Plasma Cell Neoplasms

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MULTIPLE MYELOMA
A plasma cell neoplasm

- Malignant plasma cell proliferation in the BM
- Monoclonal Immunoglobulin (or kappa or lambda light chain) in serum ± urine
Criteria for Diagnosis of Myeloma


**MGUS**
- <3 g M spike
- <10% PC

**Smouldering MM**
- ≥3 g M spike
- OR ≥10% PC

**Active MM**
- M spike +
- ≥10% PC

**End organ damage (CRAB)**
- HyperCalcemia
- Renal failure
- Anemia
- Bone lesions
- Recurrent bacterial infection, hyperviscosity, amyloidosis

**No end organ damage**
- MGUS → MM 1%/yr
- Smouldering MM → MM 10%/yr

**Treatment**
- Watchful waiting, serial monitoring M protein
## Risk Stratification Model for MGUS

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>No. of patients</th>
<th>Relative risk</th>
<th>Absolute risk of progression (ARP) at 20 years</th>
<th>ARP at 20 years with death as a competing risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk stratification model</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Low-risk</strong> (serum M spike &lt;1.5g/dL, IgG subtype, normal FLC ratio 0.26-1.65)</td>
<td>449</td>
<td>1</td>
<td>5%</td>
<td>2%</td>
</tr>
<tr>
<td><strong>Low-Intermediate-risk</strong> (Any 1 factor abnormal)</td>
<td>420</td>
<td>5.4</td>
<td>21%</td>
<td>10%</td>
</tr>
<tr>
<td><strong>High-Intermediate-risk</strong> (Any 2 factors abnormal)</td>
<td>226</td>
<td>10.1</td>
<td>37%</td>
<td>18%</td>
</tr>
<tr>
<td><strong>High-risk</strong> (All 3 factors abnormal)</td>
<td>53</td>
<td>20.8</td>
<td>58%</td>
<td>27%</td>
</tr>
</tbody>
</table>

Multiple Myeloma


98% >40 years old
61% Males
68% Bone pain (back, ribs)
62% Anemia (normochromic normocytic, Rouleaux)
88% Proteinuria
49% Bence Jones Proteinuria
79% Lytic bone lesions, pathologic fractures

Bone X-RAY survey, MRI (most sensitive) or CT

55% Renal Failure (2nd to light chain deposition + high Ca)
30% Hypercalcemia (confusion, disorientation, constipation, polyuria, polydipsia, weakness, suppressed PTH)
21% Hepatomegaly

Others  Recurrent bacterial infections, hypogamma, hyperviscosity
Lytic bone lesions in Multiple Myeloma
Punched out skull lesions in myeloma
Myeloma Work-up

- **Blood work**
  - CBC, diff
  - CRP quantitative
  - CMP, LDH, Ca, Uric acid, *albumin*
  - SPEP and immunofix
  - Serum IgG, A, M + D and E
  - Serum free-kappa and lambda
  - Beta-2 microglobulin
  - Erythropoietin level (if anemic)
- **Urine**
  - 24-hour UPEP, immunofix, free LC
- **BM asp/bx**
  - Wright-Giemsa + k/l immunostain
  - Flow (CD34, 38, 138, 10, 19, 20)
  - Cytogenetics and FISH
    - Hyperdiploid, t(11:14)
    - 13q-, 17p-, t(4:14)
  - Oncogenomics

**Check to see if**
1. Bone disease, hyper Ca
2. Renal failure
3. Dehydration
4. Anemia
5. Hyperviscosity
6. Infection
7. Amyloid signs and sx
   - Heart failure
   - Neuropathy
   - Macroglossia
   - Nephrotic syndrome
   - Racon eyes

- **Imaging**
  - Skeletal survey
  - PET
  - MRI
SPEP - Serum Protein Immunoelectropheresis

Patient

Control
Serum Protein Immunofixation
Serum Protein Immunofixation

(Light-chain myeloma)
Bone marrow aspirate in Multiple Myeloma
Bone marrow flow cytometry in Multiple Myeloma

CD38+, lambda+, kappa- population
Pathway for a patient with suspected AL amyloidosis.

