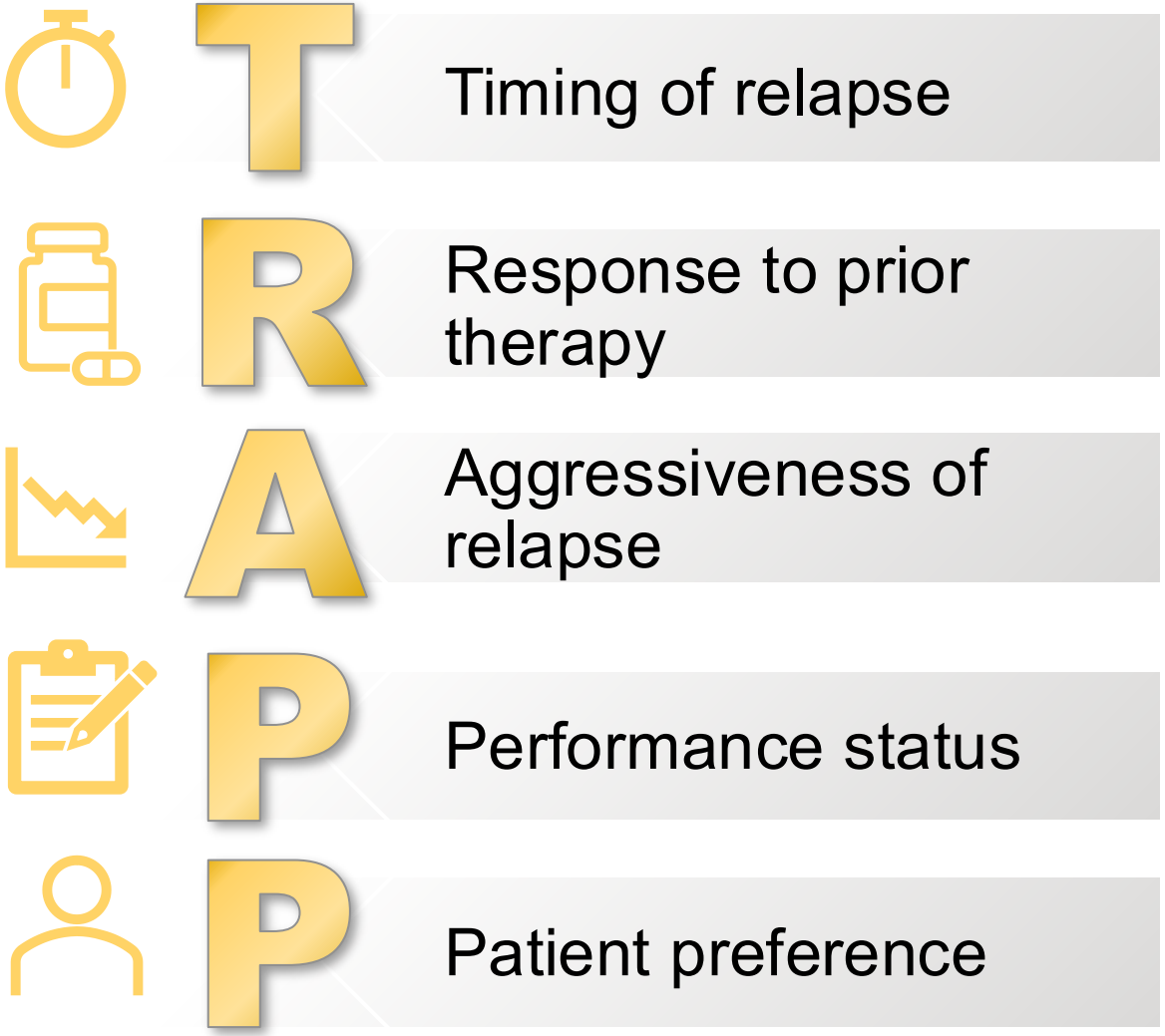
- CBC with differential; platelets
- Electrolytes; metabolic panel
- sCr & corrected serum Ca^{2+}
- M-proteins & immunoglobulins
- Serum FLC as clinically indicated
- Bone marrow aspiration & biopsy
- Assess MRD

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



- 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.

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

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		

National Comprehensive Cancer Network® (NCCN®)

NCCN Guidelines Version 2.2026
Multiple Myeloma

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

[a]2 or more prior therapies; [b]Off-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.

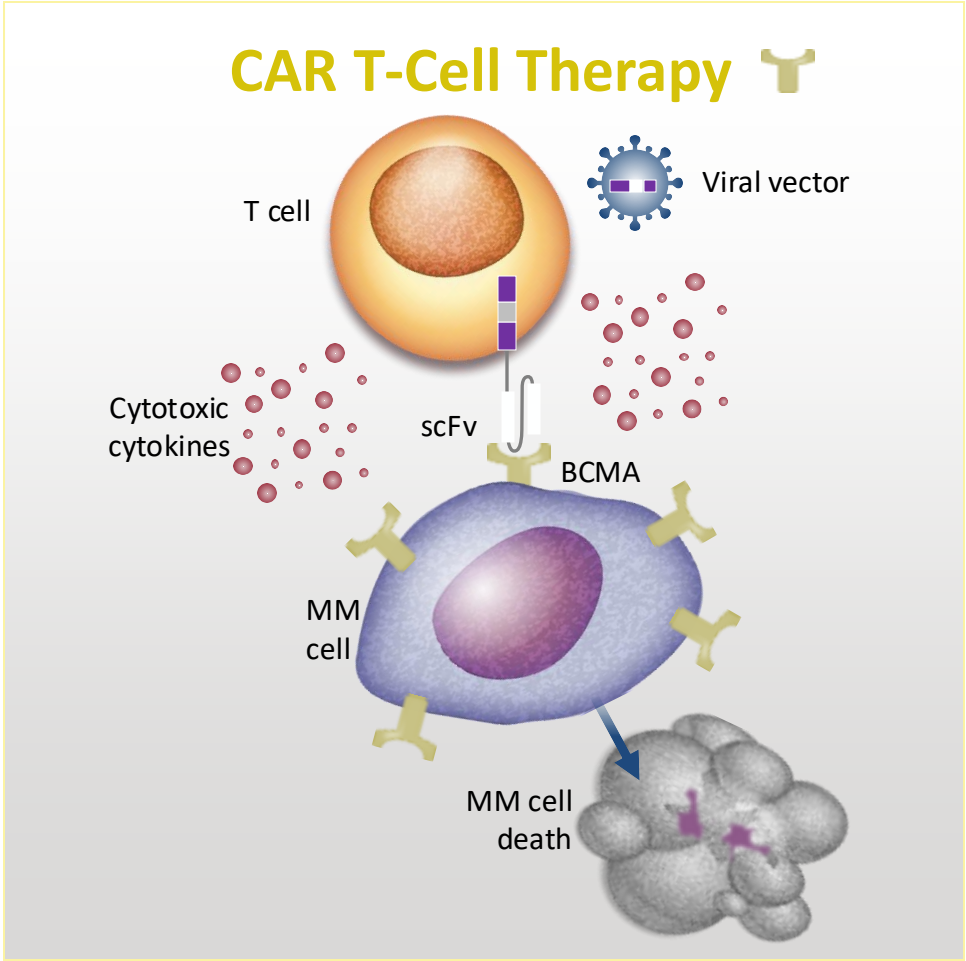
Rajkumar SV. 2024 Myeloma Algorithm. Clinical Care Options. December 27, 2023. Accessed April 4, 2025. https://clinicaloptions.com/activities/oncology/2024-mm-algorithm/18440-26989/info. Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Multiple Myeloma V.2.2026. © 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

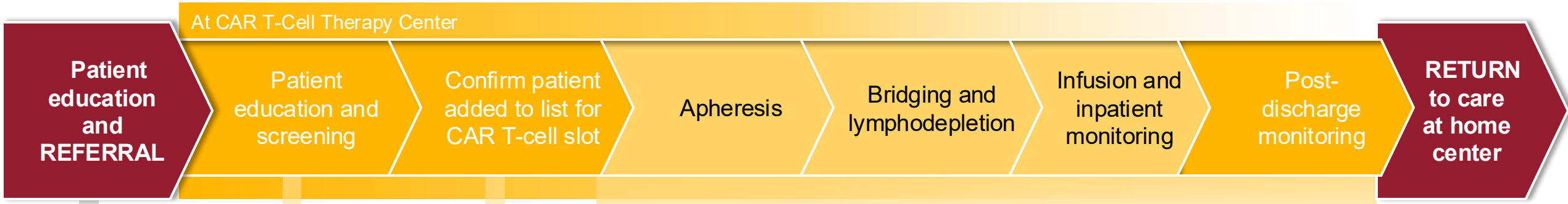
- BCMA (B-cell maturation antigen)
- Member of TNF receptor superfamily
- BCMA is expressed on late memory B cells committed to PC differentiation and PCs
- BCMA plays a role in survival of long-lived PCs
- BCMA is expressed more abundantly on malignant PCs than on normal ones



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



Refer patients to CAR T-cell center early when CAR T cell therapy could be next therapy

Most centers require several screening steps, including financial consultation

Allocation of slots is institution specific—UNDERSTAND their process to help your patients navigate

CAR T-cell therapy takes a couple of months once a patient receives a CAR T-cell therapy slot

- Extensive care partner support is typically required (especially for month after CAR T-cell infusion)
- Patients usually need to remain in proximity to the CAR T-cell therapy center for ≈ 4 weeks after CAR T-cell infusion
- Patients should not drive for ≈ 2 months after CAR T-cell infusion

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/ 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!

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.

Emerging Role of BCMA in R/R MM

Joshua Richter, MD, FACP

Belantamab Mafodotin: Mechanisms of Action

Mechanisms of action: S

- Belantamab mafodotin has multimo
  immune-independent ADC-mediate
  immune-dependent mechanisms su
  ADCC/ADCP[1,2]
- Belantamab mafodotin, a humanize
  afucosylated, anti-BCMA monoclon
  antibody conjugated to the microtub
  inhibitor, mafodotin, is the first off-th
  BCMA-targeted ADC[1,2]
- Belantamab mafodotin specifically
  eliminates myeloma cells by a mult
- Mafodotin delivered to BCMA-expre
  inhibits microtubule polymerization
  immune-independent apoptosis tha
  release of markers of ICD, which m
  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

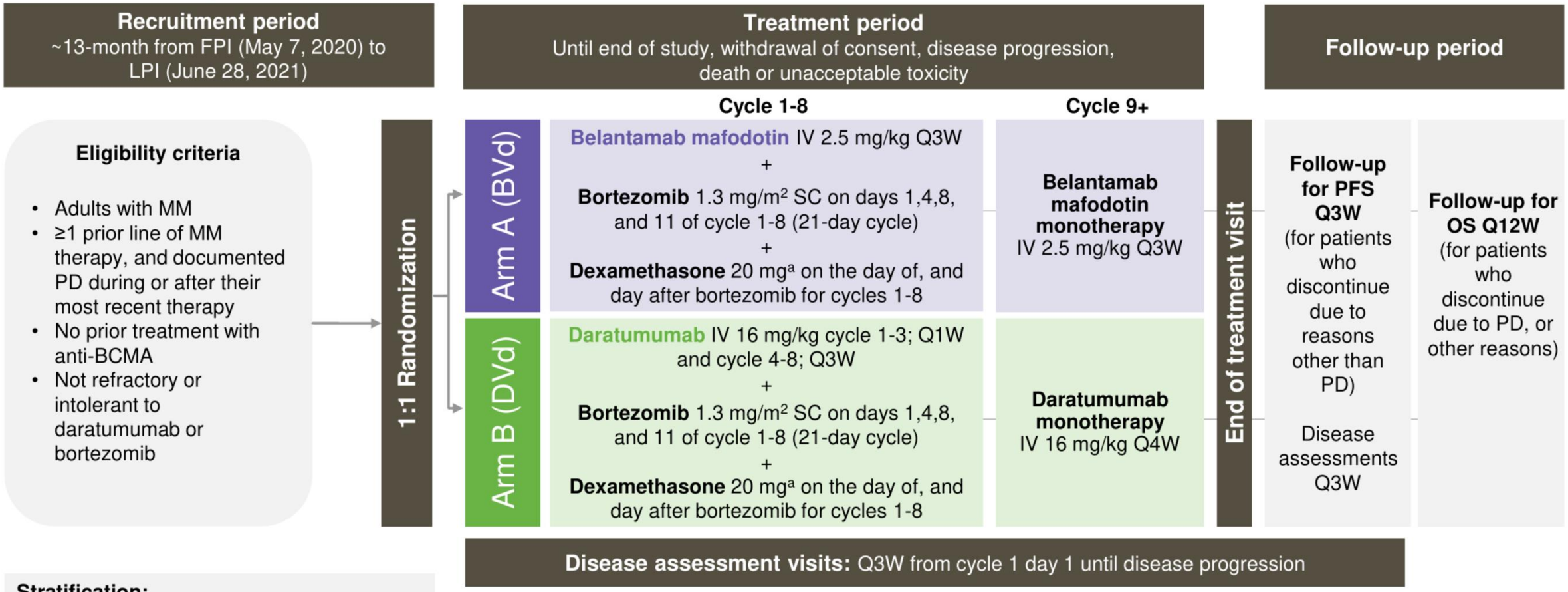
Download (PDF - 245.7KB)

- Significant unmet need for patients requires new and novel treatments[1]
- 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 triplet[2]
- *Blenrep* is the only anti-BCMA accessible in the community setting where 70% of patients receive care, and with a new streamlined REMS programme[3]
- Robust clinical development is ongoing to advance *Blenrep* in earlier lines of treatment, including newly diagnosed patients[4]

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.

