Novel Therapies for Multiple Myeloma:
Exploring New Strategies for Relapsed/Refractory Disease

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PGY-1 Pharmacy Resident
November 7th, 2017
Objectives

• Recognize the signs and symptoms of a typical patient presentation for multiple myeloma

• Identify common drug therapy regimens used for initial treatment of multiple myeloma

• Select an appropriate drug regimen for a patient with relapsed/refractory disease
Epidemiology

Population
- Men > women
- Median age of diagnosis is 69 years old (range 65-74)

New Cases
- 30,280 new cases per year
- Diagnosis rate rising by 0.8% per year

Mortality
- Mortality rate decreasing by 0.8% per year
- Overall ~50% over 5 years
Survival

- Not curable (yet) – goal is to sustain remission of multiple myeloma but relapse is inevitable

5 year Survival Rates

<table>
<thead>
<tr>
<th>Years</th>
<th>% Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>1975-77</td>
<td>25</td>
</tr>
<tr>
<td>1987-89</td>
<td>27</td>
</tr>
<tr>
<td>2006-12</td>
<td>50</td>
</tr>
</tbody>
</table>

Patient Presentation: CRAB Symptoms

- **C**: Hypercalcemia (25%)
  - Serum calcium >11.5 mg/dL

- **R**: Renal Dysfunction (50%)
  - Serum creatinine >2 mg/dL

- **A**: Anemia (70%)
  - Hemoglobin <10 g/dL or >2 g/dL from baseline
  - Fatigue

- **B**: Bone lesions (80%), fractures (30%)
  - Osteopenia, pathologic fracture, lytic lesions

*M protein
*Bone Marrow Biopsy
Disease Course

Normal Plasma Cells

Monoclonal gammopathy of undetermined significance (MGUS)

- M protein <3g/dL
- <10% bone marrow plasma cells

- No symptoms

Smoldering Multiple Myeloma

- M protein >3g/dL
- 10-60% bone marrow plasma cells

- 1%/year

Multiple myeloma

- M protein present
- >10% bone marrow plasma cells

- 10%/year

Symptoms
Question 1

- GM is a 66 YOF who presents to the emergency department with pain and fatigue. Several tests are ordered with the following results:
  
  - SCr 2.2 mg/dL, eCrCl 32 mL/min
  
  - Electrolytes: Na = 137, K = 5.3, Ca = 11.7 (corrected)
  
  - CBC: Hgb = 9 g/dL (baseline 11.5), Platelets = 50 x 10⁹ cells/L
  
  - X-ray: (see image)
Question 1

Which of the following symptoms can NOT be attributed to multiple myeloma?

- A. Lytic bone lesions
- B. Hyperkalemic
- C. Renal dysfunction
- D. Fatigue
Backbone Therapy for Multiple Myeloma
Treatment Overview

Consolidation → Hematopoietic Stem Cell Transplant*

Induction → Maintenance

- 3 drugs (Backbone)
- 2 drugs (elderly/frail)
- 1 drug (low dose)
- 3 drugs (Novel Agent)

Salvage (Relapse)
Multiple Myeloma Therapy Backbone

- **Proteosome Inhibitors**
- **Immunomodulatory Agents**
- **Corticosteroids**
- **Alkylating Agents**
Backbone Therapy - Important Facts

**Proteosome Inhibitors**
Bortezomib, Carfilzomib

- Bortezomib given weekly, subQ injection to prevent peripheral neuropathy (vs. IV)
- Carfilzomib – cardiac and pulmonary toxicities
- HSV reactivation - prophylactic antiviral therapy

**Immunomodulatory Agents**
Lenalidomide, Thalidomide, Pomalidomide

- REMS program for embryo-fetal birth defects
- VTE prophylaxis with aspirin or other anticoagulation

HSV = Herpes Simplex Virus

NCCN Clinical Practice Guidelines: Multiple Myeloma, Version 1.2018
Backbone Therapy - Important Facts

**Corticosteroid**
- Dexamethasone
  - Long-acting corticosteroid – potentiates the effects of the other agents
  - PJP prophylaxis is recommended

