
Applying the Latest Clinical Data in
MULTIPLE MYELOMA PATIENT CARE
IN THE COMMUNITY SETTING
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25th ANNIVERSARY
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RedMedEd
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Craig Emmitt Cole, MD
Assistant Professor of Medicine
Michigan State University College of Human Medicine
Karmanos Cancer Institute
Lansing, Michigan
Karmanos CANCER INSTITUTE
McLaren GREATER LANSING
In partnership with MSU Health Care
Cancer Research
MICHIGAN STATE UNIVERSITY

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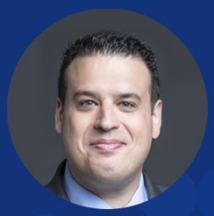
Planning Committee

Craig Emmitt Cole, MD—Presenter
Assistant Professor of Medicine
Michigan State University College of Human Medicine
Karmanos Cancer Institute
Lansing, Michigan

Laura Finn, MD, MS
Director Hematology/
Bone Marrow Transplant
Ochsner Health
New Orleans, Louisiana



Joshua Richter, MD
Associate Professor of Medicine
Tisch Cancer Institute/Icahn School of Medicine at Mount Sinai
Director of Myeloma: Blavatnik Family – Chelsea Medical Center at Mount Sinai
New York, New York

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Faculty Disclosures

Craig Emmitt Cole, MD—Presenter, has disclosed the following relevant financial relationships:
Consultant: AbbVie, AstraZeneca, Oncopeptides, Pfizer, Sanofi
Research: GSK

Laura Finn, MD, MS, has disclosed the following relevant financial relationships:
Advisory Board: Celgene, Daichi Sankyo, Janssen
Speakers Bureau: BeiGene, Bristol Myers Squibb, Jazz Pharmaceuticals, Lilly

Joshua Richter, MD, has disclosed the following relevant financial relationships:
Consultant: Celgene/Bristol Myers Squibb, Janssen, Karyopharm, Pfizer, Sanofi, Takeda
Speakers Bureau: Adaptive Biotechnologies, Bristol Myers Squibb, Janssen, Sanofi
Advisory Board: AbbVie, Celgene/Bristol Myers Squibb, Janssen, Karyopharm, Sanofi, Takeda

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The MMRF CureCloud® and MMRF Resources for Patients

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The MMRF CureCloud®: a 5,000-patient research study

MMRF CureCloud®

Together, we can make a difference for every patient with multiple myeloma.

We are making progress in the fight against myeloma because of contributions from patients like you.
People with multiple myeloma are living longer than ever before — but there's still no cure for most patients. Medical advances have been possible because patients have participated in clinical studies.

The MMRF CureCloud® study aims to identify more personalized treatments for every myeloma patient, faster.
The fastest way to find these treatments is to make information from every myeloma patient available to cancer researchers.

Myeloma is different in every patient — we need to learn more to see what's best for each patient.

It's easy and convenient to participate from home — at no cost to you or your doctor.

Unlike other studies, in the CureCloud you will not need to:
- ✖ Take any experimental medication or change your current medications.
- ✖ Go for any extra doctor's visits or see a different doctor.

Sign up online or in a CureCloud participating clinic and confirm your eligibility.
- ✔ Get a home blood test (genomic test*).
- ✔ We'll collect your medical records.

You'll help researchers find better treatments while learning more about your myeloma.
Information contributed by you and other patients will help researchers find better therapies for every myeloma patient, faster. We'll share with you anything we find out about your myeloma from your medical records.

Your data is strictly protected — the information you provide is held in a very secure database.

**Genomic test: analysis of myeloma DNA in your blood to see if there are any changes.*

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How does the MMRF CureCloud work?

MMRF CureCloud®

You'll get a blood test at home.

- After you sign up, you will receive a CureCloud bloodwork kit.
- A trained medical professional will come to your home to draw your blood.

We'll collect your medical records.

- When you sign up, you'll provide the names and contact information for the doctors who have treated your myeloma and any clinics or hospitals where you've had tests (bone scans, MRI, etc.).
- We'll contact them and collect your records.

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Multiple Myeloma Education Resources

The MMRF Patient Toolkit, the Patient Navigation Center, and Online/Hybrid Events available at:
https://themmrf.org/resources/education-programs/

Order the MMRF Patient Toolkit

Contact the MMRF's Patient Navigation Center

Attend/Stream Patient Education Events

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MMRF Scholars Program 2023

Mission: Promote the careers of Black/African American clinical and laboratory investigators in multiple myeloma

Program Features

- 4 years of funding; $100,000 per year
- Support for fellowship through first faculty position
- Additional financial support for travel to IMW and ASH
- Scholars Mentoring Committee for review of project conduct and advice on career development
- Resources for project conduct, including strategic (Mentoring Committee, collaboration matching) and operational (eg, guidance on protocol development, translational research, core technologies, and tissue banks)

Candidates

- US clinical and laboratory investigators who have completed at least 1 year of postdoctoral training
- PhD, MD, or equivalent degree
- Mentor in the field of multiple myeloma or related biological or clinical field

Applications are open. Deadline for submission is Friday, March 31, 2023.

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Today's Discussion Points

- Case presentation
- What is multiple myeloma?
- How to evaluate for a monoclonal gammopathy
- What is monoclonal gammopathy of undetermined significance (MGUS)?
- Testing to distinguish MGUS from myeloma
- Myeloma statistics
- Presenting signs and symptoms
- Treating myeloma using SCIENCE!
- Advancements in survival of multiple myeloma patients
- Conclusions

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Case Presentation

- 57-year-old African American woman with history of obesity, osteoarthritis, diabetes, and hypertension presents to her primary care provider with increasing fatigue
- Her physical exam was notable for BP 189/96 and right clavicle pain
- Called back into office for more test after work

WBC =	4.8	4.0–10.0 K/µL
Hemoglobin =	10.3	12.0–16.0 g/dL NEW
Platelet =	200	140–400 K/µL

Creatinine =	2.90	0.70–1.30 mg/dL NEW
Calcium level =	10.5	8.6–10.3 mg/dL NEW
Albumin level =	2.5	3.5–4.9 g/dL NEW

Hemoglobin A1C = 6%
Dipstick urinalysis = "normal"

SPEP: hypogammaglobulinemia
Globulin = 0.45 (0.70–1.47 g/dL)

Spot urine for Bence Jones protein: negative

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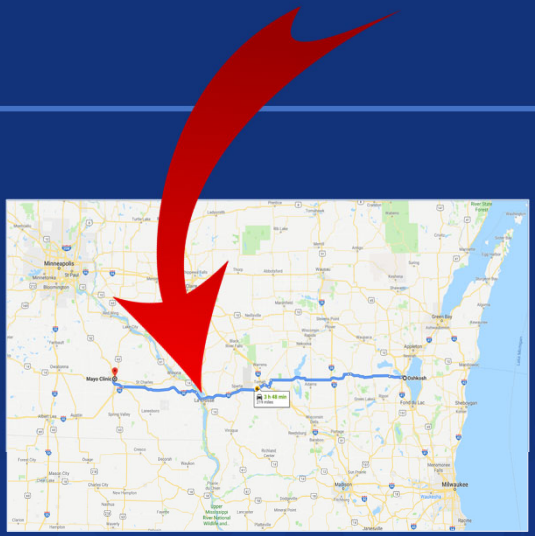
Case Presentation

