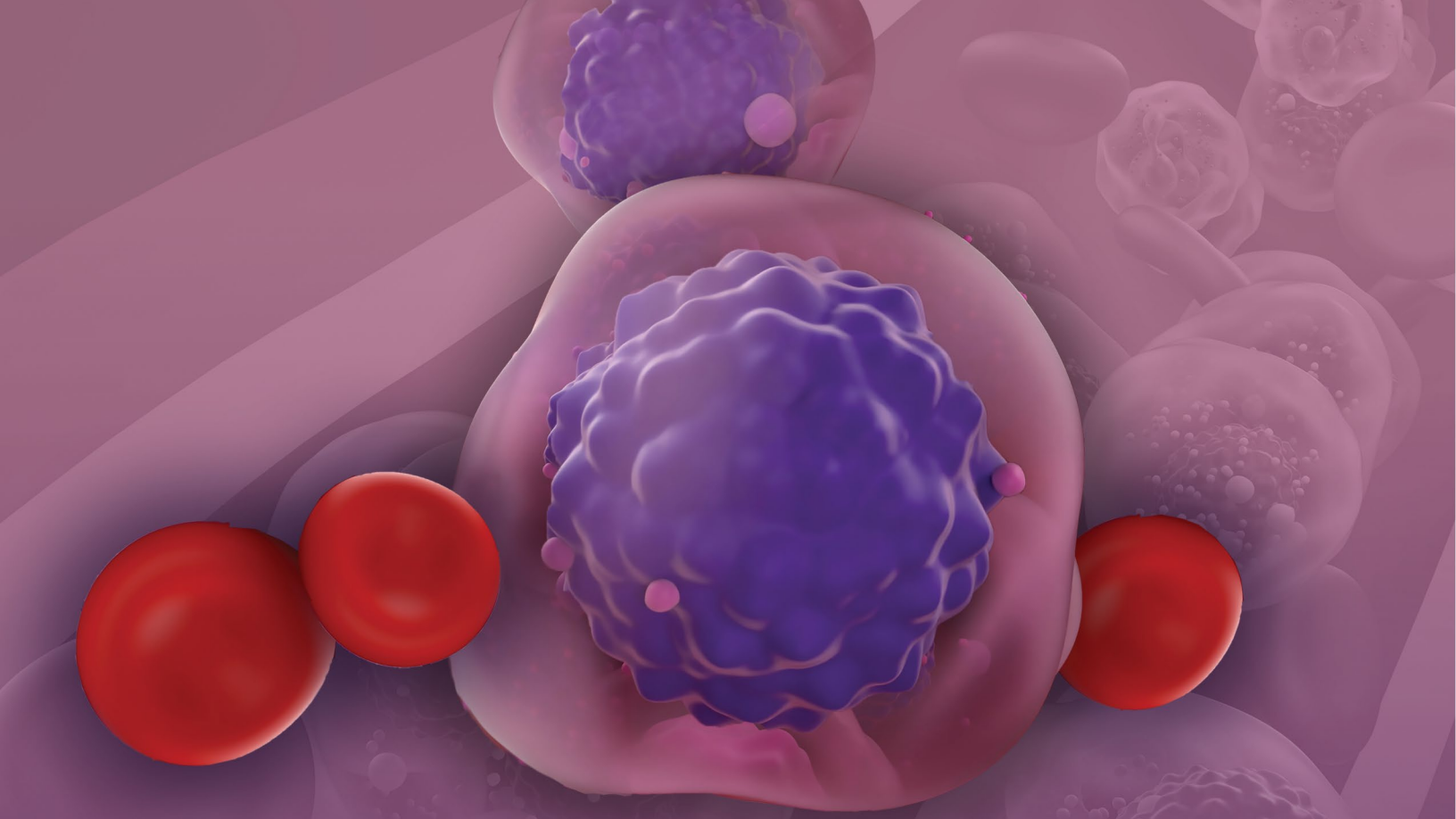

Innovations in
MULTIPLE MYELOMA CARE:
Personalizing Treatments and Managing Advanced Therapies

MED LEARNING GROUP

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This activity is supported by an educational grant from Janssen Biotech, Inc., administered by Janssen Scientific Affairs, LLC, both Johnson & Johnson companies.

Innovations in Multiple Myeloma Care: Personalizing Treatments and Managing Advanced Therapies

FACULTY

Craig Hofmeister, MD, MPH
Professor, Dept of Hematology & Oncology
Winship Cancer Institute of Emory University
Atlanta, GA

Noopur S. Raje, MD
Director, Center for Multiple Myeloma
Rita Kelley Chair, Oncology
Massachusetts General Hospital Cancer Center
Professor of Medicine
Harvard Medical School
Boston, MA

PROGRAM OVERVIEW

This program will focus on describing the mechanisms of action of current and emerging therapies in multiple myeloma and review their efficacy and safety profiles across different treatment settings. The program will also integrate patient-specific factors, prognostic indicators, and current evidence to design and implement personalized treatment plans across multiple lines of therapy. Lastly, comprehensive management strategies for patients receiving immunotherapies will be reviewed. This will include referrals to specialized treatment centers, patient and caregiver education, expected outcomes, potential complications, and proactive monitoring.

TARGET AUDIENCE

This activity is designed to meet the educational needs of academic and community hematologists/oncologists, oncology nurses, oncology NP/PAs, and oncology pharmacists to ensure the appropriate use of current and emerging therapies in relapsed/refractory multiple myeloma.

LEARNING OBJECTIVES

Upon the completion of this program, attendees should be able to:

- Describe the mechanisms of action of current and emerging therapies in multiple myeloma, critically assessing their efficacy and safety profiles across different treatment settings.
- Integrate patient-specific factors, prognostic indicators, and current evidence to design and implement personalized treatment plans for patients with multiple myeloma, integrating innovative antibody and immunotherapy platforms across all lines of therapy.
- Develop comprehensive management strategies for patients with multiple myeloma receiving immunotherapies, addressing criteria and timing for referral to specialized treatment centers, patient and caregiver education on expected outcomes and potential complications, and proactive monitoring and management of unique toxicities related to treatment.

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Speaker	Relationships	Manufacturer
Craig Hofmeister, MD	Consultant	Karyopharm Therapeutics
	Contracted research	AbbVie, Sanofi
Noopur S. Raje, MD	Consultant	Bristol Myers Squibb, Johnson & Johnson, Pfizer, Sanofi, GlaxoSmithKline, AstraZeneca, AbbVie, Regeneron, Immuneel Therapuetics, Caribou Biosciences
	Contracted research	Pfizer

All relevant financial relationships have been mitigated.

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5 min.	**Introduction and Pre-Test**
40 min.	**Didactic Content Shared by Faculty Using Slides and Infographic Data** I. **Multiple Myeloma** a. Epidemiology b. IMWG diagnostic criteria c. Revised International Staging System d. Risk categorization e. Prognostic indicators II. **Current Therapies** a. Goals of treatment b. Clinical studies **III. Emerging Therapies** a. Bispecific antibodies b. Clinical profiles of bispecific antibodies
15 min.	**Monitoring and Toxicity Management** • Cytokine release syndrome • Neurotoxicity • ICE/ICANS • Cytopenias • GPRC5D-associated toxicity
15 min.	**Case Study Discussion**
15 min.	**Conclusions, Q&A, and Post-Test**

Innovations in Multiple Myeloma Care: Personalizing Treatments and Managing Advanced Therapies

Craig Hofmeister, MD, MPH
Professor, Department of Hematology and Medical Oncology
Winship Cancer Institute of Emory University
Atlanta, GA

Noopur S. Raje, MD
Director, Center for Multiple Myeloma
Rita Kelly Chair, Oncology
Massachusetts General Hospital Cancer Center
Harvard Medical School
Boston, MA

Disclosures

- **Dr Hofmeister** discloses the following

Relationships	Manufacturer
Consultant	Karyopharm Therapeutics
Contracted research	AbbVie, Sanofi

- **Dr Raje** discloses the following

Relationships	Manufacturer
Consultant	Bristol Myers Squibb, Johnson & Johnson, Pfizer, Sanofi, GlaxoSmithKline, AstraZeneca, AbbVie, Regeneron Pharmaceuticals, Immuneel Therapeutics, Caribou Biosciences
Contracted research	Pfizer

  - During the course of this lecture, Dr Hofmeister and Dr Raje may discuss the use of medications for both US Food and Drug Administration (FDA)-approved and non-FDA-approved indications

This activity is supported by an educational grant from Janssen Biotech, Inc., administered by Janssen Scientific Affairs, LLC, both Johnson & Johnson companies.

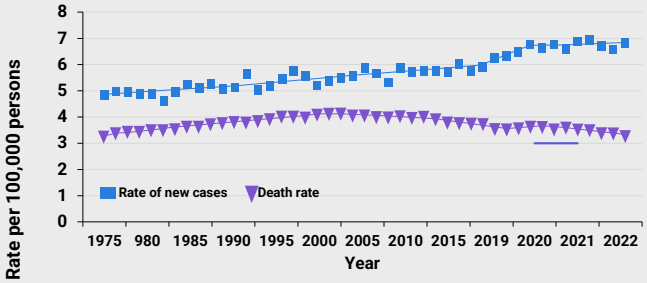
Learning Objectives

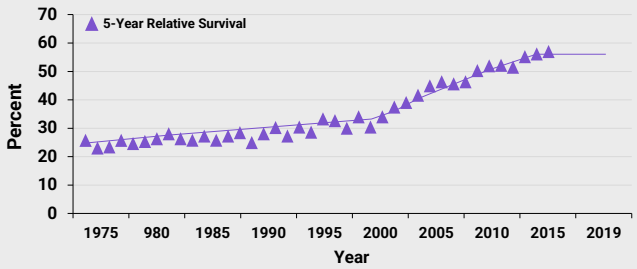
- Integrate patient-specific factors, prognostic indicators, and current evidence to design and implement personalized treatment plans for patients with multiple myeloma, integrating innovative antibody, and immunotherapy platforms across all lines of therapy
- Describe the mechanisms of action of current and emerging therapies in multiple myeloma, critically assessing their efficacy and safety profiles across different treatment settings
- Develop comprehensive management strategies for patients with multiple myeloma receiving immunotherapies, addressing criteria and timing for referral to specialized treatment centers, patient and caregiver education on expected outcomes and potential complications, and proactive monitoring and management of unique toxicities related to treatment

Multiple Myeloma Overview

Multiple Myeloma (MM)

- Characterized by clonal expansion of aberrant plasma cells in the bone marrow, with some patients having extramedullary disease (EMD)
- An estimated 179,063 people are living with MM in the United States (2021)
- The 5-year relative survival rate is 61.1%
- The estimates for 2024 indicate that
  - 35,780 new cases will be diagnosed
  - 12,540 deaths from MM





National Cancer Institute (NCI). US Surveillance, Epidemiology, and End Results (SEER) program. Cancer stat facts: myeloma. (https://seer.cancer.gov/statfacts/html/mulmy.html). Accessed 4/30/2025.

Revised IMWG Diagnostic Criteria

MGUS	Smoldering myeloma	Multiple myeloma	Amyloid light chain (AL) amyloidosis
▪ M protein <3 g/dL ▪ Clonal plasma cells in marrow <10% ▪ No SLiM-CRAB criteria	▪ M protein ≥3 g/dL (serum) or ≥500 mg/ 24 hours (urine) ▪ Clonal plasma cells in marrow 10% to 60% ▪ No SLiM-CRAB criteria	▪ Clonal marrow plasma cells ≥10% or ≥1 biopsy-proven plasmacytoma ▪ SLiM-CRAB criteria	▪ Amyloid-related systemic syndrome (renal, liver, heart, gastrointestinal [GI], peripheral nerve system [PNS]) ▪ Congo red in any tissue established to be light-chain related (mass spec or immunoelectron microscopy) ▪ Serum protein electrophoresis positive (SPEP+ve), urine protein electrophoresis positive (UPEP+ve), abnormal serum free light chain ratio (SFLC-R), or clonal marrow plasma cells

SLiM	CRAB
S Clonal plasma cells in bone marrow (BM) ≥60% **Li** Serum FLC ratio ≥100 **M** >1 MRI focal lesion ≥5 mm on MRI Any of these criteria is associated with 75% to 95% risk of progression to development of CRAB criteria in 2 years	**C** Calcium elevation (>11 mg/dL or >1 mg/dL higher than upper limit of normal [ULN]) **R** Renal insufficiency (CrCl <40 mL/min or serum creatinine >2 mg/dL) **A** Anemia (hemoglobin [Hb] <10 g/dL or 2 g/dL < normal) **B** Bone disease (≥1 lytic lesions on skeletal radiography, CT, or PET/CT)

CrCl = creatinine clearance; CT = computed tomography; FLC = free light chain; IMWG = International Myeloma Working Group; MGUS = monoclonal gammopathy of undetermined significance; MRI = magnetic resonance imaging; PET = positron emission tomography; ve = positive.

Rajkumar SV, et al. *Lancet Oncol*. 2014;15(12):e538-e548.

Revised International Staging System (R-ISS)

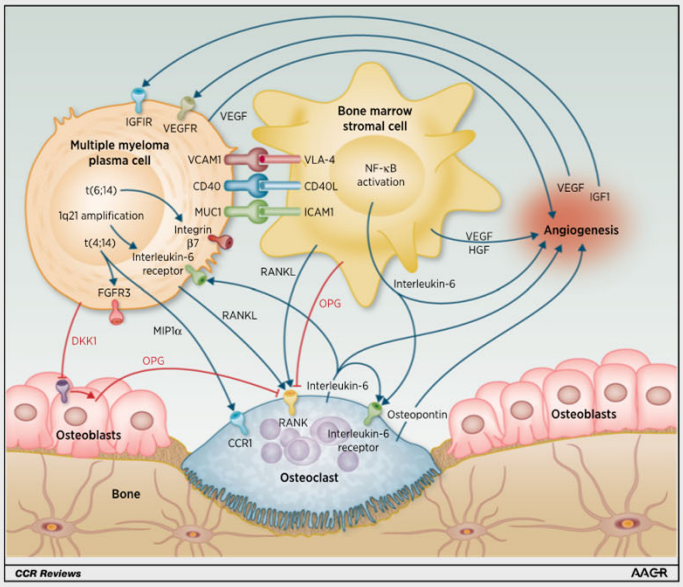
Stage	Criteria	Genetics	Survival (years)
1	$ß_2$-M <3.5 mg/L and serum albumin ≥3.5 g/dL	No del(17p) Normal LDH No t(4;14) No t(14;16)	**9**
2	Not stage 1 or 3		**6.9**
3	$ß_2$-M ≥5.5 mg/L	t(4;14) or t(14;16) or Del(17p) or High LDH	**3.6**

Palumbo A, et al. *J Clin Oncol.* 2015;33(26):2863-2869.

