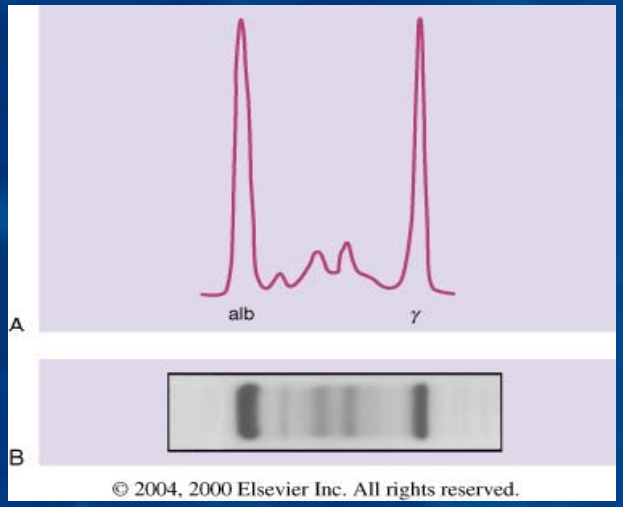
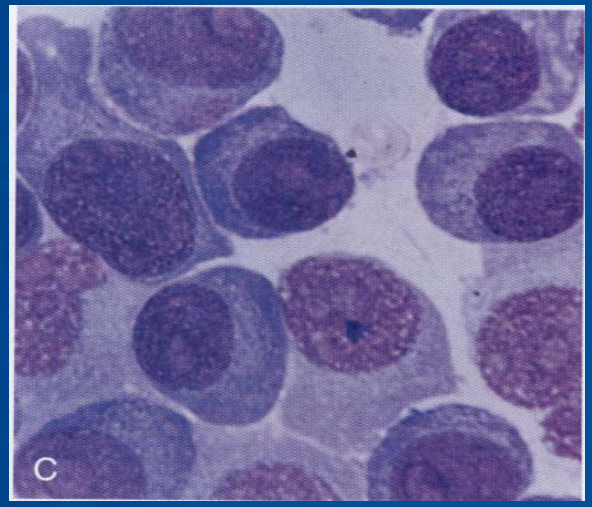
Multiple Myeloma Practice Support Case *Relapsed/Refractory Disease Management*





Patient Case Study: Recurrent Myeloma

- 44-year-old woman
- κ light chain multiple myeloma diagnosed December 2000
  - Durie-Salmon stage IIIA, ISS stage II
- Laboratory findings
  - Total proteinuria 5.80 g/day
  - Bence-Jones protein (BJP) 3.5 g/day
  - Hypogammaglobulinemia
  - Albumin 3.8 g/dL
  - β2-microglobulin 4.6 mg/L
- Mild back pain

ISS=International Staging System

Recurrent Myeloma

- Bone marrow biopsy
  - Cellularity 80% with 25% plasma cells
  - Cytogenetics 46, XX, inversion 9 (p11;q13)
- FISH not done
- Skeletal survey: extensive lytic bone disease with healing fractures of right 6^{th} and the 7^{th} ribs
- MRI of the spine: diffuse hyperintense homogenous signal on STIR sequence
- MRI of the pelvis: diffuse marrow infiltrative changes due to myeloma

FISH=fluorescence in situ hybridization; MRI=magnetic resonance imaging; STIR=short tau inversion recovery

Recurrent Myeloma

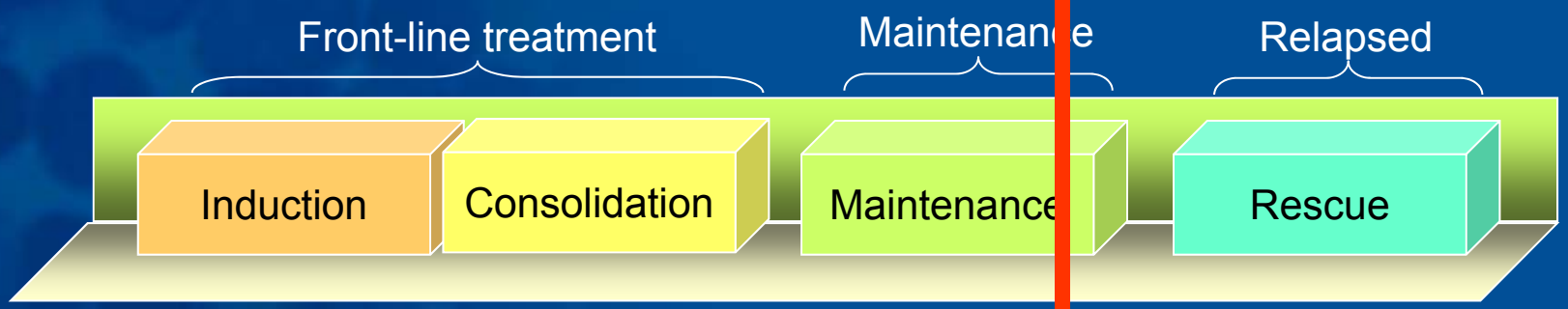
- Treatment
  - Vincristine 0.4 mg, doxorubicin 9 mg/m^2 Days 1-4; dexamethasone 40 mg Days 1-4, 9-12, 17-20; x 4 cycles
  - Followed by high-dose melphalan and stem cell transplant on June 13, 2001
- Achieved complete remission
- Maintained on pamidronate and prednisone x 1 year

