



Opening Remarks

Veronica Bohorquez, MA MMRF

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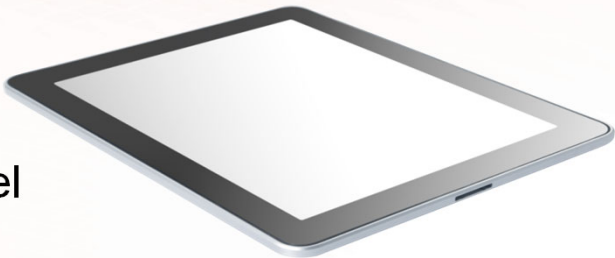
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iPads

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Program Faculty

Program Host

David H. Vesole, MD, PhD
MedStar Georgetown University Hospital
Georgetown University School of Medicine
Washington, District of Columbia
John Theurer Cancer Center, Hackensack Meridian School of Medicine
Hackensack, New Jersey

Faculty

Donna D. Catamero, ANP-BC, OCN, CCRC
Mount Sinai Hospital
New York, New York

Kenneth Shain, MD, PhD
H. Lee Moffitt Cancer Center
Tampa, Florida

Edward A. Stadtmauer, MD
Perelman School of Medicine
University of Pennsylvania
Philadelphia, Pennsylvania



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Summit Agenda

Time (ET)	Topic	Speakers
9:00 – 9:10 AM	Introduction to the MMRF	Veronica Bohorquez, MA
9:10 – 9:20 AM	Welcome	David Vesole to David H. Vesole, MD, PhD, FACP
9:20 – 10:00 AM	Myeloma 101 and Health Care Disparities in Multiple Myeloma	Kenneth Shain, MD, PhD
10:00 – 10:30 AM	Treating Relapsed/Refractory Multiple Myeloma	David Vesole to David H. Vesole, MD, PhD, FACP
10:30 – 11:00 AM	Town Hall Q&A	Panel
11:00 AM – 11:30 AM	CAR T-Cell Therapy and Bispecific Antibodies	Edward A. Stadtmauer, MD
11:30 AM – 12:00 PM	Supportive Care	Donna D. Catamero, ANP-BC, OCN, CCRC
12:00 – 1:00 PM	Lunch, Patient Journey	Thann Ingraham
1:00 – 1:30 PM	Town Hall Q&A	Panel
1:30 PM	Closing Remarks	Veronica Bohorquez, MA



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MULTIPLE MYELOMA
Research Foundation

MMRF Introduction

Mary DeRome, MS
MMRF

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The Work of the MMRF

The MMRF does three things in relentless pursuit of its mission to accelerate a cure for each and every myeloma patient.

1

We accelerate new treatments

Bringing next-generation therapies to patients faster

2

We drive precision medicine

Using data to deliver better answers and more precise treatments for patients

3

We empower patients

Putting them on The Right Track and guiding them to the right team, tests, and treatments to extend their lives

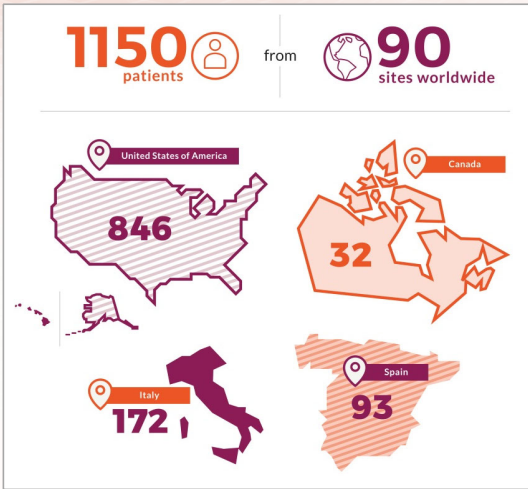


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MMRF CoMMpass Study: Advancing Personalized Medicine Research

- Landmark study focusing on the genomics of myeloma
- Goals
 - Learn which patients respond best to which therapies
 - Identify new targets and new hypotheses
- Newly diagnosed patients will be followed for at least 8 years

All participants undergo a type of detailed genetic testing called *genomic sequencing*.



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CoMMpass Is a Trial of Discovery

- CoMMpass data has
 - Provided the myeloma community with information on
 - Frequency of genetic abnormalities
 - How genetic abnormalities play a role in myeloma
 - Drive multiple myeloma cell growth and survival
 - Contribute to drug resistance
 - May predict which patients respond to which therapy
 - Genetic abnormalities that help refine risk assessment
 - Led to conception of the MyDRUG trial

All patients in CoMMpass had genomic sequencing from diagnosis to relapse. The resulting data provides detailed genetic profiles for every myeloma patient at every stage of their disease!



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MMRF CureCloud



It starts with you.

The MMRF CureCloud® is the first research study including at-home genomic testing for myeloma patients. As a participant, you receive free tests and resources that enable more productive and informed conversations with your multiple myeloma care team.



Genomic test

Get a free state-of-the-art genomics test, using the first liquid biopsy for multiple myeloma.



Personal report

Receive a free report on the genetic variations in your multiple myeloma cells.



Coming soon: Smarter treatment options

You and your care team can identify more informed treatment paths based on other patient data.

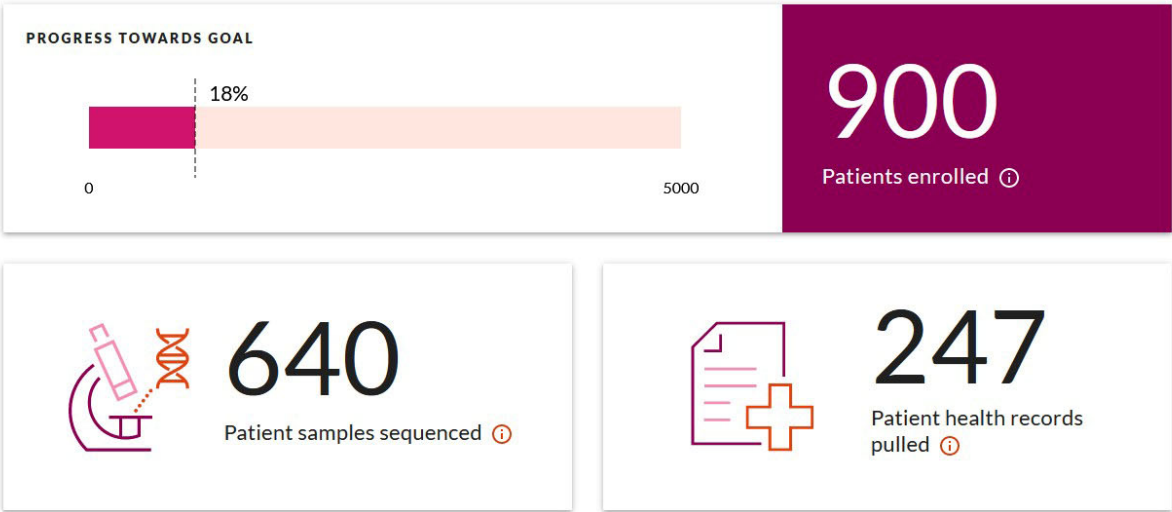
Join now — visit mmrfcurecloud.org or call 1-888-841-MMRF (6673)



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CureCloud Enrollment Tracker

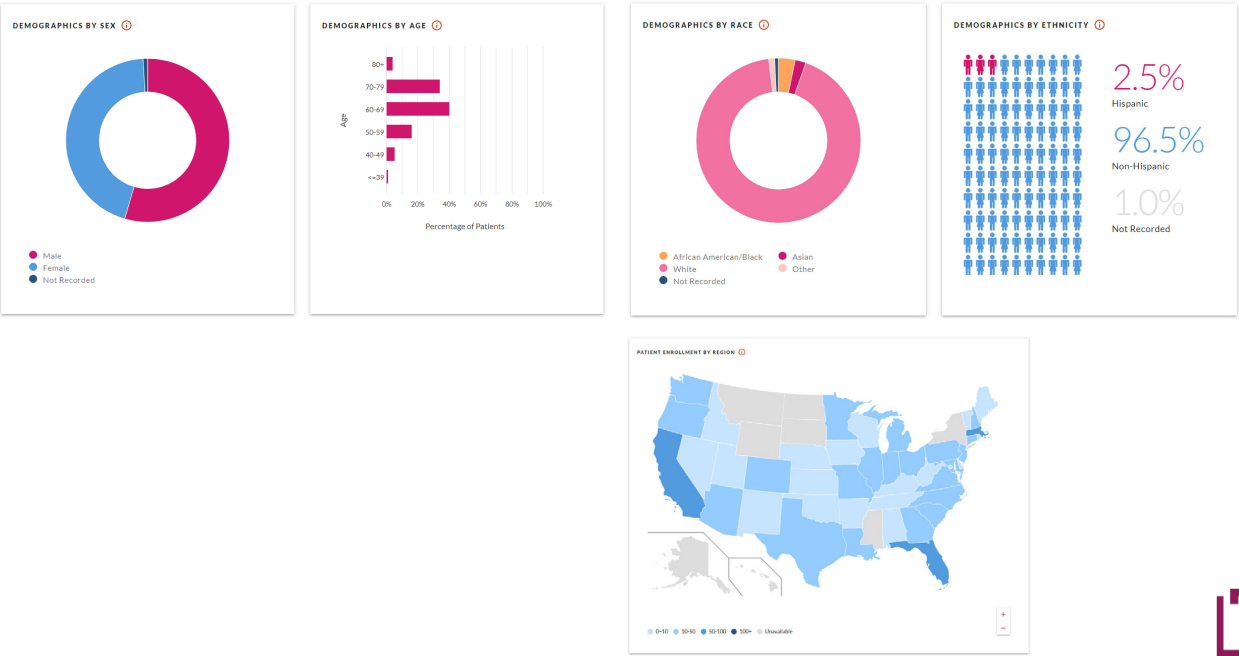
This is the total number of patients who have enrolled in the CureCloud study. Monitor enrollment progress as we work toward our goal of 5,000 patient participants over 5 years. Explore anonymous CureCloud patient data below and find more information about each section in the (i) icon.



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Demographics

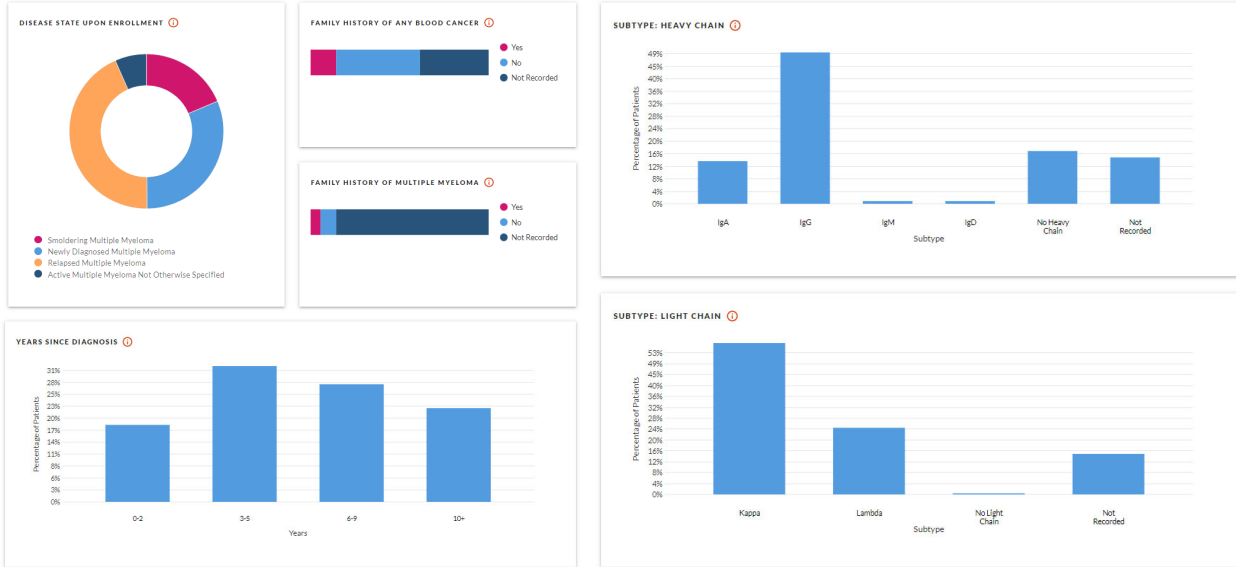
Learn about CureCloud study participant demographics by sex, age, ethnicity, race and region. Use the filter tool to find patients like you.



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Clinical

Explore clinical information from CureCloud study participants, including disease state, family history, staging information, years since diagnosis and subtype. Use the filter tool to see results relevant to the specifics of your multiple myeloma.



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Genomics

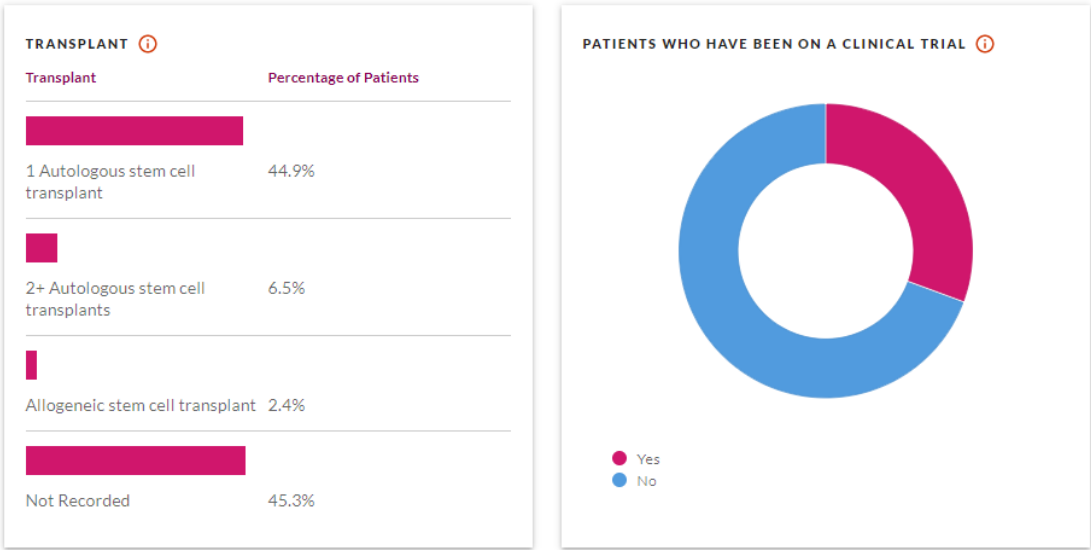
Learn about the percentage of CureCloud study participants whose DNA tests identified cytogenetic abnormalities and/or genetic mutations.



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Therapy

View the percentage of CureCloud study participants who have undergone a stem cell transplant and/or participated in a clinical trial.



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Welcome!

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Question



Are you a...

- A. Patient
- B. Caregiver (family member or friend who helps patient manage his or her disease)
- C. Other



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Question



At what stage is your myeloma? (If you are a caregiver, what is the stage of the patient's myeloma?)

- A. Newly diagnosed
- B. Relapsed/refractory
- C. Remission: still on therapy
- D. Remission: not on therapy
- E. MGUS or smoldering myeloma not currently requiring treatment
- F. Other
- G. I don't know.



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Question

Have you had a stem cell transplant?

- A. No, but I will soon!
- B. No, but I am considering one (or my doctor is discussing with me).
- C. No, my doctor tells me I am not a candidate.
- D. Yes
- E. Not applicable



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Question

Do you know if you had any molecular characterization performed on your tumor, such as FISH, cytogenetics, or sequencing?

- A. No
- B. Yes, I had FISH.
- C. Yes, I had cytogenetics.
- D. Yes, I had sequencing.
- E. Yes, I had more than one of these tests performed.
- F. I don't know.



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Question



Have you and your care team ever discussed the possibility of you joining a clinical trial that you are eligible for? (If you are a caregiver, do you know if joining a clinical trial has ever been discussed?)

- A. Yes
- B. No
- C. I don't know.



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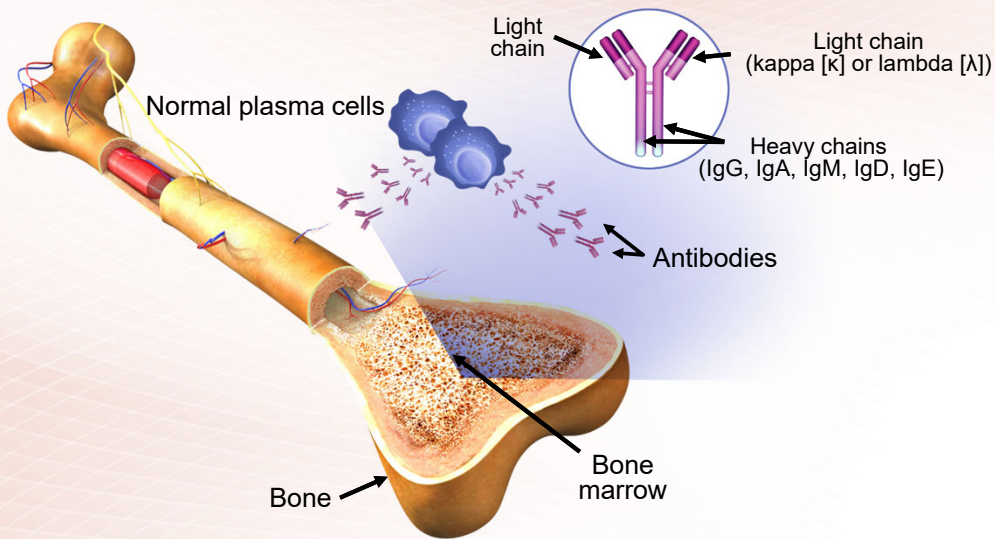
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Myeloma 101 and Health Care Disparities in Multiple Myeloma

Kenneth Shain, MD, PhD
H. Lee Moffitt Cancer Center
Tampa, Florida

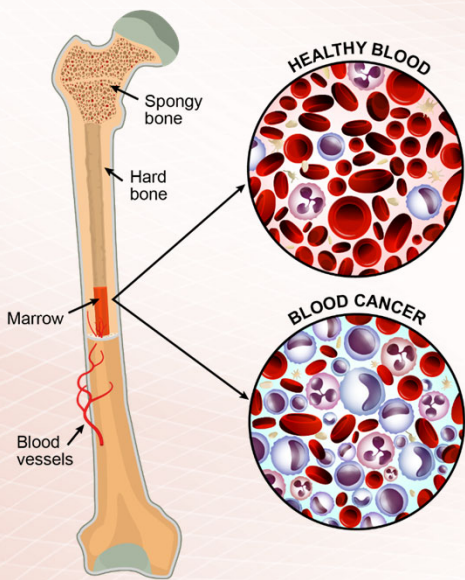
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Normal Bone Marrow



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What is multiple myeloma?