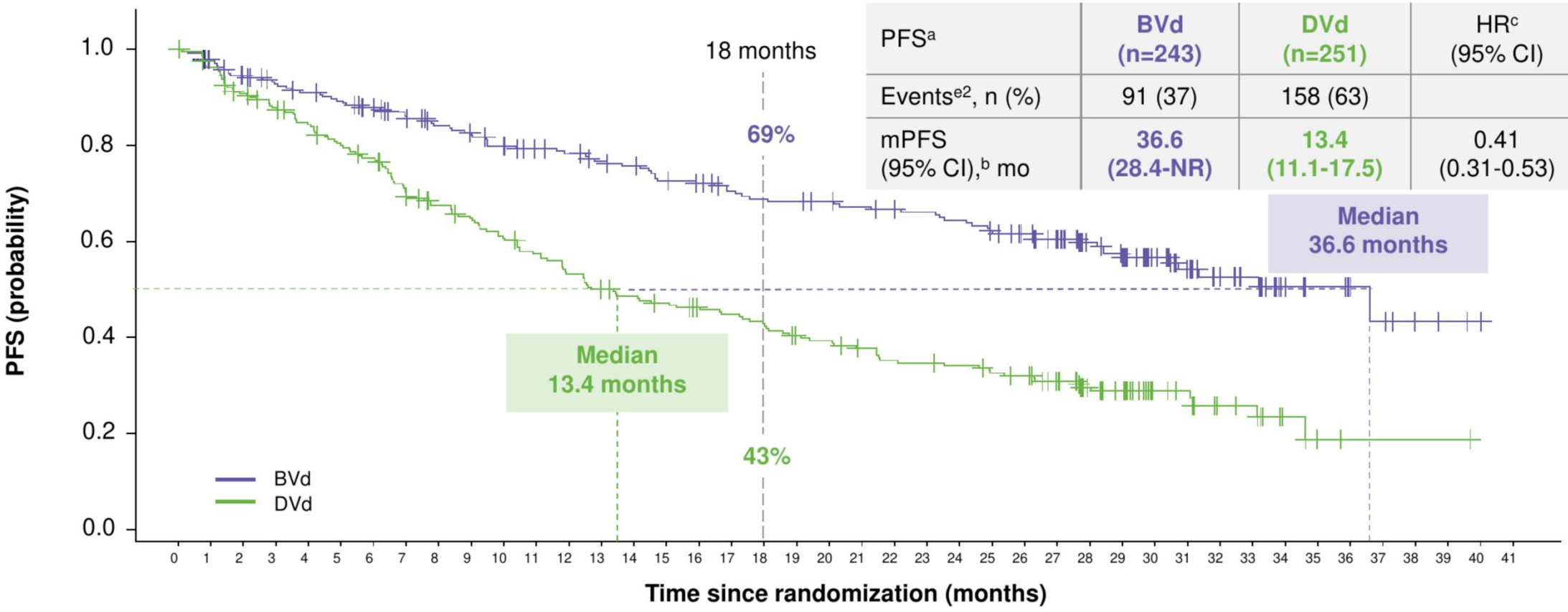
Tai YT, et al. *Blood*. 2014;123(20):3128-3138. Montes de Oca R, et al. Poster PF558. Presented at: EHA 2019; June 13-16, 2024; Amsterdam, Netherlands. Cho SF, et al. *Front Immunol*. 2018;9:1821.

Dreamm-7



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

Dreamm-7

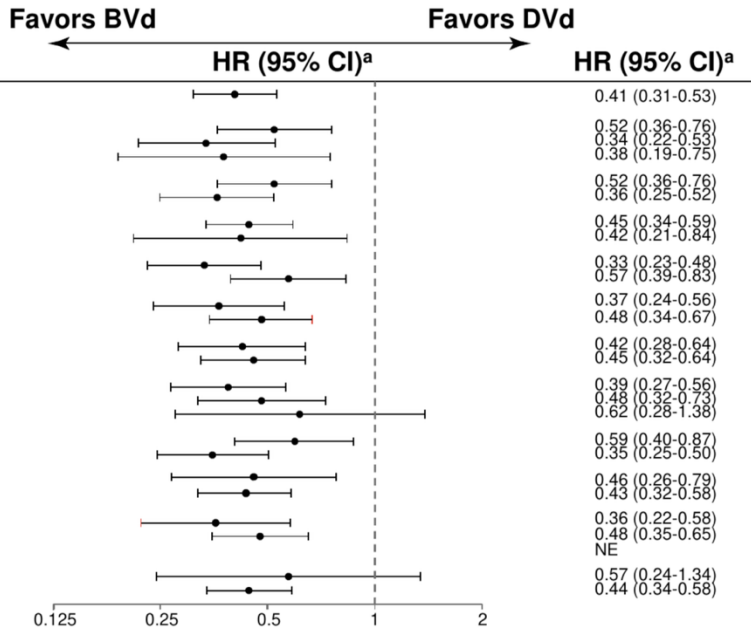


PFS[a]	BVd (n=243)	DVd (n=251)	HR[c] (95% CI)	*p*-value[d]
Events[e2], n (%)	91 (37)	158 (63)		
mPFS (95% CI),[b] mo	36.6 (28.4-NR)	13.4 (11.1-17.5)	0.41 (0.31-0.53)	<.00001

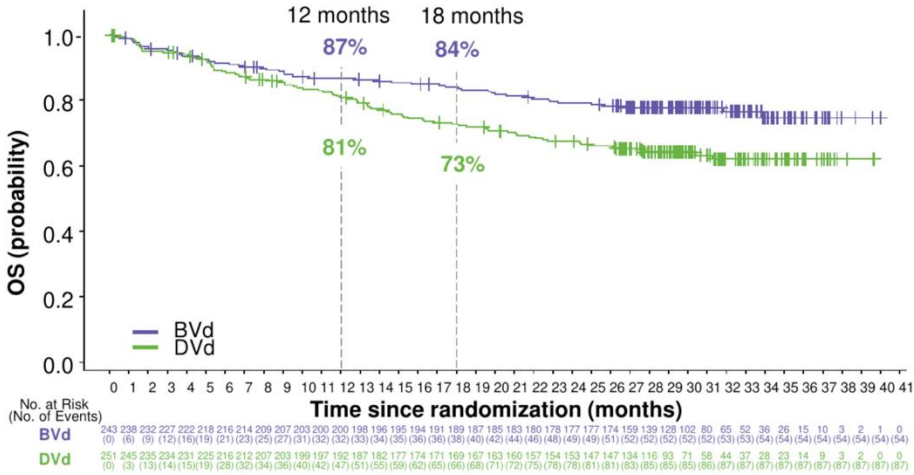
Mateos MVM, et al. Abstract 439572. Presented at: ASCO Plenary Series: February 2024 Session; 2024.

Dreamm-7

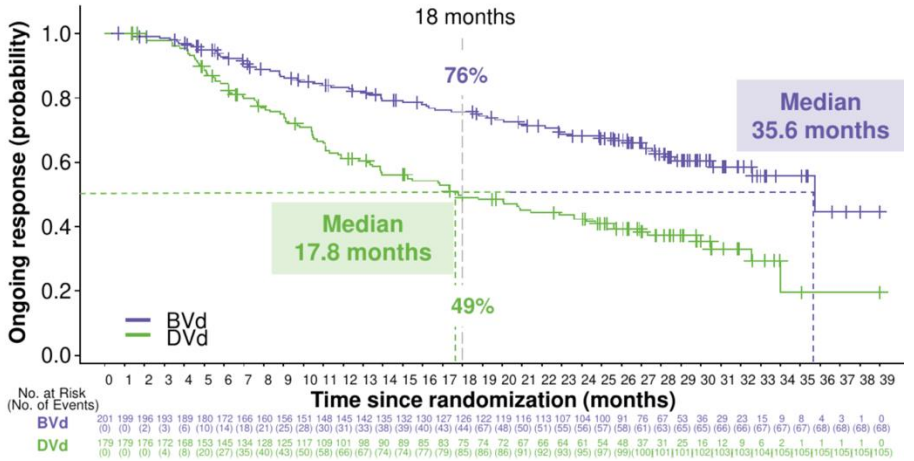
Categories	BVd n/N	DVd n/N	HR (95% CI)[a]
All Subjects (Stratified)[b]	91/243	158/251	0.41 (0.31-0.53)
Number of Prior LOT (1 vs. 2/3 vs. ≥4)			
1	46/125	76/125	0.52 (0.36-0.76)
2/3	30/88	62/99	0.34 (0.22-0.53)
≥4	15/30	20/27	0.38 (0.19-0.75)
Number of Prior LOT (1 vs. >1)			
1	46/125	76/125	0.52 (0.36-0.76)
>1	45/118	82/126	0.36 (0.25-0.52)
Prior Bortezomib			
Yes	79/210	132/211	0.45 (0.34-0.59)
No	12/33	26/40	0.42 (0.21-0.84)
Prior Lenalidomide			
Yes	44/127	88/130	0.33 (0.23-0.48)
No	47/116	70/121	0.57 (0.39-0.83)
Refractory to Lenalidomide			
Yes	33/79	64/87	0.37 (0.24-0.56)
No	58/164	94/164	0.48 (0.34-0.67)
Revised ISS Staging at Screening			
I	37/102	64/103	0.42 (0.28-0.64)
II/III	53/139	94/146	0.45 (0.32-0.64)
Age			
<65 years	42/121	84/126	0.39 (0.27-0.56)
65-<75 years	37/85	61/95	0.48 (0.32-0.73)
≥75 years	12/37	13/30	0.62 (0.28-1.38)
Gender			
Female	48/115	59/107	0.59 (0.40-0.87)
Male	43/128	99/144	0.35 (0.25-0.50)
Time to Relapse After Completion of 1L Treatment			
≤12 months	23/49	31/50	0.46 (0.26-0.79)
>12 months	68/194	127/201	0.43 (0.32-0.58)
Cytogenetics Risk			
High Risk[c]	26/67	48/69	0.36 (0.22-0.58)
Standard Risk[d]	65/175	106/175	0.48 (0.35-0.65)
Missing or Not Evaluable	0/1	4/7	NE
Extramedullary Disease at Baseline			
Yes	8/13	18/25	0.57 (0.24-1.34)
No	83/230	140/226	0.44 (0.34-0.58)



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)



