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

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
The MMRF CureCloud® and MMRF Resources for Patients

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

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.
How does the MMRF CureCloud work?

1. Sign up on the MMRF CureCloud website or in person at a CureCloud participating clinic and see if you are eligible.
2. Convenience at-home blood test. A medical professional will come to you.
3. Personalized insights. Learn more about your myeloma.
4. Medical record collection. Provide your myeloma doctors and we’ll contact them.
5. Discuss with your doctor.

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.

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
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.

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
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

<table>
<thead>
<tr>
<th>WBC = 4.8</th>
<th>4.0–10.0 K/μL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin = 10.3</td>
<td>12.0–16.0 g/dL NEW</td>
</tr>
<tr>
<td>Platelet = 200</td>
<td>140–400 K/μL</td>
</tr>
<tr>
<td>Creatinine = 2.90</td>
<td>0.70–1.30 mg/dL NEW</td>
</tr>
<tr>
<td>Calcium level = 10.5</td>
<td>8.6–10.3 mg/dL NEW</td>
</tr>
<tr>
<td>Albumin level = 2.5</td>
<td>3.5–4.9 g/dL NEW</td>
</tr>
</tbody>
</table>

Hemoglobin A1C = 6%
Dipstick urinalysis = “normal”

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

Spot urine for Bence Jones protein: negative

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
**Case Presentation**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kappa free light chains</td>
<td>0.01 (0.33–1.94 mg/dL)</td>
<td></td>
</tr>
<tr>
<td>Lambda free light chains</td>
<td>&gt;1,800 (0.57–2.63 mg/dL)</td>
<td></td>
</tr>
<tr>
<td>Kappa lambda FLC ratio</td>
<td>&lt;0.01 (0.26–1.65)</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>3.80 (0.70–1.30 mg/dL)</td>
<td></td>
</tr>
<tr>
<td>Calcium level</td>
<td>12.5 (8.6–10.3 mg/dL)</td>
<td></td>
</tr>
<tr>
<td>Albumin level</td>
<td>2.0 (3.5–4.9 g/dL)</td>
<td></td>
</tr>
<tr>
<td>Bence Jones quantitation</td>
<td>4.1 g/24 hr</td>
<td></td>
</tr>
<tr>
<td>Urine immunofixation</td>
<td>a monoclonal free Lambda light chain</td>
<td></td>
</tr>
</tbody>
</table>

**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)

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

**What is multiple myeloma?**

**BLOOD**
- Myeloma is a cancer of the blood
- Myeloma crowds out normal blood-forming cells, causing anemia

**BONES**
- Surrounding bone where myeloma cells grow is damaged/weakened
- Myeloma cells activate bone destruction → blood calcium levels

**Kidneys**
- Large amounts of M proteins can overwork or cause damage to the kidneys
Q: Where do we start looking for plasma cell disorders?

A: Monoclonal protein!
Anatomy of the Antibody

Immunoglobulin classes: IgG, IgA, and IgM

- Red – disulfide links
- Green – light chains
- Blue – heavy chains

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

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 \(\beta\) region may affect >40% of IgA monoclonal proteins
- Quantitative serum immunoglobulins can detect *immunopareshis*\(^2\)
  - 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 \(\geq 0.02\) g/dL and a urine M protein \(\geq 0.004\) g/dL
- 17% of patients with myeloma only produce light chains\(^4\)
  - Check for M protein and light chains in workup!

---

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 available²
  - 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


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

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


Establishing “Renal Reference Range” for FLC in Chronic Kidney Disease

Serum FLC concentrations in patients with CKD¹

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

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

<table>
<thead>
<tr>
<th>Protocols</th>
<th>Myeloma</th>
<th>AL amyloidosis</th>
<th>MGUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 SPE alone</td>
<td>90</td>
<td>50</td>
<td>45</td>
</tr>
<tr>
<td>2 SPE and serum IFE</td>
<td>95</td>
<td>70</td>
<td>80</td>
</tr>
<tr>
<td>3 SPE and UPE</td>
<td>95</td>
<td>75</td>
<td>70</td>
</tr>
<tr>
<td>4 SPE, UPE, serum and urine IFE</td>
<td>97</td>
<td>90</td>
<td>80</td>
</tr>
<tr>
<td>5 FLC alone</td>
<td>96</td>
<td>95</td>
<td>30–65</td>
</tr>
<tr>
<td>6 SPE and FLC</td>
<td>99</td>
<td>98</td>
<td>85</td>
</tr>
<tr>
<td>7 SPE, FLC, serum IFE</td>
<td>99</td>
<td>99</td>
<td>100</td>
</tr>
</tbody>
</table>
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


“Benign” Monoclonal Gammopathy?

