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Blood Disorders Day 2020

FOR Health Professionals

Plasma cell Disorders

From MGUS to multiple myeloma

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Presenter Disclosure

- **Faculty: Vi Dao**
- **Relationships with commercial interests: none**

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Mitigating Potential Bias

- Not Applicable

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Learning Objectives

1. Distinguish MGUS from multiple myeloma
2. Understand the overall prognosis and management of patients with multiple myeloma

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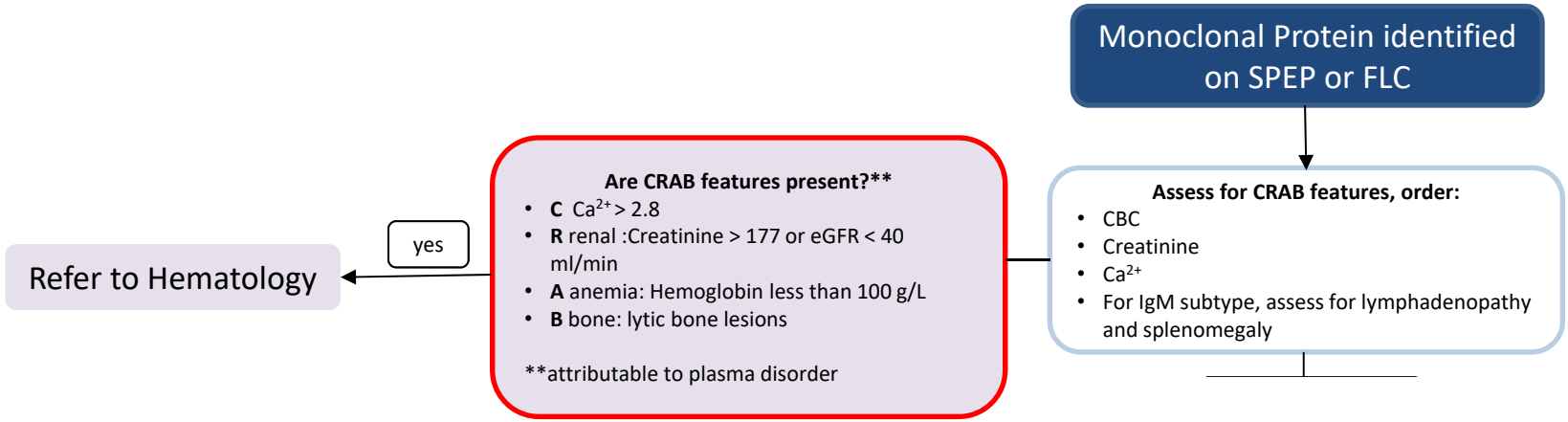

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Priority	Examples	Goal/Time line

Emergent	• Bony involvement:
	  • Spinal cord compromise
	  • Unstable lesion with risk for pathological fracture
	  • Pain (plasmacytoma/lytic lesion)
	• Laboratory involvement:
	  • Hypercalcemia (>3mmol/L)
	  • Acute renal failure (needs serial creatinine values)
	  • Anemia is <u>not</u> considered Emergent as symptoms can be readily supported with transfusion *(but please let us know if transfusion has been arranged)*
		▪ Same day phone advice (Referral to surgery or radiation oncology)
		▪ Empiric treatment (bisphosphonate, steroid)
		▪ Further investigations with CT/MRI/Renal US or Blood/Urine tests
		▪ Clinic <1 week
		▪ May need to be hospitalized

Urgent	All symptomatic or suspected myeloma that does not meet criteria for "emergent" as above	• To clinic in 2 weeks
Routine	• Asymptomatic (smoldering) myeloma • MGUS and query myeloma?	• To clinic within 4 weeks (or when results available)