- Patient is referred to a nephrologist
  - "He didn't listen to me or draw my blood"
  - Diagnosis was hypertensive/diabetic kidney disease
- Patient seeks a second opinion with a family friend who is a physician and agrees with the nephrologist
- *3 months* after original presentation, the patient travels for a third opinion at Mayo Clinic in Rochester, MN
- She has to stop in La Crosse, WI, due to shortness of breath, fever, and fatigue



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Case Presentation

Kappa free light chains = 0.01		(0.33–1.94 mg/dL)
Lambda free light chains >1,800		(0.57–2.63 mg/dL)
Kappa lambda FLC ratio <0.01		(0.26–1.65)
Creatinine =	3.80	(0.70–1.30 mg/dL)
Calcium level =	12.5	(8.6–10.3 mg/dL)
Albumin level =	2.0	(3.5–4.9 g/dL)

Bence Jones quantitation = 4.1 g/24 hr
Urine immunofixation:
a monoclonal free Lambda light chain

Quantitative immunoglobulins:

IgA = 46.2	(60.0–350.0 mg/dL)
IgG = 200.2	(700.0–1,600.0 mg/dL)
IgM = <16.9	(40.0–280.0 mg/dL)

Bilateral pneumococcal pneumonia with + blood cultures

Sepsis → multisystem organ failure → death

Autopsy: bone marrow: 55% plasma cells, light chain cast nephropathy, multiple bone lesions consistent with multiple myeloma

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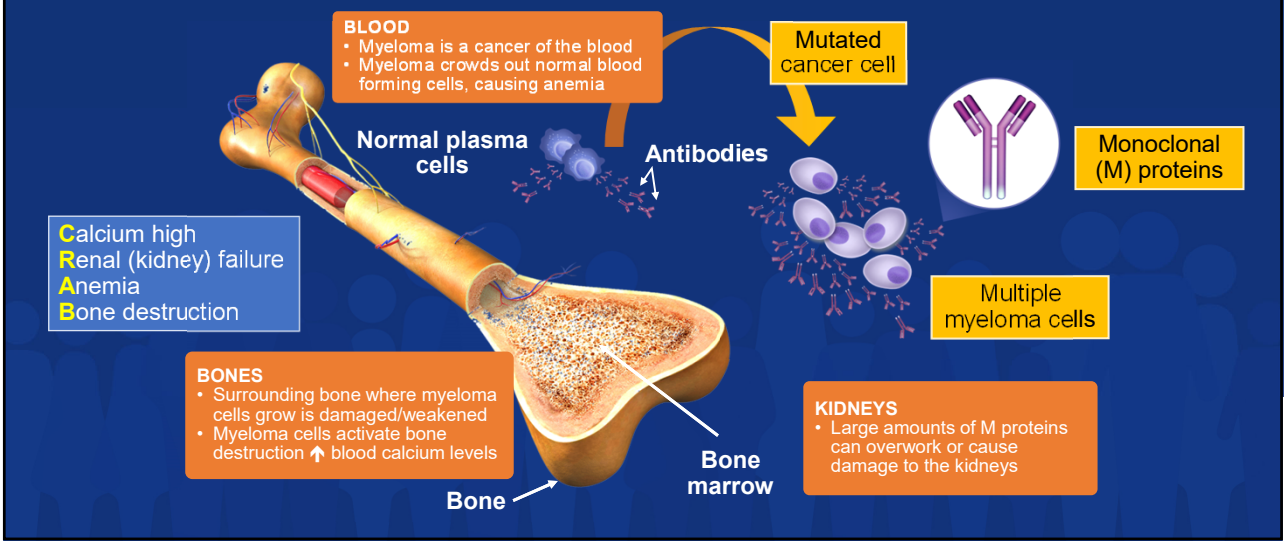
What is multiple myeloma?



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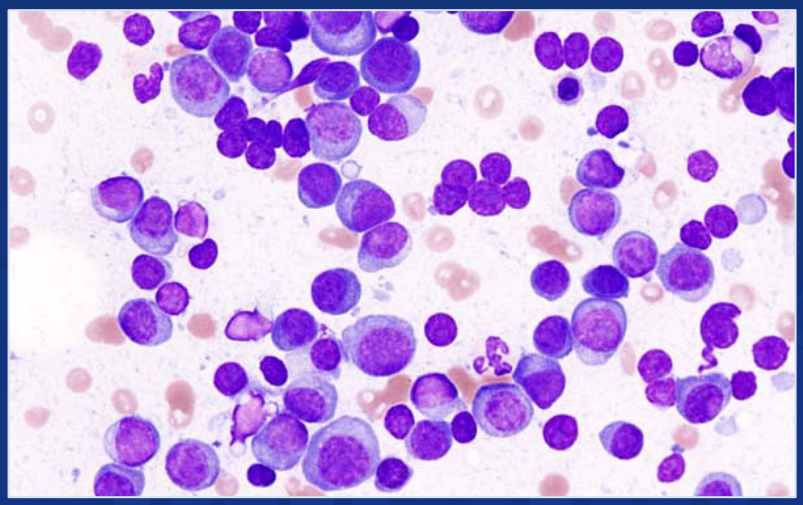
Myeloma Cells



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Q: Where do we start looking for plasma cell disorders?

A: Monoclonal protein!

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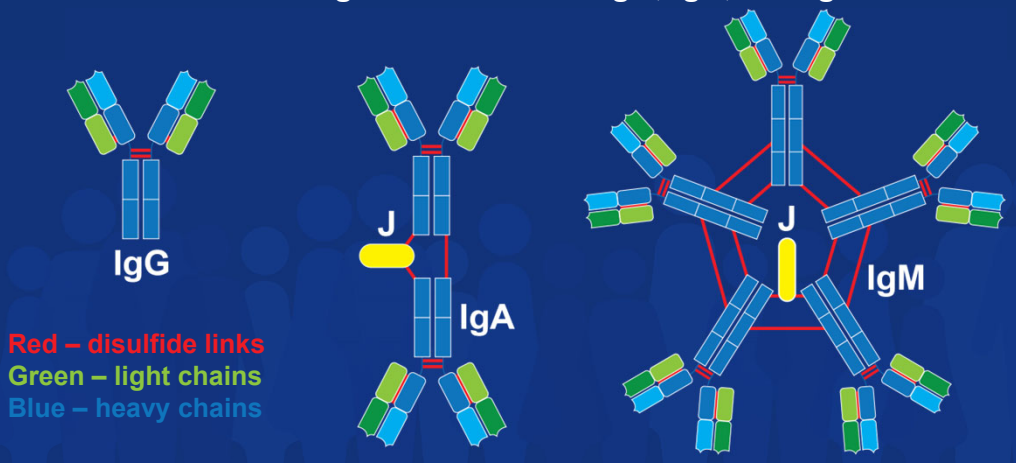
Anatomy of the Antibody