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

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\(^3\)

MGUS SE Minnesota 1960–1994

Figure 2, pg 247

Relative Risk of Progression by Serum M Protein Size

Kyle RA. Unpublished data.
MGUS Risk Stratification

Table 2, Appendix

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
Making the Diagnosis: Imaging Tests

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

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-ray</td>
<td>Conventional x-rays reveal punched-out lytic lesions, osteoporosis, or fractures in 75% of patients.</td>
</tr>
<tr>
<td>MRI</td>
<td>MRI and PET/CT appear to be more sensitive (85%) than skeletal x-rays for the detection of small lytic bone lesions.</td>
</tr>
<tr>
<td>CT scan</td>
<td></td>
</tr>
<tr>
<td>PET scan</td>
<td></td>
</tr>
</tbody>
</table>

Spectrum of Plasma Cell Disorders and Myeloma

<table>
<thead>
<tr>
<th>Condition</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>MGUS</td>
<td>Monoclonal gammopathy of uncertain significance</td>
</tr>
<tr>
<td>Smoldering myeloma</td>
<td>M protein ≥2 g/dL, AND Plasma cells in bone marrow ≥10%–60% AND ≥1 “CRAB” feature OR ≥1 SLiM “high risk” features (C: Calcium elevation (&gt;11 mg/dL), R: Renal - low kidney function (serum creatinine &gt;2 mg/dL), A: Anemia - low red blood count (Hb &lt;10 g/dL), B: Bone disease (≥1 lytic lesions on skeletal radiography, CT, or PET-CT))</td>
</tr>
<tr>
<td>High-risk smoldering</td>
<td>M protein ≥2 g/dL AND Plasma cells in bone marrow ≥10%–60% AND Free light chain ratio &gt;20 AND “Evolving type” SMM increase &gt;10% protein within 6 mo and ≥1 lytic lesions on MRI (or PET/CT scan)</td>
</tr>
<tr>
<td>Multiple myeloma</td>
<td>Malignant plasma cells seen on any biopsy (usually bone marrow) AND ≥1 “CRAB” feature OR have ≥1 SLiM “high risk” features: (S: &gt;60% plasma cells on bone marrow biopsy, L: Serum light chain ratio &gt;100, M: &gt;1 lytic lesions on MRI (or PET/CT scan))</td>
</tr>
</tbody>
</table>

Multiple Myeloma Fast Facts

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

Multiple Myeloma Incidence and Mortality in the U.S.

- Incidence rates, 2014-2018:
  - Myeloma, by state map.
- Death rates, 2015-2019:
  - Myeloma, by state map.

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

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

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Races</td>
<td>8.8</td>
<td>5.7</td>
</tr>
<tr>
<td>White</td>
<td>8.2</td>
<td>5.0</td>
</tr>
<tr>
<td>Black</td>
<td>16.3</td>
<td>12.1</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>4.8</td>
<td>3.1</td>
</tr>
<tr>
<td>American Indian/Alaska Native</td>
<td>6.8</td>
<td>4.9</td>
</tr>
<tr>
<td>Hispanic</td>
<td>8.2</td>
<td>6.0</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>8.9</td>
<td>5.7</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Races</td>
<td>4.0</td>
<td>2.5</td>
</tr>
<tr>
<td>White</td>
<td>3.8</td>
<td>2.3</td>
</tr>
<tr>
<td>Black</td>
<td>7.2</td>
<td>4.9</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>1.9</td>
<td>1.3</td>
</tr>
<tr>
<td>American Indian/Alaska Native</td>
<td>3.9</td>
<td>2.5</td>
</tr>
<tr>
<td>Hispanic</td>
<td>3.3</td>
<td>2.2</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>4.1</td>
<td>2.5</td>
</tr>
</tbody>
</table>

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

- Hematology/oncology: <3 months
- Primary care: >6 months

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

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)

---

How to Recognize Signs and Symptoms of Multiple Myeloma

How to RECOGNIZE signs and symptoms of multiple myeloma

- Fatigue 32%
- Hypercalcemia 13%
- Renal insufficiency 48%
- Anemia 73%
- Bone pain 58%
- Lytic bone lesions 67%

Total “CRAB” manifestations of MM

Other: Neuropathy, repeated infections, bruising/bleeding

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

---

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

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/
Putting the Results Together

Staging, prognosis, and risk assessment

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
Applying the Latest Clinical Data in Multiple Myeloma Patient Care in the Community Setting

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

Staging Myeloma: FISH Helps to Assign Risk in Myeloma

<table>
<thead>
<tr>
<th>Risk category</th>
<th>High risk</th>
<th>Standard risk</th>
</tr>
</thead>
</table>
| 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 |

### Revised International Staging System for Multiple Myeloma

*From International Myeloma Working Group*

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


### Revised International Staging System for Multiple Myeloma

*From International Myeloma Working Group*

<table>
<thead>
<tr>
<th>R-ISS stage</th>
<th>5-year OS (%)</th>
<th>5-year PFS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>82</td>
<td>55</td>
</tr>
<tr>
<td>II</td>
<td>62</td>
<td>36</td>
</tr>
<tr>
<td>III</td>
<td>40</td>
<td>24</td>
</tr>
</tbody>
</table>

SO..... HOW DO WE TREAT MULTIPLE MYELOMA?

