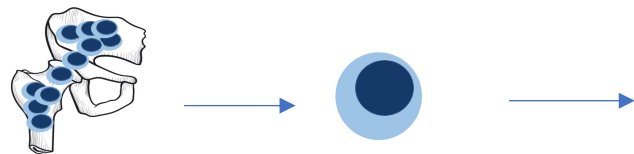


# **MULTIPLE MYELOMA Reference Handout**

## MM Pathology



→ monoclonal antibodies or light chains



Antibody (IgG > IgA > IgM)

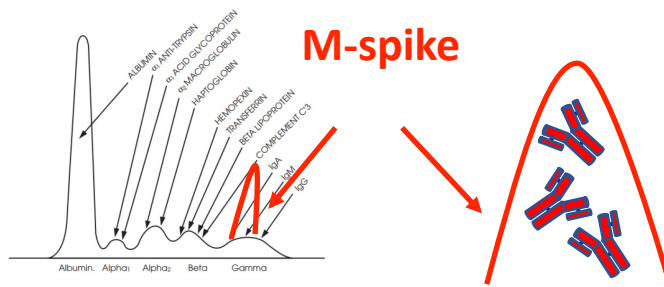


Light chain (kappa or lambda)

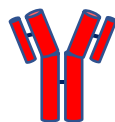
monoclonal plasma cell neoplasm

## MM Work Up

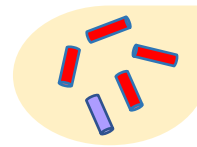
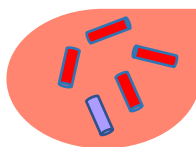
1. Serum/Urine Protein Electrophoresis  
*is there a monoclonal protein*  
m-spike > 3 g/dl



2. Serum/Urine Immunofixation  
*what is the monoclonal protein*  
IgG > IgA > IgM = common



= ?



3. Free Light Chains  
*is there a monoclonal light chain*  
Kappa / Lambda > 3

## MM Symptoms

CRAB SYMPTOMS	MECHANISM
<b>Hypercalcemia</b>	Bone destruction Impaired renal clearance PTHrP
<b>Renal Dysfunction</b>	Light chain cast nephropathy Tubular toxicity HyperCa/Hyperuricemia AL Amyloid
<b>Anemia</b>	Bone replacement Low EPO
<b>Bone Lesions</b>	Bone destruction
OTHER SYMPTOMS	MECHANISM
<b>Infections</b>	Hypogammaglobulinemia
<b>Hyperviscosity</b>	High concentration antibodies IgM > 3K, IgA > 5K, IgG > 7K
<b>Neuropathy</b>	Paraprotein nerve injury Drug effect
<b>Coagulopathy</b>	Inflammation Activation of pro-coagulant factors

## MM: Spectrum of Disease

	MGUS Monoclonal Gammopathy of Unknown Significance	Smoldering Myeloma	Multiple Myeloma
<b>M-spike</b>	< 3 g/dL	> 3 g/dL	> 3 g/dL
<b>% plasma cells in bone marrow</b>	< 10%	> 10%	> 10%
<b>CRAB symptoms</b>	NO	NO	YES
<b>SUMMARY</b>	Low [monoclonal protein] Asymptomatic	High [monoclonal protein] Asymptomatic	High [monoclonal protein] Symptomatic

## MM Diagnosis

BMB > 10 % plasma cells or extramedullary plasmacytoma with SLIM-CRAB	
SLIM CRAB	
<b>S = Sixty</b>	60% plasma cells in bone marrow
<b>Li = Light Chains</b>	Free kappa/lambda ratio > 100
<b>M = MRI lesions</b>	MRI lytic lesions
<b>CRAB Symptoms</b>	Present

## MM: Work Up

- Bone marrow biopsy**
- Skeletal survey**
- Uric acid/G6PD  
LDH  
Albumin  
B2 microglobulin**

