Multiple Myeloma.

The term multiple myeloma is considered to be synonymous with myeloma, plasma cell myeloma, active and symptomatic myeloma.

The intent is to positively identify patients with active or symptomatic myeloma requiring systemic therapy.

CLINICAL MANIFESTATION

- **CRAB . The four major areas of dysfunction are:**

  [C], Calcium Elevation

  [R], Renal Insufficiency

  [A], Anemia

  [B], Bone Abnormalities (Lytic or Osteopenic)

Solitary plasmacytoma of Bone.

Patients with early stage

- myeloma must also be distinguished from those with an isolated or solitary
- plasmacytoma. Imaging must reveal only a single lesion wich is a biopsy
- proven plasmacytoma. Routine bone marrow biopsy is normal (<10% plasma cells) and there is no organ dysfunction.

DIAGNOSTIC CRITERIA: ALL 3 REQUIRED

1. Monoclonal plasma cells in the bone marrow > 10% and/or presence of a biopsy-proven plasmacytoma
2. Monoclonal protein present in the serum and/or urine
3. Myeloma-related organ dysfunction (1 or more)
   - [C] Calcium elevation in the blood {S. Calcium >10.5 mg/l or upper limit of normal}
   - [R] Renal insufficiency {S. Creatinine > 2 mg/dl}
   - [A] Anemia {Hemoglobin < 10 g/dl or 2 g < normal}

   [B] Lytic bone lesions or osteoporosis

Solitary Plasmacytoma of bone

DIAGNOSTIC CRITERIA: ALL 3 REQUIRED

- **1. Biopsy proven monoclonal plasmacytoma of bone in a single site only. X-rays and MRI and/or FDG PET imaging (if done) must be negative outside the primary site. The primary lesion may be associated with a low* serum and/or urine M-component.**
- **2. The bone marrow contains < 10% monoclonal plasma cells.**
- **3. No other myeloma related organ dysfunction.**

Required Testing for Possible Myeloma

- History and physical examination
- Complete blood count with differential and peripheral blood smear review
- Chemistry panel including calcium and creatinine
- Serum protein electrophoresis, immunofixation
- Nephelometric quantitation of immunoglobulins
- Routine urinalysis, 24-hour urine collection for electrophoresis and immunofixation. Quantification of both urine M-component level and albuminuria.

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- Bone marrow aspirate and trephine biopsy
- Bone survey including spine, pelvis, skull, humeri, and femurs. MRI of the axial skeleton is very informative if available/feasible but is not required. Whole body
- FDG/PET imaging is also not required, but can be used to confirm MGUS or exclude unsuspected and/or extramedullary myeloma, infection and/or an associated second malignancy.
- β2 microglobulin, C-reactive protein, and lactate dehydrogenase
- Measurement of free monoclonal light chains is an option if conventional Mcomponent quantitation is negative or equivocal.

DURIE AND SALMON STAGING SYSTEM

- ***Stage I (low cell mass)***
- All of the following:
- Hemoglobin value > 10 g/dl
- Serum calcium value normal or < 10.5 mg/dl
- Bone x-ray, normal bone structure (scale 0), or solitary bone plasmacytoma only
- Low M-component production rates:
  - IgG value < 5.0 g/dl
  - IgA value < 3.0 g/dl
  - Urine light chain M-component on electrophoresis < 4 g/24h

- ***Stage II***

  Fitting neither stage I nor stage III.
- ***Stage III (high cell mass) > 1,200 billion***

  One or more of the following:
  - Hemoglobin value < 8.5 g/dl
  - Serum calcium value > 12 mg/dl
  - Advanced lytic bone lesions (scale 3)
  - High M-component production rates
    - IgG value > 7.0 g/dl
    - IgA value > 5.0 g/dl
    - Urine light chain M-component on electrophoresis > 12 g/24h

SERUM ß2 MICROGLOBULIN (β2M) AND

- **SERUM ALBUMIN (S. Alb) STAGING**
- **SWOG STAGING SYSTEM* PROPOSED IPI SYSTEM**
- **Stage I β2M < 2.5 mg/dl β2M < 3.5; S. Alb> 3.5**
- **Stage II β2M > 2.5 < 5.5 mg/dl**

  β2M < 3.5; S. Alb < 3.5 or β2M 3.5 – 5.5
- **Stage III β2M > 5.5 mg/dl. S. Alb > 3.0 g/dl**
- **Stage IV β2M > 5.5 mg/dl NO STAGE IV**

  S. Alb < 3.0 g/d

FRONTLINE THERAPY

Options Comments

- **1. Melphalan/Prednisone Still an option, especially for elderly** patients
- **2. Cytoxan alone or in combination Can be useful alone or in combination with less stem cell injury than melphalan**
- **3. Alkylating agent combinations Really only an option if stem cell transplant is not planned**
- **4. VAD regimen Still a major frontline approach; all can ave significant disadvantages**
- **5. Dexamethasone or other steroids A one A valid option, especially with renal insufficiency and/or reduced blood count values**
- **6. Thalidomide plus dexamethasone A new oral option worthy of consideration but without a long track record**