MULTIPLE MYELOMA Research Foundation

Understanding Your Lab Report

May 13, 2024

1

Tech Support

1-719-234-7952

2

3

Resources

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

Submit your questions throughout the program!

4

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

5

2023 Myeloma Accelerator Challenge Program Grant Recipients

Samir Parekh, MD

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

Pieter Sonneveld, MD, PhD

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

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.

Sagar Lonial, MD

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

6

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 increases 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.

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
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.

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.

7

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

8

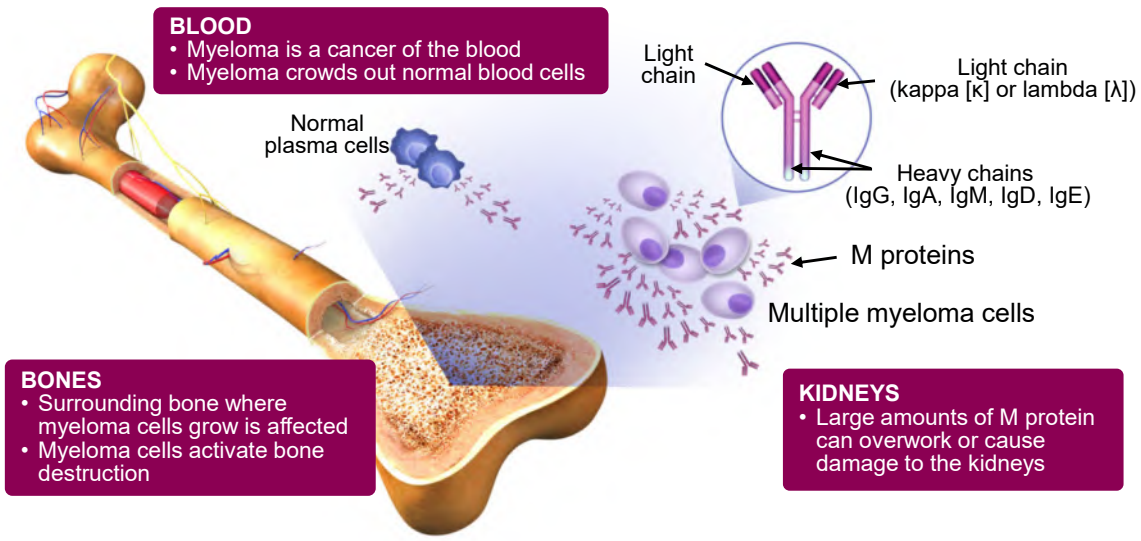
MULTIPLE MYELOMA Research Foundation

Understanding Your Blood Test

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

9

Multiple Myeloma Affects Your Bones, Blood, and Kidneys

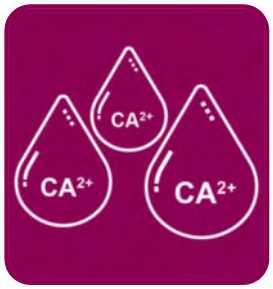


10

Multiple Myeloma Affects Your Bones, Blood, and Kidneys

The clinical features that are characteristic of multiple myeloma

C

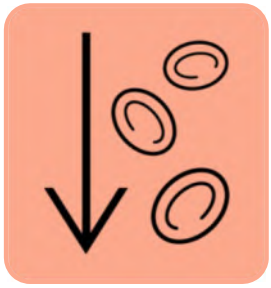


High levels of **c**alcium in the blood

R

Decreased kidney (**r**enal) function

A



Low amount of red blood cells (**a**nemia)

B

Presence of **b**one damage

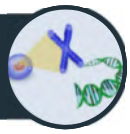
11

The Right Tests: Common Tests Conducted in Myeloma Patients

Blood tests
Urine tests

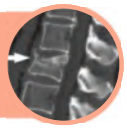
- Confirms the type of myeloma or precursor condition

