MULTIPLE MYELOMA Research Foundation

Management of Patients Who Have Relapsed After One to Three Prior Lines of Therapy

March 8, 2023

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Tech Support

1-719-234-7952

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Resources

- Resource tab includes
  - Speaker bios
  - Copy of the slide presentation
  - Exhibit Hall

Submit your questions throughout the program!

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MMRF Research Initiatives

MULTIPLE MYELOMA Research Consortium

CoMMpass Study℠

MMRF CureCloud™

For more information, please visit themmrf.org

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Speakers

Larry D. Anderson, Jr., MD, PhD
UT Southwestern Medical Center
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Dallas, Texas

Faith E. Davies, MBBCh, MD
Perlmutter Cancer Center
New York University/Langone Health
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Treatment Options and Considerations for Multiple Myeloma Patients at Relapse

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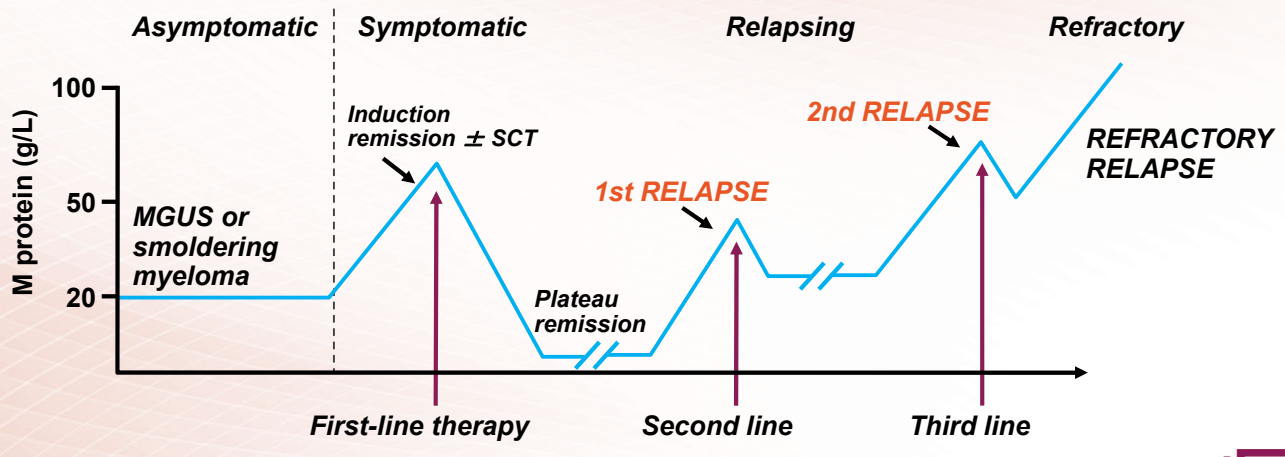
Multiple Myeloma Is a Marathon, Not a Sprint



Adapted from Borrello I. *Leuk Res*. 2012;36 Suppl. 1:S3.

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Definitions: What is relapsed/refractory disease and a line of therapy?

- ***Relapsed:*** recurrence (reappearance of disease) after a response to therapy
- ***Refractory:*** progression despite ongoing therapy
- ***Progression:*** change in M protein/light chain values
- ***Line of therapy:*** change in treatment due to either progression of disease or unmanageable side effects
  - **Note:** initial (or induction) therapy + stem cell transplant + consolidation/maintenance therapy = 1 line of therapy

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Biochemical Relapse or Clinical Relapse

Biochemical

- Patients with asymptomatic rise in blood or urine M protein, free light chains, or plasma cells

→ **Timing of therapy initiation/escalation dependent on numerous factors**

Clinical

- Based on direct indicators of increasing disease and/or end-organ dysfunction

→ **Mandates immediate initiation/escalation of therapy**

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Choosing Therapy for First or Second Relapse

Choices are broadest and guided by

- Disease biology
- Nature of relapse
- Patient preference

Factors to consider

- Prior autologous stem cell transplant
- Prior therapies
- Aggressiveness of relapse
- Comorbidities
- Psychosocial issues
- Access to care

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Options for Relapsed/Refractory Disease Continue to Increase

IMiDs	Proteasome inhibitors	Chemotherapy anthracyclines	Chemotherapy alkylators	Steroids	Novel mechanisms of action	mAbs	Cellular therapy
Thalomid (thalidomide)	Velcade (bortezomib)	Adriamycin	Cytoxan (cyclophosphamide)	Dexamethasone	XPOVIO (selinexor)	Empliciti (elotuzumab)	Abecma (idecabtagene vicleucel)
Revlimid (lenalidomide)	Kyprolis (carfilzomib)	Doxil (liposomal doxorubicin)	Bendamustine	Prednisone	Venclexta (venetoclax)*	Darzalex (daratumumab)	Carvykti (ciltacabtagene autoleucel)
Pomalyst (pomalidomide)	Ninlaro (ixazomib)		Melphalan		~~Farydak (Panobinostat)~~†	Sarclisa (isatuximab)	
					~~Pepaxto (melflufen)~~†	Blenrep (belantamab mafodotin)‡	

*Not yet FDA-approved for patients with multiple myeloma; †Withdrawn from the US market in 2021; ‡Antibody-drug conjugate

New formulations, new dosing, and new combinations, too!

