Understanding Your Lab Report

May 13, 2024

Tech Support
1-719-234-7952
Resources

- Resource tab includes
  - Speaker bios
  - Copy of the slide presentation
  - Exhibit Hall

Submit your questions throughout the program!
**MMRF Research Initiatives**

1. **MMRF Myeloma Accelerator Challenge (MAC) Grants**
   - Broad, multi-institutional research grants designed to advance clinical trial concepts in the areas of
     - High-risk newly diagnosed multiple myeloma (NDMM)
     - High-risk smoldering myeloma (SMM)
   - Each research network will be funded up to $7M over 3 years

2. **MMRF Horizon Adaptive Platform Trials**
   - Paired with MAC grants
   - Done in collaboration with 14 MMRC sites
   - Trials in relapsed/refractory myeloma, high-risk NDMM, high-risk SMM

*For more information, visit themmrf.org*

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**2023 Myeloma Accelerator Challenge Program Grant Recipients**

- **Transforming Treatment of High-Risk Myeloma**
  - Network includes: Tisch Cancer Center at Mt Sinai, Albert Einstein Medical College, Hackensack University Medical Center, Stanford University Medical Center, UCSF, Washington University of Saint Louis

- **A Systems Biology Approach to High-Risk Myeloma**
  - Network includes: Erasmus Medical Center, Rotterdam; Amsterdam University Medical Centers; Julius Maximilian University of Wurzburg; University of Turin; University of Salamanca

- **Clinical and Multi-Omics Platforms to Define High-Risk Smoldering Myeloma**
  - Network includes: Emory University, Atrium Health Levine Cancer Institute, Icahn School of Medicine at Mt. Sinai, Mass General Hospital, Mayo Clinic, MSKC Institute, Dana-Farber Cancer Institute

Each network will receive $7M over 3 years for a total $21M investment by the MMRF, meant to foster collaboration and advance compelling hypotheses that are ready for rapid testing in clinical trials.
MMRF 2023 Scholars Grant Awardees

Eden Biltibo  
Vanderbilt University Medical Center

Grant Proposal:  
Identifying Effective and Cost-Conscious Maintenance Daratumumab Dosing  
Frequent hospital visits cost money and increase exposure to bad bugs. If we prove every 8-week daratumumab works as good, patients won’t have to come to the hospital on a monthly basis.

Joselle Cook  
Mayo Clinic, Rochester

Grant Proposal:  
Prevalence Of MGUS Among Unique Populations Of Black People  
For people who test positive for MGUS, we will perform DNA testing which will inform us about ancestral origins and will give information on genetic variations that we know are associated with MGUS and MM.

Eden Biltibo, MD, MS is a Hematology/Oncology clinical fellow at Vanderbilt University Medical Center, who is passionate about developing strategies to bridge health care disparities in Multiple Myeloma care. She particularly focuses on the equitable utilization of immunotherapeutics in multiple myeloma and improving racial diversity of clinical trial participants in those trials.

Joselle Cook, MBBS is an assistant professor and Hematology/Oncology Fellow at Mayo Rochester. Dr. Cook received her medical degree from University of the West Indies Faculty of Medical Sciences. She completed her residency and fellowship training in 2022.

Speakers

Amy Blake, NP-C  
Karmanos Cancer Institute  
Detroit, Michigan

Craig Emmitt Cole, MD  
Wayne State University  
Karmanos Cancer Institute  
Detroit, Michigan

Michigan State University College of Human Medicine  
Karmanos Cancer Institute  
East Lansing, Michigan
Understanding Your Blood Test

Amy Blake, NP-C
Karmanos Cancer Institute
Detroit, Michigan

Multiple Myeloma Affects Your Bones, Blood, and Kidneys

**BONES**
- Surrounding bone where myeloma cells grow is affected
- Myeloma cells activate bone destruction

**BLOOD**
- Myeloma is a cancer of the blood
- Myeloma crowds out normal blood cells

**KIDNEYS**
- Large amounts of M protein can overwork or cause damage to the kidneys

Light chain
(kappa [κ] or lambda [λ])

Heavy chains
(IgG, IgA, IgM, IgD, IgE)