Bone marrow biopsy



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

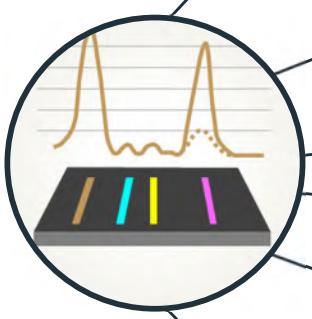
Imaging tests



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

12

Understanding Your Labs!
Blood Tests



- **CBC** – Number of red blood cells, white blood cells, and platelets
- **CMP** – Measure levels of albumin, calcium, LDH, BUN, and creatinine. Assess function of kidney, liver, and bone status and the extent of disease
- **β2M** – Determine the level of a protein that indicates the presence/extent of multiple myeloma 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; β2M; beta-2 microglobulin; SPEP, serum protein electrophoresis; IFE, immunofixation electrophoresis; SFLC, serum free light chain assay; LDH, lactate dehydrogenase; BUN, blood urea nitrogen

13

Understanding Your Labs!
Complete Blood Count (CBC) Normal Range

Sample	Blood
What is measured	The level of hemoglobin and the number of red blood cells, white blood cells, and platelets

Component*	**Normal range†**
Red blood cells	Women: 3.90 to 5.03 × 10^{12}/L Men: 4.32 to 5.72 × 10^{12}/L
Hemoglobin	Women: 12.1 to 15.1 g/dL Men: 13.8 to 17.2 g/dL
White blood cells	Total: 3.5 to 10.5 × 10^{9}/L Neutrophils (as absolute neutrophil count [ANC]): 1.7 to 7.0 × 10^{9}/L **Monocytes**: 0.2 to 1.0 × 10^{9}/L **Lymphocytes**: 1.0 to 3.0 × 10^{9}/L
Platelets	150 to 450 × 10^{9}/L

*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.

14

Understanding Your Labs!
Complete Metabolic Panel (CMP) Normal Range

Sample	Blood
What is measured	Levels of electrolytes, albumin, calcium, BUN, and creatinine
Component*	**Normal range†**
Albumin	3.4 to 5.4 g/dL
BUN (blood urea nitrogen)	6 to 20 mg/dL
Calcium	8.5 to 10.2 mg/dL
Chloride	96 to 106 mEq/L
Creatinine	0.6 to 1.3 mg/dL
Potassium	3.7 to 5.2 mEq/L
Sodium	135 to 145 mEq/L

*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.

15

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

Sample	Blood
What is measured	M protein
Component	**Normal range***
Albumin	3.8 to 5 g/dL
Alpha-1	0.1 to 0.3 g/dL
Alpha-2	0.6 to 1 g/dL
Beta	0.7 to 1.4 g/dL
Gamma	0.7 to 1.6 g/dL
M protein	0

*Normal ranges vary slightly from one institution to another.

16

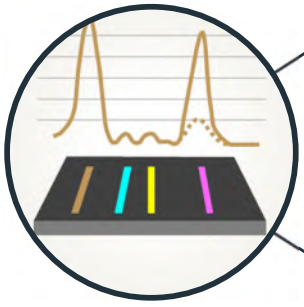
Understanding Your Labs!
Serum Free Light Change (SFLC) Normal Range

Sample	Blood
What is measured	Levels of light chains
Component	**Normal range***
Kappa (κ) free light chains	3.3 to 19.4 mg/L
Lambda (ʎ) free light chains	5.71 to 26.3 mg/L
Ratio of kappa (κ)/lambda (ʎ)	0.26 to 1.65

*Normal ranges vary slightly from one institution to another.