Risk categorization *(draft)*	Characteristics at diagnosis or during first line
High risk per International Myeloma Society	▪ FISH Del17 (≥20%); or ▪ FISH (1p- **and** 1q+); or ▪ FISH high risk 14q32 trans and (1q+ **or** 1p-) ▪ ***Genomic TP53 mutant or bi-allelic del(1p-)***
Intermediate	▪ R-ISS 3 ▪ Any of the following: t(4;14), t(14;16), t(14;20) ▪ Del17p (<20%) ▪ ≥2% circulating plasma cells (PCs) at diagnosis ▪ Extramedullary disease ▪ < VGPR after 4 to 6 cycles of induction
Standard	All others
Frail	Standard risk (as above)
	High/intermediate risk (as above)

FISH = fluorescent in-situ hybridization; VGPR = very good partial response.
Walker BA, et al. *Leukemia.* 2018;33:159-170. Corre J, et al. *Blood.* 2021;137:1192-1195. Jelinek T, et al. *J Clin Oncol.* 2023;41:1383-1392. Weinstock M, et al. *Br J Haematol.* 2015;169:851-858.

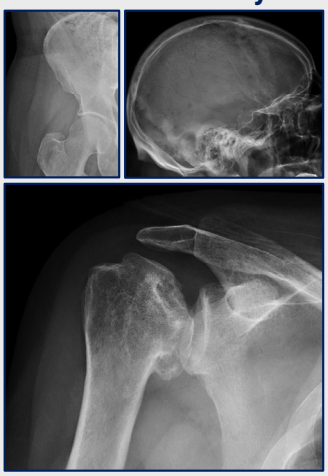
MM and Bone Marrow Stromal Cell Interaction Causes Overproduction of Factors Responsible for Uncoupled Bone Remodeling



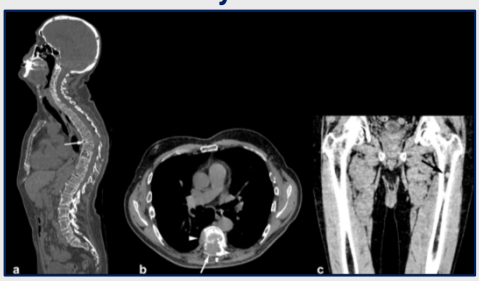
Raje N, Roodman GD. *Clin Cancer Res*. 2011;17(6):1278-1286.

Imaging for Bone Disease

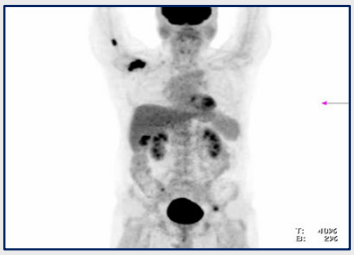
Skeletal survey



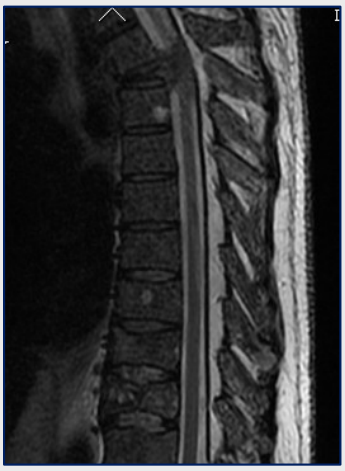
Whole body low dose CT



FDG PET scans



MRI

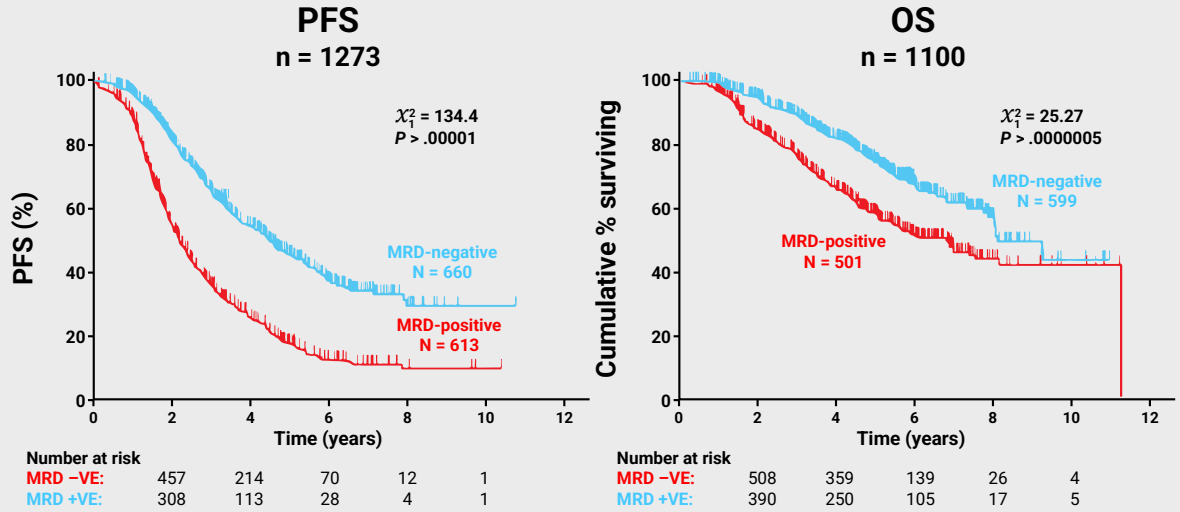


FDG = fluorodeoxyglucose.

Images courtesy of Noopur S. Raje, MD.

Prognostic Indicators

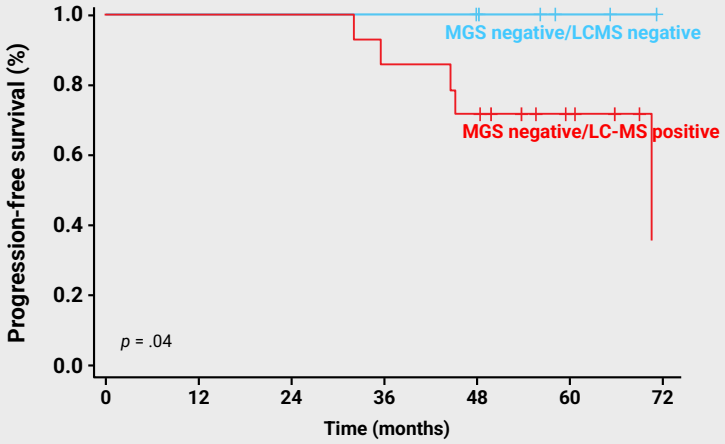
The effect of MRD status on PFS and OS
(meta-analysis)



MRD = minimal residual disease; OS = overall survival; PFS = progression-free survival.
Munshi NC, et al. *JAMA Oncol.* 2017;3(1):28-35.

MRD Assessment by LC-MS May Be Superior to NGS

PFS by MRD status after 18 cycles of KRd



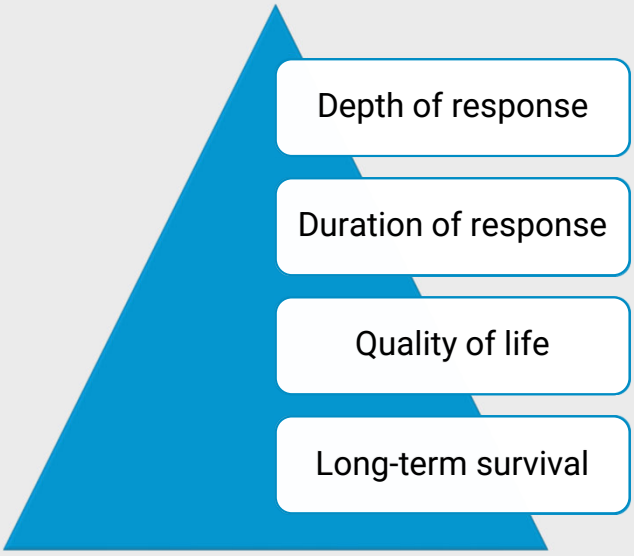
LC-MS can stratify outcomes among NGS negative patients.

NGS at 10^{-5}

KRd = carfilzomib, lenalidomide, and dexamethasone; LC-MS = liquid chromatography-mass spectrometry; NGS = next-generation sequencing.
Derman BA, et al., *Blood Cancer J.* 2021;11(2):19.

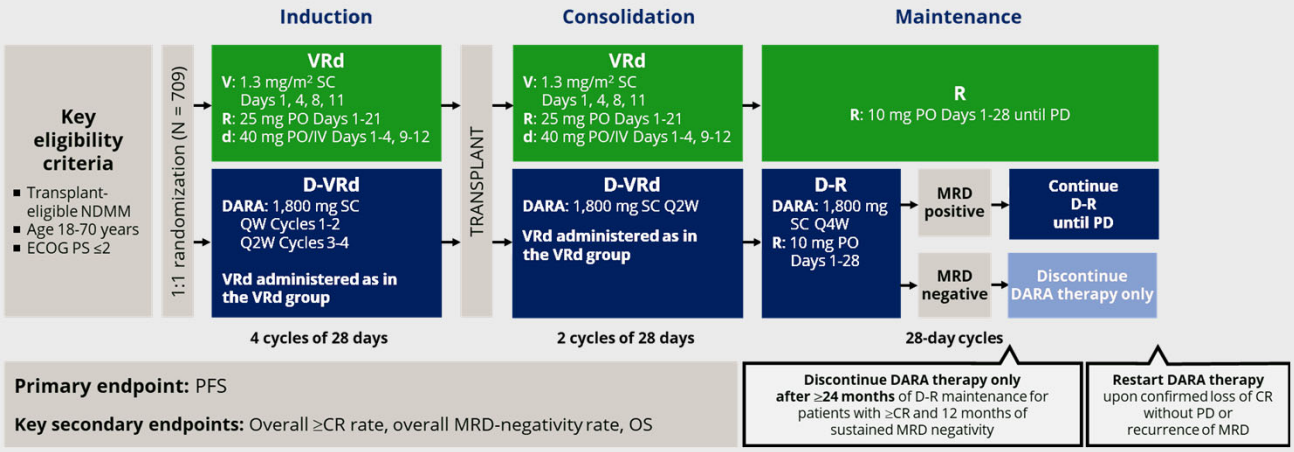
Current Therapies in Multiple Myeloma

Goals of Treatment in Multiple Myeloma



Bonello F, et al. *Cancers (Basel)*. 2019;12(1):15. Munshi NC, et al. *JAMA Oncol*. 2017;3:28-35.

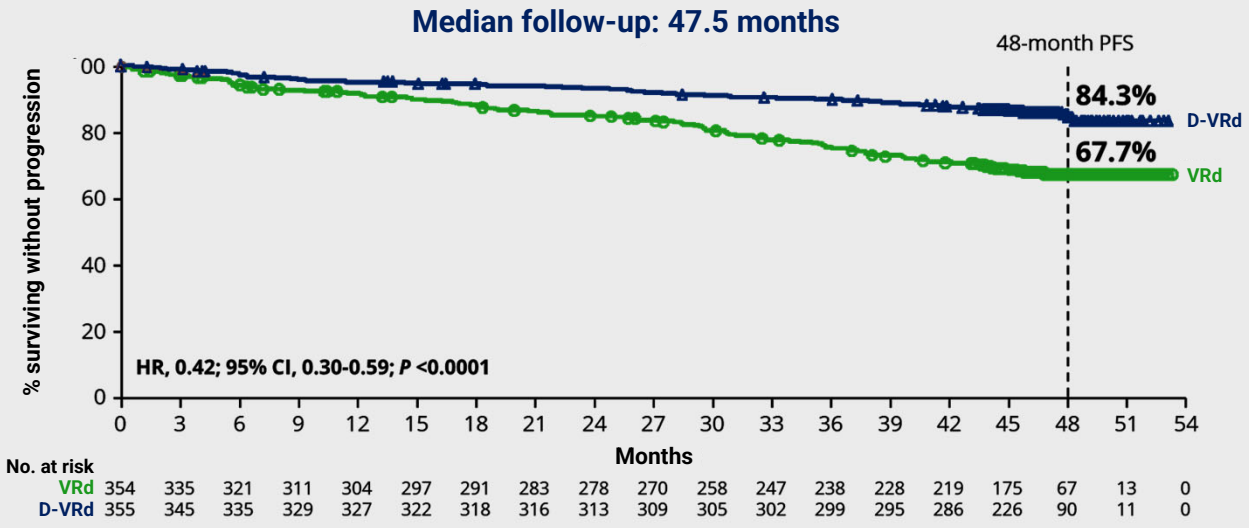
Phase 3 PERSEUS: D-VRd vs VRd



CR = complete response; DARA = daratumumab; D-VRD = daratumumab plus bortezomib, thalidomide, and dexamethasone; ECOG PS = Eastern Cooperative Oncology Group performance status; NDMM = newly diagnosed multiple myeloma; OS = overall survival; PFS = progression-free survival; R = lenalidomide maintenance therapy; SC = subcutaneous; VRd = bortezomib, lenalidomide, and dexamethasone.

Sonneveld P, et al. *Blood*. 2023;142(suppl 2); Abstract LBA1.