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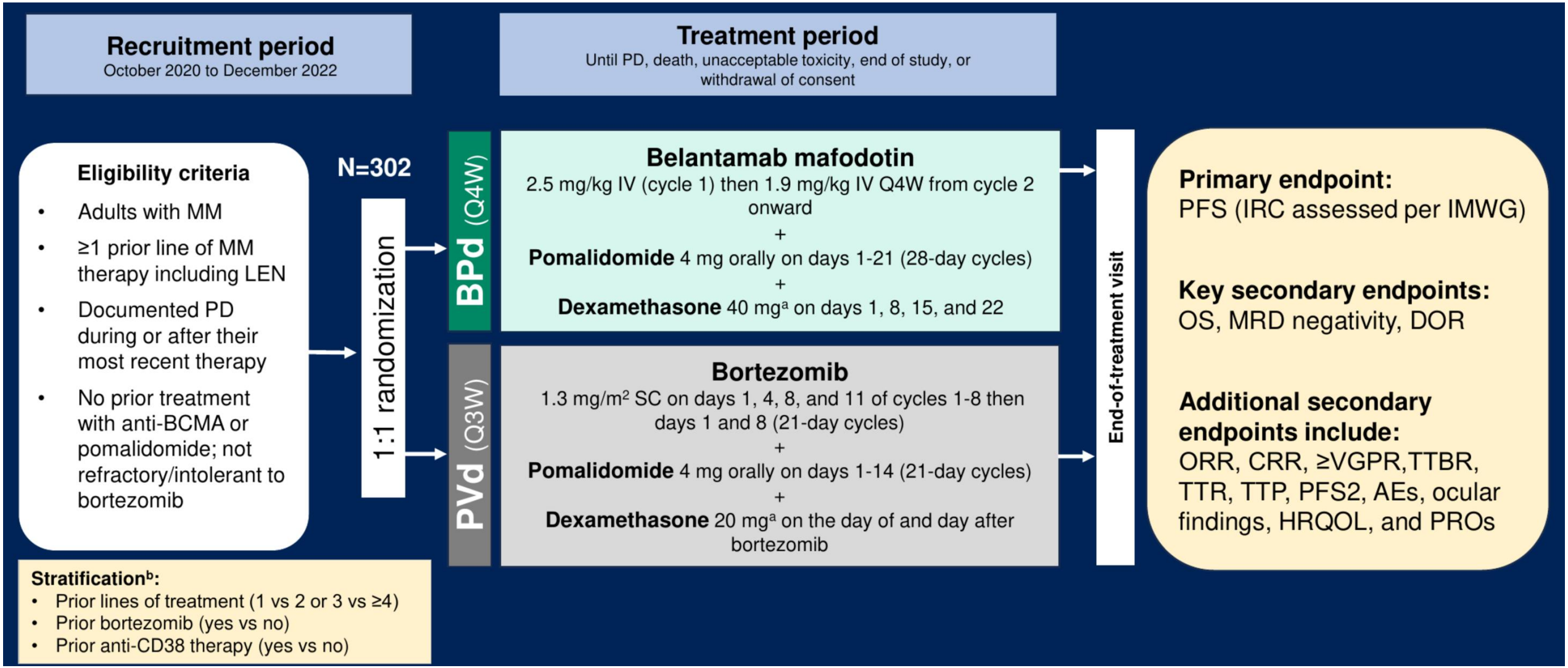
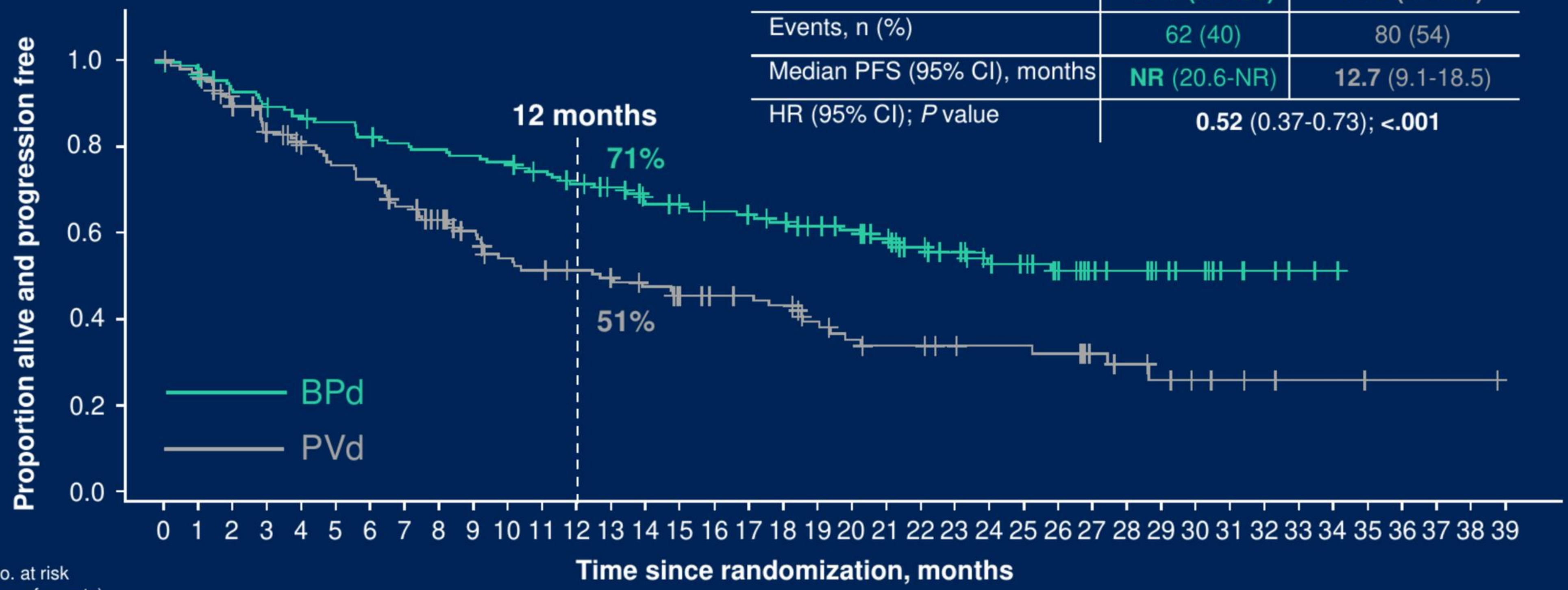
DREAMM-8



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

DREAMM-8

PFS	BPd (N=155)	PVd (N=147)
Events, n (%)	62 (40)	80 (54)
Median PFS (95% CI), months	**NR** (20.6-NR)	**12.7** (9.1-18.5)
HR (95% CI); *P* value	**0.52** (0.37-0.73); **<.001**	



No. at risk (no. of events)

	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
BPd	155 (0)	143 (5)	135 (10)	130 (15)	125 (19)	122 (21)	117 (26)	113 (28)	111 (30)	109 (32)	107 (34)	102 (37)	97 (41)	93 (42)	82 (47)	80 (47)	77 (49)	75 (50)	72 (52)	67 (53)
PVd	147 (0)	138 (4)	123 (14)	111 (23)	102 (27)	96 (33)	92 (37)	83 (45)	75 (49)	68 (52)	59 (59)	56 (62)	54 (62)	51 (64)	47 (66)	43 (68)	40 (68)	39 (68)	37 (70)	30 (73)

	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39
BPd	64 (54)	59 (56)	50 (58)	45 (59)	38 (61)	36 (61)	28 (62)	23 (62)	21 (62)	16 (62)	13 (62)	8 (62)	4 (62)	2 (62)	1 (62)	0 (62)	0 (62)	0 (62)	0 (62)	0 (62)
PVd	25 (76)	22 (77)	22 (77)	19 (77)	18 (77)	18 (77)	17 (78)	13 (78)	11 (79)	7 (80)	5 (80)	4 (80)	3 (80)	2 (80)	2 (80)	1 (80)	1 (80)	1 (80)	1 (80)	0 (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)

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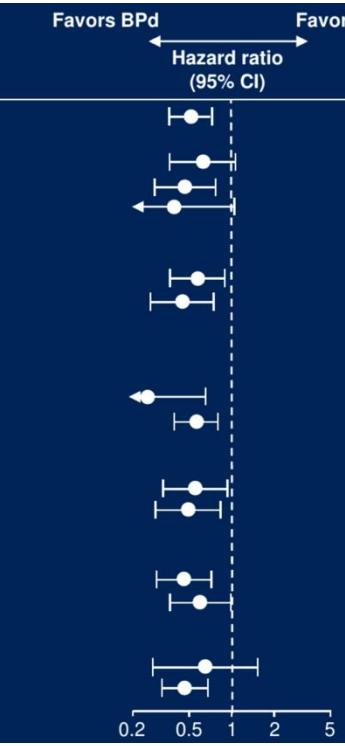
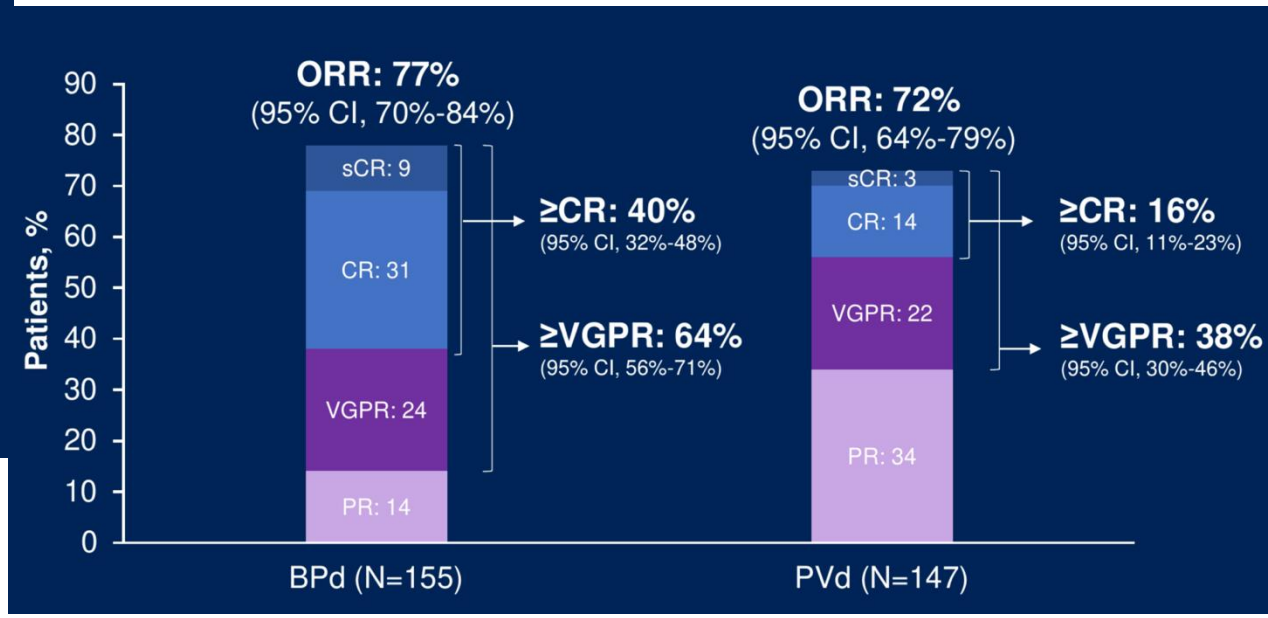
DREAMM-8

Categories	BPd n/N	PVd n/N	Hazard ratio (95% CI)
All patients (stratified)[a]	**62/155**	**80/147**	**0.52 (0.37-0.73)**
Age, years			
<65	28/64	27/53	0.64 (0.37-1.09)
65 to <75	29/72	34/59	0.48 (0.29-0.79)
≥75	5/19	19/35	0.40 (0.15-1.07)
Baseline ECOG PS			
0	34/82	48/85	0.59 (0.38-0.92)
1 or 2	28/73	32/62	0.46 (0.28-0.78)
Time to relapse after initiation of 1L treatment			
≤12 months	8/22	12/20	0.26 (0.10-0.68)
>12 months	54/133	68/127	0.58 (0.40-0.83)
Cytogenetics risk			
High risk	29/52	31/47	0.57 (0.34-0.95)
Standard risk	24/72	35/75	0.51 (0.30-0.86)
ISS stage at screening			
I	33/93	46/85	0.48 (0.30-0.75)
II/III	29/61	34/62	0.62 (0.38-1.02)
EMD at baseline			
Yes	13/20	9/11	0.67 (0.28-1.59)
No	49/135	71/136	0.48 (0.33-0.70)