17

Understanding Your Labs!
Urine Tests



UPEP

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

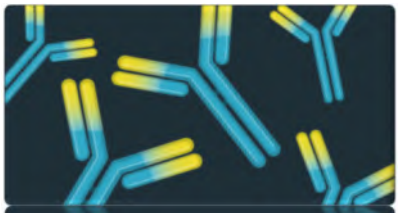
24-hr urine analysis

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

UPEP, urine protein electrophoresis

18

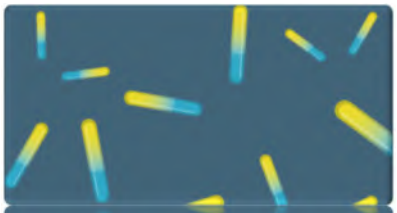
Types of Multiple Myeloma Based on Blood and/or Urine Tests



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%

19

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

20

Blood, Urine, Bone Marrow, and Imaging Tests Used to Identify MGUS, SMM, or Active Multiple Myeloma

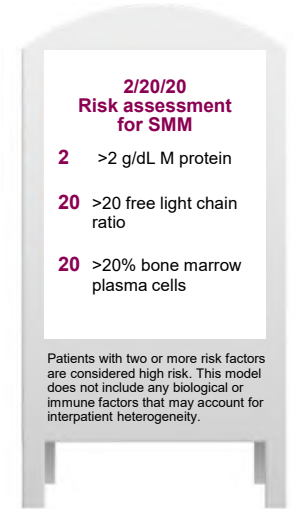
Marker Measured	MGUS	SMM	Active MM
M protein	<3 g/dL in blood	≥3 g/dL in blood **or** ≥500 mg/24 hrs in urine	≥3 g/dL in blood **or** ≥500 mg/24 hrs in urine
Plasma cells in bone marrow	<10%	≥10%–60%	≥60%
Clinical features	No myeloma-defining events*	No myeloma-defining events*	≥1 myeloma-defining event*,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

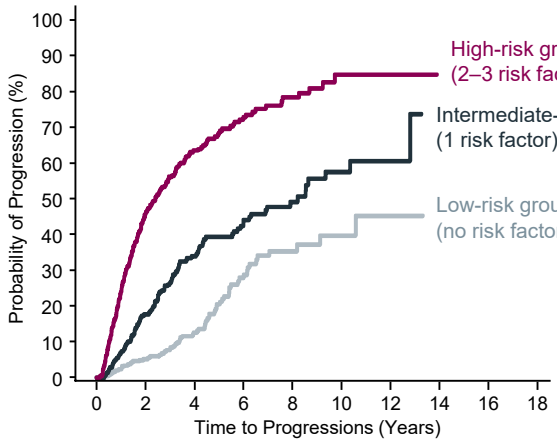
*CRAB, calcium elevation, renal insufficiency, anemia, bone disease; SLiM, >60% plasma cells in bone marrow, free light chain involved to uninvolved ratio >100, >1 focal lesion on MRI

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

21

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





Risk of progression at 2 Years
44.2%
17.9%
6.2%

Mateos MV et al. *Blood Cancer J*. 2020;10:102.

22

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!

23

MULTIPLE MYELOMA Research Foundation

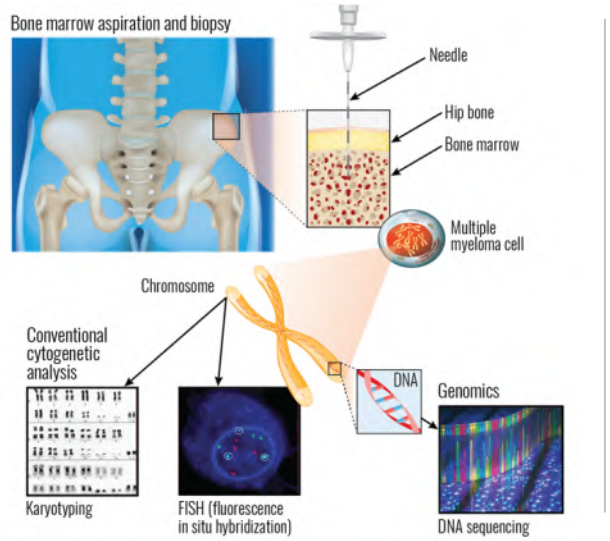
Understanding Bone Marrow Biopsy and Staging