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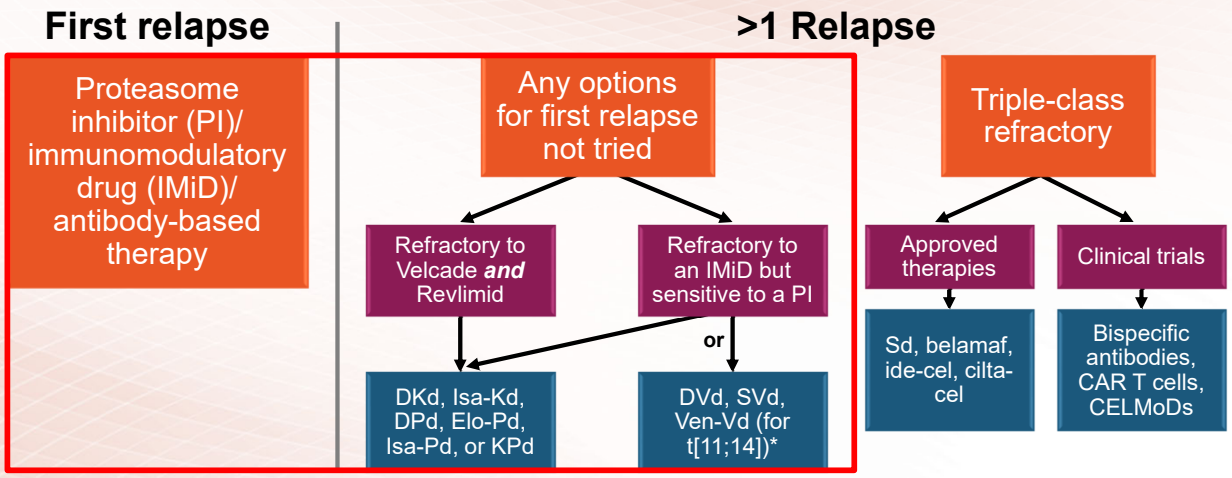
Treatment Approach



D, daratumumab (Darzalex); K, carfilzomib (Kyprolis); d, dexamethasone; Isa, isatuximab (Sarclisa); P, pomalidomide (Pomalyst); Elo, elotuzumab (Empliciti); V, bortezomib (Velcade); S, selinexor (Xpovio); Ven, venetoclax (Venclexta); belamaf, belantamab mafodotin (Blenrep); ide-cel, idecabtagene vicleucel (Abecma); cilta-cel, ciltacabtagene autoleucel (Carvykti)

*Not yet approved for use in myeloma patients

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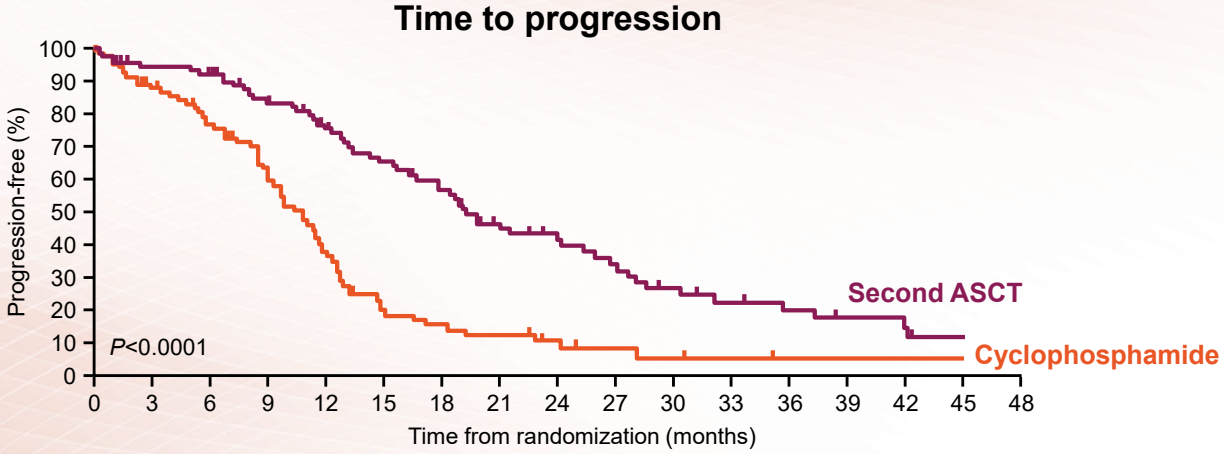
Second ASCT an Option for Early Relapse



Cook G et al. *Lancet Oncol*. 2014;15:874.

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Proteasome Inhibitor–Based Regimens for Early Relapse

	OPTIMISMM	ASPIRE	TOURMALINE-MM1	BOSTON
Regimens Compared	• Velcade-Pomalyst-dex (VPd) vs Vd	• Kyprolis-Revlimid-dex (KRd) vs Rd	• Ninlaro-Rd (IRd) vs Rd	• XPOVIO-Velcade-dex (XPO-Vd) vs Vd
Median progression-free survival favored:	• VPd: 11 vs 7 months	• KRd: 26 vs 17 months	• IRd: 21 vs 15 months	• XPO-Vd: 14 vs 9 months

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Important Considerations for Use of Proteasome Inhibitors

Velcade

- Risk of **peripheral neuropathy (PN;** numbness, tingling, burning sensations and/or pain due to nerve damage)
  - Avoid in patients with severe existing PN
  - Reduced with subcutaneous once-weekly dosing
- High risk of **shingles**
  - Use appropriate vaccination
- No dose adjustment for kidney issues; but adjust for liver issues

IV infusion or SC injection

Kyprolis

- Less **PN** than Velcade
- High risk of **shingles**
  - Use appropriate vaccination
- Monitor for **heart, lung, and kidney side effects**
  - Use with caution in older patients with cardiovascular risk factors
- High blood pressure
- No dose adjustment for kidney issues; but adjust for liver issues

IV infusion and weekly dosing

Ninlaro

- Less **PN** than Velcade
- High risk of **shingles**
  - Use appropriate vaccination
- Monitor for rashes and **gastrointestinal (GI)** side effects
  - GI effects occur early
- Needs to be taken at least 1 hour before or 2 hours after a meal

Once weekly pill

*Do not take any supplements without consulting with your doctor.

