A Caregiver’s Guide to Helping Myeloma Patients

Webinar 1, February 23, 2017
The New Normal for Caregivers of Patients With Multiple Myeloma

 Speakers

Moderator:
• Mary DeRome
  Multiple Myeloma Research Foundation
  Norwalk, Connecticut

Faculty:
• Angela A. Mayo, PA-C, MS
  Mayo Clinic
  Phoenix, Arizona
What does a caregiver do?

- Critical role in treatment process
- Ensure that patient attends appointments/treatments
- Note symptoms/side effects related to treatment or disease and report to health care team
- Ensure that patient takes the correct dosage of medications on time
- Help the patient optimize nutrition, self-care, sleep, exercise, safety, hygiene
- Another set of ears to take in information provided at office visits
- Provide love and support!

Multiple Myeloma Today

CML, chronic myeloid leukemia; CLL, chronic lymphocytic leukemia; MM, multiple myeloma; NHL, non-Hodgkin lymphoma.


A Caregiver’s Guide to Helping Myeloma Patients
The New Normal for Caregivers of Patients With Multiple Myeloma

Webinar 1, February 23, 2017
Angela A. Mayo, PA-C, MS

What is multiple myeloma?

Multiple Myeloma

Normal plasma cells
Antibodies
M proteins
Light chain
Heavy chains
Multiple myeloma cells
Bone
Bone marrow

Effects of Myeloma and Common Symptoms

Low Blood Counts
- Anemia is present in 60% of patients at diagnosis
- May lead to anemia and infection

Decreased Kidney Function
- Occurs in over half of myeloma patients

Bone Damage
- Affects 85% of patients
- Common sites include spine, pelvis, and ribs
- Leads to fractures

Bone Turnover
- Leads to high levels of calcium in blood (hypercalcemia)

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

Key Considerations for Optimal Disease Management

1. Laboratory and imaging tests, tissue banking, and diagnosis
   - Measure levels of albumin, calcium, lactate dehydrogenase (LDH), blood urea nitrogen (BUN), and creatinine. Assess function of kidney, liver, and bone status and the extent of disease.
   - Determine the level of a protein that indicates the presence/extent of MM and kidney function.
   - Detect the presence and level of M protein.

2. Staging and prognosis
   - Identify the type of abnormal antibody proteins.

3. Obtain a second opinion
   - Freelite test measures light chains (kappa or lambda).

4. Know the standard of care

5. Consider clinical trials

Diagnosing Myeloma: Learn Your Labs!

- CBC: complete blood count
- CMP: complete metabolic panel
- B2M: beta-2 microglobulin
- SPEP: serum protein electrophoresis
- IFE: immunofixation electrophoresis
- SFLC: serum free light chain assay
Diagnosing Myeloma: Learn Your Labs!

Urine Tests

- UPEP
  - Detect Bence Jones proteins (otherwise known as myeloma light chains)
  - Determine the presence and levels of M protein and Bence Jones protein

24-hr Urine Analysis

Diagnosing Myeloma: 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

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

MRI and PET/CT appear to be more sensitive (85%) than skeletal x-rays for the detection of small lytic bone lesions.
Diagnosing Myeloma: Know Your Bone Marrow Tests!

Bone Marrow Aspiration and Biopsy
- Jamshidi needle

Conventional Cytogenetic Analysis
- Karyotyping
- FISH (fluorescence in situ hybridization)

Putting the Results Together

Blood and urine test results
Genomics
Bone marrow analysis
Imaging results

Staging and Prognosis
Multiple Myeloma Staging

- B2M < 3.5 mg/dL
  - Neither stage I nor stage III
- B2M > 5.5
  - Stage III
- Albumin ≥ 3.5 g/dL
  - Stage I


How aggressive is my myeloma?

**Risk Level* (Degree of Aggressiveness)**

- High Risk
- Intermediate Risk
- Standard Risk

**Patients Affected (%)**

- FISH
  - del 17p
  - t(14;16)
  - t(14;20)
- GEP
  - High-risk signature
- FISH
  - t(4;14)*

**Currently cannot predict with great certainty all high-risk patients.**

*Based on the Updated Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) Consensus Guidelines 2013
Some Questions to Ask After Myeloma is Diagnosed

- What type of myeloma do I have?
- What is my myeloma stage?
- Do I have any cytogenetic abnormalities?
- What is my long-term prognosis?
- Can I bank my bone marrow tissue for future analysis and precision medicine?*
- What treatment options should I consider?

