Clinical Pathways Congress + Cancer Care Business Exchange

Using Clinical Pathways to Guide Treatment Selection in Multiple Myeloma

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Disclosures

- **Yuxin Liu, MD** has nothing to disclose in relation to this activity

Learning Objectives

- Summarize recent updates in clinical guidelines and their significance for MM clinical pathways
- Assess novel and emerging therapeutics for MM treatment, with emphasis on mechanisms of action, and safety and efficacy data
- Discuss strategies to align evidence-based best practices and personalized medicine, as well as formulary and cost considerations into MM clinical pathways

MM = multiple myeloma.

Clinical Pathways in Hematology Care

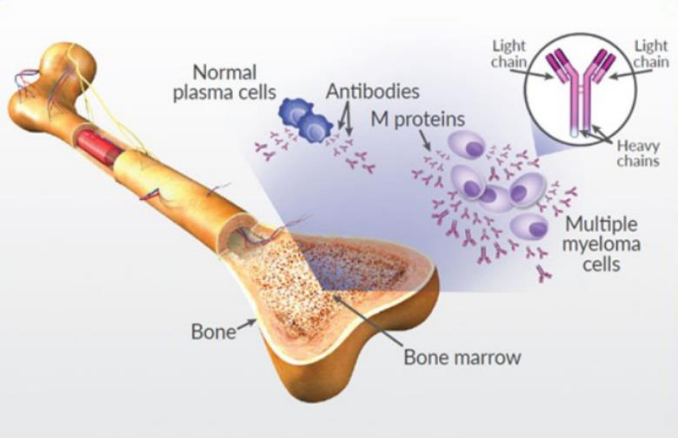
- The rapid rate of advancements in the understanding of disease biology, genomics, and immunology; the growing number of targeted small molecule, immune, and cellular therapies; and the rising number and intricacy of clinical trials—all lead to increased complexity in treatment decision-making

- Clinical pathways can play a role in bridging advances in personalized and genomic-based medicine and evidence-based medicine to assist healthcare providers in bringing optimal care to patients

Overview of Multiple Myeloma

Multiple Myeloma Disease Overview

- Hematologic cancer is characterized by malignant transformation of plasma cells in the bone marrow, leading to abnormal production of a monoclonal protein
- End-organ damage or IMWG myeloma-defining biomarker criteria warrant treatment



C

High levels of calcium in the blood

R

Decreased kidney (renal) function

A

Low amount of red blood cells (anemia)

B

Presence of bone damage

IMWG = International Myeloma Working Group.
Multiple Myeloma Research Foundation. Accessed August 30, 2024. https://themmrf.org/multiple-myeloma/.

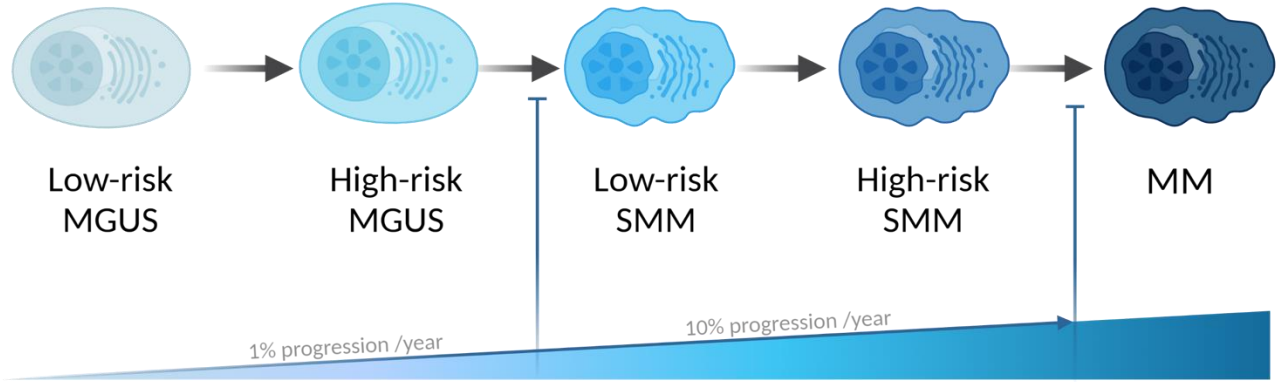
Progression from Precursor to Active Myeloma

Monoclonal gammopathy of undetermined significance (MGUS)

- Presence of monoclonal protein
- Bone marrow with <10% abnormal plasma cells
- Absence of myeloma-defining events

Smoldering multiple myeloma (SMM)

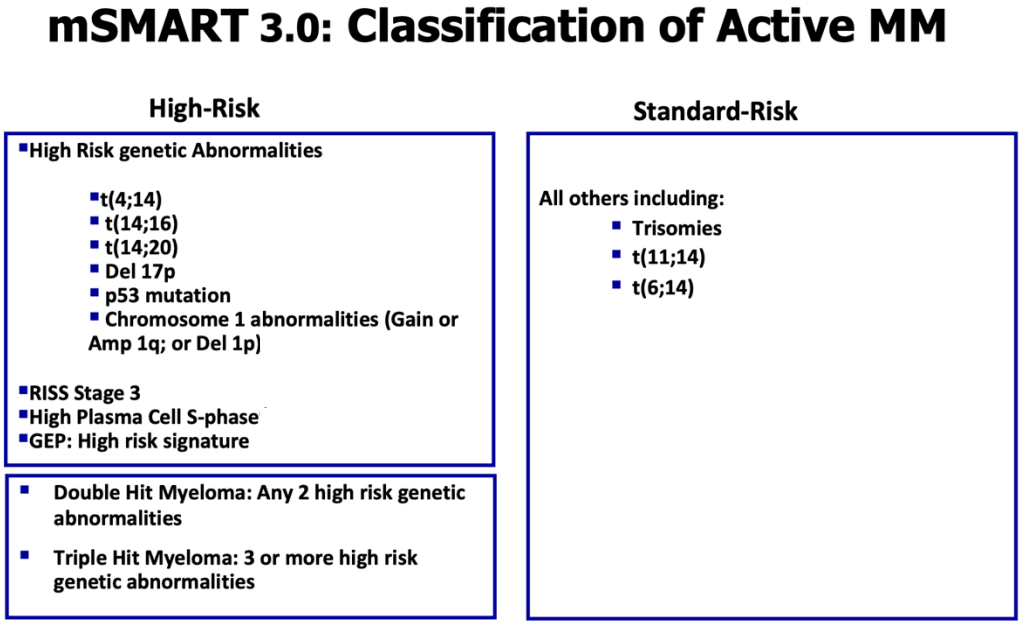
- Presence of monoclonal protein
- Bone marrow with >10% to <60% abnormal plasma cells
- Absence of myeloma-defining events



Rajkumar SV, et al. *Lancet Oncol*. 2014;15(12):e538-e548. Kyle RA, et al. *N Engl J Med*. 2007;356(25):2582-2590.
Figure: Biorender.

Genomic Aberrations in Multiple Myeloma

- Genomic aberrations are a hallmark feature of myeloma and contribute to the tumorigenesis and disease progression
- Cytogenetic abnormalities have been classified (and sometimes re-classified) into a different risk grouping as they hold prognostic significance



mSMART = Mayo Stratification of Myeloma and Risk-Adapted Therapy; RISS = revised International Staging System; GEP = gene expression profile.

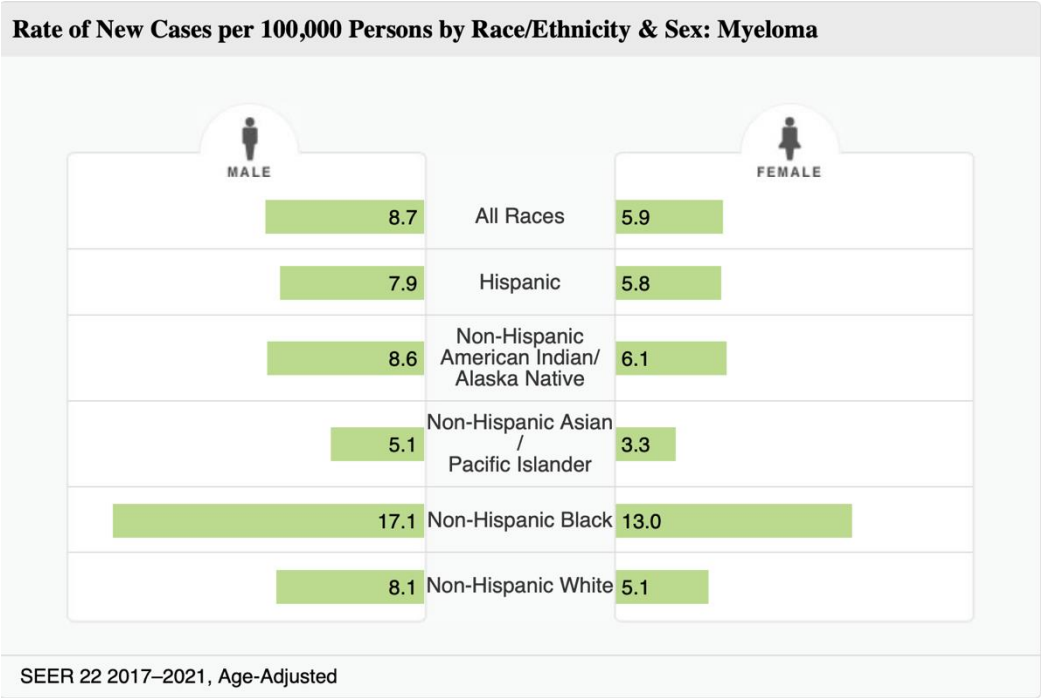
Dispenzieri A, et al. *Mayo Clin Proc*. 2007;82(3):323-341. Kumar SK, et al. *Mayo Clin Proc*. 2009;84(12):1095-1110. Mikhael JR, et al. *Mayo Clin Proc*. 2013;88(4):360-376.

