1) **Review of Plasma Cell Disorders**

- **Asymptomatic (smoldering) myeloma**
  - M-protein in serum at myeloma levels (>3g/dL); and/or
  - 10% or more clonal plasma cells in bone marrow
  - **No** related organ or tissue impairment (no end organ damage or bone lesions)

- **Symptomatic plasma cell myeloma**
  - M-protein in serum or urine (no level is included)
  - Bone marrow clonal plasma cells or plasmacytoma
  - Related organ or tissue impairment (CRAB: hypercalcemia, renal insufficiency, anemia, bone lesion)

- **Oligosecretory Myeloma**
  - A subset of myeloma where the M-protein is very low in the serum (<1 g/dL) & urine (<200 mg/24 hours).
  - Disease can be followed using serum free light chain assay (FLC) provided the ratio is abnormal & the involved FLC level is >10 mg/dL at baseline.

- **Non-secretory myeloma**
  - A subset of myeloma where the serum & urine M-protein are absent by immunofixation electrophoresis.

- **Light Chain myeloma**
  - Characterized only by a light chain in the serum or urine & lacks expression of the immunoglobulin heavy chain.
  - Disease is readily detected by UPEP & urine immunofixation.
  - Incidence of renal failure is higher in light chain myeloma.

- **Primary Amyloidosis**
  - Caused by a plasma cell (or rarely a lymphoplasmacytic neoplasm) that secretes intact or fragments of abnormal immunoglobulin light chains (or rarely heavy chains), which deposit in various tissues & form β-pleated sheet structure (AL amyloid) that binds Congo red dye with characteristic birefringence.

- **Light chain deposition disease (LCDD)**
  - Similar to amyloidosis in that abnormal light chains deposit in tissues causing organ dysfunction but do not form amyloid β-pleated sheets or bind Congo red dye.

- **POEMS**
  - A rare syndrome that includes polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes.
  - 75-85% of patients have a serum M-protein that’s either IgG lambda or IgA lambda; the quantity is typically low (median 1.1g/dL).
  - Osteosclerotic myeloma (a plasma cell neoplasm characterized by fibrosis and osteosclerotic changes in the bone trabeculae) is often a component of POEMS. In other words, these patients will not have lytic lesions on skeletal survey, but rather sclerotic white looking lesions.
2) Determining appropriate baseline to use when determining disease status

3) How to best report disease status when not all testing is done

4) Case Studies (2-3)

5) Tools
Multiple Myeloma - Defining what baseline to use when determining the best response to HSCT

1) **HSCT is planned as part of initial therapy w/out prior disease progression or relapse.**
   The baseline used to determine the best response to HSCT is the disease parameters obtained at the time of diagnosis.

2) **Patients who have not received any chemotherapy within 6 months of HSCT, untreated relapse/progression or if the recipient has never been treated (rare).**
   The baseline used to determine the best response to HSCT would be the disease parameters obtained immediately prior (within 30 days) to the start of the preparative regimen (not the disease parameters at time of diagnosis).

3) **What if the patient had a disease progression or relapse of disease before HSCT?**
   If a patient had disease progression or relapse of disease & was treated to reduce the myeloma burden before any preparative regimen was given for HSCT, the baseline used to determine the best response to HSCT would be the disease parameters obtained at the time of the relapse or progression. In other words, the baseline is reset to the time of the relapse or progression. Therefore, the disease parameters obtained at diagnosis or immediately prior to the start of the preparative regimen would not be used as the baseline to determine the best response to HSCT.

4) **What if the patient had 2 or more disease progressions before HSCT?**
   The appropriate baseline to use would be the disease parameters documenting the most recent disease progression.

5) **What if the patient's initial therapy was changed to a different regimen due to toxicity & there was not a disease progression or relapse at any time prior to HSCT, what baseline is used to determine the best response to HSCT?**
   The baseline used to determine the best response to HSCT is the disease parameters obtained at the time of diagnosis.

6) **Tandem Transplantation w/out disease progression or relapse in between.**
   Since this is considered one treatment, the pre-HSCT baseline for determining the best response following the 2nd HSCT would be the same baseline used prior to the 1st HSCT (i.e. the disease parameters at diagnosis).