Plasmacytoma
# International Staging System (ISS) for Myeloma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Criteria</th>
<th>Median Survival (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>$\beta_2m &lt; 3.5 , \text{mg/L}$&lt;br&gt;$\text{albumin} \geq 3.5 , \text{g/dL}$</td>
<td>62</td>
</tr>
<tr>
<td>II*</td>
<td>Not stage I or III</td>
<td>44</td>
</tr>
<tr>
<td>III</td>
<td>$\beta_2m &gt; 5.5 , \text{mg/L}$</td>
<td>29</td>
</tr>
</tbody>
</table>

*$\beta_2m < 3.5 \, \text{mg/L}$ and $\text{albumin} < 3.5 \, \text{g/dL}$ or $\beta_2m$ $3.5 \text{ - } < 5.5 \, \text{mg/dL}$, any albumin

**Others prognostic indicators:** LDH, Cytogenetics/FISH, DNA microarray

*Greipp et al. J Clin Oncol 2005; 23: 3412-20*
Chromosomes and Prognosis in Multiple Myeloma

Nonhyperdiploid worse prognosis than hyperdiploid

For conventional therapy
- \( t(11;14), \) hyperdiploidy \( \Rightarrow \) standard risk
- \( t(4;14), \) del(17p), del(13q14) \( \Rightarrow \) high risk

Novel treatment approaches can overcome high risk cytogenetic abnormalities, i.e. bortezomib
Life expectancy is doubled in MM Now, average 5 years after diagnosis

Kumar S K et al. Blood 2008;111:2516-20

Longer survival is directly related to depth of response to therapy
# International Myeloma Working Group Uniform Response Criteria: CR and Response Categories

<table>
<thead>
<tr>
<th>Response subcategory</th>
<th>Response criteria&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>sCR</td>
<td>CR as defined below plus</td>
</tr>
<tr>
<td></td>
<td>Normal FLC ratio and</td>
</tr>
<tr>
<td></td>
<td>Absence of clonal cells in bone marrow&lt;sup&gt;b&lt;/sup&gt; by immunohistochemistry or immunofluorescence&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>CR</td>
<td>Negative immunofixation on the serum and urine and Disappearance of any soft tissue plasmacytomas and ≤5% plasma cells in bone marrow&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>VGPR</td>
<td>Serum and urine M-protein detectable by immunofixation but not on electrophoresis or 90% or greater reduction in serum M-protein plus urine M-protein level &lt; 100 mg per 24 h</td>
</tr>
<tr>
<td>PR</td>
<td>≥50% reduction of serum M-protein and reduction in 24-h urinary M-protein by ≥90% or to &lt;200 mg per 24 h If the serum and urine M-protein are unmeasurable, &lt;sup&gt;d&lt;/sup&gt;a ≥50% decrease in the difference between involved and uninvolved FLC levels is required in place of the M-protein criteria If serum and urine M-protein are unmeasurable, and serum free light assay is also unmeasurable, ≥50% reduction in plasma cells is required in place of M-protein, provided baseline bone marrow plasma cell percentage was ≥30% In addition to the above listed criteria, if present at baseline, a ≥50% reduction in the size of soft tissue plasmacytomas is also required</td>
</tr>
<tr>
<td>SD (not recommended for use as an indicator of response; stability of disease is best described by providing the time to progression estimates)</td>
<td>Not meeting criteria for CR, VGPR, PR or progressive disease</td>
</tr>
</tbody>
</table>

Abbreviations: CR, complete response; FLC, free light chain; PR, partial response; SD, stable disease; sCR, stringent complete response; VGPR, very good partial response.

<sup>a</sup>All response categories require two consecutive assessments made at anytime before the institution of any new therapy; all categories also require no known evidence of progressive or new bone lesions if radiographic studies were performed. Radiographic studies are not required to satisfy these response requirements.

<sup>b</sup>Confirmation with repeat bone marrow biopsy not needed.