Multiple myeloma cells

Normal plasma cells
Multiple Myeloma Affects Your Bones, Blood, and Kidneys

The clinical features that are characteristic of multiple myeloma

C
High levels of calcium in the blood

R
Decreased kidney (renal) function

A
Low amount of red blood cells (anemia)

B
Presence of bone damage

The Right Tests: Common Tests Conducted in Myeloma Patients

- Blood tests
  - Confirms the type of myeloma or precursor condition

- Urine tests

- Bone marrow biopsy
  - Confirms diagnosis of myeloma
  - Determines how advanced the myeloma or precursor condition is

- Imaging tests
  - Detects the presence and extent of bone disease and the presence of myeloma outside of the bone marrow
Understanding Your Labs!

**Blood Tests**

- CBC: complete blood count
  - Number of red blood cells, white blood cells, and platelets
- CMP: complete metabolic panel
  - Measure levels of albumin, calcium, LDH, BUN, and creatinine. Assess function of kidney, liver, and bone status and the extent of disease
- β2M: beta-2 microglobulin
  - Determine the level of a protein that indicates the presence/extent of multiple myeloma and kidney function
- SPEP: serum protein electrophoresis
  - Detect the presence and level of M protein
- IFE: immunofixation electrophoresis
  - Identify the type of abnormal antibody proteins
- SFLC: serum free light chain assay
  - Freelite test measures light chains (kappa or lambda)

**Complete Blood Count (CBC) Normal Range**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>What is measured</strong></td>
<td>The level of hemoglobin and the number of red blood cells, white blood cells, and platelets</td>
</tr>
<tr>
<td><strong>Component</strong></td>
<td><strong>Normal range</strong></td>
</tr>
<tr>
<td>Red blood cells</td>
<td>Women: 3.90 to 5.03 × 10^{12}/L</td>
</tr>
<tr>
<td></td>
<td>Men: 4.32 to 5.72 × 10^{12}/L</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>Women: 12.1 to 15.1 g/dL</td>
</tr>
<tr>
<td></td>
<td>Men: 13.8 to 17.2 g/dL</td>
</tr>
<tr>
<td>White blood cells</td>
<td>Total: 3.5 to 10.5 × 10^{9}/L</td>
</tr>
<tr>
<td></td>
<td>Neutrophils (as absolute neutrophil count [ANC]): 1.7 to 7.0 × 10^{9}/L</td>
</tr>
<tr>
<td></td>
<td><strong>Monocytes:</strong> 0.2 to 1.0 × 10^{9}/L</td>
</tr>
<tr>
<td></td>
<td><strong>Lymphocytes:</strong> 1.0 to 3.0 × 10^{9}/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>150 to 450 × 10^{9}/L</td>
</tr>
</tbody>
</table>

*Additional components not listed here may be analyzed, but they are not typically used for diagnosing or managing myeloma.

*Normal ranges vary slightly from one institution to another.
### Understanding Your Labs!  
**Complete Metabolic Panel (CMP) Normal Range**

<table>
<thead>
<tr>
<th>Component*</th>
<th>Normal range†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>3.4 to 5.4 g/dL</td>
</tr>
<tr>
<td>BUN (blood urea nitrogen)</td>
<td>6 to 20 mg/dL</td>
</tr>
<tr>
<td>Calcium</td>
<td>8.5 to 10.2 mg/dL</td>
</tr>
<tr>
<td>Chloride</td>
<td>96 to 106 mEq/L</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.6 to 1.3 mg/dL</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.7 to 5.2 mEq/L</td>
</tr>
<tr>
<td>Sodium</td>
<td>135 to 145 mEq/L</td>
</tr>
</tbody>
</table>

*Additional components not listed here may be analyzed, but they are not typically used for diagnosing or managing myeloma.

†Normal ranges vary slightly from one institution to another.

### Understanding Your Labs!  
**Serum Protein Electrophoresis (SPEP) Normal Range**

<table>
<thead>
<tr>
<th>Component</th>
<th>Normal range*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>3.8 to 5 g/dL</td>
</tr>
<tr>
<td>Alpha-1</td>
<td>0.1 to 0.3 g/dL</td>
</tr>
<tr>
<td>Alpha-2</td>
<td>0.6 to 1 g/dL</td>
</tr>
<tr>
<td>Beta</td>
<td>0.7 to 1.4 g/dL</td>
</tr>
<tr>
<td>Gamma</td>
<td>0.7 to 1.6 g/dL</td>
</tr>
<tr>
<td>M protein</td>
<td>0</td>
</tr>
</tbody>
</table>

*Normal ranges vary slightly from one institution to another.
Understanding Your Labs!