## MM: Staging/Prognosis

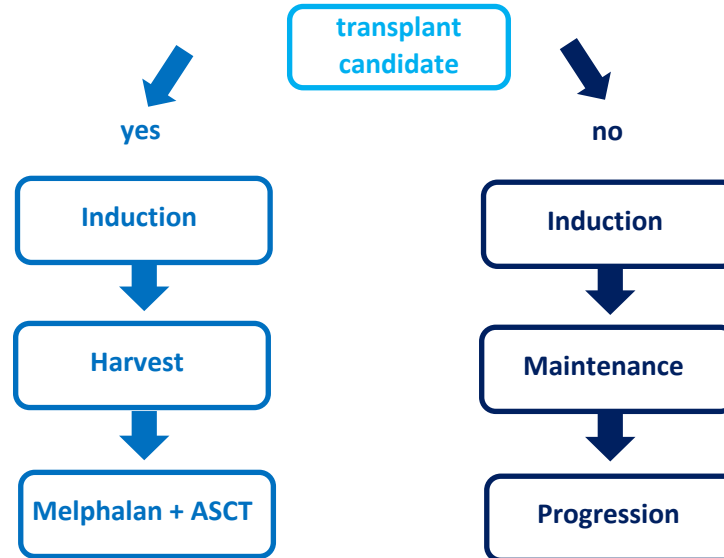
International Staging System	Labs	Median Survival
<b>I (- high risk features)</b>	B2 MG < 3.5 mg/L Albumin > 3.5 g/dL	Not reached
<b>II</b>	Not I or III	83 months
<b>III (+ high risk features)</b>	B2 MG > 5.5 mg/L	43 months
<b>High Risk Features</b>	High LDH FISH: del(17p), t(4;14), t(14;16)	

## MM: Drug Classes

DRUG CLASS	DRUGS
<b>Steroids</b>	Prednisone Dexamethasone
<b>Proteasome Inhibitors</b>	Bortezomib/Velcade (IV/SC) Carfilzomib (IV) Ixazomib (PO)
<b>Immune Modulators</b>	Lenalidomide/Revlimid (PO) Pomalidomide (PO)
<b>Monoclonal AB</b>	Daratumumab (IV) = anti-CD38 Elotuzumab (IV) = anti-SLAMF7
<b>Histone Deacetylase Inhibitors</b>	Panobinostat (PO) Ricolinostat (PO)
<b>BCL2 Inhibitor</b>	Venetoclax = in t(11;14)
<b>Selective Inhibitor Nuclear Export</b>	Selinexor

## MM: Principles of Treatment

1. Everyone who can get an auto-SCT should
2. No standard induction therapy
3. Triplet therapy > doublet therapy



### Regimen Selection

#### 1. Tolerability (Age, ECOG)

Consider doublet > triplet if older/poor ECOG

#### 2. Side Effects

Bortezomib (neuropathy, HSV re-activation)  
Lenalidomide (renal dosing, VTE)

#### 3. Onset of Action

CyBorD faster than VRD

#### 4. Transplant Eligibility

No melphalan pre-transplant

#### 4. FDA Approval

## MM: Common Regimens

VRD +/- Dara

Velcade (Bortezomib)

Revlimid (Lenalidomide)

Dexamethasone

CyBorD +/- Dara

Cyclophosphamide

Velcade (Bortezomib)

Dexamethasone

RD +/- Dara

Revlimid (Lenalidomide)

Dexamethasone

Daratumumab

(V) DPACE

+/- Velcade

Dexamethasone

Cisplatin

Adriamycin

Cyclophosphamide

Etoposide

(V) DCEP

+/- Velcade

Dexamethasone

Cyclophosphamide

Etoposide

Cisplatin

## MM: Management of Complications

Complications	Supportive Care
<b>Hypercalcemia</b> <b>mild &lt;12, moderate 12-14, severe &gt;14 mg/dL</b>	Tx = IVF [200-300 cc/hr], steroids Calcitonin = short term correction: 4u/kg BID x 48H Bisphosphonates/RANKL AB = long term correction: pamidronate, zoledronic acid, denosumab
<b>Hyperuricemia</b> <b>severe &gt;10</b>	PPx = allopurinol [300 mg QD, renally dose] Tx = rasburicase (only give if uric > 10, G6PD negative)
<b>ID Prophylaxis</b> <b>check HIV, Hepatitis prior to Tx</b>	Acyclovir if on proteasome inhibitor (bortezomib) UTD Vaccinations PCP ppx if neutropenic
<b>Bone Lesions</b> <b>lytic</b>	Tx = consider RT, surgery PPx = bisphosphonate (pamidronate, zoledronic), RANKL AB (denosumab)
<b>Thrombosis</b> <b>including PVT</b>	Low risk: No ppx Mod risk: aspirin 81 mg (receiving dex) High risk: consider LMWH (receiving dex + doxorubicin)
<b>Hyperviscosity</b> <b>viscosity &gt; 4-6 CP</b>	Sx = CNS (HA, vision, dizziness, coma, CHF, etc) Rare! More common w/ larger Ig like IgM > IgA > IgG Dx = viscosity doesn't correlate with symptoms Tx = plasmapheresis (only if sx)