Immunoglobulin classes: IgG, IgA, and IgM



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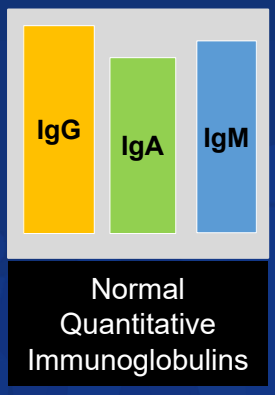
Quantitative Immunoglobulins and Immunofixation

- IgA monoclonal proteins may co-migrate with other serum proteins due to charge diversity in the IgA[1]
  - Co-migration into β region may affect >40% of IgA monoclonal proteins
- Quantitative serum immunoglobulins can detect *immunoparesis*[2]
  - Uninvolved Igs are reduced in 90% of myeloma patients



1. Boyle EM et al. *Cancer*. 2014;120(24):3952. 2. Sørrig R et al. *PLoS One*. 2017;12(12):e0188988.

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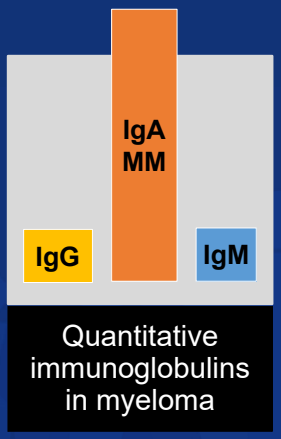
Quantitative Immunoglobulins and Immunofixation

- IgA monoclonal proteins may co-migrate with other serum proteins due to charge diversity in the IgA[1]
  - Co-migration into β region may affect >40% of IgA monoclonal proteins
- Quantitative serum immunoglobulins can detect *immunoparesis*[2]
  - Uninvolved Igs are reduced in 90% of myeloma patients
- The ***type*** of M protein is best determined by immunofixation (ifix)[3]
  - Immunofixation will detect a serum M protein ≥0.02 g/dL and a urine M protein ≥0.004 g/dL
- **17% of patients with myeloma only produce light chains[4]**
  - **Check for M protein and light chains in workup!**



Quantitative immunoglobulins in myeloma

1. Boyle EM et al. *Cancer*. 2014;120(24):3952. 2. Sørrig R et al. *PLoS One*. 2017;12(12):e0188988. 3. International Myeloma Working Group. *British J Haematol*. 2003;121(5):749. 4. Kyle RA et al. *Lancet Haematol*. 2014;1(1):e28.

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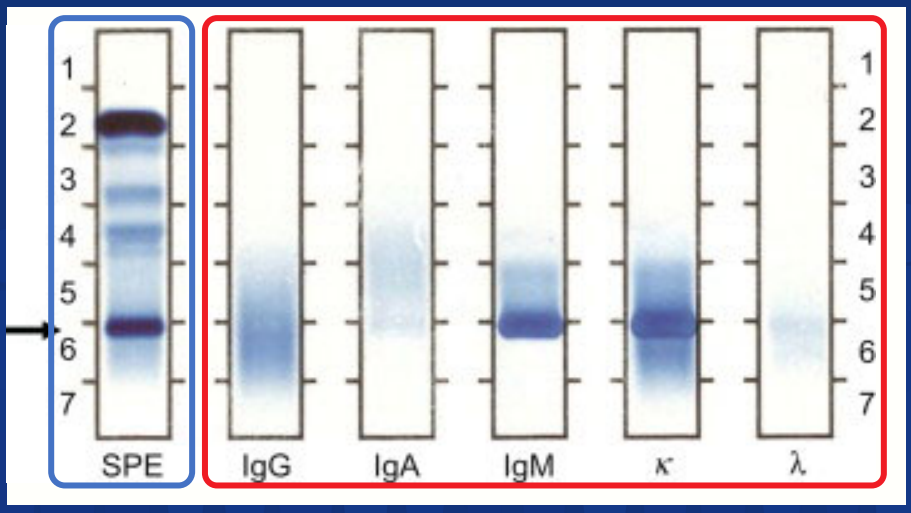
Serum Protein Electrophoresis and Immunofixation



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Light Chain Monoclonal Gammopathy Detection

- **17% of patients with myeloma only produce light chains**[1]
  - **Concentrations are too low to be detected by routine serum immunofixation**
  - Can be found with either 24-hr urine collection for UPEP or a blood test for the serum light chain analysis
  - Random (spot) Bence Jones urine protein electrophoresis alone is **not** considered adequate screening for monoclonal gammopathies
- A sensitive assay for immunoglobulin **free light chains** (FLCs) in the serum is available[2]
  - Several studies have shown the serum FLC test equivalent or superior to the 24-hr urine collection
  - Ratio helps in *diagnosis*; the total FLC value assesses response

1. Kyle RA et al. *Lancet Haematol.* 2014;1(1):e28. 2. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Multiple Myeloma. Version 2.2023.

21

Light Chain Monoclonal Gammopathy Detection

- Serum FLC assay uses κ and λ polyclonal antibodies against specific epitopes that are hidden in intact immunoglobulins but exposed on FLCs

Figure 1, pg 1388

Hutchison CA et al. Serum free light chain assessment in monoclonal gammopathy and kidney disease. *Nat Rev Nephrol.* 2009;5(11):621.

Hutchison CA et al. *Nat Rev Nephrol.* 2009;5(11):621.

22

Light Chain Monoclonal Gammopathy Detection

- Serum FLC assay uses κ and λ polyclonal antibodies against specific epitopes that are hidden in intact immunoglobulins but exposed on FLCs
- FLCs independently quantify the two isotypes
- Monoclonality can be identified by the demonstration of an abnormal **ratio** of κ:λ FLCs

Figure 2, pg 1387

Hutchison CA et al. Serum free light chain assessment in monoclonal gammopathy and kidney disease. *Nat Rev Nephrol.* 2009;5(11):621.

Hutchison CA et al. *Nat Rev Nephrol.* 2009;5(11):621.

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Establishing "Renal Reference Range" for FLC in Chronic Kidney Disease

Serum FLC concentrations in patients with CKD[1]

Figure 2

Hutchison CA et al. Quantitative assessment of serum and urinary polyclonal free light chains in patients with chronic kidney disease. *Clin J Am Soc Nephrol.* 2008;3:1684.

