Applying the Latest Clinical Data in
MULTIPLE MYELOMA PATIENT CARE
IN THE COMMUNITY SETTING

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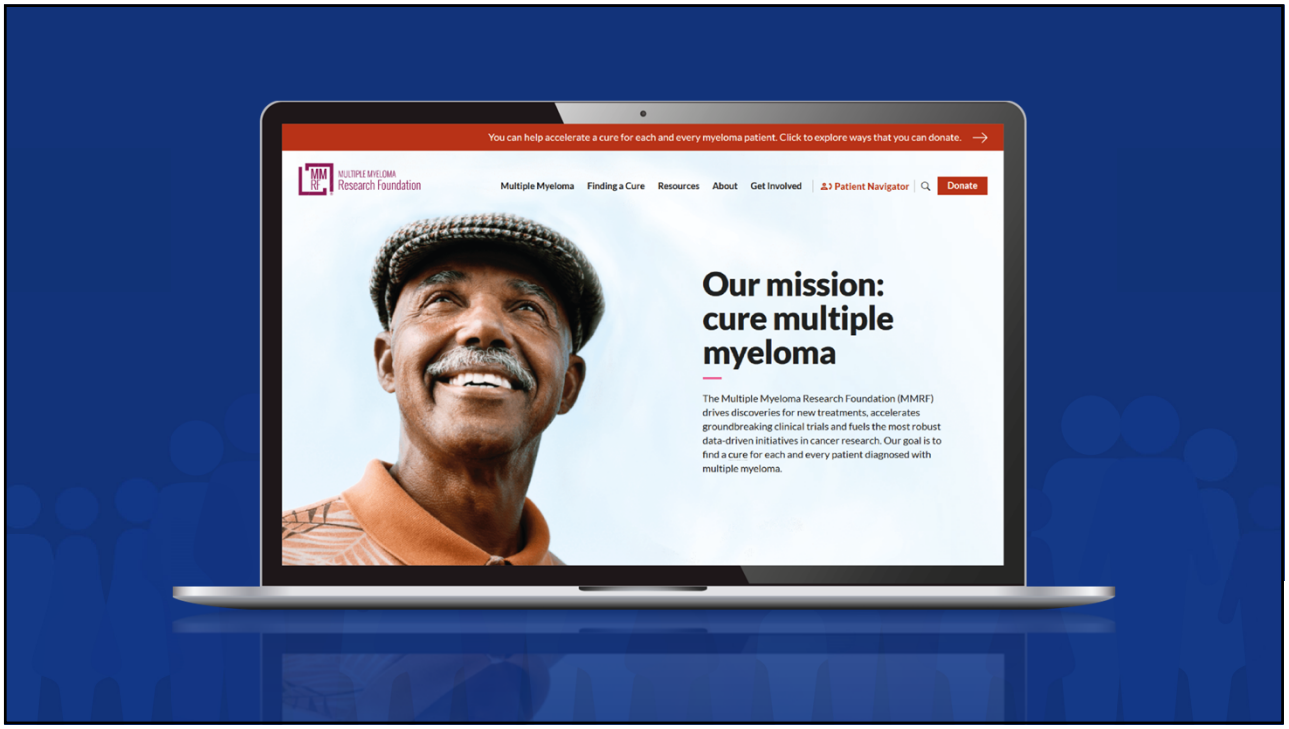
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Our mission:
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The Multiple Myeloma Research Foundation (MMRF) drives discoveries for new treatments, accelerates groundbreaking clinical trials and fuels the most robust data-driven initiatives in cancer research. Our goal is to find a cure for each and every patient diagnosed with multiple myeloma.

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Multiple Myeloma Care Among Black Patients

Initial therapy

- Median time to first-line therapy initiation significantly longer in Black patients[1]
- Black patients less likely to initiate first-line triplet therapy for multiple myeloma[2]

Utilization of stem cell transplant

- Significantly lower stem cell transplant utilization in Black patients[1-5]

Treatment outcomes

- With equal access, Black patients have superior survival compared to White patients with multiple myeloma[5,6]
- Outcomes of Black patients same as White patients in cooperative-group clinical trials[7]

1. Ailawadhi S et al. *Blood Adv*. 2019;3(20):2986. **2.** Derman BA et al. *Blood Cancer J*. 2020;10(8):80. **3.** Ailawadhi S et al. *Cancer Med*. 2017;6(12):2876.
4. Fiala M et al. *Cancer*. 2017;123(9):1590. **5**. Filmore NR et al. *Blood*. 2019;133(24):2615. **6.** Dong J et al. *Blood Cancer J* 2022;12:34. **7.** Ailawadhi S et al. *Blood Cancer J*. 2018;8:67.

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IMWG Criteria for Diagnosis of Multiple Myeloma

Monoclonal gammopathy of undetermined significance (MGUS)

- M protein <3 g/dL
- Clonal plasma cells in BM <10%
- No myeloma-defining events

Smoldering multiple myeloma (SMM)

- M protein ≥3 g/dL (serum) or ≥500 mg/24 hrs (urine)
- Clonal plasma cells in bone marrow ≥10%–60%
- No myeloma-defining events

Ultra–high-risk SMM = active myeloma

- Not CRAB but SLiM CRAB
- S (60%)
- Li (Light chains I/U >100)
- M (MRI ≥1 focal lesion)
- C (calcium elevation)
- R (renal insufficiency)
- A (anemia)
- B (bone disease)

Multiple myeloma

- Underlying plasma cell proliferative disorder
- AND ≥1 myeloma-defining events
- ≥1 CRAB* feature
- Clonal plasma cells in bone marrow ≥60%
- Serum free light chain ratio ≥100
- >1 MRI focal lesion

*C: Calcium elevation (>11 mg/dL or >1 mg/dL higher than ULN)
R: Renal insufficiency (creatinine clearance <40 mL/min or serum creatinine >2 mg/dL)
A: Anemia (Hb <10 g/dL or 2 g/dL < normal)
B: Bone disease (≥1 lytic lesions on skeletal radiography, CT, or PET-CT)

Rajkumar SV et al. *Lancet Oncol*. 2014;15:e538.

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Multiple Myeloma Prognosis and Risk Assessment

Revised-International Staging System (R-ISS)[1]

R-ISS stage	Laboratory measurements	5-year OS (%)	5-year PFS (%)
I	• Serum β2M level <3.5 mg/L • Serum albumin level ≥3.5 g/dL • No high-risk CA* • Normal LDH level	82	55
II	All other possible combinations	62	36
III	• Serum β2M level ≥5.5 mg/L • High-risk CA* or high LDH level	40	24

Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) Consensus Guidelines[2]

High risk
- High-risk genetic abnormalities
  - t(4;14)
  - t(14;16)
  - t(14;20)
  - del 17p
  - p53 mutation
  - gain 1q
- RISS Stage 3
- High plasma cell S phase
- GEP: high-risk signature

Standard risk
- All others including:
  - Trisomies
  - t(11;14)
  - t(6;14)

- *Double-hit myeloma:* any two high-risk genetic abnormalities
- *Triple-hit myeloma:* three or more high-risk genetic abnormalities

Currently cannot identify with great certainty all high-risk patients.