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

CARTITUDE-1: Phase 1b/2 Study Design

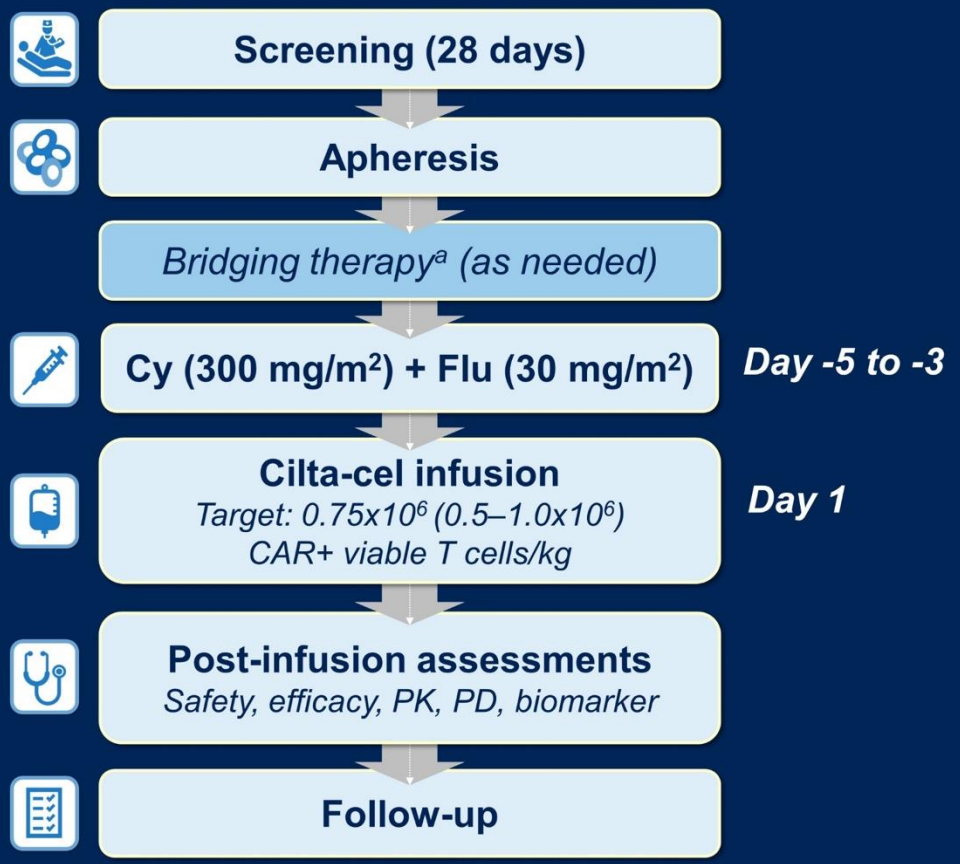
Primary Objectives

- 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

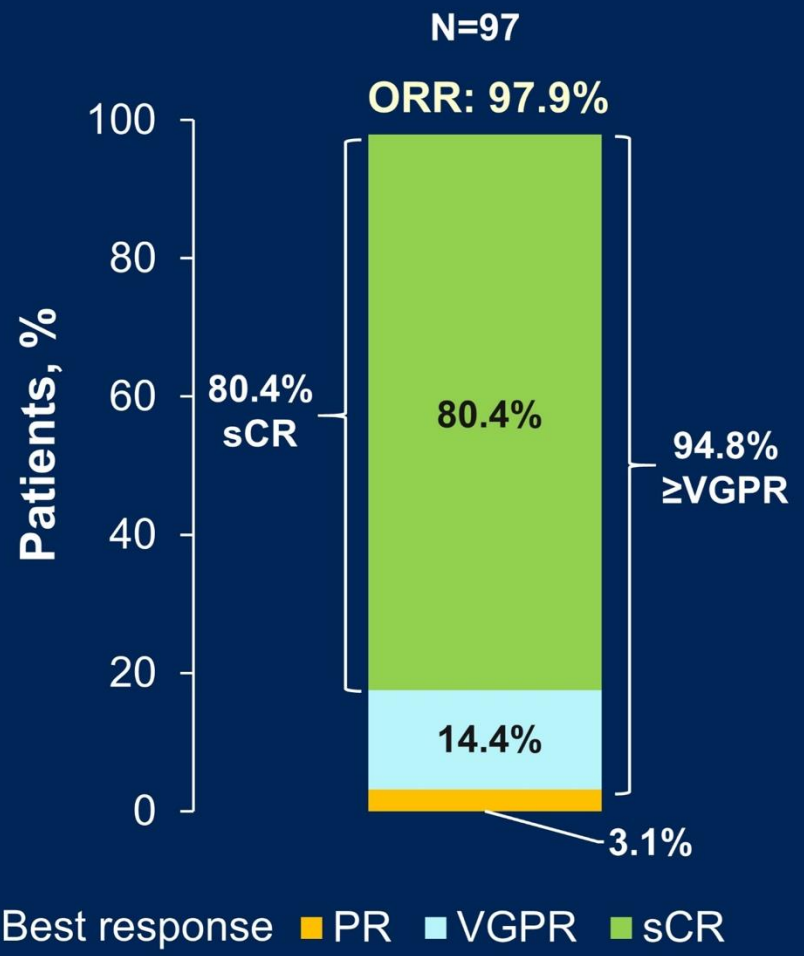
Median administered dose:
$0.71x10^6$ ($0.51–0.95x10^6$) CAR+ viable T cells/kg



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. [a]Treatment 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



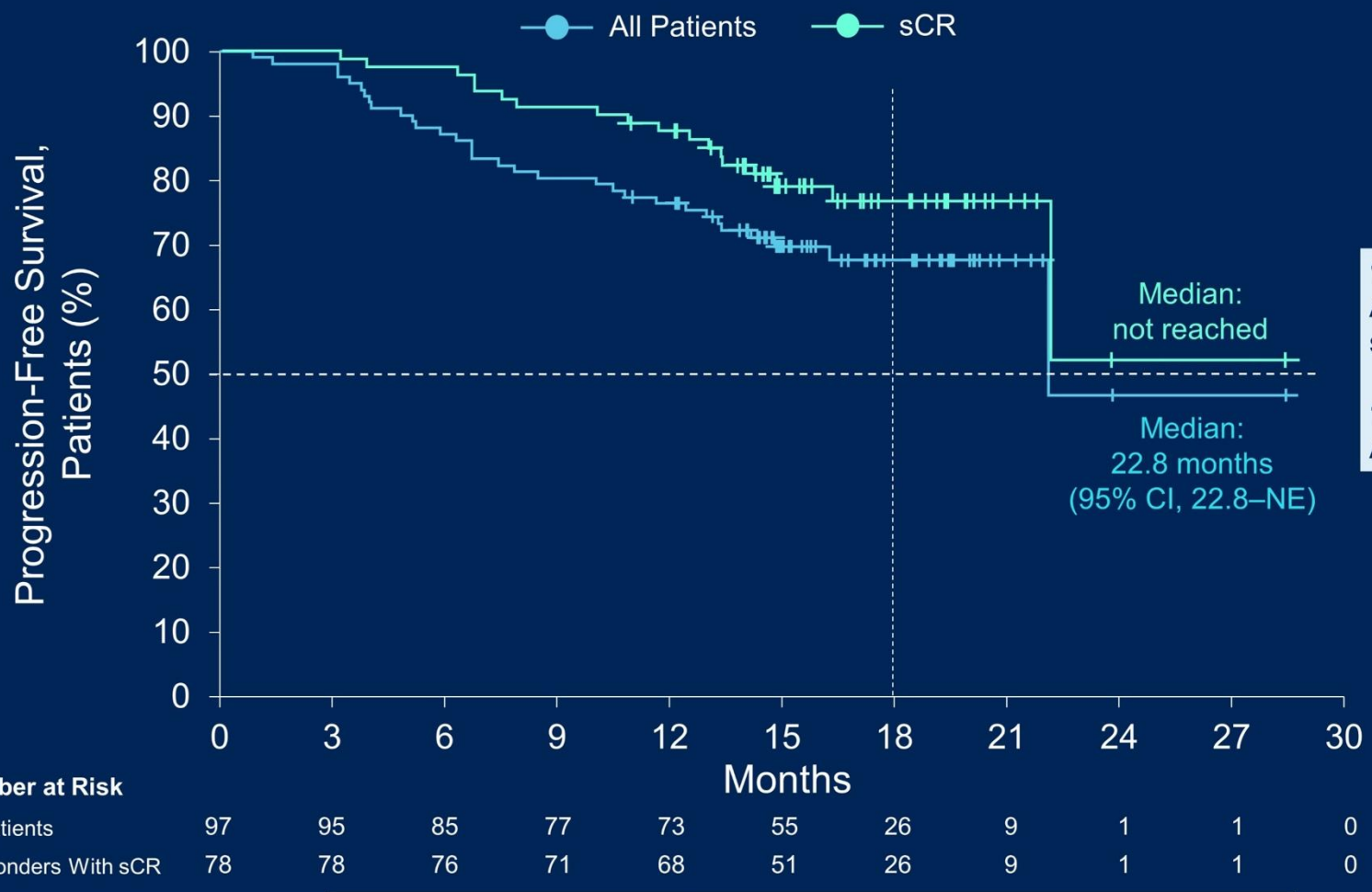
With longer follow-up, responses deepened with increasing rate of sCR

- 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 ≥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. [a]Subgroups 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 (≤30%, >30 to <60%, ≥60%), baseline tumor BCMA expression (≥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.

CARTITUDE-1: Progression-Free Survival



Number at Risk

All Patients	97	95	85	77	73	55	26	9	1	1	0
Responders With sCR	78	78	76	71	68	51	26	9	1	1	0

18-month PFS
All Patients: 66.0% (95% CI, 54.9–75.0)
sCR: 75.9% (95% CI, 63.6–84.5)

18-month OS
All patients: 80.9% (95% CI, 71.4–87.6)

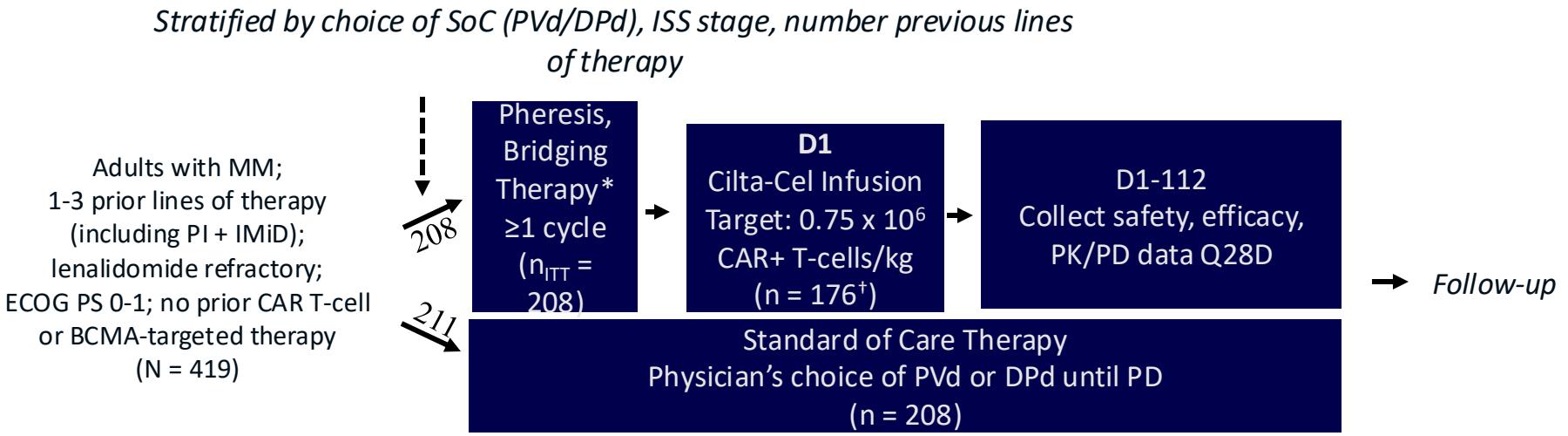
Median duration of follow-up: 18 months (range, 1.5–30.5)

NE, not estimable; PFS, progression-free survival; OS, overall survival; sCR, stringent complete response.

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

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

- Randomized, open-label phase III trial



*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.