Multiple Myeloma: Epidemiology

- 35,780 new cases/year
- 1.8% of all new cancer diagnoses
- 3rd most common blood cancer
- 179,063 individuals living with diagnosis of multiple myeloma (NIH 2021)
- 12,540 deaths expected/year
- 5-year relative survival rate: 61.1% (2014-2020)

National Cancer Institute. Surveillance, Epidemiology, and End Results Program (SEER). Accessed August 30, 2024. https://seer.cancer.gov/statfacts/html/mulmy.html.

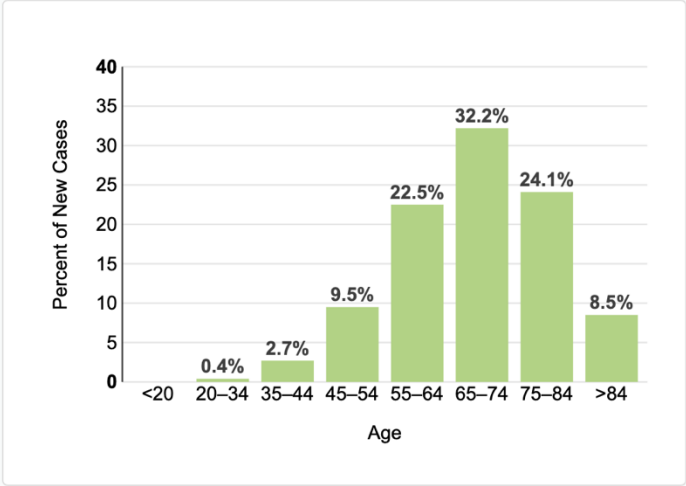
Epidemiology Continued



National Cancer Institute SEER. Accessed August 30, 2024. https://seer.cancer.gov/statfacts/html/mulmy.html.

Epidemiology Continued

Percent of New Cases by Age Group: Myeloma



Myeloma is most frequently diagnosed among people aged 65–74.

Median Age At Diagnosis

69

SEER 22 2017–2021, All Races, Both Sexes

National Cancer Institute SEER. Accessed August 30, 2024. https://seer.cancer.gov/statfacts/html/mulmy.html.

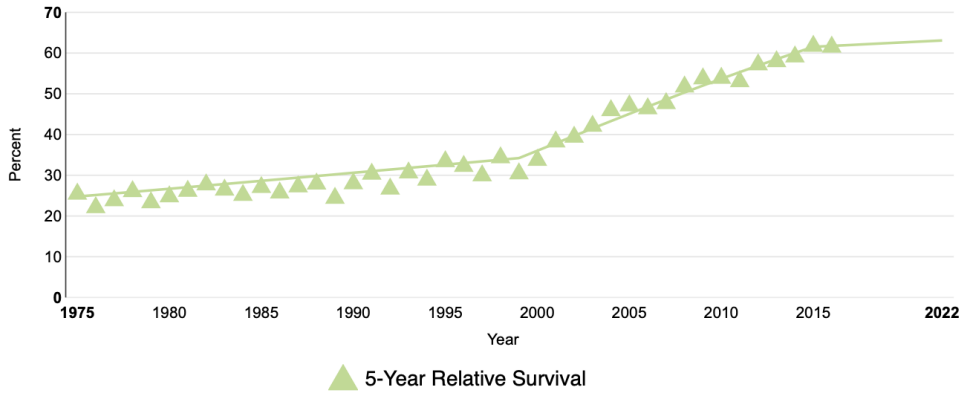
Risk Factors Associated with Multiple Myeloma

- Age: Advanced age
- Sex: Men have slightly higher risk than women
- Race and ethnicity: Black Americans have a 2 times higher chance than White Americans
- Family history: Having a first-degree relative with myeloma increases risk of myeloma by 2-4 times
- History of MGUS or other plasma cell dyscrasia
- Toxic exposures: High doses of radiation, benzene, certain pesticides, and other chemicals
- Obesity and metabolic syndrome

Boyd KD, et al. *Cancer Epidemiol Biomarkers Prev*. 2011;20(8):1703-1707.
Lynch HT, et al. *Blood*. 2009;114(4):749-750. Choa R, et al. *Blood Adv*. 2023;7(18):5510-5523.

Prognosis

- Myeloma is considered a treatable blood cancer but not curable
- 5-year survival rate has improved over time



SEER 8 5-Year Relative Survival Percent from 1975–2016, All Races, Both Sexes.
Modeled trend lines were calculated from the underlying rates using the Joinpoint Survival Model Software.

National Cancer Institute SEER. Accessed August 30, 2024. https://seer.cancer.gov/statfacts/html/mulmy.html.

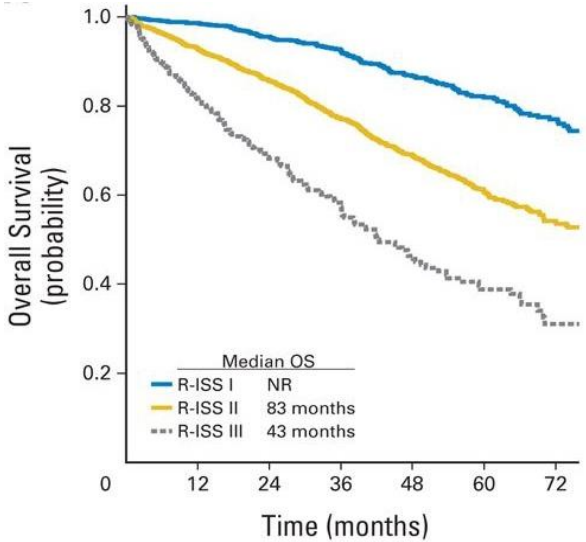
Disease Heterogeneity

- Disease severity and course varies between patients
- We use staging systems and baseline cytogenetics to help us prognosticate

Table 1. Standard Risk Factors for MM and the R-ISS

Prognostic Factor	Criteria
ISS stage	
I	Serum β_2-microglobulin < 3.5 mg/L, serum albumin ≥ 3.5 g/dL
II	Not ISS stage I or III
III	Serum β_2-microglobulin ≥ 5.5 mg/L
CA by iFISH	
High risk	Presence of del(17p) and/or translocation t(4;14) and/or translocation t(14;16)
Standard risk	No high-risk CA
LDH	
Normal	Serum LDH < the upper limit of normal
High	Serum LDH > the upper limit of normal
A new model for risk stratification for MM	
R-ISS stage	
I	ISS stage I and standard-risk CA by iFISH and normal LDH
II	Not R-ISS stage I or III
III	ISS stage III and either high-risk CA by iFISH or high LDH

Abbreviations: CA, chromosomal abnormalities; iFISH, interphase fluorescent in situ hybridization; ISS, International Staging System; LDH, lactate dehydrogenase; MM, multiple myeloma; R-ISS, revised International Staging System.

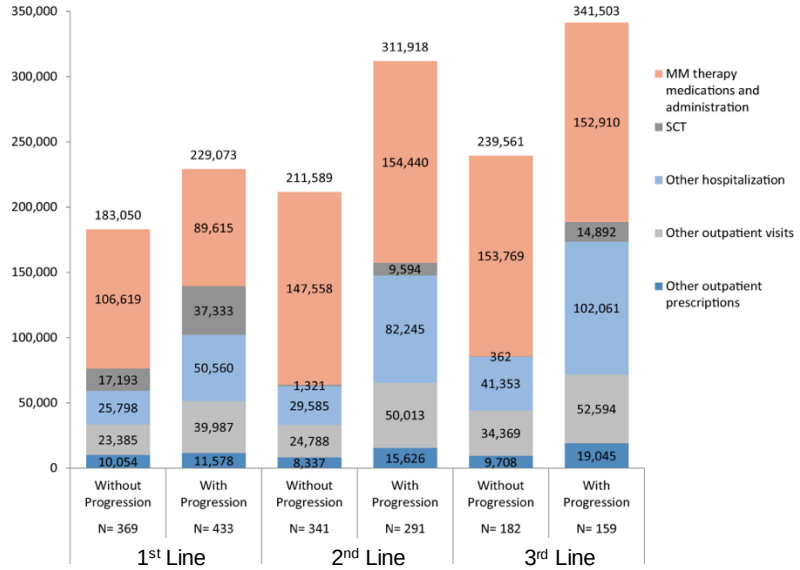


OS = overall survival.

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

Economic Burden of Multiple Myeloma

IPTW adjusted mean annual healthcare costs among transplant-eligible patients with myeloma with or without progression by line of treatment (LOT) 2013–2018



Extrapolated average cumulative healthcare costs incurred by patients with MM who received ≥4 lines of tx

Month post-index date	All-cause total healthcare costs
6	$207,658
12	$415,316
18	$622,974
24	$830,632
30	$1,038,290
36	$1,245,948

The index date was defined as the initiation date of first subsequent LOT after meeting eligibility requirements for the study (eg, received ≥4 prior LOTs)

IPTW = inverse probability of treatment weighting; SCT = stem cell transplant.

Jagannath S, et al. *Oncol Ther*. 2022;10(2):411-420. Fonseca R, et al. *Blood Cancer J*. 2021;11(2):35.

