Treatment of Relapsed Multiple Myeloma

A Case Study

Case Presentation

- Mr. V is a 61-year-old man previously diagnosed with ISS stage III IgG λ multiple myeloma with bone lesions, normal FISH and cytogenetics, and an initial hemoglobin of 10.2, albumin 3.0, and a β2 microglobulin of 5.8
- He was initially treated with 6 cycles of lenalidomide and dexamethasone and had a very good partial response (VGPR)
  - Additional treatments: aspirin 81 mg/d VTE prophylaxis; zoledronic acid was given for one year, discontinued previous to dental surgery, not restarted
- He underwent an autologous stem cell transplant with a complete response and no maintenance therapy
- After 2 years, he is seen in clinic due to back pain and was found to have lytic bone lesions, renal insufficiency, moderate hypercalcemia and an elevated M-protein
- Bone marrow (BM) biopsy: 40% plasma cells

What are the treatment options for his relapsed myeloma?

ISS=International Staging System; Ig=immunoglobulin; FISH=fluorescence in-situ hybridization; VTE=venous thromboembolism

Case Study: Laboratory Values

Lab/Normal Reference Range	Value
WBC 3.0–11.0 k/µL	8.4
Plt Ct 150–400 k/µL	117 (L)
Hgb 13.0–17.0 g/dL	10.8 (L)
Hct 39.0–51.0%	32.3 (L)
MCV 80–100 fL	97.4
RDW-CV 11.5–15.0%	13.6
Neut % 38.5–75.0%	62.0
Abs Neut 1.00–7.50 k/µL	5.2

Lab/Normal Reference Range	Value
BUN 8–25 mg/dL	23 (H)
Creatinine 0.7–1.4 mg/dL	2.1 (H)
Calcium 8.5–10.5 mg/dL	12 (H)
Albumin 3.5–5.0 g/dL	3.9
Alk Phos 40–150 U/L	164 (H)

(H)=high; (L)=low; WBC=white blood cell; Plt Ct=platelet count; Hgb=hemoglobin; Hct=hematocrit; MCV=mean corpuscular volume; RDW-CV=red cell distribution width-coefficient variation; Neut=neutrophils; Abs Neut=absolute neutrophils; BUN=blood urea nitrogen; Alk Phos=alkaline phosphatase

Case Study: Laboratory Values

SPEP: Lab/Normal Reference Range	Value
Alpha-1 0.11–0.22 g/dL	0.21
Alpha-2 Globulin 0.6–1 g/dL	0.85
Beta G 0.50–1.00 g/dL	0.64
Gamma Glob 0.60–1.35 g/dL	**1.52 (H)**
M-Spike (g/dL)	**1.87 (H)**

Lab/Normal Reference Range	Value
Serum IgG 717–1,411 mg/dL	**1,635**
Serum IgA 78–391 mg/dL	42
Serum IgM 53–334 mg/dL	19
Serum Kappa 534–1,267 mg/dL	<30
Serum Lambda 253–653 mg/dL	**896**

SPEP=serum protein electrophoresis; Gamma Glob=gamma globulin

Definition of Relapsed Myeloma

- Relapse after a complete response (CR)[1]
  - Reappearance of M-protein in the serum or urine
  - ≥5% plasma cells in the bone marrow
  - New lytic bone lesion(s), plasmacytoma, or hypercalcemia

This patient has undergone a symptomatic relapse, not just a biochemical relapse.
The time since last treatment is far greater than 6 months.

[1]National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology: multiple myeloma. v.2.2013.

Major Factors That Influence Choice of Therapy

DISEASE-RELATED[1]	REGIMEN-RELATED[1]	PATIENT-RELATED[1]
DOR to initial therapy	Prior drug exposure	Pre-existing toxicity
FISH/cytogenetics	Toxicity of regimen	Comorbidities
	Mode of administration	Age
	Previous SCT	Performance status
•Two years since last therapy; DOR was good; no high-risk features by FISH/cytogenetics	•Previous VGPR with LD treatment, achieved CR post HDT-ASCT; no toxicity related issues requiring dose reductions or discontinuations	•Bone lesions- disease related; no other comorbidities; no history of peripheral neuropathy

DOR=duration of response; SCT=stem cell transplant; HDT-ASCT=high-dose therapy/autologous stem cell transplantation

[1]Lonial SL. ASH Educational Book, 2010..

2013 NCCN Guidelines for Relapsed Myeloma

Preferred Regimens	Other Regimens
•Repeat primary induction therapy (if relapse at >6 months) **•Bortezomib (category 1)** **•Bortezomib/dexamethasone** **•Bortezomib/lenalidomide/dexamethasone** **•Bortezomib/liposomal doxorubicin (category 1)** **•Bortezomib/thalidomide/dexamethasone** •Carfilzomib* **•Cyclophosphamide/lenalidomide/dexamethasone** •Dexamethasone/cyclophosphamide/etoposide/cisplatin (DCEP) •Dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide (DT-PACE)±bortezomib (VTD-PACE) •High-dose cyclophosphamide **•Lenalidomide/dexamethasone (category 1)** •Pomalidomide*/dexamethasone •Thalidomide/dexamethasone	•Bendamustine •Bortezomib/vorinostat •Lenalidomide/bendamustine/dexamethasone

*Indicated for patients that have received at least two prior therapies including bortezomib and an immunomodulatory drug (IMiD) and have demonstrated disease progression on or within 60 days of completion of the last therapy.

NCCN. Clinical practice guidelines in oncology: multiple myeloma. v.2.2013.

Treatment Plan

- Patient was symptomatic, moderate hypercalcemia, renal insufficiency, bone lesions: observation not option
- Patient was admitted into hospital: hydrated for hypercalcemia, bisphosphonate – pamidronate was administered according to PI [90 mg IV monthly], patient had moderate renal insufficiency (45 CLcr) and was monitored after each dose as directed, additional treatment included dexamethasone and pain control
  - Immediate treatment for MM disease commenced after hypercalcemia normalization

PI=package insert; CLcr=creatinine clearance; IV=intravenous; MM=multiple myeloma

Treatment Plan

- Bortezomib-based regimen chosen (IV) for initial treatment for rapid response due to renal impairment (additional benefit to bone) with plan to switch to SQ after one to two cycles depending on depth of response; peripheral neuropathy monitoring
  - Regimen selected: bortezomib, lenalidomide, dexamethasone (NCCN category 2A)
    - Previous long duration of response with lenalidomide; addition of lenalidomide may prove synergistic since rapid, deep, and durable response is essential
    - Lenalidomide was dose-adjusted (10 mg/d) based on prescribing information for patient's creatinine clearance with plans to increase to full dose or as tolerated after clearance normalizes
- Key prophylaxis: 400 mg PO BID for HSV prophylaxis, 81 mg/d aspirin for VTE and antibiotic for neutropenia – monitor for neutropenia
- Plan to discuss clinical trial options with patient with improved renal status and disease control

SQ=subcutaneous; PO=by mouth; BID=twice a day; HSV=herpes simplex virus

Further Recommended Resource

- *Managing Myeloma*
  Multidisciplinary Practice and Care 2013
  - Focus on supportive care