OS, overall survival; PFS, progression-free survival; β2M, beta-2 microglobulin; LDH, lactate dehydrogenase; GEP, gene expression profiling

1. Palumbo A et al. *J Clin Oncol.* 2015;33:2863. **2.** Mikhael JR et al. *Mayo Clin Proc.* 2013;88:360.

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Recent Advances in the Treatment of Newly Diagnosed Multiple Myeloma (NDMM)

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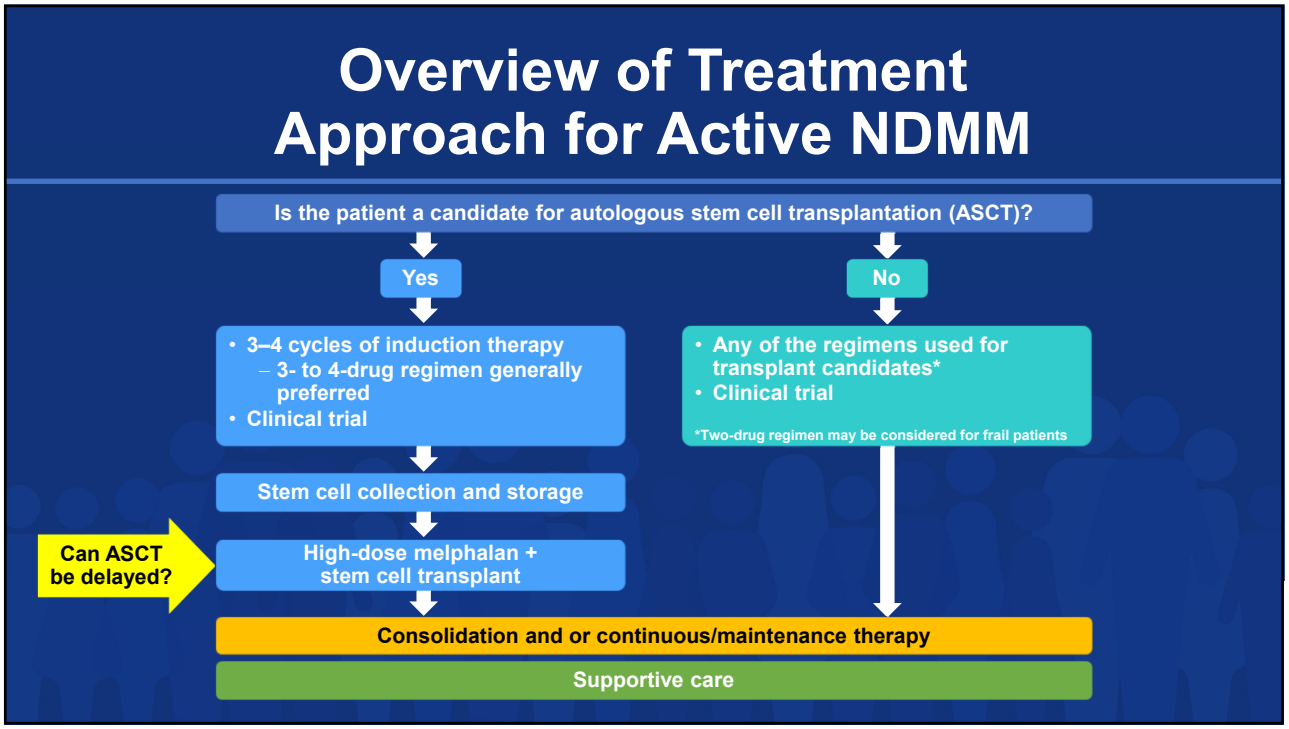
Overview of Treatment Approach for Active NDMM
Is the patient a candidate for autologous stem cell transplantation (ASCT)?
Yes
No
• 3–4 cycles of induction therapy
– 3- to 4-drug regimen generally preferred
• Clinical trial
• Any of the regimens used for transplant candidates*
• Clinical trial
*Two-drug regimen may be considered for frail patients
Stem cell collection and storage
Can ASCT be delayed?
High-dose melphalan + stem cell transplant
Consolidation and or continuous/maintenance therapy
Supportive care

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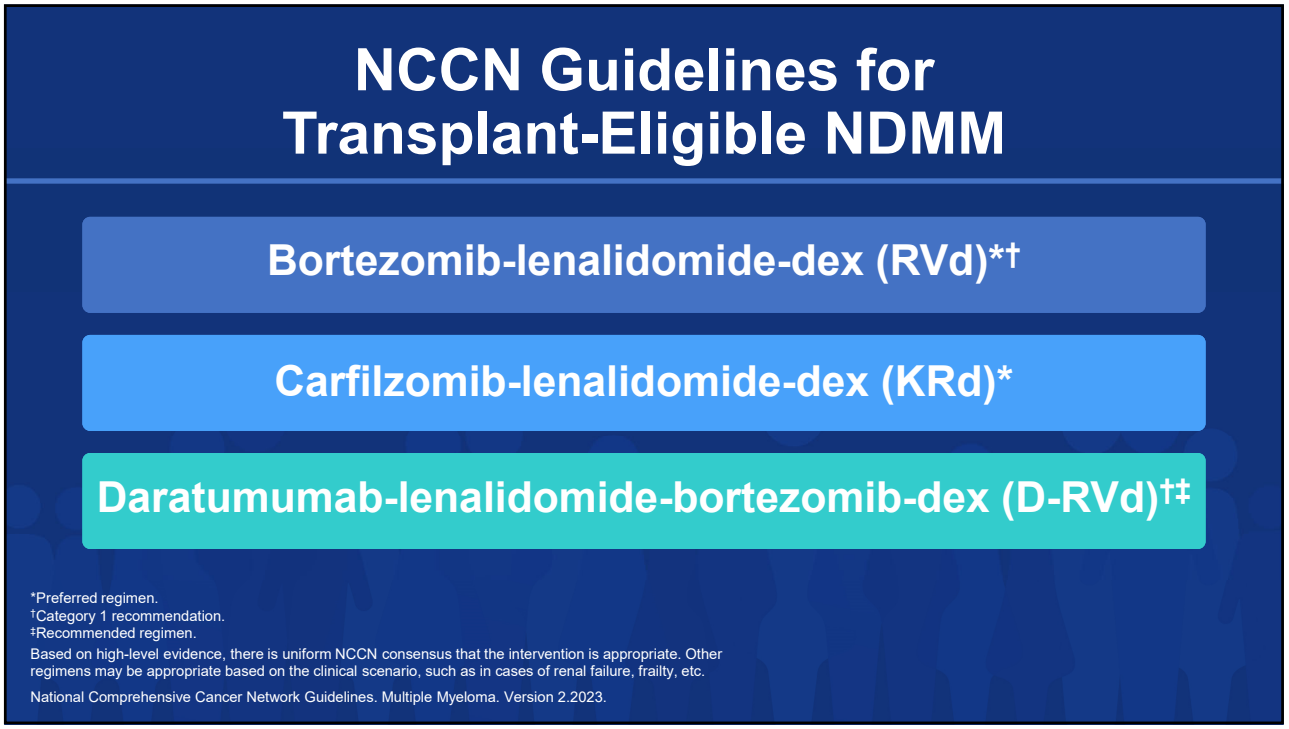
NCCN Guidelines for Transplant-Eligible NDMM
Bortezomib-lenalidomide-dex (RVd)*†
Carfilzomib-lenalidomide-dex (KRd)*
Daratumumab-lenalidomide-bortezomib-dex (D-RVd)†‡
*Preferred regimen.
†Category 1 recommendation.
‡Recommended regimen.
Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate. Other regimens may be appropriate based on the clinical scenario, such as in cases of renal failure, frailty, etc.
National Comprehensive Cancer Network Guidelines. Multiple Myeloma. Version 2.2023.