Hutchinson CA et al. established renal reference range κ:λ 0.3–3.1 in patients with renal failure and no other evidence of monoclonal protein.[2]

1. Hutchison CA et al. *Clin J Am Soc Nephrol.* 2008;3:1684. 2. Hutchinson CA et al. *BMC Nephrol.* 2008;9:11.

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SPEP+ Ifix + Light Chain Testing (UPEP or FLC)

Accuracy of diagnostic tests at clinical presentation			
Protocols	**Myeloma**	**AL amyloidosis**	**MGUS**
1 SPE alone	90	50	45
2 SPE and serum IFE	95	70	80
3 SPE and UPE	95	75	70
4 SPE, UPE, serum and urine IFE	97	90	80
5 FLC alone	96	95	30–65
6 SPE and FLC	99	98	85
7 SPE, FLC, serum IFE	99	99	100

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Incidence of Monoclonal Gammopathies

Figure 38.1

Kyle RA, Rajkumar SV. Monoclonal Gammopathy of Undetermined Significance. In: Wiernik P, Goldman J, Dutcher J, Kyle R. (eds). *Neoplastic Diseases of the Blood.* Springer; 2013.

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What is MGUS?

- "Monoclonal gammopathy of undetermined significance (MGUS) is a ***premalignant, clonal*** plasma cell disorder"
  - Presence of a monoclonal protein
    - <3 g/dL of Ig heavy chain or <500 mg/dL 24-hr urine
  - <10% clonal plasma cells in the bone marrow
  - Absence of multiple myeloma or related lymphoplasmacytic malignancies

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

27

"Benign" Monoclonal Gammopathy?

"It is not safe to assume that these patients have a benign condition even after years of observation."

Kyle RA et al. *Am J Med.* 1966;40:426.

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Incidence and Non-Modifiable Risk Factors for MGUS

- The Mayo Clinic/Olmsted County study, in which 21,463 individuals >50 years of age were screened and MGUS was found to be present in 3.2%[1]
  - 5.3% of persons >70 years
  - 8.9% of men >85 years old
- MGUS is 2× more prevalent in men than women[2]
- Prevalence increases with age, from 1.7% in those in their 50s to >5% in those older than 70[3]

Figure 2

Kyle RA et al. Prevalence of monoclonal gammopathy of undetermined significance. *N Engl J Med.* 2018;378(3):241.

1. Kyle RA et al. *N Engl J Med.* 2006;354:1362. 2. Mouhieddine TH et al. *Blood.* 2019;133(23):2484. 3. Vachon CM et al. *Blood.* 2009;114(4):785.

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MGUS SE Minnesota
1960–1994

Figure 2, pg 247

Kyle RA et al. Long-term follow-up of monoclonal gammopathy of undetermined significance. *N Engl J Med.* 2018;378(3):241.

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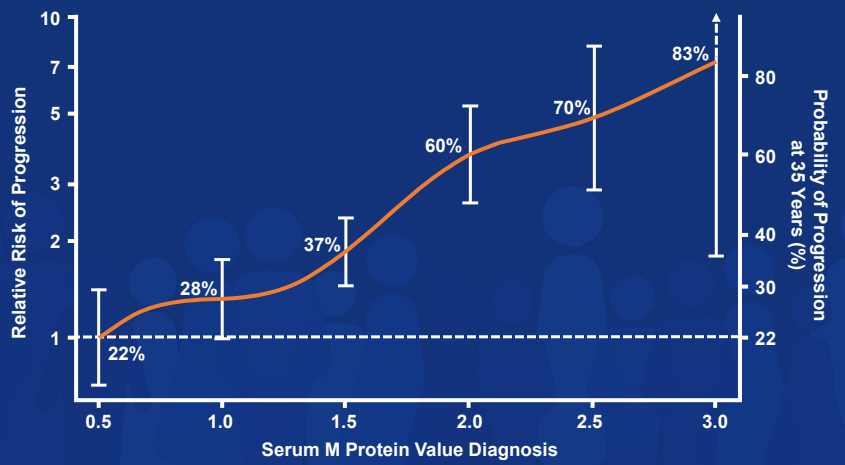
Relative Risk of Progression by Serum M Protein Size



Kyle RA. Unpublished data.

32

MGUS Risk Stratification

Table 2, Appendix

Kyle RA et al. Monoclonal gammopathy of undetermined significance (MGUS) and smoldering (asymptomatic) multiple myeloma: IMWG consensus perspectives risk factors for progression and guidelines for monitoring and management. *Leukemia.* 2010;24(6):1121.

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Evaluation of Monoclonal Gammopathies

SPEP (with ifix)
Serum FLC assay or 24 hr UPEP (with ifix)

↓

CBC, CMP, creatinine, calcium
quant immunos

↓ CRAB or ≥1 risk factor MGUS

Bone marrow biopsy and low-dose skeletal CT

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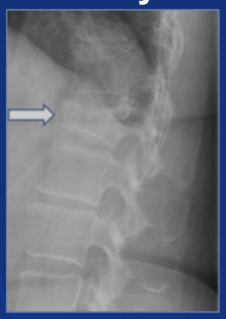
Making the Diagnosis: Imaging Tests

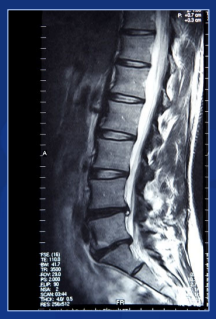
Assess changes in the bone structure and determine the number and size of tumors in the bone

X-ray

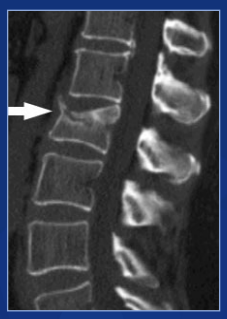


Conventional x-rays reveal punched-out lytic lesions, osteoporosis, or fractures in 75% of patients.

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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Spectrum of Plasma Cell Disorders and Myeloma

MGUS Monoclonal gammopathy of uncertain significance	Smoldering myeloma	High-risk smoldering	Multiple myeloma
M protein <3 g/dL **AND** Plasma cells in bone marrow <10% **AND** No CRAB or "SLiM" high-risk features	M protein >3 g/dL (serum) or over 500 mg/24 hrs (urine) **AND** Plasma cells in bone marrow 10%–60% **AND** **No CRAB or "SLiM" high-risk features**	M protein >2 g/dL **AND** Plasma cells in bone marrow 20%–60% **AND** Free lt chain ratio >20 "Evolving type" SMM increase >10% protein within 6 mo **AND** **No CRAB or "SLiM" high-risk features**	**Malignant plasma cells seen on any biopsy** (usually bone marrow) **AND ≥1 "CRAB" feature** **C:** Calcium elevation (>11 mg/dL) **R:** Renal - low kidney function (serum creatinine >2 mg/dL) **A:** Anemia - low red blood count (Hb <10 g/dL) **B:** Bone disease (≥1 lytic lesions on skeletal radiography, CT, or PET-CT) **OR have ≥1 SLiM "high risk" features:** **S:** >60% plasma cells on bone marrow biopsy **Li:** Serum light chain ratio >100 **M:** >1 lytic lesions on MRI (or PET/ CT scan)
1% risk of progression/year to multiple myeloma or related conditions	*10% risk of progression/year to active myeloma*	*>46% risk of progression in 2 yr to active myeloma*	
Observation **clinical trials**	**Observation** **clinical trials**	**Close observation** **clinical trials** **??Treatment??**	**Frontline treatment** **clinical trials**

Reprinted from *Lancet Oncol* 15(12). Rajkumar SV et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma, e538-e548. Copyright 2014, with permission from Elsevier.

