Case Studies in Multiple Myeloma Treatment Best Practices for Nurses

Thank you for coming!
Please help us have an on-time start.

Please do not save seats.
Case Studies in Multiple Myeloma Treatment Best Practices for Nurses

May 1, 2014
Anaheim, CA

This activity is jointly sponsored by Medical Education Resources, CMEFirst, and the International Myeloma Foundation

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Meeting space has been assigned to provide a satellite symposium supported by the International Myeloma Foundation via an educational grant during the Oncology Nursing Society’s (ONS) 39th Annual Congress, May 1, 2014, in Anaheim, CA.

The Oncology Nursing Society’s assignment of meeting space does not imply product endorsement nor does the Oncology Nursing Society assume any responsibility for the educational content of the symposium.
Welcome and Introductions

Joseph D. Tariman, PhD, ANP-BC
Beth Faiman, PhDc, MSN, APRN-BC, AOCN®
Symposium Accreditation

• Medical Education Resources is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

• This CE activity provides 1.5 contact hours of continuing nursing education.

• Medical Education Resources is a provider of continuing nursing education by the California Board of Registered Nursing, Provider Number #CEP 12299, for 1.5 contact hours.

• Please complete the Evaluation Form for CE Credit and return to the back of the room after the presentation.
Faculty Introductions

Co-Chairs

Joseph D. Tariman, PhD, ANP-BC
De Paul University
Chicago, IL

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Taussig Cancer Institute, Cleveland Clinic
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Page A. Bertolotti, RN, BSN, OCN®
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University of Arizona Cancer Center
Tucson, AZ
International Myeloma Foundation (IMF)

Improving Lives • Finding the Cure®

Dedicated to improving the quality of life of myeloma patients while working toward prevention and a cure
<table>
<thead>
<tr>
<th>Time</th>
<th>Topic</th>
<th>Faculty</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:00 PM - 12:05 PM</td>
<td>Welcome &amp; Introduction</td>
<td>Joseph D. Tariman</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Beth Faiman</td>
</tr>
<tr>
<td>12:05 PM - 12:25 PM</td>
<td>Case Study #1: Asymptomatic Smoldering Myeloma</td>
<td>Joseph D. Tariman</td>
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<td>Beth Faiman</td>
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<tr>
<td>12:25 PM - 1:00 PM</td>
<td>Case Studies #2 and #3: Newly Diagnosed Myeloma</td>
<td>Page Bertolotti</td>
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<td></td>
<td>Beth Faiman</td>
</tr>
<tr>
<td>1:00 PM – 1:25 pm</td>
<td>Case Studies #4 and #5: Relapsed Myeloma</td>
<td>Sandra Kurtin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Beth Faiman</td>
</tr>
<tr>
<td>1:25 PM - 1:30 PM</td>
<td>Closing Remarks and Q &amp; A</td>
<td>All</td>
</tr>
</tbody>
</table>
Learning Objectives

As a result of this program, you will be able to:

• Review myeloma disease state and disease stages

• Discuss new therapies and combination regimens in Multiple Myeloma, their appropriate use, and related patient management

• Identify best practices including practical tools and recommendations for long-term management and care of Multiple Myeloma patients

• Define strategies to empower nurses to incorporate best practices in their care of Multiple Myeloma patients
Patient #1: Asymptomatic Smoldering Myeloma

Joseph D. Tariman, PhD, ANP-BC
Beth Faiman, PhDc, MSN, APRN-BC, AOCN®
Myeloma Is a Cancer of Plasma Cells

- Preceded by nonmalignant state(s): MGUS or SMM
- Cancer of plasma cells
- Healthy plasma cells produce immunoglobulins: G, A, M, D & E
- Myeloma cells produce abnormal immunoglobulin continually
  - 65% IgG
  - 20% IgA
  - 5% to 10% light chains (monoclonal kappa, lambda light chains, Bence-Jones proteins)
  - Rare: IgD, IgE, IgM, or nonsecretory disease

Myeloma Is a Complex Disease

Myeloma Involves
- Cancerous plasma cell clone(s)
- Genetic changes
- Premalignant conditions: MGUS, SMM at early stages
- Complex interactions of adhesion and cytokines
- Imbalances of osteoclasts and osteoblasts, resulting in bone damage

Case #1: Ed*

Initial Presentation

• 59-year-old man
• Bank vice president
• Routine checkup with primary care physician; no specific complaint
• Abnormal blood work noted - serum total protein 10.2 g/dL; SPEP = M-protein 3.5 g/dL (IgG kappa)

Referred to heme-onc; work-up revealed:

• Bone marrow biopsy:
  - Monoclonal kappa+ plasma cells 12%
  - MFC: Normal DNA ploidy; 1% PCLI at S-phase
  - Cytogenetics: normal; 46XY
  - FISH: no deletions; no translocations

• Serum free light chain ratio = 92
• Negative skeletal survey

Diagnosis: smoldering multiple myeloma

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Case #1: Ed*

Patient Health Status
- Excellent; no comorbid conditions

Family Status
- Stay-at-home wife
- 2 children; 1 college freshman, 1 high school sophomore

Patient & Family Concerns
- Financial (college for kids, finish saving for retirement)
- Planning on traveling in retirement; spending more time together

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
# Multiple Myeloma Disease Continuum

## Premalignant

**MGUS**
(Monoclonal Gammopathy of Undetermined Significance)

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Asymptomatic</th>
<th>Asymptomatic</th>
<th>Symptomatic (~89%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active treatment needed</td>
<td>No</td>
<td>Yes for high risk*&lt;br&gt;No for others</td>
<td>Yes</td>
</tr>
<tr>
<td>M-protein (per dL)</td>
<td>&lt;3 g</td>
<td>&gt;3 g</td>
<td>M-spike or plasmacytoma</td>
</tr>
<tr>
<td>% Clonal plasma cells in bone marrow</td>
<td>&lt;10</td>
<td>&gt;10</td>
<td>&gt;10</td>
</tr>
<tr>
<td>End-organ damage</td>
<td>None</td>
<td>None</td>
<td>1 or more CRAB criteria</td>
</tr>
<tr>
<td>Likelihood of progression</td>
<td>1% per year</td>
<td>10% per year for first 5 years; 73% by 15 years</td>
<td>Not Applicable</td>
</tr>
</tbody>
</table>

* In clinical trial

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“CRAB” Criteria: A Hallmark of Symptomatic Active Multiple Myeloma

Calcium elevation

Renal complications

Anemia

Bone disease

## Symptoms Are a Result of Myeloma Cells

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Explanation</th>
<th>Impact on Patient</th>
</tr>
</thead>
</table>
| **Anemia**                     | Myeloma cells crowd out normal production of red blood cells in bone marrow | • Fatigue  
• Weakness                                           |
| **High protein level**         | Myeloma cells produce myeloma protein, which is released into the bloodstream and can pass into the urine | • Sluggish circulation; increased risk for DVT  
• Possible kidney damage  
• Fatigue                                                   |
| **Bone damage**                | Myeloma cells activate osteoclasts, which destroy bone and block osteoblasts that normally repair damaged bone | • Bone pain  
• Lytic lesions  
• Bone fracture  
• Collapse of vertebra                                  |
| **High blood calcium**         | Myeloma cells disrupt osteoclast/osteoblast balance, resulting in bone damage, which then releases calcium into bloodstream | • Mental confusion  
• Fatigue, weakness  
• Somnolence  
• Nausea & vomiting  
• Constipation  
• Possible kidney damage                                   |
| **Reduced immune system function** | Myeloma cells produce nonfunctional antibodies and crowd out normal immune cells in the bone marrow | • Susceptibility to infection  
• Delayed recovery from infection                          |

MGUS / SMM Precedes Myeloma

Light chain
- Kappa
- Lambda

Heavy chain
- IgG
- IgD
- IgA
- IgE
- IgM


In nearly all cases, myeloma is preceded by the presence of a monoclonal gammopathy.

Percent of Patient Samples With Detectable M-Protein Prior to MM

*Detected in serum for all time points; 2 years prior utilized electrophoresis, immunofixation, kappa, lambda FLC assay

Disease Progression in SMM and MGUS Patients

Smoldering Multiple Myeloma

10% risk of progression per year*
- Screen every 4 to 6 weeks
- *For first 5 years, ~3% per year for next 5 years, ~1% per year thereafter

MGUS

1% risk of progression per year
- First year: screen every 3 to 6 months
- After first year: screen at least every 1 to 2 years
- 3% of people over 50 years old
- 5% of people over 70 years old

SMM = smoldering multiple myeloma
MGUS = monoclonal gammopathy of undetermined significance

High-Risk Smoldering Multiple Myeloma

- **High-Risk SMM**
  - 50% progress within 2 yrs
  - Treat in clinical trial

- **Low-Risk SMM**
  - Few progress within 2 yrs
  - Observation

SMM = smoldering multiple myeloma

### PETHEMA Classification

- Bone marrow clonal plasma cells ≥10%
- AND a monoclonal component
  - IgG level of ≥3 g/dL OR
  - IgA level of ≥2 g/dL OR
  - Urinary Bence-Jones protein level of >1 g/24 hrs
- OR one of above (BMC involvement or monoclonal component) AND
  - at least 95% immunophenotypically aberrant plasma cells in the bone marrow plasma cell compartment by MFC, with reductions in one or two uninvolved immunoglobulins of more than 25%, as compared with normal values
- No “CRAB” criteria present

### Mayo/ECOG Classification

- Bone marrow clonal plasma cells ≥10% or sheets of plasma cells
- Monoclonal protein (M-protein) ≥3 g/dL
- ≥10% BMPCs and/or serum M-protein ≥3g/dl plus abnormal sFLC ratio (≥100 or ≤0.01)\(^3\) (update from initial Mayo Classification)
- An abnormal serum FLC ratio (<0.125 or >8.0) by sFLC assay\(^4\)
- No “CRAB” criteria present

### Others\(^5\)-\(^7\)

- MRI imaging showing diffuse abnormal marrow pattern\(^5\)
- High levels of peripheral blood circulating PCs\(^6\)
- Evolving vs. not evolving (consecutive increasing lab values)\(^7\)