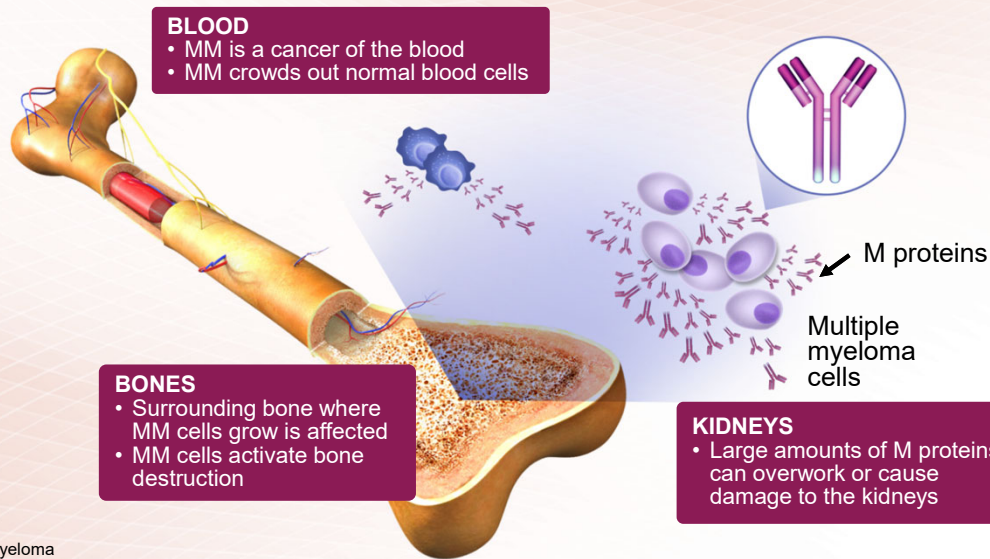


- Multiple myeloma is a **blood cancer** that starts in the **bone marrow**, the place where all **blood cells** are produced
- Multiple myeloma is caused when a type of **white blood cell** called a **plasma cell** becomes cancerous and grows out of control



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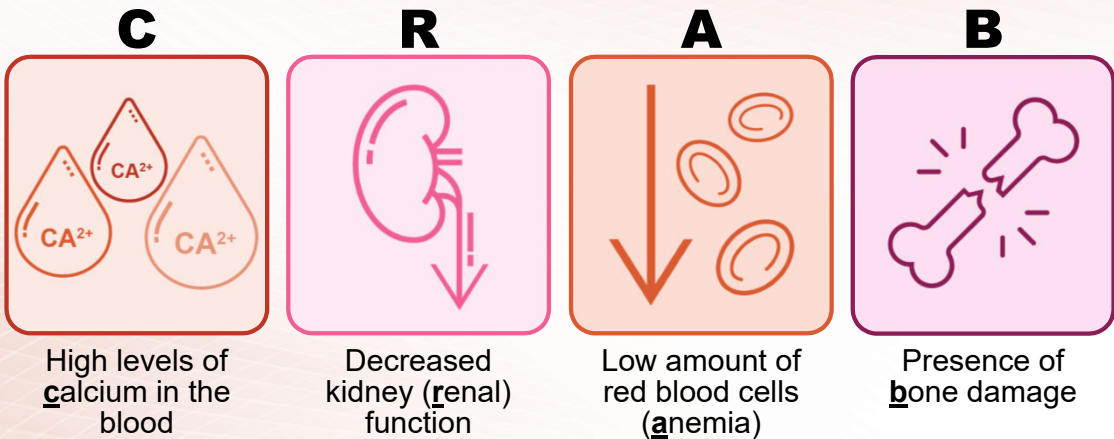
Multiple Myeloma Affects Your Bones, Blood, and Kidneys



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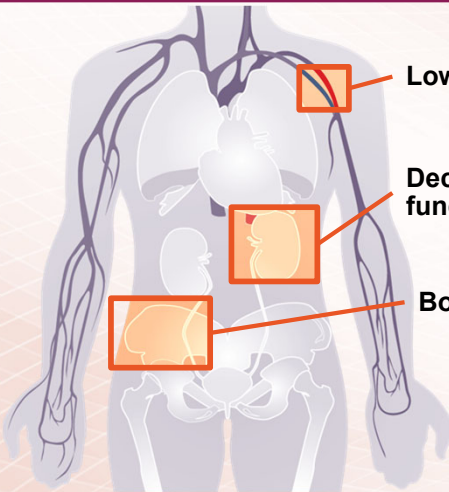
Multiple Myeloma Affects Your Bones, Blood, and Kidneys

The clinical features that are characteristic of multiple myeloma



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Effects of Myeloma and Common Symptoms



Low blood counts →

- Weakness
- Fatigue
- Infection

Decreased kidney function → Weakness

Bone damage → Bone pain

About 10% to 20% of patients with newly diagnosed myeloma do not have any symptoms.

Disease presentation and myeloma-related complications after myeloma diagnosis are different in patients by race

More common in Black patients

- Hypercalcemia
- Kidney dysfunction
 - Hemodialysis
- Anemia

Less common in Black patients

- Bone fractures

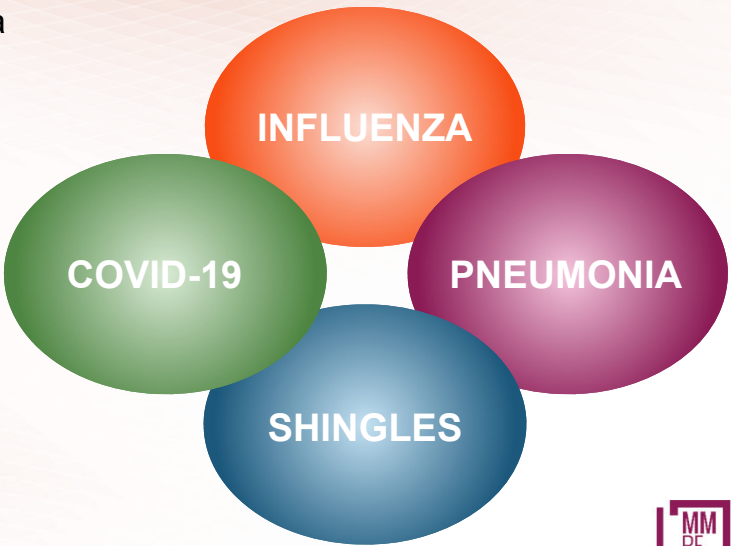
MMRF. Multiple myeloma symptoms, side effects, and complications. <https://themmrf.org/multiple-myeloma/symptoms-side-effects-and-complications/>. Campbell K. *Nurs Times*. 2014;110:12; Kyle R et al. *Mayo Clin Proc*. 2003;78:21; Ailawadhi S et al. *Cancer*. 2018;124:1710.



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Infections and Vaccinations in Multiple Myeloma

- Risk of infection higher for myeloma patients than for general population
- Types of infections include
 - Bacterial: pneumonia (an infection of the lungs), bacteremia
 - Viral: varicella zoster (shingles), influenza, COVID
- Preventive strategies (prophylaxis) are recommended
 - Hand-washing, avoiding sick contacts
 - Vaccines/pre-exposure antibodies
 - Other precautions (antibiotics, growth factors)



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Demographic Risk Factors: Multiple Myeloma

- Older age
- Male sex
- Obesity
- Race
 - ↑ Blacks (2× Whites)
 - Ashkenazi Jews
 - Europe: Ireland
 - ↓ Asian

Family history risks

One first-degree relative with multiple myeloma

Relatives of multiple myeloma patients have more monoclonal gammopathy of undetermined significance (MGUS)

Schinasi LH et al. *Br J Haematol*. 2016;175:87.
Thordardottir M et al. *Blood Adv*. 2017;1:2186.



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Following the Proper Path Will Help Patients Get the Best Treatment and Results for Their Specific Type of Myeloma



Right Team

Access experts and centers that have extensive experience treating multiple myeloma



Right Tests

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



Right Treatment

Work with your team to decide on the best treatment plan and identify clinical trials that are right for you



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The Right Team

Available resources



Connect with a myeloma specialist—a doctor who diagnoses and treats a high number of myeloma patients



MMRF's online myeloma treatment locator: themmrf.org/resources/find-a-treatment-center



Seek a second opinion at any point in your journey



Contact the MMRF Patient Navigation Center: themmrf.org/resources/patient-navigation-center
1-888-841-MMRF (6673)



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The Right Tests

Common laboratory tests conducted

Blood tests



- Complete blood count (CBC)
- Complete metabolic panel (CMP)
- Chemistries
 - Calcium
 - Creatinine
 - Lactate dehydrogenase (LDH)
 - Beta-2 microglobulin
- Serum protein electrophoresis (SPEP) with immunofixation electrophoresis (IFE)
- Serum free light chain assay (SFLC)

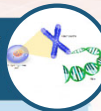
Confirms the type of myeloma

Urine tests



- Urine protein electrophoresis (UPEP) with IFE
- 24-hour urine

Bone marrow biopsy



- Conventional
 - Fluorescence in situ hybridization (FISH)
- New
 - Genomic sequencing

Determines how advanced the myeloma is and identifies the myeloma subtype

Imaging tests



- X-ray
- MRI
- Whole-body, low-dose CT scan
- PET scan
- Metastatic bone survey

Assess changes in the bone structure and determine the number and size of tumors in the bone

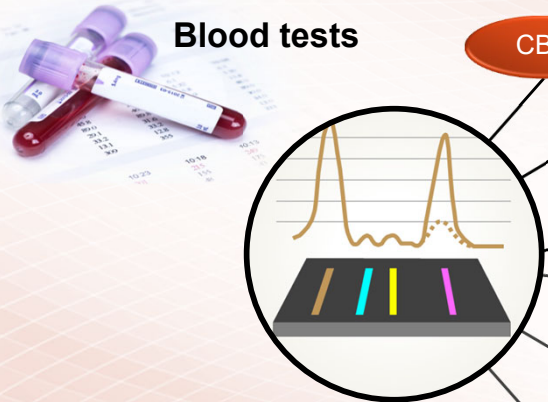
Detects the extent of bone disease and the presence of myeloma outside of the bone marrow



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Learn Your Labs!

Blood Tests



Blood tests

CBC

- Number of red blood cells, white blood cells, and platelets

CMP

- Measure levels of albumin, calcium, lactate dehydrogenase (LDH), blood urea nitrogen (BUN), and creatinine. Assess function of kidney, liver, and bone status and the extent of disease

B2M

- Determine the level of a protein that indicates the presence/extent of MM and kidney function

SPEP

- Detect the presence and level of M protein


IFE

- Identify the type of abnormal antibody proteins

SFLC

- Freelite test measures light chains (kappa or lambda)


CBC, complete blood count; CMP, complete metabolic panel; B2M; beta-2 microglobulin; SPEP, serum protein electrophoresis; IFE, immunofixation electrophoresis; SFLC, serum free light chain assay



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Learn Your Labs!

Urine Tests



Urine tests


UPEP

- Detect Bence Jones proteins (otherwise known as myeloma light chains)

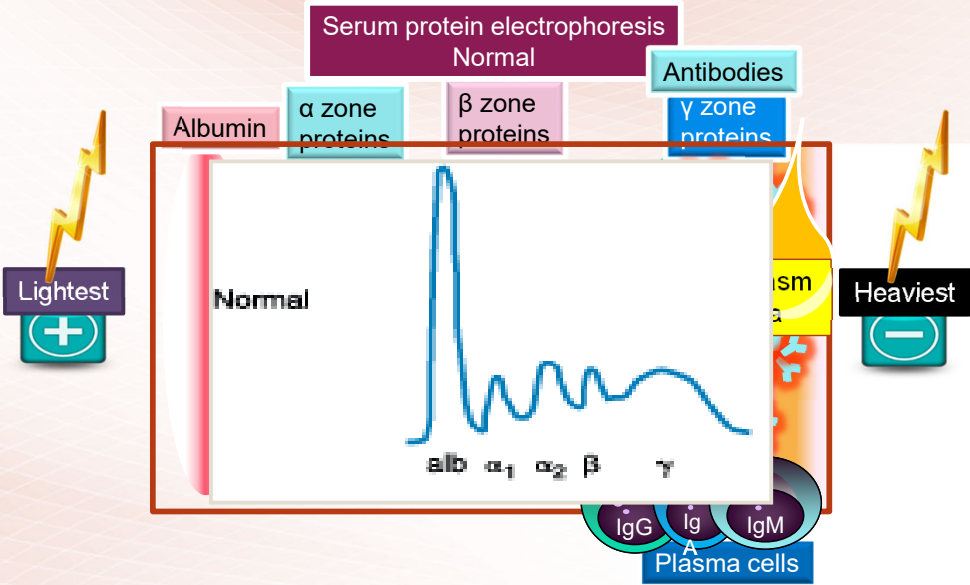
24-hr urine analysis

- Determine the presence and levels of M protein and Bence Jones protein

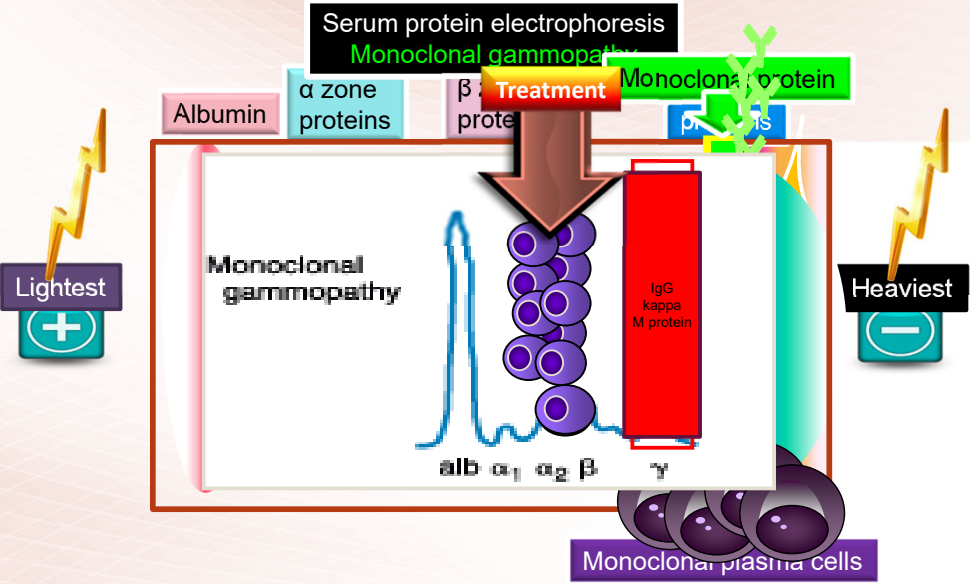
UPEP, urine protein electrophoresis



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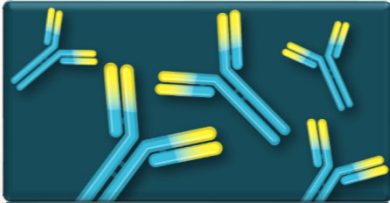


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Types of Multiple Myeloma Based on Blood or Urine Tests



Intact M protein

- Named for the type of immunoglobulin and light chain pair; for example, IgG kappa (κ) or IgG lambda (λ)

80%



Light chain only

- Also known as Bence Jones protein
- Renal failure more common in light chain multiple myeloma

20%



Non-secretory

- No M protein present

3%



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Know Your Imaging Tests!

Assess changes in the bone structure and determine the number and size of tumors in the bone

X-ray



Conventional x-rays reveal punched-out lytic lesions, osteoporosis, or fractures in 75% of patients.