**Alkylating Agents**
- Cyclophosphamide, Melphalan
  - Cyclophosphamide (IV, PO) - used in acute renal dysfunction until resolution
  - Melphalan no longer recommended by 2018 guidelines due to significant cytopenias (used mostly for SCT conditioning)

PJP = Pneumocystis jiroveci pneumonia
SCT = stem cell transplant

NCCN Clinical Practice Guidelines: Multiple Myeloma, Version 1.2018
Becker DE. Anesth Prog 2013;60(1):25-32
Multiple Myeloma Initial Therapy

Preferred Regimens (Category 1)
- Bortezomib + Lenalidomide + Dexamethasone
- Bortezomib + Cyclophosphamide + Dexamethasone

Other Category 1 Regimens
- Bortezomib + Thalidomide + Dexamethasone
- Bortezomib + Dexamethasone
- Lenalidomide + Dexamethasone

Used in acute renal dysfunction
Question 2:

GM, 66 yof, has a bone marrow biopsy that comes back positive for multiple myeloma. The team would like to start induction therapy for GM right away with the ultimate goal of stem cell transplant. Her CrCL has improved to 65 mL/min after treating her hypercalcemia.
Question 2:

Which regimen below would be the preferred induction regimen for GM’s newly diagnosed multiple myeloma?

- A. Lenalidomide, Dexamethasone
- B. Bortezomib, Cyclophosphamide, Dexamethasone
- C. Bortezomib IV weekly, Lenalidomide, Dexamethasone
- D. Bortezomib SubQ weekly, Lenalidomide, Dexamethasone
Novel Therapies
Novel Therapies Overview

- **Panobinostat**
  - Approved: February 23rd, 2015
  - First oral histone deacetylase (HDAC) inhibitor

- **Ixazomib**
  - Approved: November 20th, 2015
  - First oral proteosome inhibitor

- **Daratumumab**
  - Approved: November 21st, 2016
  - Second Monoclonal antibody approved
Panobinostat (Farydak®)

FDA Approval
- February 23rd, 2015
- Approval based on one phase 3 clinical trial

Indication
- In combination with bortezomib and dexamethasone in patients with 2 prior therapies
- Prior therapies: bortezomib and an immunomodulatory agent

Route/Dose
- Oral capsule: 20mg three times per week x 2 weeks of a 21 day cycle
- Up to 8 cycles (weekly bortezomib injection and dexamethasone PO)
Panobinostat Mechanism of Action

Histone deacetylase (HDAC) enzyme inhibitor

Unfolded/misfolded proteins → Ubiquitinated protein aggregates

Panobinostat

Proteasomal degradation
Ubiquitinated protein
Protein degradation

Bortezomib

Lysosomal degradation
Protein degradation

Microtubule

PANORAMA 1 Trial

Relapsed/refractory multiple myeloma

Randomize

- Panobinostat
- Bortezomib
- Dexamethasone

N=387

Placebo
- Bortezomib
- Dexamethasone

N=381

21-day cycles (x 8 cycles)
- Panobinostat PO on days M/W/F, M/W/F
- Bortezomib IV 1.3mg/m2 days 1, 4, 8, 11
- Dexamethasone PO days 1/2, 4/5, 8/9, 1/12

Additional 6 week cycles (x4)
- If clinical benefit at 8 weeks

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Panobinostat</th>
<th>Placebo</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression Free Survival (PFS)</td>
<td>11.9 months</td>
<td>8 months</td>
<td>HR = 0.63, p = &lt;0.0001</td>
</tr>
<tr>
<td>Overall Survival (OS)</td>
<td></td>
<td>Final analysis still pending, median OS thus far: 33.6 months panobinostat and 30.4 months placebo</td>
<td></td>
</tr>
</tbody>
</table>

## PANORAMA 1 Trial

<table>
<thead>
<tr>
<th>Safety</th>
<th>Panobinostat</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of treatment</td>
<td>5 months</td>
<td>6.1 months</td>
</tr>
<tr>
<td>Discontinuation for progression</td>
<td>21%</td>
<td>40%</td>
</tr>
<tr>
<td>Discontinuation for ADE</td>
<td>36%</td>
<td>20%</td>
</tr>
</tbody>
</table>