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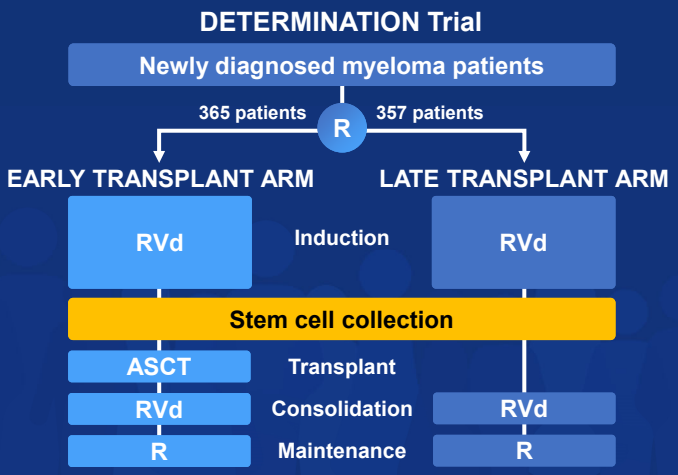
Phase 3 Study of Early vs Late ASCT in Patients With NDMM



The study enrolled 19% Black myeloma patients.

From Richardson PG et al. Triplet therapy, transplantation, and maintenance until progression in myeloma. *N Engl J Med.* 2022;387(2):132-147.

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Phase 3 Study of Early vs Late ASCT in Patients With NDMM

Progression-free survival (PFS)

PFS for early transplant was 22 months longer than for late transplant (68 mos vs 46 mos). However, Black patients did not seem to have the same PFS advantage with early transplant as other patients.

5-year PFS in MRD-negative patients was similar regardless of ASCT timing (53.5% for early transplant vs 59.2% for late transplant)

Overall survival (OS)

No difference was seen in OS between treatment groups (5-yr OS rate: 81% vs 79%)

Richardson PG et al. *N Engl J Med.* 2022;387(2):132.

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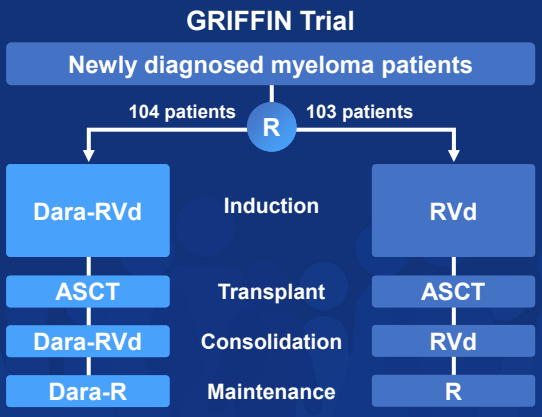
MRD-Negativity Results From Phase 2 Study of Dara-RVd vs RVd in Transplant-Eligible NDMM



Sustained MRD-negativity rates at 10^{-5} lasting ≥6 and ≥12 months were higher for D-RVd vs RVd among all high-risk subgroups.*

Dara-RVd was superior to RVd for rates of **sustained MRD negativity** lasting >12 months for patients with greater than or equal to a CR (**53.7% vs 20.3%**) and sCR (59.1% vs 17.4%).

MRD negativity rates in patients treated with Dara-RVd were **consistent across all subgroups of patients**, including those with high-risk features.

*ISS stage III or high-risk cytogenetics del(17p), t(4;14); t(14;16), t(14;20), or gain 1q

The findings support the role of D-RVd as the new standard of care for this patient population.

Rodriguez C et al. *J Clin Oncol.2022;*40. Abstract 8011.

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Lenalidomide as Maintenance Therapy

Reduction in myeloma progression (3 large studies)[1-3]

Improved survival (1 of 3 studies; meta-analysis)[3,4]

Increased risk of second cancers when used after melphalan*[3]

Approved for use as maintenance treatment after ASCT[4]

*Low risk when used in the context of ASCT

1. Attal M et al. *N Engl J Med*. 2012;366:1782. **2.** McCarthy PL et al. *N Engl J Med*. 2012;366:1770.
3. Palumbo A et al. *N Engl J Med*. 2014;371:895. **4.** McCarthy PL et al. *J Clin Oncol*. 2017;35:3279.

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Lenalidomide Maintenance Therapy: Improves Depth of Response

Disease response	Before len maintenance (n)	During/after len maintenance (n)
MRD negative	37	72
CR	57	49
VGPR	34	14
≤PR	11	4

Achievement of MRD-negative status at any time (before or during maintenance) was associated with improved PFS (median PFS 83 mos for MRD negative vs 48 mos for MRD positive, *P*<0.01)

Alonso R et al. *Blood Adv*. 2020;4(10):2163.

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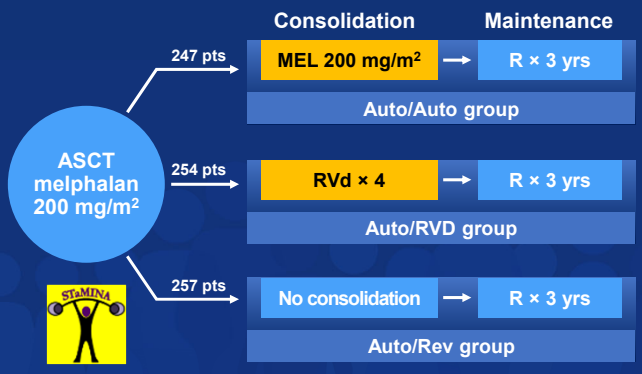
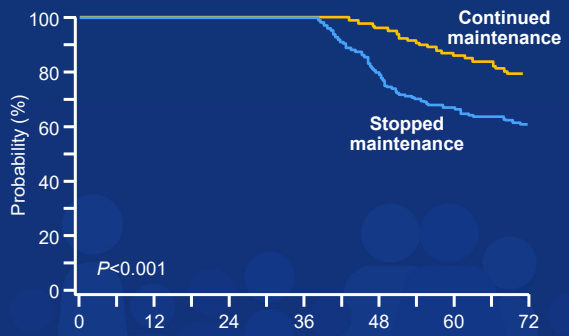
Lenalidomide Maintenance Duration

STaMINA Trial (BMT-CTN0702)



There was no difference in PFS or OS between the 3 groups.

From Fig 1 of Stadtmauer EA, et al. Autologous transplantation, consolidation, and maintenance therapy in multiple myeloma: results of the BMT CTN 0702 trial. *J Clin Oncol*. 2019 Mar 1;37(7):589-597. © 2019 by the American Society of Clinical Oncology. https://ascopubs.org/doi/pdf/10.1200/JCO.18.00685?role=tab



Discontinuation of lenalidomide @ 3 years did not affect overall second primary malignancies (SPM) rates @ 6 years

Discontinuation of lenalidomide maintenance at 3 years is not recommended because of the increased risk of disease progression.

Hari P et al. *J Clin Oncol*. 2020;38. Abstract 8506.

