Clinical Updates & Issues: Relapsed/Refractory Multiple Myeloma

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Faculty Biography

Beth Faiman, PhD, MSN, APRN-BC, AOCN is Nurse Practitioner in the Department of Hematologic Oncology and Blood Disorders at the Taussig Cancer Institute, Cleveland Clinic in Cleveland, Ohio. Dr. Faiman also serves as Adjunct Faculty at Case Western Reserve School of Nursing in Cleveland; Adjunct Faculty at Ursuline College of Nursing in Pepper Pike, Ohio; and Adjunct Faculty at Kent State University in Kent, Ohio.

Dr. Faiman received her master of science in nursing and certification as an adult nurse practitioner from Kent State University and her PhD in Clinical Research and Nursing from Case Western Reserve University.

Dr. Faiman is an active author, presenter, and educator on the topic of multiple myeloma, amyloidosis, plasma cell dyscrasias, general cancer diagnosis and treatment, as well as management of skeletal and other cancer complications. She is an appointed delegate on the International Myeloma Foundation Nurse Leadership Board. She is currently Editor-in-Chief of The Oncology Nurse APN/PA and on the editorial board of ASH Clinical News among others. She has edited several books and authored many chapters relating to diagnosis and management of multiple myeloma, blood disorders and has written numerous articles relating to the diagnosis and treatment of myeloma, pain, palliation, and cancer symptom management.

Dr. Faiman has lectured extensively internationally and nationally. She is the recipient of numerous awards, most recently receiving the 2015 Dean’s Legacy Award for Outstanding Doctor of Philosophy, Frances Payne Bolton School of Nursing at Case Western Reserve University. She received the 2012 Excellence in Medical Oncology and 2013 Commendation for Patient and Nursing Education Award sponsored by The Oncology Nursing Society.
Treating Myeloma is Not Easy....

- Accurate diagnosis is required
- Attention to Relapse, emerging data
- Goals of treatment:
  - Rapid and effective control of disease
  - Manage disease-related symptoms
  - Improve survival
  - Maintain quality of life while on therapy

Challenges of Effective Treatment

- Patient
  - Comorbid conditions
  - Trust in the provider (Impacts adherence)
- Polypharmacy
  - Confusion
  - Disease sequelae
- Healthcare
  - Access to effective drugs
  - Communication
  - Identify and intervene adverse events (AEs)

Nurses are critical in the identification and intervention of AEs, keeping patients on therapy.
Myeloma Is a Cancer of Plasma Cells

- Cancer of plasma cells
- Often preceded by nonmalignant state(s): MGUS or SMM
- Healthy plasma cells produce antibodies/immunoglobulins (Ig)
- Overproduction of a normal Ig “clone”
  - 65% IgG
  - 20% IgA
- Baseline and ongoing monitoring of the disease is essential: CBC, CMP, SPEP, UPEP, serum free light chains

MGUS = monoclonal gammopathy of undetermined significance; SMM = smoldering multiple myeloma SPEP = serum protein electrophoresis UPEP = Urine protein electrophoresis CBC = complete blood count CMP Complete metabolic panel


The Multiple Effects of Multiple Myeloma

- Renal Compromise (CMP) (30%)
- Neuropathy (33%)
- Infection (leukopenia, lymphopenia, monitor cBC (15%)
- Hypercalcemia (ca++) (15-20%)
- Bone pain (75-80%)
- Lytic lesions (70%)
- Marrow Infiltration
- M Protein (SPEP, MPA)
- Immune Deficiency- monitor Igs, infection
- Destruction of bone (skeletal imaging)
- Anemia – (CBC) (~70%)

Criteria for Diagnosis of Myeloma: CRAB

Pre-Malignant
MGUS
- < 3 g/dL M spike
- < 10% PC

More Genetic Damage
Smoldering MM
- ≥ 3 g/dL M spike
- AND/OR ≥ 10% PC

Malignant
Symptomatic MM
- Increased PC ≥ 10%
- Any M spike +

AND

AND

one or more of the following:
- Calcium ↑ in serum (> 11.5 mg/dL)
- Renal insufficiency (SCr > 2 mg/dL)
- Anemia (Hgb < 10 g/dL or 2g below nl)
- Bone lesions or osteoporosis
- Abnormal SFLC ratio >100
- MRI >1 focal lesion
- BMBX plasma cell >60%


Treatment Options Have Greatly Increased – US

Side effect identification and management is critical to keep patients “fit” for the next therapy

Approved relapsed indications for 2015/2016:
- Ixazomib + lenalidomide + dexamethasone, >1 prior therapy
- Daratumumab monotherapy >3 prior therapies
- Elotuzumab + lenalidomide + dexamethasone, >prior therapy
- Carfilzomib + lenalidomide + dexamethasone, >1-3 prior therapy
- Carfilzomib 20/56mg/m2 IV

Dex= Dexamethasone SC - subcutaneous
DRUGS@FDA.gov
## New drugs, new studies, new indications: 2015

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Study Population</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daratumumab</td>
<td>RRMM</td>
<td>Newly approved MOAB; infusion reaction, toxicities</td>
</tr>
<tr>
<td>Single agent and in combination with len/dex, pom/dex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;TOURMALINE MM&quot;</td>
<td>NDMM/RRMM</td>
<td>All oral combinations; adherence, cost</td>
</tr>
<tr>
<td>Ixazomib + len/dex + Pan/dex + Ctx/dex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;ELOQUENT-2&quot;</td>
<td>RRMM</td>
<td>Infusion – related</td>
</tr>
<tr>
<td>+ len/dex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&quot;ASPIRE&quot; - CaRd vs Rd Car/Pom/dex, Car/Pan/dex</td>
<td>RRMM</td>
<td>Timing of Carfilzomib; cardiac</td>
</tr>
<tr>
<td>Bortezomib - SWOG 0777</td>
<td>NDMM</td>
<td>3 vs 2 drugs upfront</td>
</tr>
<tr>
<td>- RVDlite</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