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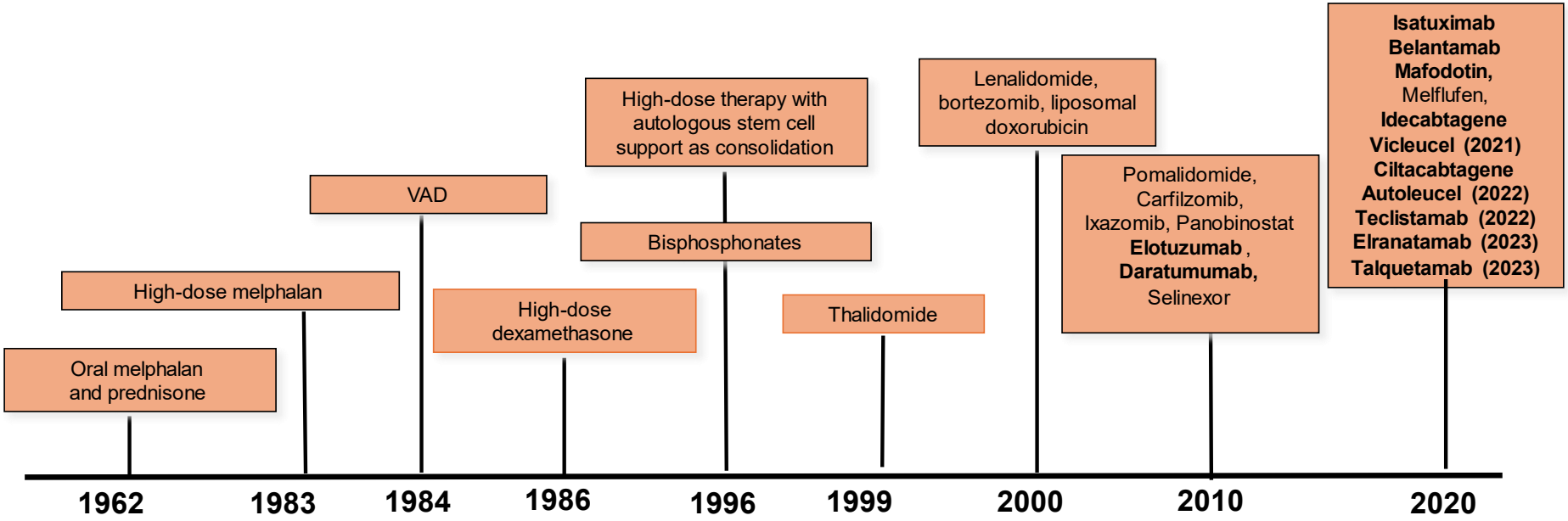
Therapeutics in Multiple Myeloma

Myeloma Therapy Evolution



VAD = vincristine, doxorubicin, and dexamethasone.
Figure used with permission from Dr. Omar Nadeem.

Myeloma Therapeutics by Class / Mechanism

Class	Drugs
Immunomodulatory drugs (IMiDs)	Lenalidomide Pomalidomide Thalidomide
Proteosome inhibitors (PIs)	Bortezomib Carfilzomib Ixazomib
Monoclonal antibodies	Daratumumab Isatuximab Elotuzumab
Steroids	Dexamethasone Prednisone
Antibody drug conjugates	*Belantamab mafodotin-blmf*[a]
XPO-1 inhibitor	Selinexor
Bispecific antibodies	Teclistamab Elranatamab Talquetamab
CAR-T	Idecabtagene autoleucel Ciltacabtagene autoleucel

[a]Received FDA accelerated approval 8/5/2020. Withdrawn from market 3/20/23.
XPO = exportin; CAR-T = chimeric antigen receptor T cell.
International Myeloma Foundation. Accessed August 30, 2024. https://www.myeloma.org/multiple-myeloma-drugs.

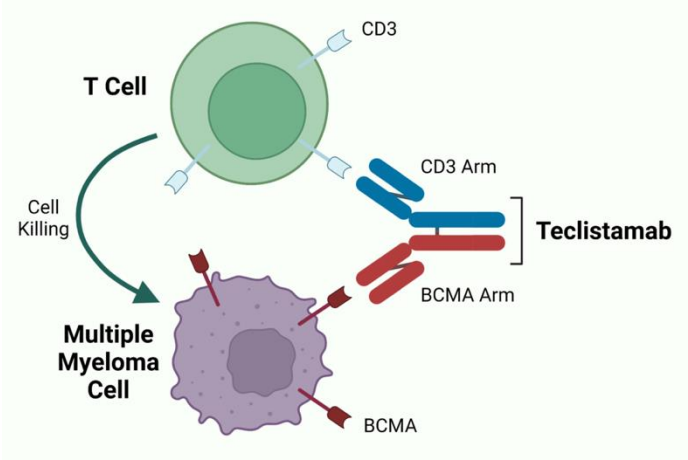
A Focus on Novel Therapies

- Immunotherapies / cellular therapies
  - Bispecific T cell engager antibodies (BiTEs)
  - Chimeric antigen receptor (CAR)-T cell therapy

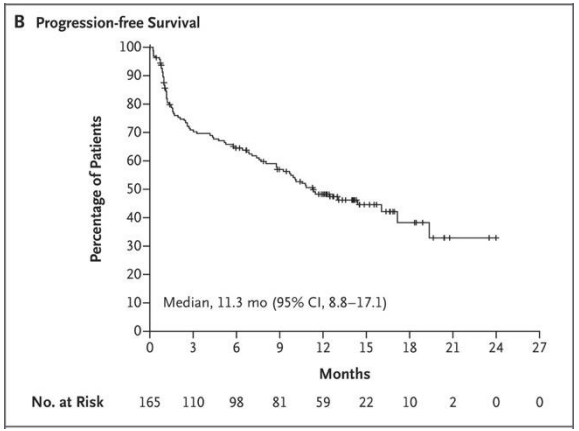
- Targeted therapies / small molecule inhibitors
  - XPO-1 inhibitors
  - BCL2 inhibitors
  - CeLMOD agents

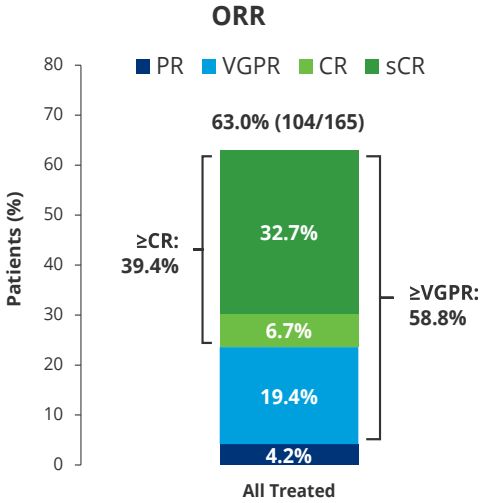
BCL2 = B-cell lymphoma 2 protein; CelMOD = cereblon E3 ligase modulator.

Bispecific T Cell Engager Therapies



Phase I Trial of Teclistamab in RRMM (MajesTEC-1)





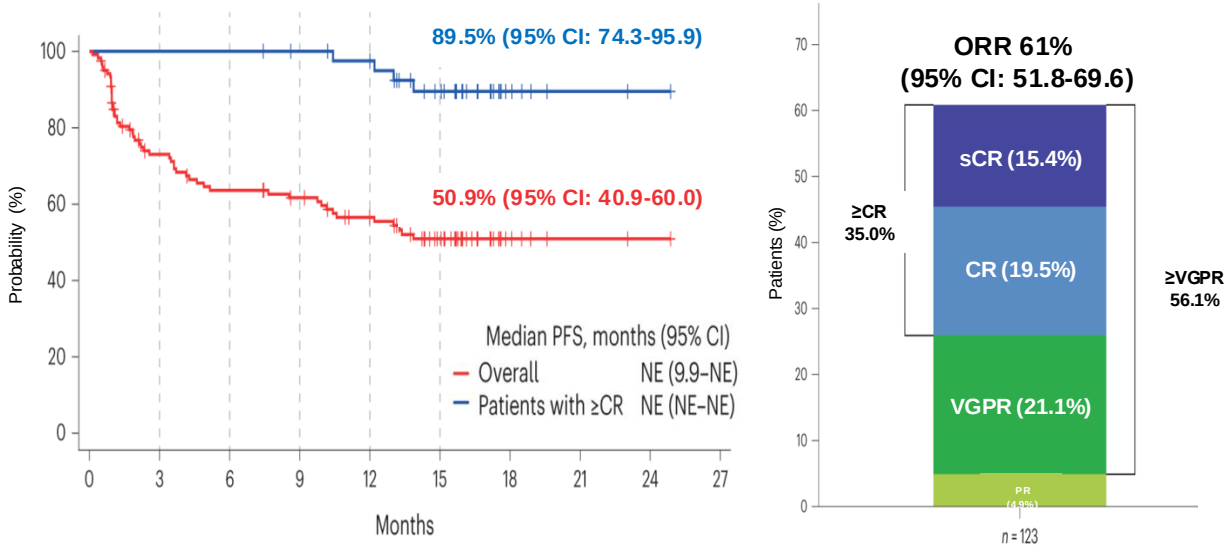
FDA approved 10/2022 for relapsed/refractory myeloma after at least 4 prior lines, including proteosome inhibitor, IMiD, and CD38 mAB

RR = relapsed/refractory.

Moreau P, et al. *N Engl J Med*. 2022;387(6):495-505. Figure adapted from Pillarisetti K, et al. *Blood Adv.* 2020;4(18):4538-4549.