*Tissue banking may not be an option at some oncology offices

Treatment Overview
Key Considerations for Optimal Disease Management

1. Know the standard of care
2. What to expect on therapy
3. Assessing your response to therapy
4. Maintenance options
5. Consider clinical trials

Overview of Treatment Approach

MGUS
- Close monitoring (observation)

SMM
- Close monitoring (observation)
  - If high risk: possible myeloma drugs?

Active myeloma
- Initial therapy
  - Myeloma drugs
  - High-dose chemotherapy/ stem cell transplantation (option, if possible)
- Maintenance option
- Therapies for relapsed/ refractory myeloma
- Bone loss: bisphosphonates + other supportive treatments
  - Clinical trial participation should be considered.
Creating a Personalized Treatment Plan: Partnering With Your Health Care Team

Your Overall Health and Characteristics of Your Myeloma
- Age and general health
- Other conditions
- Test results
- Symptoms

Your Preferences and Personal Goals
- Eliminate vs control disease
- Willingness to tolerate side effects
- Symptom relief
- Personal lifestyle/situation

No one treatment plan is right for everyone.

Goals of Therapy

- Achieving good response (≥VGPR)
- High response rate; rapid response
- Improve performance status
- Minimal side effects
### Therapeutic Options in Myeloma: The Current Landscape

<table>
<thead>
<tr>
<th>IMIDs</th>
<th>Proteasome Inhibitors</th>
<th>Chemotherapy Anthracyclines</th>
<th>Chemotherapy Alkylators</th>
<th>Steroids</th>
<th>HDAC Inhibitors</th>
<th>mAbs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thalomid (thalidomide)</td>
<td>Velcade (bortezomib)</td>
<td>Adriamycin</td>
<td>Cytoxan (cyclophosphamide)</td>
<td>Dexamethasone</td>
<td>Farydak (panobinostat)</td>
<td>Empliciti (elotuzumab)</td>
</tr>
<tr>
<td>Revlimid (lenalidomide)</td>
<td>Kyprolis (carfilzomib)</td>
<td>Doxil (liposomal doxorubicin)</td>
<td>Bendamustine</td>
<td>Prednisone</td>
<td>Zolinza (vorinostat)</td>
<td>Darzalex (daratumumab)</td>
</tr>
<tr>
<td>Pomalyst (pomalidomide)</td>
<td>Ninlaro ( ixazomib)</td>
<td>Melphalan</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Treatment Sequence in Myeloma

**Frontline treatment**
- **Now**
  - Vel/Dex
  - Rev/Dex
  - CyBorD
  - Vel/Thal/Dex
  - RVD
  - KRD

**Induction**
- Kyprolis combinations
- "More" induction
- Lenalidomide (2 months)

**Consolidation**
- Dexamethasone
- Farydak
- Darzalex

**Maintenance**
- Nothing
- Thalomid?
- Velcade
- Revlimid
- Ninlaro

**Post Consolidation**
- Combinations

**Relapsed**
- Rescue
- Novel mAbs: Isatuximab...
- Newer HDACs
- PD/PDL-1 inhibitors
- Multiple small molecules
The Pillars of Myeloma Treatment

- **Proteasome Inhibitors**
  - Velcade
  - Kyprolis
  - Nenlaro...