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BMC = bone marrow concentrate; BMPC = bone marrow plasma cells; CRAB = Durie-Salmon CRAB criteria; PC = plasma cells; sFLC = serum free light chain
PETHEMA = Programa para el Estudio de la Terapéutica en Hemopatía Maligna (a Spanish consortium)

Open-Label Phase 3 Trial of High-Risk SMM Patients: Study Design

High-Risk SMM
N=119
PETHEMA Criteria

Randomization

Treatment
• Induction: 9 cycles of 28 days
  • len 25 mg days 1-21
  • dex 20 mg days 1-4, 12-15
• Maintenance: 2 years
  • len 10 mg days 1-21 of 28

Observation

PETHEMA = Programa para el Estudio de la Terapéutica en Hemopatía Maligna (a Spanish consortium)

• Significantly longer median time to progression (TTP) for treated
  (median not reached vs. 21 months; hazard ratio for progression, 0.18;
  95% confidence interval [CI], 0.09 to 0.32; P<0.001)
• Higher 3-year overall survival rate (OS) for treated
  (94% vs. 80%; hazard ratio for death, 0.31; 95% CI, 0.10 to 0.91; P=0.03)
• Technique used to determine aberrant BMC not widely available

BMC = bone marrow concentrate; CI = confidence interval; OS = overall survival; TTP = time to progression

High Response Rates in SMM Patients

Study Design

- High-risk SMM by PETHEMA or Mayo classification
- Phase 2 single arm: 8 cycles CRd (carfilzomib-len-dex) followed by 2 yrs of len
  - Primary end point: response
  - Other end points: progression-free survival, duration of response, minimal residual disease

Preliminary Results (N=12)

<table>
<thead>
<tr>
<th>Response</th>
<th>2 cycles n/N (%)</th>
<th>4 cycles n/N(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Response Rate (≥PR)</td>
<td>12/12 (100)</td>
<td>9/9 (100)</td>
</tr>
<tr>
<td>Near Complete Response (nCR) or Better*</td>
<td>2/12 (17)</td>
<td>7/9 (78)</td>
</tr>
<tr>
<td>Very Good Partial Response (VGPR)</td>
<td>5/12 (42)</td>
<td>2/9 (22)</td>
</tr>
<tr>
<td>Partial Response (PR)</td>
<td>5/12 (42)</td>
<td>0</td>
</tr>
</tbody>
</table>

*Included complete response (CR) and stringent complete response (sCR)

Conclusions

- “After 4 cycles of CRd, 100% achieved a VGPR or better”
- “Larger clinical studies are needed to replicate and expand on these promising results”

PETHEMA = Programa para el Estudio de la Terapéutica en Hemopatía Maligna (a Spanish consortium)

Landgren et al. ASH 2013 #1939.
<table>
<thead>
<tr>
<th>Risk Group</th>
<th>% progressing* within 2 years</th>
<th>Authors' recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone marrow clonal plasma cells ≥60%</td>
<td>90</td>
<td>Treat as myeloma</td>
</tr>
<tr>
<td>Serum involved/uninvolved free light chain ratio ≥100</td>
<td>80</td>
<td>Treat as myeloma</td>
</tr>
<tr>
<td>Abnormalities on MRI (&gt;1 focal lesion)</td>
<td>70</td>
<td>Treat as myeloma</td>
</tr>
<tr>
<td>Abnormal plasma cell immunophenotype ≥95% by MFC</td>
<td>50</td>
<td>Consider preventive therapy or trials</td>
</tr>
<tr>
<td>Evolving type of SMM**</td>
<td>65</td>
<td>Consider preventive therapy or trials</td>
</tr>
<tr>
<td>t(4;14) or del 17p</td>
<td>50</td>
<td>Consider preventive therapy or trials</td>
</tr>
<tr>
<td>M-protein ≥3g/dL and bone marrow clonal plasma cells ≥10%</td>
<td>50</td>
<td>Consider preventive therapy or trials</td>
</tr>
<tr>
<td>Serum involved/uninvolved free light chain ratio ≥8 and &lt;100</td>
<td>40</td>
<td>Consider clinical trial</td>
</tr>
<tr>
<td>No high-risk factors</td>
<td>10-20</td>
<td>Observation or clinical trial</td>
</tr>
</tbody>
</table>

*R to myeloma or related disorder

**Increase in serum monoclonal protein by ≥10% on each of two successive evaluations within a 6-month period

Case #1: Ed*

Risk Assessment
• High-risk SMM

Options Discussed/Decision Point
• Observation
• Clinical Trial

Patient & Family Considerations
• Desire to treat; waiting to progression wasn’t appealing
• Treatment schedule compatible with work and family

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Myeloma Disease Trajectory: MGUS/SMM Precedes Active Myeloma

- **MGUS or SMM**
- **ASYMPTOMATIC**
- **SYMPTOMATIC**
- **REFRACTORY RELAPSE**
  - M-Protein g/L: 2, 5, 10
  - Therapy
  - Active Myeloma
  - Plateau Remission
  - Relapse

Adapted from Dr. Brian Durie
Case #1: Ed*

**Nursing Implications**

- Patient education on high-risk SMM, prognosis
- Other education needs:
  - Treatment
  - Self care/autonomy
- Patient advocacy
- Survivorship begins as diagnosis:
  - Educate on protecting bone and renal health
- Educate patient and caregiver on the importance of maintaining good health
  - Lifestyle (healthy foods, exercise)
  - General health screenings (hypertension, diabetes, etc)
  - Minimizing risk factors

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Prevalence

- 25% to 50% have renal impairment during disease
- 30% to 40% have elevated serum creatinine at presentation
- Less than 10% have severe renal failure at presentation

Nursing Implications

- Educate patients on protecting renal function
  - Hydration
  - Caution with drugs, IV contrast, etc
- Educate patient on symptoms of renal impairment


Bone Disease in Myeloma

- Approximately 85% of MM patients develop bone disease
- Bone destruction may lead to hypercalcemia and contribute to renal impairment

Nursing Implications

- Educate patients on protecting bone health
- Educate patients on symptoms of bone disease


### Partnering With Patients: NLB Survivorship Care Plan for Renal Health

**Patient Tear-Out Tool**

**Long-Term Survivor Renal Care Plan for Patients**

<table>
<thead>
<tr>
<th>Follow-Up Care for</th>
<th>Recommendations</th>
<th>Treating hematology or oncology provider</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood tests</strong></td>
<td>A complete blood count, comprehensive metabolic panel, serum protein electrophoresis, serum immunofixation electrophoresis, 24-hour urine protein electrophoresis, urine immunofixation electrophoresis, lactate dehydrogenase, serum free light chain assay, and beta-2-microglobulin every three months. Special tests for bone loss may be ordered by the kidney specialist.</td>
<td></td>
</tr>
<tr>
<td><strong>Bone surveys</strong></td>
<td>A metastatic skeletal survey annually or earlier if new skeletal symptoms occur.</td>
<td></td>
</tr>
</tbody>
</table>
| **Diagnostic imaging** | Avoid the use of IV dye or contrast with positron-emission and computed tomography or magnetic resonance image scans. | • Any provider may order one of these tests.  
• You, as the patient, should alert whoever is ordering these tests that you have a diagnosis of myeloma and IV dye may not be safe. |
| **History and physical examination** | Quarterly review of medications, changes in medical history, and physical examinations are recommended. | • Call your primary care provider for an annual physical examination.  
• Your hematology oncology practitioner will review medications at each visit. |
| **Medications**    | • Avoid the use of nonsteroidal anti-inflammatory drugs such as ibuprofen. Many medications and over-the-counter supplements can worsen renal impairment, but others can be given safely with lower doses. | All medications should be reviewed with your provider before starting, including herbal and over-the-counter medications. |


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**In Your Packet on CD and Available for free download at http://myeloma.org**
Partnersing With Patients: 
NLB Survivorship Care Plan for Bone Health

Symptoms that require immediate medical attention include:
- Sudden onset of pain (may indicate a new fracture)
- Back pain with sudden change in sensation in lower or upper extremities or loss of bowel or bladder function
- Noticeable changes in mental status such as increased somnolence, confusion, or irritability; or severe excessive thirst, and urination (may indicate increased calcium in blood)

The following guidelines will help monitor and maintain your bone health, including blood tests and radiographic evaluations, medications, supplements, and physical activity. Pain management is important for maintaining physical activity levels.

### Medical Follow-Up

<table>
<thead>
<tr>
<th>Blood and laboratory tests (performed at least annually)</th>
<th>Calcium, vitamin D, alkaline phosphate, and creatinine. Hormone levels such as parathyroid and thyroid; testosterone for men; and estradiol, follicle-stimulating, and luteinizing hormone for women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Last date tested: ___________</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Radiology and imaging (performed annually and with new onset of pain or fracture)</th>
<th>Bone survey to monitor for new bone lesions and bone density to monitor for osteoporosis. Magnetic resonance imaging, positron-emission tomography, and computed tomography performed as recommended by the healthcare provider</th>
</tr>
</thead>
<tbody>
<tr>
<td>Last date tested: ___________</td>
<td></td>
</tr>
</tbody>
</table>

### Medications and Supplements

| Bisphosphonates: If your disease status is very good partial response rate (VGPR) or better, monthly use for one year is recommended. If your disease status is less than VGPR, monthly use for two years is recommended. | Used to increase bone strength and may have antmyeloma benefit. Stop during remission or use as maintenance every three months. These guidelines continue to be reviewed and may be revised over time. |

| Pain medication: Monitor changes in your pain, such as an increase or decrease based on a pain scale of 1 (least pain) to 10 (worst pain). | Report any change in pain level. Use pain medication as prescribed by your healthcare provider. Discuss other pain management techniques if your pain is not well controlled with medication (i.e., balloon kyphoplasty or vertebroplasty, radiation, or surgical treatments). A consultation with a treatment specialist may be recommended. |