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

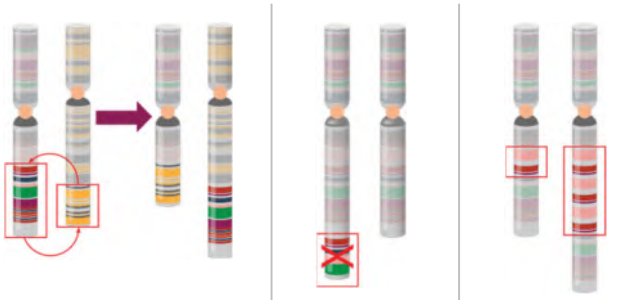
Michigan State University College of Human Medicine
Karmanos Cancer Institute
East Lansing, Michigan

24

Bone Marrow Biopsy



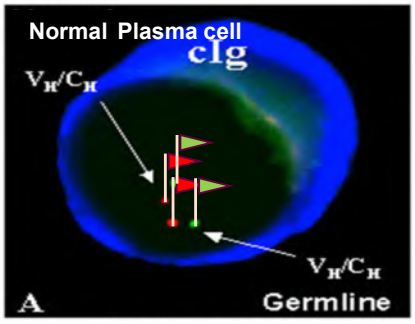
Types of chromosomal abnormalities



Translocation | Deletion | Gain or Amplification

25

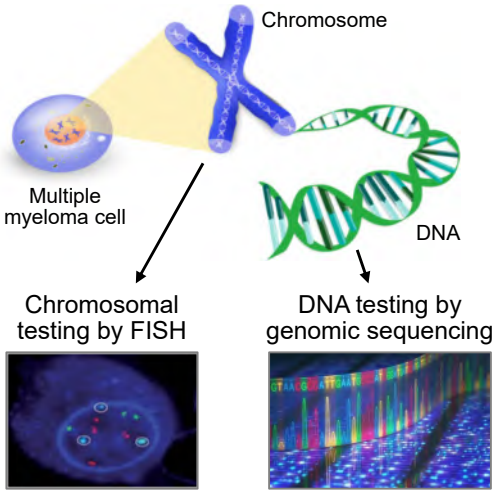
What's inside those myeloma cells?
FISH (fluorescence in situ hybridization)



26

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!

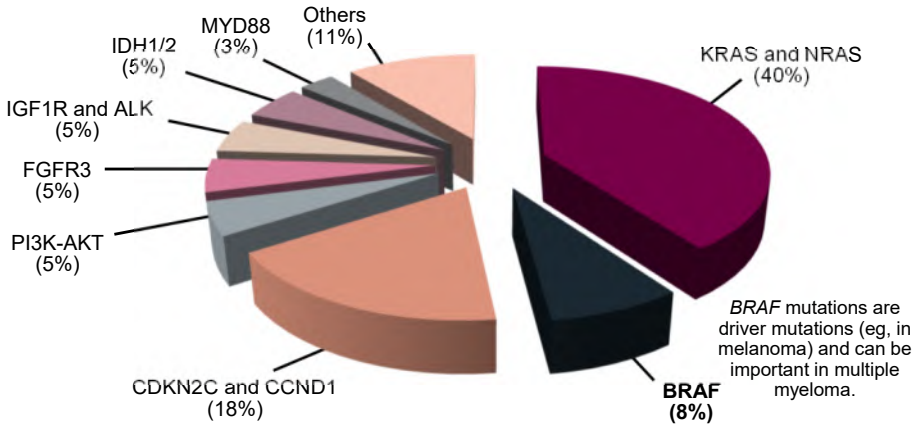


27

Actionable Alterations in MM

These alterations may be the Achilles' heel of myeloma cells.