## Multiple Myeloma Is a Clonal Disease; However, the Clones Change Over Time

- Effective treatment reduces or eliminates the dominant clone
- Other clones can still exist.
- On-going treatment to suppress clones

Monitoring Disease is Essential: IMWG Myeloma Response Criteria

<table>
<thead>
<tr>
<th>Category</th>
<th>Response Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>sCR, stringent complete</td>
<td>Normal free light chain (FLC); no clonal BM plasma cells</td>
</tr>
<tr>
<td>response</td>
<td></td>
</tr>
<tr>
<td>CR, complete response</td>
<td>Negative IFX and &lt; 5% BM plasma cells</td>
</tr>
<tr>
<td>VGPR, very good partial</td>
<td>Positive IFX and negative SPEP; &gt; 90% urine protein decrease; urine M-protein level &lt; 100 mg per 24 h</td>
</tr>
<tr>
<td>response</td>
<td></td>
</tr>
<tr>
<td>PR, partial response</td>
<td>≥ 50% decrease serum M-protein and ≥ 90% decrease in 24 h urinary M-protein</td>
</tr>
<tr>
<td>SD, stable disease</td>
<td>Not meeting criteria for CR, VGPR, PR, or progressive disease</td>
</tr>
</tbody>
</table>

sCR: Stringent Complete Response; CR = Complete Response; VGPR = Very Good Partial Response; PR = Partial Response; SD = Stable Disease; MR = Minimal Response (only in relapsed); PD = Progressive Disease


Select Preferred Regimens from the NCCN Guidelines for MM

- **NCCN Category 1**
  - Bortezomib
    - SC vs IV administration
  - Bortezomib/PLD
  - Carfilzomib/lenalidomide/dexamethasone
  - Panobinostat/bortezomib/dexamethasone
  - Lenalidomide/dexamethasone
  - Ixazomib/len/dex
  - Elotumab/len/dex

- **NCCN Category 2A**
  - Repeat primary induction therapy if relapse at > 6 mos
  - Daratumumab
  - Bortezomib combinations
    - With dex; len/dex; thalidomide
  - Carfilzomib
  - Cyclophosphamide
    - High-dose or with bort/dex or len/dex
  - Pomalidomide/dexamethasone
  - Thalidomide/dexamethasone
  - DCEP, DT-PACE, or VTD-PACE

NCCN Guidelines for Multiple Myeloma: v.3.2016.
Factors in Selecting Treatment for Relapsed/Refractory Myeloma

- Disease-related factors
  - Duration of response to initial therapy
  - High/low risk status
  - Biochemical disease progression, or symptomatic?
  - Other comorbid conditions
- Treatment-related factors
  - Previous therapy exposure (relapsed or refractory)
  - Toxicity of regimen (combination vs single agent)
  - Mode of administration (eg, oral or IV)
  - Cost and convenience (out of pocket copays for IV/Oral)

Strategies at Relapse: Start low, go slow.. or “Go for it”?

**Treating Indolent, Slow-Growing Myeloma in First Relapse**
- If initial treatment with bortezomib, len repeat or change therapy
- Ixazomib, carfilzomib and elotuzumab are all considerations with len/dex
- Consider if high/low risk disease at diagnosis

**Treating Relapsed/Refractory Myeloma**
- Any peripheral neuropathy or renal dysfunction?
- What has been tried (PI-based, IMiD-based)
- Are clinical trials available?

**Aggressive Myeloma With Rapid, Multiple Relapses**
- Transplant if not done (allo, auto)
- Chemotherapy – based salvage with aggressive clones is often necessary
- MoAb candidates

**Remember to discuss goals and costs of therapy at each stage.**
**Encourage health maintenance to maintain “fitness” for next therapy.**
Proper Dosing of Drugs Can Minimize AEs

*Geriatric assessment- Risk Factors:
• Age over 75 years
• Mild, moderate, or severe frailty (weakness, poor endurance, weight loss, low physical activity, and slow gait speed)
• Comorbidities: cardiac, pulmonary, hepatic, or renal dysfunction

<table>
<thead>
<tr>
<th>Drug</th>
<th>No risk factors</th>
<th>At least 1 risk factor Adjusted Dose</th>
<th>At least 1 risk factor plus occurrence of GR 3-4 non-hematological AE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bortezomib</td>
<td>1.3 mg/m² biweekly d1,4,8,11/3 wks</td>
<td>1.3 mg/m² weekly d1,8,15,22/5 wks</td>
<td>1.0 mg/m² weekly d1,8,15,22/5 wks</td>
</tr>
<tr>
<td>Lenalidomide</td>
<td>25 mg/d d1-21 of 28-day cycle</td>
<td>15 mg/d d1-21 of 28-day cycle</td>
<td>10 mg/d d1-21 of 28-day cycle</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>40 mg weekly d1,8,15,22/4 wks</td>
<td>20 mg weekly d1,8,15,22/4 wks</td>
<td>10 mg weekly d1,8,15,22/4 wks</td>
</tr>
<tr>
<td>Melphalan</td>
<td>0.25 mg/kg or 9 mg/m² d1-4/4-6 wks</td>
<td>0.18 mg/kg or 7.5 mg/m² d1-4/4-6 wks</td>
<td>0.13 mg/kg or 5 mg/m² d1-4/4-6 wks</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>100 mg per day</td>
<td>50 mg per day</td>
<td>50 mg qod</td>
</tr>
</tbody>
</table>

**Geriatric assessment- Risk Factors:**
- Age over 75 years
- Mild, moderate, or severe frailty (weakness, poor endurance, weight loss, low physical activity, and slow gait speed)
- Comorbidities: cardiac, pulmonary, hepatic, or renal dysfunction

