Objectives

- Identify common treatment regimens in early relapsed multiple myeloma
- Apply knowledge of nursing management of patients with multiple myeloma, including effective symptom management
New Strategies for Multiple Myeloma Care: Case Studies for Nurses
Part 2: Relapsed Multiple Myeloma

CASE #3

Steve*

- 50-year-old man diagnosed with IgA lambda MM, standard risk in 2013
- Treated with VRd then ASCT
  - No maintenance
  - Complete response

Decided against clinical trial participation due to job and family responsibilities

Now:
Slow biochemical progression

ASCT = autologous stem cell transplantation; HIPAA = Health Insurance Portability and Accountability Act; Ig = immunoglobulin; MM = multiple myeloma; VRd = bortezomib-lenalidomide-dexamethasone.
How Patients With Myeloma Relapse

**Symptomatic**
- New, worsening bone pain
- Increasing fatigue, anemia
- Next steps: relapse workup, many therapy choices

**Asymptomatic Biochemical Relapse**
- Sequentially rising myeloma protein, free light chain
- No other symptoms
- Decisions: if, when, how to treat

Relapse Workup

<table>
<thead>
<tr>
<th>Lab tests</th>
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<tbody>
<tr>
<td>Serum protein electrophoresis (SPEP)</td>
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<tr>
<td>Urine protein electrophoresis (UPEP)</td>
<td></td>
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<tr>
<td>CBC + differential + chemistry (metabolic panel)</td>
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<tr>
<td>FLC ratio of free kappa/lambda light chains (plasma)</td>
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<tr>
<td>Monoclonal protein analysis (MPA)</td>
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<table>
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<tr>
<th>Consider bone marrow biopsy</th>
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<td>Cytogenetics and FISH</td>
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<tr>
<th>Imaging</th>
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<tr>
<td>PET/CT</td>
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<tr>
<td>Skeletal survey</td>
<td></td>
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<tr>
<td>Whole-body low-dose CT</td>
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<td>MRI</td>
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</table>

Which imaging depends on individual’s symptoms and available testing options

CBC = complete blood count; CT = computed tomography; FISH = fluorescence in situ hybridization; FLC = free light chain; MRI = magnetic resonance imaging; PET = positron emission tomography.
### CASE #3

**Steve**

- **February 2020:** biochemical relapse
  - M-protein from undetectable g/dL to 0.96 g/dL over 2.5 years
  - No other symptoms
  - Lab values normal
  - Low-dose whole-body CT, no new lesions

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**Many Treatment Options at Early Relapse (1-3 Prior Therapies)**

**FDA-approved myeloma therapies**
- Bortezomib (SC admin)
- Lenalidomide
- Carfilzomib
- Pomalidomide
- Ixazomib
- Daratumumab
- Elotuzumab
- Isatuximab

**Common Combinations**
- VRd, Vd
- VRd, Rd
- KrD, Kd, Kd-Dara
- Pd, DPd, EPd, PCd
- IRd
- Dara-Rd, Dara-Vd, Dara-Pd, Dara-VMP, Dara-Kd
- ERd, EPd
- Isa-Pd

**New agents or regimens in clinical trials are always an option**

C = cyclophosphamide; D or Dara = daratumumab; d = dexamethasone; E = elotuzumab; FDA = US Food and Drug Administration; Isa = isatuximab; I = ixazomib; K = carfilzomib; M = melphalan; P = pomalidomide; PACE = cisplatin doxorubicin cyclophosphamide etoposide; R = lenalidomide; SC = subcutaneous; T = thalidomide; V = bortezomib.

*2 prior therapies.