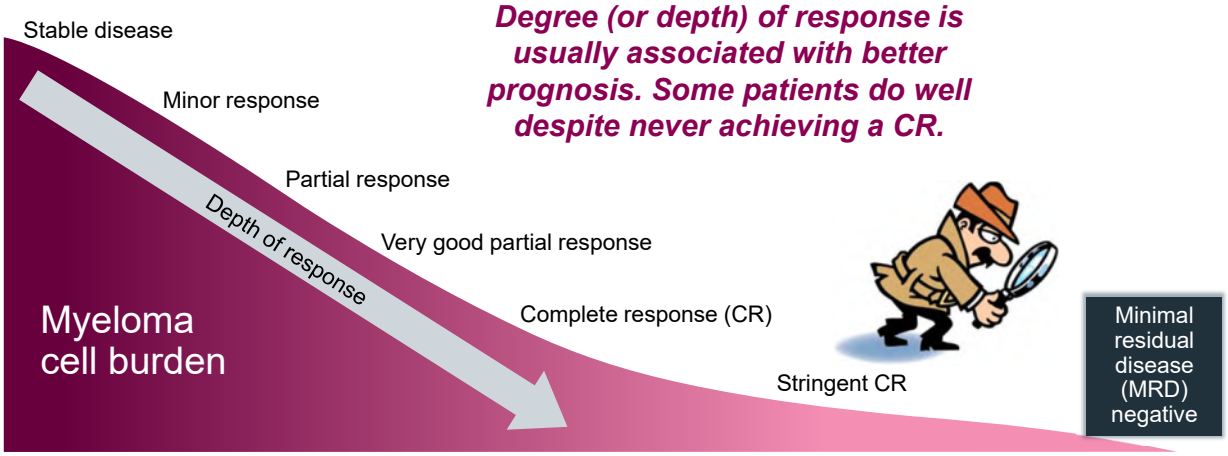
Scientists studying personalized medicine have found certain changes in DNA molecules that may be treated with drugs currently available in the clinic



BRAF mutations are driver mutations (eg, in melanoma) and can be important in multiple myeloma.

28

Measuring Response to Therapy



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

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.

29

What is MRD?

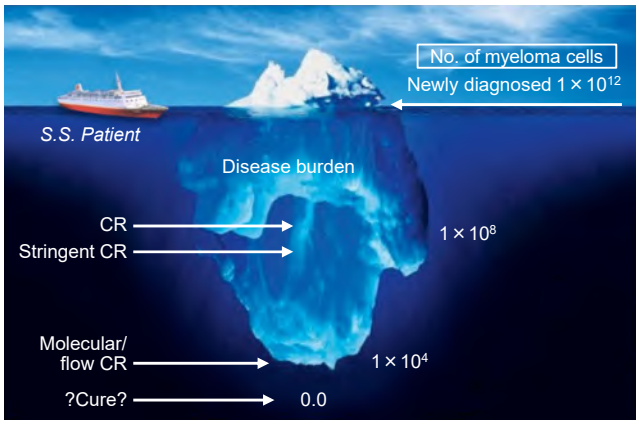
The presence of small amounts of myeloma cells in the body after treatment

MRD tests can detect at least 1 cell in 1,000,000.

30

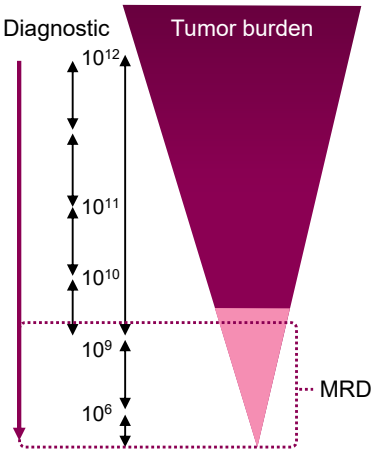
Why do we need to measure MRD?