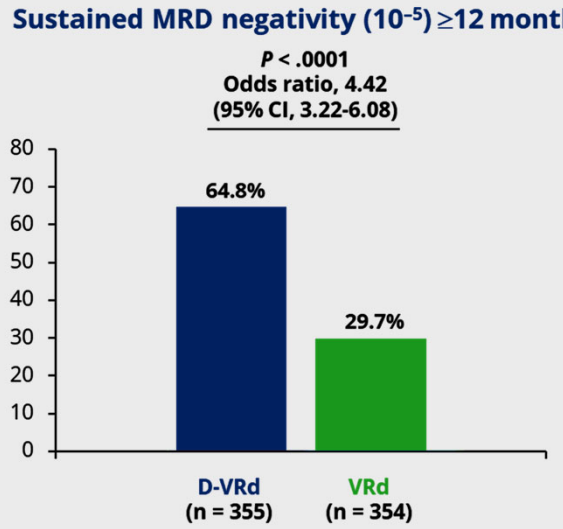
PERSEUS: Primary Endpoint—PFS



CI = confidence interval; HR = hazard ratio.

Sonneveld P, et al. *Blood*. 2023;142(suppl 2); Abstract LBA1.

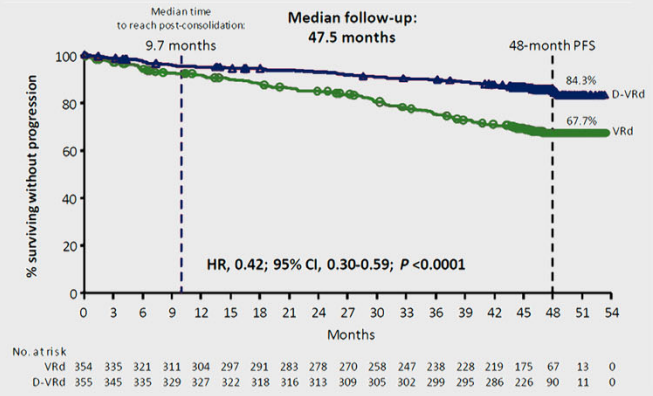
PERSEUS: Sustained MRD-Negativity Rates

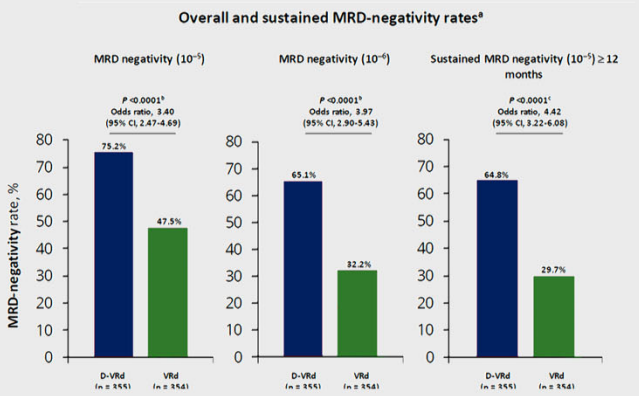


64% (207/322) of patients receiving maintenance in the D-VRd group discontinued daratumumab maintenance after achieving sustained MRD negativity (lenalidomide maintenance continued).

Sonneveld P, et al. *Blood*. 2023;142(suppl 2); Abstract LBA1.

PERSEUS Primary Analysis: D-VRd Followed by D-R Maintenance Significantly Improved PFS and Depth of Response vs VRd Followed by Lenalidomide Maintenance Therapy





58% reduction in the risk of progression or death in patients receiving D-VRd

Deep and durable MRD negativity achieved with D-VRd

[a]MRD-negativity rate was defined as the proportion of patients who achieved both MRD negativity and >CR. MRD was assessed using bone marrow aspirates and evaluated via NGS (clonosEQassay.version 2.0; Adaptive Biotechnologies, Seattle, WA, USA). [b]*P*-values were calculated with the use of the stratified Cochran—Mantel—Haenszel chi-square test. [c]*P*-value was calculated with the use of Fisher's exact test.

HR = hazard ratio; CI = confidence interval; NGS = next-generation sequencing.

Sonneveld P, et al. *N Engl J Med*. 2024;390(4):301-313.

The SKylaRk Trial:

Isatuximab, once-weekly carfilzomib, lenalidomide, and dexamethasone in transplant-eligible (TE) NDMM

Screening

Enrollment

Induction (C1-4)
- Lenalidomide 25 mg po Days 1-21
- Carfilzomib 56 mg/m2 IV Days 1, 8, 15
- Dexamethasone 20 mg po Days 1, 2, 8, 9, 15, 16
- Isatuximab 10 mg IV Q1 week for 8 weeks, then Q2 weeks for 16 weeks, thereafter Q4 weeks

Stem cell collection (SCT)

Autologous SCT

Consolidation (C5-6)
- Lenalidomide 25 mg po Days 1-21
- Carfilzomib 56 mg/m2 IV Days 1, 8, 15
- Dexamethasone 20 mg po Days 1, 2, 8, 9, 15, 16
- Isatuximab 10 mg IV Day 1

Transplant-Deferred

Induction (C5-8)
- Lenalidomide 25 mg po Days 1-21
- Carfilzomib 56 mg/m2 IV Days 1, 8, 16
- Dexamethasone 20 mg po Days 1, 2, 8, 9, 15, 16
- Isatuximab 10 mg IV Day 1

Maintenance (stratified based on cytogenetics and MRD status)
Standard-risk and/or MRD negative:
- Lenalidomide 10 mg po Days 1-21

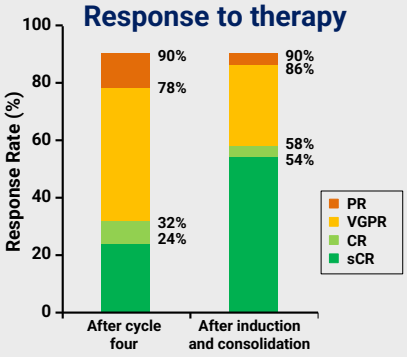
High-risk and/or MRD positive:
- Lenalidomide 10 mg po Days 1-21
- Carfilzomib 56 mg/m2 IV Days 1, 8, 15
- Isatuximab 10 mg IV Day 1

O'Donnell EK, et al. *Lancet Haematol.* 2024;11(6):e415-e424.

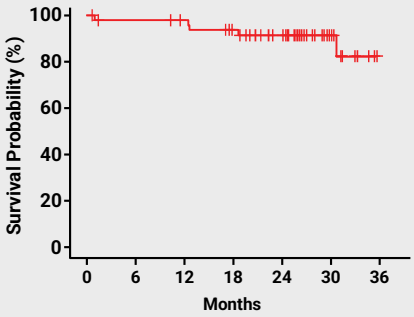
The SKylaRk Trial:

Isatuximab, once-weekly carfilzomib, lenalidomide, and dexamethasone in TE NDMM

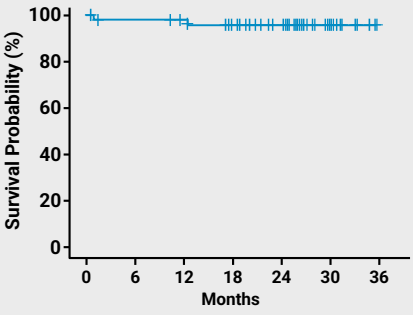
Response to therapy



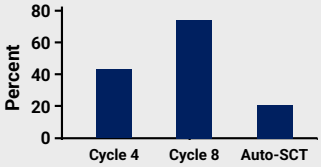
PFS



OS



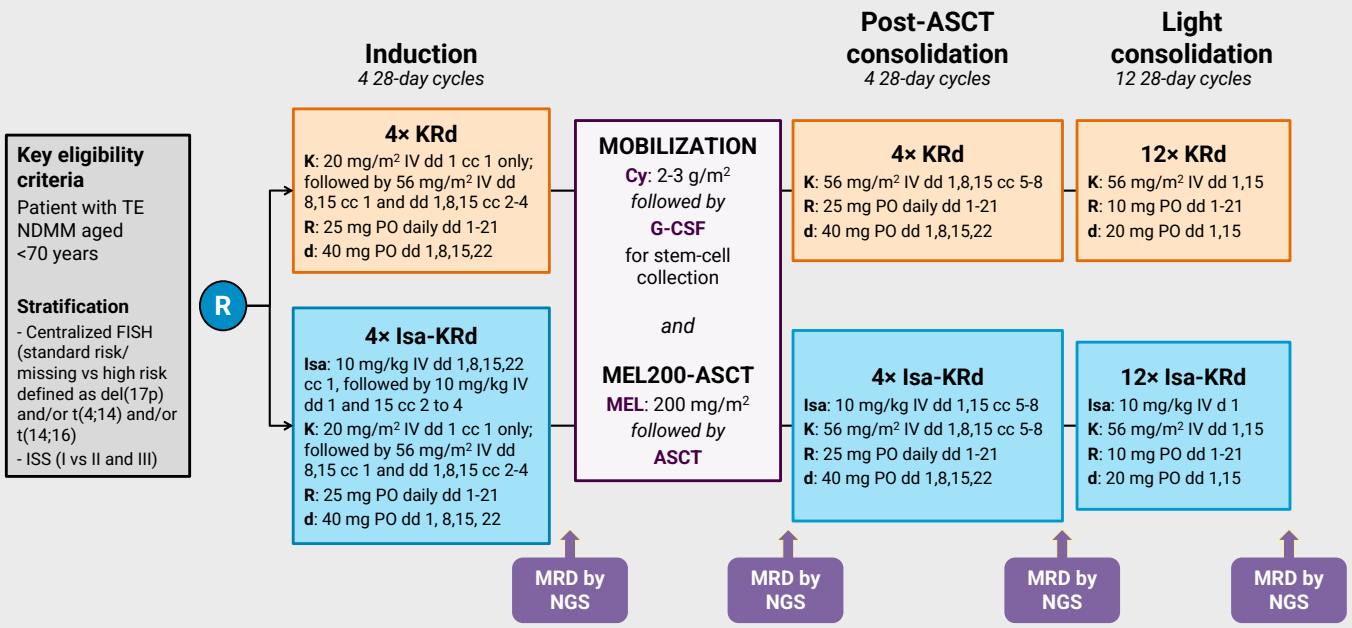
MRD negativity 10^{-5}



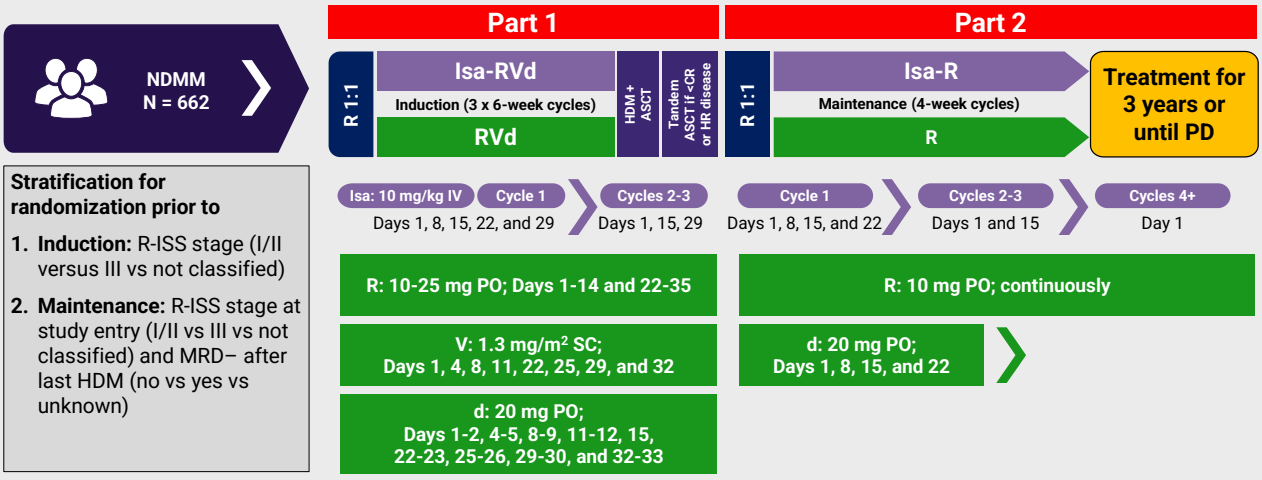
24-month PFS: 91.3%
24-month OS: 95.8%

O'Donnell EK, et al. *Lancet Haematol.* 2024;11(6):e415-e424.