Primary endpoint: PFS

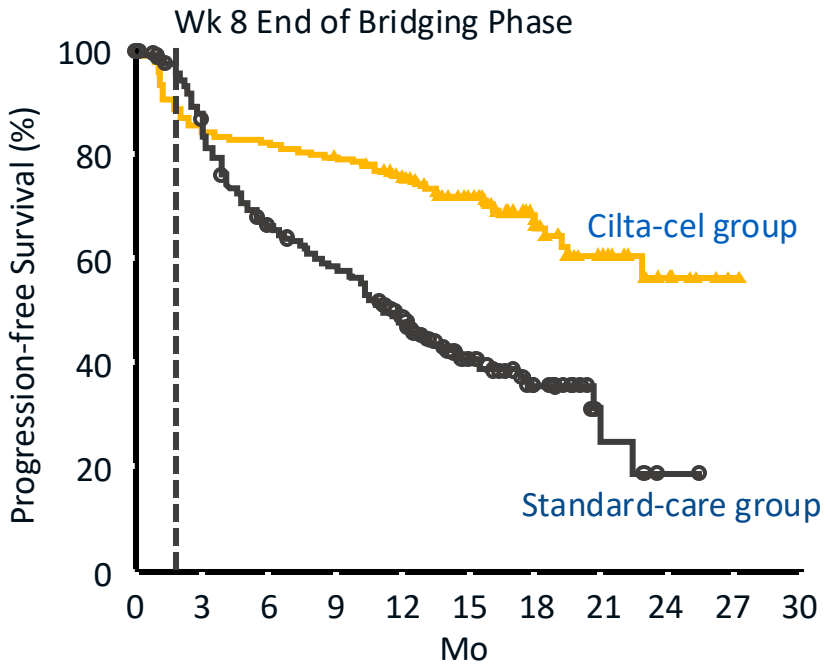
Secondary endpoints: ≥ CR, ORR, MRD negativity, OS, safety, PROs

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

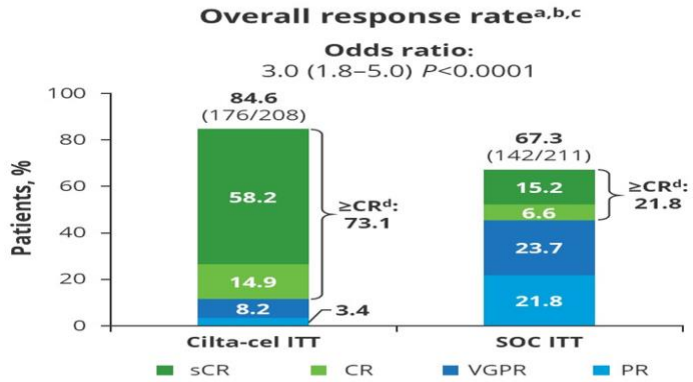
San-Miguel J, et al. *N Engl J Med*. 2023;389(4):335-347.

CARTITUDE-4: PFS and ORR (ITT Population)

Median F/U 15.9 mos



	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



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

<u>Cilta-Cel As-Treated Population</u>
ORR 99.4%
≥ CR 86.4%

San-Miguel J, et al. *N Engl J Med*. 2023;389(4):335-347.

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

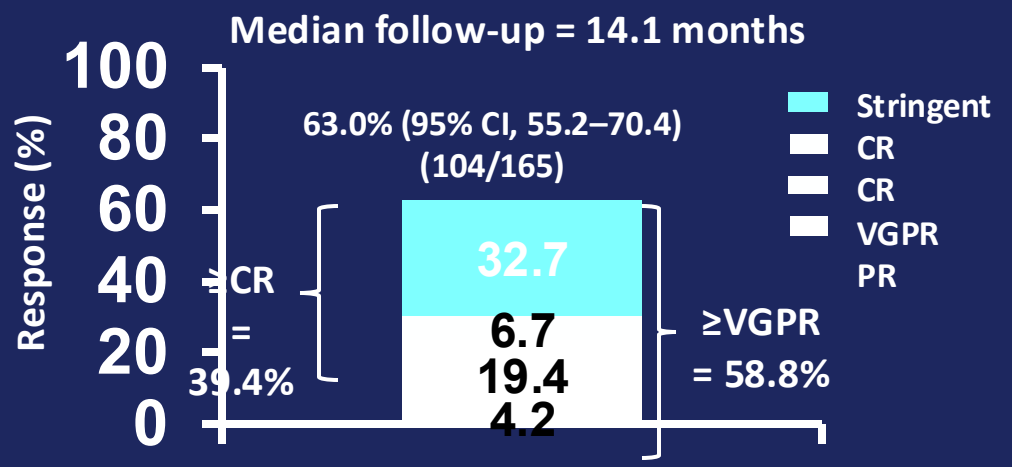
Safety

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

33% of patients had ≥2 CRS events

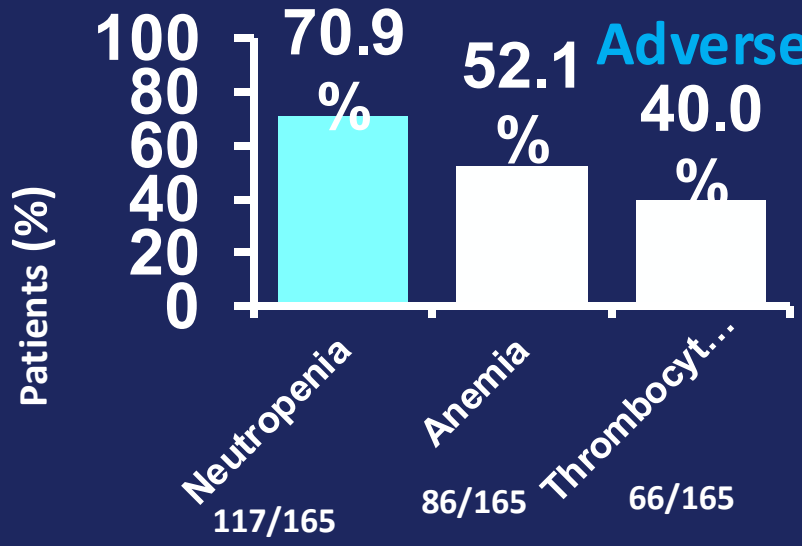
36.4% of patients with CRS required tocilizumab

Overall response



All Patients

Adverse events



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

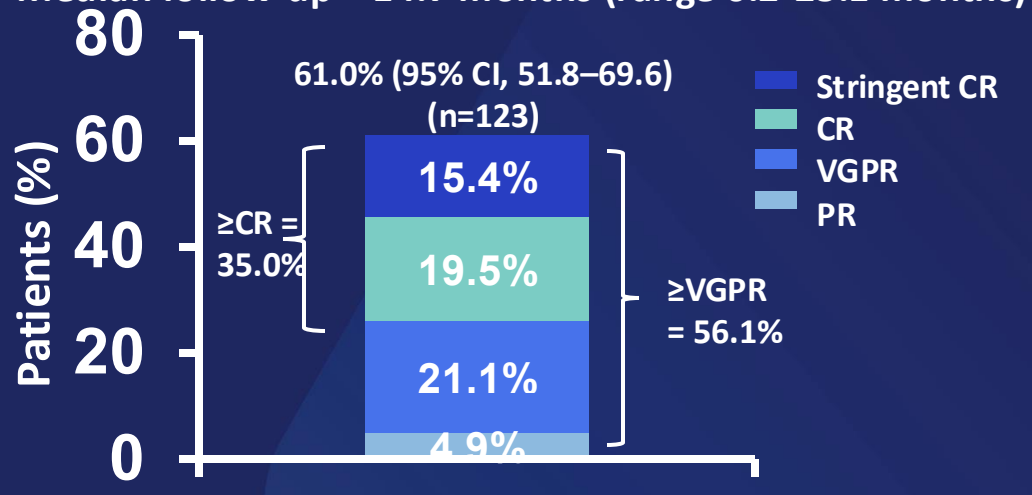
Moreau P, et al. *N Engl J Med*. 2022;387:495-505. Touzeau C, et al. *J Clin Oncol*. 2022;40(16 suppl); Abstract 8013. FDA. October 25, 2022. Accesssed November 4, 2023. www.fda.gov/drugs/resources-information-approved-drugs fda-approves-teclistamab-cqyv-relapsed-or-refractory-multiple-myeloma. Teclistamab [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

- 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

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	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)

[a]Preferred 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.

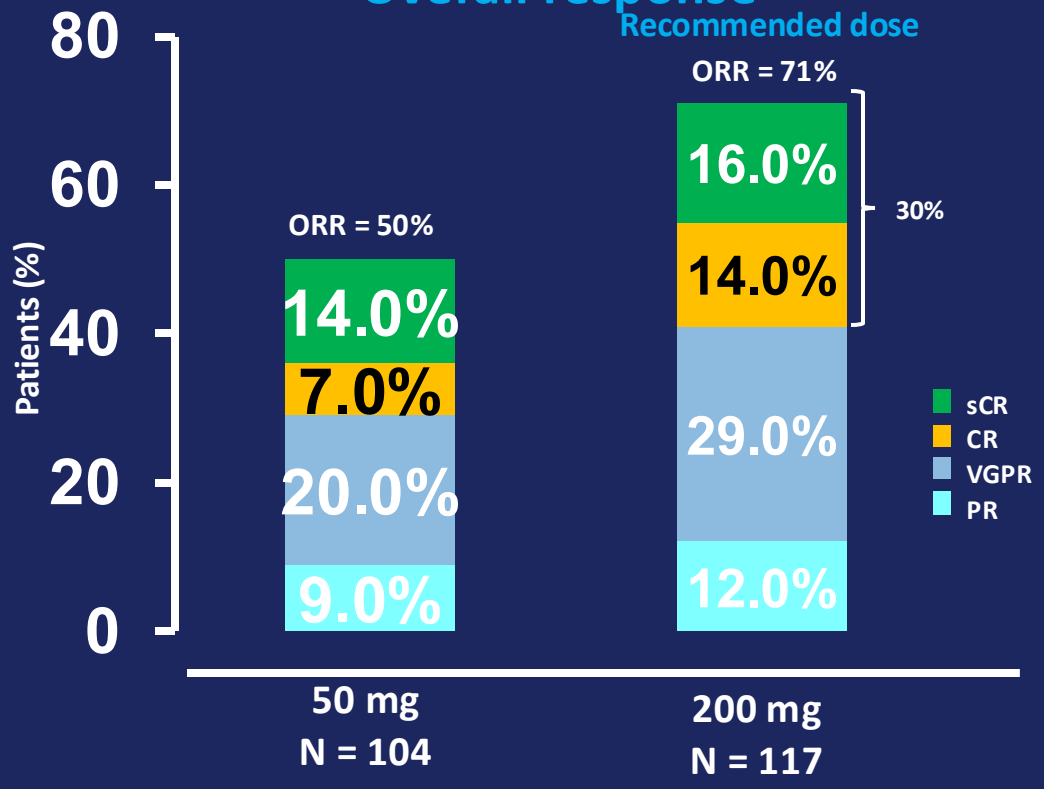
Bahlis NJ, et al. Abstract 159. ASH 2022; December 10-13, 2022; New Orleans, LA. Lesokhin AM, et al. *Nat Med*. 2023;29(9):2259-2267.

Linvoseltamab (REGN5458): LINKER-MM1

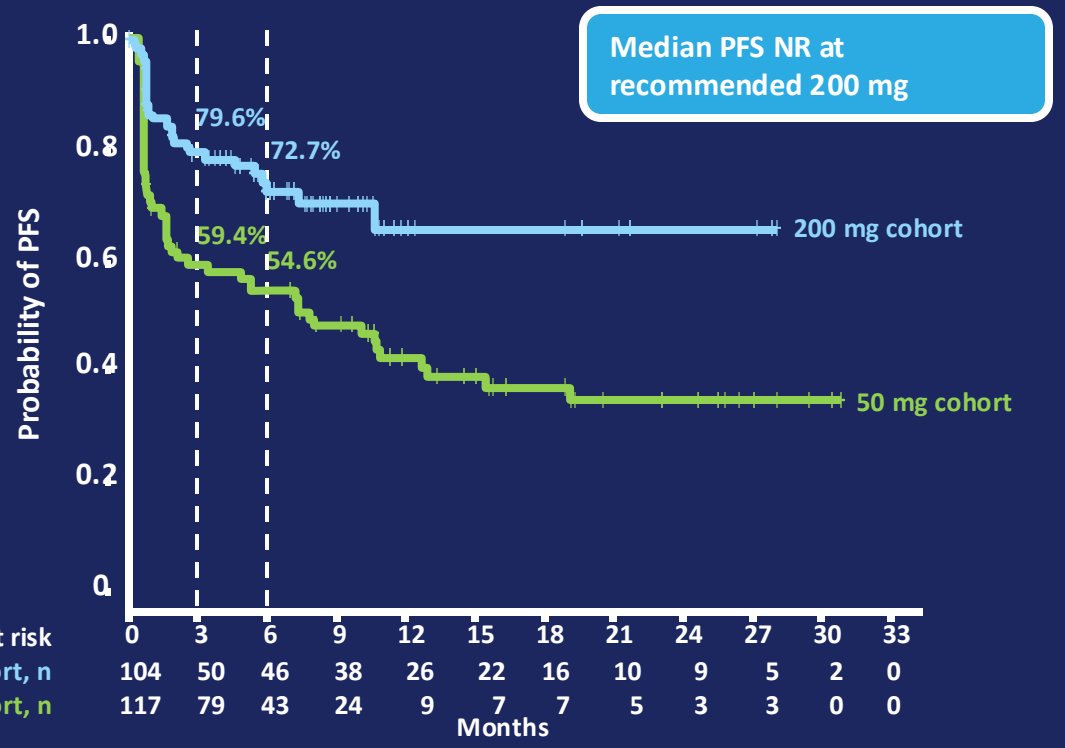
Phase 2 ORR and PFS at 50 mg and 200 mg dose regimens; BCMA x CD3