Bispecific T Cell Engager Therapies

Phase II Trial of Elranatamab in RRMM (MagnetisMM-3)

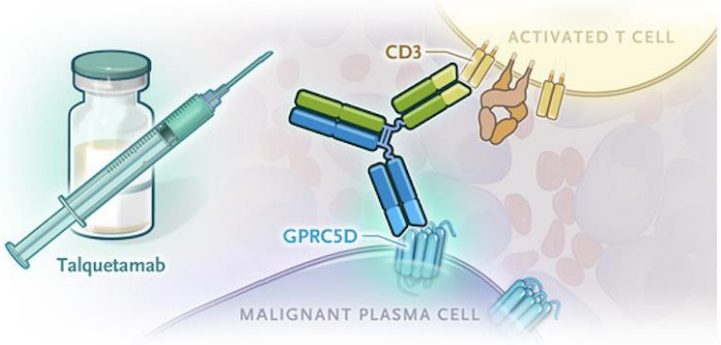


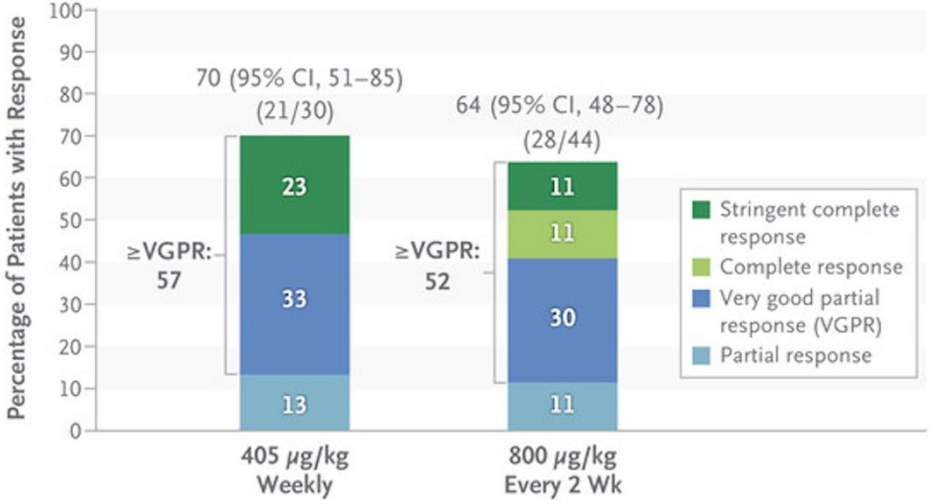
FDA approved 8/2023 for relapsed/refractory myeloma after at least 4 prior lines, including proteosome inhibitor, IMiD, and CD38 mAB

Lesokhin AM, et al. *Nat Med*. 2023;29(9):2259-2267.

Bispecific T Cell Engager Therapies

Phase I/II Trial of Talquetamab in RRMM (MonumenTAL-1)

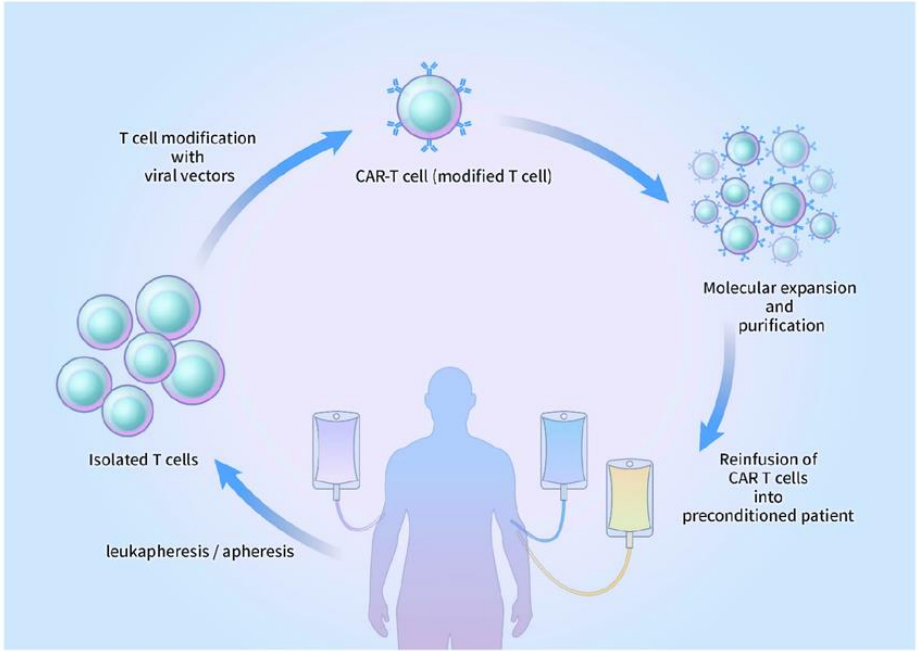




FDA approved 8/2023 for relapsed/refractory myeloma after at least 4 prior lines, including proteosome inhibitor, IMiD, and CD38 mAB

Chari A, et al. *N Eng J Med*. 2022;387(24):2232-2244.

CAR-T Cell Therapy



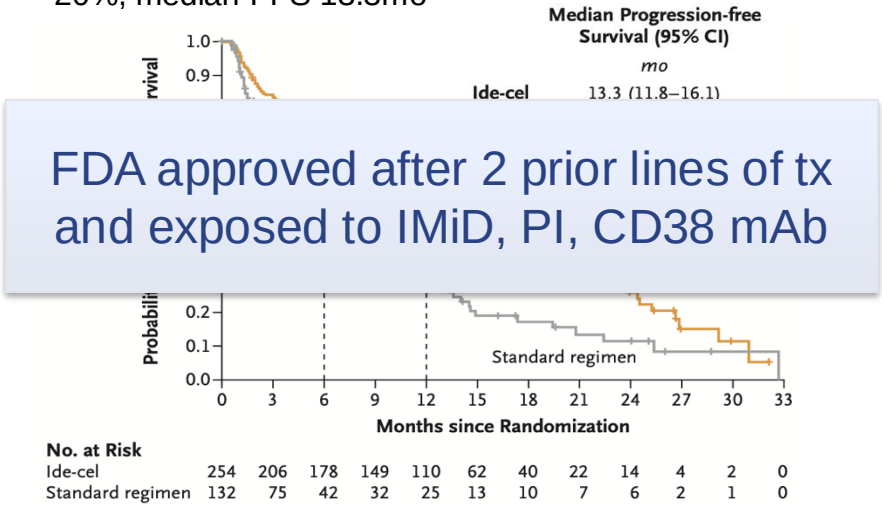
- CAR-T targets
  - BCMA (B-cell maturation antigen)
  - GPRC5D (G-coupled receptor)
- 2 FDA-approved BCMA CAR-T therapies
  - Idecabtagene autoleucel
  - Ciltacabtagene autoleucel

Young DY. *Int J Mol Sci.* 2021;22(2):640.

CAR-T Therapy in Relapsed/Refractory MM

Idecabtagene vicleucel (ide-cel)

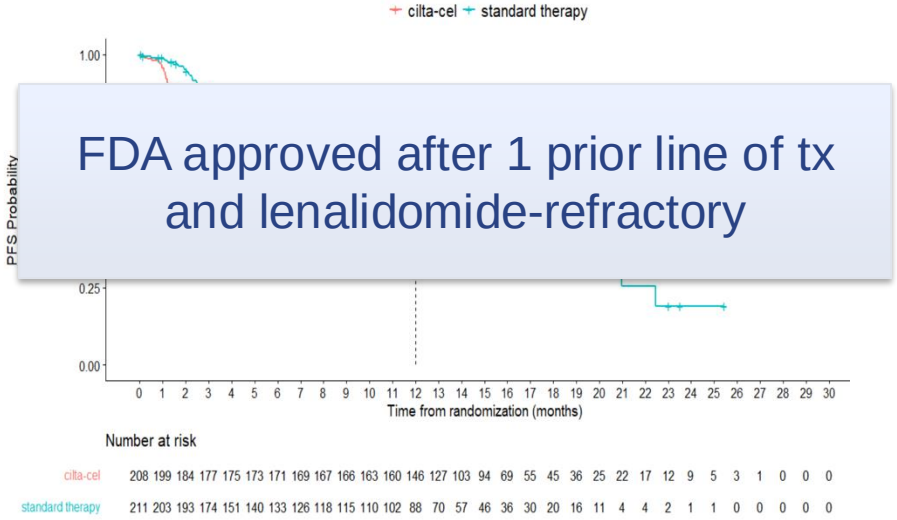
Phase III KarMMA-3: ORR 71% (39% CR) MRD-ve (10^{-5}) 20%, median PFS 13.3mo



FDA approved after 2 prior lines of tx and exposed to IMiD, PI, CD38 mAb

Ciltacabtagene autoleucel (cilta-cel)

Phase III CARTITUDE-4: ORR 84.6% (73.1% ≥CR) MRD-ve (10^{-5}) 60.6%, median PFS not reached