**Serum Free Light Change (SFLC) Normal Range**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>What is measured</td>
<td>Levels of light chains</td>
</tr>
<tr>
<td>Component</td>
<td>Normal range*</td>
</tr>
<tr>
<td>Kappa (κ) free light chains</td>
<td>3.3 to 19.4 mg/L</td>
</tr>
<tr>
<td>Lambda (λ) free light chains</td>
<td>5.71 to 26.3 mg/L</td>
</tr>
<tr>
<td>Ratio of kappa (κ)/lambda (λ)</td>
<td>0.26 to 1.65</td>
</tr>
</tbody>
</table>

*Normal ranges vary slightly from one institution to another.

Understanding Your Labs!

**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
Understanding Your Lab Report
May 13, 2024

Types of Multiple Myeloma
Based on Blood and/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%

The Multiple Myeloma Disease Spectrum

Almost all patients diagnosed with multiple myeloma have had a preceding phase of disease that is characterized by changes in the bone marrow.

- **Monoclonal gammopathy of undetermined significance (MGUS)**
- **Smoldering multiple myeloma (SMM)**
- **High-risk SMM**
- **Multiple myeloma**
Blood, Urine, Bone Marrow, and Imaging Tests Used to Identify MGUS, SMM, or Active Multiple Myeloma

<table>
<thead>
<tr>
<th>Marker Measured</th>
<th>MGUS</th>
<th>SMM</th>
<th>Active MM</th>
</tr>
</thead>
<tbody>
<tr>
<td>M protein</td>
<td>&lt;3 g/dL in blood</td>
<td>≥3 g/dL in blood or</td>
<td>≥3 g/dL in blood or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥500 mg/24 hrs in urine</td>
<td>≥500 mg/24 hrs in urine</td>
</tr>
<tr>
<td>Plasma cells in</td>
<td></td>
<td>≥10%–60%</td>
<td>≥60%</td>
</tr>
<tr>
<td>bone marrow</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical features</td>
<td>No myeloma-defining events*</td>
<td>No myeloma-defining events*</td>
<td>≥1 myeloma-defining event*,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>including either:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• ≥1 CRAB feature</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>or</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• ≥1 SLiM feature</td>
</tr>
</tbody>
</table>

*CRAB, calcium elevation, renal insufficiency, anemia, bone disease; SLiM, >60% plasma cells in bone marrow, free light chain involved to uninvolved ratio >100, >1 focal lesion on MRI


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Risk Assessment in Smoldering Myeloma: 2/20/20 Model to Identify High-Risk SMM Patients

- 2/20/20 Risk assessment for SMM
  - 2 >2 g/dL M protein
  - 20 >20 free light chain ratio
  - 20 >20% bone marrow plasma cells

Patients with two or more risk factors are considered high risk. This model does not include any biological or immune factors that may account for interpatient heterogeneity.

Understanding Your Blood Tests

Summary

Unlike other types of cancer, multiple myeloma is diagnosed, staged, and monitored through blood tests, x-rays, and bone marrow biopsies.

Blood tests allow you and your doctor to not only track the myeloma but also the function of the bone marrow, kidneys, liver, immune system, and electrolytes.

Know how to read your myeloma (M) protein level.

Understanding and monitoring your M protein and/or free light chains will allow you to know when and how well you have responded to therapy.

Understanding your blood work informs and empowers you!

You can cope with the diagnosis of multiple myeloma by empowering yourself to learn what you need to gain control, knowledge, and support!
Bone Marrow Biopsy

Types of chromosomal abnormalities

Translocation  Deletion  Gain or Amplification

FISH (fluorescence in situ hybridization)

What’s inside those myeloma cells?

FISH (fluorescence in situ hybridization)
Why is genomic sequencing important in myeloma risk assessment?