### Overall Adverse Effects

<table>
<thead>
<tr>
<th>Effect</th>
<th>Panobinostat</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>57%</td>
<td>41%</td>
</tr>
<tr>
<td>Peripheral Neuropathy</td>
<td>61%</td>
<td>67%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>68%</td>
<td>42%</td>
</tr>
<tr>
<td>Absolute Neutrophil Count</td>
<td>75%</td>
<td>36%</td>
</tr>
<tr>
<td>Thrombocytopenia*</td>
<td>98%</td>
<td>84%</td>
</tr>
</tbody>
</table>

*ADiscontinuation due to thrombocytopenia only 2%*

ADE = adverse drug event

Conclusion: Panobinostat provides another unique, effective treatment option for patients with relapsed/refractory disease.

*Category 1 recommended regimen in NCCN guidelines for relapsed/refractory (not “preferred” yet)*
Panobinostat

**Dose Adjustments**
- Nausea/vomiting/diarrhea → Decrease by 5mg
- Hepatic impairment → start at 15mg
- Platelets<50 and bleeding, ANC<750 → hold

**Clinical Pearls**
- QTc must be <450 msec to use
- Moderate emetic potential – prophylaxis needed

ANC = absolute neutrophil count

NCCN Clinical Practice Guidelines: Multiple Myeloma, Version 1.2018
### Ixazomib (Ninlaro®)

<table>
<thead>
<tr>
<th>FDA Approval</th>
</tr>
</thead>
</table>
| • September 9th, 2015 - Priority review granted  
  • November 20th, 2015 – Approval granted after one phase 3 trial |

<table>
<thead>
<tr>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Treatment of multiple myeloma in combination with lenalidomide and dexamethasone in patients with one prior therapy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Route/Dose</th>
</tr>
</thead>
</table>
| • Oral capsule: 4mg once weekly x 3 weeks of a 28 day cycle  
  • Lenalidomide (daily x 21 days) and dexamethasone (weekly x 4 weeks) - also PO tablets |
Ixazomib – Proteosome Inhibitor

Protein aggregation → cell death
TOURMALINE-MM1 Trial

Relapsed/refractory multiple myeloma

Randomize

N=360
Ixazomib
Lenalidomide
Dexamethasone

N=362
Placebo*
Lenalidomide
Dexamethasone

28-day cycles
4mg Ixazomib
days 1, 8, 15
25mg lenalidomide
days 1-21
40mg dexamethasone
PO days 1, 8, 15, 22

Additional 6 week cycles (x4)
If clinical benefit at 8 weeks

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Ixazomib</th>
<th>Placebo</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression Free survival (PFS)</td>
<td>20.6 months</td>
<td>14.7 months</td>
<td>HR 0.74, p = 0.01</td>
</tr>
<tr>
<td>Overall Survival (OS)</td>
<td></td>
<td>Not significantly different at interim analysis</td>
<td></td>
</tr>
<tr>
<td>High risk cytogenetics</td>
<td>21.4 months</td>
<td>9.7 months</td>
<td>HR 0.54, p = 0.02</td>
</tr>
</tbody>
</table>
## TOURMALINE-MM1 Trial Conclusion

### Safety

<table>
<thead>
<tr>
<th></th>
<th>Ixazomib</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Cycles</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>Discontinuation for progression</td>
<td>34%</td>
<td>40%</td>
</tr>
<tr>
<td>Discontinuation for ADE</td>
<td>17%</td>
<td>14%</td>
</tr>
</tbody>
</table>

ADE = adverse drug event

### Overall Adverse Effects

<table>
<thead>
<tr>
<th></th>
<th>Ixazomib</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral Neuropathy</td>
<td>27%</td>
<td>22%</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>31%</td>
<td>16%</td>
</tr>
<tr>
<td>Rash</td>
<td>36%</td>
<td>23%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>45%</td>
<td>39%</td>
</tr>
</tbody>
</table>

Conclusion: Ixazomib with lenalidomide and dexamethasone is an effective, tolerable, alternative regimen in relapsed/refractory multiple myeloma patients. *Preferred regimen in NCCN guidelines for relapsed/refractory*