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Important Considerations for Use of Immunomodulatory Drugs

Revlimid*

- **Rash**
  - Consider antihistamines
- **Diarrhea**
  - Consider bile acid sequestrants
- Risk of **blood clots**
- Risk of second primary **malignancies**
- Dose adjustment based on kidney function

Once-a-day pill

Pomalyst*

- **Low blood counts**
- Less **rash** than Revlimid
- Risk of second primary **malignancies**
- Risk of **blood clots**

Once-a-day pill

*Black box warning.

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Important Considerations for Use of XPOVIO

Gastrointestinal

Begin prophylactic anti-nausea medications.
Consult with your doctor if nausea, vomiting, or diarrhea occur or persist.

Low sodium (hyponatremia)

Maintain fluid intake.
Salt tabs

Fatigue

Stay hydrated and active.

Low blood counts (cytopenias)

Report signs of bleeding right away.
Report signs of fatigue or shortness of breath.

Chari A et al. Manuscript under preparation.

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Proteasome Inhibitor–Based Regimens for Early Relapse

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Regimens compared	• Velcade-Pomalyst-dex (VPd) vs Vd	• Kyprolis-Revlimid-dex (KRd) vs Rd	• Ninlaro-Rd (IRd) vs Rd	• XPOVIO-Velcade-dex (XPO-Vd) vs Vd
Median progression-free survival favored	• VPd: 11 vs 7 months	• KRd: 26 vs 17 months	• IRd: 21 vs 15 months	• XPO-Vd: 14 vs 9 months
Clinical considerations	• Consider for relapse on Revlimid • VPd associated with more low blood counts, infections, and neuropathy than Pd	• KRd associated with more upper respiratory infections and high blood pressure than Rd	• IRd an oral regimen • Gastrointestinal toxicities and rashes • Lower incidence of peripheral neuropathy	• XPO-Vd associated with low platelet counts and fatigue with triplet, but less neuropathy than the Vd

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Monoclonal Antibody–Based Regimens at Relapse

Larry D. Anderson, Jr., MD, PhD
UT Southwestern Medical Center
Simmons Comprehensive Cancer Center
Dallas, Texas

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Monoclonal Antibody–Based Regimens for Early Relapse: Darzalex

	POLLUX	CASTOR	CANDOR	APOLLO
Regimens compared	• Darzalex-Revlimid-dex (DRd) vs Rd	• Darzalex-Velcade-dex (DVd) vs Vd	• Darzalex-Kyprolis-dex (DKd) vs Kd	• Darzalex-Pomalyst-dex (DPd) vs Pd
Median progression-free survival favored	• DRd: Not reached vs 17 months	• DVd: 17 vs 7 months	• DKd: Not reached vs 16 months	• DPd: 12 vs 7 months

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Important Considerations for Use of Darzalex

Darzalex

- **Infusion reactions**
  - Less with SC use
- Risk of **shingles**
  - Use appropriate vaccination

IV infusion or SC injection

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Monoclonal Antibody–Based Regimens for Early Relapse: Darzalex

	POLLUX	CASTOR	CANDOR	APOLLO
Regimens compared	• Darzalex-Revlimid-dex (DRd) vs Rd	• Darzalex-Velcade-dex (DVd) vs Vd	• Darzalex-Kyprolis-dex (DKd) vs Kd	• Darzalex-Pomalyst-dex (DPd) vs Pd
Median progression-free survival favored	• DRd: Not reached vs 17 months	• DVd: 17 vs 7 months	• DKd: Not reached vs 16 months	• DPd: 12 vs 7 months
Clinical consider-ations	• Consider for relapses from Revlimid or Velcade maintenance • DRd associated with more upper respiratory infections, low blood white blood cell counts, and diarrhea	• Consider for patients who are Revlimid-refractory without significant neuropathy • DVd associated with more low blood cell counts	• Consider for younger, fit patients who are double-refractory to Revlimid and Velcade • DKd associated with more respiratory infections • Sever side effects (possibly fatal) in intermediate fit patients 65 and older	• Consider in patients who are double-refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro) • Severe low white blood cell counts

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Monoclonal Antibody–Based Regimens for Early Relapse: Sarclisa and Empliciti

	ELOQUENT-2	ELOQUENT-3	ICARIA-MM	IKEMA
Regimens compared	• Empliciti-Revlimid-dex vs Rd	• Empliciti-Pomalyst-dex vs Pd	• Sarclisa-Pomalyst-dex vs Pd	• Sarclisa-Kyprolis-dex vs Kd
Median progression-free survival favored:	• Empliciti-Rd: 19 vs 15 months	• Empliciti-Pd: 10 vs 5 mos	• Sarclisa-Pd: 12 vs 7 mos	• Sarclisa-Kd: Not reached vs 19 mos

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Important Considerations for Use of Monoclonal Antibodies

Sarclisa

- **Infusion reactions**
- Risk of **shingles**
  - Use appropriate vaccination

IV infusion

Empliciti

- Lower rate of **infusion reactions** than Darzalex or Sarclisa
- Risk of **shingles**
  - Use appropriate vaccination

IV infusion

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Monoclonal Antibody–Based Regimens for Early Relapse: Sarclisa and Empliciti