<sup>c</sup>Presence/absence of clonal cells is based upon the k/λ ratio. An abnormal k/λ ratio by immunohistochemistry and/or immunofluorescence requires a minimum of 100 plasma cells for analysis. An abnormal ratio reflecting presence of an abnormal clone is k/λ of >4:1 or <1:2.

<sup>d</sup>Refer to Table 4 for definitions of measurable disease.
Improvement in survival of patients with myeloma is due to

- Initial (Induction) therapy with **novel agents** (3-4 months)
- Stem Cell Transplantation ➔ Highest CR rate
- Post-transplant Maintenance ➔ Some additional benefit
- Supportive Care (Critical)
- Treatment of Relapsed Disease (Possible but expensive)
Thalidomide

- Marketed as a sedative in the 1950s
- In 1961, it was discovered to be teratogenic, affecting 10,000 infants and was taken off the market
- In 1997, Dr. Barlogie found that it was antiangiogenic in myeloma
- In 84 patients treated, response rate was 32% (Singhal S et al. NEJM 1999)
Lenalidomide

- An analog of thalidomide, immunomodulator
- Overall response rate was 71% in patients with relapsed or refractory myeloma
- In an upfront trial, lenalidomide + dexamethasone → RR: 31/34 (91%) (Rajkumar SV et al. Blood 2005)
- Approved by the FDA in 2006
- Preferred in the setting of peripheral neuropathy
Bortezomib

- Inhibition of proteasome causes apoptosis, predominantly in the malignant and proliferating cells
- Robert Orlowski showed striking anti-myeloma (9/9 patients) activity (Orlowski RZ et al. JCO 2002)
- Approved by the FDA for myeloma in 2003
- Preferred in the setting of renal impairment, t(4;14), or advanced disease
Carfilzomib: A Novel Proteasome (Chymotryptic) Inhibitor

- Novel chemical class with highly selective and irreversible proteasome binding
- Improved antitumor activity with consecutive day dosing
- No neurotoxicity in animals
- Durable responses in relapsed/refractory MM w/o neuropathy

- Carfilzomib lenalidomide Dex versus lenalidomide Dex phase III trial for new drug approval

1 Demo et al. (2007), Cancer Research, 67:6383  
Siegal et al ASH 2010
Approach to the treatment of newly diagnosed myeloma in patients eligible for transplantation (A) and not eligible for transplantation (B). *For patients who choose delayed ASCT, dexamethasone usually discontinued after 12 months and continued long-term len...
## Response to First ASCT
### Evaluable Patients

**Harousseau et al, ASH 2008**

<table>
<thead>
<tr>
<th></th>
<th>VAD (A1+A2)</th>
<th>Vel-Dex (B1+B2)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=213</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CR</strong></td>
<td>9%</td>
<td>17%</td>
<td>0.016</td>
</tr>
<tr>
<td><strong>CR + nCR</strong></td>
<td>19%</td>
<td>37%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>≥ VGPR</strong></td>
<td>38%</td>
<td>57%</td>
<td>0.0003</td>
</tr>
<tr>
<td><strong>≥ PR</strong></td>
<td>79%</td>
<td>84%</td>
<td>NS</td>
</tr>
<tr>
<td><strong>MR/SD/PD</strong></td>
<td>4%</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td><strong>No ASCT</strong></td>
<td>17%</td>
<td>13%</td>
<td></td>
</tr>
</tbody>
</table>
Upfront Induction Treatments of MM

Stewart AK, Richardson PG, San Miguel JF Blood 2009
## Summary of Results of Randomized Trials Comparing Single Autotransplant with Conventional Therapy

<table>
<thead>
<tr>
<th>CR %</th>
<th>IFM90(^1)</th>
<th>MRC7(^2)</th>
<th>PETHEMA(^3)</th>
<th>USIG(^4)</th>
<th>IMMSG(^5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC 10%</td>
<td>5</td>
<td>9</td>
<td>11</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>ASCT 30%</td>
<td>21</td>
<td>44</td>
<td>30</td>
<td>17</td>
<td>26</td>
</tr>
</tbody>
</table>