**Ixazomib**

### Dose Adjustments
- Rash, peripheral neuropathy: 4 mg → 3 mg → 2.3 mg → discontinue
- CrCL<30 or total bilirubin>1.5xULN → use 3mg
- ANC<500, platelets<35 → hold

### Clinical Pearls
- Antiviral prophylaxis against HZV
- Avoid CYP3A4 strong inducers – may decrease concentration of Ixazomib

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HZV = herpes zoster virus
ULN = upper limit of normal

NCCN Clinical Practice Guidelines: Multiple Myeloma, Version 1.2018
Daratumumab (Darzalex®)

**FDA Approval**
- November 16th, 2015 – Accelerated approval
- November 21st, 2016 – Official FDA approval

**Indication**
- Dexamethasone AND lenalidomide OR bortezomib in patients with 1 prior therapy
- Monotherapy in patients with 3 prior therapies (pending trial completion)

**Route/Dose**
- 16 mg/kg IV infusion over 4-8 hours
- With Lenalidomide: given as a weekly, biweekly, or monthly infusion
- With Bortezomib: given as an infusion every 3 weeks
Daratumumab Mechanism of Action

- Multiple Myeloma Cell
- CD38

**Direct Effects**
- Alterations in intracellular signaling
- Inhibition of function of growth factor receptors
- Inhibition of function of adhesion molecules

**ADCC**

**NK Cell**

**Fc Receptor**

**Lysis**

**Myeloma Cell**

**ADCP**

**Macrophage**

**Fc Receptor**

**Signaling Cascade**

**Antigen**

**MAC**

**C1q**

**CDC**

**Cell Death**
POLLUX Trial – Interim Analysis

Relapsed multiple myeloma

Randomize

N=286
Daratumumab
Lenalidomide
Dexamethasone

N=283
Placebo
Lenalidomide
Dexamethasone

28-day cycles
16mg/kg Daratumumab
IV weekly x 8 weeks
25mg lenalidomide
days 1-21 each cycle
40mg dexamethasone
PO weekly

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Daratumumab</th>
<th>Placebo</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression Free survival (<em>2017 update</em>)</td>
<td>24 months</td>
<td>17.5 months</td>
<td>p = &lt;0.0001</td>
</tr>
<tr>
<td>Disease progression at Interim</td>
<td>18.5%</td>
<td>41%</td>
<td>HR = 0.34, p = &lt;0.001</td>
</tr>
<tr>
<td>Overall Response Rate (ORR)</td>
<td>92.9%</td>
<td>76.4%</td>
<td>p = &lt;0.001</td>
</tr>
</tbody>
</table>

## POLLUX Trial

<table>
<thead>
<tr>
<th>Safety</th>
<th>Daratumumab</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinuation for progression</td>
<td>14.1%</td>
<td>34.2%</td>
</tr>
<tr>
<td>Discontinuation for ADE</td>
<td>6.7%</td>
<td>8.2%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Overall Adverse Effects</th>
<th>Daratumumab</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>26.9%</td>
<td>27.4%</td>
</tr>
<tr>
<td>Anemia</td>
<td>31.1%</td>
<td>34.9%</td>
</tr>
<tr>
<td>Upper Respiratory Infection</td>
<td>31.8%</td>
<td>20.6%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>42.8%</td>
<td>24.6%</td>
</tr>
<tr>
<td>Infusion reactions</td>
<td>47.7%</td>
<td>N/A</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>59.4%</td>
<td>43.1%</td>
</tr>
</tbody>
</table>

Conclusion: Interim analysis showed significant progression-free survival benefit and overall response rate with daratumumab added to standard therapy

*Preferred regimen in NCCN guidelines for relapsed/refractory*

ADE = adverse drug event

Daratumumab

Dose Adjustments
- Infusion reactions – decrease infusion rate by 50%, discontinue if three grade 3 reactions
- Premedicate: acetaminophen, antihistamine, steroid
- May delay infusion for neutrophil/platelet recovery

Clinical Pearls
- Administer antiviral prophylaxis for 3 months to prevent HZV reactivation
- Growth factors and platelet transfusions are allowed