ISKIA (EMN24)



GMMG-HD7



Stratification for randomization prior to

1. **Induction:** R-ISS stage (I/II versus III vs not classified)
2. **Maintenance:** R-ISS stage at study entry (I/II vs III vs not classified) and MRD− after last HDM (no vs yes vs unknown)

Primary endpoints: Postinduction MRD− (NGF, 10^{-5}); PFS after second randomization

Key secondary endpoints: PFS (whole study); OS (whole study and from second randomization); postinduction CR; CR and MRD− after HDM and during and after maintenance therapy

Selected secondary endpoint: PFS after first randomization

Treatment for Newly Diagnosed Multiple Myeloma

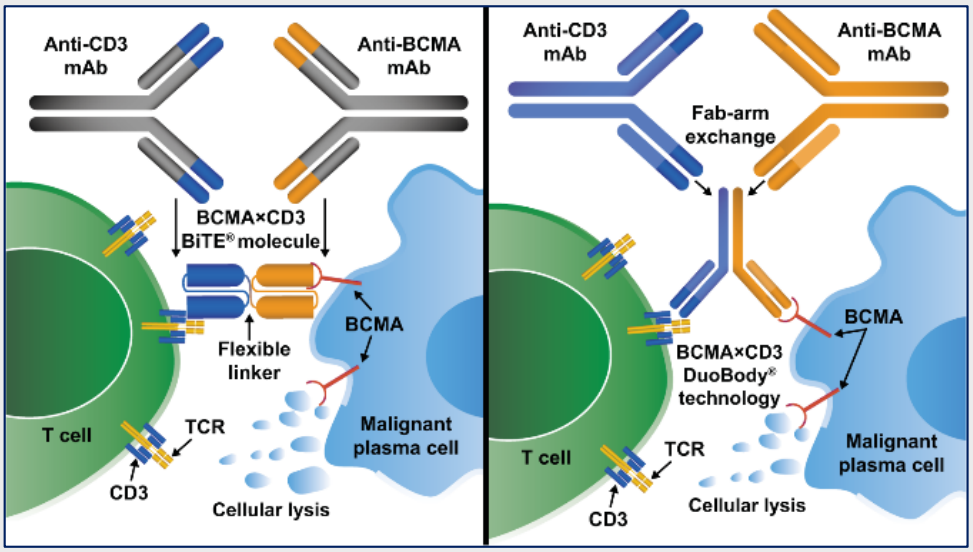
Transplant ineligible

IMROZ CD38-RVd vs RVd	CEPHEUS CD38-RVd vs RVd	BENEFIT CD38-RVd vs CD38-Rd
18–80 years 60 months follow-up	**31–80 years** 59 months follow-up	**65–79 years** 23 months follow-up
RVd with twice weekly bortezomib x 6 months; then CD38-Rd (weekly dex) until progression	RVd with twice weekly bortezomib x 6 months; then CD38-Rd (weekly dex) until progression	Dex "stops" after 12 cycles; bortezomib decreases to every other week at 1 year, then stops at 18 months
2-year total **32 x 1.3 mg/m^2** **2720 mg**	2-year total **32 x 1.3 mg/m^2** **4160 mg**	2-year total **48 x 1.3 mg/m^2** **1200 mg**
▪ 24-month est PFS 82% vs 72% ▪ CR$^+$ & MRD-ve 10^{-5} 56% vs 41%	▪ 24-month est PFS 81% vs 76% ▪ CR$^+$ & MRD-ve 10^{-5} 61% vs 39%	▪ 24-month PFS 85% vs 78% ▪ CR$^+$ & MRD-ve 10^{-5} 37% vs 17%

Early data suggest weekly bortezomib and low dose dexamethasone are preferred.

Emerging Therapies in Multiple Myeloma

Bispecific Antibodies: Mechanism of Action (MOA)



Shah N, et al. *Leukemia.* 2020;34:985-1005.

Bispecific Antibodies (BsAbs)

Bispecific molecule targets vary

Agent	Tumor cell target	T-cell target
Teclistamab	BCMA	CD3
Talquetamab	GPRC5d	CD3
Elranatamab	BCMA	CD3

"Off the shelf" advantage

- No manufacturing process, unlike CAR-T therapy (but like ADC/belantamab therapy)
- Therefore, no delay between decision to treat and administration of drug

Image from Shah N, et al. *Leukemia.* 2020;34:985-1005 (Creative Commons License: CC BY 4.0).

ADC = antibody-drug conjugate; CAR-T = chimeric antigen receptor T-cell therapy; FcRH5 = Fc receptor-homolog 5; GPRC5D = G-protein-coupled receptor, family C, group 5, member D; TCR = T-cell receptor.

Barilà G, et al. *Pharmaceuticals (Basel).* 2021;14:40. Raje N, et al. American Society of Hematology (ASH) 2022; Abstract 158. Bumma N, et al. ASH 2022; Abstract 4555.

T-Cell Engagers: Bispecific Antibodies (BsAbs)

Approved bispecific antibodies in the management of relapsed/refractory multiple myeloma

	Teclistamab (anti-BCMA)	Talquetamab (anti-GPRC5D)	Elranatamab (anti-BCMA)
	IgG1 Fc	IgG1 Fc	IgG2a Fc
			
Approved	**10/25/2022**	**8/9/2023**	**8/14/2023**

All indicated for use in relapsed/refractory (R/R) MM with ≥4 prior lines of therapy, including

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

Cho SF, et al. *Front Oncol*. 2022;12:1032775. FDA news release 10/25/2022 (www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-teclistamab-cqyv-relapsed-or-refractory-multiple-myeloma). FDA news release 8/14/2023 (https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-elranatamab-bcmm-multiple-myeloma). FDA news release 8/9/2023 (https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-talquetamab-tgvs-relapsed-or-refractory-multiple-myeloma). URLs accessed 4/30/2025.

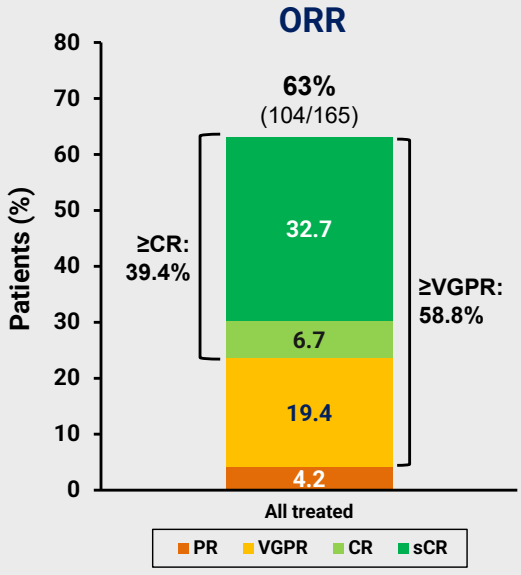
MajesTEC-1

Phase 1/2 study in R/R MM[1-3]

- 82% triple-class refractory, 30% penta-refractory

Additional response data[2]

- Median time to first response: 1.2 months
- Median duration of response (DOR): 18.4 months
- Median progression-free survival (PFS): 12.5 months
- Median overall survival (OS): 21.9 months



CR = complete response; ORR = objective response rate; PR = partial response; sCR = stringent complete response; VGPR = very good partial response.

1. Moreau P, et al. *N Engl J Med*. 2022;387(6):495-505. 2. van de Donk NWCJ, et al. American Society of Clinical Oncology (ASCO) 2023; Abstract 8011. 3. Garfall AL, et al. ASCO 2024; Abstract 7540.

Now Let's Watch an Animation

Recognizing and Managing CRS and ICANS with Bispecific Antibody Therapy in Multiple Myeloma

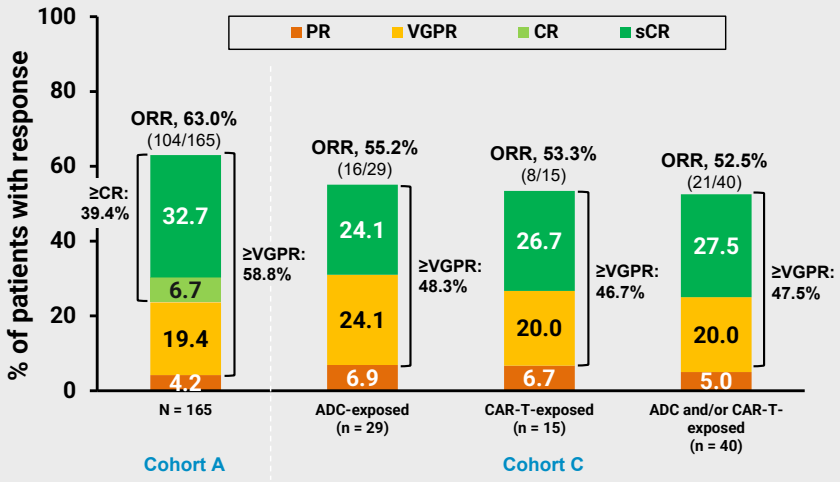
[https://youtu.be/TzHr2uXfp_U]

2-Year Follow-Up Data From MajesTEC-1

- Median PFS: 12.5 months
- Median DOR: 24 months

- Cohort A: BCMA-naïve
- Cohort C: Prior anti-BCMA therapy (CAR-T or ADC)

Response rates in patients from Cohorts A* and C†‡



*Data from Moreau P, et al. *N Engl J Med*. 2022;387:495-505.
†Data from Touzeau C, et al. *Blood*. 2024;144(23):2375-2388.
‡PR or better as per the International Myeloma Working Group 2016 criteria.

ADC = antibody-drug conjugate; CAR-T = chimeric antigen receptor T-cell therapy; CR = complete response; ORR = overall response rate; PR = partial response; sCR = stringent complete response; VGPR = very good partial response.

Sidana S, et al. *Hemasphere*. 2023;7(suppl):e62475d0. Moreau P, et al. *N Engl J Med*. 2022;387:495-505. Touzeau C, et al. *Blood*. 2024;144(23):2375-2388.

MajesTEC-1: Safety Data

Adverse event (AE), n (%)	Any grade (N = 165)	Grade 3/4 (N = 165)
Neutropenia	118 (71.5)	108 (65.5)
Anemia	90 (54.5)	62 (37.6)
Thrombocytopenia	70 (42.4)	37 (22.4)
Infections	132 (80.0)	91 (55.2)
Cytokine release syndrome (CRS)	119 (72.1)	1 (0.6)
Immune effector cell-associated neurotoxicity syndrome (ICANS)	5 (3.0)	0
Diarrhea	56 (33.9)	6 (3.6)
Nausea	45 (27.3)	1 (0.6)
Injection site erythema	43 (26.1)	0

Moreau P, et al. *N Engl J Med*. 2022;387(6):495-505. van de Donk NWCJ, et al. ASCO 2023; Abstract 8011. Garfall AL, et al. ASCO 2024; Abstract 7540.

MagnetisMM-3

Phase 1/2 study in R/R MM[1-3]

- Arm A: BCMA naïve
- 96.7% triple-class refractory, 42.3% penta-drug refractory

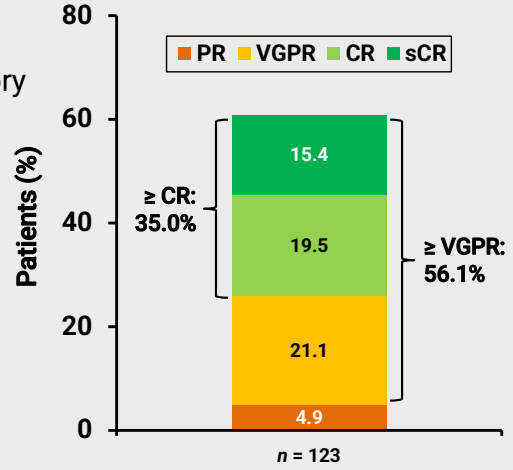
ORR 61.0%

- CR or better: 35.0%

Additional response data[3]

- Median time to first response: 1.2 months
- DOR at 24 months: 66.9%
- Median PFS: 17.2 months
- Median OS: 24.6 months
- 28/31 (90%) MRD-evaluable patients were MRD-negative (10^{-5})

ORR: 61.0% (95% CI: 51.8–69.6)[1]



1. Lesokhin AM, et al. *Nat Med*. 2023;29(9):2259-2267. 2. Tomasson M, et al. *Blood*. 2023;142(suppl 1):3385. 3. Mohty M, et al. EHA 2024; Abstract P932.

MagnetisMM-3: Safety Data

AE, n (%)	Any grade (N = 123)	Grade 3/4 (N = 123)
Neutropenia	61 (49.6)	61 (49.6)
Anemia	60 (48.8)	46 (37.4)
Thrombocytopenia	39 (31.7)	29 (23.6)
Infections	86 (69.9)	50 (40.7)
CRS	71 (57.7)	0
ICANS	6 (4.9)	0
Diarrhea	55 (44.7)	4 (3.3)
Nausea	33 (26.8)	0
Injection site erythema	33 (26.8)	0

Lesokhin AM, et al. *Nat Med*. 2023;29(9):2259-2267. Tomasson M, et al. *Blood*. 2023;142(suppl 1):3385. Mohty M, et al. EHA 2024; Abstract P932.

MonumenTAL-1: Study Design (talquetamab-tgvs)

- Multicenter, open-label phase 1/2 trial

Adults with measurable MM

Phase 1: Progression on or intolerance to all established therapies; ECOG PS 0-1

Phase 2: ≥3 prior lines of therapy that included a PI, an IMiD, and an anti-CD38 antibody; ECOG PS 0–2

→ **Talquetamab** 0.4 mg/kg SC QW* (n = 143)

→ **Talquetamab** 0.8 mg/kg SC Q2W* (n = 145)

→ Prior T-cell redirection group: **Talquetamab** Either 0.4 mg/kg SC QW or 0.8 mg/kg SC Q2W (n = 51)

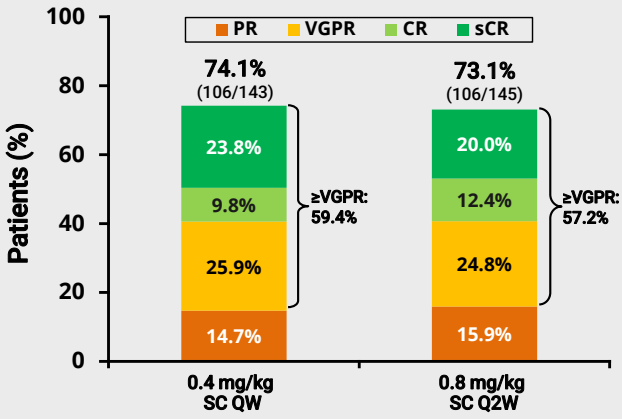
*Previous anti-BCMA therapy allowed; T-cell redirection therapy naive.

- **Primary endpoint (phase 2):** ORR
- **Secondary endpoints (phase 2):** DoR, ≥ VGPR rate, ≥ CR, sCR rate, TTR, PFS, OS, MRD, safety

ECOG PS = Eastern Cooperative Oncology Group performance status; SC = subcutaneous; Q2W = every 2 weeks; QW = every week; TTR = time to response.

Chari A, et al. ASH 2022; Abstract 157. NCT03399799 (https://clinicaltrials.gov/study/NCT03399799). NCT04634552 (https://www.jnjmedicalconnect.com/products/talvey/medical-content/talvey-monumental1-mmy1001-study). URLs accessed 4/30/2025.