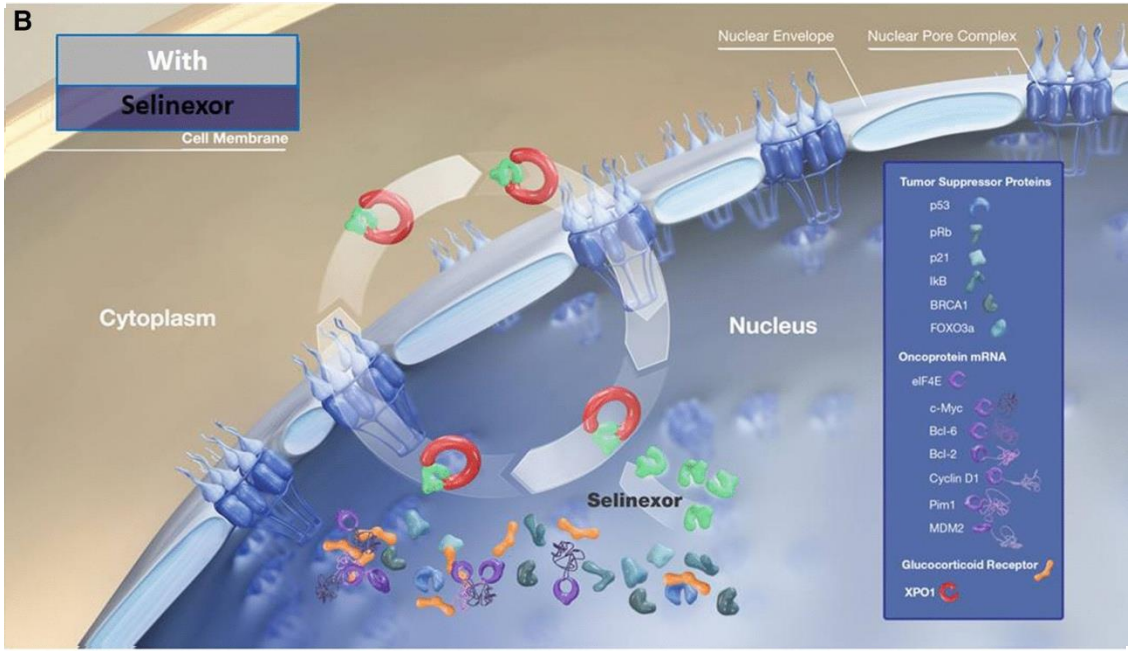
FDA approved after 1 prior line of tx and lenalidomide-refractory

MRD = minimal residual disease; ORR = objective response rate; PFS = progression-free survival.

Rodriguez-Otero P, et al. *N Engl J Med*. 2023;388(11):1002-1014. San Miguel J, et al. *N Engl J Med*. 2023;389(4):335-347. FDA Oncologic Drug Advisory Committee Meeting Briefing Document. March 15, 2024. Available at: https://www.fda.gov/media/176986/download.

Small-Molecule Inhibitors of Nuclear Export (SINE): Selinexor

- Exportin1 (XPO1) is a nuclear exporter that transports proteins, including tumor suppressor proteins (TSP), from the nucleus to the cytoplasm, preventing TSPs from exerting their anti-tumor effect
- Overexpression of XPO1 is seen in MM
- Selinexor inhibits XPO1, preventing the export of TSPs leading to cell death
- FDA approved 12/2020

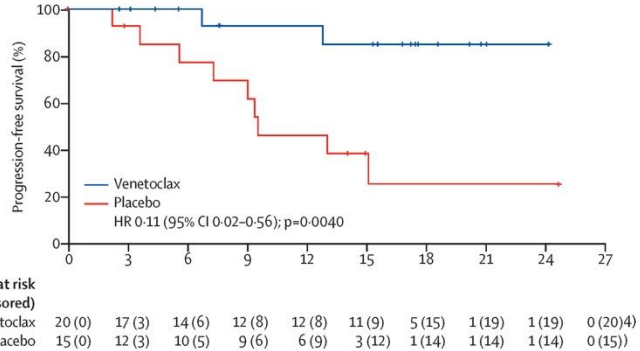


Theodoropoulos N, et al. *Target Oncol*. 2020;15(6):697-708.

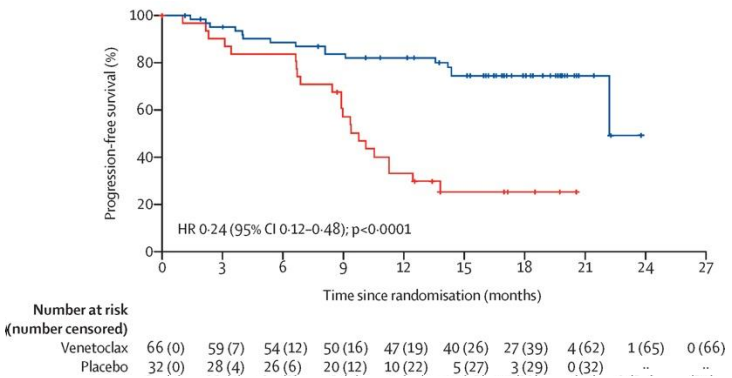
BCL-2 Inhibition in Myeloma

- t(11;14) is the most common translocation event in myeloma, occurring in 16%-24% of patients
  - Characterized by high levels of BCL-2 expression
  - Predictive biomarker that can be targeted by BCL-2 inhibitors, such as **venetoclax**
- Phase III BELLINI trial: Venetoclax-bortezomib-dex vs bortezomib-dex

PFS – t(11;14) patients



OS – t(11;14) patients



Bal S, et al. *Am J Cancer Res*. 2022;12(7):2950-2965. Kumar SK, et al. *Lancet Oncol*. 2020;21(12):1630-1642.

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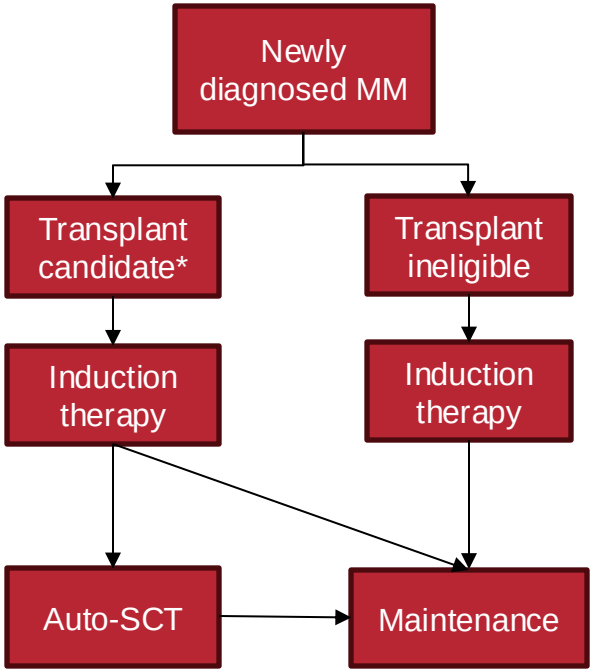
NCCN Guidelines for Treatment of Myeloma

Newly Diagnosed Myeloma

Transplant eligibility
Age
Performance status
Pulmonary function
Cardiac function



Newly Diagnosed Myeloma

PRIMARY THERAPY FOR TRANSPLANT CANDIDATES[a-d]
Preferred Regimens • Bortezomib/lenalidomide/dexamethasone (category 1) • Carfilzomib/lenalidomide/dexamethasone[k]
Other Recommended Regimens • Daratumumab/lenalidomide/bortezomib/dexamethasone
Useful In Certain Circumstances • Bortezomib/cyclophosphamide/dexamethasone[e] • Bortezomib/doxorubicin/dexamethasone • Carfilzomib/cyclophosphamide/dexamethasone[e,f,k] • Daratumumab/bortezomib/thalidomide/dexamethasone • Daratumumab/bortezomib/cyclophosphamide/dexamethasone • Daratumumab/carfilzomib/lenalidomide/dexamethasone[k] • Dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide/bortezomib[g] (VTD-PACE) • Isatuximab-irfc/lenalidomide/bortezomib/dexamethasone

National Comprehensive Cancer Network (NCCN). *Multiple Myeloma.* Accessed August 30, 2024. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf.

Newly Diagnosed Myeloma

PRIMARY THERAPY FOR NON-TRANSPLANT CANDIDATES[a-d]	
Preferred Regimens • Bortezomib/lenalidomide/dexamethasone (category 1) • Daratumumab/lenalidomide/dexamethasone (category 1)	
Other Recommended Regimens • Daratumumab/bortezomib/melphalan/prednisone (category 1) • Carfilzomib/lenalidomide/dexamethasone[k]	• Daratumumab/cyclophosphamide/bortezomib/dexamethasone
Useful In Certain Circumstances • Lenalidomide/low-dose dexamethasone (category 1)[m] • Bortezomib/cyclophosphamide/dexamethasone[e] • Bortezomib/dexamethasone	• Bortezomib/lenalidomide/dexamethasone (VRD-lite) for frail patients • Carfilzomib/cyclophosphamide/dexamethasone[f,k] • Lenalidomide/cyclophosphamide/dexamethasone

NCCN. *Multiple Myeloma.* Accessed August 30, 2024. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf.

Maintenance

Transplant eligible

MAINTENANCE THERAPY
Preferred Regimens • Lenalidomide[h] (category 1)
Other Recommended Regimens • Bortezomib
Useful In Certain Circumstancesz • Bortezomib/lenalidomide[j] • Carfilzomib/lenalidomide[j] • Daratumumab ± lenalidomide[j] • Ixazomib (category 2B)[i]

Transplant ineligible

MAINTENANCE THERAPY
Preferred Regimens • Lenalidomide (category 1)
Other Recommended Regimens • Bortezomib
Useful In Certain Circumstances • Bortezomib/lenalidomide[j] • Ixazomib (category 2B)[i]

NCCN. *Multiple Myeloma.* Accessed August 30, 2024. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf.

