Management of Multiple Myeloma: The Changing Paradigm

Supportive Care for Patients With Multiple Myeloma

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Question

Which of the following decreases the skeletal events (bone complications) in patients with myeloma?

A. Transfusions
B. Bisphosphonates (for example, Zometa or Aredia)
C. Iron and B12 supplements
D. All of the above
Question

Which of the following procedures is used for compression fractures in myeloma patients?

A. Kyphoplasty or vertebroplasty
B. Massage and chiropractic manipulations
C. Radiation
D. Iron and B12 supplements

Effects of Myeloma

- Low blood counts
- Bone damage
- Decreased kidney function
Effects of Myeloma: Bone Disease

- Occurs in 85% of patients
- Weakened bone due to lesions or “holes”
- Increased levels of calcium in the blood (hypercalcemia)
- Leads to
  - Fractures
  - Spinal cord compression/collapse

Lytic Lesions

(images of lytic lesions)
Bisphosphonates for Myeloma Bone Disease

**How they work**
- Prevent bone disease from getting worse
- Slows bone destruction
- Does not build bone

**Benefits**
- Decreases pain and reduces fractures
- Anti-myeloma effect (Zometa): increases in survival time in one major study

**Dosing**
- IV infusion in doctor's office every 3–4 weeks

**Medication types**
- Zometa (zoledronic acid): at least over 15-minute infusion
- Aredia (pamidronate): 2-hour infusion

**Side effects**
- Reduced kidney function
- Fracture of the femur
- Osteonecrosis of the jaw (ONJ): painful exposed bone in the jaw

**OC, osteoclast (inhibited, halting bone break-down); BP, bisphosphonate**

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**Bisphosphonates: Unanswered Questions**

- For whom?
- Agent of choice?
- How long?
- How frequent? Every month or every 3 months?

**My approach:**
- All patients with symptomatic myeloma
- Prefer Zometa given survival benefit in UKMRC IX study
- Monthly initially for at least 1–2 years
- After that time: less frequently based on response (every 3 months for most patients; consider every 6 months for patients in complete response; discontinue in select patients)
Reducing the Risk of ONJ: Oral Health Recommendations

- Complete major dental work before beginning bisphosphonate therapy
- Practice good oral hygiene
- Schedule regular dental visits
- Let your dentist know that you are receiving bisphosphonates
- Manage dental problems by the least invasive strategy
- Keep your doctor informed of dental issues/need for dental work
- Be attentive! ONJ seems to be related to the length of time patients are on bisphosphonates

Osteonecrosis of the Jaw (ONJ)

- Incidence: about 0.5%/year
- Lower incidence with less frequent bisphosphonates
- Management:
  - Seek expert dental evaluation
  - Avoid further bisphosphonates (unless absolutely needed)
  - Avoid major surgical interventions
  - Antibiotics: Pen VK
  - Mouthwashes: Peridex
Orthopedic Procedures to Stabilize the Spine

- Minimally invasive procedures
- Can be performed without hospitalization
- Small incision
- Cement filler stabilizes bone
- Potential for relatively rapid symptom relief (Lazarus effect) (approximately 1 month with kyphoplasty)

Vertebroplasty Kyphoplasty

Radiation Therapy for Pain Management
Additional Medications May Help Treat Bone Problems

Bone Support Drugs Being Studied

<table>
<thead>
<tr>
<th>Drug</th>
<th>Type</th>
<th>Clinical Trial</th>
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<tbody>
<tr>
<td>Xgeva* (denosumab)</td>
<td>Monoclonal antibody, RANKL inhibitor</td>
<td>• Phase 3 study in progress</td>
</tr>
<tr>
<td>Sotatercept (ACE 011)</td>
<td>Activin-A inhibitor</td>
<td>• Phase 2 study completed</td>
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*FDA approved to prevent fracture, spinal cord compression, or the need for radiation or surgery to bone in patients with bone metastases from solid tumors.

Effects of Myeloma: Low Blood Counts

- Low red blood cells = anemia
- Low white blood cells = neutropenia; can lead to infection
- Low platelets = thrombocytopenia
Anemia
(Low Red Blood Cell Count)

**Symptoms**
- Fatigue
- Depression/mood changes
- Difficulty breathing
- Weight loss
- Rapid heartbeat
- Nausea
- Dizziness
- Difficulty sleeping

**Other causes**
- Low levels of iron, folate, and vitamin B12

**Treatment**
- Identify and treat causes other than myeloma
- Supplements
- Medications to increase number of red blood cells
- Blood transfusions

Neutropenia
(Low White Blood Cell Count)

**Infection prevention**
- Vaccination (pneumonia, flu)
- Treatment with intravenous IgG
- Antifungal medications
- Antiviral prophylaxis, in some cases (herpes zoster) especially with proteasome inhibitors
- Preventive antibiotics (controversial)

**Treatment**
- Medications to stimulate production of white blood cells
- Antibiotics
- Antifungal medications
Effects of Myeloma: Decreased Kidney Function

- Detection
  - Decreased amount of urine is one sign
  - Blood test: increase in creatinine and other proteins
- Other causes beside myeloma
  - Hypertension
  - Diabetes
  - Some medications
- Treatment
  - Fluids
  - Avoid nonsteroidal anti-inflammatory drugs such as Aleve, Advil/Motrin
  - IV contrast for CT scans
  - Plasmapheresis?
  - Treat other causes
  - Dialysis (severe)

Lifestyle Enhancements

- Eat better
- Get more exercise
- Regular sleep
- Decrease alcohol consumption
- Give up tobacco
- Minimize or eliminate stress
Side Effects Management Pearls

• Revlimid/Pomalyst
  – Cramps: L-glutamine 500 mg (1–2 tabs with meals)
  – Diarrhea: avoid dairy; fibers (Metamucil); Imodium; colestipol; cholestyramine; dose reduction
  – Blood clots: prevention (aspirin or anticoagulants; stay active)
  – Fatigue: sleep hygiene, regular exercise, dose reduction

Velcade-Induced Neuropathy

• An ounce of prevention...
  – COMMUNICATE with your treatment team
  – SC vs IV
  – Weekly vs twice weekly
  – Dose modification
  – +/- vitamins!
• Management
  – Discontinue offending agent (non-neurotoxic PI)
  – Consider amyloid, other etiologies (radicular pain, mononeuritis)
  – Pain control: gabapentin, pregabalin, duloxetine, opioids (methadone)
  – Physical therapy
  – Two third get better within 3–6 months
Kyprolis

- Hypertension: common; beware of fluid overload; anti-hypertensives
- Cardiac: decreased ejection fraction; atrial fibrillation; coronary spasms.
  - Close collaboration with cardiology; these cardiac events are not uncommon in some clinical settings
  - Pretreatment evaluation in at risk population: >75 years, amyloid, existing heart disease

Summary: Supportive Care for Patients With Multiple Myeloma

- Various approaches are used to reduce the impact of common multiple myeloma complications
  - Bone damage/loss
  - Low blood counts
    - Anemia
    - Risk of infection due to low white blood counts
  - Reduced kidney function

Partner with your health care team to determine the best management plan for you.