## Myeloma Risk Factors: Most Are Not Addressable

<table>
<thead>
<tr>
<th>Not Addressable</th>
<th>Addressable</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age:</strong> Age is the biggest risk factor for multiple myeloma. Most people with this cancer are over 65 years old.</td>
<td><strong>Weight:</strong> A study by the American Cancer Society found that being overweight increases a person's risk of getting this cancer.</td>
</tr>
<tr>
<td><strong>Gender:</strong> Men are slightly more likely than women to get multiple myeloma.</td>
<td><strong>Toxin exposure:</strong> Several specific toxins are now linked to myeloma, including pesticides; insecticides; 1,3-butadiene; dioxins; benzene.</td>
</tr>
<tr>
<td><strong>Race:</strong> Multiple myeloma is almost twice as common among black Americans as white Americans. The reason is not known.</td>
<td><strong>Radiation:</strong> Exposure to radiation may increase the risk of multiple myeloma.</td>
</tr>
<tr>
<td><strong>Family history:</strong> A first-degree relative with the disease increases risk 4-fold; however, most patients have no other relatives with the disease.</td>
<td></td>
</tr>
<tr>
<td><strong>Other plasma cell diseases:</strong> Many people with other plasma cell diseases will develop multiple myeloma later.</td>
<td></td>
</tr>
</tbody>
</table>
Case #1: Ed*

Treatment:
• Entered clinical trial:
  “Phase 2 Trial Of Initial Safety and Toxicity Prior To The Phase 3 Trial Of Lenalidomide Versus Observation Alone In Patients With Asymptomatic High-Risk Smoldering Multiple Myeloma (E3A06): A Trial Coordinated By The Eastern Cooperative Oncology Group”

Update 6 months:
• Doing well – responding to therapy
• No CRAB criteria
• Family doing well
• Work going well
• Adherent to therapy/clinical trial
• Follows monthly myeloma lab monitoring as ordered by the physician

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Adherence means receiving the therapy as planned. Patients who stay on therapy have better outcomes!

**Patient Factors**
- Lack of understanding as to why the treatment is needed
- Lack of confidence in provider
- Inadequate expectations of therapy
- Difficulty getting to clinic
- Forgetfulness
- Delay in refilling prescriptions (oral)
- Overwhelmed by amount of medications for other co-morbid conditions (oral)

**Health System Factors**
- Complex dosing regimens
- Inadequate follow-up/discharge planning
- Poor patient-provider relationship/communication
- Cost
- Lack of institutional guidelines/protocols for oral cancer treatments
- Inadequate management of AEs

Nurse’s Role in IV and Oral Adherence

• Essential in both IV and oral therapy adherence
• Reinforce the rationale in ongoing/continuous treatment
  – Cancer is a chronic condition
  – Most hematologic cancers are incurable; ongoing therapy is indicated for most patients
• Set expectations for therapy (manageable vs. toxic AEs)
• Provide tools, advice for AE management
• Enlist help of caregivers (transportation to clinic, medication reminders)
• Offer advice (consistent time, alarm clocks, pillboxes, smart phone “alerts”)
• Facilitate prior authorizations
• Encourage discussion of cancer treatment and rationale so a mutual agreement can be reached

• Multiple myeloma is a cancer of the plasma cells
• Myeloma disease continuum: MGUS, SMM, MM
• A majority of patients with SMM do not require therapy
• A paradigm shift in SMM: probably 2 populations
  – “More like MGUS”
  – “More like active myeloma” ← Efforts by Mateos, Landgren, others to identify patients and treat early
• Oncology nurses must continue to keep abreast of the current science of SMM since it is changing
• Main nursing implications: education and advocacy
• Nurses play an important role in patient adherence

Patients #2 & #3: Newly Diagnosed Myeloma

Page A. Bertolotti, RN, BSN, OCN®
Beth Faiman, PhDc, MSN, APRN-BC, AOCN®
Patient #2: Rebecca*

Initial Presentation:
- 48-year-old woman
- School teacher
- Back pain
- Self-medicating with NSAIDs, but no improvement

Initial Testing:
- MRI of spine
  - L4 compression fracture; lytic lesions
- Blood work
  - Hgb below 9 mg/dL
  - Calcium 13.7 mg/dL
  - Creatinine 2.1 mg/dL

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Common Symptoms at Myeloma Diagnosis

Symptom

- Anemia: 73%
- Bone Lesions: 66%
- Bone Pain: 58%
- Kidney Issues: 48%
- Fatigue: 32%
- Weight Loss: 24%
- No Symptoms: 11%

## Imaging Techniques for Assessing Myeloma Bone Disease

<table>
<thead>
<tr>
<th>Technique</th>
<th>When to Use</th>
<th>Limitations of Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBS (skeletal survey)</td>
<td>• Baseline &amp; relapse</td>
<td>• Insensitive; bone lesions only seen when &gt;30% bone loss occurs</td>
</tr>
<tr>
<td>MRI</td>
<td>• Verify solitary plasmacytomomas; nonsecretory disease; Assess spinal cord compression</td>
<td>• Lack of specificity reflects marrow infiltration not specifically bone deterioration; Expense &amp; time</td>
</tr>
<tr>
<td>CT</td>
<td>• Soft-tissue disease; nonsecretory disease</td>
<td>• Does not differentiate between active &amp; inactive lesions; Higher levels of radiation exposure; Avoid IV contrast for myeloma patients</td>
</tr>
<tr>
<td>PET</td>
<td>• Assess extra-medullary disease; response</td>
<td>• Lack of specificity of findings may result in false-positive results; Expense; False negatives; some myelomas not PET-avid</td>
</tr>
<tr>
<td>CT/PET Fusion</td>
<td>• Assess active disease &amp; areas of bone destruction that are not active</td>
<td>• Expense; False negatives; Avoid IV contrast for myeloma patients</td>
</tr>
<tr>
<td>DEXA (bone densitometry)</td>
<td>• If comorbid conditions exist for osteoporosis</td>
<td>• Does not measure osteolytic disease</td>
</tr>
</tbody>
</table>

MBS = metastatic bone survey

### Myeloma Staging Systems: Durie-Salmon and ISS

#### Durie-Salmon Staging System

<table>
<thead>
<tr>
<th>Stage</th>
<th>Values</th>
<th>MM Cell Mass $10^{12}$ cells/m²</th>
</tr>
</thead>
</table>
| I     | All of the following:  
  - Hemoglobin $>$10 g/dL  
  - Serum calcium level $\leq$12 mg/dL  
  - Normal bone or solitary plasmacytoma on x-ray  
  - Low M component production rate: IgG $<$5 g/dL  
  - IgA $<$3 g/dL  
  - Bence-Jones protein $<$4 g/24 hr  
|        |        | low $<0.6$                       |
| II    | Not fitting stage I or III | intermediate 0.6 - 1.2           |
| III   | One or more of the following:  
  - Hemoglobin $<$8.5 g/dL  
  - Serum calcium level $>$12 mg/dL  
  - Multiple lytic bone lesions on x-ray  
  - High M-component production rate: IgG $>$7 g/dL  
  - IgA $>$5 g/dL  
  - Bence-Jones protein $>$12 g/24 hr  
|        |        | High $>1.2$                      |

**Subclassification criteria:**

- **A** Normal renal function (serum creatinine level $<2.0$ mg/dL)
- **B** Abnormal renal function (serum creatinine level $>2.0$ mg/dL)

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#### International Staging System (ISS)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Values</th>
</tr>
</thead>
</table>
| 1     | $B_2M$ $<$3.5 mg/dL  
  - $Alb$ $\geq$3.5 g/dL |
| 2     | Not Stage 1 or 3     |
| 3     | $B_2M$ $>$5.5 mg/dL  |

- $B_2M$=serum $B_2$ microglobulin in mg/dL;  
  - $Alb$=serum albumin in g/dL

- ISS should only be used in patients who meet diagnostic criteria for myeloma, since other conditions (renal dysfunction from diabetes or hypertension) may cause elevated $B_2M$ levels
- ISS is more of a prognostic index; it does not quantify tumor burden or extent of involvement
- It is recommended that ISS staging be used along with the Durie-Salmon Staging System

---

Case #2: Rebecca*

**Myeloma Work-Up:**
- Skeletal survey: Lesions spine, skull, and pelvis
- 24-hour urine: 1100 cc (decreased), 5934 mg protein
- Bone marrow
  - Plasma cells: 70%
  - Cyto: normal
  - FISH: t(4;16) – std risk
- IgG: 470
- sFLC: 197 (lambda), Ratio: 0.38
- B₂M: 5.4mg/dL
- Alb: 4.9 g/dL
- ISS Stage: II

**Diagnosis:** IgG lambda light chain MM, ISS stage II

Rebecca has “active myeloma”
- C = calcium elevation
- R = renal
- A = anemia
- B = bone disease

and needs treatment

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Case #2: Rebecca*

Family Situation
- Single, never married
- Caregiver for aging mother who
  - Lives alone
  - Arthritis, uses cane
- Brother lives across the country

Patient Concerns
- Ability to provide care to mother
- Ability to work, financial

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Nursing Implications: Discussion of Expectations, Goals

Goals of Treatment:
• Rapid and effective control of disease
• Manage disease-related symptoms
• Improve survival
• Maintain quality of life while on therapy

Expectations:
• Chronic condition; will require ongoing therapy and follow-up for life
• Prognosis: many live with myeloma for many years – “new normal”
• Optimal outcomes require active participation by patient & caregiver
  – Adherence to therapy: need to treat myeloma
  – Understanding myeloma symptoms and therapy—when to call
  – Importance of maintaining overall health; screenings, PCP, etc
  – Utilizing available support and education resources

Treatment: Transplant-Eligible or -Ineligible

Rebecca

Transplantation Eligible Induction Regimens
- Bor/Dex
- Bor/Cy/Dex
- Bor/Len/Dex
- Car/Len/Dex
- Bor/Dox/Dex
- Len/Dex
- Bor/Thal/Dex

Transplantation Candidate?
Yes

Considerations
- Age
- Performance status
- Comorbidity
- Prognostic factors
- Patient preference
- Insurance coverage

Consideration
Stem cell harvest after 4–6 cycles

Autologous hematopoietic stem cell transplantation

Non-Transplantation Eligible Induction Regimens
- Mel/Pred plus Bor, Len, or Thal
- Bor/Len/Dex
- Len/low Dex
- Cy/Bor/Dex