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Multiple Myeloma Fast Facts

- Multiple myeloma 2nd most common blood cancer
- 34,470 new cases of myeloma in 2022
- 138,415 U.S. patients living with myeloma in 2021
- Myeloma is most frequently diagnosed in people 65 to 74 years old
- Black incidence: 14.1/100,000 White incidence: 6.1/100,000

Leukemia & Lymphoma Society. Facts and Statistics. www.lls.org/facts-and-statistics/facts-and-statistics-overview#Myeloma.
SEER Cancer Stat Facts: Myeloma. National Cancer Institute. Bethesda, MD, seer.cancer.gov/statfacts/html/mulmy.html
North American Association of Central Cancer Registries (NAACCR), 2021 www.naaccr.org/DataandPublications/CINAPubs.aspx

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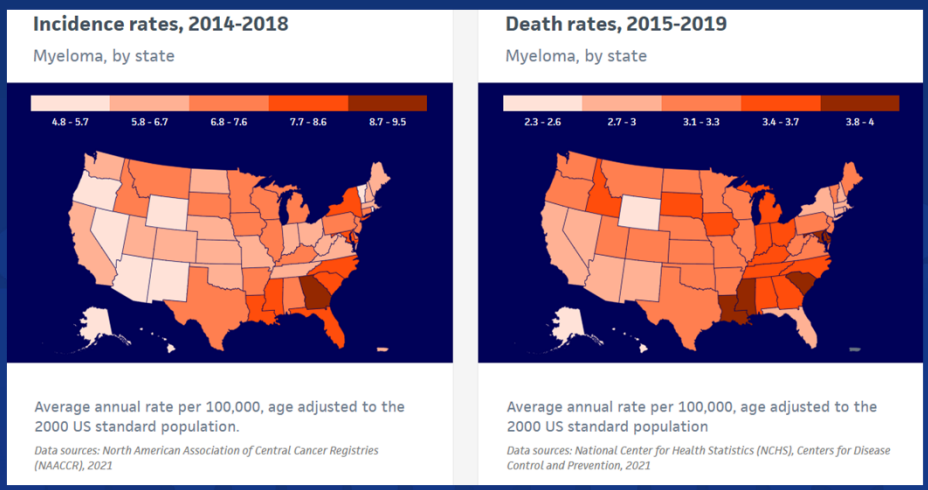
Multiple Myeloma Incidence and Mortality in the U.S.



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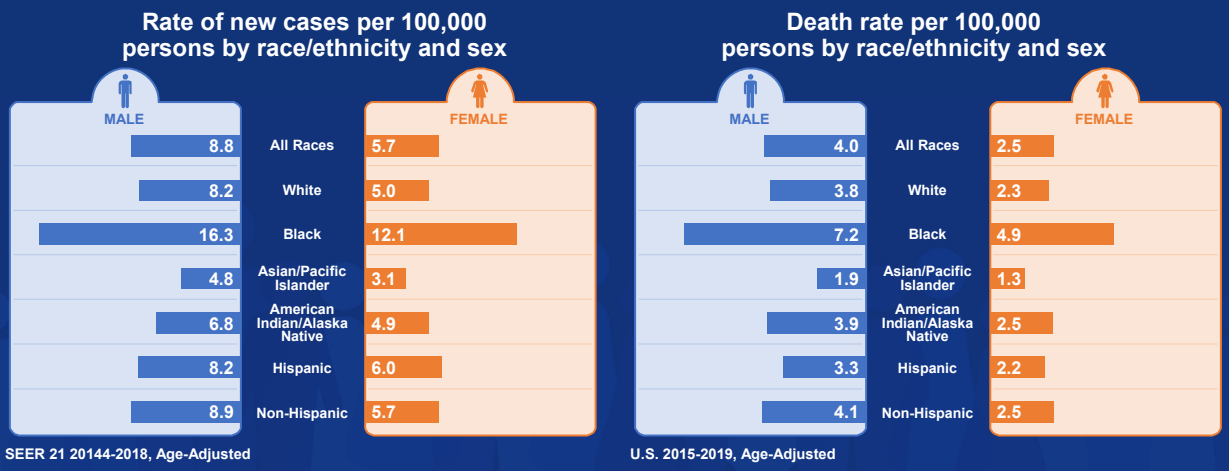
Multiple Myeloma Is Twice as Common—and Twice as Deadly—in Black Patients



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

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Variety of Specialists Assess and Diagnose Multiple Myeloma Patients

from Table 1, pg 637

Kariyawasan CC et al. Multiple myeloma: causes and consequences of delay in diagnosis. *QJM.* 2007;100(10):635.

Typical diagnostic intervals[1]
Hematology/oncology: <3 months
Primary care: >6 months

Over 50% of patients with symptomatic myeloma have 3 or more primary care visits before referral[2]

1. Kariyawasan CC et al. *QJM.* 2007;100(10):635. 2. Hossain MI et al. *Blood.* 2021;138(suppl 1):3007.

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Multiple Myeloma Demographic Risk Factors[1,2]

- Older age
- Male sex
- 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)

1. Schinasi LH et al. *Br J Haematol*. 2016;175:87. 2.Leiba M et al. *Blood*. 2013;122(21):5346.

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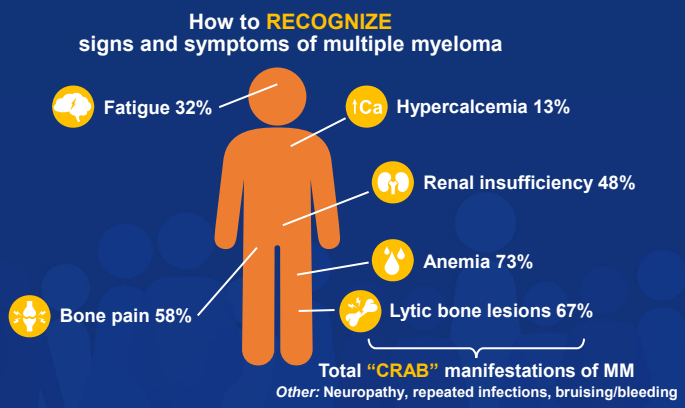
How to Recognize Signs and Symptoms of Multiple Myeloma



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

Figure 2 from Mikhael J et al. Multiple myeloma for the primary care provider: a practical review to promote earlier diagnosis among diverse populations. *Am J Med.* 2023;136(1):p33-p41. https://creativecommons.org/licenses/by/4.0/

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Disease presentation and complications of myeloma different in patients by race

More common in Black patients

- Hypercalcemia
- Kidney dysfunction
  - Hemodialysis
- Anemia

Less common in Black patients

- Bone fractures

Blacks/African Americans are *less likely* than Whites to receive a full diagnostic workup for multiple myeloma

Mikhael J et al. *Am J Med.* 2023;136:p33.