- 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)

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: 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 Philippar

Check for updates

Blood blood.2025030027.

https://doi.org/10.1182/blood.2025030027 Article history

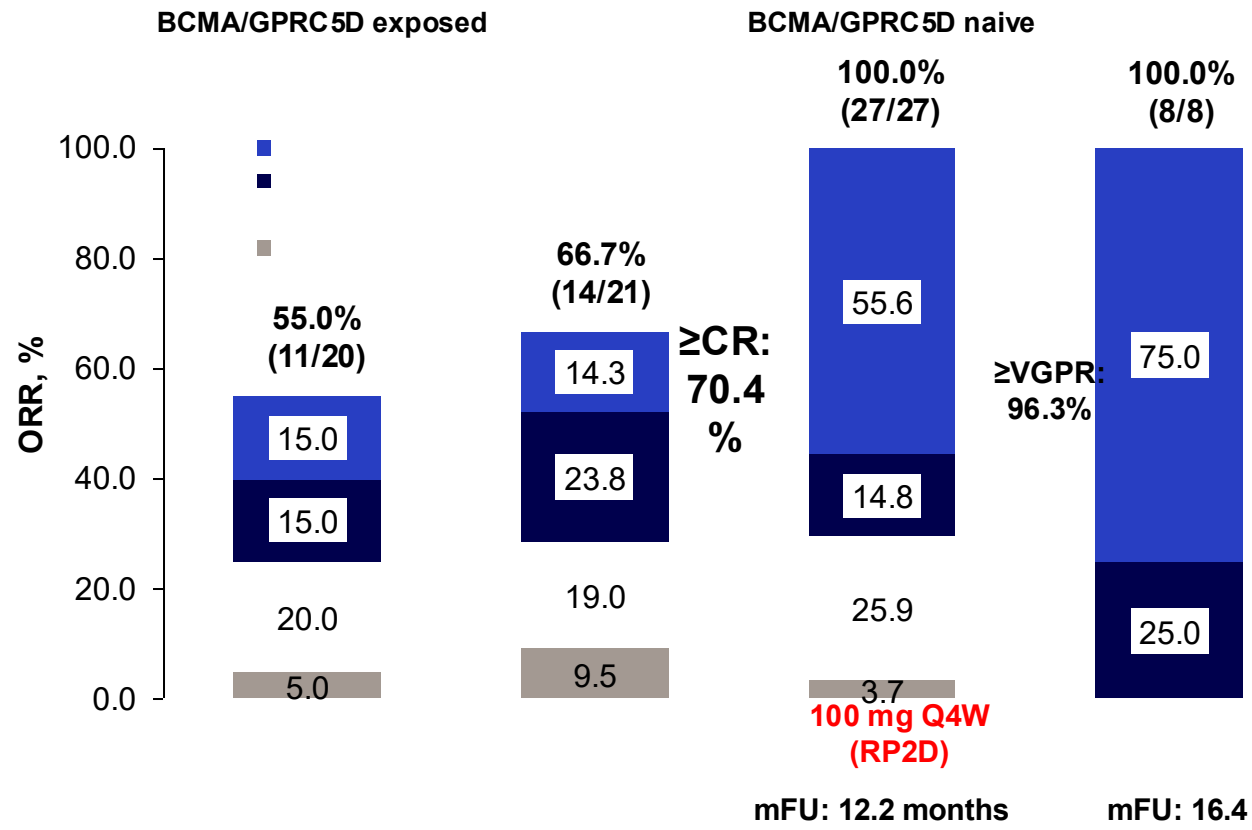
Split-Screen Share Tools PDF

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

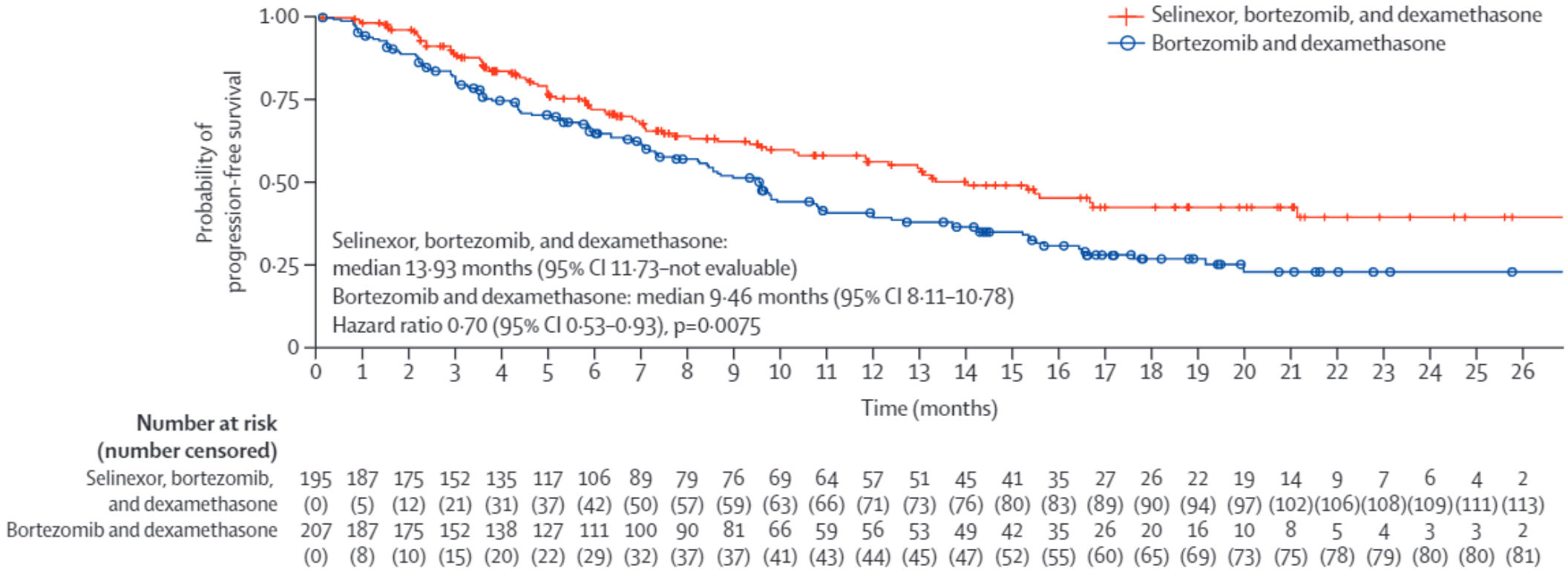
Other Novel and Emerging Therapies in R/R MM

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	

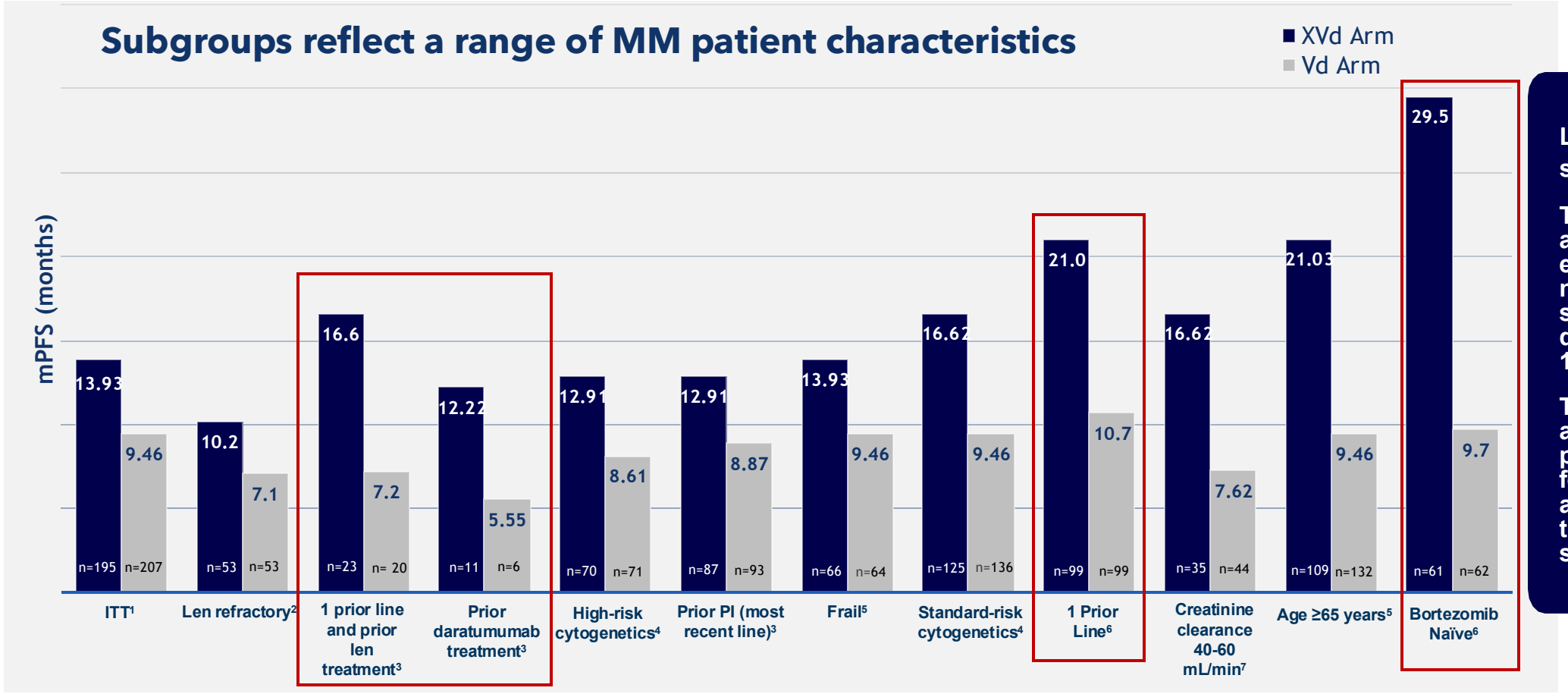
- Early PFS benefit observed with SVd vs Vd
- There was a 30% decrease in the risk of relapse with SVd vs Vd



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:

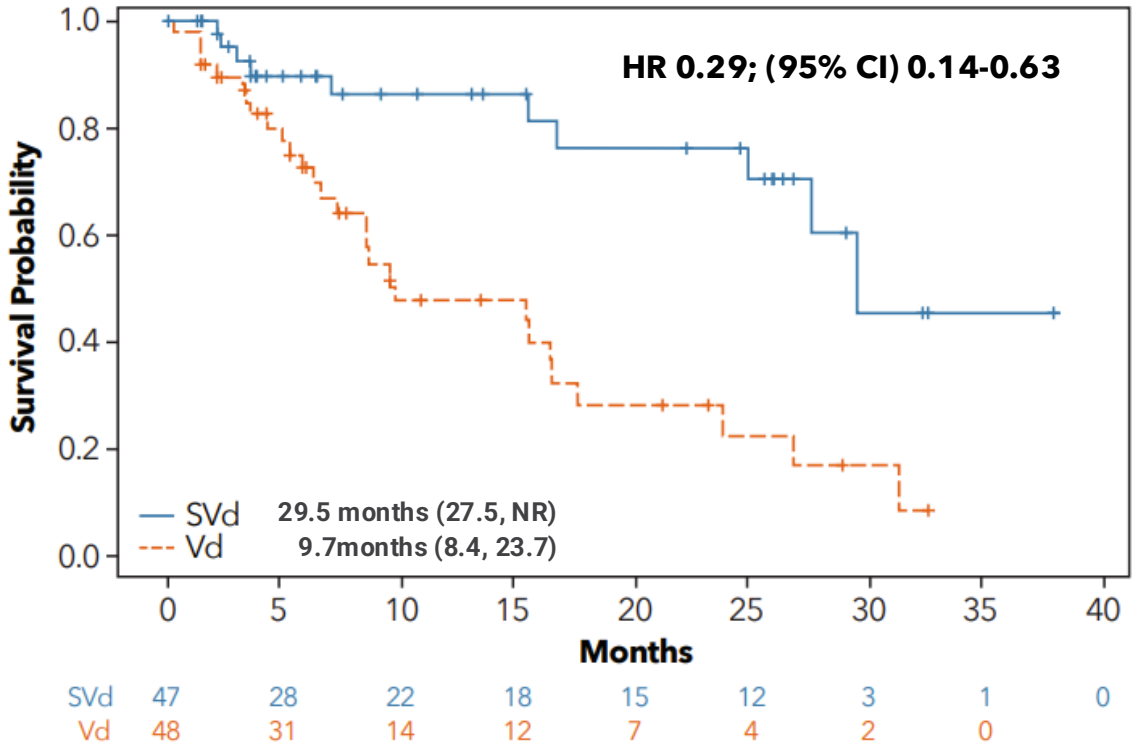
These subgroup analyses were exploratory in nature, not included in the study objectives, and do not control for type 1 error