Consideration
Continued or maintenance therapy

Bor—bortezomib; Car—carfilzomib; Cy—cyclophosphamide; Dex—dexamethasone; Dox—doxorubicin; Len—lenalidomide; Mel—melphalan; Pred—prednisone; Thal—thalidomide

Treatment Options Have Greatly Increased

- **1950**: MM Therapies Introduction
- **1958**: Melphalan
- **1960**: Prednisone
- **1962**: Melphalan + Prednisone
- **1969**: High-Dose Dexamethasone
- **1980**: 1983 Autologous Transplantation
- **1983**: Bortezomib 3rd line
- **1986**: Bortezomib 2nd line
- **1990**: Lenalidomide + Dex 2nd line
- **2000**: Thalidomide + Dex 1st line
- **2003**: Doxorubicin + Bortezomib 2nd line
- **2005**: Carfilzomib 3rd line
- **2006**: Bortezomib SC
- **2007**: Bortezomib 1st line
- **2008**: Bortezomib SC
- **2010**: FDA-Approved in MM
- **2012**: Pomalidomide ±Dex 3rd line
- **2013**: Bortezomib SC

**Key Dates and Treatments**
- **1958**: Melphalan
- **1962**: Prednisone
- **1969**: Melphalan + Prednisone
- **1983**: Autologous Transplantation
- **1986**: High-Dose Dexamethasone
- **1990**: Bortezomib 3rd line
- **2000**: Bortezomib 2nd line
- **2003**: Lenalidomide + Dex 2nd line
- **2005**: Thalidomide + Dex 1st line
- **2006**: Doxorubicin + Bortezomib 2nd line
- **2007**: Carfilzomib 3rd line
- **2010**: FDA-Approved in MM
- **2012**: Pomalidomide ±Dex 3rd line
- **2013**: Bortezomib SC
### Drugs & Drug Classes Approved for Treatment of Myeloma

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Name</th>
<th>Abbrev.</th>
<th>Brand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteasome inhibitor</td>
<td>Bortezomib</td>
<td>btz, V</td>
<td>VELCADE®</td>
</tr>
<tr>
<td></td>
<td>Carfilzomib</td>
<td>cfz</td>
<td>KYPROLIS®</td>
</tr>
<tr>
<td>Immunomodulatory agent</td>
<td>Lenalidomide</td>
<td>len, R</td>
<td>REVLIMID®</td>
</tr>
<tr>
<td></td>
<td>Thalidomide</td>
<td>thal, T</td>
<td>THALOMID®</td>
</tr>
<tr>
<td></td>
<td>Pomalidomide</td>
<td>pom</td>
<td>POMALYST®</td>
</tr>
<tr>
<td>Alkylating agent</td>
<td>Melphalan</td>
<td>mel, M</td>
<td>ALKERAN®, ALPHALAN®</td>
</tr>
<tr>
<td></td>
<td>Cyclophosphamide</td>
<td>CTX</td>
<td>CYTOXAN®</td>
</tr>
<tr>
<td>Corticosteroid</td>
<td>Prednisone</td>
<td>pred, P</td>
<td>DELTASONE®</td>
</tr>
<tr>
<td></td>
<td>Dexamethasone</td>
<td>D, d, Dex, DXM</td>
<td>DECADRON®</td>
</tr>
<tr>
<td>Bisphosphonate</td>
<td>Pamidronate</td>
<td>pmd</td>
<td>AREDIA®</td>
</tr>
<tr>
<td></td>
<td>Zoledronic Acid</td>
<td>zol</td>
<td>ZOMETA®</td>
</tr>
</tbody>
</table>
## Treatment Paradigm: Combinations

<table>
<thead>
<tr>
<th>Myeloma Preferred Induction Regimens*</th>
<th>Abbreviation(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Combination</strong></td>
<td></td>
</tr>
<tr>
<td>Bortezomib/dexamethasone (dex)†</td>
<td>VD or Vd</td>
</tr>
<tr>
<td>Bortezomib/cyclophosphamide/dex</td>
<td>CyBORD</td>
</tr>
<tr>
<td>Bortezomib/doxorubicin/dex†</td>
<td></td>
</tr>
<tr>
<td>Bortezomib/lenalidomide/dex</td>
<td>VRD or VRd</td>
</tr>
<tr>
<td>Bortezomib/thalidomide/dex†</td>
<td>VTD or VTd</td>
</tr>
<tr>
<td>Lenalidomide/dexamethasone†</td>
<td>RD or Rd</td>
</tr>
<tr>
<td><strong>Non-transp.</strong></td>
<td></td>
</tr>
<tr>
<td>Bortezomib/dex</td>
<td>VD or Vd</td>
</tr>
<tr>
<td>Lenalidomide/low-dose dex†</td>
<td>Rd</td>
</tr>
<tr>
<td>Melphalan/prednisone/bortezomib†</td>
<td>VMP or MPB</td>
</tr>
<tr>
<td>Melphalan/prednisone/lenalidomide†</td>
<td>MPR or MPL</td>
</tr>
<tr>
<td>Melphalan/prednisone/thalidomide†</td>
<td>MPT</td>
</tr>
</tbody>
</table>

Combination therapies demonstrated improved response rates, progression-free survival, and/or overall survival compared to single agents.

*NCCN Guidelines Multiple Myeloma Version 2.2014
†Category 1
Decision Making; Patient Factors

Nursing Implications:
• Patient education
  – Outcomes
  – Quality of life
• Advocacy for patients
  – Autonomy for patients
  – Patient’s considerations

Nursing Considerations:
• Patient adherence
• AE management
• Performance status
• Renal function
• Other comorbidities
• Patient preference
• Health maintenance

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy

Bortezomib: SC vs. IV Administration

**Subcutaneous (SC)**

- FDA approved SC in 2012
- Equivalent efficacy as IV (numerous studies)
- Reduced neuropathy and GI AEs with SC administration (numerous studies)
- 67.8% patients prefer SC over IV
  - 54 min less “chair time” on average
  - 46 min less clinic time on average

**Intravenous (IV)**

- FDA approved in 2003
- Highly effective myeloma therapy
- Neuropathy—a notable AE

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For subcutaneous administration
Add 1.4 mL
0.9% sodium chloride

Two ways to reconstitute a 3.5 mg vial of bortezomib

For intravenous administration
Add 3.5 mL
0.9% sodium chloride

Hydration status: a key nursing consideration, especially in patients with renal compromise

Heterogeneity in SC Bortezomib Administration

Study Design & Respondents

• 41-question electronic survey on SC bortezomib
• 43 nurses at 17 clinics responded
• 74% practicing oncology for >5 years

Results

• Heterogeneity in techniques used
• Developing a practice guideline would be important (completely agree = 77%; somewhat agree = 23%)
• Nurses would change practice to be consistent with guideline (completely agree = 67%, somewhat agree = 30%)

* Arm is not a recommended injection site in bortezomib prescribing information

In the study, nurses reported using various injection sites and techniques for SC bortezomib, with the most common being the abdomen (98%), followed by the arm (53%) and thigh (19%). The least used site was the arm. For injection techniques, air purge was used by 49% of nurses, while air bubble was used by 51%.

Study Design & Respondents
• Injection site reactions (ISRs) evaluated in 300 SC bortezomib injections in 20 patients

Results
• Significantly fewer injection site reactions in abdomen than thighs
• Significantly fewer injection site reactions in cycle 2 or later than first cycle

Nursing Implications: Consider prioritizing abdomen over thigh as injection site. Especially monitor first cycle for injection site reactions

Air Sandwich: Administration Technique

“Air Sandwich” Technique

- Site selection: amount of fatty tissue
- Attach fresh needle (4 to 6 mm) to syringe with prepared medication
- Do not purge needle (air in needle)
- Maximum volume for SC injection is 2 mL per site
- Pull 0.5 to 1.0 mL air into syringe
- Use index finger and thumb to “pinch an inch” — avoid pinching the underlying muscle
- Invert syringe and inject, including air behind the drug
  - 90 ° angle for 4-6-mm needles
  - 45 ° angle for ≥8-mm needle
- Remove needle promptly
- Apply gentle pressure to site

Use “air sandwich” technique to avoid seeding of irritating medication in the injection track

Improving Renal Function With Novel Agents

**Study:**
- 112 newly diagnosed MM patients with renal impairment
- Received thalidomide-based regimen, bortezomib-based regimen, or lenalidomide-based regimen
- Complete renal responses (CRR) or partial renal responses (PRR) determined by glomerular filtration rate

**Conclusions:**
- Novel MM agents can improve renal function
- Bortezomib- and thalidomide-based regimens statistically better for improving renal function

**Results:**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Renal response</th>
<th>Median time to first renal response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Complete</td>
<td>Complete + Partial</td>
</tr>
<tr>
<td>Bortezomib-based</td>
<td>70%*</td>
<td>80%*</td>
</tr>
<tr>
<td>Thalidomide-based</td>
<td>53%*</td>
<td>55%*</td>
</tr>
<tr>
<td>Lenalidomide-based</td>
<td>34%</td>
<td>38%</td>
</tr>
</tbody>
</table>

*P<0.05 vs. lenalidomide-based regimen

**Bone Health Supportive Care**

**Pharmaceuticals:** used to build bone and reduce skeletal events (fractures, etc.)
- Pamidronate
- Zoledronic acid
- Denosumab (biological in phase 3 for MM)

**Nursing implications for BPs:**
- Acute phase reaction: 11% fever, chills
- Dental health (dental exams every 6 months)
- Renal (24-hr urine)

**Surgical interventions:**
- Vertebroplasty
- Kyphoplasty
- Surgery

**Radiation:** used to kill myeloma cells in a lytic lesion or extramedullary disease

Osteonecrosis of the jaw can be a consequence of bisphosphonates

Kyphoplasty uses a “balloon” to create a cavity for bone cement to reduce vertebral fracture & pain

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# Guidelines for Bone Disease