Five Years Later

- January 11, 2006
  - Urine total protein 545 mg/day
  - Creatinine clearance 86 mL/minute
  - BJP 100 mg/day
  - Urine IFE free κ light chain
  - Serum free κ 750 mg/L
  - Free λ 15 mg/L
  - κ:λ ratio 50
  - Multiple new lytic lesions of the skull
- MRI spine and pelvis January 11, 2006
  - New focal lesion at L3 and L4 vertebral body

IFE=immunofixation electrophoresis

Multiple Myeloma Treatment Lines*



Induction	Consolidation	Maintenance	Rescue
Bort/Dex Bort/Cyclo/Dex Bort/Dox/Dex Bort/Len[a]/Dex Bort/Thal/Dex Len[a]/Dex	SCT	Observation Thal[b] Len[c] Bort[d]	Repeat primary induction (if relapse is > 6 mo) Bendamustine[e] Bort Bort/Dex Bort/Len/Dex Bort/Liposomal Dox Cyclo/Bort/Dex Cyclo/Len/Dex DCEP[f,g] DT-PACE or VDT-PACE[f,g] High-dose Cyclo Len/Dex Thal/Dex

[a]Lenalidomide is not FDA approved for treatment of newly diagnosed, multiple myeloma (MM) patients.
[b]Thalidomide is not FDA approved as maintenance therapy for MM patients.
[c]Lenalidomide is not FDA approved as maintenance therapy for MM patients.
[d]Bortezomib is not FDA approved as maintenance therapy for MM patients.
[e]Bendamustine is not FDA approved for the treatment of multiple myeloma.
[f]Etoposide is not FDA approved for the treatment of multiple myeloma.
[g]Cisplatin is not FDA approved for the treatment of multiple myeloma.

*Transplant eligible patients; Bort=bortezomib; Dex=dexamethasone; Cyclo=cyclophosphamide; Dox=doxorubicin; Thal=thalidomide; Len=lenalidomide; SCT=stem-cell transplant; VTD=bortezomib (Velcade), thalidomide, dexamethasone; DCEP=dexamethasone, cyclophosphamide, etoposide, cisplatin (Platinol); DT PACE= dexamethasone, thalidomide, cisplatin (Platinol), doxorubicin (Adriamycin), cyclophosphamide, etoposide; FDA=Food and Drug Administration

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology-Multiple Myeloma 2011 (v1.2012).

Patient's Initial Therapy of Relapse

- Since patient had never been exposed to IMiD or proteosome inhibitor, these would be first choice
  - Relatively low tumor bulk so double therapy reasonable
  - Goal is to achieve good response
- Treated with lenalidomide 25 mg/d PO QAM days 1-21 and weekly dexamethasone 40mg/d PO QAM x 3 months → stable disease
- Bortezomib added at a dose of 1.3 mg/m^2 days 1-4-8 and 11 to each cycle with reduction of lenalidomide to 15mg/d PO QAM days 1-14 every 21-day cycle; dexamethasone 40mg PO QAM on days 1, 2, 4, 5, 8, 9, 11, and 12.

Lenalidomide Prescribing Information. Bortezomib Prescribing Information. Jimenez-Zepeda VH et al. ASH Annual Meeting Abstracts 2011: abstract 2936. Richardson PG, et al. *J Clin Oncol.* 2009;27:5713-5719. Anderson KC, et al. *J Clin Oncol*. 2009;27:15S (abstract 8536). Weber D, et al. *N Engl J Med*. 2007;357:2133-2142.Dimopoulos M, et al. *N Engl J Med*. 2007;357:2123-2132.

Take Home Pearls

- Consider type of relapse
  - Does the patient need to be treated
- Prior therapies
  - Transplant naïve or not
  - On maintenance or not
- Availability of stem cells
- Tempo of disease
- Previous toxicities and response
- Time of previous remission
- Pragmatic concerns (access, geography, age, preference)
- To sequence or combine existing approved drugs?
- Consider referral for participation in clinical trial
  - Advances in survival are directly attributable to clinical advances in multiple myeloma