MonumenTAL-1: ORR



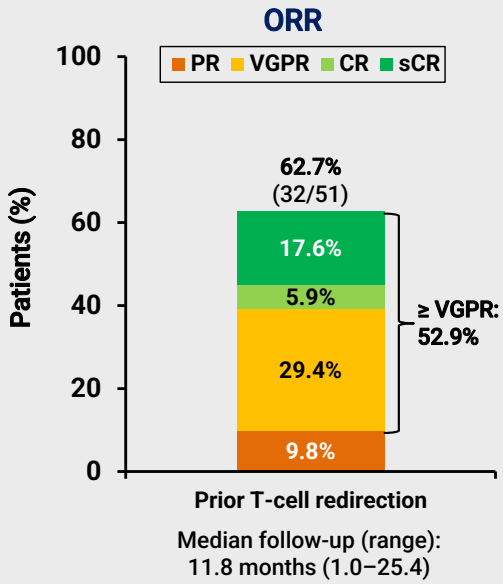
ORR was similar for both dosing schedules

- Triple-class refractory: 72.6% (63.1-80.9) QW and 71.0% (61.1–79.6) Q2W
- Penta-drug refractory: 71.4% (55.4–84.3) QW and 70.6% (52.5–84.9) Q2W

Chari A, et al. ASH 2022; Abstract 157.

MonumenTAL-1: ORR in Patients With Prior T-Cell Redirection

Characteristic	Patients (n = 51)
Median prior lines of therapy, n (range)	6 (3–15)
Exposure status, n (%) ▪ CAR T-cell ▪ Bispecific antibody	36 (70.6)* 18 (35.3)*
Refractory status, n (%) ▪ Belantamab	4 (7.8)
Median DOR, months (range)	12.7 (3.7–NE)
ORR by prior therapy, % (95% CI) **▪ CAR T-cell** **▪ Bispecific antibody**	**72.2 (54.8–85.8)** **44.4 (21.5–69.2)**



Median follow-up (range): 11.8 months (1.0–25.4)

CI = confidence interval; DOR = duration of response; NE = not estimable.

Chari A, et al. ASH 2022; Abstract 157.

MonumenTAL-1: Adverse Events (AEs)

AEs (≥20% of any RP2D cohort), n (%)	0.4 mg/kg SC QW (n = 143)		0.8 mg/kg SC Q2W (n = 145)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
CRS	**113 (79.0)**	**3 (2.1)**	**105 (72.4)**	**1 (0.7)**
Skin-related AEs	**80 (55.9)**	**0**	**98 (67.6)**	**1 (0.7)**
Nail-related AEs	74 (51.7)	0	63 (43.4)	0
Distorted sense of taste (dysgeusia)	**69 (48.3)**	**NA**	**67 (46.2)**	**NA**
Rash-related AEs	56 (39.2)	2 (1.4)	39 (26.9)	8 (5.5)
Decreased weight	57 (39.9)	3 (2.1)	47 (32.4)	2 (1.4)

AEs, %	0.4 mg/kg SC QW (n = 143)		0.8 mg/kg SC Q2W (n = 145)	
	Any grade	Grade 3/4	Any grade	Grade 3/4
Infections	57.3	16.8	50.3	11.7
Opportunistic infections	3.5	--	2.8	--
COVID-19	9.1	0.7	11.0	2.1
Received IVIG	13.3	--	9.7	--

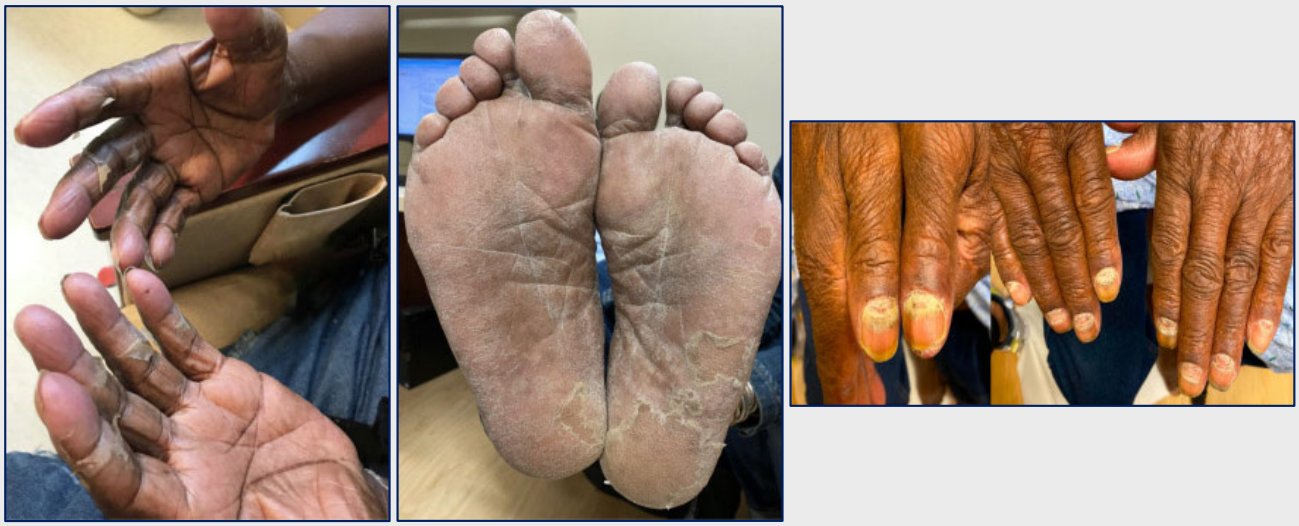
- Majority of high-grade hematologic AEs were cytopenias, which resolved with later cycles
- No patients died due to drug-related AEs at time of data cutoff

Event, %	0.4 mg/kg SC QW (n = 143)	0.8 mg/kg SC Q2W (n = 145)
Discontinuation due to AEs	4.9	6.2
Dose delays due to AEs	8.4	13.8
Dose reductions due to AEs	14.7	6.2

AE = adverse event; COVID-19 = coronavirus disease 2019; IVIG = intravenous immunoglobulin; RP2D = recommend phase 2 dose.

Chari A, et al. ASH 2022; Abstract 157.

MonumenTAL-1: Adverse Events Skin Toxicity



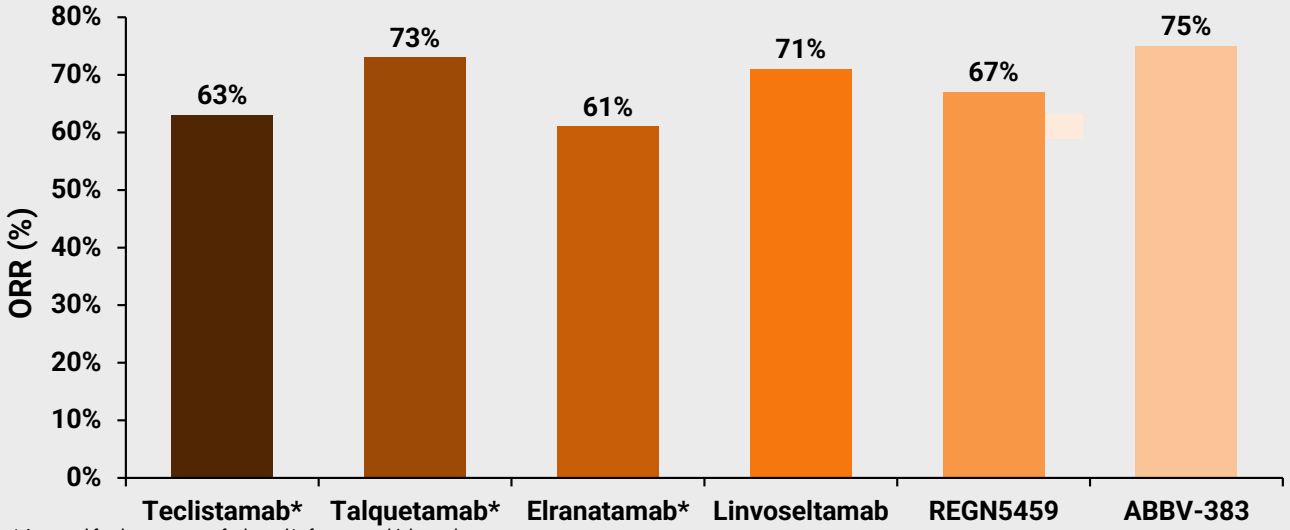
Overview of Safety Data

	Talquetamab	Teclistamab	Elranatamab
CRS	76% (grade 1: 57%, grade 2: 17%, grade 3: 1.5%)	72% (grade 1: 50%, grade 2; 21%, grade 3: 0.6%)	58% (grade 1: 44%, grade 2: 14%, grade 3: 0.5%)
Neurologic toxicity, including ICANS	55% (grade 3/4: 6%)	57% (grade 3/4: 2.4%)	59% (grade 3/4: 7%)
Hematologic toxicities	Grade 3/4 neutropenia (35%) Grade 3/4 thrombocytopenia (22%)	Grade 3/4 neutropenia (56%)	Grade 3/4 neutropenia (51%)
TEAEs of special interest	Skin toxicity (62% overall, 0.3% grade 3) Hepatotoxicity (eg, ALT elevations in 33%)	Infections (grade 3/4: 35%, grade 5: 4.2%) Hepatotoxicity (eg, ALT elevations in 34%)	Infections (grade 3/4: 31%, grade 5: 7%) Hepatotoxicity (eg, ALT elevations in 36%)

ALT = alanine transaminase; TEAE = treatment-emergent adverse event.

Talquetamab PI 2023 (https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=9001355e-003d-4d4e-b4ce-337e0fd14952). Teclistamab PI 2023 (https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid= 54e0f974-ccee-44ea-9254-40e9883cee1e). Elranatamab PI 2023 (https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=aa044060-5b4b-4692-bf0f-9a50e140b10e). URLs accessed 4/30/2025.

Efficacy Across Approved* Bispecific Antibodies and BCMA-Directed Bispecific Antibodies in Development

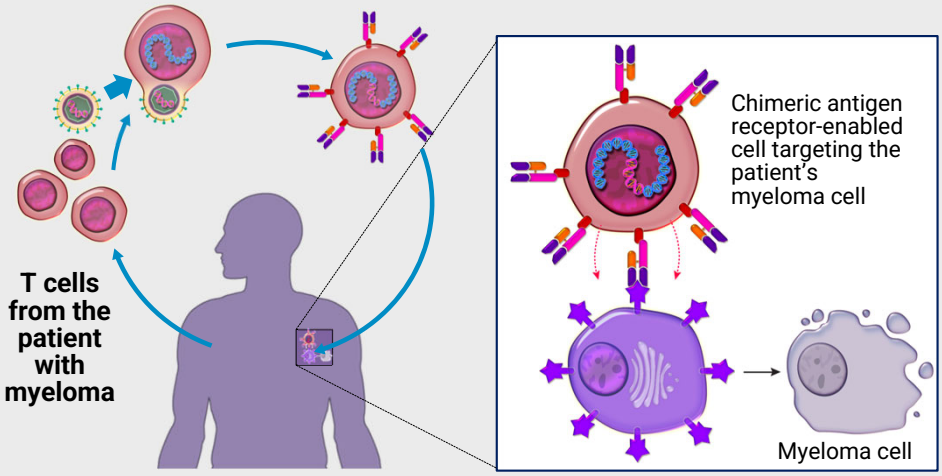


* Approved for the treatment of relapsed/refractory multiple myeloma.

Moreau P, et al. *N Engl J Med*. 2022;387:495-505 and supplement. Searle E, et al. *Blood*. 2022;140(suppl 1):394-396. Chari A, et al. *Blood*. 2022;140(suppl 1):384-387. Lesokhin AM, et al. *Nat Med*. 2023;29(9):2259-2267. Richter J, et al. IMS 2023; Abstract P-044 (https://imsannual2023.eventscribe.net/fsPopup.asp?efp=T0dKRktCQkMxMzg1OA&PosterID=604868&md=0.27828&mode=posterinfo). Suvannasankha A, et al. American Association for Cancer Research (AACR) 2023 (https://www.abstractsonline.com/pp8/#!/10828/presentation/10253). Wong SW, et al. *Hemasphere*. 2023;7(suppl): e1220745. Voorhees PM, et al. *Blood*. 2022;140(suppl 1):4401-4404. URLs accessed 4/30/2025.

The First T-Cell Engagers: Chimeric Antigen Receptor T-Cell (CAR-T)

Lentivirus containing instructions in its DNA to create chimeric receptor for a particular target (eg, BCMA, GPRC5D, etc)



DNA = deoxyribonucleic acid; GPRC5D = G protein-coupled receptor, class C, group 5, member D.

Timmers M, et al. *Front Immunol*. 2019;10:1613

Current BCMA-Targeted Therapies: Idecabtagene Ciloleucel (ide-cel) (KarMMa Trial)

Overview

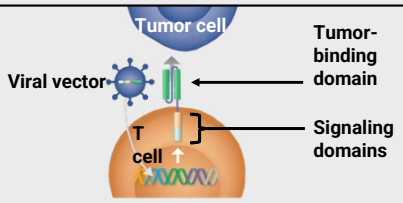
- At 450 x 106 CAR-T, ORR 81% with CRR (CR + sCR) of 39%
- Median peak CAR+ T cell expansion at 11 days
- 59% detectable vector at 6 months, 36% at 12 months
- Median DOR = 11.3 months at 450 x 106
- Median PFS if achieve CR/sCR (20.2 months)

Side effects

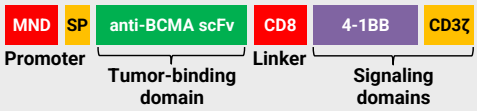
- 91% grades 1 and 2 CRS; 6% grade 3
- 20% neurotoxicities (6% grade 3+), all in patients with CRS
- Delayed recovery (>1 month) of grade ≥3 neutropenia in 41% of patients and thrombocytopenia in 48%
- Infections were common (69%) including aspergillus pneumonia and CMV pneumonia

CD = cluster of differentiation; CMV = cytomegalovirus; CR = complete response; CRS = cytokine release syndrome; DOR = duration of response; ORR = objective/overall response rate; PFS = progression-free survival; scFv = single-chain variable fragment; sCR = stringent complete response.

Munshi NK, et al. *N Engl J Med*. 2021;384:705-716. Anderson LD Jr. *Future Oncol*. 2022;18(3):277-289.