- Genetic changes in myeloma cells may affect prognosis and treatment selection
- Using samples from the bone marrow—specific tests look at these genetic changes
- Some tests are used routinely and look at the chromosomal changes (FISH)
- Newer tests assess changes in the DNA (gene expression profiling and next-generation sequencing)
  - Ask your doctor if these tests are available
- All patients in the MMRF CoMMpass study had genomic sequencing from diagnosis to relapse. The resulting data provides detailed genetic profiles for every myeloma patient at every stage of their disease!

Actionable Alterations in MM

Scientists studying personalized medicine have found certain changes in DNA molecules that may be treated with drugs currently available in the clinic

- KRAS and NRAS (40%)
- BRAF (8%)
- IDH1/2 (5%)
- MYD88 (3%)
- Others (11%)
- IGF1R and ALK (5%)
- FGFR3 (5%)
- PI3K-AKT (5%)
- CDKN2C and CCND1 (18%)

These alterations may be the Achilles’ heel of myeloma cells.
Measuring Response to Therapy

Degree (or depth) of response is usually associated with better prognosis. Some patients do well despite never achieving a CR.

- Stable disease
- Minor response
- Partial response
- Very good partial response
- Complete response (CR)
- Stringent CR

Myeloma cell burden

ClonoSEQ is an FDA-approved next-generation sequencing (NGS) test to measure MRD in MM patients

What is MRD?

- The presence of small amounts of myeloma cells in the body after treatment
- MRD tests can detect at least 1 cell in 1,000,000.
Why do we need to measure MRD?

• With new and more effective treatments, more patients achieve CR
• However, achieving a CR does not necessarily mean that all myeloma cells are gone
• Routine blood tests are not sensitive enough to detect these remaining cells

How is MRD measured?

- Diagnostic
- Tumor burden
- MRD

- Flow cytometry
- Next-generation DNA sequencing
Key Terms for MRD

- **MRD positive or MRD positivity (MRD+)**
  - Myeloma cells are still detectable

- **MRD negative or MRD negativity (MRD-)**
  - Myeloma cells are not detected

- **Sustained MRD-**
  - Two measurements of MRD negativity performed at least 12 months apart

Level of sensitivity can be different depending on methodology used: next-generation sequencing (NGS) or next-generation flow cytometry (NGF).

How is a Patient's Response to Treatment Assessed?

- Right now, measurement of MRD depends on counting cells or DNA sequences in bone marrow samples
- Imaging (with PET/CT scan) is also required to detect residual disease outside of the bone marrow
- What about other areas of the body?
Why is it important to achieve MRD negativity?

Patients who achieve MRD negativity following treatment experience longer remission than those who are still MRD positive after treatment.

MRD by next-generation sequencing (sensitivity $1 \times 10^{-5}$)


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MRD used to Accelerate MM Clinical Trials

- On Friday, April 12th 2024, the U.S. Food and Drug Administration (FDA) held an Oncologic Drugs Advisory Committee (ODAC) meeting “to discuss the adequacy of available data to support the use of minimal residual disease (MRD) as an endpoint to support accelerated approval of new therapies for patients with multiple myeloma (MM).”
- ODAC unanimously voted in favor of MRD testing (12-0)
- If approved by the FDA, MRD testing as an early endpoint would expedite the development of FDA-approved myeloma drugs and therapies and bring them into the market much sooner

https://www.fda.gov/media/177652/download
Know Your Imaging Tests!

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

- **X-ray**
- **MRI**
- **CT scan**
- **PET scan**

Putting the Results Together

- Imaging results
- Blood and urine test results
- Bone marrow analysis

Staging, prognosis, and risk assessment
Multiple Myeloma Prognosis and Risk

Revised International Staging System (R-ISS)