MRI



CT scan



PET scan



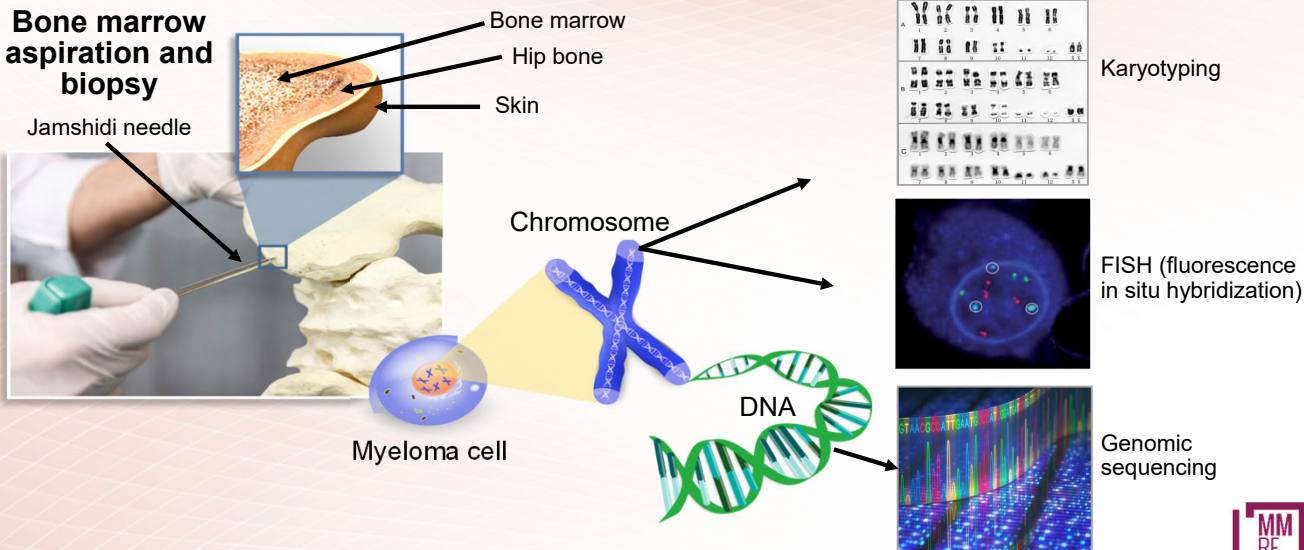
MRI and PET/CT appear to be more sensitive (85%) than skeletal x-rays for the detection of small lytic bone lesions.



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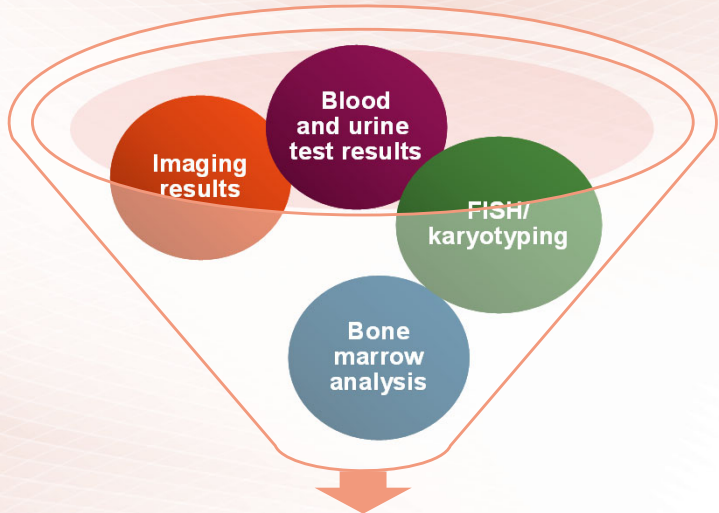
Know Your Bone Marrow Tests!

Bone marrow aspiration and biopsy



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Putting the Results Together



Staging, prognosis, and risk assessment

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Multiple Myeloma Prognosis and Risk

Revised-International Staging System (R-ISS)

R-ISS stage	Laboratory measurements
I	<ul style="list-style-type: none">Serum β2M level <3.5 mg/LSerum albumin level ≥3.5 g/dLNo high-risk CA*Normal LDH level
II	All other possible combinations
III	<ul style="list-style-type: none">Serum β2M level ≥5.5 mg/LHigh-risk CA* or high LDH level

*High-risk chromosomal abnormality (CA) by FISH: del(17p) and/or t(4;14) and/or t(14;16)

β2M; beta-2 microglobulin; LDH, lactate dehydrogenase
Greipp PR et al. *J Clin Oncol.* 2005;23:3412.; Palumbo A et al. *J Clin Oncol.* 2015;33:2863; Mikhael JR et al. *Mayo Clin Proc.* 2013;88:360.

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

High risk

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

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

Standard risk

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

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



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Multiple Myeloma Prognosis and Risk

Many blood test and bone marrow biopsy test results can determine a patient's risk for myeloma that is aggressive (high risk) or not (standard risk) based on the revised-International Staging System (R-ISS)

Standard risk



- Serum β2M level <3.5 mg/L
- Serum albumin level ≥3.5 g/dL
- No high-risk chromosomal abnormality*
- Normal LDH level



All other possible combinations of the test results means that a patient is **R-ISS stage II**

High risk



- Serum β2M level ≥5.5 mg/L
- High-risk chromosomal abnormality* or high LDH level

*High-risk chromosomal abnormality by FISH: del(17p) and/or t(4;14) and/or t(14;16)
β2M; beta-2 microglobulin; LDH, lactate dehydrogenase; FISH, fluorescent in situ hybridization



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The Right Treatment



Know the treatment options available to you based on your myeloma subtype at each stage of your disease.



Be aware of the pros and cons of each option.



Clearly communicate your treatment goals and concerns to the care team.



Find clinical trials that are right for you.



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Getting the Right Treatment: Goals of Multiple Myeloma Therapy



Reduce the amount of M protein (as measured by serum protein electrophoresis) or light chains (as measured via the free light chain test) to the lowest level possible.



Eliminate myeloma cells from the bone marrow (as measured via minimal residual disease [MRD] testing).



Improve quality of life with as few treatment side effects as possible.



Provide the longest possible period of response before first relapse.



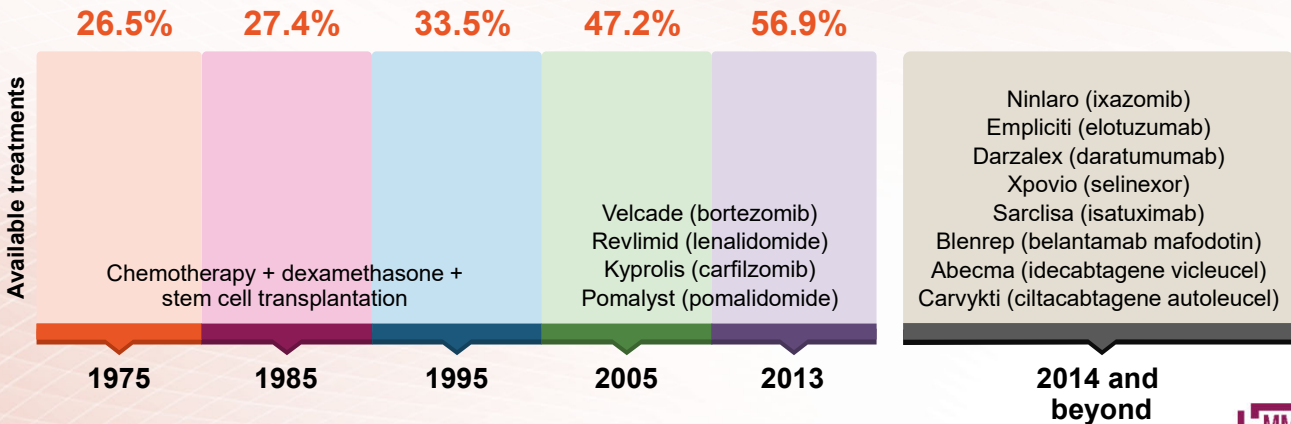
Prolong overall survival.



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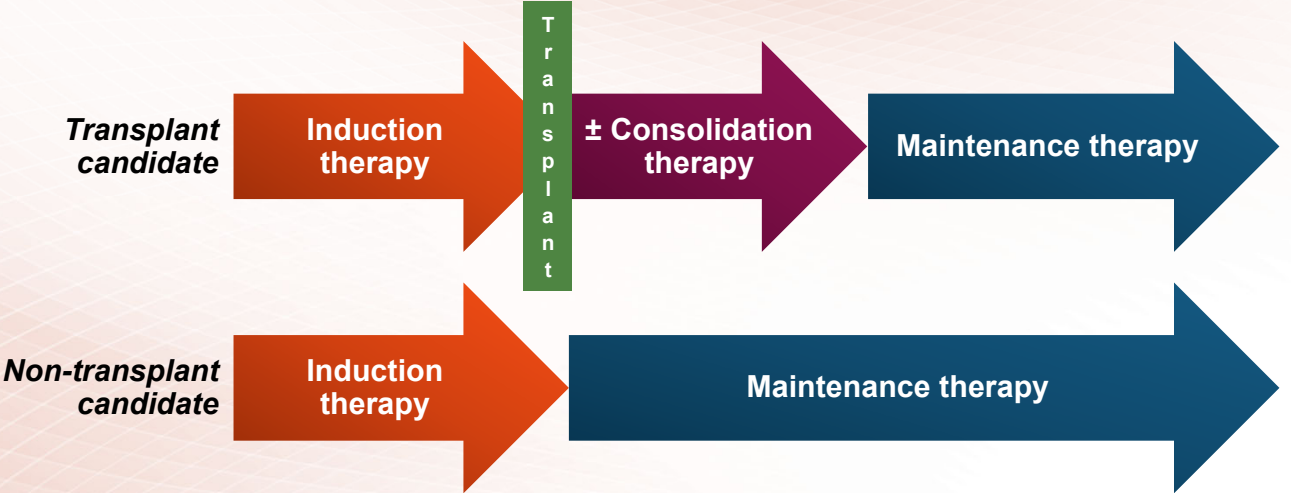
Myeloma Survival Has Improved Over Time Mainly Due to Current Drugs

The percentage of people expected to survive 5 years or more after being diagnosed with myeloma



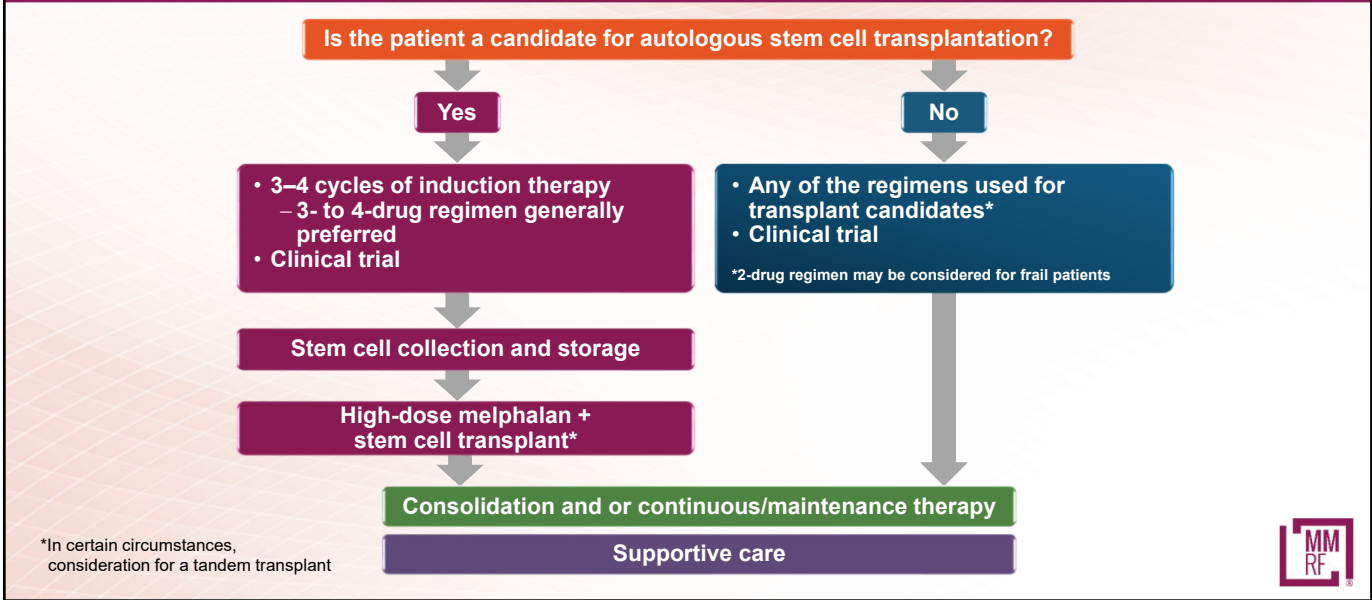
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Current Treatment Paradigm for Newly Diagnosed Multiple Myeloma



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Overview of Treatment Approach for Active Multiple Myeloma



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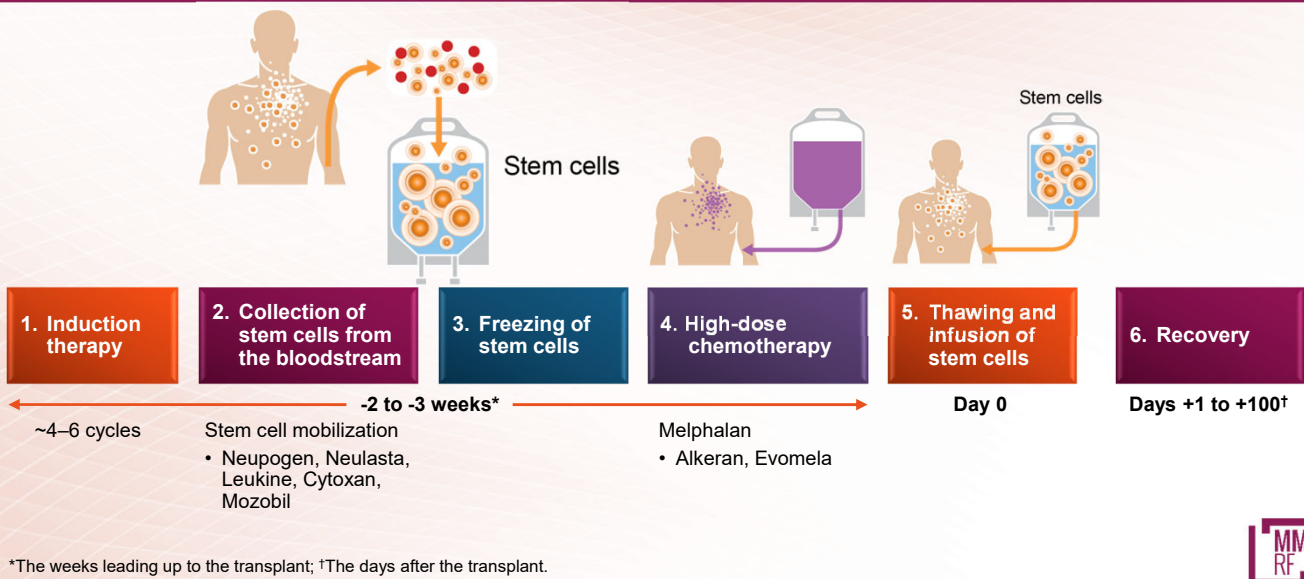
Induction Therapy Regimens

	Preferred	Recommended	Certain circumstances
Transplant eligible	<ul style="list-style-type: none">• Revlimid-Velcade-dex (RVd)*	<ul style="list-style-type: none">• Kyprolis-Revlimid-dex (KRd)• Ninlaro-Revlimid-dex (IRd)• Darzalex-Revlimid-Velcade-dex (D-RVd)	<ul style="list-style-type: none">• Velcade-Cytosan-dex (VCd)• Kyprolis-Cytosan-dex (KCd)• Ninlaro-Cytosan-dex (ICd)• Revlimid-Cytosan-dex (RCd)• Velcade-Thalomid-dex (VTd)*• Velcade-Doxil-dex (VDd)• Darzalex-Velcade-Revlimid-dex (D-VRd)• Darzalex-Kyprolis-Revlimid-dex (D-KRd)• Darzalex-Cytosan-Velcade-dex (D-VCd)• Darzalex-Velcade-Thalomid-dex (D-VTd)• VTD-PACE
Transplant ineligible	<ul style="list-style-type: none">• Revlimid-Velcade-dex (RVd)*• Darzalex-Revlimid-dex (DRd)*	<ul style="list-style-type: none">• Kyprolis-Revlimid-dex (KRd)• Ninlaro-Revlimid-dex (IRd)• Darzalex-Velcade-melphalan-prednisone (D-VMP)*• Darzalex-Cytosan-Velcade-dex (D-VCd)	<ul style="list-style-type: none">• Velcade-dex (Vd)• Revlimid-dex (Rd)*• Velcade-Cytosan-dex (VCd)• Revlimid-Cytosan-dex (RCd)• Kyprolis-Cytosan-dex (KCd)• Revlimid-Velcade-dex (RVd)-lite

*Category 1 recommendation. Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
National Comprehensive Cancer Network Guidelines Version 1.2022. Multiple Myeloma.