Relapsed/Refractory Myeloma (RRMM)

THERAPY FOR PREVIOUSLY TREATED MULTIPLE MYELOMA[a-d,n-o,q] Relapsed/Refractory Disease After 1–3 Prior Therapies	
Preferred Regimens* *Order of regimens does not indicate comparative efficacy*	
Bortezomib-Refractory[p]	**Lenalidomide-Refractory[p]**
• Carfilzomib/lenalidomide/dexamethasone (category 1) • Daratumumab/carfilzomib/dexamethasone (category 1) • Daratumumab/lenalidomide/dexamethasone (category 1) • Isatuximab-irfc/carfilzomib/dexamethasone (category 1) • Carfilzomib/pomalidomide/dexamethasone *After one prior therapy including lenalidomide and a PI* ‣ Daratumumab/pomalidomide/dexamethasone (category 1) *After two prior therapies including lenalidomide and a PI* ‣ Isatuximab-irfc/pomalidomide/dexamethasone (category 1)	• Daratumumab/bortezomib/dexamethasone (category 1) • Daratumumab/carfilzomib/dexamethasone (category 1) • Isatuximab-irfc/carfilzomib/dexamethasone (category 1) • Pomalidomide/bortezomib/dexamethasone (category 1) • Selinexor/bortezomib/dexamethasone (category 1) • Carfilzomib/pomalidomide/dexamethasone • Elotuzumab/pomalidomide/dexamethasone *After one prior therapy including lenalidomide and a PI* ‣ Daratumumab/pomalidomide/dexamethasone (category 1) *After two prior therapies including lenalidomide and a PI* ‣ Isatuximab-irfc/pomalidomide/dexamethasone (category 1) *After two prior therapies including an IMiD and a PI and with disease progression on/within 60 days of completion of last therapy* ‣ Ixazomib/pomalidomide/dexamethasone
CAR T-Cell Therapy *After one prior therapy including IMiD and a PI, and refractory to lenalidomide* ‣ Ciltacabtagene autoleucel (category 1) *After two prior therapies including an IMiD, an anti-CD38 monoclonal antibody and a PI* ‣ Idecabtagene vicleucel (category 1)	

NCCN. *Multiple Myeloma.* Accessed August 30, 2024. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf.

Relapsed/Refractory Myeloma (RRMM)

THERAPY FOR PREVIOUSLY TREATED MULTIPLE MYELOMA[a-d,n-r] Relapsed/Refractory Disease After 1–3 Prior Therapies	
Other Recommended Regimens	
• Carfilzomib (twice weekly)/dexamethasone (category 1) • Elotuzumab/lenalidomide/dexamethasone (category 1) • Ixazomib/lenalidomide/dexamethasone (category 1) • Bortezomib/cyclophosphamide/dexamethasone • Bortezomib/lenalidomide/dexamethasone • Carfilzomib/cyclophosphamide/dexamethasone • Daratumumab/cyclophosphamide/bortezomib/dexamethasone • Elotuzumab/bortezomib/dexamethasone • Ixazomib/cyclophosphamide/dexamethasone • Lenalidomide/cyclophosphamide/dexamethasone	*After two prior therapies including an IMiD and a PI and disease progression on/within 60 days of completion of last therapy* ▸ Pomalidomide/cyclophosphamide/dexamethasone See Evidence Blocks on MYEL-G (EB-4)
Useful in Certain Circumstances	
• Bortezomib/dexamethasone (category 1) • Bortezomib/liposomal doxorubicin/dexamethasone (category 1) • Lenalidomide/dexamethasone (category 1) • Carfilzomib/cyclophosphamide/thalidomide/dexamethasone • Carfilzomib (weekly)/dexamethasone • Selinexor/carfilzomib/dexamethasone • Selinexor/daratumumab/dexamethasone • Venetoclax/dexamethasone ± daratumumab or PI only for t(11;14) patients	*After two prior therapies including IMiD and a PI and with disease progression on/within 60 days of completion of last therapy* ▸ Pomalidomide/dexamethasone (category 1) ▸ Ixazomib/pomalidomide/dexamethasone ▸ Selinexor/pomalidomide/dexamethasone *For treatment of aggressive MM* ▸ Dexamethasone/cyclophosphamide/etoposide/cisplatin (DCEP) ▸ Dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide (DT-PACE) ± bortezomib (VTD-PACE) *After at least three prior therapies including a PI and an IMiD or are double-refractory to a PI and an IMiD* ▸ Daratumumab See Evidence Blocks on MYEL-G (EB-5)

NCCN. *Multiple Myeloma.* Accessed August 30, 2024. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf.

Relapsed/Refractory Myeloma (RRMM)

THERAPY FOR PREVIOUSLY TREATED MULTIPLE MYELOMA[a-d,n-o] Relapsed/Refractory Disease After 3 Prior Therapies
Preferred Regimens
After at least four prior therapies, including an anti-CD38 monoclonal antibody, a PI, and an IMiD[s] ▸ *CAR T-cell Therapy:* ◊ **Ciltacabtagene autoleucel** ◊ **Idecabtagene vicleucel** ▸ *Bispecific Antibodies:* ◊ **Elranatamab-bcmm** ◊ **Talquetamab-tgvs** ◊ **Teclistamab-cqyv**
Other Recommended Regimens
• **Bendamustine[t]** • **Bendamustine/bortezomib/dexamethasone[t]** • **Bendamustine/carfilzomib/dexamethasone[t]** • **Bendamustine/lenalidomide/dexamethasone[t]** • **High-dose or fractionated cyclophosphamide** *After at least four prior therapies and whose disease is refractory to at least two PIs, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody* • **Selinexor/dexamethasone**
Useful in Certain Circumstances
After at least four prior therapies, including an anti-CD38 monoclonal antibody, a PI, and an IMiD • **Belantamab mafodotin-blmf (if available through compassionate use program)**

NCCN. *Multiple Myeloma.* Accessed August 30, 2024. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf.

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Treatment Sequencing

Treatment Considerations at Diagnosis

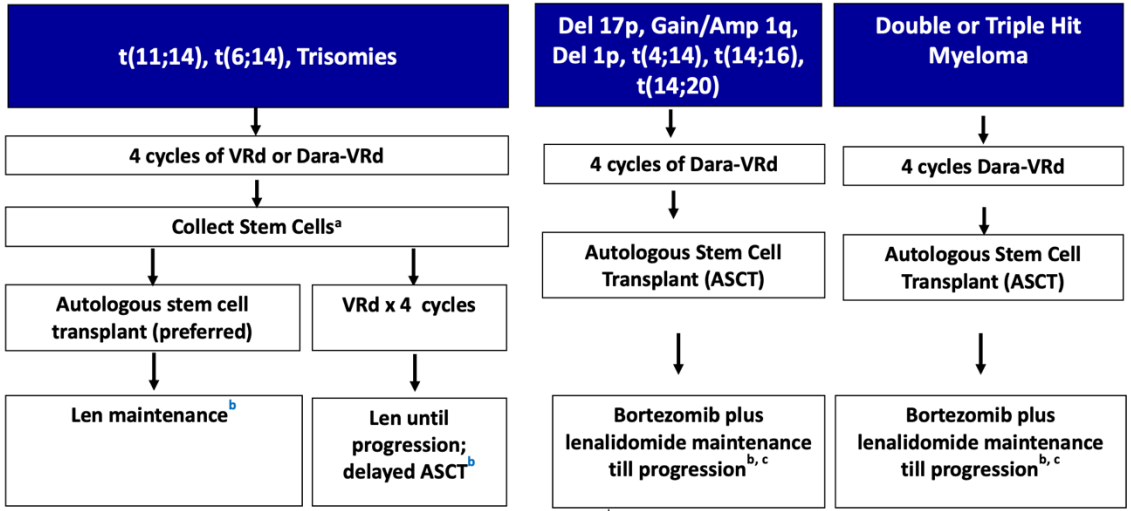
- Patient features
  - Age
  - Frailty status
  - Comorbidities
  - Organ function (renal failure)
- Disease features
  - Cytogenetics
  - R-ISS risk stratification
  - Circulating plasma cells, plasma cell leukemia
- Transplant eligibility and decision for delayed or upfront transplant
- Drug availability and indications

Costello CL. *Hematology Am Soc Hematol Educ Program*. 2022;2022(1):539-550.