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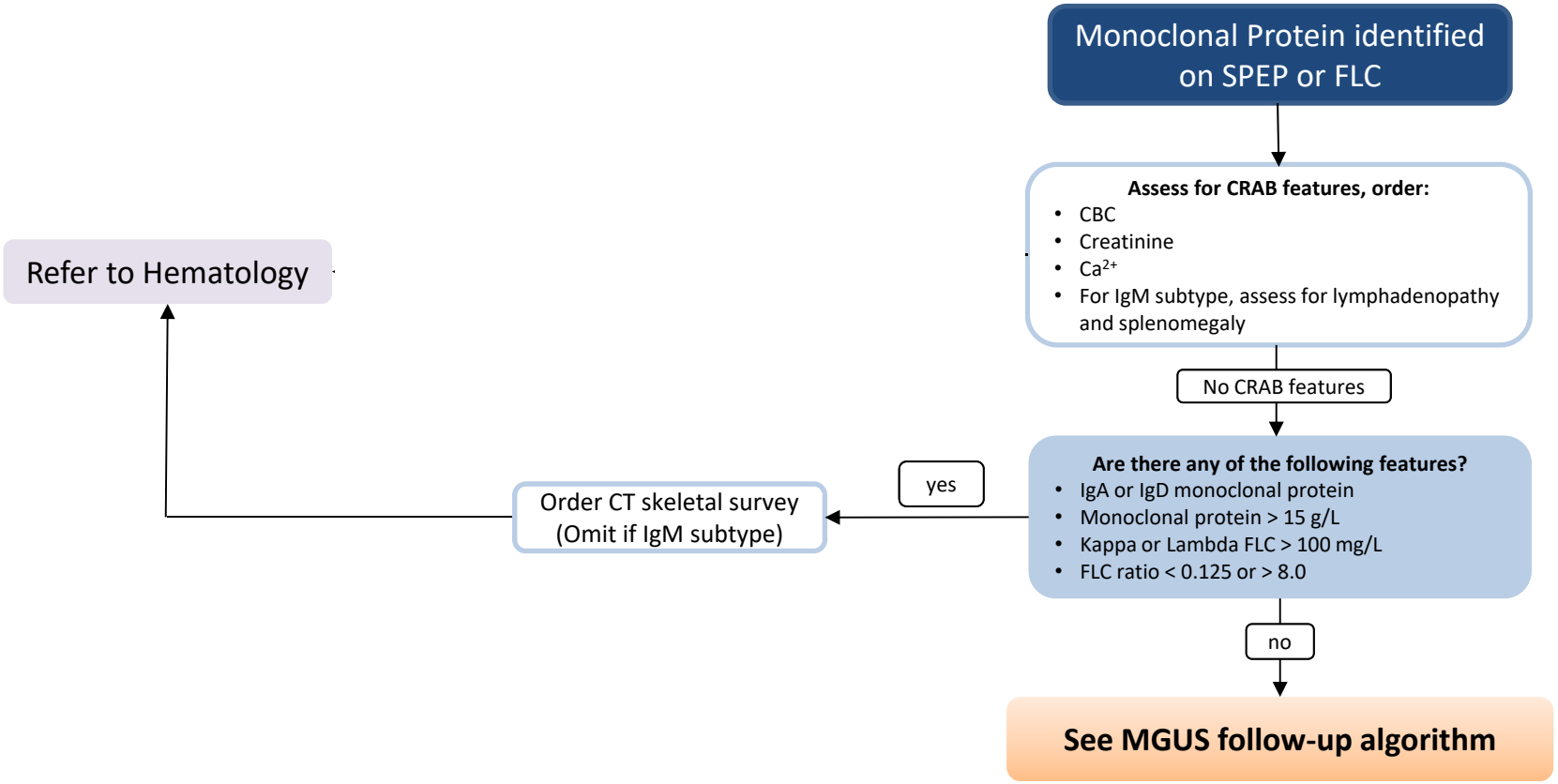

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MGUS is common

- 3% of general population >50 years old (increases with age)
- ~50% are low-risk
- 3 types of MGUS with variable risk of progression
  1. IgM MGUS (15%)
  2. Light chain MGUS
  3. Non-IgM MGUS (80%)

- Harms of testing?

  ~40% of patients with MGUS have anxiety, stress or fear related to diagnosis
  Cost of follow-up – 100 million annually in the US alone

How I Manage MGUS. Go et al. Blood 2018;131:163-173

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Disorders associated with M protein

Plasma cell disorders

- MGUS
- Smoldering Myeloma
- Multiple Myeloma
- AL amyloidosis
- POEMS syndrome
- Light or heavy chain deposition disease

B-cell disorders

- Waldenstroms macroglobulinemia/lymphoplasmacytic lymphoma
- Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
- Marginal zone lymphoma

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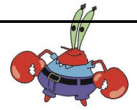
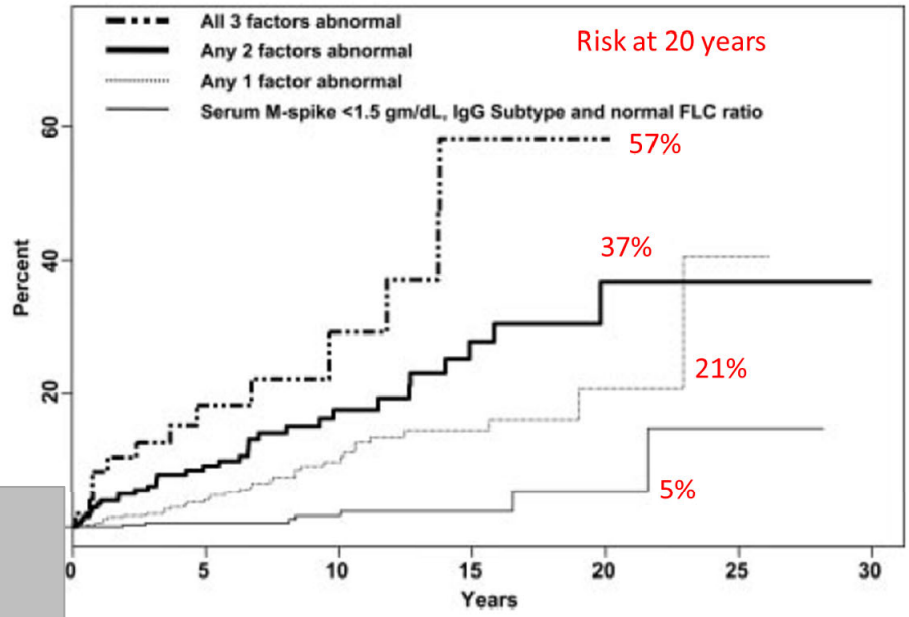
Monoclonal Gammopathy of Undetermined Significance (MGUS)	Smoldering Multiple Myeloma	Multiple Myeloma
M protein in serum <30g/l **and**	M protein >30g/l **and / or**	Any level of M protein (none in non-secretory) **and**
Clonal Bone Marrow Plasma Cells <10% **and**	Clonal plasma cells >10% **and**	Clonal plasma cells >10% **and**
No myeloma related "**CRAB**"	**No** myeloma related "**CRAB**"	Myeloma related "**CRAB**"
No evidence of other B cell LPD or light chain associated Amyloidosis or other tissue damage		**Or: "SLiM" criteria** 1. BM plasma cells >60% 2. FLCR >100 or <0.01 3. >1 focal lesion on MRI