**Improvement in EFS with ASCT (9 months)**

| Improvement in EFS with ASCT (9 months) | 9 | 12 | 8 | 4 | 12 |

**Improvement in OS with ASCT (12 months)**

| Improvement in OS with ASCT (12 months) | >23 | 12 | 5 | 5 | 15 |

**References:**
1 – Attal et al; 2 – Child et al; 3- Blade et al; 4- Barlogie et al; 5- Italian Study Group, Turin 2004

**NOTE:** colored values indicate statistical significance
Double Autotransplantation Improves Survival in MM

IMF 94  399 pts

### Autotransplantation (m 140 mg/m² 8Gy) vs Autotransplantation (m 140 mg/m² 8Gy)

<table>
<thead>
<tr>
<th></th>
<th>Autotransplant (m 140 mg/m² 8Gy)</th>
<th>Autotransplant (m 140 mg/m² 8Gy)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR/VGPR</td>
<td>42%</td>
<td>50%</td>
<td>0.10</td>
</tr>
<tr>
<td>7 yr prob EFS</td>
<td>10%</td>
<td>20%</td>
<td>0.03</td>
</tr>
<tr>
<td>7 yr prob OS</td>
<td>21%</td>
<td>42%</td>
<td>0.01</td>
</tr>
<tr>
<td>7 yr prob OS (no VGPR)</td>
<td>11%</td>
<td>43%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Low β2m, young age, low LDH, and treatment are associated with longer survival

Pamidronate With or Without Thalidomide as Post-transplantation Maintenance Therapy

<table>
<thead>
<tr>
<th>CR/VGPR</th>
<th>No maintenance</th>
<th>Pamidronate</th>
<th>Pamidronate+Thal</th>
<th>P=0.03</th>
</tr>
</thead>
<tbody>
<tr>
<td>3yr EFS</td>
<td>36%</td>
<td>37%</td>
<td>52%</td>
<td>p&lt;0.009</td>
</tr>
<tr>
<td>4 yr OS</td>
<td>77%</td>
<td>74%</td>
<td>87%</td>
<td>p&lt;0.04</td>
</tr>
</tbody>
</table>

Longer EFS significantly associated with: low beta2m (p<0.03); treatment arm (p<0.02); lack of del 13 (p<0.03); and lack of VGPR to transplant (p<0.004).

No decrease in bone events with maintenance pamidronate

CALGB 100104 Schema

Registration

Restaging Days 90–100

Randomization

S-D Stage 1-3, <70 years
≥ 2 cycles of induction
Attained SD or better
≤1 yr from start of therapy
2 x 10^6 CD34 cells/kg

Mel 200

ASCT

CR

PR

SD

Placebo

Lenalidomide*
10 mg/d with ↑↓ (5–15 mg)

McCarthy et al ASCO 2010

Stratification based on diagnostic β-2M and thalidomide and lenalidomide use during Induction
ITT Analysis with a Median Follow-up from transplant of 18 months as of 12/17/2009 ($p < 0.0001$)
OS based on all follow-up forms to Nov 2010 on an ITT basis ($p<0.078$)}
Continued Therapy, Second Cancers

- In January, 2010, 122 lenalidomide patients and 86 placebo patients were receiving lenalidomide.
- As of Feb 2011, 101 lenalidomide patients have received lenalidomide within 6 months and 26 have not for > 6 months.
- As of Feb 2011, 52 placebo patients have received lenalidomide within 6 months and 34 have not received lenalidomide for > 6 months.
- No 2\textsuperscript{nd} cancers in cross over placebo patients as of Feb 2011.
- 30 new cancers reported out of 568 registered patients (5.3\%, 4.0\% excluding all skin cancers) at a median follow-up of 26 months (Feb 2011).
- **Lenalidomide 14/231 (6\%) versus Placebo 4/229 (2\%)** excluding pre randomization and non-melanoma skin cancers (Feb 2011).
IFM 2005-02: Study design