Lenalidomide

- **Class:** IMiD (thalidomide analogue)
- **FDA approval:** 2006
- **Administration:** oral
- **Dose:** 25 mg once daily orally on Days 1-21 of q 28-day
- **Dose adjust for renal insufficiency**

**Indication**
- Multiple myeloma, in combination with dexamethasone for NDMM, RRMM
- In combination with Elo, Ixa, Carfilzomib

**Adverse Events**
Most common (≥20%):
- **Fatigue**, neutropenia, constipation, diarrhea, muscle cramp, anemia, pyrexia, peripheral edema, nausea, back pain, upper respiratory tract infection, dyspnea, dizziness, thrombocytopenia, tremor and rash

****Educate and evaluate:**
- REMS: Embryo-fetal toxicity
- Hematologic toxicity – neutropenia and thrombocytopenia
- Venous thromboembolism – DVT and PE

IMiD = immunomodulatory drug; REMS = Risk Evaluation and Mitigation Strategy; DVT = deep vein thrombosis; PE = pulmonary embolism.

Lenalidomide® Prescribing Information, 2013.
Bortezomib

- **Class:** proteasome inhibitor
- **FDA approval:** 2003
- **Administration:** subcutaneous or intravenous
- **Dose:** recommended starting dose is 1.3 mg/m²
  - Administered intravenously at a concentration of 1 mg/mL as a 3 to 5 second bolus IV injection
  - Administered subcutaneously at a concentration of 2.5 mg/mL

**Indication**
- Treatment of patients with multiple myeloma

**Most Commonly Reported Adverse Reactions (incidence ≥ 20%) in Clinical Studies**
- Nausea, diarrhea, thrombocytopenia, neutropenia, peripheral neuropathy, fatigue, neuralgia, anaemia, leukopenia, constipation, vomiting, lymphopenia, rash, pyrexia, and anorexia.

Possible Side Effect of Treatment: Peripheral Neuropathy (PN)

- **Sensory, motor, autonomic**
- **Risk**
- **Symptoms**
- **Side effect of MM treatment or the disease**

Cavaletti et al., 2007; Smith et al., 2013
Peripheral Neuropathy (PN): Risk Factors and General Considerations

Non-MM Causes of PN:
- Endocrine disorders
  - Hypothyroidism
  - Diabetes
- Nutritional disease
  - Vitamin B deficiency
  - ETOH
- Connective tissue disease
- Vascular disease
- Medications
- Herpes zoster
- Most common symptoms
  - Sensory deficits, pain

MM Disease- and Treatment-Related Hyperviscosity syndrome
- Hypergammaglobulinemia
- Incidence of PN in untreated pts: 39%
- Incidence of grade 3/4 PN
  - Bortezomib: 26% to 44%
    - ↓ with weekly vs twice weekly dosing
  - Thalidomide: 28% to 41%
    - ↑ with higher doses duration
  - Carfilzomib: overall 14%
  - Pomalidomide: Mild, up to 9%


Minimize PN with Bortezomib SC

Peripheral Neuropathy
- Major reason for dose reduction, discontinuation
- SC and weekly can minimize risk of PN

Subcutaneous (SC)
- FDA approved SC in 2012
- Equivalent efficacy as IV
- Reduced neuropathy and GI AEs with SC
- Skin / Infection site reactions
- Reconstitution

Peripheral Neuropathy (PN) Management

• Prevention / management:
  • Once-weekly or SC administration of bortezomib
  • Dose reduce thalidomide or other agent (mild PN is associated with pomalidomide, carfilzomib)
  • Ensure no other causes of PN (check b vitamins, glucose)
  • Recommend exercise, massage to stimulate blood flow
  • Safe environment: rugs, furnishings, shoes, driving

• Pharmacologic:
  • Supplements are generally safe: B-complex vitamins (B1, B6, B12), folic acid, and/or amino acids but do not take on day of bortezomib infusion
  • L glutamine, b vitamins, alpa-lipoic acid,
  • Duloxetine (30-60 mg/day), gabapentin, pregabalin
  • Opioid analgesic agents

• Mild:
  • Consider holding, dose reduction or discontinuation of offending agent
• If moderate to severe:
  • Stop the drug


Carfilzomib: IV Administration 2 Days per Week

Carfilzomib: Approved for RRMM in the US at Two Dose levels:
1) 20/27 mg/m2 with len/dex, or
2) 20/56 mg/m2 monotherapy

• ASPIRE: 792 patients randomly assigned to carfilzomib/len/dex or len/dex; median PFS 26.3 months, vs. 17.6 months
• ENDEAVOR: 929 pts randomly assigned to carfilzomib/dex or bortezomib/dex median PFS 18.7 months, vs. 9.4 months
• Pre-medicate and hydrate
  – Antiemetic and fluids before carfilzomib C1
  – After (optional)
• Administer carfilzomib IV
  – over 30 minutes
• Monitor: may require dose adjustment for toxicities
• DVT risk

Carfilzomib 28-day Cycle

| Cycle 1, week 1: | 20 mg/m² |
| Cycle 1, week 2+: | 27 or 56 mg/m² |

Source: Amgen, 2016. Carfilzomib prescribing information
**ENDEAVOR:** Carfilzomib/dex results in 2-fold increase in median PFS vs bortezomib/dex in relapsed MM

- **Pts with symptomatic RR MM after 1-3 prior treatments with ≥ PR to ≥ 1 prior regimen (N = 792)**
- Significant PFS improvement and higher response rates with carfilzomib/dex vs bortezomib/dex in relapsed MM; ORR: 77% vs 63% (P < .0001), respectively

![Graph showing PFS benefit for carfilzomib/dex vs bortezomib/dex](image)