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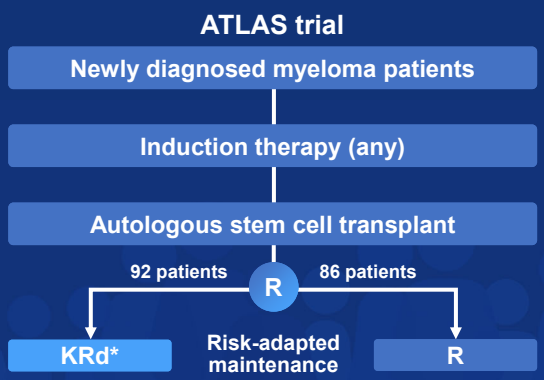
Phase 3 Trial of KRd vs R as Maintenance After ASCT



	KRd	R
MRD negativity after 6 cycles (%)†	47	29
Median PFS (mos)	59	41.4
≥G3 side effects (%)		
Low white blood cell counts (neutropenia)	47	59
Low platelet counts (thrombocytopenia)	13	7
Infections	15	6
Cardiovascular	4	5
Secondary malignancies	2	2

The first randomized phase 3 trial demonstrating superior PFS with extended post-transplant KRd therapy compared to R maintenance

*Response assessed after first six cycles and patients who are standard risk and achieve MRD negativity proceeded on R maintenance. High risk considered to have t(4;14), t(14;16), or del(17p).
† MRD negativity ≥10^{-5} or higher by NGS
Dytfeld D et al. *J Clin Oncol.2022*;40. Abstract 8001.

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NCCN Guidelines for Transplant-Ineligible NDMM

Bortezomib-lenalidomide-dex (RVd)*†

Daratumumab-lenalidomide-dex (DRd)*†

Daratumumab-bortezomib-melphalan-prednisone (D-VMP)†‡
Carfilzomib-lenalidomide-dex (KRd)‡
Ixazomib-lenalidomide-dex (IRd)‡
Daratumumab-cyclophosphamide-bortezomib-dex (D-VCd)‡

*Preferred regimen.
†Category 1 recommendation.
‡Recommended regimen.
Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate. Other regimens may be appropriate based on the clinical scenario, such as in cases of renal failure, frailty, etc.
National Comprehensive Cancer Network Guidelines. Multiple Myeloma. Version 2.2023.

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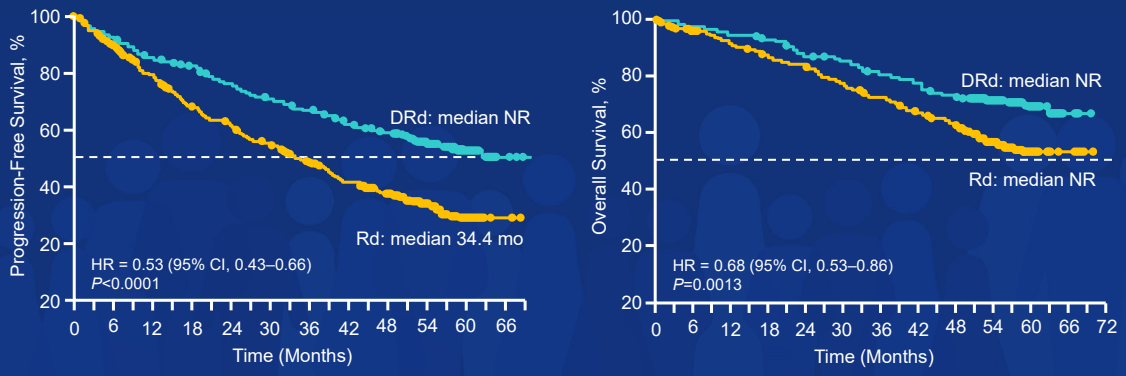
MAIA: Adding Daratumumab to Rd in Non-ASCT Candidates Substantially Improved PFS and OS

After ~5 years of follow-up, a significant and clinically meaningful OS improvement was demonstrated with DRd versus Rd, representing a 32% reduction in the risk of death[1]



Reprinted from Facon T, et al. Daratumumab, lenalidomide, and dexamethasone versus lenalidomide and dexamethasone alone in newly diagnosed multiple myeloma (MAIA): overall survival results from a randomised, open-label, phase 3 trial. *Lancet Oncol* 22(11):1582-1596. Copyright 2021, with permission from Elsevier.

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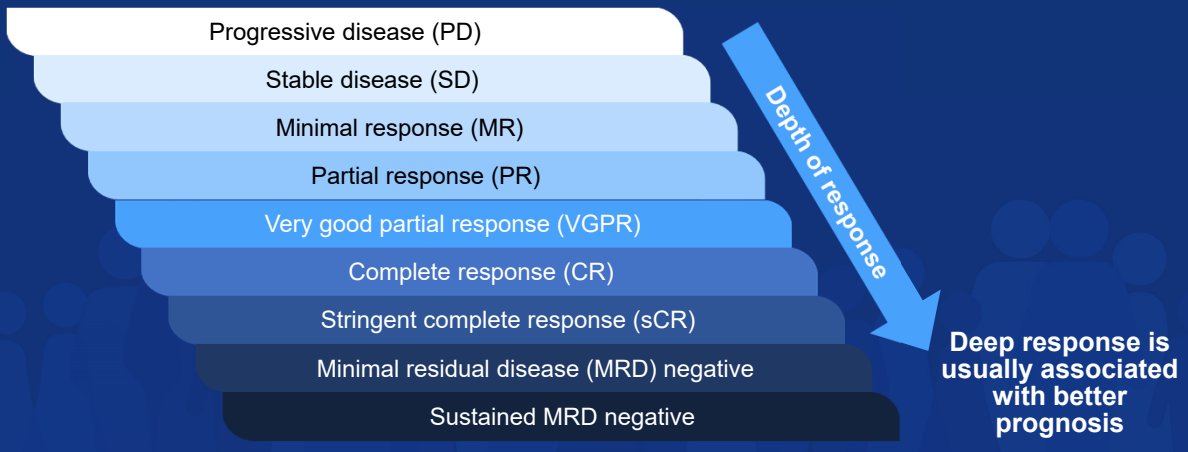
Response Evaluation in Myeloma Therapy



ClonoSEQ is an FDA-approved next-generation sequencing (NGS) test to measure MRD in MM patients.

Palumbo A et al. *J Clin Oncol.* 2014;32:587.
Kumar S et al. *Lancet Oncol.* 2016;17:e328.

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Guiding Principles for NDMM Management

- Use at least three drugs for induction therapy
  - Consider four-drug induction regimen for high-risk disease
- Aim for the deepest response (includes MRD)
- Prolonged maintenance therapy with lenalidomide improved depth of response
- Consider stem cell transplant either now or later
- Approach, regimens, and goals must be individualized based on age, organ function, risk assessment, and personal factors

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The Expanding Treatment Armamentarium for RRMM

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NCCN Guidelines for Early RRMM
Category 1 Recommendations (1–3 Prior Therapies)

- Carfilzomib/lenalidomide/dex*
- Daratumumab + Vd, Kd, Pd, or Rd*
- Isatuximab + pom/dex or Kd*
- Ixazomib/lenalidomide/dex*
- Pom/bortezomib/dex*

- Bortezomib/liposomal doxorubicin/dex†
- Carfilzomib (twice weekly)/dex†
- Elotuzumab/lenalidomide/dex†
- Selinexor/bortezomib/dex†

Triplets, including antibody-based options, are among the recommended strategies.

*Preferred regimen.
†Other recommended regimen.
Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate. Other regimens may be appropriate based on the clinical scenario, such as in cases of renal failure, frailty, etc.

National Comprehensive Cancer Network Guidelines. Multiple Myeloma. Version 2.2023.