Ide-cel CAR design

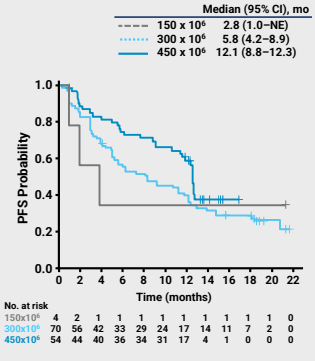


Ide-cel CAR-T cell design

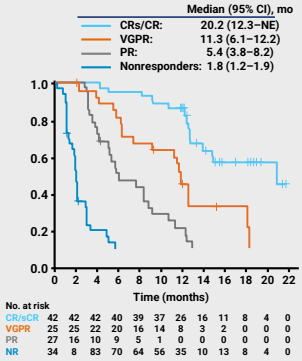
- Autologous T cells transduced with lentiviral vector encoding CAR specific for human BCMA
- Targeting domain: Anti-BCMA
- Costimulatory domain: 4-1BB
- T-cell activation domain: CD3ζ

KarMMa: PFS and MRD-Negativity

PFS by Target Dose



PFS by best response

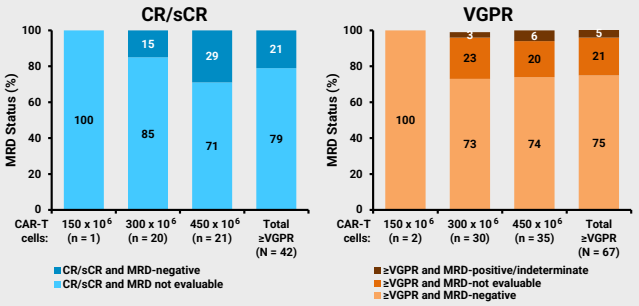


- PFS increased with higher target dose
- Median PFS was 12 months at 450 x 10⁶ CAR+ T cells

- PFS increased by depth of response
- Median PFS was 20 months in patients with CR/sCR

Median OS 24.8 months (95% CI: 19.9–31.2) among all treated patients

MRD-negativity by target dose



Target dose, CAR+ T cells	150 x 10⁶	300 x 10⁶	450 x 10⁶	Total
All ide-cel treated	N=4	N=70	N=54	N=128
MRD-negative and >CR, n (%) [95% CI]	1 (25) [0.6-80.6]	17 (24) [14.8-36.0]	15 (28) [16.5-41.6]	33 (26) [18.5-34.3]
MRD-negative and >VGPR, n (%) [95% CI]	2 (50) [6.8-93.2]	22 (31) [20.9-43.6]	26 (48) [34.4-62.2]	50 (39) [30.6-48.1]

NR = nonresponders.

Munshi NK, et al. *N Engl J Med*. 2021;384:705-716.

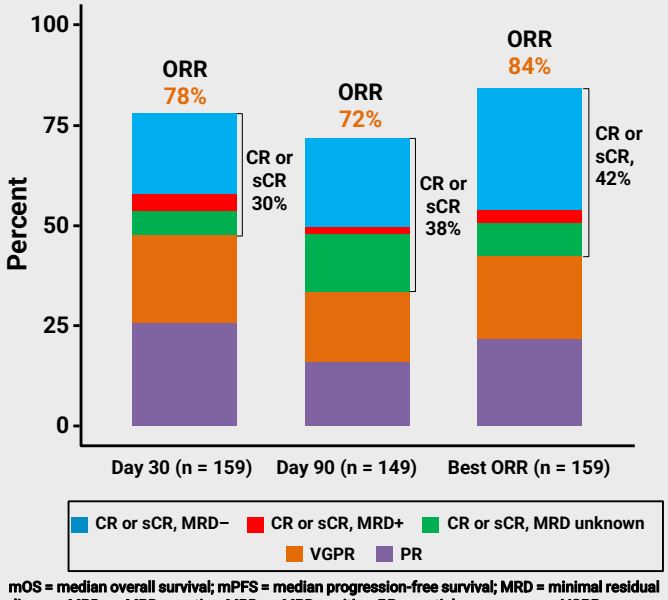
Ide-Cel: Real-World Efficacy Data

- Autologous anti-BCMA CAR-T therapy with idecabtagene ciloleucel is approved for R/R MM on the basis of phase 2 pivotal KarMMa trial, in which ORR was 73% and CR rate was 33%
- In retrospective study of patients with R/R MM, safety and efficacy were comparable with results of KarMMa trial despite 75% of patients not meeting trial eligibility criteria due to comorbidities at time of leukapheresis
  - 196 patients underwent leukapheresis, of whom 159 (81%) received idecabtagene ciloleucel
  - Manufacturing failure rate = 6%
- Key efficacy outcomes
  - Best ORR = 84%
  - CR = 42%
  - Median PFS = 8.5 months (95% CI, 6.5–NR)
  - Median OS =12.5 months (95% CI, 11.3–NR)

CI = confidence interval; NR = not reached; OS = overall survival; R/R = relapsed/refractory.

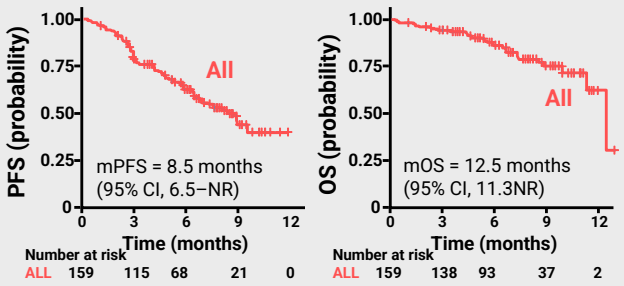
Hansen DK, et al. *J Clin Oncol*. 2023;JCO2201365.

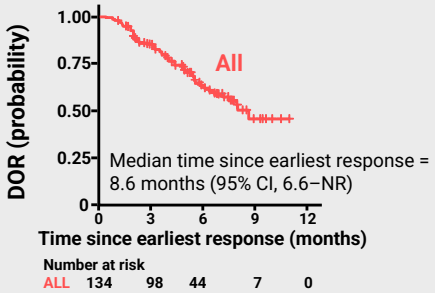
Ide-Cel: Real-World Efficacy Outcomes



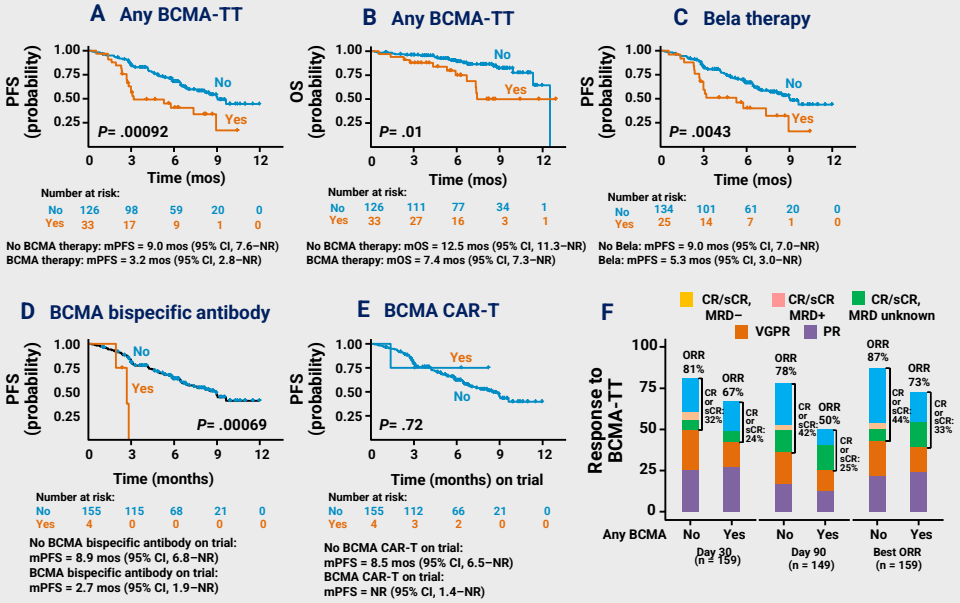
mOS = median overall survival; mPFS = median progression-free survival; MRD = minimal residual disease; MRD− = MRD negative; MRD+ = MRD positive; PR = partial response; VGPR = very good partial response.

Hansen DK, et al. *J Clin Oncol*. 2023;JCO2201365.





Ide-Cel: Responses in Patients Treated With Prior Anti-BCMA Therapy



- Use of any prior anti-BCMA therapy was associated with significantly lower rate of PFS (A) and OS (B)
- These differences varied by type of prior anti-BCMA therapy used, including prior Bela (C), prior anti-BCMA-bispecific antibody (D), or prior CAR-T therapy (E)
- ORRs also varied by prior use of BCMA therapy (F)

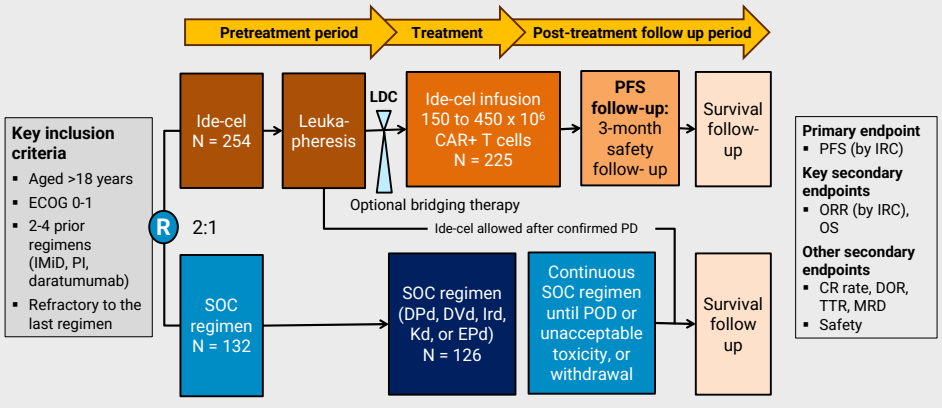
TT = targeted therapy.

Hansen DK, et al. *J Clin Oncol*. 2023;JCO2201365.

KarMMa-3: Ide-Cel vs Standard of Care (SOC) After 2 to 4 Lines

Phase 3 KarMMa-3 study compared ide-cel vs SOC in patients with R/R MM after 2 to 4 prior lines

Trial design



Stratification factors

- Age (<65 years vs >65 years)
- Number of prior regimens (2 vs 3 or 4)
- High-risk cytogenetics (t(4;14), t(14;16), or del17p: yes vs absent/unknown)
- Data cutoff: 4/2022
- Median duration of follow-up: 18.6 (0.4–35.4) months

Baseline characteristics

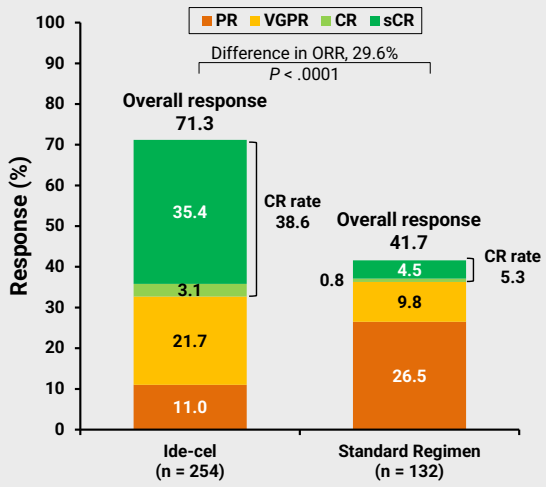
Median age	63 years
Median time since diagnosis	4.1 years
Median prior therapies	N = 3
Triple-class refractoriness	66%
Daratumumab refractoriness	95%
High-risk cytogenetics	44%

Rodriguez-Otero P, et al. *N Engl J Med*. 2023;388:1002-1014.

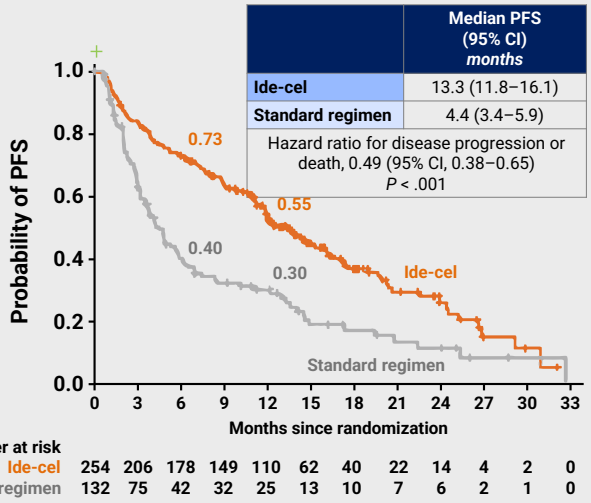
KarMMa-3: Response and PFS

Phase 3 KarMMa-3 study compared ide-cel vs SOC in patients with R/R MM after 2 to 4 prior lines

Response



Progression-free survival



Rodriguez-Otero P, et al. *N Engl J Med.* 2023;388:1002-1014.