- Rates of d/c due to AEs similar (14% vs 16%), but rates of grade ≥ 3 hypertension (25% vs 9%), dyspnea (5% vs 2%), and heart failure (5% vs 2%) increased with carfilzomib vs bortezomib; rates of grade ≥ 2 peripheral neuropathy increased with bortezomib/Dex vs carfilzomib/dex (32% vs 6%)

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**Phase III ASPIRE:** Len/Dexamethasone ± Carfilzomib in RR MM

- Randomized, open-label, multicenter phase III trial

- **Stratified by β2-microglobulin, prior bortezomib, and prior lenalidomide**

- **KRx**
  - Carfilzomib* 27 mg/m² IV Days 1, 2, 8, 9, 15, 16 (20 mg/m² Days 1, 2, cycle 1 only) + Lenalidomide 25 mg Days 1-21 + Dexamethasone 40 mg Days 1, 8, 15, 22 (n = 396)

- **Rd**
  - Lenalidomide 25 mg Days 1-21 + Dexamethasone 40 mg Days 1, 8, 15, 22 (n = 396)

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Len/Dexamethasone ± Carfilzomib in RR MM (ASPIRE): PFS (ITT)

Risk Group by FISH

<table>
<thead>
<tr>
<th></th>
<th>KRd (n = 396)</th>
<th>Rd (n = 396)</th>
<th>HR</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median PFS, Mos</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>48</td>
<td>52</td>
<td>13.9</td>
<td>0.70</td>
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<tr>
<td>Standard</td>
<td>147</td>
<td>170</td>
<td>19.5</td>
<td>0.66</td>
</tr>
</tbody>
</table>


ASPIRE: Select Adverse Events

<table>
<thead>
<tr>
<th>Select Adverse Events</th>
<th>KRd (n = 392)</th>
<th>Rd (n = 389)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonhematologic AEs occurring in ≥25% of pts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Diarrhea</td>
<td>42.3</td>
<td>33.7</td>
</tr>
<tr>
<td>• Fatigue</td>
<td>32.9</td>
<td>30.6</td>
</tr>
<tr>
<td>• Cough</td>
<td>28.8</td>
<td>17.2</td>
</tr>
<tr>
<td>• Pyrexia</td>
<td>28.6</td>
<td>20.8</td>
</tr>
<tr>
<td>• Upper respiratory tract infection</td>
<td>28.6</td>
<td>19.3</td>
</tr>
<tr>
<td>• Hypokalemia</td>
<td>27.6</td>
<td>13.4</td>
</tr>
<tr>
<td>• Muscle spasms</td>
<td>26.5</td>
<td>21.1</td>
</tr>
</tbody>
</table>

Hematologic AEs occurring in ≥25% of pts

| • Anemia                                 | 42.6          | 39.8         |
| • Neutropenia                            | 37.8          | 33.7         |
| • Thrombocytopenia                       | 29.1          | 22.6         |

Other AEs of Interest

| • Dyspnea                                | 19.4          | 14.9         |
| • Peripheral neuropathy                  | 17.1          | 17.0         |
| • Hypertension                           | 14.3          | 6.9          |
| • Acute renal failure                    | 8.4           | 7.2          |
| • Cardiac failure                        | 6.4           | 4.1          |
| • Ischemic heart disease                 | 5.9           | 4.6          |

Implications

Monitor blood counts
Monitor for infection
Cardiac
- EKG for patients with cardiac history
- ECHO baseline
- Diuretics, inhalers, minimize fluids, longer infusion time (30 mins)
- Advise patient on
  - Shortness of breath (dyspnea)
  - Fatigue
  - Cytopenias
  - Infection prevention
  - VTE prophylaxis

Source: Amgen, 2016. Carfilzomib prescribing information
**Pomalidomide**

**Pomalidomide**

- **Class:** IMiD
- **Indication:** patients with MM
  - Have received at least 2 prior therapies
  - PD within 60 days of last therapy
- **FDA Approval:** February 8, 2013
- **Administration:** Oral
- **Metabolism/Clearance:**
  - Liver via CYP1A2 and CYP3A4
- Can be ± low-dose dex
- **REMS Program**

**Pomalidomide Prescribing Information Highlights.**

- Pomalidomide prolongs survival
- Pomalidomide has a manageable safety profile with few discontinuations due to AE’s
- Pomalidomide maintains quality of life and provides oral convenience for patients

**Pomalidomide Implications: Administration**

**Implications:**
- Anti-thrombotic treatment
- Embryonic/fetal toxicity
  - Child-bearing age female
    - Two negative pregnancy tests
    - Abstinence or 2 forms birth control
  - Male: drug present in semen
    - Latex or synthetic condom with females of reproductive potential
- Pomalidomide REMS™ Program

**Discuss Administration With Patient:**
- 4 mg once daily on days 1-21 of 28-day cycle
- Available in strengths: 1, 2, 3 or 4 mg capsules
- Take without food
  - At least 2 hrs before or after a meal
- Do not break, chew, or open the capsules
- Adherence: consistent schedule (AM or PM)
  - Take immediately if <12 hours since missed dose
  - Skip and take next regular dose if >12 hours

Pomalidomide prescribing information highlights.
Pomalidomide Implications: AEs & Patient Management