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Practical Approach to Treatment of Patients With Relapsed Myeloma

Disease-related factors
- Duration of response to initial therapy
- High-risk vs low-risk status
- Molecular relapse vs symptomatic relapse
- Other comorbid conditions, patient frailty

Treatment-related factors
- Previous/current therapy exposure (relapsed or refractory)
- Toxicity/tolerability of previous regimen
- Mode of administration (ie, PO or IV)
- Cost and convenience (out-of-pocket copays for IV vs po)
- Patient preference

Carfilzomib (K): IV Proteasome Inhibitor

- IV proteasome inhibitor, indications:
  - In combination with dex or len-dex in patients with relapsed or refractory MM who have received 1-3 lines of therapy
  - As a single agent in patients with relapsed or refractory multiple myeloma who have received 1 or more lines of therapy

- Clinical pearls
  - Escalate dose
  - Dose-dependent 10- or 30-min infusion
  - Hydration but not overhydration
  - Premedication (dex)
  - Aspirin vs full anticoagulation
  - Monitor blood counts, response
  - Monitor for infection
    - Herpesvirus prophylaxis
    - Know cardiac and pulmonary status and optimize heart failure and blood pressure management
    - Diuretic (furosemide or torsemide) or inhalers if needed
    - Avoid dyspnea over the weekend; start new patients first dose early in the week
Once-Weekly Carfilzomib Dosing in ARROW Clinical Trial

Patients with R/R MM
2 or 3 previous lines of therapy with IMiD and PI exposure (no carfilzomib or oprozomib)
ECOG PS 0/1, and CrCl ≥30 mL/min
(N=478)

Weekly Carfilzomib (70 mg/m²)a + dex (n=240)
Twice-Weekly Carfilzomib (27 mg/m²)a + dex (n=238)

Overall Response Rate

<table>
<thead>
<tr>
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<th>ORR (%)</th>
<th>ORR (%)</th>
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<tr>
<td>Once Weekly</td>
<td>62.9%</td>
<td>40.8%</td>
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<td>Twice Weekly</td>
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CANDOR Phase 3: Carfilzomib Dexamethasone ± Daratumumab in Patients With R/R MM

Design
- Multicenter, randomized phase 3
  - 466 patients with R/R MM 1-3 prior therapies
  - ECOG PS 0-2; CrCl ≥20 mL/min; LVEF ≥40%

Results
- Median time to first response was 1 month in the KdD and Kd arms

<table>
<thead>
<tr>
<th>Responses, %</th>
<th>KdD (n=152)</th>
<th>Kd (n=154)</th>
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<tbody>
<tr>
<td>ORR</td>
<td>84.3*</td>
<td>74.7*</td>
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<tr>
<td>VGPR or better</td>
<td>69.2</td>
<td>48.7</td>
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<tr>
<td>CR or better</td>
<td>28.5</td>
<td>10.4</td>
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<tr>
<td>MRD negative at 12 months (10⁻⁵ threshold)</td>
<td>17.6</td>
<td>3.9</td>
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<tr>
<td>MRD-negative CR at 12 months (10⁻⁵ threshold)</td>
<td>12.5†</td>
<td>1.3†</td>
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<tr>
<td>Best MRD-negative CR (10⁻⁵ threshold)</td>
<td>13.8</td>
<td>3.2</td>
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CANDOR Conclusions
- 37% reduction in risk of progression or death with KdD compared with Kd
- 10× higher MRD-negative CR rate with KdD compared with Kd
- PFS benefit maintained for len-refractory patients
New Strategies for Multiple Myeloma Care: Case Studies for Nurses
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Consider Full Anticoagulation for Patients on Carfilzomib Regimens

ASA = aspirin; KRd = carfilzomib lenalidomide dexamethasone; RVd = bortezomib lenalidomide dexamethasone; VTE = venous thrombotic embolism.


New data suggest rivaroxaban may be a more-effective antithrombotic agent for patients on KRd.