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Autologous Stem Cell Transplantation



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Continuous or Maintenance Therapy Options

	Preferred	Recommended	Certain circumstances
Transplant eligible	• Revlimid*	• Ninlaro* • Velcade	• Velcade-Revlimid ± dex
Transplant ineligible	• Revlimid*	• Ninlaro* • Velcade	• Velcade-Revlimid

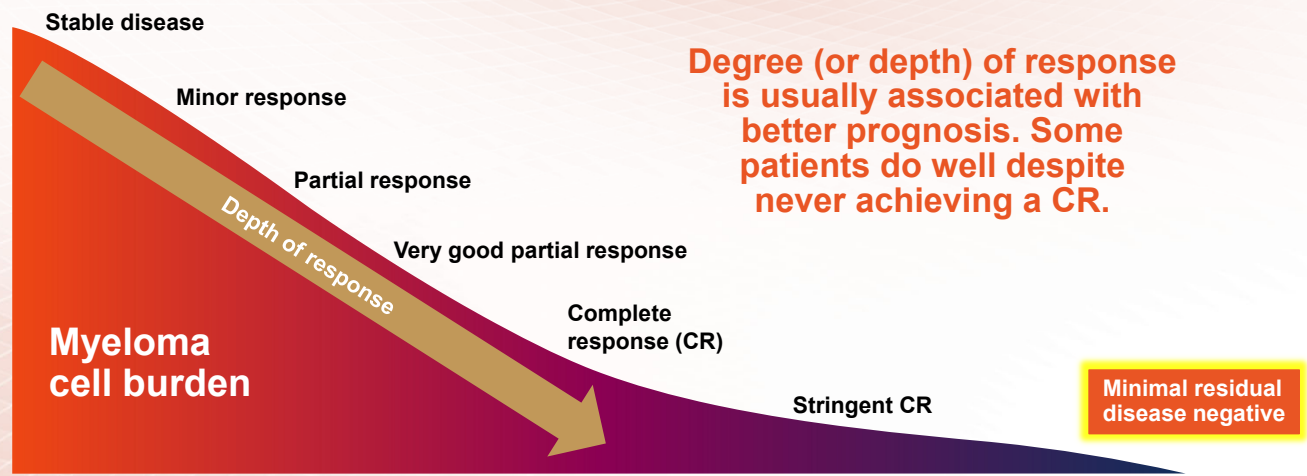
Additional agents under investigation: Darzalex, Empliciti, Kyprolis

*Category 1 recommendation. Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
National Comprehensive Cancer Network Guidelines Version 1.2022. Multiple Myeloma.



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Measuring Response to Therapy



ClonoSEQ is an FDA-approved next-generation sequencing (NGS) test to measure MRD in MM patients.
Palumbo A et al. *J Clin Oncol*. 2014;32:587.
Kumar S et al. *Lancet Oncol*. 2016;17:e328.



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Where is the myeloma field going?

- Staging with genomics and advanced imaging
- Higher efficacy using four-drug regimens
- Precision medicine and targeted therapies in subsets of patients—for example, t(11;14)
- MRD-driven therapy
- Minimize long-term toxicities since myeloma patients living (much) longer
- New drug classes and immunotherapies



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Summary

- Multiple myeloma is a rare blood cancer that can negatively affect the bones, kidneys, and the bone marrow, leading to lowered blood counts.
- The prognosis of multiple myeloma depends on the genetic makeup of myeloma cell chromosomes; R-ISS is used for staging in multiple myeloma.
- Survival rates are improving because of new drugs and new combinations of drugs.
- The treatment paradigm will continue to change with the approval of additional novel agents.
- Knowledge is power: right team, right test, right treatment.

Be an informed and empowered part of your health care team!



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**Please take a moment to
answer two questions
about this presentation.**



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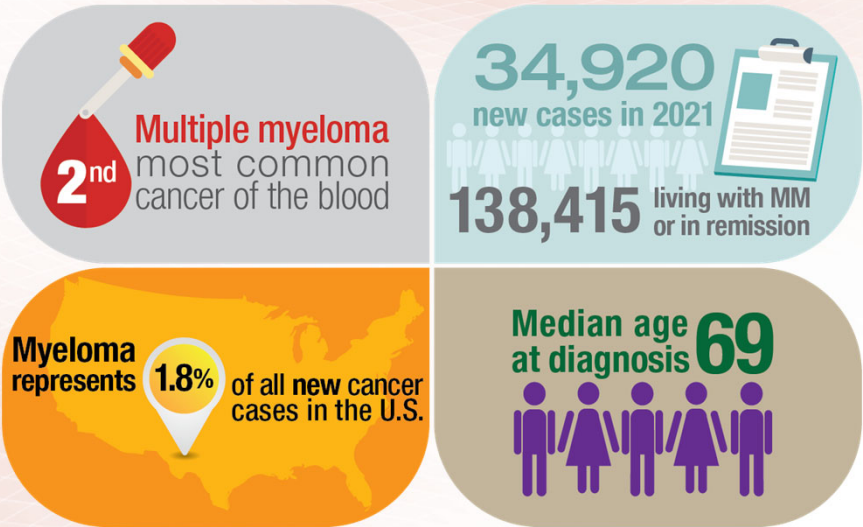


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Health Care Disparities in Multiple Myeloma

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How common is multiple myeloma?

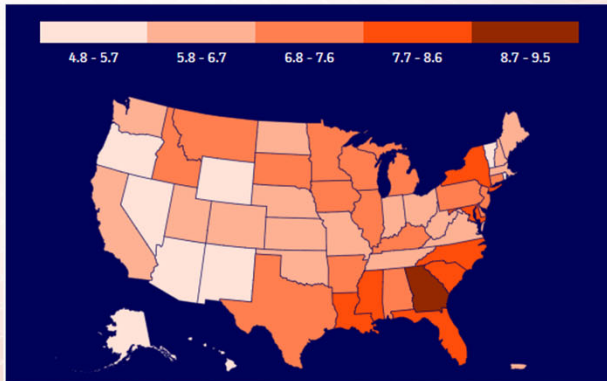


SEER Cancer Stat Facts: Myeloma. National Cancer Institute. Bethesda, MD, <http://seer.cancer.gov/statfacts/html/mulmy.html>



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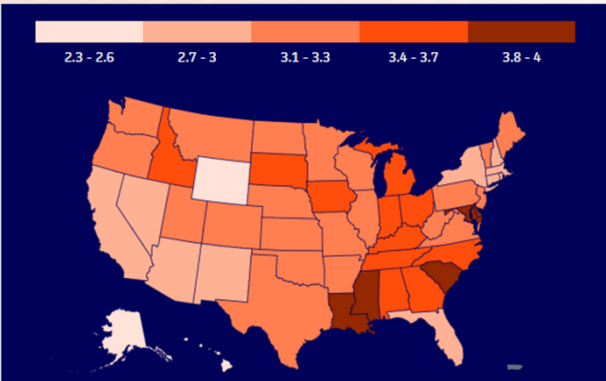
Incidence rates, 2014–2018
Myeloma, by state



Average annual rate per 100,000, age adjusted to the 2000 US standard population.

Data sources: North American Association of Central Cancer Registries (NAACCR), 2021

Death rates, 2015–2019
Myeloma, by state



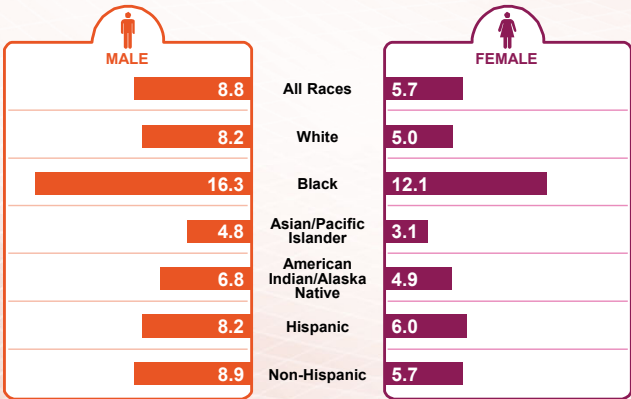
Average annual rate per 100,000, age adjusted to the 2000 US standard population.

Data sources: National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention, 2021



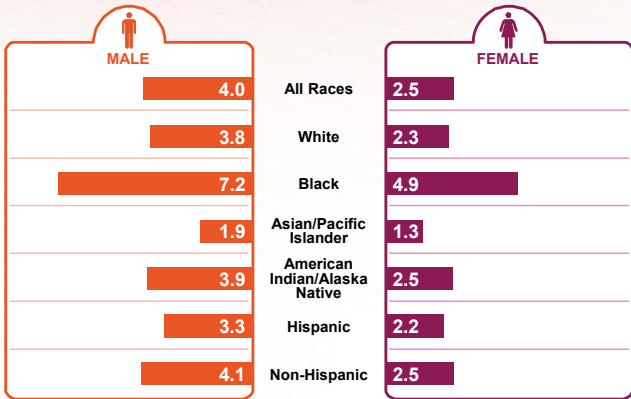
Multiple Myeloma Is Twice
as Common in Black Patients

Rate of new cases per 100,000
persons by race/ethnicity and sex



SEER 21 2014-2018, Age-Adjusted

Death rate per 100,000
persons by race/ethnicity and sex



U.S. 2015-2019, Age-Adjusted

SEER Cancer Stat Facts: Myeloma. National Cancer Institute. Bethesda, MD, <http://seer.cancer.gov/statfacts/html/mulmy.html>

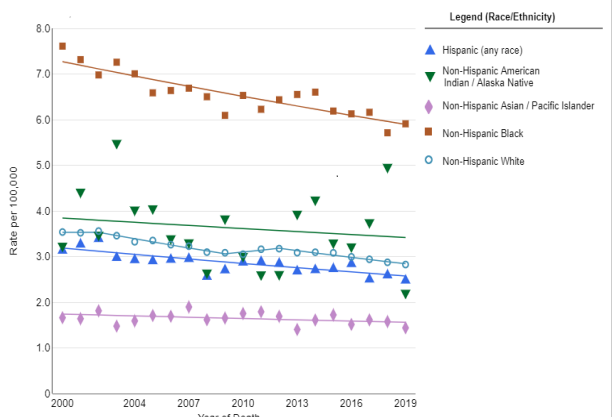


Multiple Myeloma Incidence and Mortality by Race/Ethnicity

Myeloma
Recent Trends in SEER Age-Adjusted Incidence Rates, 2000-2019
By Race/Ethnicity, Delay-adjusted SEER Incidence Rate, Both Sexes, All Ages, All Stages



Myeloma
Recent Trends in U.S. Age-Adjusted Mortality Rates, 2000-2019
By Race/Ethnicity, Both Sexes, All Ages



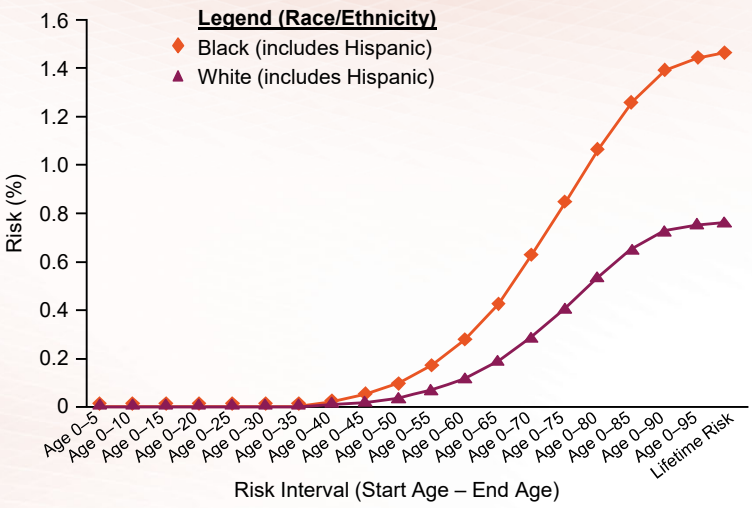
SEER Cancer Stat Facts: Myeloma. National Cancer Institute. Bethesda, MD. <https://seer.cancer.gov/statistics-network/explorer/application.html>



59

Risk of Myeloma Diagnosis by Age

Black patients are diagnosed at an earlier age and have a twofold risk of being diagnosed with multiple myeloma



Data from National Cancer Institute
Surveillance, Epidemiology, and End Results Program (SEER)



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Multiple Myeloma in Black Patients



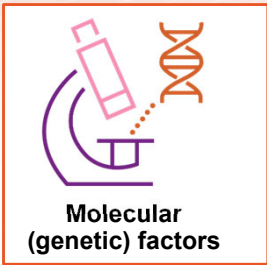
Demographics

- ↑ Myeloma prevalence (2× White patients)¹
- Older adults have ↑ prevalence of the myeloma precursor condition MGUS²
- Younger³⁻⁵



Clinical factors

- ↑ Comorbidities^{3,6}
- ↑ Incidence of all myeloma-defining events (for example, hypercalcemia, renal dysfunction, anemia, dialysis) **except bone fractures**⁷



Molecular (genetic) factors

- Significant differences in the frequency of certain chromosomal abnormalities:
 - High risk cytogenetics including del17p are seen **less frequently**⁸
 - Some other mutations seen more frequently but significance not known⁹



Treatment

- Significantly lower stem cell transplant utilization^{7,9-13}

1. SEER Cancer Stat Facts: Myeloma. National Cancer Institute. Bethesda, MD. <http://seer.cancer.gov/statfacts/html/mulmy.html>. 2. El-Khoury H et al. *Blood*. 2021;138. Abstract 152. 3. Blue B et al. *Br J Haematol*. 2017;176:322. 4. Waxman AJ et al. *Blood*. 2010;116:5501. 5. Ailawadhi S et al. *Blood Cancer J*. 2018;8:67. 6. Schoen MW et al. *Blood*. 2019;134. Abstract 383. 7. Ailawadhi S et al. *Cancer*. 2018;124:1710. 8. Baker A et al. *Blood*. 2013;121:3147. 9. Manojlovic Z et al. *PLoS Genet*. 2017;13:e1007087. 10. Ailawadhi S et al. *Cancer Med*. 2017;6:2876. 11. Fiala M et al. *Cancer*. 2017;123:1590. 12. Costa LJ et al. *Biol Blood Marrow Transplant*. 2015;21:701. 13. Vardell VA et al. *Blood*. 2019;134. Abstract 423.



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Disparities in Care in Black Patients

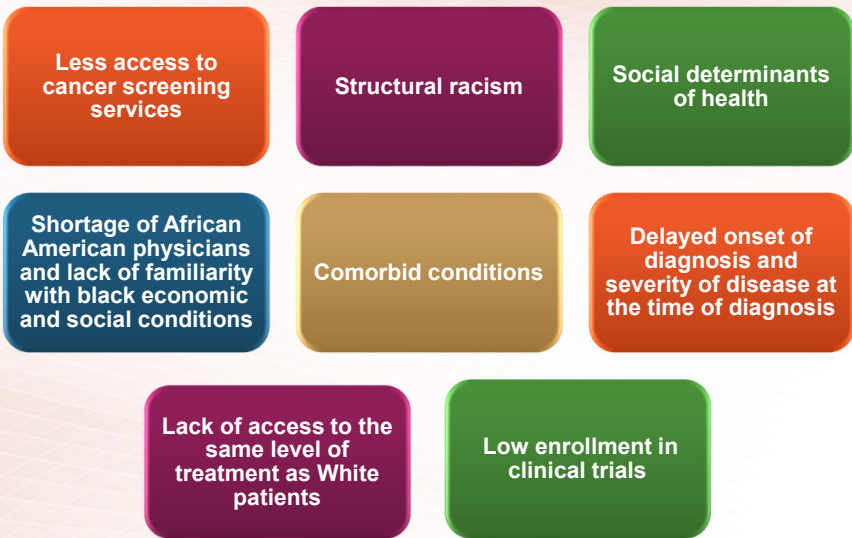
- Several studies have shown that the use of standard therapies tends to be significantly lower in Black patients
- However, with equal access to standard therapy, the outcome in Black patients is equal or superior to that of White patients

Treatment type	Use in Black patients	Use in White patients	P value
Triplet therapy	47%	61%	0.004
Stem cell transplantation	30%	40%	0.034



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Reasons for Disparities in Outcomes for Black Americans With Multiple Myeloma and Other Cancers



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Key Points

- Despite disparities in incidence and outcomes of multiple myeloma among Black patients, evidence suggests that these disparities can be overcome:
 - ✓ Ensure equal access to appropriate therapeutic options for Black patients
 - ✓ Increase awareness of these disparities and their solutions to patients, physicians, and the communities



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**Please take a moment to
answer two questions
about this presentation.**



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Town Hall Questions & Answers



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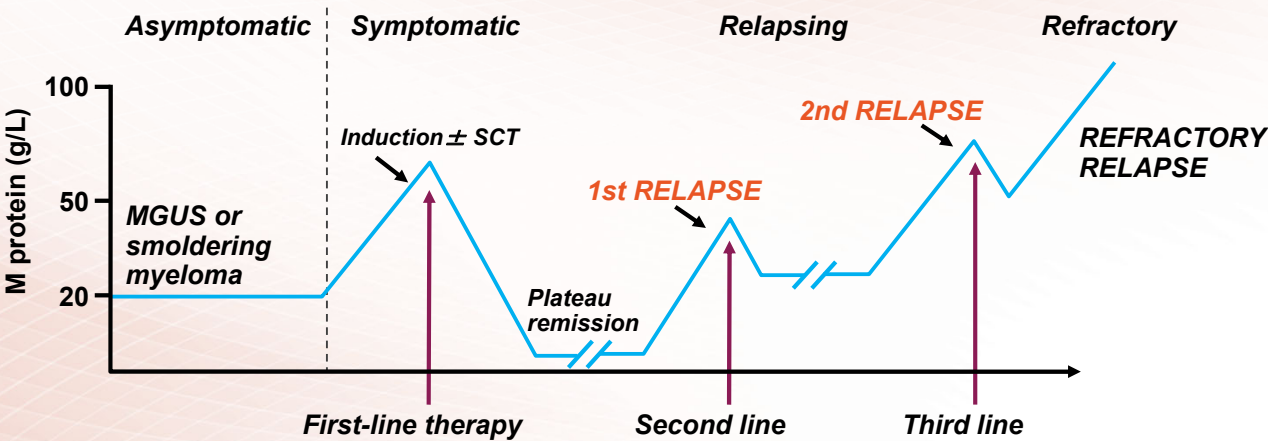
Treating Relapsed/Refractory Multiple Myeloma

