

1 **Multiple myeloma: an overview and looking into the future**

Ola Landgren, MD; Mary Ann Yancey, RN; Marcia Mulquin, RN
www.multiplemyeloma.cancer.gov

2 **Outline**

- Clinical presentation of multiple myeloma (symptoms, diagnosis, prognosis, basic therapeutic strategies, complications)
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- Risk stratify myeloma precursor disease
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- Future directions for multiple myeloma and its precursor disease (new therapeutic strategies, new types of drugs, role of early intervention)

3 **Previously healthy 64-year-old man**

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- Presents with persistent pain in his lower back and fatigue
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- CBC reveals a hemoglobin level of 9.6 g/dL
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- A monoclonal-(M)-protein is detected on serum protein electrophoresis (IgG kappa)
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- Radiologic skeletal bone survey shows lytic bone lesions of the vertebrae and the pelvis

4 **Previously healthy 64-year-old man**

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- Multiple myeloma (MM) is confirmed by bone marrow aspiration showing infiltrate of plasma cells
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- Serum calcium and creatinine levels are normal
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- Albumin is 3.7 g/dL and beta2-microglobulin is 2.8 mg/L
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- Fluorescence in situ hybridization (FISH) of bone marrow plasma cells shows deletion of chromosome 13

5 **Previously healthy 64-year-old man**

- Interpretation:
 - Relatively young age
 - Absence of coexisting illnesses
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- A hematologist recommends:
 - Induction therapy followed by...
 - High-dose therapy with autologous hematopoietic stem-cell transplantation (ASCT) as initial treatment

6 **Multiple myeloma in the U.S.**

- 20,580 new cases (11,680 men; 8,980 women) and 10,580 deaths per year
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- Average age at dx 65-70 yrs (<40 yrs; ~2%)

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- The 2nd most common hematologic malignancy in whites; in Blacks it is #1

7 **Myeloma an increasing problem due to the aging population**

8 **Symptoms**

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11 **Clinical work-up
and diagnostic criteria**

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17 **Differential diagnosis**

- MGUS
- SMM
- Solitary plasmacytoma
- Amyloidosis
- Light chain deposition disease
- Waldenström's macroglobulinemia
- Lymphoproliferative disorders
- Infections (e.g. CMV)
- Rheumatologic autoimmune disorders
- Certain skin or neurologic disorders

18 **Prognosis**

19 **Overall survival according to age
and date of diagnosis**

20 **Current clinical tools**

21 **Mayo Clinic "mSMART 2.0 classification" of active MM**

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24 **Current treatment principles**

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26 **Old treatment strategy before novel drugs**

27 **Three of our novel myeloma drugs**

28 **Transplant eligible and transplant ineligible patients**

29 **Transplant eligible and transplant ineligible patients**

30 **Treatment strategies for relapsed/refractory patients**

- Initial treatment can be repeated in selected patients
 - Commonly used with alkylating agents (cyclophosphamide + prednisone is alternative to repeated MP)
 - Also high-dose melphalan + ASCT
 - Data emerging that novel agents can be used again
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- Novel agents can be introduced
 - As single agents
 - With steroids
 - In 3-4 drug regimens with conventional chemotherapy and/or other novel agents

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Upfront therapy
for multiple myeloma

33 **High response rates prior high-dose melphalan/ASCT**

34 **Upfront versus delayed high-dose melphalan therapy/ASCT**

- Primary objectives: determine the MTD and response rate of RVD at MTD
- Secondary objectives: response rates, DOR, PFS (with/without ASCT), OS, toxicity, stem cell collection/engraftment

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37 **IFM 2005-02: study design**

38 **IFM-2005-02: survival outcomes**

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40 **CALGB 100104: survival outcomes**

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Characterizing Natural Hx of MGUS and SMM Vascularity: IHC and DCE-MRI

46 **High Risk SMM with Aggressive Features**

47 **Current (IMWG 2010) clinical recommendations for SMM**

- Baseline bone marrow biopsy and skeletal survey
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- Repeat pertinent lab tests 2-3 months after initial recognition. If stable, repeat every 4-6 months for a year, and if stable every 6-12 months
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- Treatment is not indicated unless it is part of a clinical trial. Consider clinical trials for selected patients; with the aim to delay and/or prevent progression to symptomatic myeloma

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51 **Skeletal bone survey
– still the gold standard...**

52 **SMM patient with back pain; skeletal survey was negative**

53 **Molecular imaging from MGUS to MM**

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62 **Clinical myeloma studies
at NCI in 2011-**

- Precursor disease (MGUS and smoldering myeloma)
 - Natural history study (individualized profiling)
- Smoldering myeloma treatment
 - Anti-KIR
 - Carfilzomib (*coming soon*)
 - Oral proteasome inhibitor (*coming soon*)
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