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

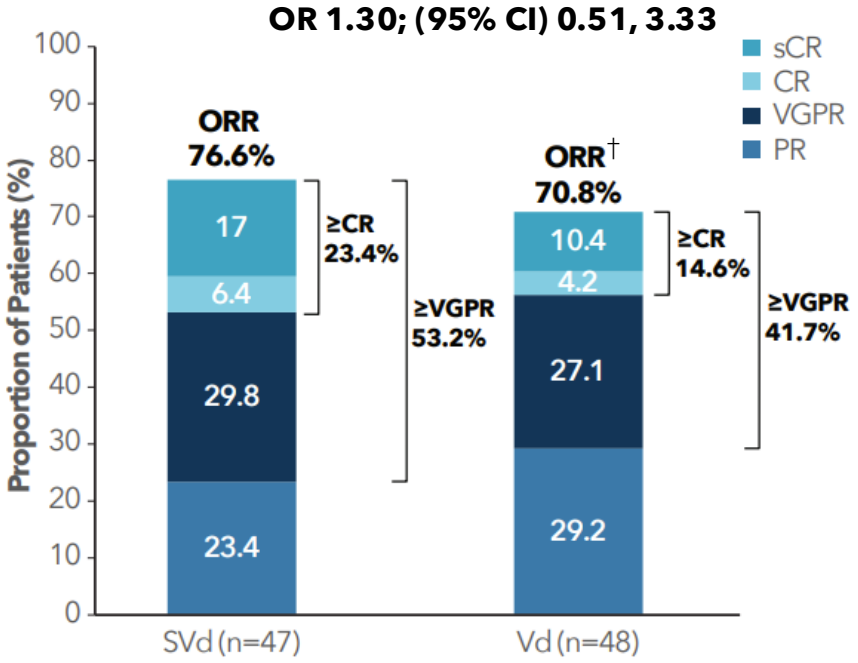
Grosicki S, et al. *Lancet*. 2020;396(10262):1563-1573. Mateos MV, et al. Poster #P886. Presented at: EHA Hybrid Congress 2023; June 8-11, 2023. Karyopharm Therapeutics. Accessed October 2025. https://investors.karyopharm.com/2020-05-28-Karyopharm-Reports-Positive-Phase-3-BOSTON-Data-in-Oral-Presentation-at-the-American-Society-of-Clinical-Oncology-2020-Virtual-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



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.

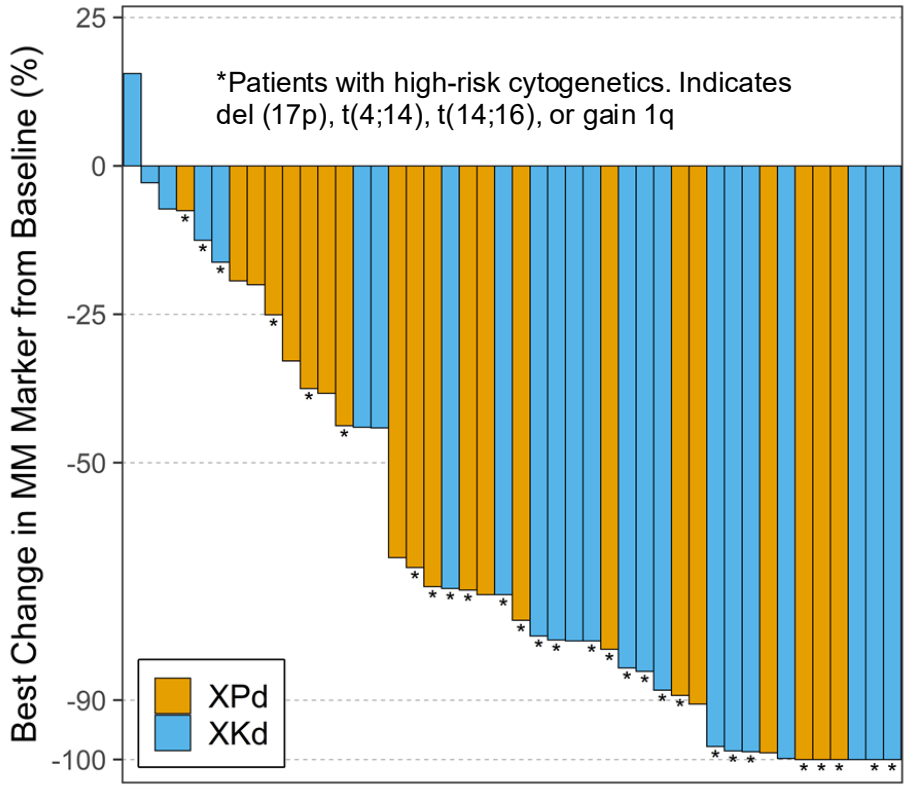
These subgroup analyses were exploratory in nature, not included in the study objectives and do not control for type 1 error. The analyses were not powered or adjusted for multiplicity to assess efficacy outcomes across these subgroups.

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.

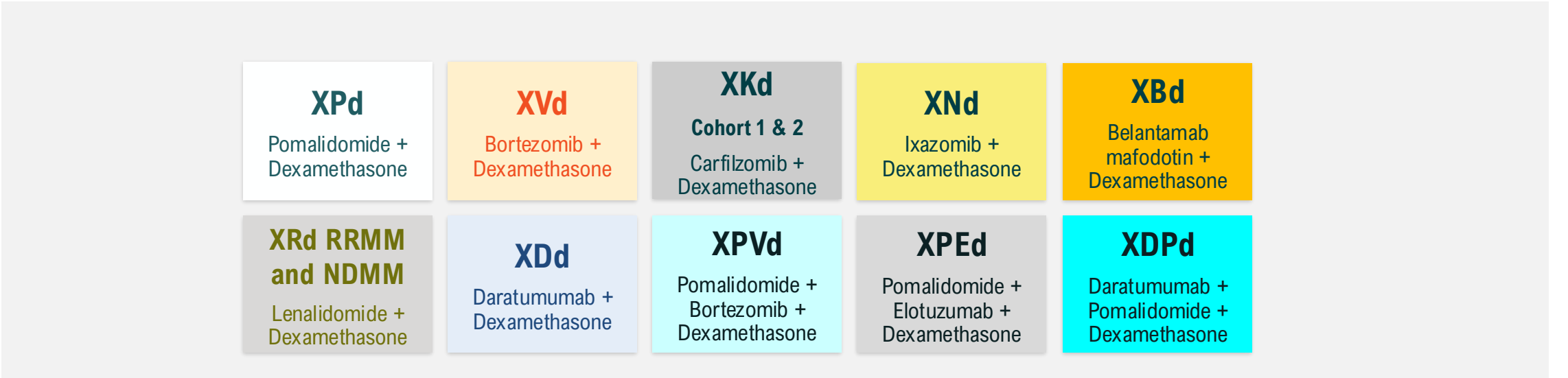
Lentzsch S, et al. Abstract 1651. Presented at: 63rd American Society of Hematology Annual Meeting; December 10-14, 2021; Atlanta, GA.

STOMP: Study Overview & Objectives

Selinexor and backbone **T**reatments **O**f multiple **M**yeloma **P**atients (**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.

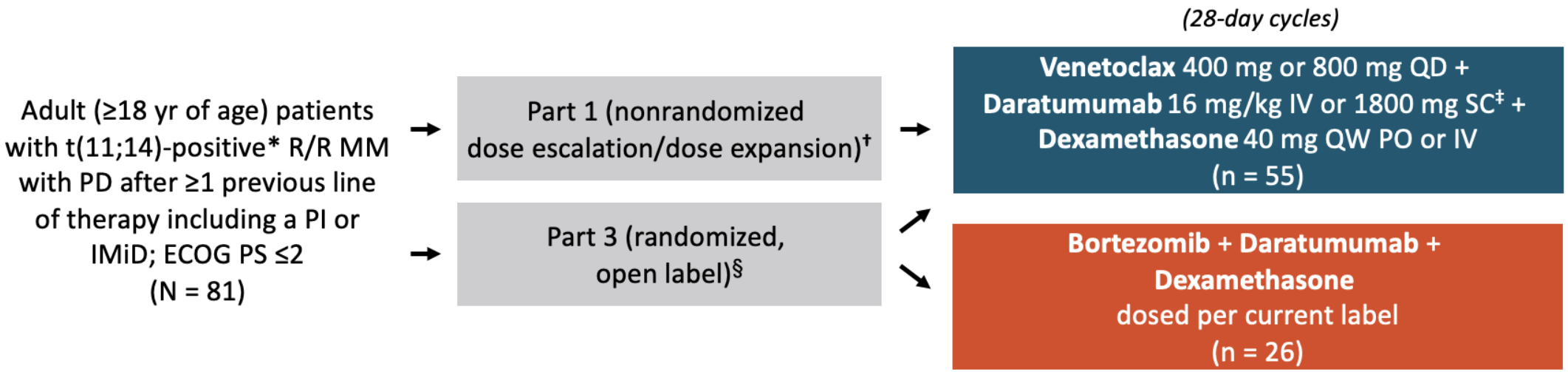


CBR = clinical benefit rate; CTCAE = common terminology criteria for adverse events; DOR = duration of response; MM = multiple myeloma; MTD = maximum tolerated dose; RP2D = recommended phase 2 dose; NDMM = newly diagnosed multiple myeloma; ORR = overall response rate; OS = overall survival; PFS = progression-free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

Bahlis NJ, et al. Abstr 338. Presented at: ASH 2023; December 9-12, 2023; San Diego, CA.

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%)

Bahlis NJ, et al. Abstr 338. Presented at: ASH 2023; December 9-12, 2023; San Diego, CA.

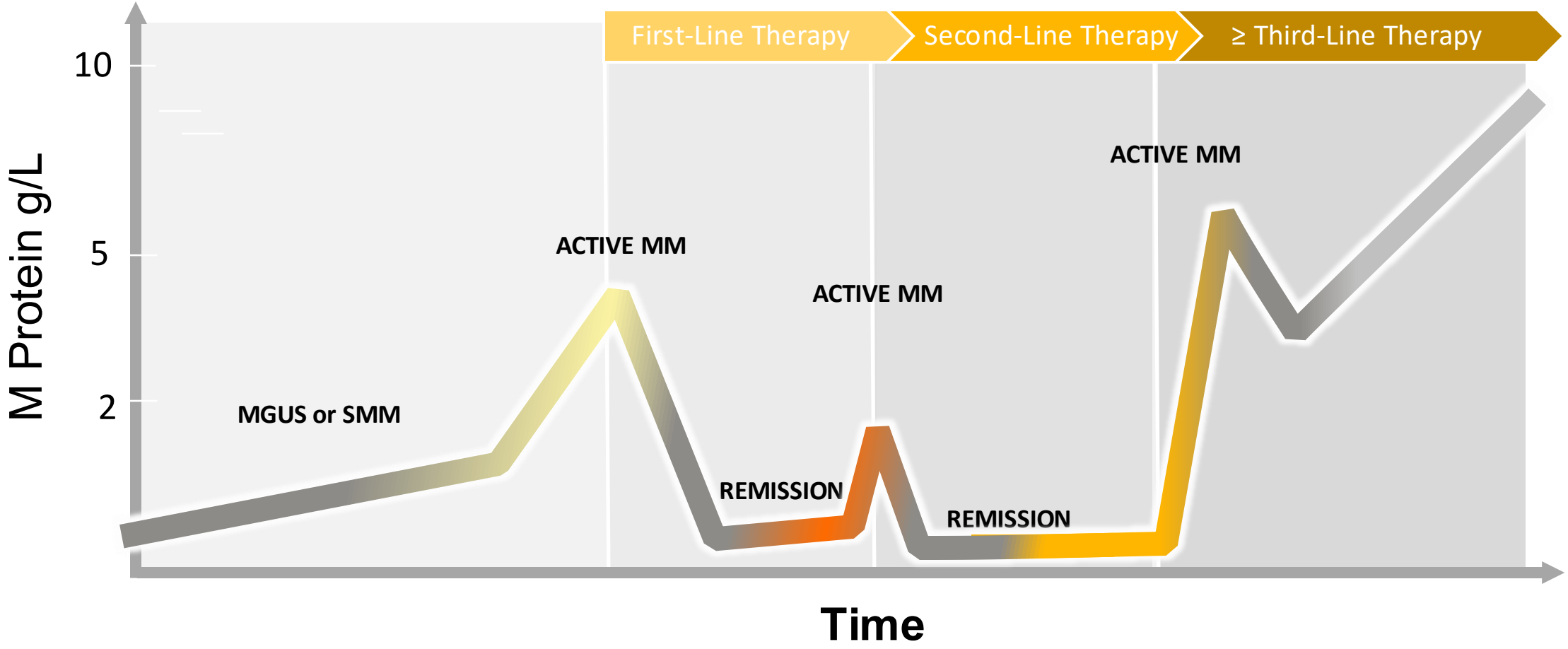
Key Take-Aways

- 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!