Treatment Algorithms for Newly Diagnosed

mSMART – Off-Study

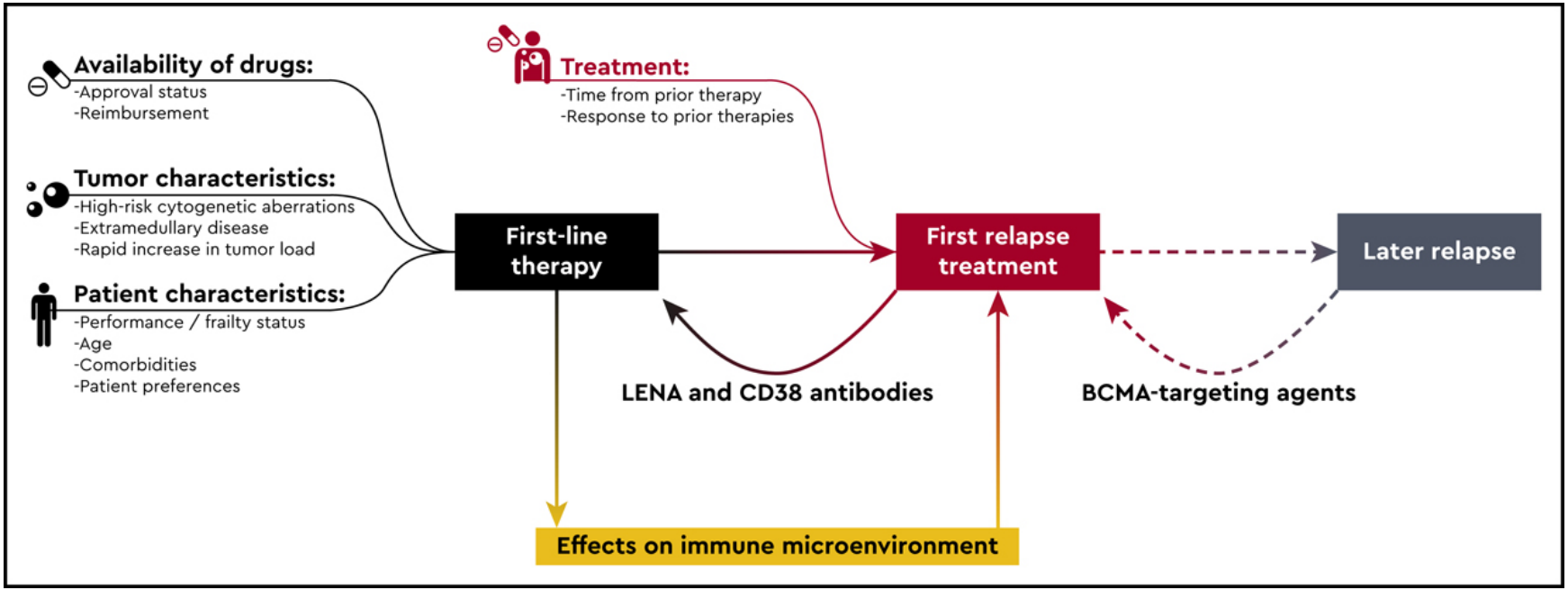
Transplant Eligible



[a] If age >65 or > 4 cycles of VRd, consider mobilization with G-CSF plus cytoxan or plerixafor; [b] Duration usually until progression based on tolerance; [c] In patients with grade 2 or higher neuropathy at baseline, and for patients in whom bortezomib needs to be dose reduced or discontinued due to neuropathy, consider carfilzomib instead.

Dispenzieri A, et al. *Mayo Clin Proc*. 2007;82(3):323-341. Kumar SK, et al. *Mayo Clin Proc*. 2009;84(12):1095-1110. Mikhael JR, et al. *Mayo Clin Proc*. 2013;88(4):360-376.

Treatment Considerations at Relapse



van de Donk NWCJ. *Hematology Am Soc Hematol Educ Program*. 2020;2020(1):248-258.

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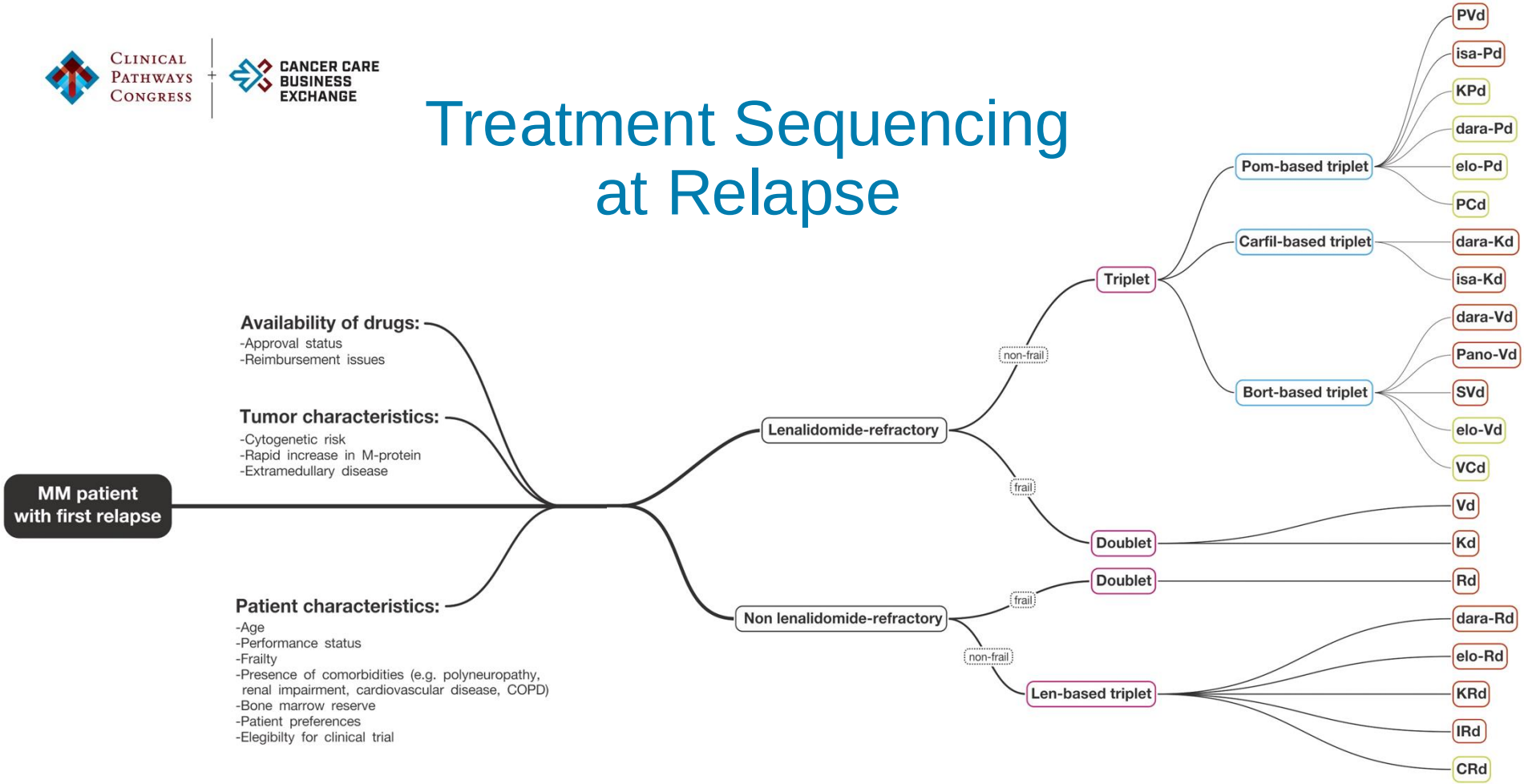
Treatment Sequencing at Relapse



clinicalpathwayscongress.oncnet.com

C = cyclophosphamide; R = lenalidomide; d = dexamethasone; K = carfilzomib; P = pomalidomide; V = bortezomib; elo = elotuzumab; I = ixazomib; len = lenalidomide; Pano = panobinostat; Pom = pomalidomide; S = selinexor.

van de Donk NWCJ. *Hematology Am Soc Hematol Educ Program*. 2020;2020(1):248-258.

Treatment Tolerability

- With multiple different agents that are often employed together, the therapeutic profile and commonly associated adverse events (AEs) must be considered with patient comorbidities during treatment selection

AE	Common Agents
Myelosuppression	IMiDs, alkylating chemotherapy
Immunosuppression	Monoclonal antibodies, IMiDs, PIs, alkylators, BiTEs, CAR-T cells
Peripheral neuropathy	Bortezomib, chemotherapy
Thromboembolism	IMiDs (lenadlidomide, pomalidomide)
Cardiotoxicity	Carfilzomib
Ocular toxicity	Belantamab mafodotin
Gastrointestinal toxicity	Lenalidomide, ixazomib, cyclophosphamide, selinexor
Cytokine release syndrome/neurotoxicity	CAR-T, bispecific antibodies

Pozzi S, et al. *Cancers*. 2021;13(19):4978.

Adverse Event Management

- In addition to dose reduction and adjusted dose schedules, we have concurrent supportive care therapies and measures to address or try to mitigate some of the side effects of myeloma-directed therapies

AE	Management Strategy / Supportive Care
Thromboembolic risk with IMiDs	Thromboprophylaxis with aspirin or anticoagulation
Immunosuppression	Shingles prophylaxis Antibiotic prophylaxis Vaccinations Intravenous immunoglobulin (IVIg)
Skeletal-related events	Bisphosphonates or RANK-L inhibitors
Peripheral neuropathy	Once-weekly bortezomib dosing
Cytokine release syndrome	Steroids, tocilizumab

Pozzi S, et al. *Cancers*. 2021;13(19):4978. Ludwig H, et al. *Lancet Oncol*. 2023;24(6):e255-e269.

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Clinical Pathways Applications in Multiple Myeloma

Guideline-Directed Pathways

Clinical Practice Guidelines	
International Myeloma Working Group (IMWG)	Range of publications, including consensus definitions of diagnosis, risk-stratification, imaging and response assessment, treatment guidelines for relapsed myeloma, and optimal usage of bispecific antibodies and other therapies
NCCN	Provides guidelines for the entire continuum of cancer care; incorporates evidence-based and expert consensus approaches (both tabular and algorithm); ad-hoc meetings for staying more up-to-date on new data and approvals; and extensive footnotes
American Society of Clinical Oncology (ASCO)	Provides evidence-based recommendations
American Society of Hematology (ASH)	Currently no practice guidelines pertaining to multiple myeloma