Phase III randomized, placebo-controlled trial
N= 614 patients, from 78 centers, enrolled between 7/2006 and 8/2008

**Patients** < 65 years, with non-progressive disease, ≤ 6 months after ASCT in first line

Randomization: stratified according to Beta-2m, del13, VGPR

**Consolidation:**
Lenalidomide alone 25 mg/day p.o.
days 1-21 of every 28 days for 2 months

**Arm A=**
Placebo
(N=307)
until relapse

**Arm B=**
Lenalidomide
(N=307)
10-15 mg/d until relapse

**Primary end-point:** PFS,
**Secondary end-points:** CR rate, TTP, OS, feasibility of long-term lenalidomide….

Atal et al, ASCO, 2010
IFM 2005-02: PFS from randomization

p < 10^{-7}
## Grade 3-4 Adverse Events during treatment

<table>
<thead>
<tr>
<th>AE (grade 4)</th>
<th>Arm A</th>
<th>Arm B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>2% (1%)</td>
<td>4% (2%)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>6% (2%)</td>
<td>12% (5%)</td>
</tr>
<tr>
<td><strong>Neutropenia</strong></td>
<td><strong>14% (3%)</strong></td>
<td><strong>43% (11%)</strong></td>
</tr>
<tr>
<td>Febrile Neutropenia</td>
<td>0%</td>
<td>2% (1%)</td>
</tr>
<tr>
<td>Infections</td>
<td>5% (1%)</td>
<td>10% (1%)</td>
</tr>
<tr>
<td>DVT</td>
<td>0%</td>
<td>2% (0.3%)</td>
</tr>
<tr>
<td>Skin disorders</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0%</td>
<td>1%</td>
</tr>
<tr>
<td>Peripheral Neuropathy</td>
<td>0.3%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Hematologic malignancies (n)</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Non hematologic malignancies (n)</td>
<td>1</td>
<td>6</td>
</tr>
</tbody>
</table>

Discontinuation for AE: placebo = 15% vs lenalidomide = 21%
Treatment in transplant ineligible patients
Phase III Trial: MP vs MPR vs MPR-R

N=459, 82 centers in Europe, Australia and Israel

Cycles (28-day) 1-9

MPR-R
M: 0.18 mg/kg, days 1-4
P: 2 mg/kg, days 1-4
R: 10 mg/day po, days 1-21

MPR
M: 0.18 mg/kg, days 1-4
P: 2 mg/kg, days 1-4
R: 10 mg/day po, days 1-21

MP
M: 0.18 mg/kg, days 1-4
P: 2 mg/kg, days 1-4
PBO: days 1-21

Cycles 10+

Lenalidomide Continued Tx

10 mg/day,
days 1-21

Disease progression

Lenalidomide
(25 mg/day)
+/-
dexamethasone

Stratified by age (≤ 75 vs. > 75 years) and stage (ISS 1,2 vs. 3)

Palumbo et al, ASH 2009

M, melphalan; P, prednisone; R, lenalidomide; PBO, placebo.
# Best Response: MP vs MPR vs MPR-R

<table>
<thead>
<tr>
<th>Best Overall Response&lt;sup&gt;a&lt;/sup&gt;</th>
<th>MPR-R&lt;sup&gt;1&lt;/sup&gt; N = 152</th>
<th>MPR N = 153</th>
<th>MP N = 154</th>
<th>P Value (MPR-R vs. MP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR</td>
<td>77%</td>
<td>67%</td>
<td>49%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CR&lt;sup&gt;b&lt;/sup&gt;</td>
<td>18%</td>
<td>13%</td>
<td>5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥ VGPR&lt;sup&gt;c&lt;/sup&gt;</td>
<td>32%</td>
<td>33%</td>
<td>11%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PR</td>
<td>45%</td>
<td>34%</td>
<td>37%</td>
<td>---</td>
</tr>
<tr>
<td>Progressive Disease</td>
<td>0%</td>
<td>1%</td>
<td>0%</td>
<td>---</td>
</tr>
<tr>
<td>Median time to first response, months</td>
<td>1.9</td>
<td>1.9</td>
<td>2.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