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Current Guidelines and Evidence for Use of Triplet Combinations Anchored by Anti-CD38 Antibodies in RRMM

Preferred antibody-based regimens (Category 1)[1]

Daratumumab + Vd, Kd, Pd, or Rd

CANDOR[2]	KdD (n=312)	Kd (n=154)
Median PFS, mo	**28.6**	**15.2**
HR for KdD vs Kd (95% CI)	**0.59** (0.45–0.78), *P*<0.001	

APOLLO[3]	DPd (n=151)	Pd (n=153)
Median PFS, mo	**12.4**	**6.9**
HR for DPd vs Pd (95% CI)	**0.63** (0.47–0.85), *P*=0.0018	

Isatuximab + Pd or Kd

ICARIA-MM[4]	IsaPd (n=154)	Pd (n=153)
Median PFS, mo	**11.5**	**6.4**
HR for IsaPd vs Pd (95% CI)	**0.536** (0.4360–0.814), *P*=0.001	

IKEMA[5]	IsaKd (n=179)	Kd (n=123)
Median PFS, mo	**NR**	**19.15**
HR for IsaKd vs Kd (95% CI)	**0.53** (0.4360–0.814), *P*=0.0007	

1. National Comprehensive Cancer Network Guidelines. Multiple Myeloma. Version 2.2023. **2.** Usmani S et al. *Lancet Oncol*. 2022;23:65.
3. Dimopoulos MA et al. *Lancet Oncol*. 2021;22:801. **4.** Attal M et al. *Lancet*. 2019;394:2096. **5.** Moreau P et al. *Lancet*. 2021;397:2361.

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NCCN Guidelines for Late Relapses (>3 Prior Therapies)

After ≥4 prior therapies, including an anti-CD38 mAb, a PI, and an IMiD

- Idecabtagene vicleucel
- Ciltacabtagene autoleucel
- Teclistamab-cqyv

After ≥4 prior therapies and in patients whose disease is refractory to ≥2 PIs, ≥2 IMiDs, and an anti-CD38 mAb

- Selinexor/dexamethasone

National Comprehensive Cancer Network Guidelines. Multiple Myeloma. Version 2.2023.

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BOSTON: Adding Selinexor to Bortezomib/Dex Improved PFS in RRMM

	SVd (n=195)	Vd (n=207)
Median PFS (mos) Hazard ratio (*P* value)	13.93 0.70 (0.0075)	9.46
ORR (%) Hazard ratio (*P* value)	76.4 1.96 (0.0012)	62.3
≥VGPR (%)	44.6	32.4
DOR (months)	20.3	12.9

Grosicki S et al. *Lancet*. 2020;396:1563.

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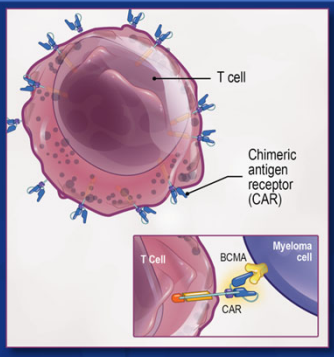
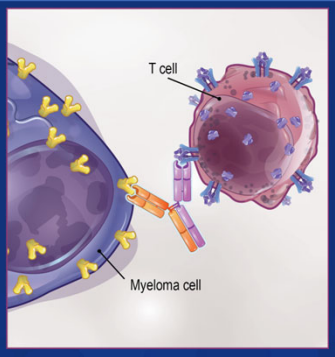
BCMA-Targeted Therapies for MM



CAR T-cell therapies
Idecabtagene vicleucel
Ciltacabtagene autoleucel



Bispecific T-cell engagers
Teclistamab
Elranatamab
Talquetamab

Figure 3 from Yu B et al. BCMA-targeted immunotherapy for multiple myeloma. *J Hematol Oncol.* 2020;13:125. Available under a Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by/4.0/).
Figure 1B of Shah N et al. B-cell maturation antigen (BCMA) in multiple myeloma: rationale for targeting and current therapeutic approaches. *Leukemia.* 2020;34(4):985-1005. http://creativecommons.org/licenses/by/4.0/.

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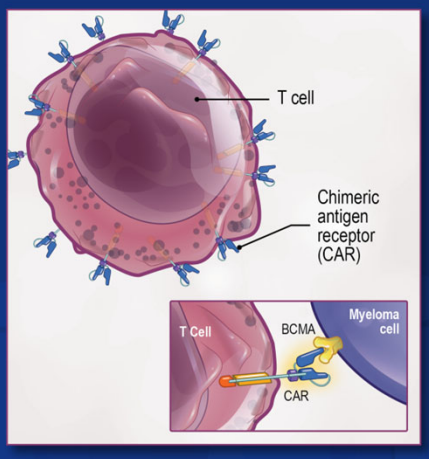
CAR T-Cell Therapy



- 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 the myeloma cell
- CAR T cells can persist for long periods 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
- Approved:
  Idecabtagene vicleucel (ide-cel)
  Ciltacabtagene autoleucel (cilta-cel)

CAR, chimeric antigen receptor.
Cohen A et al. *Clin Cancer Res.* 2020;26:1541.

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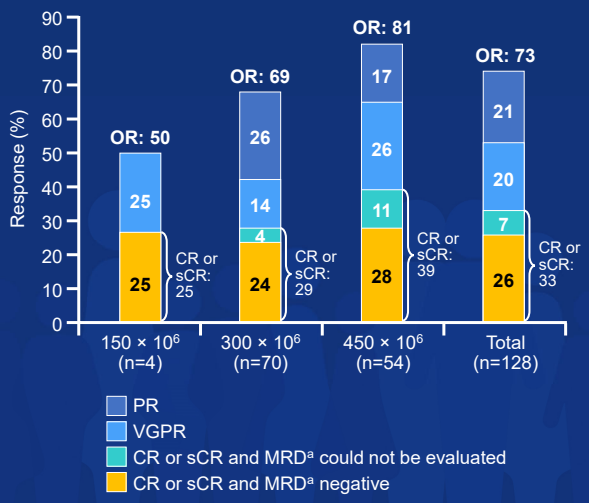
KarMMa: Ide-Cel in Triple-Class–Refractory MM

- Primary (ORR >50%) and key secondary (CRR >10%) end points were met in the ide-cel–treated population
  - ORR: 73% (95% CI, 65.8–81.1; *P*<0.0001)
  - CRR (CR/sCR): 33% (95% CI, 24.7–40.9; *P*<0.0001)
- Median PFS
  - 8.8 months (95% CI, 5.6 to 11.6) in Total
  - 12.1 months (95% CI, 8.8 to 12.3) at the 450 × 10^6 dose
  - 20.2 months in patients with CRR (CR/sCR)



From Munshi NC, et al. Idecabtagene vicleucel in relapsed and refractory multiple myeloma. *N Engl J Med* 384:705-716. Copyright © 2021 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

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CARTITUDE-1: 2-Year Follow-Up With Cilta-Cel in RRMM

2 years post-last patient in (LPI) results

- ORR[a] remained 97.9%
- 83% of patients achieved a sCR with longer follow-up
- Cilta-cel is being assessed in earlier lines of therapy
  - CARTITUDE-3, CARTITUDE-4, CARTITUDE-5, CARTITUDE-6

[a]ORR assessed by independent review committee; [b]No patient had CR or stable disease
Usmani SZ et al. *Clin Lymphoma Myeloma Leuk*. 2022;22 Suppl 2:S410.