<table>
<thead>
<tr>
<th><strong>Bisphosphonates (BPs) should be considered in ALL MM patients receiving first-line anti-myeloma therapy</strong></th>
<th>IMWG¹</th>
<th>NCCN²</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZOL or PAM are preferred BPs; dosed every 3 to 4 weeks; ZOL demonstrated survival benefit for MM patients</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>IMWG¹</strong></th>
<th><strong>NCCN²</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Continue BPs in patients with active disease &amp; resume after disease relapse if discontinued in CR/VGPR patients</td>
<td>✓</td>
</tr>
<tr>
<td>Monitor for renal dysfunction and osteonecrosis of the jaw</td>
<td>✓</td>
</tr>
<tr>
<td>Use of BPs in SMM in clinical trial setting</td>
<td>✓</td>
</tr>
<tr>
<td>Orthopedic consultation for long-bone fractures (actual and impending), spinal cord compression, or vertebral instability</td>
<td>✓</td>
</tr>
<tr>
<td>Consider kyphoplasty for symptomatic vertebral compression fractures</td>
<td>✓</td>
</tr>
<tr>
<td>Low-dose RT (10 to 30 Gy) as palliative for bone pain, impending pathologic fracture or spinal cord compression</td>
<td>✓</td>
</tr>
</tbody>
</table>

* vertebroplasty also recommended

IMWG = International Myeloma Working Group; NCCN = National Cancer Center Network

2. NCCN Multiple Myeloma Guidelines v 2.2014.
Patient #2: Rebecca*

Update
- On 3rd cycle of CyBorD combination
- VGPR (Very Good Partial Response) after 2 cycles
- Kidney function normal
- Planning on transplant in summer and lenalidomide maintenance post transplant
- Received kyphoplasty; back pain reduced
- Began zoledronic acid for bone support

Nursing Implications
- Educate patient on transplant, need for caregiver
- Coordinate with transplant center; PCP
- Patient management: AEs, pain, psychological, infection prevention
- Discuss long-term health maintenance post transplant (health screenings)
- Post-transplant immunizations

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy

Nurse Leadership Board CJON Supplement on Transplantation in MM

Resources for Nurses:
- Transplant process
- Caregiver information
- Clinical update
- Frequently asked questions

In your packet & available free from myeloma.org

## IMWG Response Criteria

<table>
<thead>
<tr>
<th>Response</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Better</td>
<td><strong>sCR</strong></td>
</tr>
<tr>
<td></td>
<td>CR as defined below plus:</td>
</tr>
<tr>
<td></td>
<td>Normal FLC ratio and absence of clonal cells in bone marrow by immunohistochemistry or immunofluorescence</td>
</tr>
<tr>
<td>CR</td>
<td>Negative immunofixation on the serum and urine + disappearance of any soft-tissue plasmacytomas and &lt;5% plasma cells in bone marrow</td>
</tr>
<tr>
<td>VGPR</td>
<td>Serum and urine M-protein detectable by immunofixation but not by electrophoresis or ≥90% reduction in serum M-protein plus urine M-protein level &lt;100 mg/24 hr</td>
</tr>
<tr>
<td>PR</td>
<td>≥50% reduction of serum M-protein and reduction in 24-hr urinary M-protein by ≥90% or to &lt;200 mg/24 hr. If serum &amp; urine M-protein are not measurable:</td>
</tr>
<tr>
<td></td>
<td>• ≥50% decrease in the difference between involved and uninvolved FLC levels is required</td>
</tr>
<tr>
<td></td>
<td>• AND if serum free light assay is also not measurable, ≥50% reduction in plasma cells is required, provided baseline bone marrow plasma cell percentage was ≥30%</td>
</tr>
<tr>
<td></td>
<td>In addition to the above criteria, if present at baseline, a ≥50% reduction in the size of soft-tissue plasmacytomas is also required</td>
</tr>
<tr>
<td>SD</td>
<td>Not meeting criteria for CR, VGPR, PR, or progressive disease</td>
</tr>
<tr>
<td>Worse</td>
<td><strong>PD</strong></td>
</tr>
<tr>
<td></td>
<td>Increase of &gt;25% from lowest response value in any one or more of M-component (serum or urine), difference between involved and uninvolved FLC, bone marrow plasma cell percentage, new bone lesions/plasmacytomas or increase in size of existing lesions/plasmacytomas, hypercalcemia attributed solely to myeloma</td>
</tr>
</tbody>
</table>

**Legend:**
- **sCR** = stringent complete response; **CR** = complete response; **VGPR** = very good partial response; **PR** partial response; **SD** stable disease; **PD** progressive disease

Sequencing Method to Detect MRD

Background
Most MM patients relapse due to persistence of myeloma cells termed minimal residual disease (MRD)

Study Design
BM samples from patients in GEM00 or GEM05 trials evaluated for MRD by 3 methods:
• LymphoSIGHT™ sequencing method
• Multiparameter flow cytometry (MFC)
• Allele-specific oligonucleotide (ASO) PCR

Results
• LymphoSIGHT detected MM rearrangement in 121 of 133 (91%) of patients
• High correlation among MRD detection methods: LymphoSIGHT, MFC, ASO-PCR
• LymphoSIGHT MRD had significant prognostic value

Conclusion: “MRD assessment by LymphoSIGHT is useful and can determine molecular CR in MM”

Nursing Implications: MRD testing may be used to educate patients and guide decision making

Martinez-Lopez, J et al. ASH 2013 #1848.
MRD Detection in ASCT Autografts

Study Design
Compared MRD detection methods (LymphoSIGHT™ sequencing method, allele-specific oligonucleotide (ASO) PCR) in ASCT autografts in autologous peripheral blood stem cell (PBSC)

Results
• MRD in autografts assessed in 36/36 (100%) by LymphoSIGHT method and 30/36 (83%) by ASO-PCR
• LymphoSIGHT method was more sensitive than ASO-PCR
• With no post-ASCT therapy, patients with MRD-negative autograft had significantly longer PFS than patients with MRD-positive autograft
• Trend for improved PFS in patients with MRD-positive allografts that received post ASCT ther

Progression Free Survival

Nursing Implications:
MRD testing may be used in ASCT setting to
• Educate patients
• Guide decision making

Patient #3: Karl*

Initial Presentation

- 79-year-old male
- Retired minister
- Type 2 diabetes; peripheral neuropathy; pulmonary htn
- Emergency room visit for fall (daughter brought him); complained of pain in ribs
- Chest x-ray revealed rib fractures, lytic lesions
- Referred to oncologist
- Myeloma work up:
  - FISH: t(4,14)
  - M-protein: 12g/dL
  - PC in BM: 15%
  - ISS Stage II Myeloma
  - B2M: 4.2 mg/dl
  - Cr: 1.4mg/dL
  - Hg: 11 g/dL

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Patient #3: Karl*

Family Situation
- Widower
- Living alone
- Caregiver: married daughter with school-aged children

Patient Concerns
- Prognosis
- Maintaining independence
- Becoming a burden to family

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Treatment: Transplant-Eligible or-Ineligible

Transplantation Eligible Induction Regimens
- Bor/Dex
- Bor/Cy/Dex
- Bor/Len/Dex
- Car/Len/Dex
- Bor/Dox/Dex
- Len/Dex
- Bor/Thal/Dex

Transplantation Candidate?
Yes

Consideration
Stem cell harvest after 4–6 cycles

Autologous hematopoietic stem cell transplantation

Bor—bortezomib; Car—carfilzomib; Cy—cyclophosphamide; Dex—dexamethasone; Dox—doxorubicin; Len—lenalidomide; Mel—melphalan; Pred—prednisone; Thal—thalidomide

No

Non-Transplantation Eligible Induction Regimens
- Mel/Pred plus Bor, Len, or Thal
- Bor/Len/Dex
- Len/low Dex
- Cy/Bor/Dex

Consideration
Continued or maintenance therapy

Karl

### Therapies Studied

<table>
<thead>
<tr>
<th>Source</th>
<th>Therapies Studied</th>
<th>Key Conclusions</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Palumbo | Rd (doublet) MPR or CPR (triplet) | In community-based population, triplet alkylating combo did not lead to different PFS or OS benefit over doublet | • ≥Grade 3 hematological AEs in 51% MPR/CR vs. 29% Rd ($P<0.001$)  
• ≥Grade 3 hematological AEs in 67% MPR and 31% CPR ($P<0.001$) |
| | Dose adjustments made for >75 years old N=659 patients (2:1) randomization for triplet and doublet, respectively | Newly diagnosed MM | |
| | | | |
| Larocca | VP VCP VMP | In community-based population, similar PFS and OS in low-intensity regiments tested | • >75 years old; NO exclusion criteria  
• Patients rated as fit, unfit, or frail based on multiple screening instruments  
• SAEs: VP 22%, VCP 20%; VMP 30% |
| | Reduced intensity subcutaneous bortezomib 1.3 mg/m$^2$ days 1, 8, 15, 22 of 28 | | |
| | N=152 newly diagnosed MM | | |

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Higher Cumulative Dose of Bortezomib Results in Better Overall Survival

**Study Design**
- VISTA trial: VMP vs. MP in transplant-ineligible patients
- Analysis of OS based on total bortezomib dose administered

**Results**
Landmark analysis (alive at 180 days):
- Longer OS in pts with ↑cumulative dose
  - 60.4 months in pts with ≥39 mg/m²
  - 50.3 months in pts with <39 mg/m²
- Hazard ratio (HR) 0.709, P=0.0356

**Conclusion**: “Higher cumulative bortezomib dose, reflecting prolonged treatment duration and/or dose intensity, is associated with improved OS”

**Nursing Implications**
- Patient education: Importance of therapy (↑cum dose, improved OS)
- Actively manage patients (AEs, dose/schedule adjust, etc) to keep on therapy

FIRST Trial for Transplant-Ineligible MM Patients: Study Design (Phase 3)

- Previously untreated symptomatic MM
- 65 yrs+ or transplant-ineligible
- ECOG performance 0,1,2
- Renal impairment allowed but not dialysis requirement

Randomization 1:1:1

LEN + Lo-DEX (Rd): 18 Cycles (72 weeks)
LEN + Lo-DEX (Rd) Continuously
MEL+PRED+THAL (MPT): 12 Cycles (72 weeks)

End points
Primary:
- PFS
Secondary:
- OS
- Response
- DOR
- TTR
- TTF
- 2nd AMT
- TTP
- Safety
- QoL

Stratification: age, country, and ISS stage
Dose adjustment for patients >75 years old
Enrolled: 1,623 patients worldwide