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

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

**Implications**
- DVT prophylaxis
- Monitor blood counts
- Monitor for neuropathy although less common

**Educate patients on**
- DVT prophylaxis
- Infection risk / blood counts
- Fatigue
- REMS

Source: Pomalidomide Prescribing Information Highlights

Newly approved drugs and indications- 2015

<table>
<thead>
<tr>
<th>Indication</th>
<th>Panobinostat</th>
<th>Ixazomib</th>
<th>Daratumumab</th>
<th>Elotuzumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDA approved in 2015 combination with bortezomib and dexamethasone, in</td>
<td>FDA approved on 11/20/15 [len + dex] ± ixazomib in adult patients with</td>
<td>FDA approved on 11/16/15 in patients with ≥ 3 prior lines of therapy,</td>
<td>FDA approved on 11/30/15 [len + dex] ± elotuzumab in adult patients with</td>
<td>FDA approved on 11/30/15 [len + dex] ± elotuzumab in adult patients with</td>
</tr>
<tr>
<td>patients who have received ≥ 2 prior regimens, including bortezomib and</td>
<td>relapsed/refractory multiple myeloma who have received 1-3 prior therapies,</td>
<td>including both a proteasome inhibitor and an immunomodulatory agent, or</td>
<td>relapsed/refractory multiple myeloma who have received 1-3 prior therapies,</td>
<td>relapsed/refractory multiple myeloma who have received 1-3 prior therapies,</td>
</tr>
<tr>
<td>an immunomodulatory agent</td>
<td>or who are refractory to a proteasome inhibitor and an immunomodulatory</td>
<td>who are refractory to a proteasome inhibitor and an immunomodulatory</td>
<td>who are refractory to a proteasome inhibitor and an immunomodulatory agent,</td>
<td>who are refractory to a proteasome inhibitor and an immunomodulatory agent,</td>
</tr>
<tr>
<td></td>
<td>agent</td>
<td>agent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Administration</td>
<td>20 mg, taken orally once every other day for 3 doses per week (on Days 1, 3,</td>
<td>4 mg taken orally on Days 1, 8, 15</td>
<td>16 mg/kg IV on Days 1, 8, 15, and 22 of cycles 1 and 2 (weekly dosing, on</td>
<td>10 mg/kg IV, weekly, on Days 1, 8, 15, 22 (cycles 1 &amp; 2); Days 1 and</td>
</tr>
<tr>
<td></td>
<td>5, 8, 10, and 12) of Weeks 1 and 2 of each 21-day cycle for 8 cycles</td>
<td></td>
<td>Days 1 and 15 of cycles 3 to 6 (every 2 weeks dosing), and on Day 1 of cycle</td>
<td>15 (cycles 3 and beyond)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7 and subsequent cycles (every 4 weeks dosing)</td>
<td></td>
</tr>
</tbody>
</table>

FDA.gov; prescribing information
Phase III PANORAMA 1: Bort/Dex ± Panobinostat in RR Myeloma

- Randomized, double-blind trial
- Primary endpoint reached: median PFS ↑ by 3.9 mos

Stratified by prior lines of therapy and prior bortezomib

Treatment Phase I:
Eight 21-day cycles (24 wks)

Panobinostat 20 mg 3x/wk
Bortezomib 1.3 mg/m<sup>2</sup> IV d1,4,8,11
Dexamethasone 20 mg d1,2,4,5,8,9,11,12
(n = 387)

Placebo 3x/wk
Bortezomib 1.3 mg/m<sup>2</sup> IV d1,4,8,11
Dexamethasone 20 mg d1,2,4,5,8,9,11,12
(n = 381)

Pts with symptomatic RR MM after 1-3 prior treatments (bortezomib-refractory excluded) (N = 768)

Pts with ≥ SD in tx phase I can proceed to tx phase II

Panobinostat + bortezomib, dexamethasone

Panobinostat (Oral) – CYCLES 1-8 (28-Day Cycles)

<table>
<thead>
<tr>
<th>Week 1</th>
<th>Week 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1</td>
<td></td>
</tr>
<tr>
<td>D2</td>
<td></td>
</tr>
<tr>
<td>D3</td>
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<tr>
<td>D4</td>
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<tr>
<td>D5</td>
<td></td>
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<tr>
<td>D6</td>
<td></td>
</tr>
<tr>
<td>D7</td>
<td></td>
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<tr>
<td></td>
<td>D1</td>
</tr>
<tr>
<td></td>
<td>D2</td>
</tr>
<tr>
<td></td>
<td>D3</td>
</tr>
<tr>
<td></td>
<td>D4</td>
</tr>
<tr>
<td></td>
<td>D5</td>
</tr>
<tr>
<td></td>
<td>D6</td>
</tr>
<tr>
<td></td>
<td>D7</td>
</tr>
</tbody>
</table>

Panobinostat: ✓
Bortezomib: ✓
Dexamethasone: ✓

Panobinostat (Oral) – CYCLES 9-16 (28-Day Cycles)

<table>
<thead>
<tr>
<th>Week 1</th>
<th>Week 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>D1</td>
<td></td>
</tr>
<tr>
<td>D2</td>
<td></td>
</tr>
<tr>
<td>D3</td>
<td></td>
</tr>
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<td>D4</td>
<td></td>
</tr>
<tr>
<td>D5</td>
<td></td>
</tr>
<tr>
<td>D6</td>
<td></td>
</tr>
<tr>
<td>D7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>D1</td>
</tr>
<tr>
<td></td>
<td>D2</td>
</tr>
<tr>
<td></td>
<td>D3</td>
</tr>
<tr>
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<td>D4</td>
</tr>
<tr>
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<td>D5</td>
</tr>
<tr>
<td></td>
<td>D6</td>
</tr>
<tr>
<td></td>
<td>D7</td>
</tr>
</tbody>
</table>

Panobinostat: ✓
Bortezomib: ✓
Dexamethasone: ✓


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### PANORAMA 1: Safety and implications