	ELOQUENT-2	ELOQUENT-3	ICARIA-MM	IKEMA
Regimens compared	• Empliciti-Revlimid-dex vs Rd	• Empliciti-Pomalyst-dex vs Pd	• Sarclisa-Pomalyst-dex vs Pd	• Sarclisa-Kyprolis-dex vs Kd
Median progression-free survival favored	• Empliciti-Rd: 19 vs 15 months	• Empliciti-Pd: 10 vs 5 mos	• Sarclisa-Pd: 12 vs 7 mos	• Sarclisa-Kd: Not reached vs 19 mos
Clinical consider-ations	• Consider for non-Revlimid refractory, frailer patients • Overall survival benefit with Empliciti-Rd • Empliciti-Rd associated with more infections	• Consider for patients refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro)	• Consider for patients refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro) • Sarclisa-Pd associated with severe low white blood cell counts, more dose reductions, upper respiratory infections, and diarrhea	• Consider for patients refractory to Revlimid and Velcade • Sarclisa-Kd associated with higher MRD negativity rates • Sarclisa-Kd associated with severe respiratory infections

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Current and Emerging Therapies for Relapsed/Refractory Multiple Myeloma

Current therapies

Antibody-drug conjugates

- Blenrep
- Targets BCMA
- A monoclonal antibody conjugated by a protease-resistant linked to a microtubule-disrupting agent

Chimeric antigen receptor (CAR) T cells

- Abecma and Carvykti
- Targets BCMA
- Genetically modified autologous T cells that attack myeloma cells

Emerging therapies

Bispecific antibodies

- Teclistamab, elranatamab, and others
- Targets BCMA on myeloma cells and CD3 on T cells
- Redirects T cells to myeloma cells

Cereblon E3 ligase modulators (CELMoDs)

- Iberdomide
- Targets cereblon
- Enhances tumoricidal and immune-stimulatory effects compared with immunomodulatory agents

Small molecule inhibitors

- Venetoclax
- Targets Bcl-2
- Induces multiple myeloma cell apoptosis

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Summary

- **We now have many different options for relapsed myeloma depending on patient and myeloma factors at relapse.**
- **Therapy choices will depend on teamwork between physician and patient and caregivers and are based on multiple decision points.**
- **Combinations of proteasome inhibitors with either immunomodulatory drugs or selinexor improve progression-free survival.**
- **We have three different monoclonal antibodies that improve progression-free survival when added to other standard therapies without significantly increasing side effects.**
- **In general, three-drug combinations are going to work better than two drugs.**
- **Many other exciting immunotherapy options are in trials and look very promising.**

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Recent Updates

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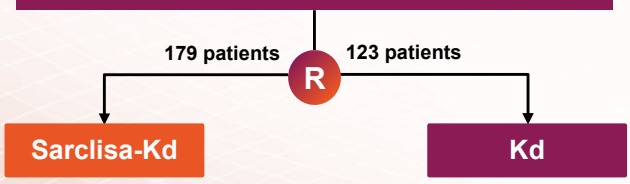
Sarclisa After Early or Late Relapse

IKEMA Study

Patients with relapsed/refractory myeloma who received 1–3 prior therapies, had no prior therapy with Kyprolis, and were not refractory to prior anti-CD38 antibody



Data evaluated according to patients who experienced an early* versus late† relapse.

	Early relapse		Late relapse	
	Sarclisa-Kd	Kd	Sarclisa-Kd	Kd
Median PFS (months)	24.7	17.2	42.7	21.9
Overall response rate (%)	82	82.6	90.4	86.1
≥VGPR rate (%)	67.2	52.2	76	58.3
MRD negativity rate (%)	24.6	15.2	37.5	16.7
MRD-negative CR rate (%)	18	10.9	30.8	13.9

Regardless of early or late relapse, RRMM patients benefit from the use of isa-Kd with respect to depth of response and prolonged PFS.

*<12 months from initiation of most recent line of therapy (for patients who had ≥2 lines of therapy); <18 months (for patients who had 1 prior line of therapy) and <12 months from ASCT
†≥12 months from initiation of most recent line of therapy (for patients who had ≥2 lines of therapy; ≥18 months for patients who had 1 prior line of therapy)

Facon T et al. *Blood*. 2022;140. Abstract 753.

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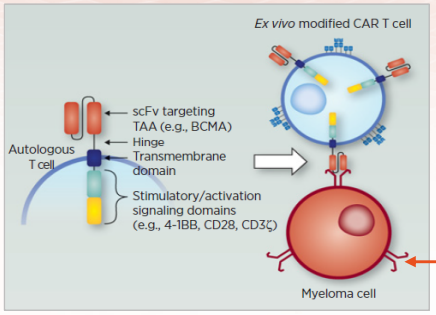
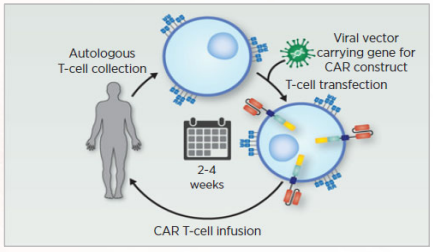
CAR T-Cell Therapy

- Genetically modified T cells designed to recognize specific proteins on myeloma cells
- CAR T cells are activated once in contact with the myeloma cell and can destroy it
- CAR T cells can persist for long periods of time in the body
- CAR T cells are created from a patient's own blood cells, but the technology is evolving to develop "off-the-shelf" varieties



B-cell maturation antigen (BCMA)



Two CAR T-cell therapies approved!
- Abecma (ide-cel)
- Carvykti (cilta-cel)

CAR, chimeric antigen receptor; MM, multiple myeloma; BCMA, B-cell maturation antigen

Cohen A et al. *Clin Cancer Res.* 2020;26:1541.