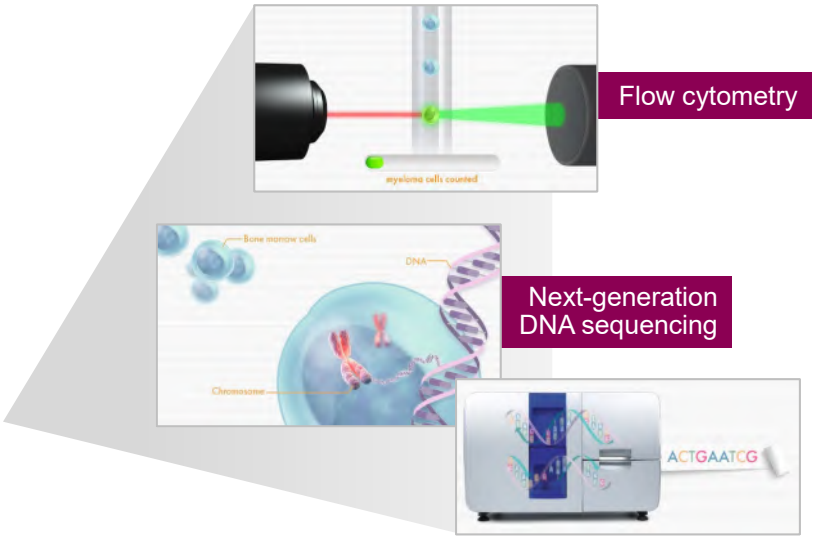
- With new and more effective treatments, more patients achieve CR
- However, achieving a CR does not necessarily mean that all myeloma cells are gone
- Routine blood tests are not sensitive enough to detect these remaining cells



31

How is MRD measured?





32

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).

33

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

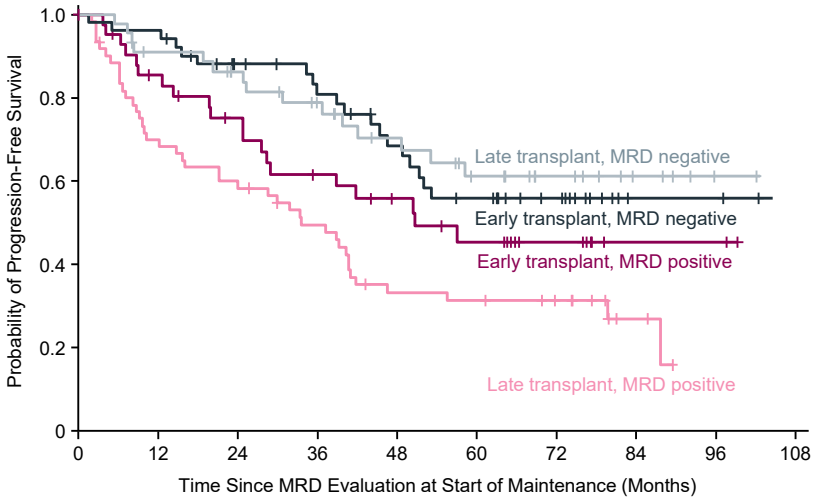
What about other areas of the body?

Imaging (with PET/CT scan) is also required to detect residual disease outside of the bone marrow

34

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 ×10^{-5})
Determination Study. Richardson PG et al. *N Engl J Med*. 2022;387:132.

35

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

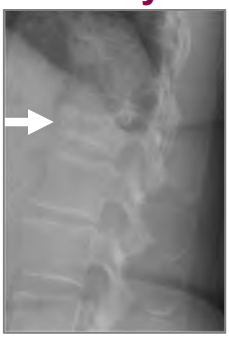
https://www.fda.gov/media/177652/download

36

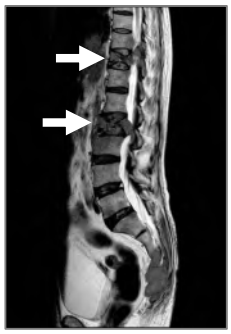
Know Your Imaging Tests!