<table>
<thead>
<tr>
<th>Select AEs (≥ 10% Incidence and ≥ 5% Greater Incidence With Pan), %</th>
<th>Pan + Bort/Dex (n = 381)</th>
<th>Pbo + Bort/Dex (n = 377)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Grades</td>
<td>Grade 3/4</td>
<td>All Grades</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>68</td>
<td>25</td>
</tr>
<tr>
<td>Nausea</td>
<td>36</td>
<td>6</td>
</tr>
<tr>
<td>Vomiting</td>
<td>26</td>
<td>7</td>
</tr>
<tr>
<td>Fatigue</td>
<td>60</td>
<td>25</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>29</td>
<td>2</td>
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<tr>
<td>Thrombocytopenia</td>
<td>97</td>
<td>67</td>
</tr>
<tr>
<td>Anemia</td>
<td>62</td>
<td>18</td>
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<tr>
<td>Neutropenia</td>
<td>75</td>
<td>34</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>81</td>
<td>23</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>82</td>
<td>53</td>
</tr>
</tbody>
</table>

**Cardiac, GI and Heme toxicity**

Evaluate and treat diarrhea, fatigue, watch for myelosuppression

Peripheral neuropathy with bortezomib

---

### Tourmaline RRMM: Ixazomib + len/dex vs len/dex

- 722 patients randomized 1:1 to receive ixazomib 4 mg or matching placebo weekly on d 1, 8, and 15, plus lenalidomide 25 mg PO on d 1-21 and dexamethasone 40 mg PO on d 1, 8, 15, and 22, in 28-d cycles
- Many high-risk patients and prior exposure to btz; study favored IRd to Rd in early relapse MM

<table>
<thead>
<tr>
<th></th>
<th>IRd</th>
<th>Rd</th>
<th>HR / OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median PFS, mos</td>
<td>20.6</td>
<td>14.7</td>
<td>HR 0.742; 95% CI: 0.587-0.939; P = 0.012</td>
</tr>
<tr>
<td>Confirmed ORR, %</td>
<td>78.3</td>
<td>71.5</td>
<td>OR 1.44; P = 0.035</td>
</tr>
<tr>
<td>CR</td>
<td>11.7</td>
<td>6.6</td>
<td>OR 1.87; P = 0.019</td>
</tr>
<tr>
<td>≥ VGPR</td>
<td>48.1</td>
<td>39.0</td>
<td>OR 1.45; P = 0.014</td>
</tr>
<tr>
<td>Median time to first response (ITT analysis), mos</td>
<td>1.1</td>
<td>1.9</td>
<td></td>
</tr>
<tr>
<td>Median duration of response (≥ PR), mos</td>
<td>20.5</td>
<td>15.0</td>
<td></td>
</tr>
</tbody>
</table>

### Phase III TOURMALINE-MM1: IRD vs RD in Relapsed and/or Refractory MM

<table>
<thead>
<tr>
<th>System Organ Class, n(%)</th>
<th>IRd, N=360</th>
<th>Rd, N=360</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td>Grade 3</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>69 (19)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Peripheral neuropathies</td>
<td>100 (28)</td>
<td>7 (2)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>151 (42)</td>
<td>22 (6)</td>
</tr>
<tr>
<td>Constipation</td>
<td>122 (34)</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Nausea</td>
<td>92 (26)</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>79 (22)</td>
<td>4 (1)</td>
</tr>
<tr>
<td>Rash</td>
<td>68 (19)</td>
<td>9 (3)</td>
</tr>
<tr>
<td>Back pain</td>
<td>74 (21)</td>
<td>2 (&lt;1)</td>
</tr>
<tr>
<td>Edema, peripheral</td>
<td>91 (25)</td>
<td>8 (2)</td>
</tr>
</tbody>
</table>

### Ixazomib: An oral proteosome inhibitor, three times monthly dosing

**IXAZOMIB (Oral) – 28-DAY CYCLES**

<table>
<thead>
<tr>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>D 1</td>
<td>D 2-7</td>
<td>D 8</td>
<td>D 9-14</td>
</tr>
<tr>
<td>D 15</td>
<td>D 16-21</td>
<td>D 22</td>
<td>D 23-28</td>
</tr>
</tbody>
</table>

- **Ixazomib**: ✓ ✓ ✓ ✓
- **Lenalidomide**: ✓ ✓ ✓ ✓ ✓ ✓
- **Dexamethasone**: ✓ ✓ ✓ ✓ ✓ ✓

**Implications:**
- Dose reduce for hepatic impairment
- Nausea, rash and thrombocytopenia can occur
- HSV prophylaxis
- Rapidly absorbed
**ELOQUENT-2: Results and Safety**

- Pts with relapsed/refractory MM and 1-3 prior therapies (N = 646), randomized to elo+ Rd or Rd
- Significant PFS improvement and higher response rates with elotuzumab + RD vs RD alone in relapsed MM
  - ORR: 79% vs 66% (P = .0002), respectively
- Infusion reactions reported in 10% of pts (9% grade 1/2; 1% grade 3); 70% occurred with initial dose; 2 discontinuations (1%) due to infusion reaction

<table>
<thead>
<tr>
<th>Nonhematologic in &gt; 1% of pts</th>
<th>Elo-Ld (n = 318)</th>
<th>Ld (n = 317)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphopenia</td>
<td>77</td>
<td>49</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>34</td>
<td>44</td>
</tr>
<tr>
<td>Infection</td>
<td>28*</td>
<td>24*</td>
</tr>
<tr>
<td>Fatigue</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

*Incidence similar after controlling for duration of therapy.