David H. Vesole, MD, PhD, FACP

MedStar Georgetown University Hospital
Georgetown University School of Medicine
Washington, District of Columbia
John Theurer Cancer Center, Hackensack Meridian School of Medicine
Hackensack, New Jersey

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Multiple Myeloma Is a Marathon, Not a Sprint



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



68

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

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



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Biochemical Relapse or Clinical Relapse

Biochemical

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



Timing of therapy initiation/escalation dependent on many factors

Clinical

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



Requires immediate initiation/escalation of therapy



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Choosing Therapy for First or Second Relapse

Choices are broadest and guided by

Disease biology

Nature of relapse

Patient preference

Factors to consider

Prior autologous stem cell transplant

Prior therapies

Aggressiveness of relapse

Comorbidities

Psychosocial issues

Access to care



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Options for Relapsed/Refractory Disease Continue to Increase

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

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

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



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Treatment Approach

First relapse

Proteasome inhibitor (PI)/ immunomodulatory drug (IMiD)/ antibody-based therapy

>1 Relapse

Any options for first relapse not tried

Refractory to Velcade **and** Revlimid

DKd, Isa-Kd, DPd, Elo-Pd, Isa-Pd, or KPd

Refractory to an IMiD but sensitive to a PI

DVd, SVd, Ven-Vd (for t[11;14])*

or

Triple-class refractory

Approved therapies

Sd, belamaf, ide-cel, cilta-cel, Tecvayli

Clinical trials

Bispecific/ trispecific antibodies, cellular therapies (CAR T-cells, NK cells), CELMoDs

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

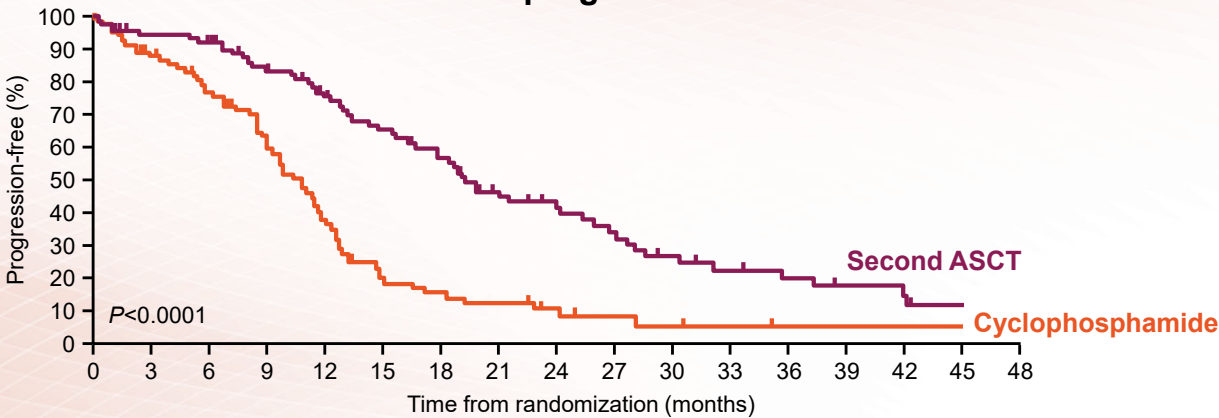
*Not yet approved for use in myeloma patients.



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Second ASCT an Option for Early Relapse

Time to progression



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









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Proteasome Inhibitor– and Immunomodulatory Drug–Based Regimens for Early Relapse



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Currently Available Agents for One to Three Prior Lines of Therapy

Drug		Formulation	Approval
Velcade (bortezomib)		<ul style="list-style-type: none">• IV infusion• SC injection	<ul style="list-style-type: none">• For relapsed/refractory myeloma
Kyprolis (carfilzomib)		<ul style="list-style-type: none">• IV infusion• Weekly dosing	<ul style="list-style-type: none">• For relapsed/refractory myeloma as a single agent, as a doublet with dexamethasone, and as a triplet with Revlimid or Darzalex plus dexamethasone
Ninlaro (ixazomib)		Once-weekly pill	<ul style="list-style-type: none">• For relapsed/refractory myeloma as a triplet with Revlimid and dexamethasone
Revlimid (lenalidomide)*		Once-daily pill	<ul style="list-style-type: none">• For relapsed/refractory myeloma in combination with dexamethasone
Pomalyst (pomalidomide)*		Once-daily pill	<ul style="list-style-type: none">• For relapsed/refractory myeloma in combination with dexamethasone
XPOVIO (selinexor)		Once-weekly pill	<ul style="list-style-type: none">• For relapsed/refractory myeloma as a triplet with Velcade and dexamethasone

*Black box warnings: embryo-fetal toxicity; hematologic toxicity (Revlimid); venous and arterial thromboembolism

IV, intravenous; SC, subcutaneous



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Proteasome Inhibitor– and Immunomodulatory Drug–Based Regimens for Early Relapse

	OPTIMISMM	ASPIRE	TOURMALINE-MM1	BOSTON
Regimens compared	• Velcade-Pomalyst-dex (VPd) vs Vd	• Kyprolis-Revlimid-dex (KRd) vs Rd	• Ninlaro-Rd (IRd) vs Rd	• XPOVIO-Velcade-dex (XPO-Vd) vs Vd
Median progression-free survival favored	• VPd: 11 vs 7 months	• KRd: 26 vs 17 months	• IRd: 21 vs 15 months	• XPO-Vd: 14 vs 9 months
Clinical considerations	• Consider for relapse on Revlimid • VPd associated with more low blood counts, infections, and neuropathy than Pd	• KRd associated with more upper respiratory infections and high blood pressure than Rd	• IRd an oral regimen • Gastrointestinal toxicities and rashes • Lower incidence of peripheral neuropathy	• XPO-Vd associated with low platelet counts and fatigue with triplet, but less neuropathy than the Vd



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Important Considerations for Use of Proteasome Inhibitors

Velcade <ul style="list-style-type: none">• Risk of peripheral neuropathy (PN); numbness, tingling, burning sensations and/or pain due to nerve damage<ul style="list-style-type: none">– Avoid in patients with severe existing PN– Reduced with subcutaneous once-weekly dosing• High risk of shingles<ul style="list-style-type: none">– Use appropriate vaccination• No dose adjustment for kidney issues; adjust for liver issues	Kyprolis <ul style="list-style-type: none">• Less PN than Velcade• High risk of shingles<ul style="list-style-type: none">– Use appropriate vaccination• Monitor for heart, lung, and kidney side effects<ul style="list-style-type: none">– Use with caution in older patients with cardiovascular risk factors• High blood pressure• No dose adjustment for kidney issues; adjust for liver issues	Ninlaro <ul style="list-style-type: none">• Less PN than Velcade• High risk of shingles<ul style="list-style-type: none">– Use appropriate vaccination• Monitor for rashes and gastrointestinal (GI) side effects<ul style="list-style-type: none">– GI effects occur early• Needs to be taken at least 1 hour before or 2 hours after a meal
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Important Considerations for Use of Immunomodulatory Drugs

Revlimid*

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

Pomalyst*

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

*Black box warning



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Important Considerations for Use of XPOVIO



Gastrointestinal

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



Low sodium (hyponatremia)

Maintain fluid intake.
Salt tabs



Fatigue

Stay hydrated and active.



Low blood counts (cytopenias)

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

Chari A et al. *Clin Lymphoma Myeloma Leuk.* 2021;21:e975.






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Monoclonal Antibody–Based Regimens at Relapse



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Currently Available Naked Monoclonal Antibodies for One to Three Prior Lines of Therapy

Drug		Formulation	Approval
Darzalex (daratumumab)		SC once a week for first 8 weeks, then every 2 weeks for 4 months, then monthly	• For relapsed/refractory myeloma as a single agent and as a triplet with Revlimid or Velcade or Kyprolis or Pomalyst plus dexamethasone
Empliciti (elotuzumab)		IV once a week for first 8 weeks, then every 2 weeks (or every 4 weeks with pom)	• For relapsed/refractory myeloma as a triplet with Revlimid or Pomalyst and dexamethasone
Sarclisa (isatuximab)		IV once a week for first 4 weeks, then every 2 weeks	• For relapsed/refractory myeloma as a triplet with Pomalyst or Kyprolis and dexamethasone

IV, intravenous; SC, subcutaneous



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Monoclonal Antibody–Based Regimens for Early Relapse: Darzalex

	POLLUX	CASTOR	CANDOR	APOLLO
Regimens compared	• Darzalex-Revlimid-dex (DRd) vs Rd	• Darzalex-Velcade-dex (DVd) vs Vd	• Darzalex-Kyprolis-dex (DKd) vs Kd	• Darzalex-Pomalyst-dex (DPd) vs Pd
Median progression-free survival favored	• DRd: 45 vs 18 months	• DVd: 17 vs 7 months	• DKd: 29 vs 15 months	• DPd: 12 vs 7 months
Clinical considerations	<ul style="list-style-type: none">• Consider for relapses from Revlimid or Velcade maintenance• DRd associated with more upper respiratory infections, low blood white blood cell counts, and diarrhea	<ul style="list-style-type: none">• Consider for patients who are Revlimid-refractory without significant neuropathy• DVd associated with more low blood cell counts	<ul style="list-style-type: none">• Consider for younger, fit patients who are double-refractory to Revlimid and Velcade• DKd associated with more respiratory infections• Severe side effects (possibly fatal) in intermediate fit patients 65 and older	<ul style="list-style-type: none">• Consider in patients who are double-refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro)• Severe low white blood cell counts



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Important Considerations for Use of Darzalex

Darzalex
<ul style="list-style-type: none">• Infusion reactions<ul style="list-style-type: none">– Less with SC use• Risk of shingles<ul style="list-style-type: none">– Use appropriate vaccination• Increased risk of hypogammaglobulinemia and upper respiratory infections<ul style="list-style-type: none">– Bactrim prophylaxis– IVIG support



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

	ELOQUENT-2	ELOQUENT-3	ICARIA-MM	IKEMA
Regimens compared	• Empliciti-Revlimid-dex vs Rd	• Empliciti-Pomalyst-dex vs Pd	• Sarclisa-Pomalyst-dex vs Pd	• Sarclisa-Kyprolis-dex vs Kd
Median progression-free survival favored	• Empliciti-Rd: 19 vs 15 months	• Empliciti-Pd: 10 vs 5 mos	• Sarclisa-Pd: 12 vs 7 mos	• Sarclisa-Kd: 36 vs 19 mos
Clinical considerations	<ul style="list-style-type: none">• Consider for non-Revlimid refractory, frailer patients• Overall survival benefit with Empliciti-Rd• Empliciti-Rd associated with more infections	<ul style="list-style-type: none">• Consider for patients refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro)	<ul style="list-style-type: none">• Consider for patients refractory to Revlimid and a proteasome inhibitor (Velcade, Kyprolis, Ninlaro)• Sarclisa-Pd associated with severe low white blood cell counts, more dose reductions, upper respiratory infections, and diarrhea	<ul style="list-style-type: none">• Consider for patients refractory to Revlimid and Velcade• Sarclisa-Kd associated with higher MRD negativity rates• Sarclisa-Kd associated with severe respiratory infections



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Important Considerations for Use of Monoclonal Antibodies

Empliciti <ul style="list-style-type: none">• Infusion reactions• Risk of shingles<ul style="list-style-type: none">– Use appropriate vaccination	Sarclisa <ul style="list-style-type: none">• Infusion reactions• Risk of shingles<ul style="list-style-type: none">– Use appropriate vaccination
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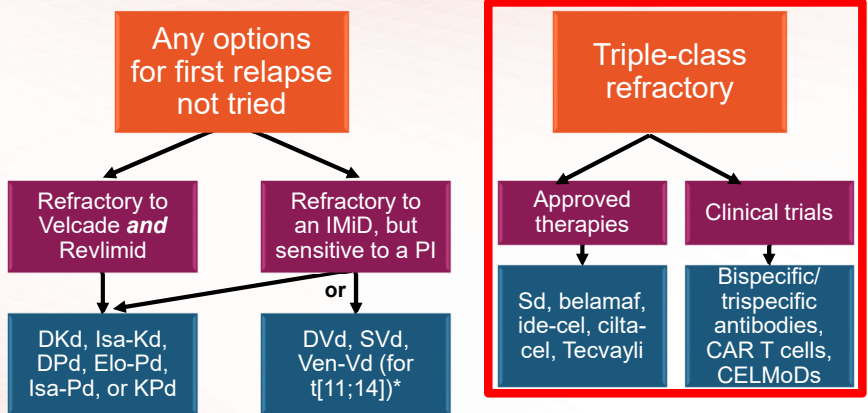
86

Treatment Approach

First relapse

Proteasome inhibitor (PI)/ immunomodulatory drug (IMiD)/ antibody-based therapy

>1 Relapse



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

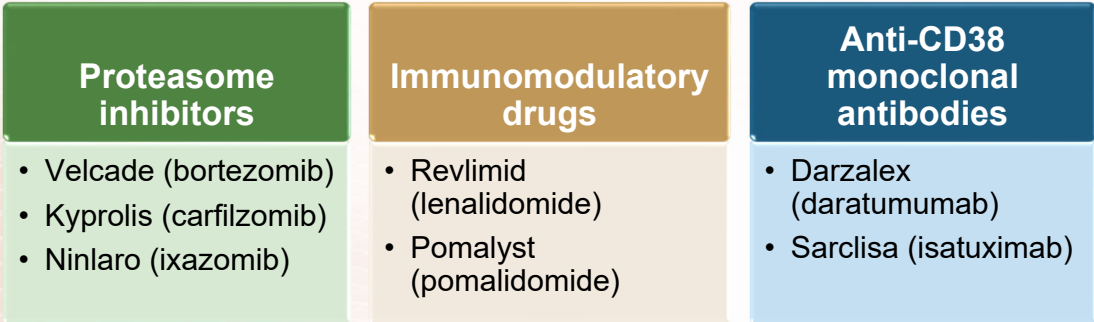
*Not yet approved for use in myeloma patients.



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Triple-Class Refractory

- For patients with relapsed or refractory multiple myeloma who have received treatment with—and did not respond satisfactorily to, or progressed while on treatment with—the three main classes of drugs currently used to treat myeloma are...



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Currently Available Drugs for Triple-Class Refractory Myeloma

Class	Drug		Formulation	Approval
Nuclear export inhibitor	XPOVIO (selinexor)		Twice-weekly pill	• For relapsed/refractory myeloma in combination with dexamethasone (after at least 4 prior therapies and whose disease is refractory to at least 2 PIs, at least 2 IMiDs, and an anti-CD38 mAb)
Antibody-drug conjugate	Blenrep (belantamab mafodotin)*		2.5 mg/kg IV over approximately 30 minutes once every 3 weeks	• For relapsed/refractory myeloma (after at least 4 prior therapies including an anti-CD38 mAb, a PI, and an IMiD)
Chimeric antigen receptor (CAR) T cell	Abecma (idecabtagene vicleucel)†		300 to 460 × 10 ⁶ genetically modified autologous CAR T cells in one or more infusion bags	• For relapsed/refractory myeloma (after 4 or more prior lines of therapy, including an IMiD, a PI, and an anti-CD38 mAb)
CAR T cell	Carvykti (ciltacabtagene autoleucel)‡		0.5 to 1.0 × 10 ⁶ genetically modified autologous CAR T cells/kg of body weight	• For relapsed/refractory myeloma (after 4 or more prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb)

IMiD, immunomodulatory agent; PI, proteasome inhibitor; mAb, monoclonal antibody

*Black box warning: changes in the corneal epithelium resulting in changes in vision; Blenrep is available only through a restricted distribution program

†Black box warning: cytokine release syndrome; neurologic toxicities; hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS); prolonged cytopenia

‡Black box warning: cytokine release syndrome; neurologic toxicities; Parkinsonism and Guillain-Barré syndrome; hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS); prolonged cytopenia
Abecma and Carvykti are available only through a restricted distribution program



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XPOVIO + Dexamethasone in Relapsed/Refractory Myeloma

	No. patients with ≥PR (%) ¹
Total	32 (26)
Previous therapies to which the disease was refractory, n (%)	
Velcade, Kyprolis, Revlimid, Pomalyst, and Darzalex	21 (25)
Kyprolis, Revlimid, Pomalyst, and Darzalex	26 (26)
Velcade, Kyprolis, Pomalyst, and Darzalex	25 (27)
Kyprolis, Pomalyst, and Darzalex	31 (26)

Additional analyses showed clinical benefit with XPOVIO regardless of patient age and kidney function.^{2,3}

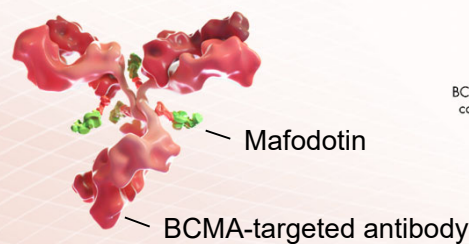
1. STORM Trial. Chari A et al. *N Engl J Med*. 2019;381:727; 2. Gavriatopoulou M et al. Presented at the 17th International Myeloma Workshop; September 12-15, 2019. Abstract FP-110; 3. Vogl DT et al. Presented at the 17th International Myeloma Workshop; September 12-15, 2019. Abstract FP-111.