Current BCMA-Targeted Therapies: Ciltacabtagene Autoleucel (cilta-cel)

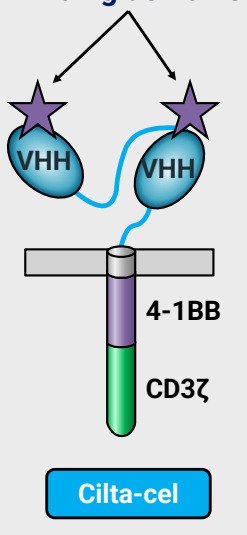
Overview

- 2 BCMA-targeting antibodies
- Most patients had undetectable CAR+ T cells at 6 months
- 12-month PFS 76%

Side effects

- 94% grade 1 and 2 CRS but time to onset in median of 7 days
- 20% neurotoxicities (10% grade 3+), all in patients with CRS
  - ICANS: 16% (time to onset 8 days)
  - Other neurotoxicities (time to onset 27 days)
- Delayed recovery (>1 month) of grade ≥3 neutropenia in 10% of patients and thrombocytopenia in 26%
- Infections were common (58%)

Binding domains



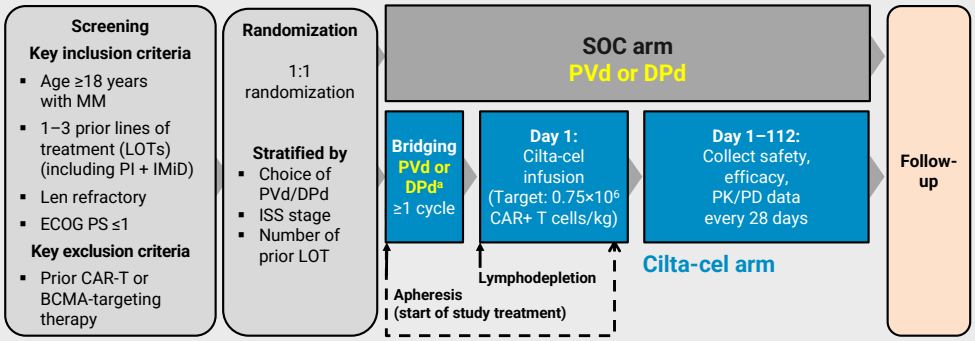
ICANS = immune effector cell-associated neurotoxicity syndrome.

Ciltacabtagene autoleucel (Carvykti™) PI 2024 (www.janssenlabels.com/package-insert/product-monograph/prescribing-information/CARVYKTI-pi.pdf). Accessed 4/30/2025. Berdeja JG, et al. *Lancet.* 2021;398:314-324. Martin T, et al. *J Clin Oncol.* 2023;41:1265-1274.

CARTITUDE-4: Cilta-Cel vs DPd/PVd After 1 to 3 Lines

Phase 3 CARTITUDE-4 compared cilta-cel vs SOC in patients with R/R MM after 1 to 3 prior lines

Trial design



Baseline characteristics

Median age	61.5 years
Median time since diagnosis	3 years
Median prior therapies	N = 2
Triple-class refractoriness	14.4%
Daratumumab refractoriness	23.1%
High-risk cytogenetics	59.4%

Primary endpoint

- PFS

Secondary endpoints

- Efficacy: ≥ CR, ORR, MRD negativity, OS
- Safety
- Patient-reported outcomes (PROs)

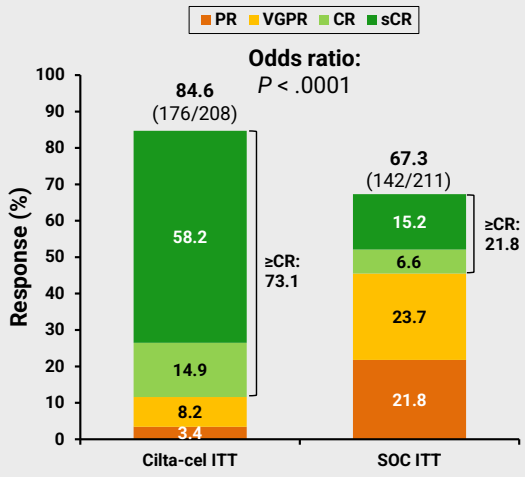
PK/PD = pharmacokinetic/pharmacodynamic.

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

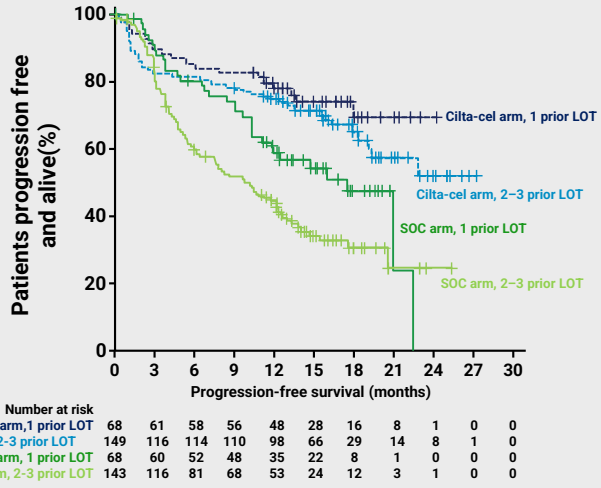
CARTITUDE-4: Response and PFS

Phase 3 CARTITUDE-4 compared cilta-cel vs SOC in patients with R/R MM after 1 to 3 prior lines

ORR



PFS by treatment and number of prior lines



Number at risk

Cilta-cel arm,1 prior LOT	68	61	58	56	48	28	16	8	1	0	0
Cilta-cel, 2-3 prior LOT	149	116	114	110	98	66	29	14	8	1	0
SOC arm, 1 prior LOT	68	60	52	48	35	22	8	1	0	0	0
SOC arm, 2-3 prior LOT	143	116	81	68	53	24	12	3	1	0	0

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

KarMMa-3/CARTITUDE-4: CRS and Neurotoxicity (NT)

KarmMMa-3

	Ide-cel (n = 225)
CRS, n (%) Any grade Grade 3/4 Grade 5	197 (88) 9 (4) 2 (1)
Median (range) time to first onset, days	1.0 (1.0–14.0)
Median (range) duration, days	3.5 (1.0–51.0)
Investigator-identified NT, n (%) Any grade Grade 3/4 Grade 5	34 (15) 7 (3) 0
Median (range) time to first onset, days	3.0 (1.0–317.0)
Median (range) duration, days	2.0 (1.0–37.0)

CARTITUDE-4

	As-treated patients (n = 176)				
AEs, n (%)	Any grade	Grade 3/4	Median time to onset, days	Median duration, days	Resolved n
CRS	134 (76.1)	2 (1.1)	8	3	134
Neurotoxicity	36 (20.5)	5 (2.8)			
ICANS	8 (4.5)	0	10	2	9
Other	30 (17.0)	4 (2.3)			
Cranial nerve palsy	16 (9.1)	2 (1.1)	21	77	14
Peripheral neuropathy	5 (2.8)	1 (0.6)	63	201	3
Movement NT	1 (0.6)	0	85	—	0

Rodriguez-Otero P, et al. *N Engl J Med.* 2023;388:1002-1014. San-Miguel J, et al. *N Engl J Med.* 2023;389:335-347.

Black Box Warnings for CAR-T

Secondary cancer	Experimental arm	Control arm
Cilta-cel (CARTITUDE-1)	10/97 MDS and AML	
Ide-cel (KarMMa-2)	1/128 MDS	
Cilta-cel (CARTITUDE-4)	5/208 MDS, AML, PTCL	**0**/208
Ide-cel (KarMMa-3)	3/225 MDS, AML	**0**/126

- As of 12/31/2023, FDA now aware of 22 cases of T-cell cancers after treatment with 5 of 6 available CAR-T products
- In 3/22 cases for which genetic sequencing has been performed to date, the CAR transgene has been detected in the malignant clone, which indicates that the CAR-T product was most likely involved in the development of the T-cell cancer

Verdun N, Marks P. *N Engl J Med.* 2024;390(7):584-586.

Case Study 1

- CCH is a 74-year-old with kappa light chain myeloma who initially presented with sepsis after a diabetic foot ulcer led to pseudomonas bacteremia; while inpatient imaging revealed lytic lesions extensively, serum protein electrophoresis was negative, and serum free light chains showed kappa light chains 810 mg/L with lambda light chains 5 mg/L
- Fluorescent in-situ hybridization (FISH) studies on the diagnostic bone marrow biopsy revealed hyperdiploid disease
- He was discharged to a subacute rehab facility but the family petitioned for him to be discharged home early so that he could show up to your oncology clinic

Case Study 1

The best induction therapy, balancing the progression-free survival with toxicity, would be

a) The patient is a candidate for autologous transplant; induction should include 2 inpatient cycles of bortezomib, dexamethasone, thalidomide with infusion of cisplatin, doxorubicin, cyclophosphamide, and etoposide (PACE) chemotherapy, cyclophosphamide stem cell mobilization, then autologous transplant

b) The patient is unlikely a candidate for autologous transplant; induction should begin with daratumumab, lenalidomide (dose adjusted based on estimated glomerular filtration rate [eGFR]), and low dose dexamethasone for 4 cycles, dexamethasone should be discontinued, and the patient should be continued on the daratumumab and lenalidomide until progression

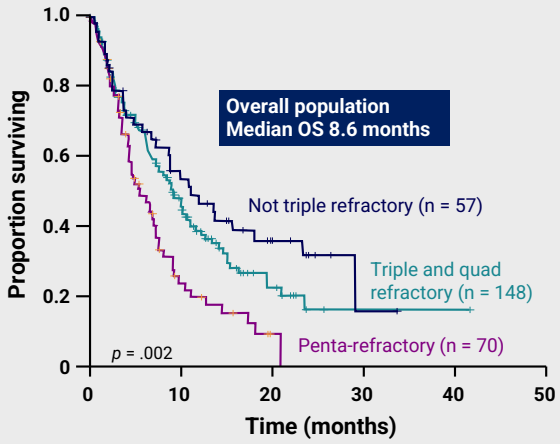
c) The patient is not a candidate for autologous transplant; induction should begin with daratumumab, lenalidomide 25 mg Days 1 to 14, bortezomib twice weekly, and dexamethasone 20 mg on Days 1, 4, 8, and 11 for 8 cycles followed by daratumumab, lenalidomide 25 mg on Days 1 to 21, and dexamethasone 40 mg weekly until progression

Personalized Treatment Plans

MAMMOTH Study: Suboptimal Outcomes in Disease Refractory to ANTI-CD38 Monoclonal Antibodies

275 patients refractory to anti-CD38 monoclonal antibodies (daratumumab, isatuximab)

	Median OS months	
Not triple refractory	11.2	Refractory to 1 CD38 mAb, and not both PI and IMiD
Triple and quad refractory	9.2	Refractory to 1 CD38 mAb + 1 PI + 1 or 2 IMiD compounds, etc.
Penta refractory	5.6	Refractory to 1 CD38 mAb + 2 PIs + 2 IMiD compounds
Overall cohort	8.6	



249 patients received further treatment

- ORR 31%
- Median PFS 3.4 months
- Median OS 9.3 months

Patient population for BCMA-targeted therapy has challenging disease to treat.

Gandhi UH, et al. *Leukemia*. 2019;33(9):2266-2275.

Case Study 2

- SL is a 60-year-old patient with immunoglobulin A light chains (IgA-L) multiple myeloma who initially presented with a beta2 microglobulin of 2.9, albumin 4.0, and fluorescent in-situ hybridization studies (FISH) on the diagnostic bone marrow biopsy revealed a gain of 1q [10%], t(4;14) [10%], and deletion of 17p [25%]
- SL received daratumumab, bortezomib, lenalidomide, and dexamethasone followed by autologous transplant and then bortezomib + pomalidomide maintenance until progression; his serum IgA decreased to 20 mg/dL after 1 year of maintenance treatment and now is 2010 mg/dL

Case Study 2

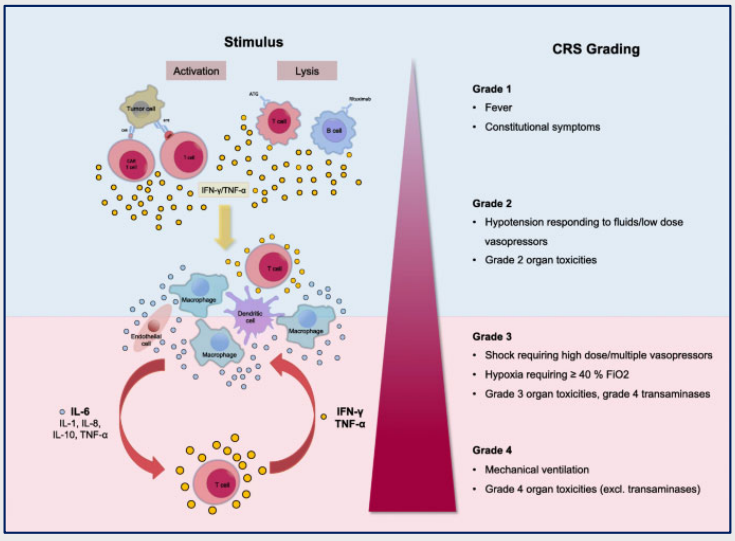
The treatment associated with the highest response rate is

a) Carfilzomib, cyclophosphamide, and dexamethasone
b) Bortezomib, selinexor, and dexamethasone
c) Cilta-cel (Carvykti)
d) Bortezomib + dexamethasone, cyclophosphamide, etoposide, and cisplatin (DCEP) infusional chemotherapy

Monitoring and Toxicity Management

Cytokine Release Syndrome (CRS)

- 44% to 72% depending on product
- Median time to onset: 11 to 48 hours
- Primarily grade 1 to 2
- Risk factors not well defined
- Treatment options
  - Symptom management (eg, antipyretic)
  - Corticosteroids
  - Tocilizumab
  - Severe: Anakinra



Shimabukuro-Vornhagen A, et al. *J Immunother Cancer*. 2018;6(1):56. Markouli M, et al. *Curr Oncol*. 2023;30(7):6330-6352. Rodriguez-Otero P, et al. *Lancet Oncol*. 2024;25:e205-e216.