**Elotuzumab: Dose and Schedule**

**Implications:**
- Infusion reaction prevention
- HSV prophylaxis
- DVT prophylaxis (lenalidomide)

**ELOTUZUMAB (IV) – CYCLES 1 AND 2 (28-Day Cycles)**

<table>
<thead>
<tr>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>D 1</td>
<td>D 2-7</td>
<td>D 8</td>
<td>D 15</td>
</tr>
<tr>
<td></td>
<td>D 9-14</td>
<td>D 16-21</td>
<td>D 22</td>
</tr>
<tr>
<td></td>
<td>D 23-28</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Elotuzumab
- Lenalidomide
- Dexamethasone

**ELOTUZUMAB (IV) – CYCLES 3 AND BEYOND (28-Day Cycles)**

<table>
<thead>
<tr>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>D 1</td>
<td>D 2-7</td>
<td>D 8</td>
<td>D 15</td>
</tr>
<tr>
<td></td>
<td>D 9-14</td>
<td>D 16-21</td>
<td>D 22</td>
</tr>
<tr>
<td></td>
<td>D 23-28</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Elotuzumab
- Lenalidomide
- Dexamethasone

Prescribing information, 2015
**Phase II SIRIUS: Daratumumab Monotherapy in Heavily Pretreated RR MM**

- **Open-label, international, multicenter, 2-stage study**

  Pts with MM and ≥ 3 prior lines of therapy including PI and IMiD or refractory to most recent PI and IMiD (N = 53)

  - **Stage 1: Response assessment**
  - **Stage 2: Enrollment of additional pts at 16 mg/kg (outcomes reported for all pts at 16 mg/mg dose)**

- **Primary objective: ORR**

  - Daratumumab 8 mg/kg q4w (n = 18)
  - Daratumumab 16 mg/kg QW x 8 then q2w x 16, then q4w thereafter (n = 16)
  - Daratumumab 16 mg/kg QW x 8 then q2w x 16, then q4w thereafter (n = 90)

- **Median PFS:** 3.7 mos (95% CI: 2.8-4.6); 1-yr OS: 65% (95% CI: 51.2-75.3)

- **Most common grade 3/4 AEs:** thrombocytopenia (25%), anemia (24%), neutropenia (14%); infusion-related reactions occurred in 43% (most grade 1/2)


---

**Daratumumab**

<table>
<thead>
<tr>
<th>DARATUMUMAB (IV) – WEEKS 1-8</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daratumumab</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DARATUMUMAB (IV) – WEEKS 9-24</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
</tr>
</thead>
<tbody>
<tr>
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<td>✓</td>
<td>✓</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>DARATUMUMAB (IV) – WEEKS 25+</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daratumumab</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>

- Daratumumab-related sAEs:
  - Pneumonia, neutropenia, diarrhea (1 pt each receiving 16 mg/kg, early infusion program);
  - Laryngeal edema (1 pt receiving 16 mg/kg, accelerated infusion program)

19 of 45 pts reported infusion-related reactions; mostly grade 1/2

- Must pre-post medicate with hydrocortisone
- Moneleukast and loratadine 10mg each the night before and for 48 hrs after infusion
- Type/cross match and antibody workup necessary

Daratumumab. PI. 2015.
Additional Agents Currently in Development

<table>
<thead>
<tr>
<th>Agent</th>
<th>MOA</th>
<th>Phase in Development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ibrutinib</td>
<td>Tyrosine kinase inhibitor (BTK, ERK1/2, others)</td>
<td>I and II</td>
</tr>
<tr>
<td>Filanesib</td>
<td>Kinesin spindle protein (KSP) inhibitor</td>
<td>II</td>
</tr>
<tr>
<td>Indatuximab ravidansine</td>
<td>CD138 antibody-drug conjugate</td>
<td>I and II</td>
</tr>
<tr>
<td>Ricolinostat</td>
<td>HDAC inhibitor</td>
<td>I and I/II</td>
</tr>
<tr>
<td>Selinexor (KPT-330)</td>
<td>XPO1 nuclear transport inhibitor</td>
<td>I and II</td>
</tr>
<tr>
<td>MOR202 (MOR03087)</td>
<td>anti-CD38 antibody</td>
<td>I/II</td>
</tr>
<tr>
<td>Venetoclax (ABT-199/GDC-0199)</td>
<td>Selective BCL-2 inhibitor</td>
<td>I</td>
</tr>
<tr>
<td>Oprozomib</td>
<td>Proteosome inhibitor, oral</td>
<td>III</td>
</tr>
<tr>
<td>SAR650984</td>
<td>Anti CD38 antibody</td>
<td>I/II</td>
</tr>
</tbody>
</table>

Clinicaltrails.gov

Adherence to treatment must be addressed

• Cancer should be a reason to take medications
• Can be intentional and non-intentional
• Reasons why people don’t take their pills or office visits:
  “I feel fine”, “I forgot”, “I can’t remember all these pills!”,
  “I don’t need them anymore”, “can’t afford treatments”

• Discuss reasons for non-adherence (intentional, non-intentional) and employ strategies to improve adherence
  • Telephone reminders, alarms, calendars, help from significant others

Other considerations to manage side effects: Myelosuppression and Infection

- Myelosuppression is associated with both myeloma and the drugs used to treat it; treat MM if disease related
  - Risk of infection increased due to hypogammaglobulinemia
  - Dose-modifications, growth factors for neutropenia
  - Mild leukopenia, anemia and thrombocytopenia can be treatment related
- Infection prophylaxis
  - Pts should remain up to date on appropriate vaccinations (influenza, pneumonia)
  - HSV prophylaxis when receiving Pis, MOAbs
  - Use of IVIG or prophylactic antibiotics is controversial and should only be used when warranted
  - Pt education emphasizing importance of alerting treating clinicians of potential infection can reduce unnecessary antibiotics


Gastrointestinal (GI)

- Constipation, nausea, and diarrhea can occur
- GI symptoms are generally mild
- Nausea
  - Make sure the patient is on PPI
  - Assess for other competing meds that may cause
- Constipation
  - Bowel regimen
- Diarrhea
  - Rule out cdiff or other infection, investigate other causes, imodium or lomotil

Treatment Side Effect: Steroids

- Side effects affect every body system
  - AM v PM dosing
  - Take with food
  - Mood stabilizers
  - Monitor for hyperglycemia

---

Venous Thromboembolic Events: Signs and Symptoms of clot in MM

**DVT**
- Slight fever
- Rapid heart rate
- Unilateral swelling, erythema, warm extremity
- Cyanosis/cool skin if blockage
- Dull ache, pain, tight feeling over area and palpation
- Homan’s sign (35% patients)