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CAR T-Cell Therapy Insights

Prognostic value of depth of response following CAR T-cell therapy[1]
- Achieving sustained, undetectable MRD after Abecma is associated with prolonged PFS
- Only MRD status—not complete response (CR) status—predicted early relapse 1 month after Abecma
- Both MRD and CR status at 12 months were required to identify patients with longer PFS

Real-world outcome with Abecma after BCMA-targeted therapy[2]
- 11 US academic centers conducted a retrospective analysis on the real-world outcome for patients treated with Abecma after previously receiving BCMA-targeted therapy
- Prior BCMA-targeted treatment is associated with inferior PFS and a trend toward inferior outcomes for patients receiving Abecma within 6 months of having received prior BCMA-targeted therapy
- Warrants further investigation into the optimal timing of Abecma infusion

Outcomes and options following relapse from CAR T[3]
- A retrospective analysis of 78 patients with RRMM who received BCMA-targeted CAR T-cell therapy
- Patients who had previously been refractory to a specific drug class re-responded after CAR-T relapse
- Median OS after progressing on CAR T was 14.8 months and 18 months for patients who received subsequent BCMA CAR T or BCMA bispecific antibodies within 6 months of progressing on CAR T

Assessment of cytopenias from CAR T[4]
- Retrospective review of data from 90 patients 4 months after CAR T-cell infusion
- Patients with poor hematologic recovery (28%) compared with adequate recovery (72%) were older, more heavily pretreated, and more likely to have received ≥1 ASCT

Abecma in earlier lines of treatment[5]
- KarMMa-2 phase 2 multicenter study of Abecma in 37 patients with RRMM with high-risk disease*
- Results show a benefit to Abecma in earlier line of treatment

*Early relapse after frontline therapy or inadequate response after frontline ASCT

1. Paiva B et al. *Blood*. 2022;140. Abstract 868. **2.** Ferreri CJ et al. *Blood*. 2022;140. Abstract 766. **3.** Reyes KR et al. *Blood*. 2022;140. Abstract 250. **4.** Thibaud S et al. *Blood*. 2022;140. Abstract 249. **5.** Usmani S et al. *Blood*. 2022;140. Abstract 361.

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What's next for CAR T-cell therapy?

	BMS-986354[1]	FasT CAR-T GC012F[2]	BMS-986393[3]
Features	• Targets BCMA with a shortened manufacturing time through the NEXT-T process	• Targets BCMA *and* CD19 • Manufacturing process that takes as little as 24 hours	• Targets GPRC5D
Trial details	• Phase 1 trial of 55 patients with RRMM with a median of 5 prior lines of therapy	• Phase 1 trial of 13 newly diagnosed high-risk myeloma patients ineligible for stem cell transplant	• Phase 1 trial of 17 heavily pretreated patients with RRMM, including those who relapsed from BCMA CAR-T therapy
Results	• CRS occurred in 80% of patients with only 1 patient experiencing ≥G3 • Neurotoxicity occurred in 10.9% of patients (one grade 4) • Overall response rate was 98.1% with 57.4% achieving ≥VGPR (29.6% ≥CR)	• 100% of patients achieved ≥VGPR (69% sCR) • All patients achieved MRD negativity (by EuroFlow) • CRS observed in 23% of patients (all low grade)	• Neutropenia and thrombocytopenia most frequent grade 3/4 adverse events • Additional adverse events include skin- and nail-related; CRS; ICANS; dysgeusia/dysphagia • 86% evaluable patients responded, including 7 of 11 patients treated with prior BMCA-targeted treatment

1. Costa LJM et al. *Blood*. 2022;140. Abstract 566. **2.** Du J et al. *Blood*. 2022;140. Abstract 366. **3.** Bal S et al. *Blood*. 2022;140. Abstract 364.

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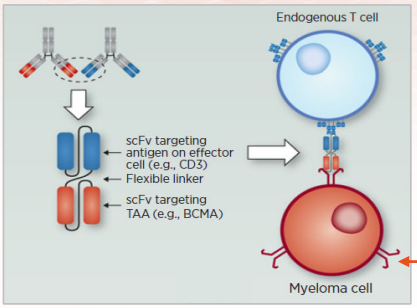
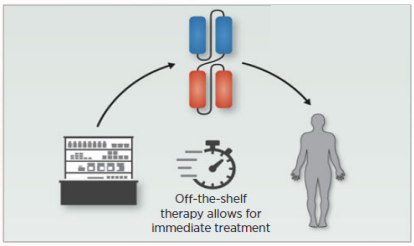
Bispecific Antibodies

- Bispecific antibodies are also referred to as *dual specific antibodies, bifunctional antibodies,* or *T-cell engaging antibodies*
- Bispecific antibodies can target two cell surface molecules at the same time (one on the myeloma cell and one on a T cell)
- Many different bispecific antibodies are in clinical development; none are approved for use in myeloma
- Availability is off-the-shelf, allowing for immediate treatment





One BCMA-targeted bispecific antibody approved!
- Tecvayli (teclistamab)

Cohen A et al. *Clin Cancer Res.* 2020;26:1541.