Facon T, et al. ASH 2013 #2.
FIRST Trial Study Results: Lenalidomide-Dex Continuous Therapy Was Superior

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Median TTP</th>
<th>Median Time to 2nd AMT</th>
<th>4-year OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rd (n=536)</td>
<td>32.5 mos†‡</td>
<td>39.1†‡</td>
<td>59.4%*</td>
</tr>
<tr>
<td>Rd18 (n=541)</td>
<td>21.9 mos</td>
<td>28.5</td>
<td>55.7%</td>
</tr>
<tr>
<td>MPT (n=547)</td>
<td>23.9 mos</td>
<td>26.7</td>
<td>51.4%</td>
</tr>
</tbody>
</table>

†Highly statistically significant difference RD vs. RD18
‡ Highly statistically significant difference RD vs. MPT
*Statistically significant difference RD vs. MPT

- Continuous Rd significantly extends PFS, with an OS benefit vs. MPT
  - Consistent benefit across most subgroups
  - Rd superior to MPT across all other efficacy secondary end points
- Safety profile with continuous RD was manageable
  - Heme and non-heme AEs were as expected for Rd and MPT
  - Incidence of hematological SPM lower with RD vs. MPT
- “In newly diagnosed transplant ineligible patients, the FIRST trial establishes continuous Rd as a new standard of care”

Nursing Implications
- Continuous Rd therapy is superior to shorter duration
- Manage AEs, adherence to keep patients on therapy

Facon T, et al. ASH 2013 #2.
Patient #3: Karl*

Treatment Plan
• Rd continuous therapy
• Zoledronic acid

Kidney Function Calculations (Cr: 1.4mg/dL)
• GFR (MDRD): 54 mL/min/1.73 m²
• GFR (CKD-EPI†) : 47 mL/min/1.73 m²
• CLcr (Cochcroft Gault): 49 mL/min

Starting Dose Adjustment
• For CLcr30-60mL/min:
  lenalidomide 10mg/24 hrs
  (Velcade® prescribing information)

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
† CKD-EPI calculation provides better prognostic value than MDRD in MM patients
  (Dimopoulous MA, et al. ASH 2013 #1867.)
Patient #3: Karl*

Nursing Considerations

- Discuss importance of therapy, adherence; involve caregiver
- Weekly CBCs for first 8 weeks
- Check blood sugars
- Antiviral prophylaxis (if shingles history)
- DVT prophylaxis
- Educate patient and caregiver on
  - Renal function
  - Bone health
  - Dental and oral care
  - Steroid side effects
  - Safety and mobility recommendations

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy

Free Patient Education Tools From IMF

Patient Educational Tools Created by IMF’s Nurse Leadership Board

- Preventing Blood Clots and Thromboembolic Events
- Managing Myelosuppression
- Managing Steroid Side Effects
- Managing Peripheral Neuropathy
- Managing Gastrointestinal Side Effects

Available as a free download from http://myeloma.org

- Select “health professionals” tab, then “nurse leadership board”
- Reproducible for non-commercial use
Safety and Mobility for MM Patients

Factors Affecting Risk of Falling and Injury

- **Patient Specific**
  - Age
  - Vision
  - Comorbidities (diabetes, orthostatic hypotension)
  - Nutrition & hydration
  - Medications

- **Environmental**
  - Home (stairs, rugs)
  - Living alone
  - Footwear
  - Weather & climate

- **MM Disease Related**
  - Fatigue
  - Neuropathy
  - Bone disease
    - Pain (reduces activity)
    - Fracture risk

- **MM Treatment Related**
  - Steroids
    - Muscle weakness
    - Loss of bone density
    - Hyperglycemia
  - Bortezomib
    - Neuropathy
    - GI disturbance
  - Thalidomide
    - Somnolence

**Table 1. Factors Associated With Reduced Mobility and Increased Risk of Fall**

<table>
<thead>
<tr>
<th>FACTOR</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Aging is associated with changes in body composition, and a decrease in muscle and bone mass. These changes can promote functional decline (Singh, 2002).</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>Identification of alcohol use, a common problem in older adults, is associated with falls, fractures, global state alteration, multiple drug interactions, loss of activities of daily living, and neuropsychological alterations (Bux et al., 2007).</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
</tr>
<tr>
<td>• Arthritis</td>
<td>Arthritis, often a disease of older adults, may predispose patients with multiple myeloma to fall-related fractures (Rubenstein &amp; Josephson, 2006).</td>
</tr>
<tr>
<td>• Cardiovascular</td>
<td>Orthostatic hypotension may result from a variety of factors, including medication, fluid or blood loss, or adrenal insufficiency, and can lead to falls, fractures, functional decline, and myocardial ischemia (Gupta &amp; Lipstiz, 2007).</td>
</tr>
<tr>
<td>• Dementia</td>
<td>Dementia is a frequent disease in older adults and places individuals at risk for falling. Causes include cognitive and behavioral disorders, visual and motor problems, gait and balance disturbances, malnutrition, adverse effects of medication, and fear of falling (Thurman et al., 2008).</td>
</tr>
<tr>
<td>• Diabetes</td>
<td>Studies have shown that type 1 and type 2 diabetes are associated with an increased risk of hip fracture and other fractures. More frequent falls may account for some of the increased risk, but reduced bone strength also may play a role (Schwartz &amp; Sellmeyer, 2007).</td>
</tr>
<tr>
<td>• Hormonal deficiency</td>
<td>Low levels of sex hormones are associated with impaired mobility and low muscle strength in men, but not in</td>
</tr>
</tbody>
</table>

Patient #3: Karl*

Update
• Achieved PR after 2 cycles
• Achieved VGPR after 8 cycles
• Continuous therapy planned
• Continuing to live independently
  – Daughter phoning daily, visiting frequently
  – Reviewed home for safety
  – Rechecked vision
• AEs are managed well

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Summary

• Transplant eligibility is major decision in MM therapy

• “Air Sandwich” technique and abdominal site may reduce likelihood of site reactions with subcutaneous bortezomib

• Minimal residual disease testing predicts outcomes; new testing methods are available

• Keeping patients on therapy (total cumulative dose, continuous therapy) improves outcomes

• Nurses are increasingly crucial in patient adherence, setting patient expectation, coordinating care, educating patients and caregivers

Patients #4 & #5: Relapsed Myeloma

Sandra Kurtin, RN, MS, AOCN®, ANP-C
Beth Faiman, PhDc, MSN, APRN-BC, AOCN®
Myeloma Disease Trajectory: Relapsed/Refractory Disease

M-protein troughs used to become shallower with more treatment regimens, but now seeing deeper responses with new agents

Adapted from Dr. Brian Durie
Carfilzomib and Pomalidomide Are New Options for Relapsed/Refractory Patients

- 1950: Melphalan
- 1960: Prednisone
- 1962: Melphalan + Prednisone
- 1969: High-Dose Dexamethasone
- 1983: Autologous Transplantation
- 1986: Melphalan + Prednisone
- 2003: Bortezomib 3rd line
- 2005: Bortezomib 2nd line
- 2006: Lenalidomide + Dex 2nd line
- 2006: Thalidomide + Dex 1st line
- 2007: Doxorubicin + Bortezomib 2nd line
- 2008: Bortezomib 1st line
- 2010: FDA-Approved in MM
- 2012: Bortezomib SC
- 2012: Pomalidomide ± Dex 3rd line
- 2013: Carfilzomib 3rd line
Case #4: Indira*

Patient History:

• Diagnosed with IgG kappa myeloma 6 years ago at 61 (currently 67)
  – Plasma cells: 4%
  – FISH: normal
  – Cytogenetics: normal

• Treated with bortezomib-dex for 4 cycles, followed by an autologous transplant
  – No maintenance therapy
  – Remission for 6 years

• Routine follow-up:
  – Four increasing SFLC and M-protein readings
    • Checked at more frequent intervals
  – Progressive and symptomatic anemia
    • Fatigue
  – Rising creatinine
  – Rising B2 microglobulin

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Relapse Work-Up:

- **Skeletal survey**: New lytic lesions (ribs, cranium)
- **Bone marrow**:
  - Plasma cells: 14%
  - Cytogenetics: Del 17p
  - FISH: not repeated
- **Myeloma profile**:
  - IgG: 2310 (624 - 1440 mg/dL)
  - Kappa LC: 11.7 (0.33 - 1.94 mg/dL)
  - Kappa/Lambda ratio: 9.14 (0.26 - 1.65)
  - M component percent – 16.4%
  - M component total – 1.3 g/dL
- **CBC with chemistry**:
  - Hgb 9.1 mg/dL
  - Calcium 7.3 mg/dL (ULN 8.0)
  - Albumin 3.3 (LLN 3.5)
  - Creatinine 2.3 mg/dL (ULN 1.3)
  - B2 microglobulin: 3.21 (1.42 - 3.21 mg/L)

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy

**Diagnosis**: relapsed MM with clonal evolution
Multiple Myeloma Is a Clonal Disease; However, the Clones Change Over Time

MM clones (detected by FISH, cytogenetics) change over time, especially after treatment rounds.

Effective myeloma treatment reduces or eliminates the dominant clone; however, other clones can still exist. Relapse can occur when another clone no longer has to compete for space with the formerly dominant clone or acquires additional mutation(s), providing a growth and/or survival advantage.

Background
• Despite the introduction of several new drugs, relapse remains inevitable
• A 2nd AHSCT often allows continued disease control

Study
• Examined outcomes in 105 patients undergoing 2nd AHSCT for relapsed MM

Results
• Median time between AHSCTs was 46 mos (10 to 130 mos)
• Treatment-related mortality was seen in 5 (5%) patients
• Partial response or better was seen in 95 (90%) patients, including a stringent CR in 10%, CR in 19%, and VGPR in 21%
• Median PFS and OS after 2nd AHSCT were 10.4 and 33 mos, respectively

Conclusions
• 2nd AHSCT is an effective therapy for eligible patients relapsing after other treatments
• It provides a meaningful duration of response and appears to be well-tolerated
• Patients with longer duration of response to first transplant and those achieving a CR appear to have maximum benefit

AHSCT = autologous hematological stem cell transplant; CR = complete response; mos = months; OS = overall survival; PFS = progression-free survival; VGPR = very good partial response.