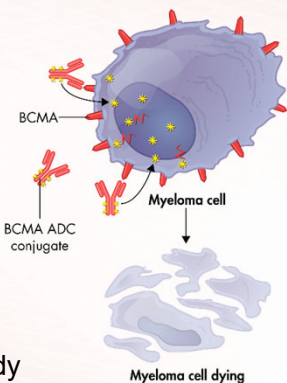
90

Blenrep: Antibody-Drug Conjugate (ADC)

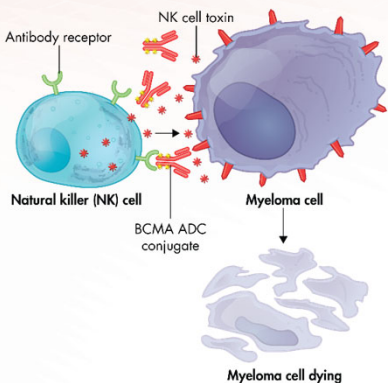
ADCs can selectively target and deliver drugs to myeloma cells.



Active cytotoxic drug is released inside the cell



NK-cell killing via ADCC



ADCC, antibody-dependent cellular cytotoxicity; BCMA, B-cell maturation antigen
Figure adapted from Cho S-F et al. *Front Immunol.* 2018;9:1821. Trudel S et al. *Lancet Oncol.* 2018;19:1641.



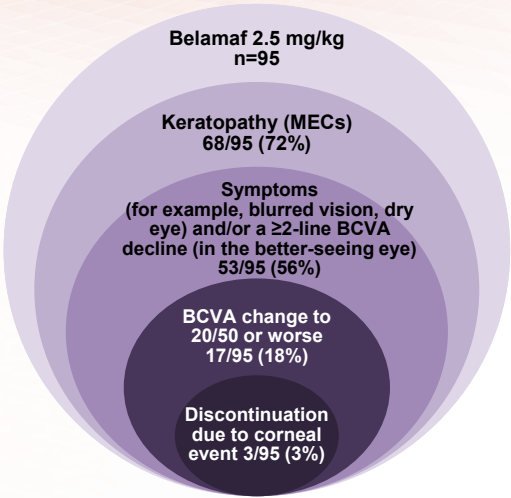
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Blenrep First ADC Approved in MM

DREAMM-2 Study	Blenrep (2.5 mg/kg)
N	97
Median no. lines of therapy, n (range)	7 (3–21)
Overall response rate (%)	31
Median progression-free survival (mos)	2.9
Duration of response (mos)	11

DREAM-2 Study. Lonial S et al. *Lancet Oncol.* 2020;21:207.

Ocular Adverse Events



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Currently Available ADC Side Effects

Blenrep

- Thrombocytopenia
- Keratopathy
- Decrease visual acuity
- Nausea
- Blurred vision
- Fever
- Infusion-related reactions
- Fatigue




Management

- Available only through a Risk Evaluation and Mitigation Strategies (REMS) due to the risk of ocular toxicity
- Patients receive ophthalmic examinations at baseline (within 3 weeks prior to the first dose), prior to each dose, and promptly for worsening symptoms
- Patients are advised to use preservative-free lubricant eye drops at least 4 times a day starting with the first infusion and continuing until end of treatment
- Patients should also avoid use of contact lenses unless directed by an ophthalmologist

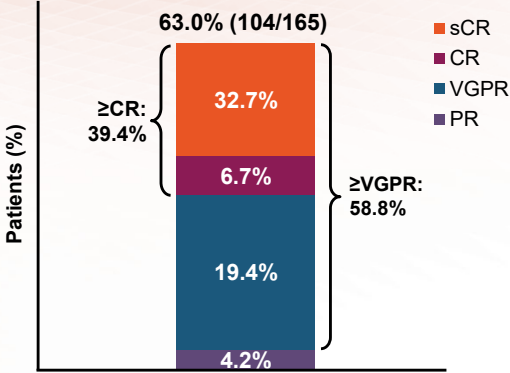


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Now Approved: Tecvayli, the First Bispecific Antibody!

Drug	Formulation	Approval
Tecvayli (teclistamab)*	 Step-up dosing† the first week then once weekly thereafter by subcutaneous injection	• For relapsed/refractory myeloma (after 4 or more prior lines of therapy, including an IMiD, a PI, and an anti-CD38 mAb)

IMiD, immunomodulatory agent; PI, proteasome inhibitor; mAb, monoclonal antibody
*Black box warning: cytokine release syndrome; neurologic toxicities
†Patients are hospitalized for 48 hours after administration of all step-up doses.
Tecvayli is available only through a restricted distribution program.



Median duration of response
18.4 months

Moreau P et al. *N Engl J Med.* 2022;387:495.



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Emerging Therapies for Relapsed/Refractory Multiple Myeloma

Bispecific antibodies

- Elranatamab, talquetamab, cevostamab, and others
- Target BCMA, GPRC5D, or FcRH5 on myeloma cells and CD3 on T cells
- Redirects T cells to myeloma cells

Cereblon E3 ligase modulators (CELMoDs)

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

Small molecule inhibitors

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



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Summary

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



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**Please take a moment to
answer two questions
about this presentation.**



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CAR T-Cell Therapy and Bispecific Antibodies

Edward A. Stadtmauer, MD
Perelman School of Medicine, University of Pennsylvania
Philadelphia, Pennsylvania

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Triple-Class Refractory

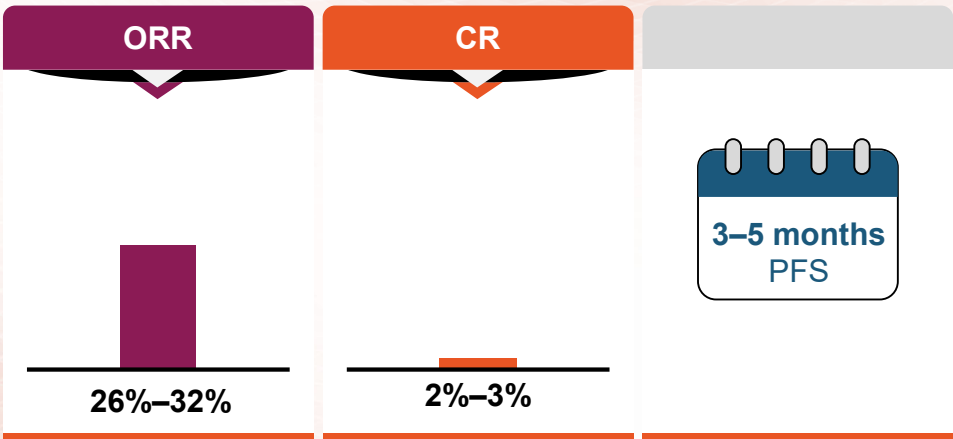
- For patients with relapsed or refractory multiple myeloma who have received treatment with—and did not respond satisfactorily to, or progressed while on treatment with—the three main classes of drugs currently used to treat myeloma are...

Proteasome inhibitors	Immunomodulatory drugs	Anti-CD38 monoclonal antibodies
<ul style="list-style-type: none">Velcade (bortezomib)Kyprolis (carfilzomib)Ninlaro (ixazomib)	<ul style="list-style-type: none">Revlimid (lenalidomide)Pomalyst (pomalidomide)	<ul style="list-style-type: none">Darzalex (daratumumab)Sarclisa (isatuximab)



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Where We've Been: Outcomes for Later-Line Triple Class-Exposed Patients With RRMM



Exposed to an immunomodulatory imide drug, proteasome inhibitor, and CD38 monoclonal antibody
Gandhi UH et al. *Leukemia*. 2019;33(9):2266.



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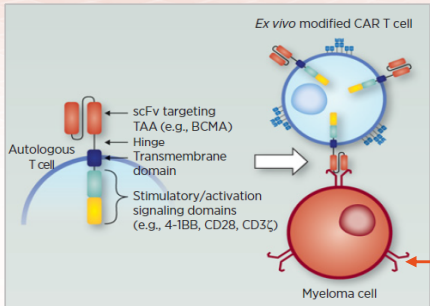
Where We're Going: CAR T-Cell Therapy

Genetically modified T cells designed to recognize specific proteins on MM cells

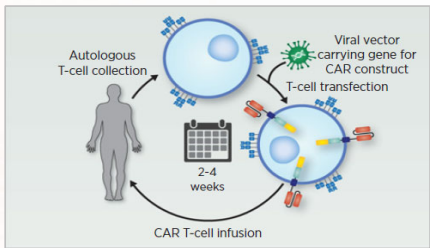
CAR T cells are activated once in contact with the MM cell and can destroy the MM cell

CAR T cells can persist for long periods of time in the body

CAR T cells are created from a patient's own blood cells, but the technology is evolving to develop "off-the-shelf" varieties



B-cell maturation antigen (BCMA)



Examples:

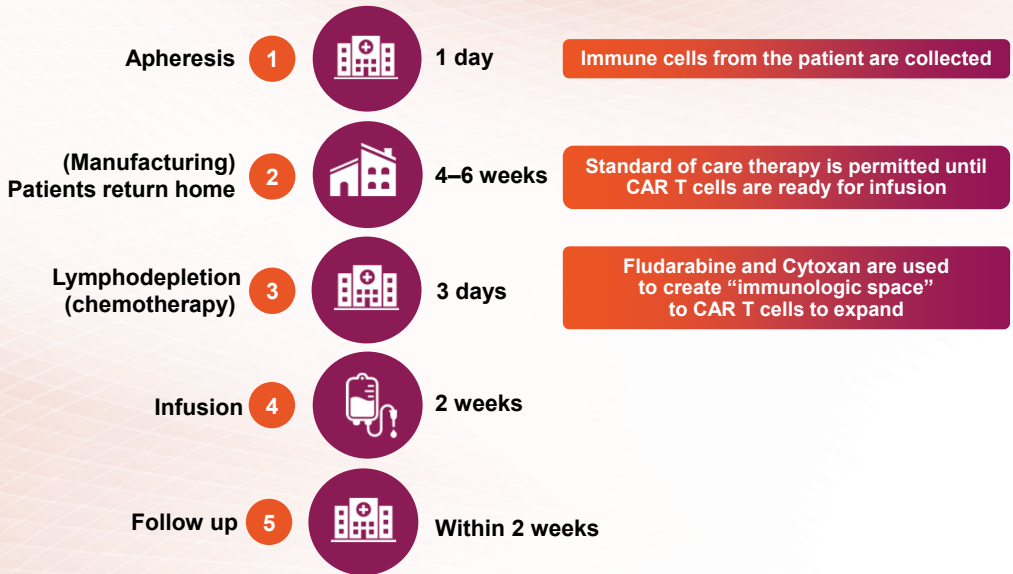
- Abecma (ide-cel)
- Carvykti (cilta-cel)
- CT103A
- Gamma secretase inhibitor followed by CAR T-cells

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





101

CAR T-Cell Therapy Patient Journey



102

Two CAR T-Cell Therapies Approved!

Drug		Formulation	Approval
Abecma (idecabtagene vicleucel)*		300 to 460 × 10 ⁶ genetically modified autologous CAR T cells in one or more infusion bags	• For relapsed/refractory myeloma (after 4 or more prior lines of therapy, including an IMiD, a PI, and an anti-CD38 mAb)
Carvykti (ciltacabtagene autoleucel)†		0.5 to 1.0 × 10 ⁶ genetically modified autologous CAR T cells/kg of body weight	• For relapsed/refractory myeloma (after 4 or more prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb)

IMiD, immunomodulatory agent; PI, proteasome inhibitor; mAb, monoclonal antibody

*Black box warning: cytokine release syndrome; neurologic toxicities; hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS); prolonged cytopenia

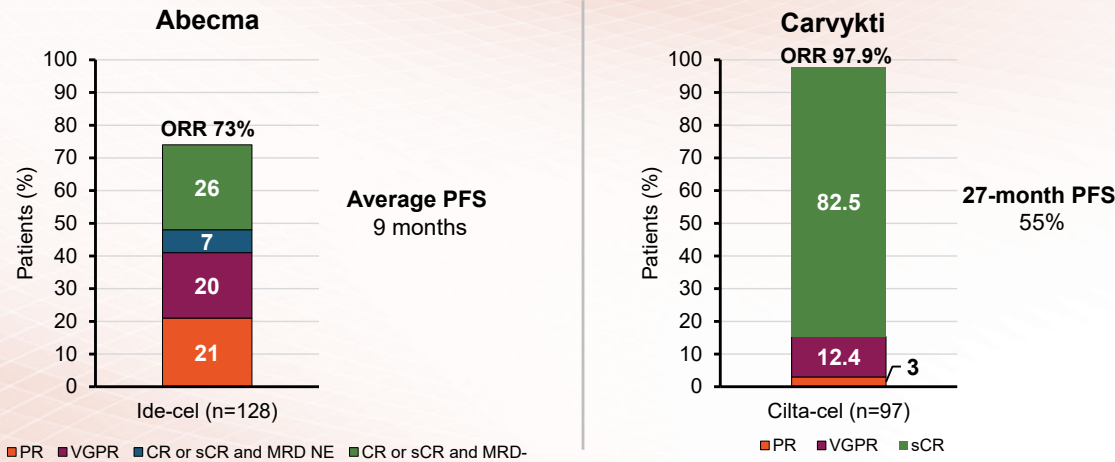
†Black box warning: cytokine release syndrome; neurologic toxicities; Parkinsonism and Guillain-Barré syndrome; HLH/MAS; prolonged cytopenia

Abecma and Carvykti are available only through a restricted distribution program.



103

Abecma and Carvykti in Relapsed and Refractory Multiple Myeloma



ORR, overall response rate; PR, partial response; VGPR, very good partial response; CR, complete response; sCR, stringent complete response; MRD, minimal residual disease; PFS, progression-free survival

KarMMa Trial. Munshi NC et al. *N Engl J Med*. 2021;384:705.
CARTITUDE-1 Trial. Berdeja JG et al. *Lancet*. 2021;398:314; Martin T et al. *J Clin Oncol*. June 4, 2022 [Epub ahead of print].



104

CAR T: Expected Toxicities



Cytokine release syndrome (CRS)



Neurotoxicity (ICANS)



Cytopenias



Infections

	CRS	ICANS
Onset	1–9 days after CAR T-cell infusion	2–9 days after CAR T-cell infusion
Duration	5–11 days	3–17 days
Symptoms	<ul style="list-style-type: none">• Fever• Difficulty breathing• Dizziness• Nausea• Headache• Rapid heartbeat• Low blood pressure	<ul style="list-style-type: none">• Headache• Confusion• Language disturbance• Seizures• Delirium• Cerebral edema
Management	<ul style="list-style-type: none">• Actemra (tocilizumab)• Corticosteroids• Supportive care	<ul style="list-style-type: none">• Antiseizure medications• Corticosteroids

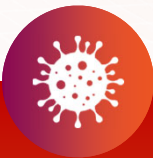
^{*}Based on the ASTCT consensus; [†]Based on vasopressor; [‡]For adults and children >12 years; [§]For children ≤12 years; [¶]Only when concurrent with CRS

Xiao X et al. *J Exp Clin Cancer Res.* 2021;40(1):367. Lee DW et al. *Biol Blood Marrow Transplant.* 2019;25:625; Shah N et al. *J Immunother Cancer.* 2020;8:e000734.



105

CAR T-Cell Therapy Themes: Myeloma



All patients were very heavily pretreated, at least six prior therapies. Many patients on the trials were considered *triple-class refractory*.



All have similar side effects, causing cytokine release syndrome, confusion, and low blood counts.



Most patients respond well to treatment and responses are durable; unfortunately, most patients eventually progress.



106

Transplant vs CAR T Cells

Cellular therapies	CAR T-cell therapy	Autologous stem cell transplantation
Patient's cells collected	Yes	Yes
Types of cells collected	T cells*	Stem cells†
Collected cells are genetically engineered in a lab	Yes	No
Patient given chemotherapy before cells are infused back into patient	Yes, lymphodepleting therapy	Yes, melphalan
When in the course of myeloma is this usually done?	After multiple relapses	As part of initial treatment
Side effects of treatment	Cytokine release syndrome; confusion	Fatigue, nausea, diarrhea

*An immune cell that is the "business end" of the system, in charge of maintaining order and removing cells.
†Precursor cells that give rise to many types of blood cells. We actually collect CD34+ve cells.