HZV = herpes zoster virus
# Novel Therapy Summary

<table>
<thead>
<tr>
<th>Panobinostat</th>
<th>Ixazomib</th>
<th>Daratumumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Oral histone deacetylase (HDAC) inhibitor (novel mechanism)</td>
<td>• First oral proteosome inhibitor (completely oral regimen)</td>
<td>• First of two monoclonal antibodies approved</td>
</tr>
</tbody>
</table>

### NCCN Preferred Regimens – Previously Treated

- Repeat primary induction therapy (relapse at >6 months)
- **Daratumumab** + Lenalidomide + Dexamethasone (category 1)
- **Daratumumab** + Bortezomib + Dexamethasone (category 1)
- **Ixazomib** + Lenalidomide + Dexamethasone (category 1)

### Other Recommended Regimens

- **Panobinostat** + Bortezomib + Dexamethasone (category 1)
- **Daratumumab** + Pomalidomide + Dexamethasone
Question 3

- GM presents to the emergency room with typical C.R.A.B. symptoms as well as a QTc prolongation of 500 milliseconds.
  - She has detectable levels of M-protein in her blood and urine signifying a relapse in her multiple myeloma.
  - GM completed her first round of induction therapy with Bortezomib/ Lenalidomide/ Dexamethasone 3 months ago.
  - You also hear her mention how hard it was to come back to the hospital every week for an injection.
Question 3

• Which therapy is most appropriate to treat GM’s first relapsed multiple myeloma episode?
  • A. Repeat induction therapy (Bortezomib/Lenalidomide/Dexamethasone)
  • B. Panobinostat + Bortezomib + Dexamethasone
  • C. Ixazomib + Lenalidomide + Dexamethasone
  • D. Daratumumab + Bortezomib + Dexamethasone
Conclusion

• Multiple Myeloma remains an incurable disease
  • Our goal is to maintain remission
  • Novel therapies are important to maintaining remission as patient’s develop resistance to our current therapies
• As additional oral regimens are developed, multiple myeloma is treated as more of a chronic disease with long-term therapy
Questions & Discussion
## Cost

<table>
<thead>
<tr>
<th>Drug</th>
<th>AWP</th>
<th>Cost Per Cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panobinostat 20mg</td>
<td>$8,800.01 for 6 capsules</td>
<td>$8,800.01</td>
</tr>
<tr>
<td>Ixazomib 4mg</td>
<td>$3,787.20 per capsule</td>
<td>$11,361.60</td>
</tr>
<tr>
<td>Daratumumab 100mg/5mL</td>
<td>$583.22 per vial</td>
<td>$2,332.88</td>
</tr>
<tr>
<td>Daratumumab 400mg/20mL</td>
<td>$2,332.90 per vial</td>
<td>$9,331.60</td>
</tr>
</tbody>
</table>

AWP = average wholesale price

**Venetoclax**

- MOA: BCL-2 inhibitor (anti-apoptotic protein)
- Approved in CLL patients with a 17p deletion with one prior therapy
- Oral tablet
- Phase 1b trial in multiple myeloma

**CAR T-cells**

- Genetically modified T cells – target and kill malignant cells
- Target the B-cell maturation antigen (BCMA)
- Early trials promising, high complete response rates, low immune-related side effects

MOA = mechanism of action  
CLL = chronic lymphocytic leukemia  
ALL = acute lymphoblastic leukemia

Moreau, et al. *Blood* 2017; pre-published online.  
Cytogenetics/Mutations

- Mix of genetic mutations and cytokines drive the progression of multiple myeloma

- Primary cytogenetic abnormalities
  - 50% Translocations:
    - Chromosome 14 with chromosomes 4, 6, 11, 16, 20
    - (4;14), (6;14), (11;14), (14;16), (14;20)

- Secondary cytogenetic abnormalities
  - Deletions: chromosomes 17p, 13
  - KRAS, MYC, p53 mutations
Diagnosis/work-up

- Complete blood count
- Serum calcium, serum creatinine
- Serum and urine protein electrophoresis to detect monoclonal ("M") protein
- X-ray, CT skeletal survey, MRI/PET
- Bone marrow biopsy → fluorescence in situ hybridization (FISH), for percentage of clonal cells
- Albumin levels
- Serum B₂-microglobulin

CT = computerized tomography
MRI = magnetic resonance imaging
PET = positron emission tomography