Gonsalves WI, et al. ASCO 2012 #8092.
Treatment Paradigm: Salvage Regimens

<table>
<thead>
<tr>
<th>Preferred Salvage Regimens*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repeat primary induction (if relapse &gt;6 mos)</td>
</tr>
<tr>
<td>Bortezomib†</td>
</tr>
<tr>
<td>Bortezomib/dexamethasone</td>
</tr>
<tr>
<td>Bortezomib/lenalidomide/dexamethasone</td>
</tr>
<tr>
<td>Bortezomib/liposomal doxorubicin†</td>
</tr>
<tr>
<td>Bortezomib/thalidomide/dex</td>
</tr>
<tr>
<td>Carfilzomib</td>
</tr>
<tr>
<td>Cyclophosphamide/bortezomib/dex</td>
</tr>
<tr>
<td>Cyclophosphamide/lenalidomide/dex</td>
</tr>
<tr>
<td>Dexamethasone/cyclophosphamide/etoposide/cisplatin</td>
</tr>
<tr>
<td>Dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide ± bortezomib</td>
</tr>
<tr>
<td>High-dose cyclophosphamide</td>
</tr>
<tr>
<td>Lenalidomide/dexamethasone</td>
</tr>
<tr>
<td>Pomalidomide + dexamethasone†</td>
</tr>
<tr>
<td>Thalidomide/dexamethasone</td>
</tr>
</tbody>
</table>

Treatment selection depends on many factors:
- Previous therapy & response
- Length of time since last therapy
- Performance status & comorbidities
- Adverse event profile
- Patient preference

Optimal treatment regimens and sequencing of therapy is being explored via clinical trials.

Optimal treatment regimens for relapsed/refractory myeloma patient will likely evolve in coming years.

* Preferred regimens according to NCCN Guidelines Version 2.2014; †Category 1
Case #4: Indira*

Treatment:
- Declined 2nd transplant
- Bortezomib, lenalidomide, dex combination
- Pamidronate

Update:
- 4 cycles response: VGPR
- 4 additional cycles response: CR
- Lenalidomide maintenance ongoing
- Pamidronate continued

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Case #4: Indira*

Family Situation:
• Married; Husband 69, retired engineer
• 3 grown children with families
  – 2 live near by <1 hour away

Patient Concerns
• Prognosis
• Enjoying life, grandkids
• Treatment side effects

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Myeloma: Treated as Outpatient, Caregivers Important in Patient Care

- Majority of care provided in the outpatient setting
- Patients and their caregivers are expected to take a primary role in the self-management of their disease
- Assimilating complex information, often very rapidly, and developing skills for self-management of many complex processes is expected
- Caregivers may be formal or informal
- Caregiver stress is common
  - Unexpected changes in the plan of care
  - Sudden change in day-to-day activities
  - Uncertainty about the ability to provide care
  - Physical, social, emotional, and financial stressors

**FIGURE 2. Selected Problems Faced by Caregivers**

<table>
<thead>
<tr>
<th>Physical Health Problems</th>
<th>Pain, loss of physical strength, sleep disorders, fatigue and exhaustion, changes in appetite, sexual dysfunction, decreased libido, and exacerbation of preexisting health problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social Problems</td>
<td>Changes in usual routines and lifestyle; social isolation; reduced contact with outside family, friends, colleagues; and changes in work status, such as increased days off, distraction, loss of employment</td>
</tr>
<tr>
<td>Emotional Problems</td>
<td>Anxiety, fear, uncertainty, despair, disbelief, depression, sorrow and a sense of loss, loneliness, feelings of inequity, powerlessness, and feeling a lack of control</td>
</tr>
<tr>
<td>Financial Problems</td>
<td>Loss of wages, difficulty in paying bills; lack of sick leave; managing health claims and bills; premature use of retirement funds, often with penalty; and inability to contribute to 401(k) with loss of employer-matched contributions</td>
</tr>
</tbody>
</table>

Caregivers: Educate, Assess, Provide

**Educate Caregivers**
- Stresses and expectations they will face during the patient’s journey with multiple myeloma
- Consistent information across setting and providers
- Frequent reinforcement of key concepts
- Active participation of the patient and family

**Assess Caregivers**
- Quality of life
- Physical and emotional demands of assisting the patient through pre- and post-treatment phases of care

**Provide Assistance**
- Resources to help them cope with added responsibility
- Self-care tips and resources
  - Support groups
  - Maintain medical and dental care
  - Staying well – diet, exercise, sleep
  - Rejuvenating activities
  - Journaling
  - Ask for help – be specific

Case #4: Indira*

Update: 14 months of maintenance
• Rising IgG, kappa LC and M-protein
• 3 sequential visits
• Progressive anemia

Relapse Work-Up:
• Skeletal survey: no new lesions
• Bone marrow: 8% plasma cells
• Cytogenetics: Del 17p, t(4;14)
• Myeloma profile:
  – IgG: 2310 (624 - 1440 mg/dL)
  – Kappa LC: 13.1 (0.33 - 1.94 mg/dL)
  – Kappa/Lambda ratio: 8.5 (0.26 - 1.65 )
  – M component percent – 10.4%
  – M component total – 0.8 g/dL
• CBC with chemistry:
  – Hgb 10.2 mg/dL
  – Calcium 8.0 mg/dL (ULN 8.0)
  – Albumin 3.3 (LLN 3.5)
  – Creatinine 2.3 mg/dL (ULN 1.3)
  – β2 microglobulin: 2.65 (1.42 – 2.64 mg/L)

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
**Patients Refractory to Bortezomib and IMiDs Had Poor Outcomes**

<table>
<thead>
<tr>
<th>Author</th>
<th>Key Results</th>
</tr>
</thead>
</table>
| Kumar  | • Retrospective study  
• Patients who are refractory to bortezomib and ineligible to receive thalidomide or lenalidomide have poor outcomes  
  - Median time to progression (TTP) = 5 months  
  - Median overall survival (OS) = 13 months |
| Kumar  | • 286 pts with relapsed MM that were refractory to btz & relapsed following, refractory to, or ineligible to receive, an IMiD  
• Patients received 1 to 8 therapies  
• At least a partial response in 32% after one therapy; minor response or better was seen after one therapy in 44%  
• Median overall survival: 9 months  
• Median event-free survival: 5 months |

These studies were conducted prior to FDA approval of carfilzomib and pomalidomide. Both drugs are indicated for patients who have previously received a proteasome inhibitor and IMiD.

Case #4: Indira*

Treatment Plan:
• Pomalidomide – dex
• Pamidronate

Nursing Implications:
Patient & Caregiver Education
• Set expectations for therapy
• 4 mg once daily on days 1 to 21 of 28-day cycle
• Take without food (may be changing)
  – At least 2 hrs before a meal
  – At least 2 hrs after a meal
• Do not break, chew, or open the capsules

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Pomalidomide: New IMiD for Relapsed/Refractory MM Patients

Pomalidomide
POMALYST®
• Class: IMiD
• Indication: patients with multiple myeloma who
  – Have received at least 2 prior therapies including lenalidomide and bortezomib and
  – Have demonstrated disease progression on or within 60 days of completion of the last therapy
• FDA approval: February 8, 2013
• Administration: Oral
• Metabolism/Clearance
  – Liver via CYP1A2 and CYP3A4
• Can be ± low-dose dex
• REMS program

Pomalyst® Prescribing Information Highlights.
# Pomalidomide Nursing Implications: AEs & Patient Management

<table>
<thead>
<tr>
<th>Pomalidomide Grade 3/4 AEs in &gt;10%</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>47</td>
</tr>
<tr>
<td>Anemia</td>
<td>22</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>22</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>16</td>
</tr>
<tr>
<td>Fatigue &amp; asthenia</td>
<td>11</td>
</tr>
<tr>
<td>Back pain</td>
<td>12</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pomalidomide Common AEs (in &gt;30%)</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue and asthenia</td>
<td>55</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>52</td>
</tr>
<tr>
<td>Constipation</td>
<td>38</td>
</tr>
<tr>
<td>Nausea</td>
<td>36</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>34</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>34</td>
</tr>
<tr>
<td>Upper resp. tract infection</td>
<td>32</td>
</tr>
<tr>
<td>Back pain</td>
<td>32</td>
</tr>
<tr>
<td>Pyrexia (pom+dex)</td>
<td>30</td>
</tr>
</tbody>
</table>

**Nursing Implications**

**AE Management**
- DVT prophylaxis
- Monitor blood counts

**Education**
- DVT prophylaxis
- Infection risk/blood counts
- Fatigue

**REMS Program:** Embryonic/fetal toxicity
- Implications for females with child-bearing potential
- Implications for men
- Paperwork

Source: Pomalyist® Prescribing Information Highlights
Case #4: Indira*

Nursing Implications:
Adherence

• Importance of therapy
• Consistent schedule (AM or PM)
  – Take immediately if <12 hours since missed dose
  – Skip and take next regular dose if >12 hours
• Refill procedure

Optimizing Therapy

• Early identification of adverse events and prompt intervention
• Familiarity with moderate asymptomatic adverse events that may not require change in therapy
• Continued supportive care

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy

Pomalyst® prescribing information highlights.
Case #4: Indira*

**Patient Update**
- PR after 2 cycles
- VGPR after 4 cycles
- Continuing on therapy

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Case #5: Roberto*

Patient History:

• Retired businessman
• Diagnosed with myeloma 3 years ago at age 66
  – Plasma cells: 70%
  – Cytogenetics: t(4;14)
  – FISH: normal myeloma
  – Anemia
• Treated with CyBorD for 4 cycles, followed by an autologous transplant
  – Lenalidomide maintenance planned for 2 years
  – Zoledronic acid
• 6 months post-transplant: rising sFLC

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Case #5: Roberto*

Family Situation:
- Married
- Lives 45 minutes from the treatment center
- Wife 67 - homemaker
- 5 grown children all but 1 live out of town
- 10 grandchildren

Patient Concerns:
- Transportation
- Time to visit family

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Case #5: Roberto*

Relapse Work-Up:
- Skeletal survey: new lytic lesions: femur, pelvis
- Bone marrow: 20% plasma cells; Cytogenetics: t(4;14); FISH: normal