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Don't Delay Testing for Multiple Myeloma

- Initiate preliminary lab testing for:
  - Persistent bone or back pain
  - Unexplained fracture
  - Incidental findings associated with myeloma
    - Anemia
    - Hypercalcemia or leukopenia
    - Lytic bone lesions
    - Impaired kidney function
    - Neuropathy
    - Osteopenia/osteoporosis atypical of age and/or gender

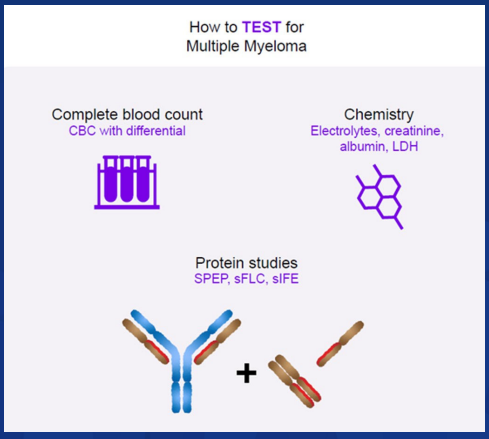

Figure 2 from Mikhael J et al. *Am J Med.* 2023;136(1):33. https://creativecommons.org/licenses/by/4.0/

Dimopoulos M et al. *Blood.* 2011;117(18):4701.

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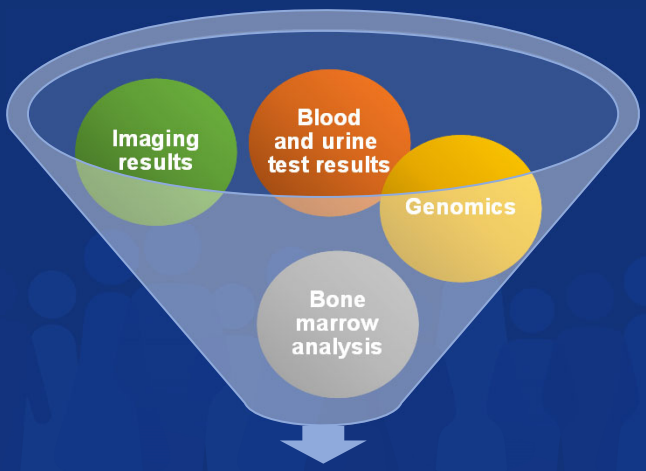
Putting the Results Together



Staging, prognosis, and risk assessment

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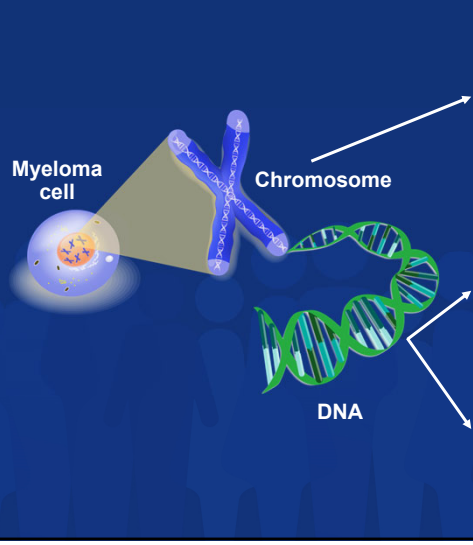
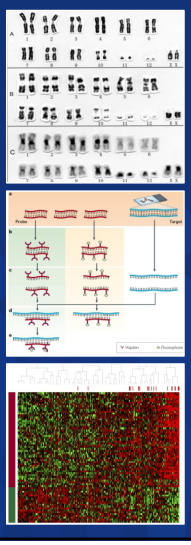
Staging Myeloma: The Importance of Genomic Testing





Conventional cytogenetic analysis (karyotyping)

FISH (fluorescence in situ hybridization)

Advances
- Genetic expression profiling (GEP)
- Whole-genome/whole-exome sequencing
- Plasma cell next-generation sequencing

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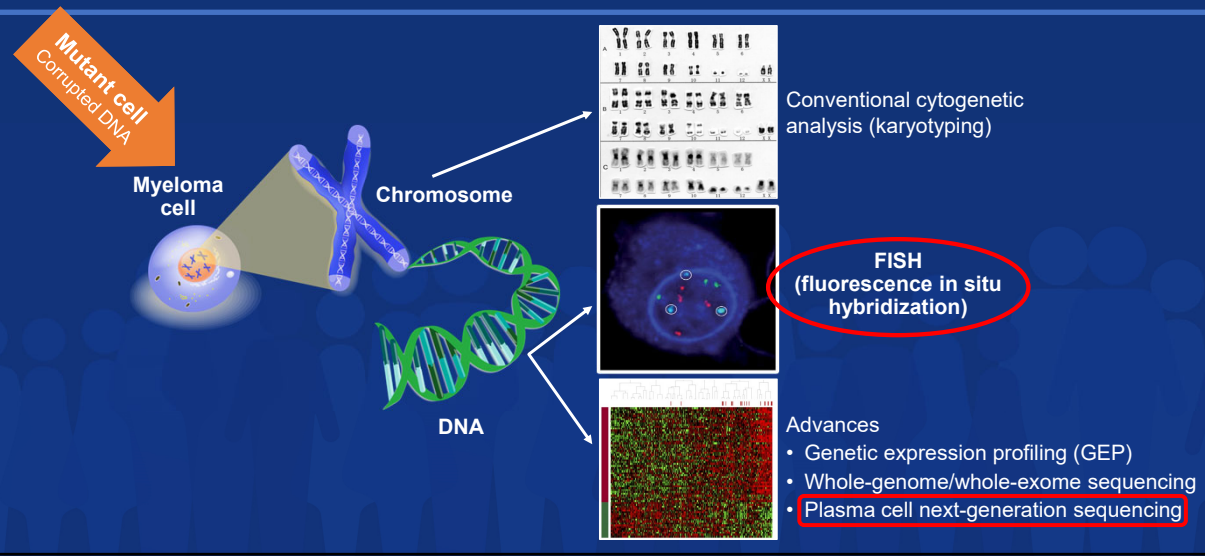
Staging Myeloma: The Importance of Genomic Testing



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Staging Myeloma: FISH Helps to Assign Risk in Myeloma

Risk category	High risk	Standard risk
Findings on chromosome (FISH) analysis results in the bone marrow	**FISH:** • **Deletion 17th chromosome** • **Gain of chromosome 1q** • **Translocation 4 and 14** • **Translocation 14 and 16** • **Translocation 14 and 20** **NGS: p53 mutation** (on chrom 17) • **Double-hit myeloma: 2 high-risk genetic abnormalities** • **Triple-hit myeloma: 3 or more high-risk genetic abnormalities**	**FISH:** • **Hyperdiploid: *More than 1 pair of chromosomes (trisomies)*** • **Translocation 11 and 14** • **Translocation 6 and 14** • **Others** • **Normal**

Mikhael JR et al. *Mayo Clin Proc.* 2013;88:360.