CRS Grading

Grade	Action	Other
If grade 1 CRS + low risk at home (fever but stable)	Triage to ICC for tocilizumab Advise patient to take home doses of dexamethasone + diphenhdyramine + acetaminophen	
Grade 1 Fever >100.4° F (38° C)	Administer tocilizumab 8 mg/kg IV over 1 hour (maximum 800 mg) in ICC	Observation in ICC for about 8 hours and discharge home if stable If symptoms persist, consider admission
Grade 2 CRS	▪ Give tocilizumab 8 mg/kg IV over 1 hour (maximum 800 mg) every 8 hours as needed max of 3 doses and ▪ Consider dexamethasone 20 mg IV every 12 hours if no improvement. If hypotensive: IV fluid bolus (NS 1 L)	Must be observed inpatient
Grade 3 CRS fever >100.4° F (38° C) plus 1 of the following: Hypotension requiring vasopressors or hypoxia requiring high flow oxygen	Admit to hospital for management	Dexamethasone 10 to 20 mg IV q6hr (max 9) and tocilizumab 8 mg/kg IV every 8 hours (max 3) IF hypotensive: IV fluids/vasopressors ICANS: Initiate Keppra 500 mg BID
Grade 4 CRS fever > 100.4° F (38° C) plus 1 of the following: Hypotension requiring multiple vasopressors or hypoxia requiring positive pressure oxygen	Admit to hospital for management	Dexamethasone 10 to 20 mg IV q6hr (max 9) and tocilizumab 8 mg/kg IV every 8 hours (max 3) If hypotensive: IV fluids/vasopressors ICANS: Initiate Keppra 500 mg BID Refractory: Consider alternative therapies (ie, anakinra)

Emory Windsor Cancer Institute 2024.

VEF0

Neurotoxicity

- Most common included headache, peripheral neuropathy, and immune effector cell-associated neurotoxicity syndrome (ICANS)
- ICANS incidence 2% to 11% depending on product
- Risk factors not well defined
- Treatment options
  - Corticosteroids
  - Tocilizumab (if concurrent CRS)
  - Antiseizure prophylaxis
  - Anakinra

Markoull M, et al. *Curr Oncol.* 2023;30(7):6330-6352. Rodriguez-Otero P, et al. *Lancet Oncol.* 2024;25:e205-e216.

Immune Effector Cell-Associated Encephalopathy (ICE) Score

Topic	Tasks	Score
Orientation	Orientation to year, month, city, hospital	4 points
Naming	Name 3 objects	3 points
Following commands	Follow simple commands (eg, Show me 2 fingers or close your eyes and stick out your tongue)	1 point
Writing	Ability to write a standard sentence	1 point
Attention	Count backwards from 100 by 10	1 point

Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;35(4):625-638.

ICANS Grading

Neurotoxicity domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE score*	7–9	3–6	0–2	0 (patient is unarousable)
Depressed level of consciousness†	Awakens spontaneously	Awakens to voice	Awakens only to tactile stimulus	Patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse; stupor or coma
Seizure	N/A	N/A	Any clinical seizure focal or generalized that resolves rapidly or non-convulsive seizures on EEG that resolve with intervention	Life-threatening prolonged seizure (>5 min), repetitive clinical or electrical seizures without return to baseline in between
Motor findings‡	N/A	N/A	N/A	Deep focal motor weakness such as hemiparesis or paraparesis
Elevated ICP/ cerebral edema	N/A	N/A	Focal/local edema on neuroimaging§	Diffuse cerebral edema on neuroimaging, decerebrate or decorticate posturing, cranial nerve VI palsy, papilledema, or Cushing's triad

ICANS grade is determined by the most severe event not attributable to any other cause.
*A patient with an ICE score of 0 may be classified as grade 3 ICANS if awake with global aphasia, but a patient with an ICE score of 0 may be classified as grade 4 ICANS if unarousable.
†Attributable to no other cause (eg, no sedating medication).
‡Tremors and myoclonus associated with immune effector cell therapies may be graded according to CTCAE V.5.0, but they do not influence ICANS grading.
§Intracranial hemorrhage with or without associated edema is not considered a neurotoxicity feature and is excluded from ICANS grading. It may be graded according to CTCAE V5.0.
ASTCT = American Society for Transplantation and Cellular Therapy; CTCAE = Common Terminology Criteria for Adverse Events; EEG = electroencephalogram; ICANS = immune effector cell-associated neurotoxicity syndrome; ICE = effector cell-associated encephalopathy; ICP = intracranial pressure; N/A = not applicable.

Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;35(4):625-638.

Management of Cytopenias

- Often seen early in therapy and resolve with continued treatment
- Neutropenia
  - Filgrastim as needed
  - Consider holding therapy for absolute neutrophil count (ANC) <500/mL
  - Levofloxacin and fluconazole for ANC <500/mL
- Thrombocytopenia
  - Consider addition of thrombopoietin receptor agonist for grade >4
  - Consider holding therapy until platelets >50,000
- Anemia
  - Consider transfusions and erythropoetin-stimulating agents as needed
- Consider extended dosing intervals when resuming

Rodriguez-Otero P, et al. *Lancet Oncol*. 2024;25:e205-e216.

Consensus Recommendations for Monitoring, Prophylaxis, and Treatment of Infections

Viral

- Valacyclovir or acyclovir prophylaxis
- Screen for HBV prior to treatment initiation
- Consider CMV and EBV monitoring
- Vaccination as appropriate

***Pneumocystis jirovecii* pneumonia**

- Recommend prophylaxis for all patients

Bacterial

- Consider fluoroquinolone prophylaxis at treatment initiation and when ANC <500/mm^3
- Vaccination as appropriate

Fungal

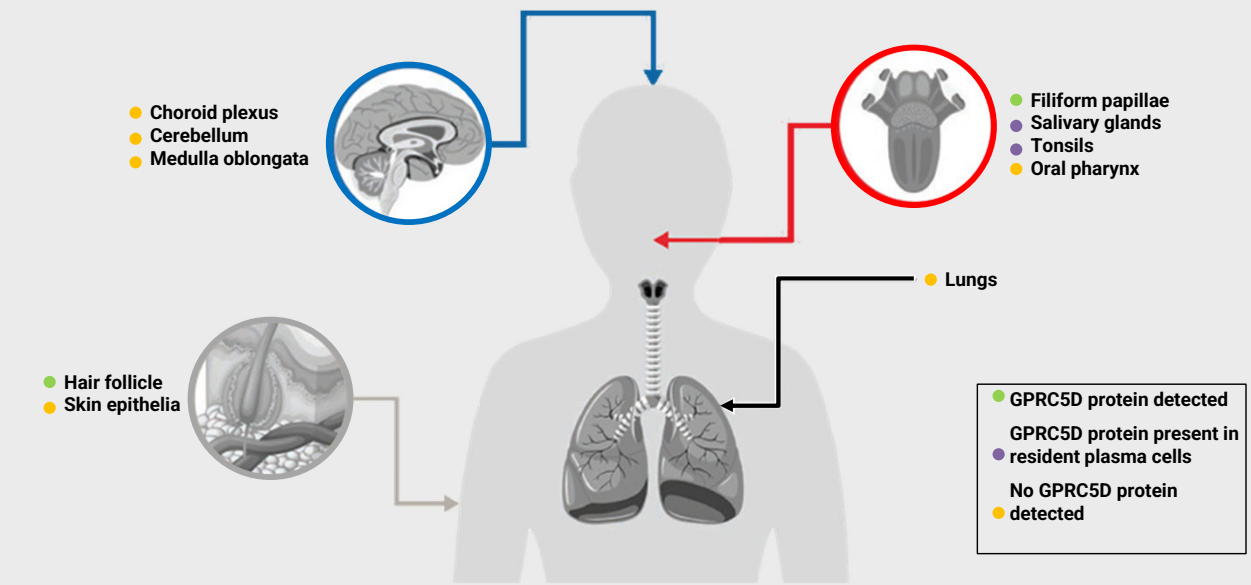
- Consider prophylaxis for ANC <500/mm^3

Other supportive care

- IVIG for IgG <400 mg/dL or patients with history of recurrent infections
- G-CSF as needed for ANC < 500/mm^3

Raje N, et al. *Blood Cancer J*. 2023;13:116. Rodriguez-Otero P, et al. *Lancet Oncol*. 2024;25:e205-e216.

GPRC5D Associated Toxicity



Chari A, et al. *Clin Lymphoma Myeloma Leuk.* 2024;2024;24(10):665-693.

GPRC5D-Related Toxicity

Oral	Skin	Nail
Prophylaxis		
▪ Oral hygiene and oral hydration ▪ Baking soda and salt-water rinses ▪ Consider saline nasal spray if seasonal allergies ▪ Consider zinc supplementation	▪ Adequate oral hydration ▪ Liberal topical hydration with emollient moisturizers ▪ Consider urea-based cream on hands and feet ▪ Reduce friction to sensitive areas such as hands and feet	Liberal topical moisturizer and adequate oral hydration
Treatment		
▪ Assess for oropharyngeal candidiasis ▪ Encourage fluid intake ▪ Consider budesonide oral slurry swish and swallow ▪ Nutrition consult ▪ Hold therapy, and consider dose modification ▪ Dysgeusia: Explore taste profiles such as sweet, sour, bitter, salty, and umami ▪ Dry mouth: Sugar free lozenges, saliva sprays, dry mouth disc	▪ Ammonium lactate 12% cream BID ▪ Topical steroids (ie, triamcinolone 0.1% twice a day) ▪ Oral steroids for diffuse rashes ▪ Antihistamines for diffuse itching ▪ Consider dermatology consult ▪ Hold therapy, and consider dose modification	▪ Topical moisturizers, nail soaks ▪ Topical steroids ▪ Vitamin E oil ▪ Assess for fungal infection – Avoid nail hardeners, acrylics, and gels—increased risk of fungal infection ▪ Consider dose modification

Chari A, et al. *Clin Lymphoma Myeloma Leuk.* 2024;24(10):665-693. Schinke C, et al. *Curr Med Res Opin.* 2024;40(10):1705-1711.

Case Study 3

- JK is a 52-year-old patient with multiple myeloma who was induced with RVd followed by autologous transplant then daratumumab + lenalidomide maintenance until progression; then relapse was treated with carfilzomib + pomalidomide + dexamethasone (KPd) and the next relapse with isatuximab + selinexor + dexamethasone
- He was diagnosed with relapsed myeloma with biochemical progression and was started on teclistamab; he received 0.06 mg/kg as a first dose, 0.3 mg/kg as a second dose with prophylactic tocilizumab, and then 1.5 mg/kg
- He tolerated this well until 12 hours after the 1.5 mg/kg dose when he developed an oral temperature of 101°F, heart rate 110 beats per minute, but no other symptoms

Case Study 3

When JK called the oncologic immediate care center for guidance, the best course of action is for him to

a) Immediately come to the emergency room to be evaluated with a CBC/d/p, BMP, respiratory viral swab, and CT chest to look for opportunistic infection

b) Immediately come to the immediate care center for CBC/d/p, CMP, and tocilizumab 8 mg/kg over 1 hour for presumed cytokine release syndrome

c) Take ibuprofen 600 mg, acetaminophen 1000 mg, and call in the next few days with any confusion

d) Immediately come to the immediate care center to be tested with CBC/d/p, CMP, and receive tocilizumab 8 mg/kg over 1 hour and dexamethasone 40 mg for presumed cytokine release syndrome (CRS) with immune effector cell-associated neurotoxicity syndrome (ICANS)

Thank you

Innovations in Multiple Myeloma Care: Personalizing Treatments and Managing Advanced Therapies

Resource	Address
A Study of Talquetamab in Participants With Relapsed or Refractory Multiple Myeloma (MonumenTAL-1). ClinicalTrials.gov identifier: NCT04634552. Last updated April 27, 2025.	https://clinicaltrials.gov/study/NCT04634552
Anderson LD Jr. Idecabtagene vicleucel (ide-cel) CAR T-cell therapy for relapsed and refractory multiple myeloma. *Future Oncol*. 2022;18:277-289.	https://pubmed.ncbi.nlm.nih.gov/34854741/
Barilà G, Rizzi R, Zambello R, Musto P. Drug conjugated and bispecific antibodies for multiple myeloma: Improving immunotherapies off the shelf. *Pharmaceuticals (Basel).* 2021;14:40.	https://www.mdpi.com/1424-8247/14/1/40
Berdeja JG, Madduri D, Usmani SZ, et al. Ciltacabtagene autoleucel, a B-cell maturation antigen-directed chimeric antigen receptor T-cell therapy in patients with relapsed or refractory multiple myeloma (CARTITUDE-1): A phase 1b/2 open-label study. *Lancet.* 2021;398:314-324.	https://pubmed.ncbi.nlm.nih.gov/34175021/
Bonello F, Mina R, Boccadoro M, Gay F. Therapeutic monoclonal antibodies and antibody products: Current practices and development in multiple myeloma. *Cancers (Basel)*. 2020;12:15.	https://www.mdpi.com/2072-6694/12/1/15
Bumma N, Richter J, Brayer J,et al. Updated safety and efficacy of REGN5458, a BCMAxCD3 bispecific antibody, treatment for relapsed/refractory multiple myeloma: A phase 1/2 first-in-human study. *Blood*. 2022;140(suppl 1):10140-10141.	https://ashpublications.org/blood/article/140/Supplement%201/10140/490712/Updated-Safety-and-Efficacy-of-REGN5458-a-BCMAxCD3
Carvykti® (ciltacabtagene autoleucel). Prescribing information. Johnson & Johnson; 2024.	https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/CARVYKTI-pi.pdf
Chari A, Krishnan A, Rasche L, et al. Clinical management of patients with relapsed/refractory multiple myeloma treated with talquetamab. *Clin Lymphoma Myeloma Leuk*. 2024;2024;24:665-693.	https://pubmed.ncbi.nlm.nih.gov/38871558/
Chari A, Touzeau C, Schinke C, et al. Talquetamab in patients with relapsed/refractory multiple myeloma: Phase 1/2 results from MonumenTAL-1. Presented at the 64th ASH Annual Meeting & Exposition. December 10-13, 2022; New Orleans, LA; Abstract 157.	https://www.myeloma.org/videos/talquetamab-patients-relapsedrefractory-multiple-myeloma-phase-12-results-monumental-1
Chari A, Touzeau C, Schinke C, et al. Talquetamab, a G protein-coupled receptor family C group 5 member D x CD3 bispecific antibody, in patients with relapsed/refractory multiple myeloma (RRMM): Phase 1/2 results from MonumenTAL-1. *Blood*. 2022;140(suppl 1):384-387.	https://ashpublications.org/blood/article/140/Supplement%201/384/491033/Talquetamab-a-G-Protein-Coupled-Receptor-Family-C

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