Myeloma Profile:
- IgA: 3292 (69 - 517 mg/dL)
- Lambda LC: 63.80 (0.57 - 2.63 mg/dL)
- M component percent – 0%
- M component total – 0

CBC with chemistry:
- Hgb 10.6 mg/dL
- Calcium 7.3 mg/dL (ULN 8.0)
- Albumin 3.1 (LLN 3.5)
- Creatinine 3.0 mg/dL (ULN 1.3)
- B2 microglobulin: 4.65 (1.42 – 2.64 mg/L)

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Case #5: Roberto*

**Diagnosis:**
- Relapsed MM
- Renal compromise

**Treatment plan:**
- Carfilzomib continuous therapy
- Zoledronic acid

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Carfilzomib: New Proteasome Inhibitor for Relapsed/Refractory MM Patients

**Carfilzomib**

**KYPROLIS®**

- **Class:** proteasome inhibitor
- **Indication:** patients with multiple myeloma who
  - Have received at least 2 prior therapies including bortezomib and an immunomodulatory agent
  - **AND**
  - Have demonstrated disease progression on or within 60 days of completion of last therapy
- **FDA Approval:** July 20, 2012
- **Administration:** IV
- **Metabolism/Clearance**
  - Renal function status had no effect on clearance; cycle 1 start dose 15 mg/m²
  - CYP450 plays a minor role

Kyprolis® prescribing information; FDA.gov
Carfilzomib Administration

- Pre-medicate: 4 mg dexamethasone before carfilzomib in
  - All doses cycle 1
  - 1st dose cycle 2
  - Additional doses/cycles if infusion reactions develop or reappear

- Hydrate: 250 to 500 mL IV saline
  - Before carfilzomib
  - After (optional)
  - For all doses cycle 1; additional if needed
  - Monitor for overhydration

- Administer carfilzomib IV
  - over 2 to 10 minutes (longer if needed)
  - Rinse IV with saline before & after

- Monitor: may require dose adjustment for toxicities

Source: Kyprolis® prescribing information
## Carfilzomib AEs

### Carfilzomib Grade 3 or 4 AEs >10%

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>GR3%</th>
<th>GR4%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>21</td>
<td>1</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>10</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>10</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

### Carfilzomib AEs (all grades) in >30%

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>56</td>
</tr>
<tr>
<td>Anemia</td>
<td>47</td>
</tr>
<tr>
<td>Nausea</td>
<td>45</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>36</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>35</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>33</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>30</td>
</tr>
</tbody>
</table>

### Nursing Implications:

**Avoid starting first cycle at the end of the week**

**Adherence**

- Monitor blood counts
- Monitor for infection
- HSV prophylaxis
- Cardiac eval/EKG for patients with cardiac history
- Know cardiac and pulmonary status

### Education

- Shortness of breath (dyspnea)
- Fatigue
- Anemia/thrombocytopenia
- Infection prevention
- Shingles prevention (Acyclovir)
- Tumor lysis syndrome

Source: Kyprolis® prescribing information
Case #5: Roberto*

Update:
• 3 cycles: PR
• 5 cycles: VGPR
• Continued treatment
  – Until disease progression of unacceptable toxicity
  – Eliminate need for dexamethasone premedication
  – Continue supportive care
  – Negotiate schedule to allow travel

* HIPAA compliant: not actual name, stock photo, patient details modified to protect privacy
Many More New Agents in Development May Be Available in Coming Years

<table>
<thead>
<tr>
<th>Molecule Class</th>
<th>Compound</th>
<th>Alternate Names</th>
<th>Admin</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humanized antibody</td>
<td>Elotuzumab</td>
<td>BMS-901608 HuLuc63</td>
<td>IV</td>
<td>Bristol Myers Squibb &amp; Abbott</td>
</tr>
<tr>
<td></td>
<td>Daratumumab</td>
<td>HuMax-CD38</td>
<td>IV</td>
<td>Genmab / Janssen</td>
</tr>
<tr>
<td>Proteasome inhibitor</td>
<td>Ixazomib</td>
<td>MLN9708</td>
<td>Oral</td>
<td>Millennium</td>
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<td>Oprozomib</td>
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<td>HDAC inhibitor</td>
<td>Vorinostat</td>
<td>SAHA, MK-O683</td>
<td>Oral</td>
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<td>Panobinostat</td>
<td>LBH589</td>
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<td>Perifosine</td>
<td>KRX-0401</td>
<td>Oral</td>
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<td>Kinase inhibitor</td>
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<td>Amifostine</td>
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<td>Injection</td>
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<td>Argy-520</td>
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<td>Darinaparsin</td>
<td>ZIO-101</td>
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<td>Ridaforolimus</td>
<td>AP23573</td>
<td>Oral</td>
<td>Ariad</td>
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Elotuzumab (Elo)

- **Humanized monoclonal antibody**
- **Target:** CS1, a cell surface protein highly expressed on myeloma cells
- **Phase 2 results:**
  - Open label, relapsed myeloma
  - Elotuzumab (10 or 20 mg/kg) with lenalidomide, low-dose dex
    - 10 mg/kg dose (N=36) ORR: 92%, median PFS: 33 months
    - 20 mg/kg dose (N=37) ORR: 76%, median PFS: 18.6 months
- **In phase 3 development:**
  - ELOQUENT-1 (NCT01335399): first-line myeloma (open for enrollment)
  - ELOQUENT-2 (NCT01239797): relapsed/refractory myeloma (fully enrolled)
- **Conclusion:** “Elo with Len/LoDex was well tolerated and effective in the treatment of relapsed/refractory multiple myeloma”

Nursing Implications: Ab administration & premedication, monitoring

Daratumumab (DARA)

- **Humanized monoclonal antibody**
- **Target:** CD38
- **Phase 1/2 design:** DARA single agent
  - Daratumumab 3 + 3 dose escalation
  - Patients with relapsed/refractory MM, 2+ lines of therapy, autologous transplant ineligible
- **Results:**
  - n=32, median prior therapies = 6
  - 5 PRs and 3 MRs; 7 of these had 50% to 100% reduction in BMPC
  - Infusion-related events in 44%
- **Conclusion:** “Highest response rates seen for a single agent mAb treatment in MM”

- **Phase 1/2 design:** DARA + Len+dex
  - Open label, multicenter relapsed myeloma
  - Daratumumab dose escalation (2 or 16mg/kg) with lenalidomide, low-dose dex
- **Results:**
  - n=6; median age 63.5; median prior therapies 2.5
  - Manageable safety profile
  - Response rates of PR or better
- **Conclusion:** “Worked in combination regimen with manageable safety profile”

Nursing Implications: Ab administration (pre med Tylenol, methylprednisolone, benadryl); V/S monitoring during 1st infusion

Ixazomib Citrate (MLN9708)

**Drug type:** Oral proteasome inhibitor, currently in phase 3

**Study Design:**
Single arm: ixazomib citrate (twice weekly dosing) + len + dex for up to 16 21-day cycles; then ixazomib citrate maintenance (twice weekly dosing)

**Results:**
- n=64; median age=64; newly diagnosed
- 93% PR or better: 67% ≥VGPR; 24% CR (14% sCR)
- 54% had 100% decrease in M-protein or sFLC from baseline
- Median time to best response 2.07 months
- No drug-related Grade 4 AEs; frequent AEs: rash (61%), fatigue (50%), peripheral edema (50%), diarrhea (41%), peripheral neuropathy (36%)

**Conclusion:** “MLN9708 plus len-dex is feasible and active in newly dosed MM patients”

**Nursing Implications:** adherence, AE management
Oprozomib

Drug type: Oral proteasome inhibitor

Study Design:
• Open-label phase 1b/2, relapsed MM patients
• Dose escalation

Results:
• n=42, median age=62-64
• Pts receiving 240 mg/d achieved depth and duration of response similar to carfilzomib (20/27mg/m²)
• Grade 3-4 AEs included diarrhea, anemia, nausea, neutropenia, hypophosphatemia
• ≥80% inhibition of PBMCs was observed on the first day of Cycle 1

Conclusion: “Once daily modified release OPZ tablets continue to have acceptable safety and promising anti-tumor activity”

Nursing Implications: adherence, AE management
Key Points

• Relapse or progression is inevitable for the majority of MM patients

• Patients who fail first-line proteasome inhibitors and immunomodulatory agents have been shown to have poor overall survival

• Effective management of RRMM requires an understanding of
  – The pathobiology of MM, including high-risk features and currently available therapies for all phases of the disease
  – The key elements of risk-adapted treatment selection in the RRMM setting, including clinical management of adverse events

• Caregivers are essential for the effective management of the MM patient and require specific assessment and support

Thank You for Sharing in Some of Our Patients’ Stories*

* HIPAA compliant: not actual names, stock photos, patient details modified to protect privacy
IMF: Website, Hotline, Pamphlets Are Source for Additional MM Information

International Myeloma Foundation Website:
http://myeloma.org

International Myeloma Foundation Hotline:
800.452.CURE (2873)
• US & Canada
• 9:00 am to 4:00 pm Pacific

• Nurses, patients, caregivers, others welcome to call
• Trained staff available to answer questions about finding clinical trials, etc.
As a result of this program, you will be able to:

• Review myeloma disease state and disease stages

• Discuss new therapies and combination regimens in Multiple Myeloma, their appropriate use, and related patient management

• Identify best practices including practical tools and recommendations for long-term management and care of Multiple Myeloma patients

• Define strategies to empower nurses to incorporate best practices in their care of Multiple Myeloma patients
And Gained Practical Tips and Resources to Enhance Your Ability to Care for Your MM Patients

Also Available for free download from http://myeloma.org
Select “Health Professionals” tab then “Nurse Leadership Board”
Also CD-ROM in your Packet
Thank You

On behalf of the International Myeloma Foundation, we thank you for your attendance and participation.

Please Contact Us for Further Information and Resources:

1-800-452-CURE
(1-800-452-2873)
TheIMF@myeloma.org
http://www.myeloma.org

Please leave CE Credit & Eval Form at back tables

Slides available for download at http://nurses.myeloma.org