Best Practice Guideline

I. Monclonal Gammopathy of Undetermined Significance

II. Disease and Diagnosis:

Most identified as incidental SPEP finding, i.e.) workup of peripheral neuropathy, vasculitis, hemolytic anemia, skin rashes, hypercalcemia, elevated ESR.

MGUS defined as:
M-protein <3.0g/dL
<10% plasma cells on marrow
No CRAB features
(>10% marrow plasma cells and/or M-protein >3.0g/dL = Smoldering Myeloma)

Incidence is 5% in pts >70y.o, 9% in men>85, and twice as frequent in AA vs Caucasians

III. Prognostic Markers:

Risk of progression to overt MM is **0.25% to 3%** per year - varies with risk-stratified subtype:

Predictors of progression	Low Risk	Intermediate and High Risk (1 or 2, and 3 risk factors, respectively)
Size of M-protein*	<1.5g/dL	(>1.5g.dL)
M-protein	IgG type	Non-IgG type (IgM/IgA)
SFLC ratio	Normal	<0.66 or >2.75

most significant prognostic determinant of risk of progression.

IV. Surveillance/Follow-Up Strategies:

Management:	Low Risk:	Intermediate and High risk

Initial **<u>If not already done:</u>** **CBC, Serum Creatinine, Serum calcium, Quantitative immunoglobulins, SFLC**	• <u>H&P</u> w focus on s/s of MM or AL amyloid: (Bone pain, B-symptoms, Bleeding, Neuropathy, Macroglossia, HSM). ***Skeletal survey and bone marrow biopsy are not routinely indicated if otherwise asymptomatic.***	In Addition: • <u>Consider bone marrow biopsy</u>: -renal dysfunction, cytopenias, changes in disease tempo • <u>Skeletal survey</u> • <u>If IgM</u>: obtain CT abdomen to look for occult retroperitoneal lymphadenopathy. • <u>urine studies</u> for protein/bence jones/UPEP
Follow Up	Repeat SPEP, Immunoglobulins, SFLC in 6months. Then Q yearly x 2. If no change, then refer back to PMD with monitoring parameters: ie) reconsult for M-spike increase by 50% or new CRAB features.	→ If results negative for MM or WM, repeat CBC, Cr, Calcium, Immunoglobulins, SFLC Q3-6months. (depending on risk factors)

V. <u>Considerations:</u>

- Peripheral blood flow cytometry not helpful. (flow data more relevant on marrow)
- Higher risk groups: African American, Agricultural workers, Obese. – Consider shorter interval follow up for intermediate and high risk patients.
- Increased risk of osteoporosis, thromboembolic events, and secondary malignancies:
    - Obtain DEXA and age appropriate screening. No indication for routine VTE prophylaxis.

References:

KYLE RA, DURIE BG, RAJKUMAR SV, et al. Monoclonal gammopathy of undetermined significance (MGUS) and smoldering (asymptomatic) multiple myeloma: IMWG consensus perspectives risk factors for progression and guidelines for monitoring and management. *Leukemia. 2010;24(6):1121*.

KYLE RA, BUADI FI, RAJKUMAR SV. Management of Monoclonal Gammopathy of Undetermined Significance (MGUS) and Smoldering Multiple Myeloma (SMM). *Oncology (Williston Park, NY)*. 2011;25(7):578-586.