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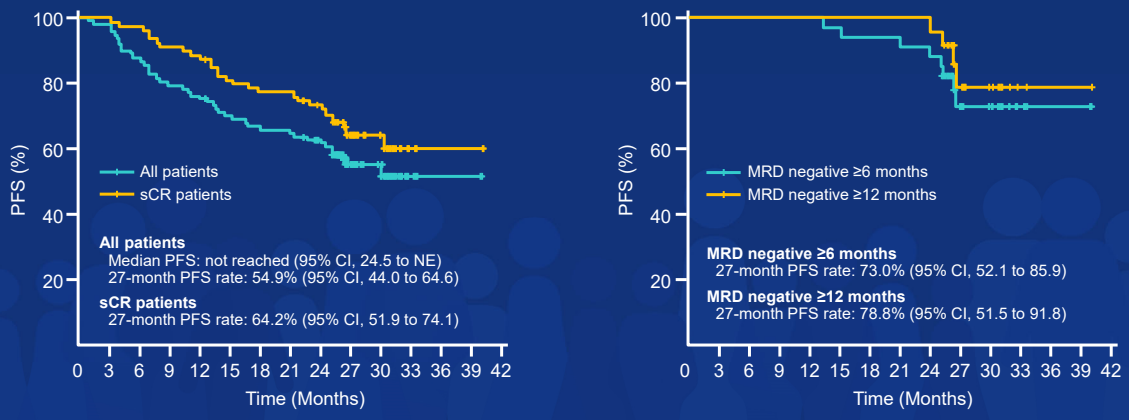
CARTITUDE-1: PFS Follow-Up 2 Years With Post-LPI With Cilta-Cel in RRMM



From Fig 2 of Martin T, et al. Ciltacabtagene autoleucel, an anti–B-cell maturation antigen chimeric antigen receptor T-cell therapy, for relapsed/refractory multiple myeloma: CARTITUDE-1 2-Year Follow-Up. *J Clin Onc* Jun 4;JCO2200842. © 2022 by American Society of Clinical Oncology. https://ascopubs.org/doi/figure/10.1200/JCO.22.00842

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CRS and ICANS With CAR T Therapy

Safety	Cilta-cel, % (n)[1]	Ide-cel, % (n)[2]
CRS (all, grade 3 or 4)	95 (5)	84 (5)
Median onset CRS	7 days	1 day
ICANS (all, grade 3 or 4)	17 (2)	18 (3)
Infections (all, grade 3 or 4)	58 (20)	69 (22)
Grade 3 or 4 neutropenia >1 mo, n	10	41
Grade 3 or 4 thrombocytopenia >1 mo, n	25	48
Delayed neurotoxicity (all, grade 3 or 4)	12 (9)	None

1. Martin T et al. *Blood*. 2021;138(Suppl 1):549. **2.** Anderson LD et al. ASCO 2021. Abstract 8016.

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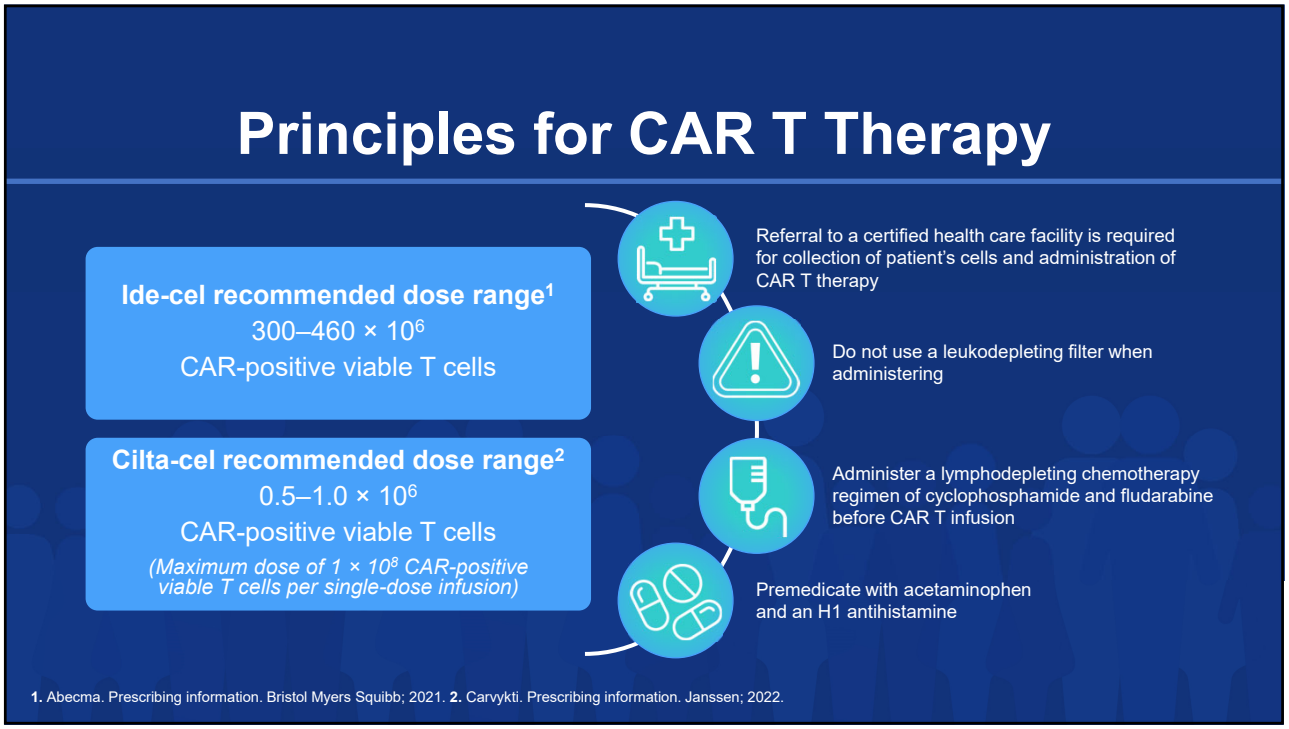
Principles for CAR T Therapy
Ide-cel recommended dose range[1]
300–460 × 10^6
CAR-positive viable T cells
Cilta-cel recommended dose range[2]
0.5–1.0 × 10^6
CAR-positive viable T cells
(Maximum dose of 1 × 10^8 CAR-positive viable T cells per single-dose infusion)
Referral to a certified health care facility is required for collection of patient's cells and administration of CAR T therapy
Do not use a leukodepleting filter when administering
Administer a lymphodepleting chemotherapy regimen of cyclophosphamide and fludarabine before CAR T infusion
Premedicate with acetaminophen and an H1 antihistamine
1. Abecma. Prescribing information. Bristol Myers Squibb; 2021. 2. Carvykti. Prescribing information. Janssen; 2022.

