Hot Topics in Multiple Myeloma Treatment
Webinar 1, September 20, 2017
Minimal Residual Disease

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Multiple Myeloma Research Foundation

**Moderator:**
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  Multiple Myeloma Research Foundation  
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**Speakers**

- C. Ola Landgren, MD, PhD  
  Memorial Sloan Kettering Cancer Center  
  New York, New York

- Donna Mastey, RN, BSN  
  Memorial Sloan Kettering Cancer Center  
  New York, New York

- Louise Miller Lavin, BSN, MSN, LPCC  
  Akron, Ohio
Topics for Discussion

- The concept of minimal residual disease (MRD)
- How MRD affects outcome
- How MRD is measured/how to interpret results
- What MRD results mean for patients
- Can you get MRD testing at your doctor’s office?

Why do we need to measure minimal residual disease (MRD)?

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

PR, partial response; nCR, near complete response
What is minimal residual disease?

The presence of small amounts of myeloma cells left in the bone marrow following the achievement of a CR after treatment.

MRD tests can detect at least 1 cell in 100,000 or better. Ideally, we want to use more sensitive assays that can find 1 cell in a million.

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.

Level of detection can be different depending on methodology used.
Why is it important to achieve minimal residual disease negativity?

Patients Who Achieve MRD Negativity Following Treatment Experience Longer Remission Than Those Who Are Still MRD Positive After Treatment

MRD at post-maintenance for patients in CR

Patients Without Progression (%)

Months Since Randomization

P-value: p<0.0001

MRD measured by sequencing.
Patients Who Achieve MRD Negativity Following Treatment Live Longer Than Those Who Are MRD Positive

Key Points From 14 Studies Analyzed*

- Being MRD negative is correlated with longer progression-free and overall survival
- MRD negativity may not (?) carry the same weight in patients with standard-risk versus high-risk disease

*5 trials included stem cell transplantation/10 studies included maintenance

Annual MRD Meeting in NYC

- New technologies, including blood tests, imaging, and bone marrow assays
- Reviewed MRD as an end point in clinical trials
- Discussed how to make MRD testing an end point for drug approval in the near future

Friday, June 16, 2017

ADVANCES IN MRD TESTING IN MYELOMA NYC 2017
MRD: What are the main techniques used to count cells left after treatment?

- Flow cytometry
- VDJ sequencing

Advantages and Disadvantages of Current Methodologies to Test for MRD

**Advantages**

**Flow cytometry**
- Can work for every patient
- Does not require sample taken at diagnosis for comparison
- Widely available

**VDJ sequencing**
- More sensitive, can detect 1 cell in 1 million or better
- Frozen samples can be used so sample can be taken and then stored before counting or shipped to a lab
- Fully standardized

**Disadvantages**

**Flow cytometry**
- Sample needs to be fresh, cannot be stored for more than a day or two
- More difficult technique, hard to standardize

**VDJ sequencing**
- Requires a sample to be taken at diagnosis for comparison
- Equipment is not (yet) widely available in labs

Sensitivity Matters

When fewer cells are detected after maintenance ends, survival is longer.

Limitation to MRD Response Assessment

- Right now, measurement of MRD depends on counting cells in samples from bone marrow
- What about other areas of the body?
  - Imaging (for example PET scan or CT scan) is also required to detect residual disease outside of the bone marrow

### IMWG 2016 Criteria for Response and MRD Assessment in MM

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<tbody>
<tr>
<td>VDJ sequencing</td>
<td>MRD-negative</td>
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<tr>
<td>Flow cytometry</td>
<td>MRD-negative</td>
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<td>Sustained MRD-negative</td>
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<tr>
<td>Imaging (PET/CT) plus</td>
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### Final Thoughts

**MRD Measurement in Practice: Not Quite Ready For Prime Time**

**Benefits**
- Combination novel therapies +/- new immune agents can now attain MRD
- MRD negativity correlates with clinical benefit

**Precautions**
- May be premature to base treatment decisions on results in community
- Technology to measure MRD is evolving

**Unanswered Questions**
- Should MM patients who are MRD+ get more treatment?
- Should MM patients who go from MRD- to MRD+ get treatment before development of clinical symptoms?

However, routine MRD from a prognostic perspective would be helpful to patients.
What do MRD results mean to patients?

Emotional Response to Initial Diagnosis

- Shock
- Sense of being overwhelmed
- Feeling of sadness, loss, and despair
- Uncertainty
- Fear
- Anger
- Loss of control
Become an Informed Patient

- Learn about multiple myeloma
  - What is multiple myeloma?
  - What diagnostic and laboratory tests are performed?
  - How often is diagnostic testing done?
  - What treatments are available?
  - How is the effectiveness of the treatments measured?

Communicate Effectively With Your Treatment Team

- Answer all questions openly and honestly
- Share your concerns
- Ask questions about treatment
- Request additional explanations as needed
Hope for the Best; Prepare for the Worst

- Waiting for MRD results is anxiety provoking
- Try to find ways that help you cope while waiting for results
- Recognize that MRD results, whether positive or negative, are important and provide valuable information concerning treatment

Understanding the Importance of MRD Results

- All MRD results, whether negative or positive, provide valuable treatment information
  - Indicate if treatment was effective
  - Measure the degree of effectiveness of treatment
  - Document which combination of medications leads to desired results
  - Reveal which combination of medications was ineffective
Hot Topics in Multiple Myeloma Treatment
Webinar 1: Minimal Residual Disease

MRD-Negative Result

• Indicates a positive response to treatment and to what degree
• Is related to improved overall survival and progression-free survival
• Represents an exciting moment in the life of a patient

MRD-Positive Results

• Indicate that treatment did not lead to optimal results
• Provide valuable information concerning future treatment
• May indicate that a new treatment regimen needs to be established
• Prevent the loss of valuable treatment time
Decisions, Decisions, Decisions

- If MRD negative, treatment options include
  - Stem cell transplant
  - Harvesting and freezing stem cells for a future transplant
  - Possibility of maintenance medication

Decisions, Decisions, Decisions

- IF MRD positive
  - Consider other treatment options, including a stem cell transplant
Become a Patient Advocate

- Advocate for yourself and other myeloma patients
- Request MRD testing
- Explain the importance of MRD testing to your treatment team
- If it is not available at your treatment center, explore the possibility of having the test performed elsewhere
- Be assertive
- Don’t give up

“Unless someone like you cares a whole awful lot, nothing is going to get better. It’s not.”

—Dr. Seuss, *The Lorax*
Questions & Answers

Closing
Resources for You!

**MMRF Patient Support Center**
Have questions about the trials or information you heard today? Call our MMRF Nurse Patient Navigators.

Our MMRF Nurse Patient Navigators can guide you through your multiple myeloma journey every step of the way. Call Monday–Friday, 9–7 ET

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  Saad Z. Usmani, MD—Chair
  Peter M. Voorhees, MD—Co-Chair
  Levine Cancer Institute

- **Friday, November 3, 2017**
  New York City, New York
  Ajai Chari, MD—Chair
  Mount Sinai Health System

- **Saturday, November 18, 2017**
  Los Angeles, California
  James Berenson, MD—Co-Chair
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