Maintenance Therapy in Multiple Myeloma

A Case Study

Case 1: 62-Year-Old Male Presents after Initial MM Therapy

- History: Symptomatic multiple myeloma (MM)
- Skeletal survey – diffuse lytic bone lesions
- Normocytic, normochromic anemia
  - Hemoglobin 9 g/dL↓ [Normal range 12.4 to 14.9 gm/dL]
- Ca^{+2} 13.3 mg/dL ↑ [Normal range 8.5 to 10.2 mg/dL]
- Creatinine 2.5 mg/dL ↑ [Normal range 0.6 to 1.3 mg/dL]
- IgG kappa paraproteinemia
- Bone marrow: 45% plasmacytosis
- Cytogenetics: Diploid
- FISH: poor risk including 17p deletion, t(14;16) and t(14;20)
- Staging: Salmon-Durie Stage III, ISS Stage II
- No comorbidities

Ca^{+2}=calcium; IgG=immunoglobulin G; FISH= fluorescent in situ hybridization; ISS=International Staging System

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- Post-correction for renal insufficiency and hypocalcemia [hydration, bisphosphonate, transfusion, dexamethasone and pain management]
- Initial induction therapy
  1. RVD x 4 cycles [NCCN category 2A]
  2. G-CSF alone for SC mobilization
  3. ASCT using melphalan 200 mg/m^2

RVD=lenalidomide/bortezomib/dexamethasone; G-CSF=granulocyte-colony stimulating factor; SC=stem cell; ASCT=autologous stem cell transplantation

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology: Multiple Myeloma. 2013; version 2.2013. Release date 3/8/2013.

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- Patient achieved complete response (CR)
  - Negative immunofixation on serum, urine
  - No soft tissue plasmacytomas
  - 5% non clonal plasma cells in bone marrow
- Considerations for maintenance therapy were discussed with patient

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- Decision Tree – Step One
- Should this patient receive maintenance therapy?
  - Yes: Patient has high-risk disease by FISH/cytogenetics
    - Even having achieved a CR, the durability of the response is of concern
    - Goal: maintain the depth of response achieved with primary therapy for as long as possible

Maintenance Options 2013

- ~~Alkylators~~ (not listed by NCCN)
- ~~IFN-alpha~~ (Category 2b)
- ~~Steroids~~ (Category 2b)

- Thalidomide (Category 1)
- Lenalidomide (Category 1)
- Bortezomib (Category 2A)

NCCN preferred maintenance drugs 2013

The US FDA has not approved thalidomide, lenalidomide, bortezomib, IFN-α, alkylating agents, or steroids for use as maintenance therapy for multiple myeloma.

IFN=interferon

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Decision Tree

- Which regimen based on history, biology, cytogenetics?
  - Lenalidomide or bortezomib are acceptable options
  - Thalidomide ruled out based on MRC Myeloma IX trial:
    - No benefit in FISH-defined high-risk patients
    - Patients with adverse iFISH receiving thalidomide showed no significant PFS benefit and worse OS (*P* = .009)
- Bortezomib SQ was selected based on patient's high-risk FISH/cytogenetics and history of renal impairment as well as patient preference
  - Route reduces risk of peripheral neuropathy
  - Dose: 1.3 mg/m^2 SQ q2wks (follow your institutional protocols for dose and schedule, duration of therapy, and side-effect monitoring and management planning)

MRC=Medical Research Council; iFISH=interphase FISH; PFS=progression-free survival; OS=overall survival; SQ=subcutaneous;
Morgan GJ, et al. *Blood.* 2011;119(1): 7-15.; Ludwig H, et al. *Blood*. 2012;119:3003-3115.

Decision Tree

- Duration of therapy?
  - Selected duration due to high-risk disease: until progression or patient can no longer tolerate
- Side-effect and comorbidity management plan
  - Side-effect threshold (not to exceed grade 1); continue to monitor for PN though route reduces risk; acyclovir prophylaxis for herpes zoster; monitor for thrombocytopenia; continue zoledronic acid up to 2 years and re-evaluate

PN=peripheral neuropathy

Morgan GJ, et al. *Blood.* 2011;119(1): 7-15.; Ludwig H, et al. *Blood*. 2012;119:3003-3115.