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<tr>
<th>Treatment</th>
<th>VTE</th>
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<tbody>
<tr>
<td>RVd + ASA</td>
<td>0%</td>
<td>4.0%</td>
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<tr>
<td>KRd + ASA</td>
<td>1.0%</td>
<td>5.2%</td>
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<tr>
<td>KRd + rivaroxaban</td>
<td>2.2%</td>
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Ixazomib: Oral Proteasome Inhibitor

- **Oral** proteasome inhibitor
  - Indication: patients with multiple myeloma who have received at least 1 prior therapy
  - In combination with Rd

- **Administration**
  - Oral capsule 1× per week; do not crush, chew capsules or open capsule
  - Empty stomach: 1 hour before or 2 hours after food

- **Clinical pearls**
  - Adherence, schedule, viral prophylaxis
  - Rapid response (1.1 months); fast absorption (if vomit, do NOT repeat dose)
  - Monitor blood counts: cyclic thrombocytopenia
  - Peripheral neuropathy, peripheral edema
  - Herpes prophylaxis
  - In combination with Rd, so DVT prophylaxis

DVT = deep vein thrombosis; FDA = US Food and Drug Administration; Rd = lenalidomide dexamethasone.

Ixazomib: Oral Proteasome Inhibitor

- FDA approved November 2015

Ixazomib + Rd
New Strategies for Multiple Myeloma Care: Case Studies for Nurses
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IRd: All-Oral Regimen Dosing Calendar

Ixazomib dosing
28-day cycle

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Recommended starting doses:
- Ixazomib 4 mg
- Lenalidomide 25 mg
- Dexamethasone 40 mg

CASE #3

Steve*

- Deciding among many excellent options
  - Not refractory to bortezomib, lenalidomide
  - Has not received monoclonal antibodies
- Given COVID-19 situation and uncertainty, considering an all-oral regimen: IRd
- Opportunity to use risk-adapted approach


*HIPAA-compliant, stock photo (not actual patient).
Special Considerations With Antibody Therapy

• Potential interference with laboratory tests
  – Co-migration of therapeutic antibody with M-protein: overestimation of M-protein and reduced CR rates

• Solutions
  – Awareness
  – Laboratory assays to minimize effects (eg, high-resolution mass spectrometry)

Daratumumab, elotuzumab, and isatuximab are all IgG antibodies

Mass Spectrometry Can Resolve Antibody Interference

• Molecular mass can identify amount of monoclonal protein specifically
• Has the potential to resolve antibody interference

The result is a highly sensitive and specific approach to monitor M-proteins

CR = complete response; Ig = immunoglobulin; M-protein = monoclonal protein.

Mass spectrometry can resolve antibody interference

M-protein = monoclonal protein.
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Daratumumab (DARA, D): Monoclonal Antibody

Summary
• Monoclonal antibody targeting CD38
  — New SC dosing and original IV
• Multiple indications for MM—prescribing information for details

Clinical pearls
• SC dose form for SC only; IV for IV only
• Antibody interference—type and cross BEFORE starting
• Premeds: corticosteroids, antipyretics, and antihistamine, montelukast
• Post-med: oral corticosteroid for 2 days after
• Educate patients/caregivers about expectations
• Herpes prophylaxis
• Remember appropriate prophylaxis for combination partner drugs

Daratumumab (DARA, D) Cont’d

SC Clinical Pearls:

- INJECTION INTO ABDOMEN
  - NEW
  - Inject 15 mL into subcutaneous tissue over 3-5 minutes
  - 3” from navel on right or left side
  - Pause or slow if patient experiences pain

IV Clinical Pearls:

- SLOW FIRST INFUSION
  - then FASTER
  - ALTERNATIVE: DIVIDED FIRST INFUSION
- DAY 1
  - 8 mg/kg
- DAY 2
  - 8 mg/kg
- DAY 1 and 2
  - 8 mg/kg
- 3-4 weeks after 1st/2nd dose

Example: 4-week cycle with Rd

- Schedule becomes less frequent
- If no injection/infusion reaction after 3 doses, consider discontinuing corticosteroid pre/post medications
Elotuzumab (E): Monoclonal Antibody