- **Immunomodulatory drugs (IMiDs)**
  - Thalidomide
  - Lenalidomide
  - Pomalidomide

- **Proteasome inhibitors (PIs)**
  - Bortezomib
  - Ixazomib
  - Carfilzomib

- **Antibodies against myeloma (immunotherapy)**
  - Daratumumab
  - Isatuximab
  - Elotuzumab

*Belantamab mafodotin was withdrawn from the US market in November 2022

**AND OTHER NOVEL THERAPIES**
- Selinexor (Xpovio)
- Belantamab mafodotin (Blenrep)*
- Idecabtagene vicelle or Ide-cel (Abecma)
- Ciltacabtagene autoleucel or cila-cel (Carvykti)
- Tecentriq (Tecvayli)

More to come...
### Understanding Myeloma Biology Resulted in Targeted Therapies for Multiple Myeloma

Figure 4, pg 611


---

### Treatment Sequence and Regimens for Active Myeloma

**Frontline treatment**

**Induction**
- Bortezomib-thalidomide-dex (VTD)
- Lenalidomide-thalidomide-dex (CyBoRd)
- Daratumab-thalidomide-dex (DRd)
- Carfilzomib-thalidomide-dex (KRd)
- Clinical trials

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

**Maintenance**
- Lenalidomide
- Bortezomib
- Observation
- Thalidomide
- Daratumumab
- Clinical trial

**Relapsed**

**Rescue**
- (1–3 Prior Therapies)
  - Carfilzomib-thalidomide-dex
  - Daratumumab + Velcade, Pd, or Rd
  - Isatuximab + pom/dex or Rd
  - Ixazomib-thalidomide-dex
  - Pom-bortezomib-dex
  - Daratumumab-bortezomib-dex
  - Carfilzomib (twice weekly)-dex
  - Elotuzumab-thalidomide-dex
  - Selinexor-bortezomib-dex

- (4+ Prior Therapies)
  - Idecabtagene vilocilubine
  - Ciltacabtagene autoleucil
  - Tiseluxamab-covac
  - After 24 prior therapies and in patients whose disease is refractory to 22 PIs, 22 IMiDs, and an anti-CD38 mAb

*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.

Applying the Latest Clinical Data in Multiple Myeloma Patient Care in the Community Setting

January 26, 2023

Myeloma Treatment Paradigm

Diagnosis, staging, clinical assessment

Is the patient a candidate for autologous stem cell transplant? Y N

Induction 3 or 4 drugs

Consolidation (SCT)

Maintenance

Induction followed by continuous therapy 3 or 4 drugs

Supportive care

Tumor burden

Goal: achieve deep response and maintain it

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

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Major Response</th>
<th>All Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melphalan prednisone</td>
<td>4%</td>
<td>35%</td>
</tr>
<tr>
<td>Thalidomide + dex</td>
<td>4%</td>
<td>63%</td>
</tr>
<tr>
<td>Bortezomib + dex</td>
<td>37%</td>
<td>78%</td>
</tr>
<tr>
<td>Lenalidomide + dex</td>
<td>32%</td>
<td>91%</td>
</tr>
<tr>
<td>Melphalan + prednisone + thalidomide</td>
<td>21%</td>
<td>62%</td>
</tr>
<tr>
<td>Bortezomib + lenalidomide + dex</td>
<td>43%</td>
<td>83%</td>
</tr>
<tr>
<td>Ixazomib + lenalidomide + dex</td>
<td>63%</td>
<td>80%</td>
</tr>
<tr>
<td>Carfilzomib + lenalidomide + dex</td>
<td>49%</td>
<td>86%</td>
</tr>
<tr>
<td>Daratumumab + melphalan + prednisone + thalidomide</td>
<td>72%</td>
<td>90%</td>
</tr>
<tr>
<td>Daratumumab + bortezomib + lenalidomide + dex</td>
<td>90%</td>
<td>99%</td>
</tr>
<tr>
<td>Daratumumab + lenalidomide + dex</td>
<td>79%</td>
<td>92%</td>
</tr>
<tr>
<td>Daratumumab + lenalidomide + carfilzomib + dex</td>
<td>95%</td>
<td>100%</td>
</tr>
</tbody>
</table>
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

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!

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

Questions and Answers
We wish to thank AbbVie; Bristol Myers Squibb; and Janssen Biotech, Inc., administered by Janssen Scientific Affairs, LLC for providing educational grants in support of this activity.