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Bispecifics Discussed at ASH in 2022

BCMA
- Highly expressed only on the surface of plasma cells
- Myeloma patients have significantly higher serum BCMA levels than healthy individuals

GPRC5D
- Highly expressed on myeloma cells in the bone marrow
- Lowly expressed on hair follicles, but not on other healthy cells
- Expression on myeloma cells is independent of BCMA

FcRH5
- Selectively expressed on B cells and plasma cells

CD3: a T-cell receptor

Bispecific antibody	Target (on MM cell × T cell)
Tecvayli (teclistamab)	BCMA × CD3
Elranatamab	BCMA × CD3
Linvoseltamab	BCMA × CD3
Alnuctamab	BCMA × CD3
ABBV-383	BCMA × CD3
Talquetamab	GPRC5D × CD3
Forimtamig (RG6234)	GPRC5D × CD3
Cevostamab	FcRH5 × CD3

GPRC5D, G protein-coupled receptor family C group 5 member D

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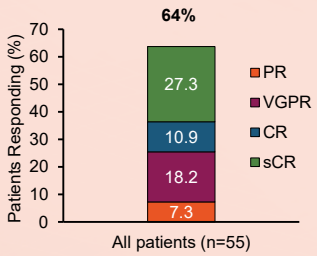
Elranatamab in Patients With Relapsed/Refractory Multiple Myeloma

Updated efficacy and safety results with elranatamab (MagnetisMM-1 Study)[1]

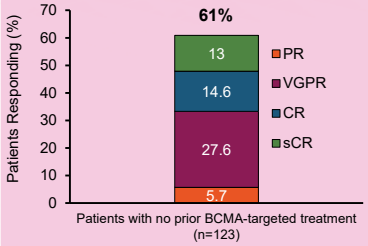
Phase 1 study in RRMM
(91% triple-class refractory)



Median duration of response 17.1 months.

MagnetisMM-3 study of elranatamab[2]

Phase 2 study in RRMM refractory to at least 1 PI, 1 IMiD, and 1 anti-CD38 antibody—no prior BMCA-targeted treatment



Elranatamab to be investigated alone and in combination with other drugs in phase 3 studies.

IMiD, immunomodulatory drug; PI, proteasome inhibitor

1. Raje N et al. *Blood*. 2022;140. Abstract 158. **2.** Bahlis NJ et al. *Blood*. 2022;140. Abstract 159.

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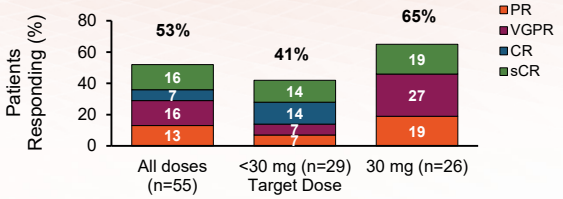
Phase 1 Study of Alnuctamab in Patients With Relapsed/Refractory Multiple Myeloma

Intravenous Formulation Results

	IV alnuctamab (n=70)
Median follow up (months)	8.0
Overall response rate (%)	39
Median duration of response (months)	33.6
Responses ongoing (%)	48
Median PFS (months)	
All patients	3.1
Responders	36.4
Nonresponders	1.7

Subcutaneous Formulation Results



Most frequent adverse events, %	Any grade	Grade 3/4
Hematologic		
Anemia	38	25
Neutropenia	37	32
Thrombocytopenia	24	9
Non-hematologic		
CRS	53	0
Infections	34	9
ICANS	3	0
ALT increase	12	6

Wong SW et al. *Blood*. 2022;140. Abstract 162.

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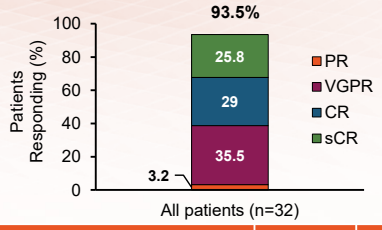
Tecvayli in Combination With Darzalex and Revlimid

Phase 1b study (MajesTEC-2) in RRMM with 1–3 prior lines of therapy (including an IMiD and a PI)

32 patients—who had received at least 2 prior lines of therapy—received treatment with the triplet and Tecvayli at 2 different doses (0.72 mg/kg and 1.5 mg/kg) subcutaneously



Most frequent non-hematologic adverse events, %	Any grade	Grade 3/4
CRS	81.3	0
Fatigue	46.9	6.3
Infections (≥1)	90.6	37.5
COVID-19	37.5	12.5
Upper respiratory	31.3	0
Pneumonia	25	15.6
COVID pneumonia	12.5	3.1
Sepsis	9.4	9.4
Pneumonia pseudomonal	6.3	6.3
CMV	6.3	6.3

IMiD, immunomodulatory drug; PI, proteasome inhibitor

1. Searl E et al. *Blood*. 2022;140. Abstract 160.

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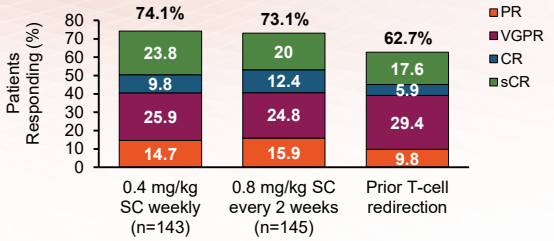
Talquetamab in Patients With Relapsed/Refractory Multiple Myeloma

Phase 1/2 study (MonumenTAL-1) in RRMM

288 patients—with no prior T cell-redirecting therapies—received treatment with talquetamab at 2 different doses (0.4 mg/kg every week and 0.8 mg/kg every other week) subcutaneously

Data from this trial was recently used to submit a Biologics License Application to the US Food and Drug Administration for the treatment of patients with relapsed or refractory multiple myeloma.