<table>
<thead>
<tr>
<th>R-ISS stage</th>
<th>Laboratory measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Serum β2M level &lt;3.5 mg/L</td>
</tr>
<tr>
<td></td>
<td>Serum albumin level ≥3.5 g/dL</td>
</tr>
<tr>
<td></td>
<td>No high-risk CA*</td>
</tr>
<tr>
<td></td>
<td>Normal LDH level</td>
</tr>
<tr>
<td>II</td>
<td>All other possible combinations</td>
</tr>
<tr>
<td>III</td>
<td>Serum β2M level ≥5.5 mg/L</td>
</tr>
<tr>
<td></td>
<td>High-risk CA* or high LDH level</td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>High risk</th>
<th>Standard risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>• High-risk genetic abnormalities</td>
<td>• All others including:</td>
</tr>
<tr>
<td>• t(4;14)</td>
<td>− Trisomies</td>
</tr>
<tr>
<td>• t(14;16)</td>
<td>− t(11;14)</td>
</tr>
<tr>
<td>• t(14;20)</td>
<td>− t(6;14)</td>
</tr>
<tr>
<td>• del 17p</td>
<td>• Double-hit myeloma: any two high-risk genetic abnormalities</td>
</tr>
<tr>
<td>• p53 mutation</td>
<td>• Triple-hit myeloma: three or more high-risk genetic abnormalities</td>
</tr>
<tr>
<td>• gain 1q</td>
<td>Current cannot identify with great certainty all high-risk patients.</td>
</tr>
</tbody>
</table>

R-ISS, Revised International Staging System; β2M, beta-2 microglobulin; LDH, lactate dehydrogenase; FISH, fluorescence in situ hybridization.

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 R-ISS.
Additional High-Risk Features

<table>
<thead>
<tr>
<th>Disease Features</th>
<th>Patient Features</th>
<th>Response Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Other cytogenetic and genetic abnormalities</td>
<td>• Comorbidities</td>
<td>• Lack of response to therapy</td>
</tr>
<tr>
<td>• Plasma cell leukemia</td>
<td>• Frailty</td>
<td>• Short first PFS</td>
</tr>
<tr>
<td>• Extramedullary disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Renal failure</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Understanding Bone Marrow Biopsy and Staging

**Summary**

- Bone marrow biopsies are a pain in the butt; but give us key insight into the biology of your myeloma.

- The genetic information we obtain from the biopsy can give us not only prognostic information but also guide us towards the optimal drug choice.

- Bone marrow biopsies can also let us know how deep your remission is.

- There are multiple ways of staging myeloma, with the newer ones using genetic information.

- X-rays, CTs, PET scans, and MRIs are all used to stage and re-stage myeloma.
Questions & Answers

For more information, visit themmrf.org/educational-resources/
MMRF Patient Resources

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 myeloma 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.
Join the MMRF Community!

National Walk/Run Program
- Atlanta | 10.26.24
- Boston | 10.12.24
- Chicago | 9.8.24
- Dallas | 11.16.24
- Detroit | 9.21.24
- Houston | 11.23.24
- Los Angeles | 8.17.24
- National Virtual | 12.14.24

New York City | 10.5.24
Philadelphia | 10.19.24
San Francisco | 8.24.24
Scottsdale | 12.7.24
Tampa | 11.2.24
Washington D.C. | 9.28.24

Other MMRF Event Programs
- Moving Mountains for Multiple Myeloma
- Half and Full Marathons
- Bike/Road to Victories
- Create Your Own Fundraiser

Upcoming Patient Education Events

Save the Date

<table>
<thead>
<tr>
<th>Program</th>
<th>Date and Time</th>
<th>Speakers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Understanding Lab Report FAQs</td>
<td>Friday, June 7, 2024 3:00 PM</td>
<td>Joshua Richter, MD, Michelle Lyn, NP</td>
</tr>
</tbody>
</table>

For more information or to register, visit themmrf.org/educational-resources
Resources

- Resource tab includes
  - Exhibit Hall
  - Speaker bios
  - Copy of the slide presentation
Need help with travel to a clinical study?

• The MMRF has partnered with the Lazarex Cancer Foundation to help provide more equitable access to clinical studies for multiple myeloma patients
• This partnership is one facet of the MMRF’s commitment to improve diversity and representation in myeloma clinical studies
• MMRF has provided $100,000 over 2 years to Lazarex to fund travel, lodging, and food for patients (and a travel companion) so that they can participate in clinical studies that are appropriate for them
• Patients are funded according to income guidelines and will be reimbursed for allowed expenses
• For more information on this program and to be connected with Lazarex, call our Patient Navigation Center at 1-888-841-6673

Thank you!