- IV monoclonal antibody targeting SLAMF-7
- Prescribed with len-dex or pom-dex
  - DVT prophylaxis (for len or pom)
  - Steroid side effects and schedule (AM vs PM)
- Clinical pearls
  - Risk of infusion reaction: 10%
    - 3-24 hours before = dex 28 mg; 45-90 minutes before = dex 8 mg IV, H1, H2, and acetaminophen
  - Infuse at rate of 0.5 mL/min and escalate to 5 mL/min over time
  - Give weekly for 8 weeks then twice monthly until progressive disease
- Monitoring
  - Blood counts (hold/adjust dose if needed)
  - Response assessment (monthly); interference
  - Glucose (dex can affect)
  - Renal, hepatic function

Isatuximab New Anti-CD38 Monoclonal Antibody: Approved in Combination with Pd

- Monoclonal antibody targeting CD38; IV administration
  - Indication: at least 2 prior therapies, including lenalidomide and a proteasome inhibitor
- Improved ORR: 60.4% Isa-Pd vs 35.3% Pd

ICARIA-MM Phase 3 Clinical Trial

Significant increase in median PFS demonstrated with isatuximab + Pd vs Pd alone

40% reduction in the risk of disease progression or death in patients treated with isatuximab + Pd vs Pd alone
New Strategies for Multiple Myeloma Care: Case Studies for Nurses
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Isatuximab: Safety and Clinical Pearls

Safety
- IRR (38%): the most common AR specific to isatuximab
- Isa-Pd common ARs: cytopenias, IRR, infections, dyspnea, GI ARs

Clinical pearls
- IRR protection: premedicate with
  - Dexamethasone: 40 mg oral or IV (or 20 mg for patients ≥75 years)
  - Acetaminophen: 650 mg to 1000 mg
  - H2 antagonists
  - Diphenhydramine: 25 mg to 50 mg oral or IV; IV preferred for at least the first 4 infusions
- Antibody interference—type and cross BEFORE starting
- In combo with pomalidomide + dex: DVT prophylaxis
- Herpes prophylaxis
- No dose adjustments for isatuximab

Pomalidomide

- Oral immunomodulatory drug active in R-refractory patients
- Indication: at least 2 prior therapies, including R and a PI, and have demonstrated disease progression on or within 60 days of completion of the last therapy
- Monitor
  - Blood counts—neutropenia most-frequent Grade 3/4 AE
  - Liver function
  - Response
- Proactive AE management
- Clinical pearls
  - Adherence and REMS
  - DVT prophylaxis
  - Monitor blood counts (neutopenia), liver enzymes
  - Refrain from smoking (reduces pom exposure)
  - Protect renal health (renal excretion of pom)
    - Hydration
    - Avoid NSAIDS, IV contrast, other drugs with renal interactions

AE = adverse event; Ara = aramidemab; DVT = deep vein thrombosis; EPd = elotuzumab pomalidomide dexamethasone; FDA = US Food and Drug Administration; IV = intravenous; NSAI = nonsteroidal anti-inflammatory drug; Pd = pomalidomide dexamethasone; PI = proteasome inhibitor; R = lenalidomide; REMS = Risk Evaluation and Mitigation Strategies.
New Strategies for Multiple Myeloma Care: Case Studies for Nurses
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CASE #4

Michelle*

- 72-year-old woman diagnosed with IgG lambda MM, standard risk in June 2014
- Treated with RVd lite continuous × 2 years
- Declined ASCT due to caregiver issues
- Biochemical disease progression
- Started ixazomib lenalidomide dex January 2018
- Symptomatic relapse (pain, new bone lesions on PET-CT)
- Started isatuximab pomalidomide dex May 2020

ASCT = autologous stem cell transplantation; CT = computed tomography; dex = dexamethasone; HIPAA = Health Insurance Portability and Accountability Act; Ig = immunoglobulin; MM = multiple myeloma; PET = positron emission tomography; RVd = lenalidomide bortezomib dexamethasone.

*HIPAA compliant, stock photo (not actual patient).

Resources to Enhance Your Ability to Care for Your Patients With MM: Download or Receive a USB Drive by Mail

...and Much, Much More

Instructions for accessing these resources are provided in the post-course evaluation.