107

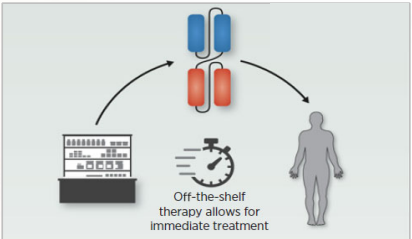
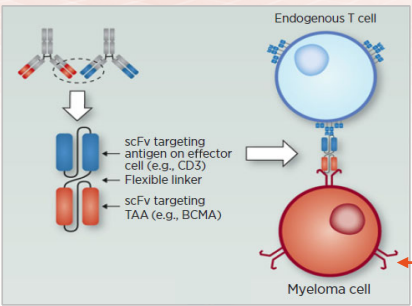
Bispecific Antibodies

Bispecific antibodies are also referred to as *dual specific antibodies, bifunctional antibodies, or T-cell engaging antibodies*

Bispecific antibodies can target two cell surface molecules at the same time (one on the myeloma cell and one on a T cell)

Many different bispecific antibodies are in clinical development; none are approved for use in myeloma

Availability is off-the-shelf, allowing for immediate treatment



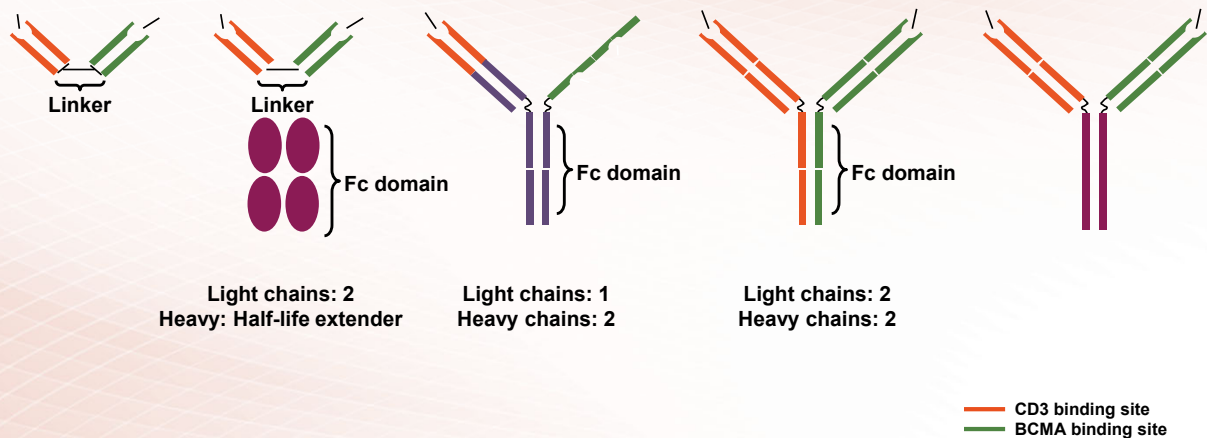
- Examples:
- Elranatamab
 - Teclistamab
 - TNB-303B (ABBV-383)
 - REGN5458
 - Cevostamab
 - Talquetamab



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

108

There Are Different Types of Bispecific T-Cell Engagers/Antibodies



109

Bispecific Antibodies: >20% Activity


Myeloma cell target	Bispecific agent	Patients responding*
BCMA	Teclistamab	63%
BCMA	REGN5458	73%
BCMA	Elranatamab	73%
BCMA	TNB383B	60%
BCMA	CC93269	89%
BCMA	AMG701	83%
GPRC5D	Talquetamab	70%
FCRH5	Cevostamab	55%

*Based on a recent sampling

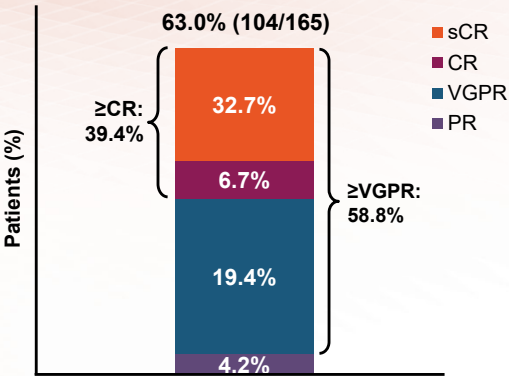


110

Now Approved: Tecvayli, the First Bispecific Antibody

Drug	Formulation	Approval
Tecvayli (teclistamab)*	 Step-up dosing† the first week then once weekly thereafter by subcutaneous injection	• For relapsed/refractory myeloma (after 4 or more prior lines of therapy, including an IMiD, a PI, and an anti-CD38 mAb)

IMiD, immunomodulatory agent; PI, proteasome inhibitor; mAb, monoclonal antibody
*Black box warning: cytokine release syndrome; neurologic toxicities
†Patients are hospitalized for 48 hours after administration of all step-up doses.
Tecvayli is available only through a restricted distribution program.



Median duration of response
18.4 months

Moreau P et al. *N Engl J Med*. 2022;387:495.



111

Bispecific Antibodies: Expected Toxicities

- Cytokine release syndrome (CRS)
- Neurotoxicity (ICANS)
 - Usually occurs within first 1–2 weeks
 - Frequency (all grade and grade 3–5) higher with CAR T
- Cytopenias
- Target unique
 - For example, rash, taste disturbance seen with GPRC5D, but not with BCMA
- Infections
 - Incidence for bispecifics at RP2D not yet known
 - Viruses: CMV, EBV
 - PCP/PJP
 - Ongoing discussions regarding prophylactic measures
 - IVIG
 - Anti-infectives



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Similarities and Differences Between CAR T-Cell Therapy and Bispecific Antibodies

	CAR T-cell therapy	Bispecific antibody
Approved product	Abecma, Carvykti	Tecvayli
Efficacy	++++	+++
How given	One-and-done	IV or SC, weekly to every 3 weeks until progression
Where given	Academic medical centers	Academic medical centers
Notable adverse events	CRS and neurotoxicity	CRS and neurotoxicity
Cytokine release syndrome	+++	++
Neurotoxicity	++	+
Availability	Wait time for manufacturing	Off-the-shelf, close monitoring for CRS and neurotoxicity



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Key Points

- CAR T and bispecific antibodies are very active even in heavily pre-treated patients.
- Side effects of CAR T cells and bispecific antibodies include cytokine release syndrome, confusion, and low blood counts, all of which are treatable.
- Abecma and Carvykti are only the first-generation CAR T cells and target the same protein. Different CAR Ts and different targets are on the way.
- Bispecific antibodies represent an “off-the-shelf” immunotherapy; Tecvayli was approved in October 2022.
- Several additional bispecific antibodies are under clinical evaluation.



114

**Please take a moment to
answer two questions
about this presentation.**



115

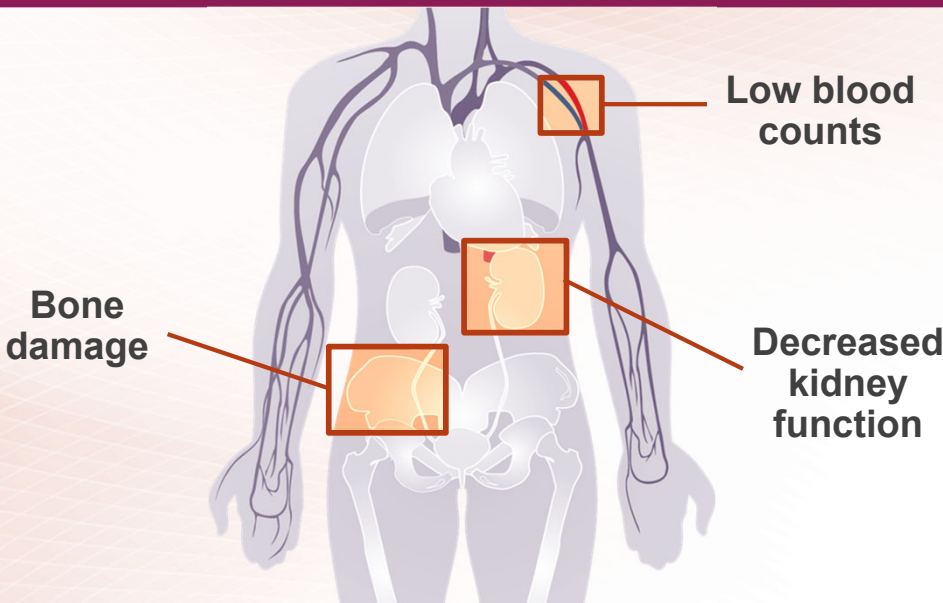


Supportive Care

Donna D. Catamero, ANP-BC, OCN, CCRC
Mount Sinai Hospital
New York, New York

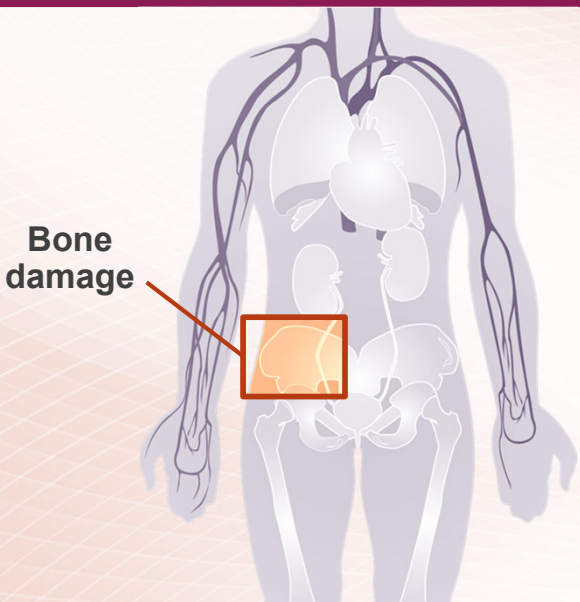
116

Effects of Myeloma



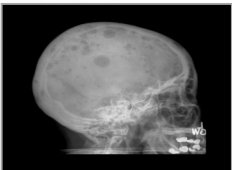
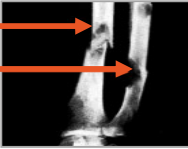
117

Effects of Myeloma: Bone Disease



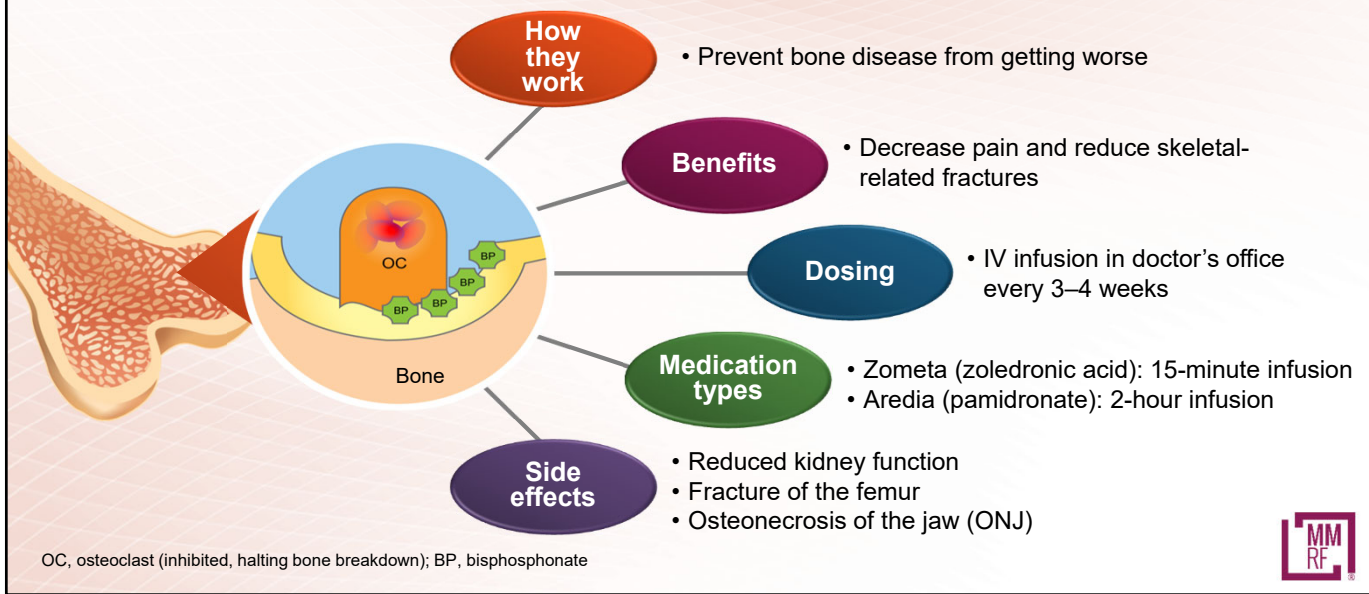
- Occurs in 85% of patients
- Weakened bone due to lesions or “holes”
- Increased levels of calcium in the blood (hypercalcemia)
- Leads to
 - Pathologic fractures
 - Spinal cord compression/collapse
 - Bone pain

Fracture
caused
by lesion
Lesions



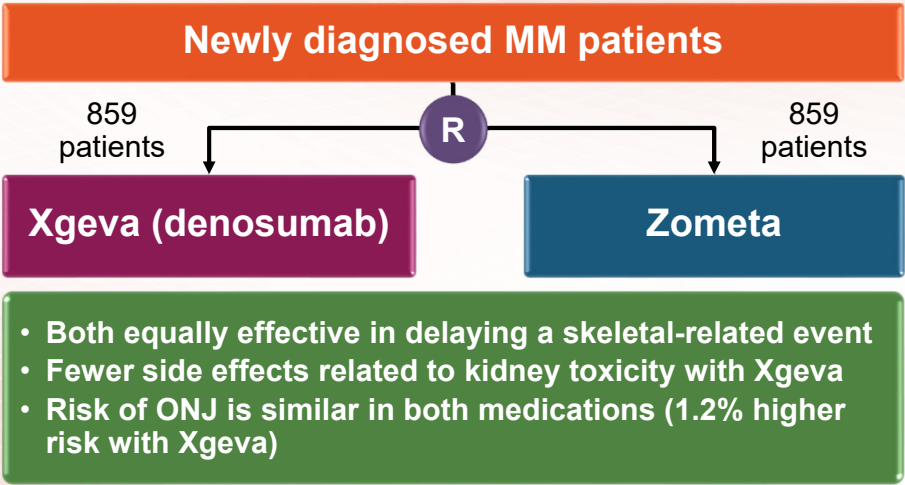
118

Bisphosphonates for Myeloma Bone Disease



119

Xgeva (denosumab) for Bone Loss



Raje NS et al. *J Clin Oncol*. 2017;35. Abstract 8005.
Terpos E et al. *Haematologica*. 2017;102. Abstract S782.

120

Recommendations for Reducing the Risk of ONJ

- Complete major dental work before beginning treatment for bone disease
- Practice good oral hygiene
- Schedule regular dental visits
- Let your dentist know that you are receiving treatment for bone disease
- Keep your doctor informed of dental issues/need for dental work
- Be attentive! ONJ seems to be related to the length of time patients are on treatment for bone disease



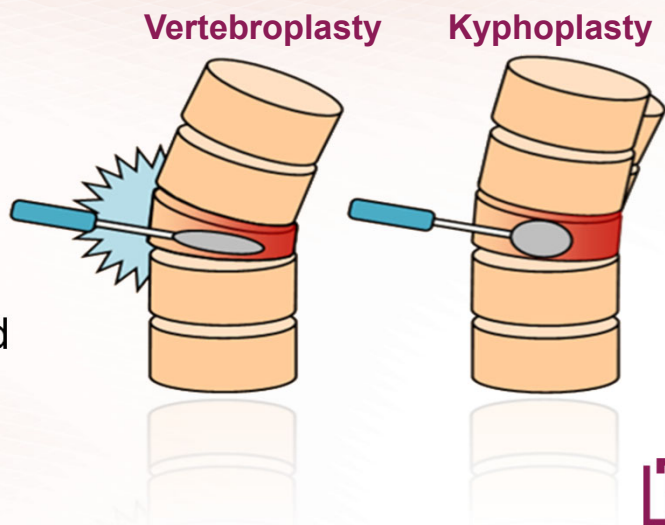
ONJ, osteonecrosis of the jaw



121

Orthopedic Procedures to Stabilize the Spine

- Minimally invasive procedures
- Can be performed without hospitalization
- Small incision
- Cement filler stabilizes bone
- Potential for relatively rapid symptom relief (approximately 1 month with kyphoplasty)



122

Radiation Therapy for Pain Management



123

Pain Management Medications

Acetaminophen (Tylenol)

Will not hurt your
kidneys; high dosage
can hurt your liver

NSAIDs (nonsteroidal anti-inflammatory drugs)

Prefer to avoid with
MM due to increased
risk of kidney injury

Opioids

Will not hurt kidneys,
liver, stomach;
potential for
constipation,
sedation, confusion,
dependence,
addiction

Corticosteroids (dexamethasone, prednisone)

Will not hurt kidneys;
can raise blood
sugar; short- and
long-term effects

Gabapentin

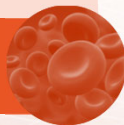


124

Effects of Myeloma: Low Blood Counts

- Symptoms
 - Fatigue; depression/mood changes; difficulty breathing; rapid heartbeat; dizziness
- Other causes
 - Low levels of iron, folate, and vitamin B12

Low red blood cells (anemia)



Treatment: Identify and treat causes other than myeloma; supplements; medications to increase number of red blood cells; blood transfusions

- Symptoms
 - Fatigue; frequent infections
- Other causes
 - Radiotherapy
 - Infection

Low white blood cells (leukopenia)



Treatment: Medications to stimulate production of white blood cells; antibiotics; antifungal medications; infection prevention

- Symptoms
 - Easy or excessive bruising; superficial bleeding into the skin; prolonged bleeding from cuts; bleeding from the gums or nose; blood in urine or stool
- Other causes
- Viral infection (hep B or C); immune thrombocytopenia; medications

Low platelets (thrombocytopenia)

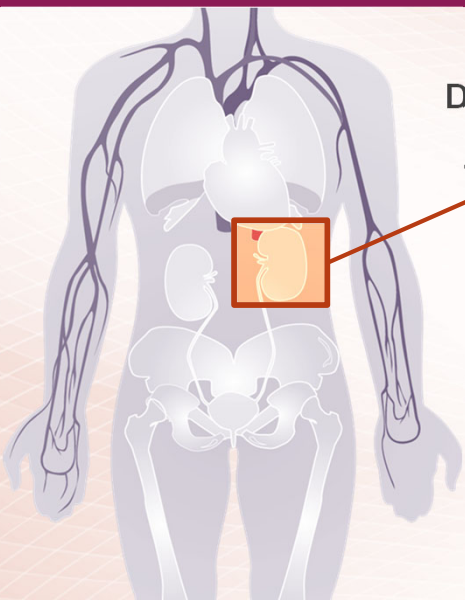


Treatment: Identify and treat causes other than myeloma; platelet transfusion; hold anticoagulation