- **Immunomodulatory**
  - Thalidomide
  - Revlimid
  - Pomalyst

- **Monoclonal Antibodies**
  - Darzalex
  - Empliciti
  - Isatuximab

- **Alkylators**
  - Melphalan,
  - Cyclophosphamide

- **Steroids**

- **Others?**

Measuring Response to Therapy

<table>
<thead>
<tr>
<th>Response Type</th>
<th>Abbreviation</th>
<th>M-Protein Reduction</th>
<th>Tests</th>
<th>Bone Marrow</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Blood</td>
<td>Urine</td>
<td>Immunofixation</td>
</tr>
<tr>
<td>Complete response</td>
<td>CR</td>
<td>0</td>
<td>0</td>
<td>Negative</td>
</tr>
<tr>
<td>Stringent complete response</td>
<td>sCR</td>
<td>0</td>
<td>0</td>
<td>Negative</td>
</tr>
<tr>
<td>Immunophenotypic complete response</td>
<td>iCR</td>
<td>0</td>
<td>0</td>
<td>Negative</td>
</tr>
<tr>
<td>Molecular complete response</td>
<td>mCR</td>
<td>0</td>
<td>0</td>
<td>Negative</td>
</tr>
<tr>
<td>Very good partial response</td>
<td>VGPR</td>
<td>&gt;90%</td>
<td>&lt;100 mg/24 hrs</td>
<td>–</td>
</tr>
<tr>
<td>Partial response</td>
<td>PR</td>
<td>&gt;50%</td>
<td>&gt;90%</td>
<td>–</td>
</tr>
<tr>
<td>Stable disease</td>
<td>SD</td>
<td>–</td>
<td>–</td>
<td>Does not meet criteria for response or progressive disease</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>PD</td>
<td>–</td>
<td>–</td>
<td>An increase of 25% in M protein; an increase of 10% in bone marrow plasma cells</td>
</tr>
</tbody>
</table>

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

*By multiparametric flow cytometry. †Allele-specific oligonucleotide PCR.

When Considering a Treatment Regimen, Find Out From Your Doctor...

- What treatment options should I consider?
- What lab values and test results are important to track for a response or to monitor for side effects?
- Is there a clinical trial that might be better suited for my type of myeloma or prognosis?
- Can I bank my bone marrow?*  

*Tissue banking may not be an option at some oncology offices

Dealing With Relapsed/Refractory Disease

- **Relapsed**: recurrence after a response to therapy  
- **Refractory**: progression despite ongoing therapy
Options for Relapsed/Refractory Disease Continue to Increase

When did you relapse from your initial therapy?

≤6 months  >6 months

Different therapy  Different therapy

Stem cell transplant  Stem cell transplant

Clinical trial

Treatment Approach

First Relapse

Steroid

Dexamethasone
Prednisone

Additional drug if early response not achieved

Pomalyst
Farydak

>1 Relapse

IMiD, immunomodulatory drug
Factors to Consider in Treatment Selection

**DISEASE-RELATED**
- DOR to initial therapy
- FISH/cytogenetics/genomics profile

**PRIOR TREATMENT-RELATED**
- Prior drug exposure
- Toxicity of regimen
- Mode of administration
- Previous SCT

**PATIENT-RELATED**
- Pre-existing toxicity
- Presence of other conditions
- Age
- General health
- Personal lifestyle and preferences

---

**Summary: Relapsed/Refractory Myeloma**

- Relapsed/refractory multiple myeloma is treatable
- Patients typically receive multiple lines of therapy
- Treatment may sometimes be continued for an extended period of time
- Six new drugs (Kyprolis, Pomalyst, Farydak, Darzalex, Empliciti, Ninlaro) introduced in last 4 years
- With the introduction of each new drug, potential for additional combinations
- Many promising new drugs/new combinations in clinical development—consider a clinical trial
Evolution of Multiple Myeloma Treatment: 10 New Drugs Approved in ≤12 Years

Conventional Therapy
- High-dose chemotherapy with autologous bone marrow transplant
- VAD (vincristine, doxorubicin, dexamethasone)
- High-dose chemotherapy with autologous, blast cell support
- High-dose melphalan and prednisone
- Bisphosphonates

Novel Therapy
- Revlimid
- Kyprolis
- Ninlaro
- Velcade
- Dovast
- Farydak
- Empliciti
- Darzalex
- Ninlaro
- Kyprolis

Chemotherapy
Steroid
Transplant
IMiD
Proteasome inhibitor
Monoclonal antibody
Bone support
Proteasome inhibitor
HDAC inhibitor
Monoclonal antibody
Bisphosphonates

Continuing Evolution of Multiple Myeloma Treatment: New Classes and Targets

Novel Therapies and Immunotherapy
- Revlimid
- Kyprolis
- Ninlaro
- Velcade
- Dovast
- Farydak
- Empliciti
- Darzalex
- Ninlaro
- Pembrolizumab
- Atezolizumab
- Nivolumab
- Vaccines
- Filanesib
- CAR-T
- Oprozomib
- Selinexor
- Oprozomib

PLD, pegylated liposomal doxorubicin; IMiD, immunomodulatory drug; HDAC, histone deacetylase; KSP, kinesin spindle protein; SINE, selective inhibitor of nuclear export
*Not yet FDA approved; only available in clinical trials
†Treatments studied in MMRC trials
‡FDA-approved for a non-MM indication
Impact of MM Clinical Trials: Dramatic Improvements in Survival in <10 Years