Staging Systems

<table>
<thead>
<tr>
<th>Stage</th>
<th>International Staging System (ISS)</th>
<th>Revised-ISS (R-ISS)*</th>
</tr>
</thead>
</table>
| I     | Serum beta-2 microglobulin <3.5 mg/L  
       Serum albumin ≥3.5 g/dL | Standard-risk cytogenetics  
       AND  
       Serum LDH ≤ ULN |
| II    | Not ISS stage I or II  
       Serum albumin <3.5 g/dL | Not R-ISS stage I or II |
| III   | Serum beta-2 microglobulin ≥5.5 mg/L | High-risk cytogenetics  
       OR  
       Serum LDH > ULN |

* R-ISS groups must also fit the original ISS stage
M-SMART Cytogenetic Classification

<table>
<thead>
<tr>
<th>High Risk</th>
<th>Intermediate Risk</th>
<th>Standard Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Deletion 17p</td>
<td>• (4;14) translocation</td>
<td>• (11;14) translocation</td>
</tr>
<tr>
<td>• (14;16) translocation</td>
<td>• Gain 1q</td>
<td>• (6;14) translocation</td>
</tr>
<tr>
<td>• (14;20) translocation</td>
<td></td>
<td>• All others</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Factor</th>
<th>High Risk</th>
<th>Intermediate Risk</th>
<th>Standard Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>20%</td>
<td>20%</td>
<td>60%</td>
</tr>
<tr>
<td>Median Overall Survival</td>
<td>3 years</td>
<td>4-5 years</td>
<td>8-10 years</td>
</tr>
</tbody>
</table>
Prognostic factors

- Tumor burden – ISS, R-ISS
- Cytogenetic Risk – mSMART
- Performance status, co-morbidities
- Increased plasma cell proliferation rate
- LDH level, SCr, platelet count
- Age
- Response to therapy (minimal residual disease)
Risk Factors for Disease Development

• Male
• African American
  • Incidence twice as high due to higher MGUS prevalence
• Older age (>60 years old)
• Overweight/obesity
• Ionizing radiation history
• Pesticide exposure
• Chronic infection
Question 1

GM is a 66 YOF who presents to the emergency department with pain and fatigue. Several tests are ordered with the following results:

- SCr 2.2 mg/dL, eCrCl 32 mL/min
- Electrolytes: Na = 137, K = 5.3, Ca = 11.7 (corrected)
- CBC: Hgb = 9 g/dL (baseline 11.5), Platelets = 50 x 10⁹ cells/L
- X-ray: (see image)

Which of the following symptoms can NOT be attributed to multiple myeloma?

- A. Lytic bone lesions
- B. Hyperkalemia
- C. Renal dysfunction
- D. Fatigue
Question 2:

• GM’s bone marrow biopsy comes back positive for multiple myeloma. The team would like to start induction therapy for GM right away with the ultimate goal of stem cell transplant. Her CrCL has improved to 65 mL/min after treating her hypercalcemia.

• Which regimen below would be the preferred induction regimen for GM’s newly diagnosed multiple myeloma?
  • A. Lenalidomide/ Dexamethasone
  • B. Bortezomib/ Cyclophosphamide/ Dexamethasone
  • C. Bortezomib IV weekly/ Lenalidomide/ Dexamethasone
  • D. Bortezomib SubQ weekly/ Lenalidomide/ Dexamethasone

CrCl = Creatinine Clearance
Question 3

GM presents to the emergency room with typical C.R.A.B. symptoms as well as a QTc prolongation of 500 milliseconds. She has detectable levels of M-protein in her blood and urine signifying a relapse in her multiple myeloma. GM completed her first round of induction therapy with Bortezomib/ Lenalidomide/ Dexamethasone 3 months ago. You also hear her mention how hard it was to come back to the hospital every week for an injection.

Which therapy is most appropriate to treat GM’s first relapsed multiple myeloma episode?

- A. Repeat induction therapy (Bortezomib/Lenalidomide/Dex)
- B. Panobinostat + Bortezomib + Dexamethasone
- C. Ixazomib + Lenalidomide + Dexamethasone
- D. Daratumumab + Bortezomib + Dexamethasone