Spectrum of Monoclonal Gammopathy of Undermined Significant (MGUS) to Multiple Myeloma (from Triple Threat's academic summaries AY 2021-22)

	MGUS (Meets each box)	**Smoldering Multiple Myeloma** (Meets each box)	**Multiple Myeloma** (>=1 Multiple Myeloma Defining Event* + 1 BM finding)
Progression	0.5-1%/year to MM	10-20%/5 years to MM	
Work-up	• **Blood tests:** CBC, BMP w/ electrolytes, Serum protein electrophoresis (SPEP) with immunofixation, Serum free light chain assay • **Urine studies:** Urine protein electrophoresis (ideally 24 hour) • **Bone marrow biopsy** • **Imaging:** Whole –body MRI, Whole-body low-dose CT, or FDG-PET		
Serum/urine protein anomalies	• Monoclonal protein (IgM[#] or non-IgM) < 3 g/dL **OR** • Abnormal free-light chain (FLC) ratio <0.26 or >1.65 • Increased levels of involved FLC (i.e., kapp or lambda) • Absence of immunoglobulin heavy chain • 24 hour urine <500 mg monoclonal protein	• Monoclonal protein (IgG or IgA) >3 g/dL **AND/OR** • Urine monoclonal protein >= 500 mg/24 hours **(FLC ratio >20 is high risk feature)** **(M-spike > 2g/dL is high risk feature)**	**Any**
Bone marrow (BM) findings	**Clonal plasma cells < 10%**	**Clonal plasma cells 10-60%** **(>20% is high risk feature)**	• Clonal plasma cells >= 10% **OR** • Biopsy-proven plasmacytoma **OR** • ***Clonal plasma cells >= 60%
Organ involvement	**Absence of end-organ damage (i.e., no C-R-A-B criteria) or amyloid light chain deposition[%]** ***Note:*** ***MG w/ clinical significance (MGCS)[&] is MGUS plus:*** • ***Renal impairment*** • ***Peripheral neuropathy*** • ***Skin deposition*** ***(POEMS – Polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes)***	**Absence of end-organ damage (i.e., no C-R-A-B criteria) or amyloid light chain deposition[%]**	***Multiple Myeloma Defining Events:** • >=1 C-R-A-B Criteria: • Hyper**C**alcemia (Ca > 1 mg/dL higher than upper limit of normal or >= 11 mg/dL) • **R**enal insufficiency (GFR=<40 mL o Cr > 2 mg/dL) • **A**nemia (Hgb =< 10 g/dL or >2 g/dL below lower limit of normal) • **B**one lesions (>=1 osteolytic lesion) • >=1 Lesion (>5 mm) on MRI • Involved : Uninvolved serum FLC ratio >=100 with involved FLC >= 100 mg/L

***Multiple Myeloma Defining Event**

[#]IgM gammopathy is consistent with continuum from IgM-MGUS to Waldenstrom Macroglobulinemia (WM). Asymptomatic WM has similar diagnostic criteria to smoldering myeloma. If presents of monoclonal IgM and symptoms (e.g.,) then diagnosis is WM (e.g., constitutional symptoms, hyper-viscosity syndrome, numbness, etc.)

[&]MGCS can cause similar isolated organ damage (through ill-defined mechanisms) and has clonal, but not malignant, proliferation.

[%]AL Amyloidosis requires biopsy of involved organ with verification by red-green birefringence after Congo red staining un cross-polarized light microscopy.