Reference: CRITERIA FOR EVALUATING DISEASE RESPONSE AND PROGRESSION IN PATIENTS WITH MULTIPLE MYELOMA TREATED BY HIGH-DOSE THERAPY AND HAEMOPOIETIC STEM CELL TRANSPLANTATION

10/28/10; updated 02/17/14
Multiple Myeloma Case Studies

Case #1

A 65 yo patient is diagnosed with IgG kappa myeloma.
- Serum M-spike = 6 g/dL (or 6000 mg/dL)
- 24-hr urine M-protein = 1000 mg/24 hrs
- Bone marrow biopsy- 40% plasma cells

Patient is treated with Velcade, Doxil & Dexamethasone (VDD) x 4 cycles

Patient re-evaluated after 4 cycles of VDD.
- Serum M-spike = 2400 mg/dL
- Bone marrow aspirate- 15% plasma cells
- Disease status- PR

Patient received Cytoxan for autologous stem cell mobilization. Labs were obtained immediately prior to the start of the prep regimen.
- Serum M-spike = 1600 mg/dL
- Bone marrow aspirate- 8% plasma cells

What is the patient’s disease status immediately prior to the start of the preparative regimen?
- A) Very Good Partial Remission (VGPR)
- B) Partial Remission (PR)
- C) Stable Disease (SD)
- D) I don’t know- not enough information provided to make determination

The patient underwent their autologous HCT. Lab studies were obtained at 60 & 100 days post HCT.
- SPEP/UPEP are negative for an M-spike at Day 60 & 100
- Serum & Urine Immunofixation are positive for IgG kappa at Day 60 & 100
- Bone marrow biopsy <5% plasma cells at Day 100

What disease response would you report for this recipient at 100 days post-HCT?
- A) Partial Remission (PR)
- B) Very Good Partial Remission (VGPR)
- C) Near Complete Remission (nCR)
- D) Complete Remission (CR)
Case #2

A 55 year old AA male is diagnosed with IgG lambda myeloma. Results of the initial work-up include:

- Serum M-spike = 4 g/dL (or 4000 mg/dL)
- 24-hr urine M-protein = 1000 mg/24 hr
- Bone marrow aspirate = 60% plasma cells

Patient received 2 cycles of Revlimid & Dex, then re-evaluated:

- Serum M-spike = 2000 mg/dL
- 24-hr urine M-protein = 190 mg/24 hr

What is the patient's disease response after two cycles of Rev/Dex?

A) Very Good Partial Remission (VGPR)
B) Partial Remission (PR)
C) Stable Disease (SD)

The patient's PR status was confirmed with a 2nd measurement. The patient received two additional cycles of Rev/Dex & re-evaluated for disease response.

- Serum M-spike = 2900 mg/dL
- 24-hr urine M-protein = 600 mg/24 hr
- Bone marrow aspirate = 30% plasma cells

What is the patient's disease response after a total of 4 cycles of Rev/Dex?

A) Very Good Partial Response (VGPR)
B) Partial Response (PR)
C) Stable Disease (SD)
D) Progressive Disease (PD)

Patient is switched to Vincristine, Adriamycin & Decadron (VAD) and is re-evaluated after two cycles.

- Serum M-spike = 1400 mg/dL
- 24-hr urine M-protein = 190 mg/24 hr
- Bone marrow aspirate = 15% plasma cells

The plan is to give IV Cytoxan mobilization. What is the patient’s disease response to the 2 cycles of VAD?

The patient achieved a PR after two cycles of VAD. What studies were used as a baseline to make that determination?

A) The studies obtained at diagnosis
B) The studies obtained after first two cycles of Rev/Dex
C) The studies obtained at time of progression
The patient underwent their autologous PBSC HSCT & has been evaluated monthly for the 1st three months post HCT.