<sup>a</sup> As measured using EBMT criteria<sup>1</sup>

<sup>b</sup> Immunofixation negative with or without bone marrow confirmation

<sup>c</sup> VGPR: >90% reduction in M-protein

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Palumbo et al, ASH 2009
MPR-R vs. MPR
47% Reduced Risk in PFS

Palumbo et al, ASH 2009

Median PFS
- MPR-R: Not reached
- MPR: 13.2 months

HR 0.530
95% CI [0.350, 0.802]
Logrank P=0.002

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>MPR-R</th>
<th>MPR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>152</td>
<td>153</td>
</tr>
<tr>
<td>5</td>
<td>115</td>
<td>122</td>
</tr>
<tr>
<td>10</td>
<td>70</td>
<td>78</td>
</tr>
<tr>
<td>15</td>
<td>36</td>
<td>20</td>
</tr>
<tr>
<td>20</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>25</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>30</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

PFS Time (months)

Patients without Event (%)
VISTA: VELCADE as Initial Standard Therapy in multiple myeloma: Assessment with melphalan and prednisone

- Randomized, international, phase III trial of VMP vs MP in previously untreated MM patients who were not candidates for HDT-ASCT
- Patients: Symptomatic multiple myeloma/end organ damage with measurable disease
  - ≥65 yrs or <65 yrs and not transplant-eligible; KPS ≥60%

**VMP**
- Cycles 1-4
  - Bortezomib 1.3 mg/m² IV: days 1,4,8,11,22,25,29,32
  - Melphalan 9 mg/m² and prednisone 60 mg/m² days 1-4
- Cycles 5-9
  - Bortezomib 1.3 mg/m² IV: days 1,8,22,29
  - Melphalan 9 mg/m² and prednisone 60 mg/m² days 1-4

**MP**
- Cycles 1-9
  - Melphalan 9 mg/m² and prednisone 60 mg/m² days 1-4

9 x 6-week cycles (54 weeks) in both arms

- Primary Endpoint: TTP
- Secondary Endpoints: CR rate, ORR, TTR, DOR, PFS, TNT, OS, QoL (PRO)

San Miguel et al, ASH 2008 Abstr 650
VISTA: VMP vs MP Updated Follow-Up and Results of Subsequent Therapy

Mateos et al ASH 2009

- Updated data with over 3-year follow-up confirm that VMP results in **significantly longer OS** vs. MP
- Subsequent salvage therapies were similarly effective in pts from both arms, demonstrating that use of bortezomib does not preclude use of novel agents at relapse
- Retreatment with bortezomib-based therapies resulted in a 47% ORR
Supportive Care

• Bisphosphonates
  – Reduces SREs
    • Morgan G. MRC Myeloma IX. Lancet Oncol. 2011
  – Associated with improved survival in the MRC trial
    • Morgan G. MRC Myeloma IX. Blood. 2012

• Vertebroplasty/Kyphoplasty
  – Pain control in vertebral compression and collapse

• Anti-microbials
ASCO Clinical Practice Guidelines
Bisphosphonates:

• Indicated for MM pts w/ lytic bone disease or osteopenia
• Reduce skeletal events such as fractures
• Useful as an adjunct for pts w/ bone pain
• The bisphosphonates recommended are either
  – Zoledronic acid: 4 mg over 15 mins, IV q 3-4 wks
  – Pamidronate (PAM): 90 mg over > 2 hrs, IV q 3-4 wks
• Monitoring serum creatinine (both BPs) and/or urine albumin (for palmidronate only)
• PAM preferred in setting of renal dysfunction
• Re-evaluate after 2 years and stop if stable disease
• Potential side effects:
  • Hypocalcemia
  • Renal dysfunction
  • Osteonecrosis of jaw (ONJ)

Kyle R, et al. JCO. 200725: 2464-2472
Questions?