**PE**
- Anxiety
- Sudden shortness of breath
- Chest discomfort
- Rapid pulse and heart rate
- Low-grade fever
- Pleural friction rub, crackles, diminished breath sounds, wheezing
Risk Assessment for VTEs in Pts Receiving Imids or carfilzomib

- MM is an inherently coagulable state and risk can change over time
- VTE prophylaxis for individual risk factors (eg, age or obesity) or myeloma-related risk factors (eg, immobilization or hyperviscosity)
  - If ≤ 1 risk factor present, aspirin 81-325 mg/day
  - If ≥ 2 risk factors present, LMWH (equivalent to enoxaparin 40 mg/day) or full-dose warfarin (target INR: 2-3)
  - Higher incidence VTEs with carfilzomib
- VTE prophylaxis for myeloma therapy–related risk factors (eg, high-dose dexamethasone, IMiDs, doxorubicin, multiagent chemotherapy)
  - LMWH (equivalent to enoxaparin 40 mg/day) or full-dose warfarin (target INR: 2-3)
  - Direct acting oral anticoagulants?

LMWH = low molecular weight heparin.

Current Management of Bone Disease

- Treat the myeloma
- Novel therapies have benefits
  - Direct effect on inflammatory cytokines
  - Inhibition of bone resorption
  - Osteoclast stimulation
- Bisphosphonates
  - Pamidronate
  - Zoledronic acid
- Supplement with calcium and vitamin D3 to maintain calcium homeostasis
- Radiotherapy (low dose)
  - Impending fracture
  - Cord compression
  - Plasmacytomas
- Vertebroplasty/kyphoplasty
- Orthopedic consultation
  - Impending or actual long-bone fractures
  - Bony compression of spinal cord
  - Vertebral column instability

Routine dental visits, watch for osteonecrosis of the jaw, a rare but serious complication

Survivorship in MM: Key Points

- Survivorship begins at diagnosis
- Patients are living longer than ever
- Health maintenance practices are highly important
- Adherence to therapies are critical to maintain remission, remain healthy for next therapy
- Prevention of infection, falls
- Care of the caregivers


---

Table 1: Adverse events commonly associated with multiple myeloma therapeutic agents

<table>
<thead>
<tr>
<th>PKs</th>
<th>PN</th>
<th>MDS</th>
<th>PLA</th>
<th>IMNs</th>
<th>Chemotherapy</th>
<th>Corticosteroids</th>
<th>DAs</th>
<th>mAs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
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<td></td>
<td></td>
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</tr>
<tr>
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<td>X</td>
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</tr>
<tr>
<td>Lenalidomide</td>
<td>X</td>
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<td>X</td>
<td>X</td>
<td>X</td>
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</tr>
<tr>
<td>Cyclophosphamide</td>
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<td>X</td>
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<td>Desamethasone</td>
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<td>Pomidoxone</td>
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</tbody>
</table>

NK natural killer, PN peripheral neuropathy, VTE venous thromboembolism

Important Factors When Providing Care: Assessment and Management in MM

<table>
<thead>
<tr>
<th>Cardiovascular/VTE</th>
<th>Risk of VTE on IMiDs: Cardiac monitoring (carfilzomib, panobinostat, doxorubicin)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone</td>
<td>Imaging yearly, Do they require bisphosphonates, and for how long? Regular dental exams; Vitamin D, Calcium</td>
</tr>
<tr>
<td>Infectious diseases</td>
<td>Is your patient at high risk for infection? (neutropenia; hypogammaglobulinemia) (myelosuppression from disease/treatment) – Weekly CBC, differential for 8 weeks with lenalidomide, pomalidomide – HSV prophylaxis with bortezomib, carfilzomib – IV Ig for recurrent infections (a result of hypogammaglobulinemia)</td>
</tr>
<tr>
<td>GI</td>
<td>Antiemetic prior to treatment, antidiarrheal agent, laxatives Assess for diarrhea (bortezomib, lenalidomide), constipation (thalidomide, doxorubicin)</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Review increased risk of PN with bortezomib and thalidomide Prompt intervention can prevent irreversible PN symptoms</td>
</tr>
<tr>
<td>Renal</td>
<td>Avoid renal toxic agents, 24-hour urine albumin (bisphosphonates), dose reduction (lenalidomide, melphalan, opioids, acyclovir)</td>
</tr>
<tr>
<td>Disease Monitoring</td>
<td>SPEP, UPEP, 24-hour urine, sFLC monthly</td>
</tr>
<tr>
<td>Health Maintenance</td>
<td>Cancer and cardiovascular surveillance</td>
</tr>
<tr>
<td>Survivorship</td>
<td>Financial, psychosocial issues (years life lost, retirement); Adherence to appts, drugs</td>
</tr>
</tbody>
</table>

VTE = venous thromboembolism; IMiDs = immunomodulatory drugs; MM = multiple myeloma; CBC = complete blood count; HSV = herpes simplex virus; IV = intravenous; Ig = immunoglobulins; GI = gastrointestinal; PN = peripheral neuropathy; SPEP = serum protein electrophoresis; UPEP = urine protein electrophoresis; sFLC = serum free light chain. Kyle et al, 2007; NCCN, 2015; Smith et al, 2008; Faiman et al, 2011; Micali et al, 2011; Kurkin, 2013.

Conclusion

- Explosion of new therapies to treat MM
- Nurses are positioned to educate patients, identify and intervene side effects
- Knowledge of the drugs and class effects allow for better education, surveillance and continued therapy
- Research is desperately needed to inform sequencing of agents
Questions

Remember: **Nurses** are like icebergs. At any one time you are only seeing about 1/5 of what they are actually doing.

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