**Day +30 evaluation:**
- Serum M-spike = 1000 mg/dL
- Serum immunofixation (+) for IgG lambda
- 24-hr urine M-protein = 190 mg/24 hrs
- Bone marrow aspirate = 7% plasma cells

**Day +60 evaluation:**
- SPEP/UPEP- no monoclonal band
- Serum/Urine immunofixation (+) for IgG lambda
- 24-hr urine for M-protein = 90 mg/24 hrs

**Day +100 evaluation:**
- SPEP/UPEP- no monoclonal band
- Serum/Urine immunofixation (+) for IgG lambda
- 24-hr urine for M-protein = 0 mg/24 hrs
- Bone marrow aspirate <5% plasma cells

**What is the best disease response to HCT that you would report at Day +100 for this patient?**
- A) Stable Disease (SD)
- B) Partial Remission (PR)
- C) Very Good Partial Remission (VGPR)
- D) Near Complete Remission (nCR)
- E) Complete Remission (CR)
Case #3

A 60 yo male was diagnosed with symptomatic myeloma (IgG kappa) in May 2011. He had a prior history of smoldering myeloma diagnosed in November 2010. His treatment plan included tandem auto HCTs.

Labs at diagnosis of symptomatic myeloma:
- Serum M-spike = 1.0 g/dL
- Serum immunofixation (+) for IgG kappa
- Serum FLC κ/λ ratio = 12.69
- Urine M-spike = 175 mg/24 hours
- Bone marrow aspirate = 45% plasma cells

Can urine studies be used to monitor the disease response to treatment?

Patient received 2 cycles of Velcade & his disease was reassessed.
- Serum M-spike = 0.7 g/dL
- Serum immunofixation (+) for IgG kappa
- Serum FLC κ/λ ratio = 11.24

What is the disease status after 2 cycles of Velcade?

A) Very Good Partial Response (VGPR)
B) Partial Response (PR)
C) Stable Disease (SD)

Patient received 2 additional cycles of Velcade prior to HCT #1 & his disease was reassessed.
- Serum M-spike = 0.6 g/dL
- Serum immunofixation (+) for IgG kappa
- Serum FLC κ/λ ratio = 8.82
- Bone marrow aspirate = 10%

What is the disease status after 4 cycles of Velcade?

A) Very Good Partial Response (VGPR)
B) Partial Response (PR)
C) Stable Disease (SD)

The patient underwent their first autologous PBSC HSCT & was evaluated at Day 30 & Day 60.

Day +30 evaluation:
- Serum M-spike = 0.6
- Serum immunofixation (+) for IgG kappa
- Serum FLC κ/λ ratio = 6.87
Day +60 evaluation:
- Serum M-spike = 0.5
- Serum immunofixation (+) for IgG kappa
- Serum FLC κ/λ ratio = 6.21
- Bone marrow aspirate = 5% plasma cells

What baseline was used to determine disease status at Day +60 post HCT #1?
A) Labs obtained prior to conditioning for HCT #1
B) Labs obtained at diagnosis

Patient undergoes HCT #2 in April 2012 & was evaluated at Day +30 & Day +100.

Day +30 evaluation:
- Serum M-spike = 0.4
- Serum immunofixation (+) for IgG kappa
- Serum FLC κ/λ ratio = 7.37

Day +100 evaluation:
- Serum M-spike = 0.7
- Serum immunofixation (+) for IgG kappa
- Serum FLC κ/λ ratio = 2.35

What baseline was used to determine disease status at Day +30 & Day +100 post HCT #2?
A) Labs obtained prior to conditioning for HCT #2
B) Labs obtained prior to conditioning for HCT #1
C) Labs obtained at diagnosis

What is the disease status at Day +30?
A) Stable Disease (SD)
B) Partial Remission (PR)
C) Very Good Partial Remission (VGPR)

What is the disease status at Day +100?
A) Progressive Disease (PD)
B) Stable Disease (SD)
C) Partial Remission (PR)

Patient started Revlimid & Dexamethasone at Day +120 for persistent disease & was evaluated at 6 months post HCT #2.

Six month evaluation:
- Serum M-protein = 0.4
- Serum immunofixation (+) for IgG kappa
What is the disease status at 6 months?
A) Stable Disease (SD)
B) Partial Remission (PR)
C) Very Good Partial Remission (VGPR)
# Multiple Myeloma Summary

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**MR#:**

**Diagnosis:**

**Physician:**

**Stage:**

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