125

Effects of Myeloma: Decreased Kidney Function



Decreased
kidney
function

- Detection
 - Decreased amount of urine
 - Increase in creatinine and other proteins
- Other causes beside myeloma
 - Hypertension
 - Diabetes
 - Some medications
- Treatment
 - Fluids
 - Avoid nonsteroidal anti-inflammatory drugs such as Aleve, Advil/Motrin
 - Plasmapheresis
 - Treat other causes
 - Dialysis (severe)

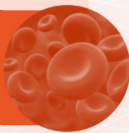


126

Main Body Systems Affected by Myeloma Treatment

- MM patients are at increased risk of developing blood clots
- Several MM drugs are associated with an increased risk of deep vein thrombosis (DVT)

Blood



- Peripheral neuropathy is a condition that affects the nerves, resulting in pain, tingling, burning sensations, and numbness in the hands and feet
- Peripheral neuropathy may be caused by MM or its treatments

CNS



- Cardiovascular side effects (including high blood pressure or congestive heart failure) can occur with some MM drugs

Cardio-vascular



- Commonly used MM drugs may cause a variety of gastrointestinal problems, such as constipation, diarrhea, and nausea/vomiting

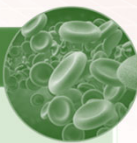
Gastro-intestinal



127

Class: Immunomodulatory Drugs Side Effects and Management

Revlimid*



- Potential for blood clots
- Reduced blood counts
- Rash
- Fatigue
- Muscle pain or muscle cramping
- Diarrhea
- Small chance of second new cancers when given with melphalan

Pomalyst*



- Fatigue and weakness
- Low white blood cell counts
- Anemia
- GI effects
- Shortness of breath
- Upper respiratory infection
- Back pain
- Fever
- Blood clots
- Mental foginess

Management



- Blood thinners
- Tonic water/increased fluid intake for cramps
- GI toxicity: avoid dairy; fibers (Metamucil); Imodium; colestipol; cholestyramine; dose reduction
- Sleep hygiene, regular exercise, dose reduction for fatigue

*Black box warning.
GI, gastrointestinal



128

Class: Proteasome Inhibitors Side Effects and Management

Velcade



- PN (numbness, tingling, burning sensations and/or pain due to nerve damage)
- Low platelets
- GI problems: nausea, diarrhea, vomiting, loss of appetite
- Fatigue
- Rash

Kyprolis



- Fatigue
- Anemia
- Nausea
- Low platelets
- Shortness of breath
- Diarrhea
- Fever
- Hypertension
- Cardiac toxicity

Ninlaro



- Diarrhea
- Constipation
- Low platelets
- PN
- Nausea
- Peripheral edema
- Vomiting
- Back pain

Management



- PN occurs less often when subcutaneous or once weekly dosing is used for Velcade
- Other PN prevention:
 - Vitamins and other supplements*
 - Certain medications such as gabapentin, pregabalin, duloxetine, opioids
 - Acupuncture
 - Physical therapy
- Shingles-prevention pills
- Blood thinners

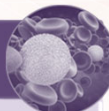
*Do not take any supplements without consulting with your doctor.
PN, peripheral neuropathy; GI, gastrointestinal



129

Class: Monoclonal Antibodies Side Effects and Management

Empliciti



- Low blood counts
- Infusion reactions

Darzalex*/Sarclisa



- Infusion reactions
- Fatigue
- Upper respiratory tract infection

*Now approved as subcutaneous injection with fewer side effects.

Management



- Premedication in anticipation of infusion reactions
- Post-infusion medications (Darzalex)



130

XPOVIO: Selective Inhibitor of Nuclear Export Side Effects and Management



Gastrointestinal

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



Low sodium (hyponatremia)

Maintain fluid intake



Fatigue

Stay hydrated and active



Low blood counts (cytopenias)

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

Chari A et al. *Clin Lymphoma Myeloma Leuk.* 2021;21:e975.



131

Class: Antibody-Drug Conjugate Side Effects and Management

Blenrep

- Thrombocytopenia
- Keratopathy
- Decrease visual acuity
- Nausea
- Blurred vision
- Fever
- Infusion-related reactions
- Fatigue



Ocular toxicity management

- Available only through a Risk Evaluation and Mitigation Strategies (REMS) due to the risk of ocular toxicity
- Patients receive ophthalmic examinations at baseline (within 3 weeks prior to the first dose), prior to each dose, and promptly for worsening symptoms
- Patients are advised to use preservative-free lubricant eye drops at least 4 times a day starting with the first infusion and continuing until end of treatment
- Patients should also avoid use of contact lenses unless directed by an ophthalmologist



132

Bispecific Antibodies

Tecvayli

- Cytokine release syndrome
- Injection-related reactions
- Injection-site reaction
- Infections
- Neutropenia
- Anemia
- Thrombocytopenia



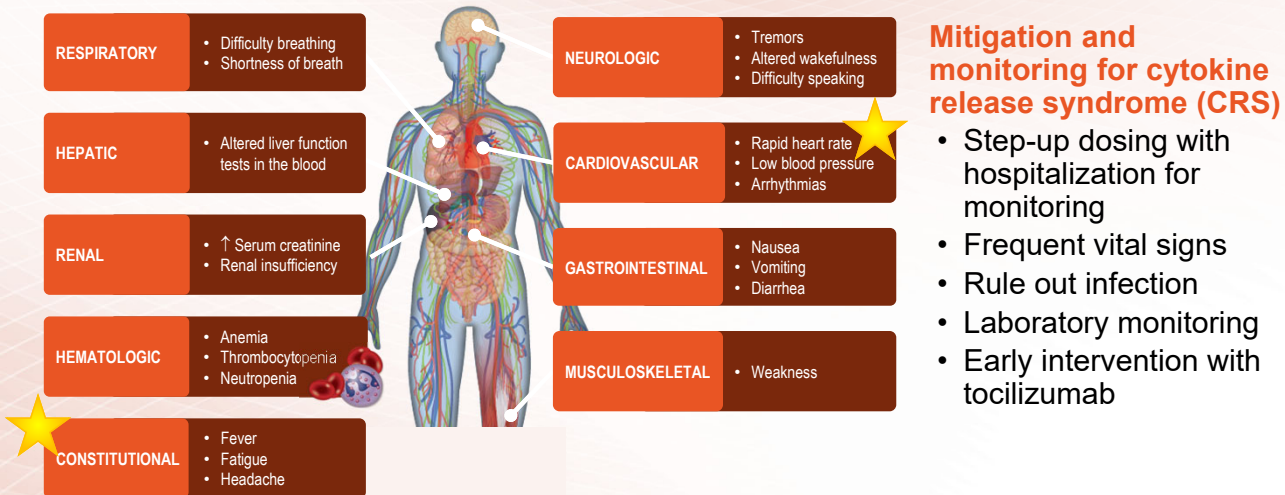
Management

- Available only through a Risk Evaluation and Mitigation Strategies (REMS) due to the risk of cytokine release syndrome
- Patients will receive step-up dosing and will be monitored in an inpatient setting
- Cytokine release syndrome is managed in the same fashion as CAR T
- Injection reactions are managed with oral antihistamines and topical steroids
- Infection prevention!
- COVID precautions



133

CRS With Bispecifics Severity Is Typically Mild: Early Recognition and Treatment Is Key

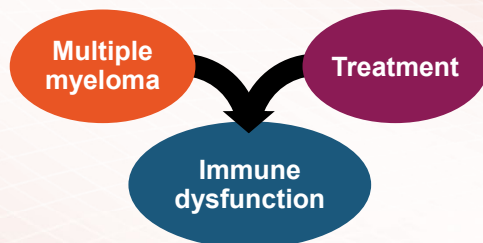


ALP, alkaline phosphatase; CPK, creatine phosphokinase; CRP, C-reactive protein; CRS, cytokine release syndrome; LDH, lactate dehydrogenase; O₂, oxygen; TLS, tumor lysis syndrome. Oluwole OO, Davila ML. *J Leukoc Biol*. 2016;100:1265. June CH, et al. *Science*. 2018;359:1361. Brudno JN, Kochenderfer JN. *Blood*. 2016;127(26):3321. Brudno JN, Kochenderfer JN. *Blood Rev*. 2019;34:45. Shimabukuro-Vornhagen, et al. *J Immunother Cancer*. 2018;6:56. Lee DW, et al. *Biol Blood Marrow Transplant*. 2019;25:625.



134

Infection Can be Serious for Patients With Myeloma



7-10–fold increased risk of bacterial and viral infections for people with myeloma

Report fever of more than 100.4°F, shaking chills even without fever, dizziness, shortness of breath, low blood pressure to HCP as directed.

General infection-prevention tips

- Good personal hygiene (skin, oral)
- Environmental control (wash hands, avoid crowds and sick people, etc)
- Growth factor (Neupogen [filgrastim])
- Immunizations (NO live vaccines)
- Medications (antibacterial, antiviral)

As recommended by your health care team

Brigle K, et al. *Clin J Oncol Nurs*. 2017;21(5)suppl:60. Faiman B, et al; IMF Nurse Leadership Board. *Clin J Oncol Nurs*. 2011;15(Suppl):66. Miceli TS, et al. *Clin J Oncol Nursing*. 2011;15(4):9. ASH Website. COVID-19 Resources. <https://www.hematology.org/covid-19/covid-19-and-multiple-myeloma>



135

BCMA-Targeted Therapies Are Associated With an Increased Risk of Infections

- Both viral and bacterial
 - Up to 1/3 of patients in clinical trials have serious infections (requiring IV antibiotics or hospitalization)
- Increased risk of serious COVID complications despite history of vaccination
 - Antibody levels
 - Tixagevimab co-packaged with cilgavimab (EVUSHELD)
 - Immediate treatment once diagnosed nirmatrelvir with ritonavir (Paxlovid)
 - Start as soon as possible; must begin within 5 days of when symptoms start



136

Infection Prevention

- Avoid crowds
- Ensure handwashing, hygiene
- Growth factor (eg, filgrastim)
- IVIG for hypogammaglobulinemia
 - Know your healthy IgG level
- Immunizations (No live vaccines)
 - COVID-19 vaccination + booster(s)
 - Pneumococcal 20-valent conjugate vaccine
 - Seasonal inactivated influenza vaccine (×2 or high-dose)
 - Shingles vaccine: zoster vaccine recombinant, adjuvanted
- COVID-19 prevention
 - Antibody levels
 - Tixagevimab co-packaged with cilgavimab

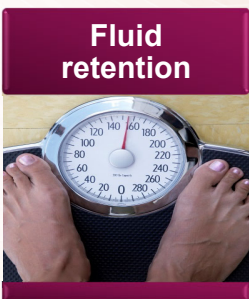


137

Side Effects of Steroids (Dexamethasone)



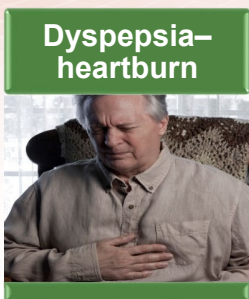
- Healthy sleep habits
- Timing
- Medication to assist with sleeping as needed



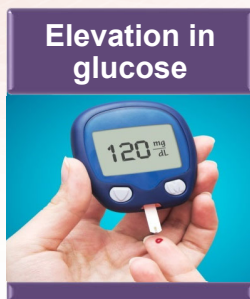
- Monitor for swelling of extremities and "puffy" face
- Monitor weight changes/gain
- Reduce dose



- Irritable, anxiety, difficulty concentrating
- Severe cases → depression, euphoria



- Dietary modifications (spicy, acidic foods)
- Avoid NSAIDs
- Acid-blocking medications
- Take steroid with food; use enteric-coated aspirin with food



- Monitor glucose and refer/treat as needed



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Symptom Management Constipation

- Stimulant laxatives
 - Mild: senna/sennoside (Senokot)
 - 1–2 pills twice a day
 - More potent: bisacodyl (Dulcolax)
- Osmotic laxatives
 - Gentle, pulls water into the intestine
 - Lactulose
 - Miralax
- Bulking agents
 - Soluble fiber: psyllium (Metamucil)



139

Symptom Management Acid Reflux/Heartburn

- Our stomachs make a powerful acid to digest food, hydrochloric acid
- Hydrochloric acid can also digest our stomach lining → leads to gastritis and ulcers

A few ways to treat

1. Decrease the amount of acid that stomach is making
 - a. Zantac, Pepcid
 - b. Prilosec, Prevacid, Protonix, Nexium
2. Absorb excess acid: Tums, Maalox, Mylanta
3. Coat stomach: Carafate
4. Avoid late night eating



140

Symptom Management Insomnia

- Causes: anxiety, stress, meds—dexamethasone
- Sleep hygiene
 - Routine: go to bed, wake up at routine times
 - Exercise
 - No TV or screen displays when trying to sleep
 - Relaxation training; use a mantra
 - Counseling support
- Medications: useful but all have drawbacks
 - Lorazepam (Ativan)
 - Zolpidem (Ambien)
 - Diphenhydramine (Benadryl)



141

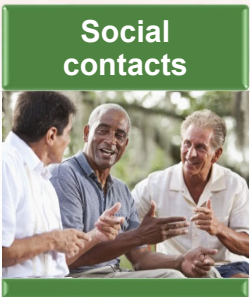
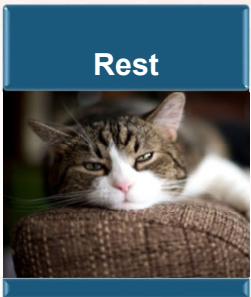
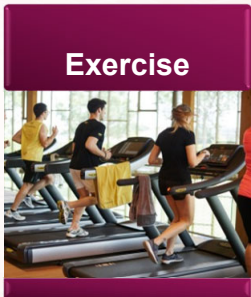
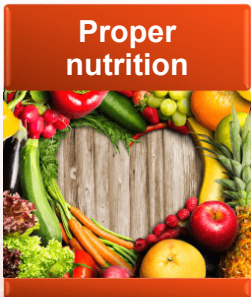
Marijuana

- Claims and hype: advocates and detractors
 - Promoted as relieving pain and muscle spasm, improving appetite, decreasing nausea, helping anxiety and insomnia, *and even curing cancer*
- Laws vary by state
- Marijuana contains 100 **cannabinoids**, most notably **THC** and **CBD**
- Sativex contains equal parts THC and CBD
 - Available in Great Britain and Canada
 - Double-blind trial in 2015: effective but no more effective than placebo for cancer pain; not available in U.S.
- Bottom line: Marijuana has been shown to have modest benefits in symptom management; claims of dramatic results are anecdotal and have not been proven



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Daily Living



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Taking Care of Yourself



Talk to your provider about side effects... there is usually a way to make treatment tolerable.



Pay attention to your own needs and don't be afraid to ask for help.



Learn more about multiple myeloma.



Look for the positive.



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**Please take a moment to
answer two questions
about this presentation.**



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Patient Experience

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Town Hall Questions & Answers



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Thank you!



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Don't Forget!

Complete your evaluation
Leave the iPad at your seat

An iPad displaying the MMRF Patient Summit evaluation interface. The screen shows the MMRF logo, the text "Welcome Multiple Myeloma Patient Summit Atlanta, Georgia April 23, 2022", and a navigation bar with options like "PRESENTATION", "AGENDA", "FACULTY BIOS", "GLOSSARY", and "EVALUATION" (which is highlighted). At the bottom, there are icons for "Tech Support", "ASK QUESTION", "TAKE NOTE", "RATE SLIDE", and "SAVE SLIDE".

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Upcoming Patient Education Events

Save the Date

Topic	Date and Time	Speakers
<i>Treatment Options for Patients With Multiple Myeloma Who Have Relapsed After Three or More Lines of Therapy</i> (including updates on Tecvayli approval)	Friday, December 2 1:00 PM – 2:00 PM (ET)	Monique A. Hartley-Brown, MD, MMSc Urvi A. Shah, MD
<i>Patient Summit</i> (live and online)	Friday, December 9 12:00 PM – 4:30 PM (CT) New Orleans, Louisiana	Laura Finn, MD—Host Ambuga R. Badari, MD Amrita Y. Krishnan, MD Suzanne Lentzsch, MD, PhD Paul G. Richardson, MD A. Keith Stewart, MBChB
<i>Expert Session: Multiple Myeloma Highlights From the 2022 American Society of Hematology Meeting</i>	Tuesday, December 20 1:00 PM – 3:00 PM (ET)	Joshua Richter, MD

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



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MMRF Patient Resources

EXPECT GUIDANCE.

MMRF Patient Navigation Center

- Information & Resources
- Expert Advice
- Support

MULTIPLE MYELOMA Research Foundation

MMRF Patient Navigation Center

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

MMRF Patient Navigators include:

- Grace Allison, RN, BSN, OCN, RN-BC
- Brittany Hartmann, RN-BSN
- Erin Mensching, RN-BSN, OCN

THE RIGHT TRACK

Get on the right track for you

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

Right Team

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

Right Tests

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

Right Treatment

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

Contact the Patient Navigation Center Today

Looking for guidance? We're here to help.

Monday – Friday | 9:00am – 7:00pm ET

Phone: 1-888-941-MMRF (6673) | Online: [TheMMRF.org/PatientNavigationCenter](https://themmrf.org/PatientNavigationCenter)

Email: patientnavigator@themmrf.org

Supported By



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

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

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



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MMRF Events

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

Endurance Events



5K Walk/Run Events



Independent Events



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



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