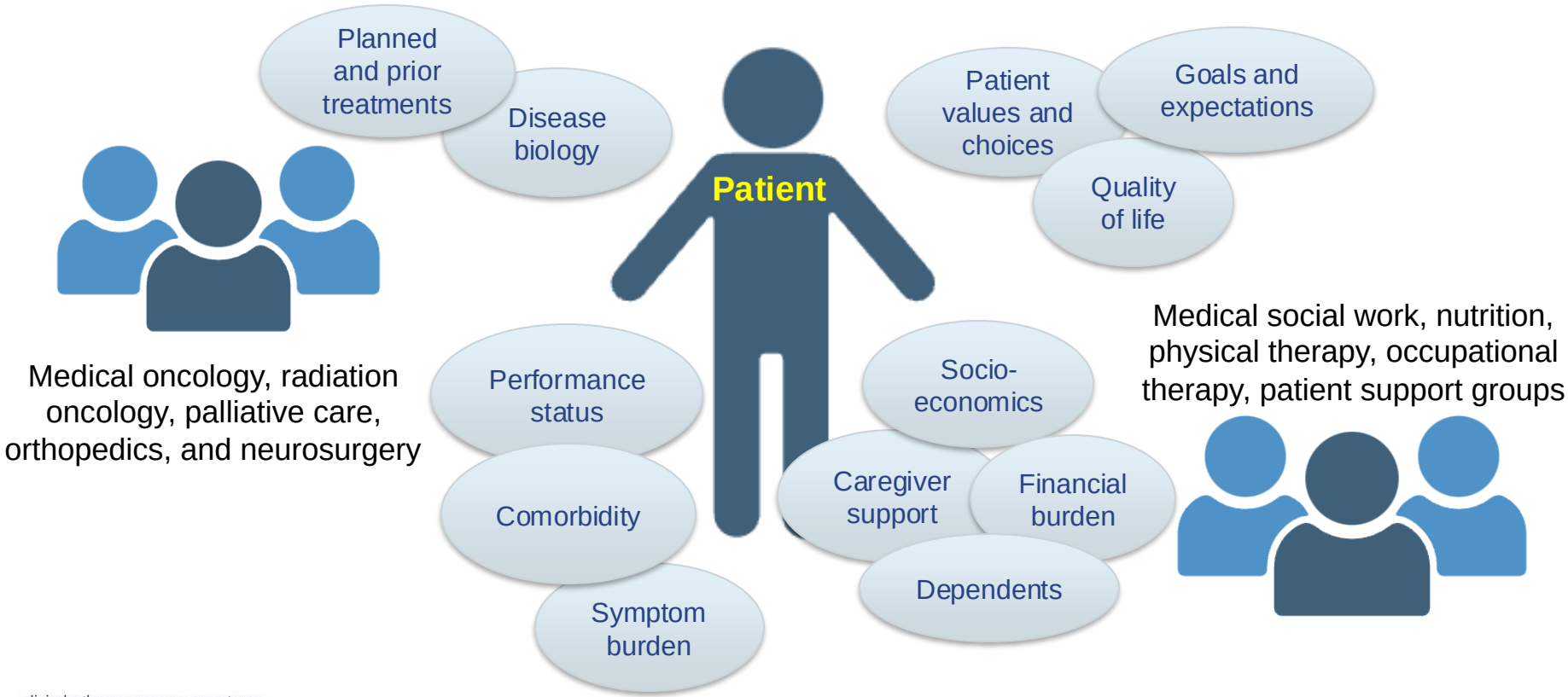
International Myeloma Foundation. Accessed September 4, 2024. https://www.myeloma.org/imwg-publications.
NCCN. *Multiple Myeloma*. Accessed August 30, 2024. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf.

Treatment Considerations

Line of Therapy	Drug Class-Refractory
≥1 complete cycle of a single agent, combination of multiple drugs, or a planned sequence of regimens	Stratification based on number of drugs/drug class refractoriness also correlates with clinical outcome, potentially better than LOT
Number of treatment lines has been associated with clinical outcome	Considers the usage of novel therapies (eg, monoclonal antibody therapies) in earlier lines of therapies
Used to determine inclusion in clinical trials and used in FDA label indications	Allows us to discriminate between drug exposure with likelihood of drug sensitivity vs drug resistance
Limitations: Assumes uniformity in lines of therapy, but patients may have received vasty different regimens and have LOT changes due to other reasons outside of progression	**Limitations:** Does not consider the possibility of loss of resistance or differential resistance to drugs that are part of a combination regimen

Rajkumar SV, et al. *Blood*. 2015;126(7):921-922. Goel U, et al. *Blood Cancer J*. 2023;13(1):11.

Patient-Centered Multidisciplinary Care



Cerchione C, et al. *Am Soc Clin Oncol Educ Book*. 2023;43:e390202.

Cost Considerations

	Approximate Drug Cost per Year* (in U.S. Dollars)	Comment
Drugs		
Lenalidomide	168,000	
Pomalidomide	192,000	
Bortezomib	50,000	
Ixazomib	111,000	
Carfilzomib	130,000	260,000 (at 56 mg/m^2)
Daratumumab	120,000	
Elotuzumab	120,000	
Cyclophosphamide	5800	
Melphalan IV	10,000	Per transplant
Dexamethasone	3,400	
Regimens		
VRd	220,000	
KRd	300,000	
VCd	60,000	
DRd	290,000	
D-VRd	340,000	

- Financial burden and request for financial assistance is common, even among insured patients with MM
- Younger age, lower household income, and longer time from diagnosis is associated with higher financial toxicity
- Patients also face time toxicity (frequent myeloma-related health interactions), which is correlated to disease status
- For CAR-T therapies there is additional need for 24-hour caregiver support, which is not financially feasible for some patients

Rajkumar SV. *Am Soc Clin Oncol Educ Book*. 2018;38:662-666. Huntington SF, et al. *Lancet Haematol*. 2015;2(10):e408-e416. Banerjee R, et al. *Clin Lymphoma Myeloma Leuk*. 2024;24(7):446-454.e3.

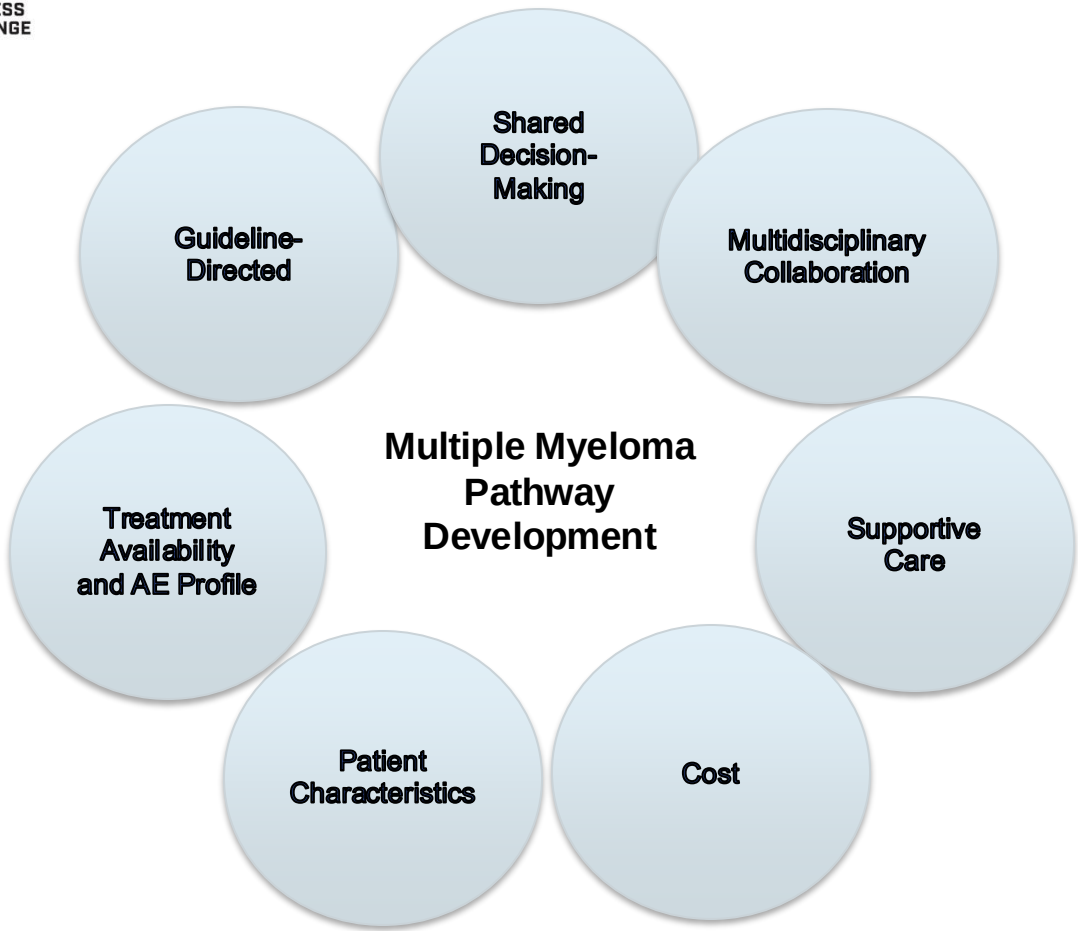
Disparities in Myeloma

- African American patients make up approximately 20% of all patients with MM in the United States, but they have been underrepresented in clinical trials compared
- Analysis of patient outcomes in the era of novel therapies show equal or superior disease-specific outcomes in African Americans vs White patients after *adjustment* of demographics, comorbidity, and treatment factors

Biologic Differences/ Disparities	Non-Biologic Disparities
Hereditary and familial	Systemic racism
biology	
	Access to quality care and clinical trials

Can a mindfully constructed clinical pathway help combat disparities in myeloma care?

Bhutani M, et al. *Blood Cancer J.* 2023;13(1):189.


Shared Decision-Making
Multidisciplinary Collaboration
Supportive Care
Cost
Patient Characteristics
Treatment Availability and AE Profile
Guideline-Directed
Multiple Myeloma Pathway Development

Key Learning Points

- Multiple myeloma is a very heterogenous hematologic malignancy in regard to disease biology, presentation, and disease course
- Outcomes are gradually improving for patients with myeloma, but this remains an incurable malignancy
- 19 FDA-approved medications for myeloma, with hopefully more to come
- Treatment sequencing has become increasingly complex with growing number of therapeutic options, and changes in drug labeling and indications
- Clinical pathways development will need to factor in multiple priorities to optimize patient care while allowing ability to personalize treatment for patient's unique disease and health characteristics

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Thank You!

Q&A Session