	0.4 mg/kg		0.8 mg/kg	
Most frequent adverse events, %	**Any grade**	**Grade 3/4**	**Any grade**	**Grade 3/4**
Hematologic				
Anemia	44.8	31.5	39.3	24.8
Neutropenia	34.3	30.8	28.3	22.1
Lymphopenia	28	25.9	26.2	25.5
Thrombocytopenia	27.3	20.3	26.9	16.6
Infections	57.3	16.8	50.3	11.7

IMiD, immunomodulatory drug; PI, proteasome inhibitor

Chari A et al. *Blood*. 2022;140. Abstract 157.

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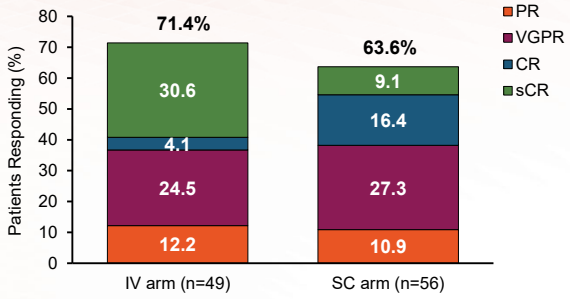
Forimtamig (RG6234) in Patients With Relapsed/Refractory Multiple Myeloma

Phase 1 study in RRMM

105 patients received treatment with RG6234 in 2 different formulations (intravenous and subcutaneous)



Carlo-Stella C A et al. *Blood*. 2022;140. Abstract 161.

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Expected Toxicities With T-Cell Activating Therapies (CAR T and Bispecific Antibodies)

Cytokine release syndrome (CRS)

Infections

- Viruses: CMV, EBV
- PCP/PJP
- Ongoing discussions regarding prophylactic measures
  - IVIG
  - Anti-infectives

Cytopenias

Neurotoxicity (ICANS)

- Usually occurs within first 1–2 weeks
- Frequency (all grade and grade 3–5) higher with CAR T

Off-target effects (with GPRC5D-targeted agents)

- **Cytokeratin changes/rash**
- **Dysgeusia**

ICANS, immune effector cell-associated neurotoxicity syndrome; CMV, cytomegalovirus; EBV, Epstein-Barr virus; PCP/PJP, pneumocystis pneumonia/pneumocystis jiroveci pneumonia

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Pretreatment With Tocilizumab Reduces Incidence and Severity of CRS

Cevostamab is an FcRH5-targeted bispecific antibody under investigation in patients with RRMM

An ongoing phase 1 study evaluating the use of tocilizumab (an IL-6 antibody) prior to the first dose of cevostamab. A single 8 mg/kg dose of tocilizumab was administered to 28 patients 2 hours prior to cevostamab

35.7% of patients receiving tocilizumab experienced CRS compared to 90.9% of patients who didn't receive tocilizumab.

Grade 3 CRS was observed in only one patient in each group and no G4/5.

The frequency of neutropenia was higher for patients receiving tocilizumab compared with those who didn't (64.3% vs 38.6% G3/4).

No impact on response was observed with tocilizumab pretreatment.

Trudel S et al. *Blood*. 2022;140. Abstract 567.

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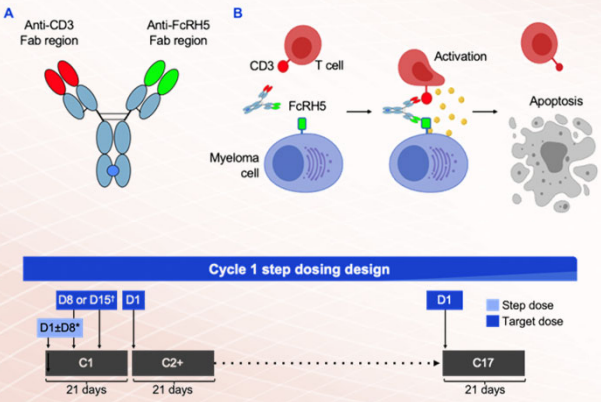
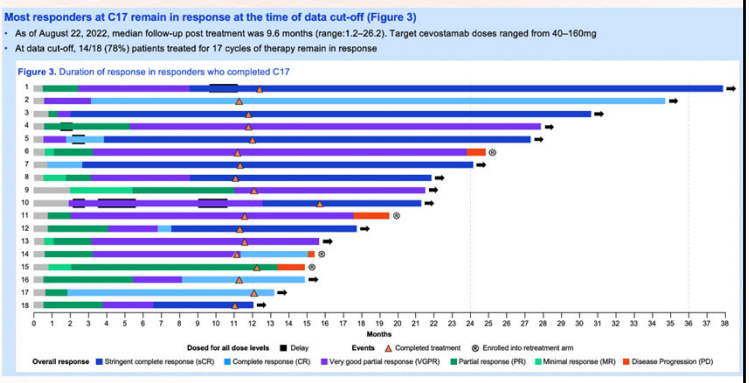
Fixed-Duration Therapy With Bispecifics Cevostamab





At the time of this presentation, no patients who achieved an sCR have relapsed!

Lesokhin AM et al. *Blood*. 2022;140. Abstract 1924.