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Revised International Staging System for Multiple Myeloma

From International Myeloma Working Group

Stage 1	Stage 2	Stage 3
β2 microglobulin under 3.6 mg/L + **Normal** Lactate dehydrogenase (LDH) **AND** **NO high-risk cytogenetics (FISH)**	**Does not meet criteria for Stage 1 or 3**	β2 microglobulin over 5.5 mg/L + **HIGH** Lactate dehydrogenase (LDH) **AND/OR** **High-risk cytogenetics (FISH)** Deletion 17th chromosome Translocation 4th and 14th Translocation 14th and 16th Translocation 14th and 20th

*Based on the Updated Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) Consensus Guidelines 2013 Mikhael JR et al. *Mayo Clin Proc.* 2013;88:360.
Palumbo A et al. *J Clin Oncol.* 2015;33(26):2863.

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Revised International Staging System for Multiple Myeloma

From International Myeloma Working Group

R-ISS stage	5-year OS (%)	5-year PFS (%)
I	82	55
II	62	36
III	40	24

*Based on the Updated Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) Consensus Guidelines 2013 Mikhael JR et al. *Mayo Clin Proc.* 2013;88:360.
Palumbo A et al. *J Clin Oncol.* 2015;33(26):2863.

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SO…..
HOW DO WE TREAT
MULTIPLE MYELOMA?

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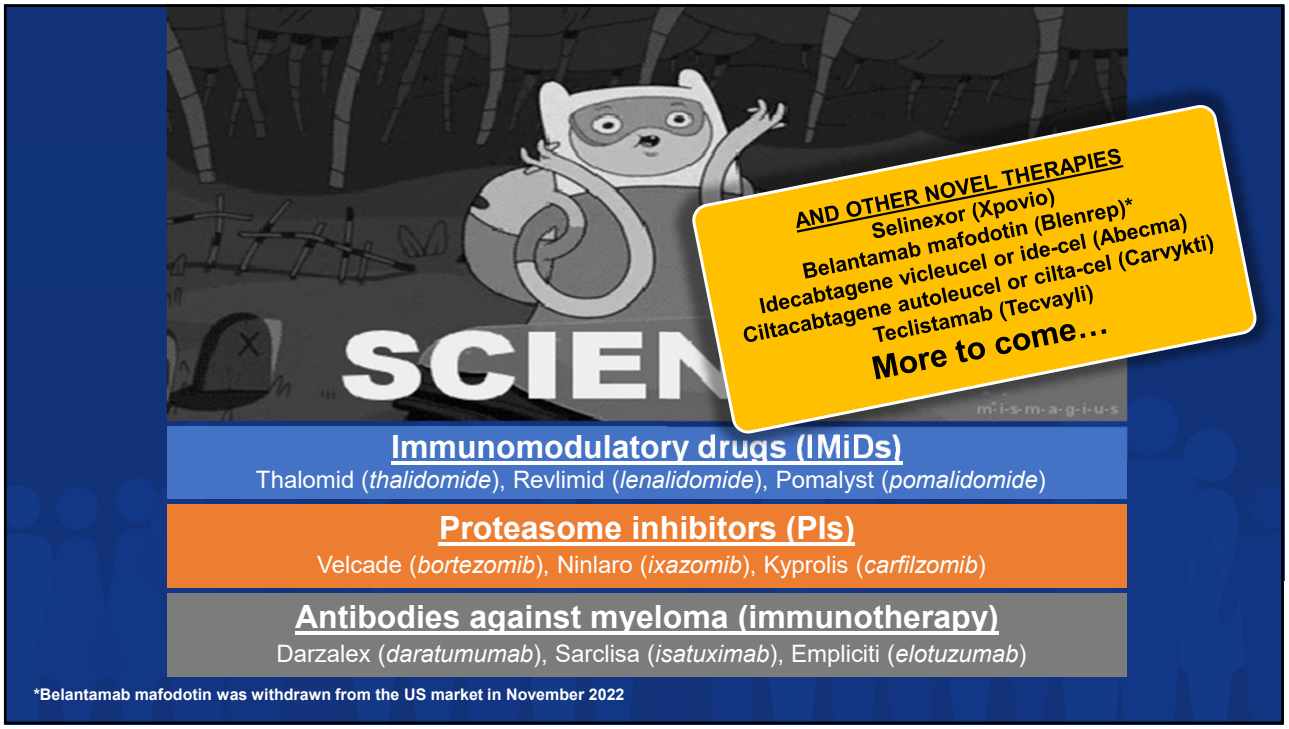

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Understanding Myeloma Biology Resulted in Targeted Therapies for Multiple Myeloma

Figure 4, pg 611

Hideshima T et al. Advances in biology of multiple myeloma: clinical applications. *Blood.* 2004;104:607.

Hideshima T, Anderson KC. *Nature Rev Cancer.* 2002;2:927.
Hideshima T et al. *Blood.* 2004;104:607.
Hideshima T, Anderson KC. *Nat Rev Cancer.* 2007;7:585.

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Treatment Sequence and Regimens for Active Myeloma

Frontline treatment

Induction

- **Bortezomib-lenalidomide-dex (RVd)*†**
- Bortezomib-thalidomide-dex: (VTD)
- **Cyclophosphamide-bortezomib-dex: (CyBorD)**
- Daratumumab-lenalidomide-dex (DRd)*†
- Daratumumab-lenalidomide-melphalan-dex
- Daratumumab-lenalidomide-thalidomide-dex
- **Carfilzomib-lenalidomide-dex (KRd)***
- **Daratumumab-lenalidomide-bortezomib-dex (D-RVd)†‡**
- **Clinical trials**

Consolidation

- **Stem cell transplant**
- Continue induction
- **Clinical trial**

Maintenance

- **Lenalidomide**
- Bortezomib
- Ixazomib
- Observation
- Thalidomide
- **Daratumumab-lenalidomide**
- **Clinical trial**

Relapsed

Rescue

(1–3 Prior Therapies)

- **Carfilzomib-lenalidomide-dex***
- **Daratumumab + Vd, Kd, Pd, or Rd***
- **Isatuximab + pom/dex or Kd***
- **Ixazomib-lenalidomide-dex***
- **Pom-bortezomib-dex***
- Bortezomib-liposomal doxorubicin-dex†
- Carfilzomib (twice weekly)-dex†
- Elotuzumab-lenalidomide-dex†
- Selinexor-bortezomib-dex†

(>3 Prior Therapies)

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

- **Idecabtagene vicleucel**
- **Ciltacabtagene autoleucel**
- **Teclistamab-cqyv**

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

- **Selinexor/dexamethasone**

CLINICAL TRIALS!