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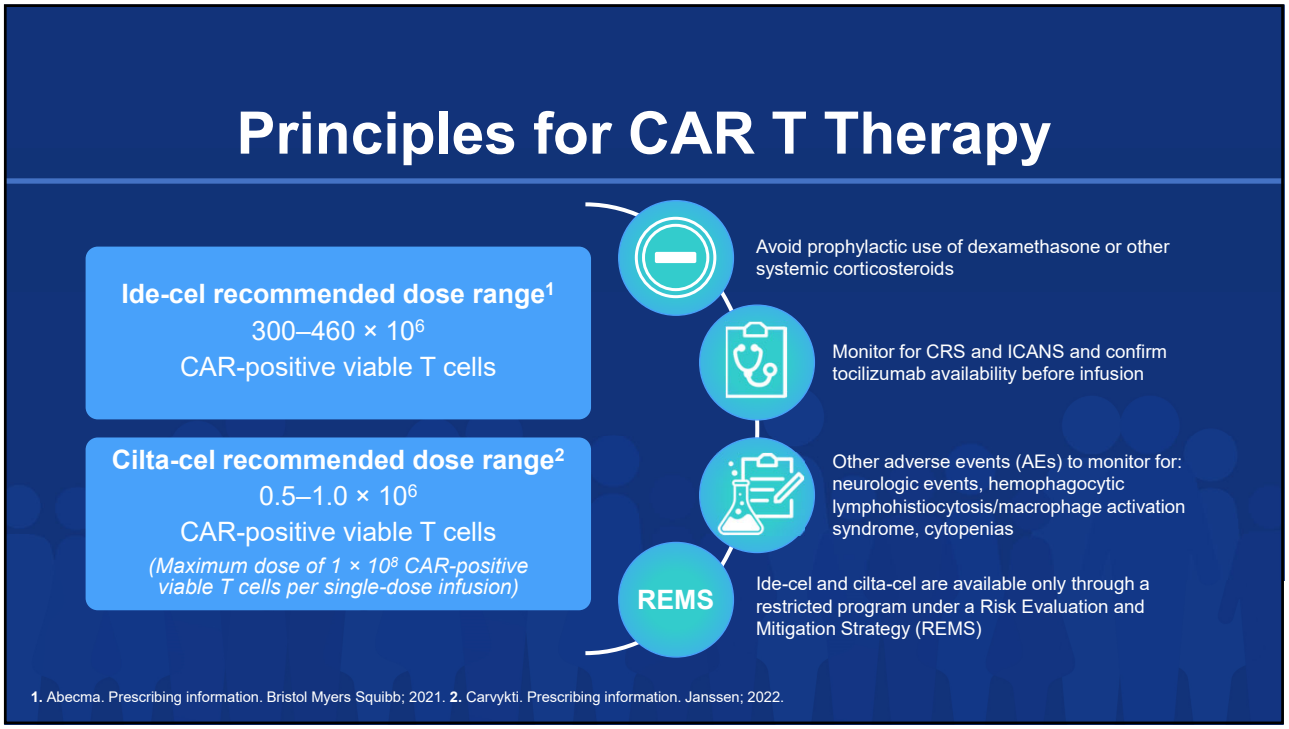
Principles for CAR T Therapy
Ide-cel recommended dose range[1]
300–460 × 10^6
CAR-positive viable T cells
Cilta-cel recommended dose range[2]
0.5–1.0 × 10^6
CAR-positive viable T cells
(Maximum dose of 1 × 10^8 CAR-positive viable T cells per single-dose infusion)
Avoid prophylactic use of dexamethasone or other systemic corticosteroids
Monitor for CRS and ICANS and confirm tocilizumab availability before infusion
Other adverse events (AEs) to monitor for: neurologic events, hemophagocytic lymphohistiocytosis/macrophage activation syndrome, cytopenias
REMS
Ide-cel and cilta-cel are available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS)
1. Abecma. Prescribing information. Bristol Myers Squibb; 2021. 2. Carvykti. Prescribing information. Janssen; 2022.

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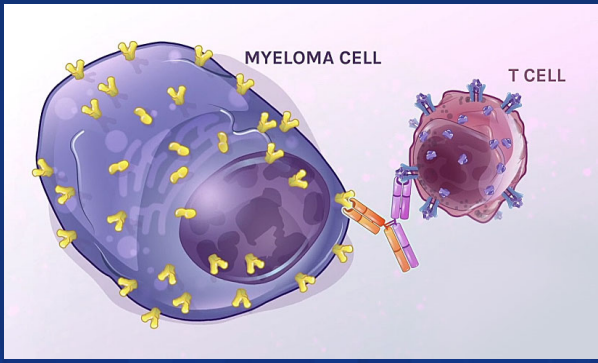
Bispecific Antibodies

- 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; teclistamab is the only one approved for use in myeloma
- Availability is off-the-shelf allowing for immediate treatment



Examples:
- Teclistamab
- Elranatamab
- Talquetamab
- Cevostamab
- TNB-303B (ABBV-383)
- REGN5458

Modified from Figure 3 of Shah N et al. B-cell maturation antigen (BCMA) in multiple myeloma: rationale for targeting and current therapeutic approaches. *Leukemia.* 2020;34(4):985-1005. http://creativecommons.org/licenses/by/4.0/.

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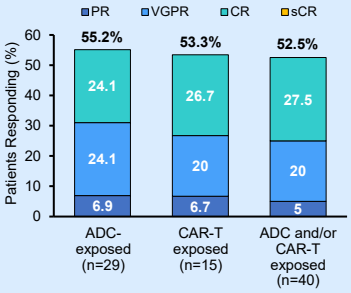
Teclistamab (BCMA × CD3 Bispecific Antibody) in Patients With RRMM

Updated efficacy and safety results with teclistamab (MajesTEC-1 study)[1]

Outcome	Patients Responding (%), n=165
sCR	32.7
CR	6.7
VGPR	19.4
PR	4.2

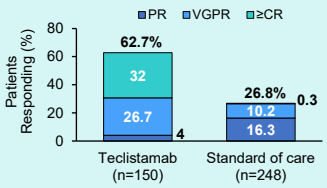
Deep and durable responses in heavily pretreated RRMM patients. Phase 3 studies under way.

Teclistamab in patients *with prior* BCMA-targeted treatment (MajesTEC-1 study)[2]



A potential off-the-shelf T-cell–redirecting therapy for patients with RRMM and prior exposure to other BCMA-targeted agents.

Teclistamab experience vs real-world clinical practice (LocoMMotion study)[3]



	Teclistamab	Standard of Care
Progression-free survival (mos)	10.1	4.3
Overall survival (mos)	18.3	13.0

A potential treatment option for patients with RRMM who have been exposed to three or more lines of therapy.

1. Moreau P et al. *N Engl J Med.* 2022;387:495. **2.** Touzeau C et al. *HemaSphere.* 2022;6:(Suppl 3):176. **3.** van de Donk NWCJ et al. *J Clin Oncol.* 2022;40. Abstract 8016.

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Elranatamab (BCMA × CD3 Bispecific Antibody) in Patients With RRMM

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

- 64% of patients responded who received elranatamab at a dose greater than or equal to 215 µg/kg
- 35% of patients achieved a CR or better
- 54% of patients who received prior BCMA-directed therapy responded to elranatamab treatment (2 sCR, 1CR, 3 VGPR, and 1 PR)
- 100% of patients who achieved CR and sCR also achieved MRD negativity

Durable clinical and molecular responses, consistent with clinical findings from other investigational BCMA-targeted bispecific antibodies

Elranatamab in patients with *no prior* BCMA-directed treatment (MagnetisMM-3 study)[2]

- Patients had a median of five prior lines of therapy and were treated with a weekly dose of elranatamab
- 61% of patients responded

The trial is ongoing with results expected later this year.

1. Jakubowiak AJ et al. *J Clin Oncol*. 2022;40. Abstract 8014. **2.** Lesokhin AM et al. *J Clin Oncol*. 2022;40. Abstract 8006.