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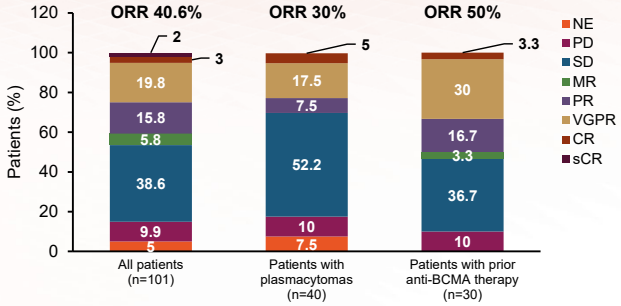
Mezigdomide: A Cereblon E3 Ligase Modulator (CELMoD)

CELMoDs are related to the immunomodulatory drugs (IMiDs) but are more potent and may overcome resistance to IMiDs

A phase 1/2 study of mezigdomide combined with dex in relapsed/refractory patients

101 patients who had received at least 6 prior lines of therapy (all were triple-class refractory; one third were previously exposed to anti-BCMA therapy) received treatment with mezigdomide-dex



Most hematologic frequent adverse events, %	Grade 3	Grade 4
Neutropenia	21.8	53.5
Anemia	34.7	1.0
Thrombocytopenia	13.9	13.9
Febrile neutropenia	12.9	2.0

Most frequent non-hematologic adverse events, %	Grade 3	Grade 4
Infections	28.7	5.9
Pneumonia	12.9	3.0
COVID-19	6.9	0

Richardson PG et al. *Blood*. 2022;140. Abstract 568.

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Questions & Answers

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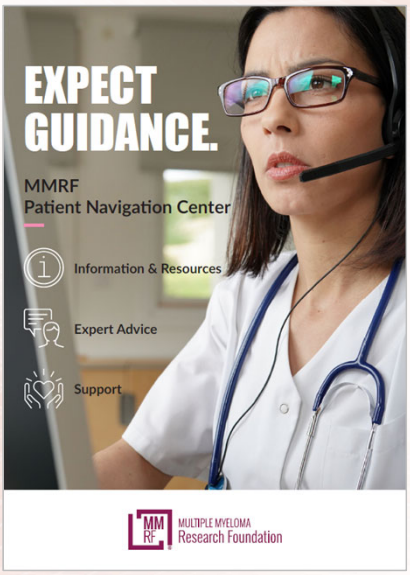
MMRF Patient Resources



MMRF Patient Navigation Center

You and your care team will have many decisions to make along your treatment journey. The Patient Navigation Center is a space for multiple myeloma patients and their caregivers to connect with patient navigators — who are professionals specializing in oncology — for guidance, information, and support. You can connect with a patient navigator via phone, or email. Whatever questions you may have, our patient navigators are here to help.

MMRF Patient Navigators include:
- Grace Allison, RN, BSN, OCN, RN-BC
- Brittany Hartmann, RN-BSN
- Erin Mensching, RN-BSN, OCN

THE RIGHT TRACK

Get on the right track for you

The MMRF's Right Track program puts you on the path to the best results for you.

Right Team
Access experts and centers that have extensive experience treating multiple myeloma.

Right Tests
Get the information, tests, and precise diagnoses to make the right treatment decisions.

Right Treatment
Work with your team to consider the best treatment plan and identify clinical trials that are right for you.

Contact the Patient Navigation Center Today

Looking for guidance? We're here to help.

Monday – Friday | 9:00AM – 7:00PM ET

Phone: 1-888-841-MMRF (6673) Online: TheMMRF.org/PatientNavigationCenter

Email: patientnavigator@themmrf.org

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Myeloma Mentors®

Myeloma Mentors® allows patients and caregivers the opportunity to connect with trained mentors. This is a phone-based program offering an opportunity for a patient and/or caregiver to connect one-on-one with a trained patient and/or caregiver mentor to share his or her patient journeys and experiences.

No matter what your disease state—smoldering, newly diagnosed, or relapsed/refractory—our mentors have insights and information that can be beneficial to both patients and their caregivers.

Contact the Patient Navigation Center at 888-841-6673 to be connected to a Myeloma Mentor or to learn more.

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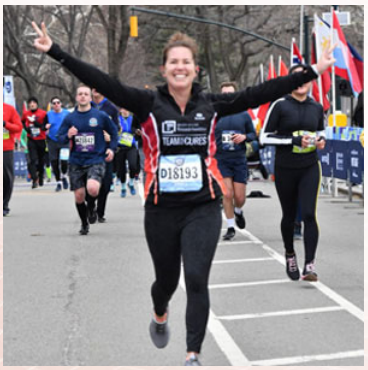
MMRF Events

Our events are returning live and in-person, and there are so many ways to get involved. Most have a virtual option, too. Join us today!

Endurance Events



5K Walk/Run Events

Independent Events

FIND AN EVENT AND JOIN US: themmrf.org/get-involved/mmrf-events/

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Upcoming Patient Education Events

Save the Date

Topic	Date and Time (ET)	Speakers
Patient Summit Hackensack, NJ	Saturday, March 11 9:00 AM to 1:40 PM ET	David Vesole, MD, PhD Noa Biran, MD Kimberley Doucette, MD Ann McNeill, RN, MSN, APN Susan Kumka, APN
Facebook Live FAQs	Tuesday, March 14 3:00 to 4:00 PM ET	Gurbakhash Kaur, MD Sonia Patel, MPH, MSN, AGACNP-BC, APRN, AOCNP
Webinar: *BCMA-Targeted Bispecific Antibodies in Multiple Myeloma*	Tuesday, March 21 4:00 to 5:00 PM ET	Jesus Berdeja, MD Amrita Krishnan, MD
Patient Summit Scottsdale, AZ *In collaboration with Arizona Myeloma Network*	Saturday, March 25 9:00 AM to 3:45 PM MT	Leif Bergsagel, MD Clarence Adoo, MD Jonathan Keats, PhD Sumit Madan, MD Suzanne Hyde, MSW, LCSW Barbara Kavanagh, MSW, LCSW Joan Koerber-Walker William Brown
Webinar (rebroadcast): *Multiple Myeloma Precursor Conditions*	Wednesday, April 5 2:30 to 3:30 PM ET	Sagar Lonial, MD Omar Nadeem, MD

For more information or to register, visit themmrf.org/resources/education-program

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Thank you!
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