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

National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Multiple Myeloma. Version 2.2023.

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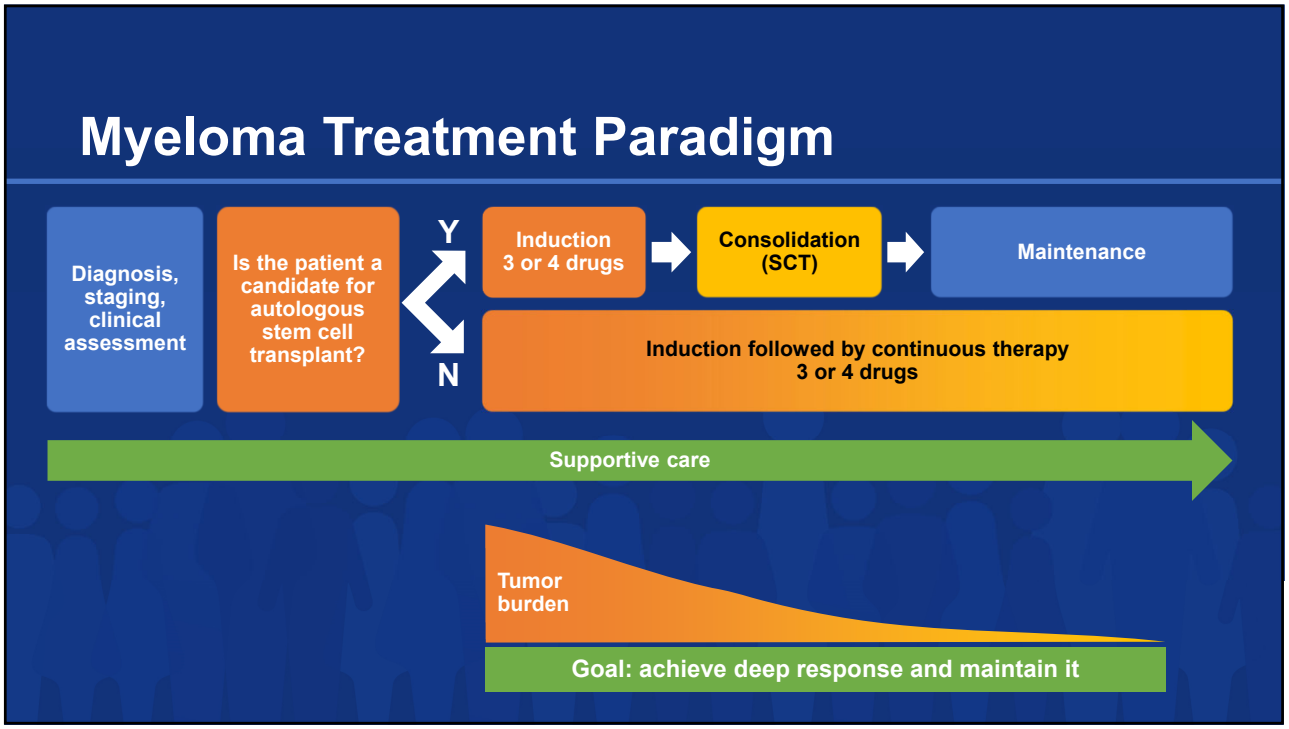

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Advancements in Newly Diagnosed Myeloma: An Achievement of the Patient-Doctor Relationship

Regimen	Major Response	All Reponses
Melphalan prednisone	4%	35%
Thalidomide + dex	4%	63%
Bortezomib + dex	37%	78%
Lenalidomide + dex	32%	91%
Melphalan + prednisone + thalidomide	21%	62%
Bortezomib + lenalidomide + dex	43%	83%
Ixazomib + lenalidomide + dex	63%	80%
Carfilzomib + lenalidomide + dex	49%	86%
Daratumumab + melphalan + prednisone + thalidomide	72%	90%
Daratumumab + bortezomib + lenalidomide + dex	90%	99%
Daratumumab + lenalidomide + dex	79%	92%
Daratumumab + lenalidomide + carfilzomib + dex	95%	100%

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Guiding Principles for Multiple Myeloma Management

- Use at least three drugs for induction therapy
- Aim for the deepest response (includes minimal residual disease)
- Consider stem cell transplant either now or later
- Provide maintenance therapy to prolong response
- Approach, regimens, and goals must be individualized based on age, organ function, risk assessment, and personal factors
- Consider clinical trials

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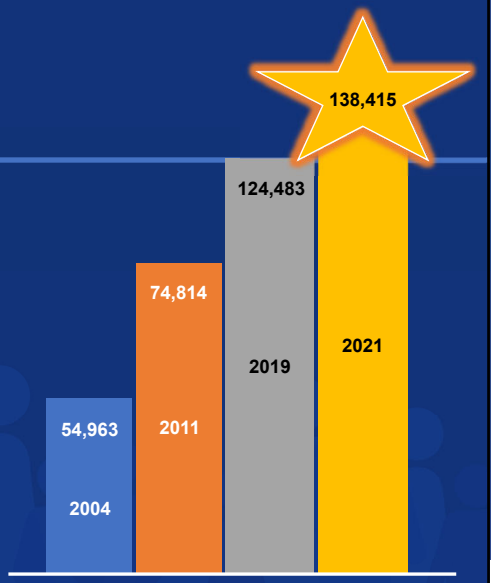
Advancements in Survival of Multiple Myeloma

- With new 3- and 4-drug treatment regimens, the response rates are now >99%
- We have had 31 treatment options FDA approved for myeloma during 2015–2022!
- With novel therapies used at diagnosis, survival has improved dramatically
  - From 3.8 years to >9 years!
  - The 10-year relative survival rate has nearly doubled in the past 20 years

Myeloma is not curable…yet. But it is survivable now!



Pashos CL et al. *Blood.* 2011;118. Abstract 5070.
Costa LJ et al. *Blood Adv.* 2017;1(4):282.

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

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In Conclusion

- Multiple myeloma is the second most common blood cancer
- It frequently presents like many other medical conditions
  - Fatigue, infections, bone pain/fractures, hypercalcemia, renal insufficiency, or anemia
- To evaluate for myeloma, need to test for the myeloma protein
  - SPEP+ free serum light chains immunofixation and quantitative immunoglobulins
- Myeloma and MGUS have twice the incidence in Blacks compared to other races
- Stage and risk are based on myeloma laboratory test and cytogenetics
- The treatment is now based on myeloma biology and surface markers which has improved response rates and survival

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Questions and Answers

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