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

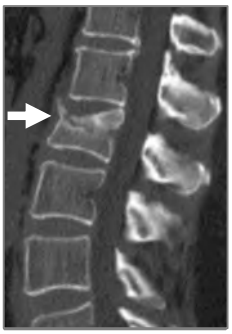
X-ray



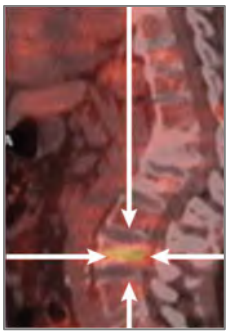
MRI



CT scan

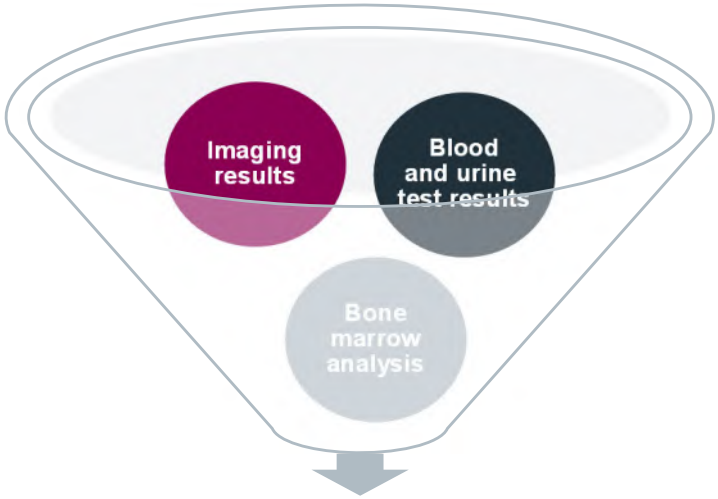


PET scan



37

Putting the Results Together



Staging, prognosis, and risk assessment

38

Multiple Myeloma Prognosis and Risk

Revised International Staging System (R-ISS)

R-ISS stage	Laboratory measurements
I	• Serum β2M level <3.5 mg/L • Serum albumin level ≥3.5 g/dL • No high-risk CA* • Normal LDH level
II	All other possible combinations
III	• Serum β2M level ≥5.5 mg/L • High-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)

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
- R-ISS 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.

β2M; beta-2 microglobulin; LDH, lactate dehydrogenase; GEP, gene-expression profiling

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.

39

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 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)

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

40

Additional High-Risk Features

Disease Features

- Other cytogenetic and genetic abnormalities
- Plasma cell leukemia
- Extramedullary disease
- Renal failure

Patient Features

- Comorbidities
- Frailty

Response Features

- Lack of response to therapy
- Short first PFS

41

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.

42

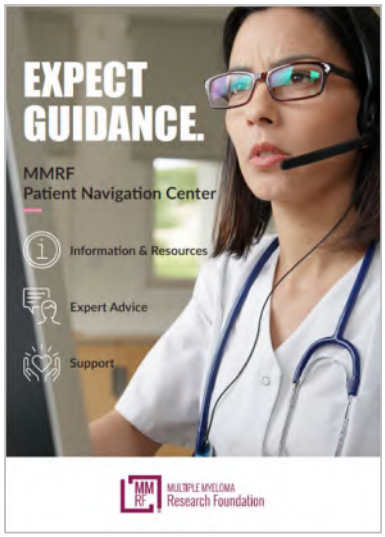
MULTIPLE MYELOMA Research Foundation

Questions & Answers

43

44

MMRF Patient Resources



45

Myeloma Mentors®

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.

46

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
Twin Cities | 9.14.24
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

47

Upcoming Patient Education Events
Save the Date

Program	Date and Time	Speakers
Understanding Lab Report FAQs *Livestream*	Friday, June 7, 2024 3:00 PM	Joshua Richter, MD Michelle Lyn, NP

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

48

49

Resources

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

50

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

It's About Living
Lazarex
CANCER FOUNDATION

51

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Thank you!

52