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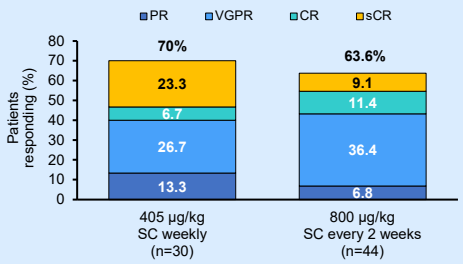
Talquetamab (GPRC5D × CD3 Bispecific Antibody) in Patients With RRMM

Updated efficacy and safety results with talquetamab (MonumenTAL-1 study)



Highly promising efficacy in heavily pretreated RRMM patients, including those who received three or more lines of prior therapy or were double refractory to a proteasome inhibitor and an immunomodulatory drug.

GPRC5D, G protein-coupled receptor family C group 5 member D
Minnema MC et al. *J Clin Oncol*. 2022;40. Abstract 8015.

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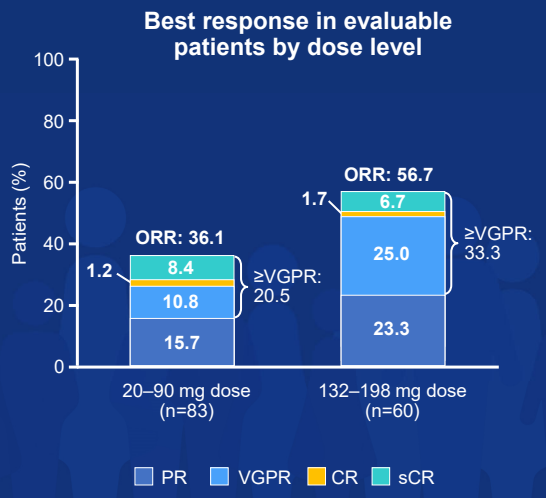
Cevostamab in RRMM: Response

- Responses occurred ≥20 mg target dose level (n=143)
- ORR increased with target dose
  - ORR in cycle 1 single step-up expansion (3.6 mg/90 mg): 29.0%
  - ORR in first cycle of double step-up expansion (0.3 mg/3.6 mg/160 mg): 54.8%

Outcome	Cevostamab (N=161)
Median time to response among responders, mo (range)	1.0 (0.7–5.9)
Median time to best response, mo (range)	2.1 (0.7–11.4)
MRD negativity at $<10^{-5}$ in patients with ≥VGPR, n/N (%)	7/10 (70)



Trudel S et al. *Blood*. 2021;138(Suppl 1):157. Abstract 653.

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Bispecific Antibodies: Expected Toxicities

Cytokine release syndrome

Cytopenias

Neurotoxicity (ICANS)

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

Cytokeratin change/rash

Infections

- Incidence for bispecifics at RP2D not yet known
- Viruses: CMV, EBV
- PCP/PJP
- Ongoing discussions regarding prophylactic measures
  - IVIG
  - Anti-infectives

ICANS, immune effector cell-associated neurotoxicity syndrome; RP2D, randomized phase 2 dose; CMV, cytomegalovirus; EBV, Epstein-Barr virus; PCP/PJP, pneumocystis pneumonia/*Pneumocystis jiroveci* pneumonia

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Key Takeaways for NDMM

- Black patients disproportionately affected by disparities in access to care
- Imperative to identify high-risk patients and to provide them with the most effective therapy
  - Attaining and maintaining a deep remission are key treatment goals
  - MRD negativity may emerge as a new goal of therapy
- RVd with or without ASCT followed by R maintenance is current standard of care for frontline therapy
- Quadruplet therapy is highly active as up-front therapy and may be the future of care
  - DETERMINATION: ASCT can be delayed in some cases
- Studies are evaluating new MRD-directed maintenance therapy

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Key Takeaways for RRMM

- Use of triplets containing an anti-CD38 antibody supported by current guidelines and evidence for use in early relapse
- BCMA-targeted CAR T-cell therapies are highly effective treatment options for triple-class refractory and beyond
  - CAR T-cell therapy: requires careful monitoring and management of CRS and ICANS
- Bispecific antibody are an “off-the-shelf” therapy that can target multiple cell surface proteins: BCMA, GPRC5D, FCRH5
- Small molecules with novel MOA such as selinexor are approved for RRMM

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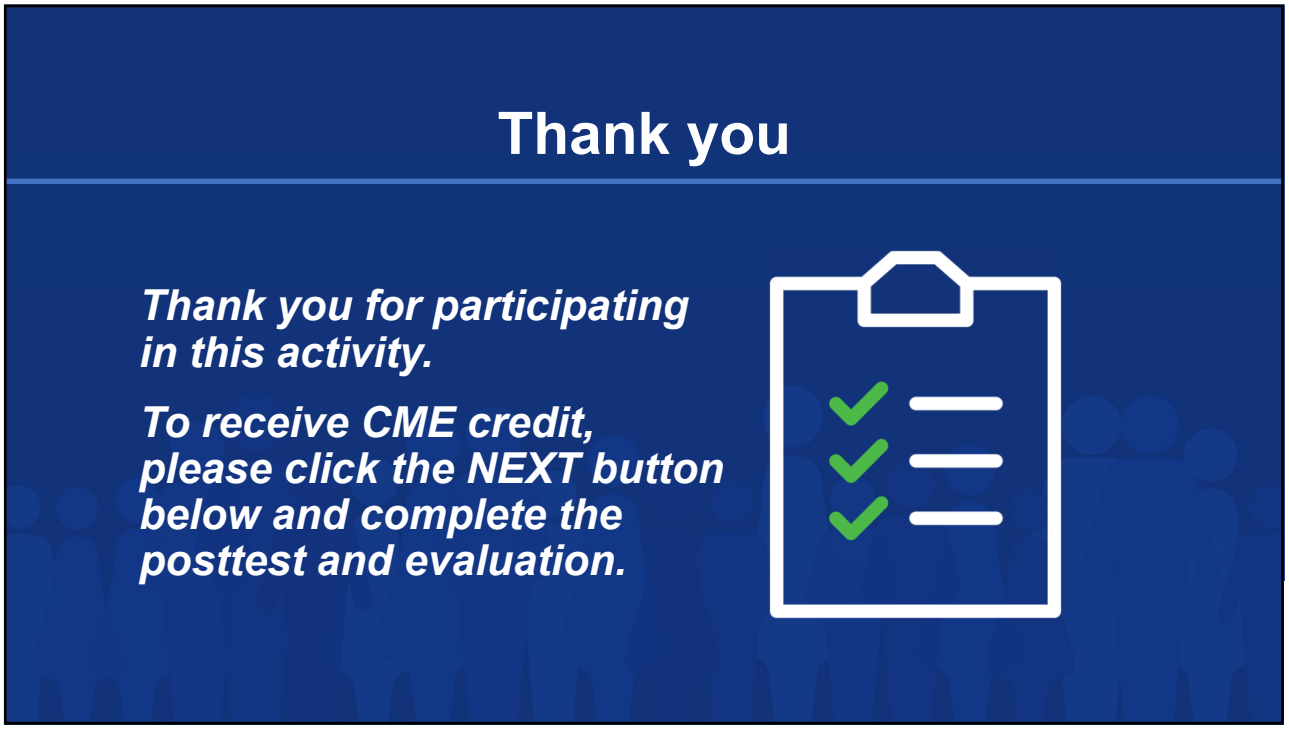
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