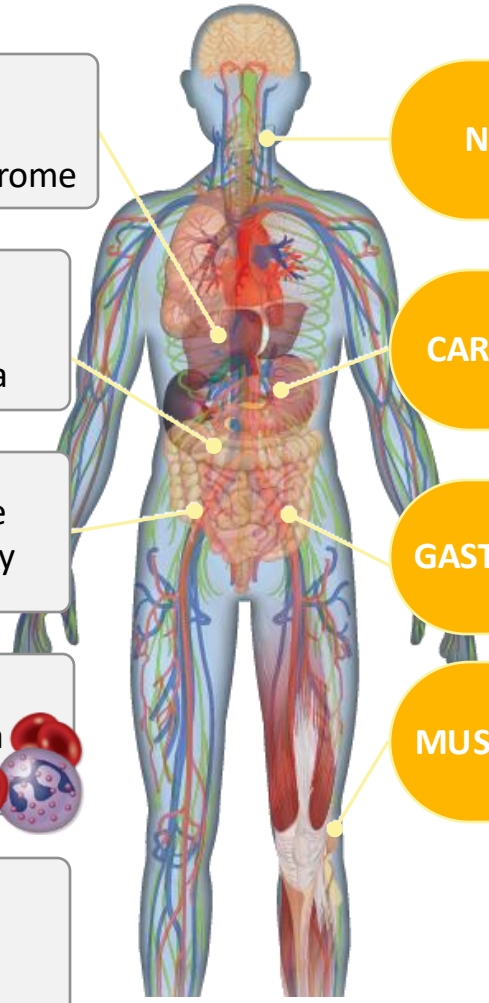
Benefits to Patients

- 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

Agency for Healthcare Research and Quality. Accessed April 4, 2025. https://www.ahrq.gov/sdm/share-approach/index.html.

ASTCT CRS Monitoring, Grading (BsAb and CART)



RESPIRATORY
Hypoxia
Dyspnea
Capillary leak syndrome

LIVER
Transaminitis
↑ ALP
Hyperbilirubinemia

KIDNEY
↑ Serum creatinine
Kidney insufficiency

HEMATOLOGIC
Anemia
Thrombocytopenia
Neutropenia

CONSTITUTIONAL
Fever
Fatigue, malaise
Headache

NEUROLOGIC
Delirium
Somnolence
Dysphagia

CARDIOVASCULAR
Sinus tachycardia
Hypotension
Arrhythmias

GASTROINTESTINAL
Nausea
Vomiting
Diarrhea

MUSCULOSKELETAL
Myalgia

Monitoring for CRS

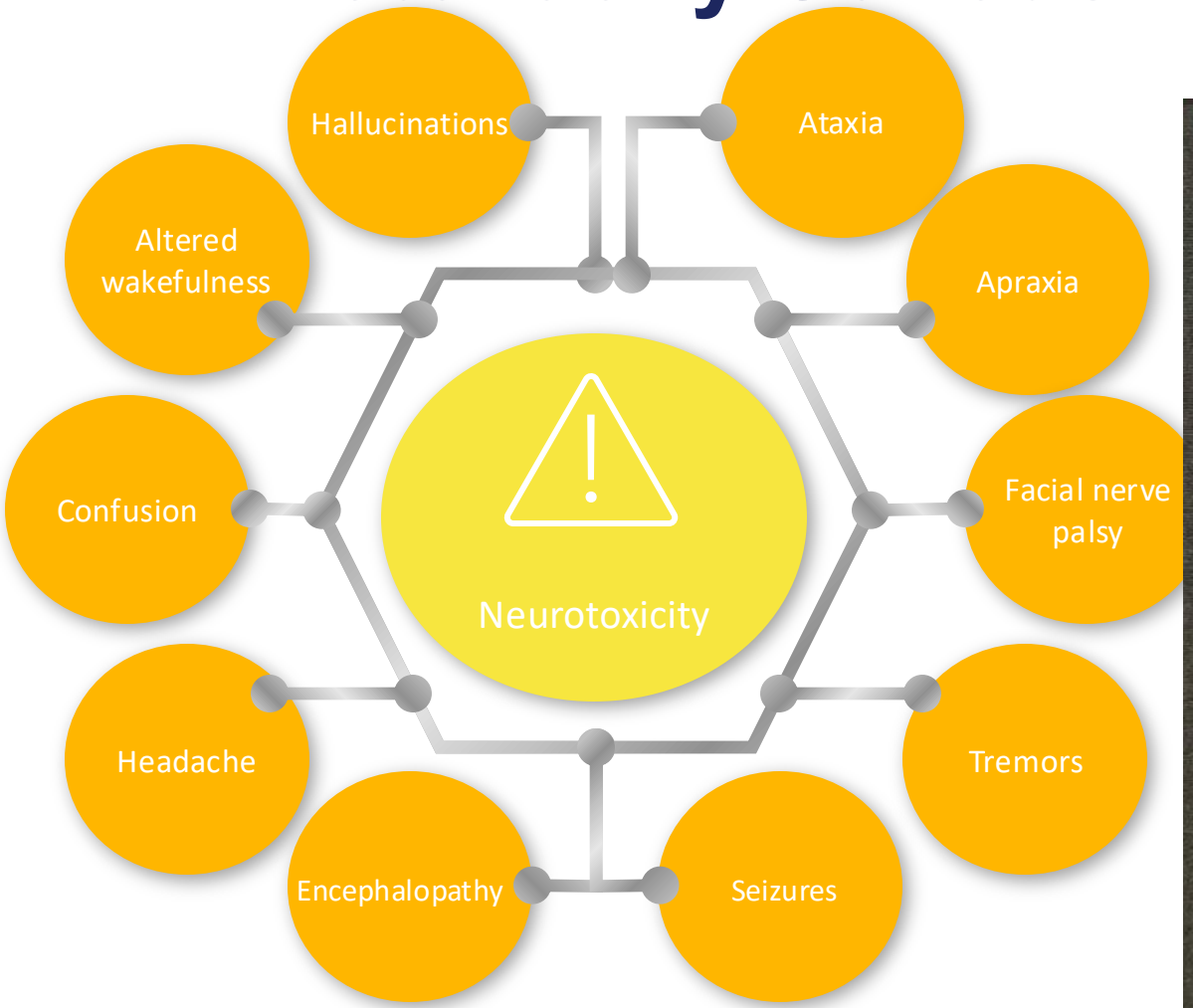
- **Vital signs (temperature, O_2 saturation, etc.)**
- **Fever is hallmark – treat**
- Review of systems and physical exam
- Laboratory monitoring
  - CRP, Ferritin, LDH

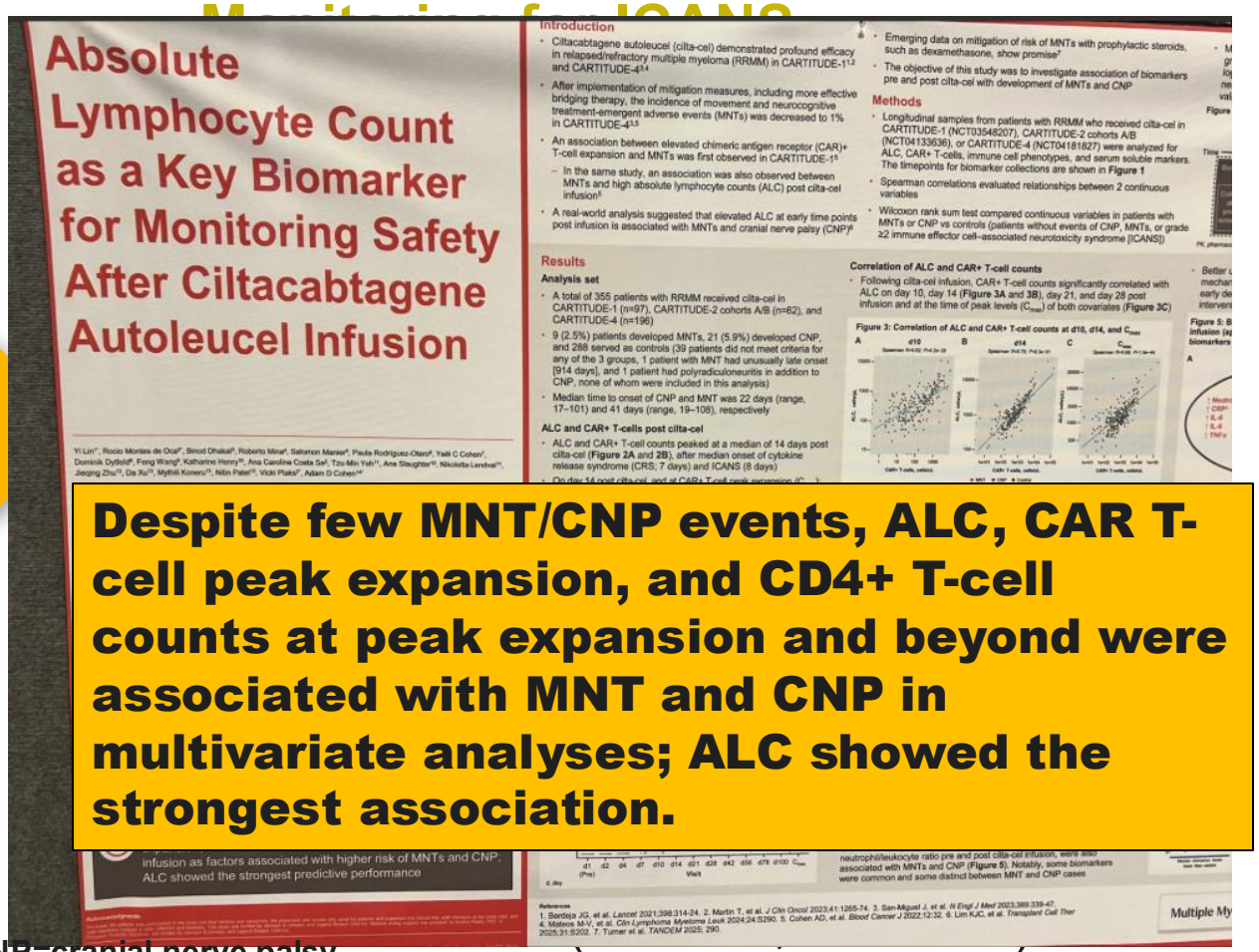
CRS Parameter	Grade 1	Grade 2	Grade 3	Grade 4
Fever[a]	Temperature ≥ 38° C	Temperature ≥ 38° C	Temperature ≥ 38° C	Temperature ≥ 38° C
		With		
Hypotension	None	Not requiring vasopressors	Requiring a vasopressor with or without vasopressin	Requiring multiple vasopressors (excluding vasopressin)
		and/or[b]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

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)





Despite few MNT/CNP events, ALC, CAR T-cell peak expansion, and CD4+ T-cell counts at peak expansion and beyond were associated with MNT and CNP in multivariate analyses; ALC showed the strongest association.

MNT= movement and neurocognitivetreatment-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
Pneumocystis jirovecii 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/µL (general infection risk)	Consider GCSF 2 or 3 times/week (or as frequently as needed) to maintain ANC > 1000 cells/µL 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

[a]IVIG is indicated in all patients with MM with IgG < 400 mg/dL and recurrent life-threatening infections; [b]Alternatives: 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

Patient Education
- Treatment expectations
- Self-care training

Primary Care
- Secondary Cancer Monitoring, health maintenance

Care Coordination
- MDs, APPs, pharmacists, labs, infusion suites

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

Symptom & Toxicity Mgmt
- Peripheral neuropathy, CRS, cytopenias, infections

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

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 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

Thank You