- Survival rates have nearly doubled; further improvements expected in near future
- Ten new drugs approved since 2003
  - IMiDs: Thalomid, Revlimid, Pomalyst
  - Proteasome inhibitors: Velcade, Pomalyst, Ninlaro
  - Histone deacetylase inhibitor: Farydak
  - Monoclonal antibodies: Darzalex, Empliciti
  - Chemotherapy: Doxil
- Many new drugs being studied in clinical trials
- Understanding of the biology of myeloma improving, with the eventual goal of personalized medicine

Clinical Trials in the Treatment of Myeloma

<table>
<thead>
<tr>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tests safety</td>
<td>Tests how well treatment works</td>
<td>Compares new treatment to standard treatment</td>
</tr>
</tbody>
</table>
Clinical Trials

Phase 1
- All patients receive the experimental therapy
- Phase 1 trials find the optimal dose of a new drug or drug combination
- Patients get higher doses as the study continues
- Determine side effects of new drugs or combinations
- Explore how the drug is metabolized by the body
- Important for all stages of myeloma

Phase 2
- Determine if a new drug or combination is effective against the cancer
- May be added to a phase 1 study once the ideal dose is found
- Patients usually receive the experimental therapy
- In some cases, the study may include two arms comparing either two different doses or a different treatment (another combination of drugs)
  - Patients will be randomly assigned to one of the study arms

Phase 3
- Highest form of clinical evidence. Typically a large number of patients are required
  - Usually required for FDA approval
- Patients receive either an experimental therapy (one or more drugs) or the current standard treatment
  - The patient is randomly assigned to a treatment, a process called randomization
  - Neither the physician or the patient can determine which treatment is given
- May be placebo controlled, if no standard treatments are available
- Very closely monitored for effectiveness and side effects

Preparing for Treatment: It Takes a Village

Nurse coordinator
Physician assistant/nurse practitioner
Physician
Clinical nurse
Social worker
Coping and Support for Caregivers

1. Learn enough about multiple myeloma to help your loved one make decisions about his/her care.
2. Ask questions about treatment options, side effects.
3. Look into support groups where you can meet and speak with others who are caregiving, or where your loved one can talk to others facing multiple myeloma.
4. Establish and maintain a strong support system for yourself.
5. Encourage your loved one to establish and maintain support as well.
6. Friends and family are vital. Enlist help so you can share the responsibilities. Be specific about the help you need.
7. Educate yourself and your loved ones about multiple myeloma so that you and those around you know what to expect.
8. Provide care for yourself: nutrition, exercise, sleep, spirituality…see your own health care provider, too.
9. Maintaining some normalcy (work, relationship, travel, social activities both with and without loved one).

Taking Care of Yourself

- Eat healthy foods and eat regularly
- Get more exercise
- Regular sleep
- Decrease alcohol consumption
- Give up tobacco
- Minimize or eliminate stress
A Caregiver’s Guide to Helping Myeloma Patients
The New Normal for Caregivers of Patients With Multiple Myeloma

Webinar 1, February 23, 2017
Angela A. Mayo, PA-C, MS

MMRF Resources

Multiple Myeloma Disease Overview brochure
Multiple Myeloma Treatment Overview brochure

MMRF CoMMunity Gateway
www.mmrfcommunitygateway.org

Additional Multiple Myeloma Education Resources

The Multiple Myeloma Research Foundation (themmrf.org)
The International Myeloma Foundation (myeloma.org)
Leukemia and Lymphoma Society (lls.org)
Blood and Marrow Transplant Information Network (bmtinfonet.org)
The Myeloma Beacon (myelomabeacon.com)

Questions & Answers

Closing
Additional Information

Speak to an MMRF Nurse Specialist
Call Monday – Friday, 9:00 AM – 7:00 PM EST
866-603-MMCT (6628)

MMRF CoMMunity Gateway

Join our trusted multiple myeloma community! Continue the conversation with other patients, caregivers, and experts!
Join today: www.MMRFCoMMunityGateway.org
Upcoming Webinar

- Webinar 2, March 16, 2017 (1:00 PM ET)
  - Managing the Ups and Downs of Caring for Multiple Myeloma Patients: Including Stem Cell Transplantation and Other Facets of the Treatment Journey

For more information or to register, visit: http://web.xyvid.com/mmrfcaregiver/