Rajkumar et al. 2014 Lancet Oncology; 15:e538-48

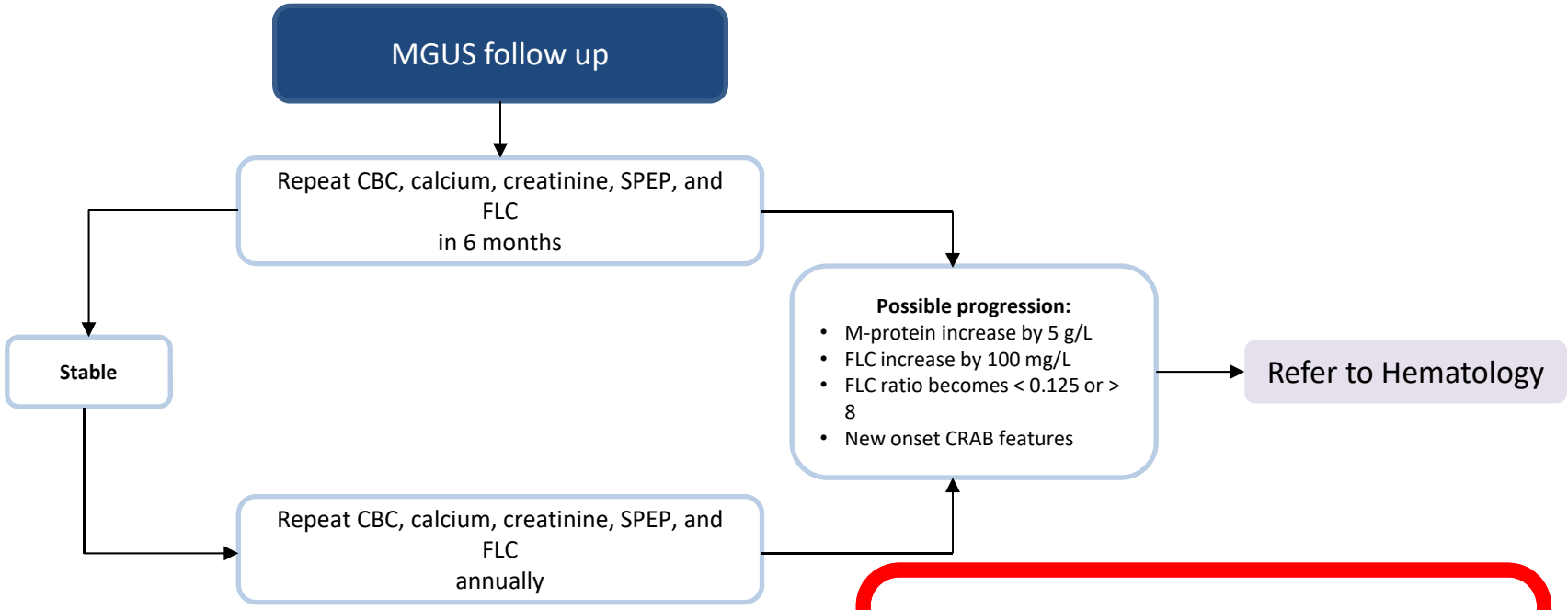
What does it mean to have MGUS?



3 adverse risk factors:

1. M band > 15 g/L
2. Non – IgG subtype (IgA, IgM, IgD)
3. Abnormal FLCI ratio (<0.26 or >1.65)

Rajkumar et al, Blood 2005;106:812-7



ANNUAL RISK OF PROGRESSION FOR MGUS SUBTYPES

Pathways are subject to clinical j
patterns may not always follow the p

MGUS Subtype	Risk	Associated disorders
IgM MGUS	1% per year	Waldenstroms macroglobulinemia
Non-IgM MGUS	0.5% per year	Multiple myeloma, plasmacytoma, amyloidosis
Light chain MGUS	0.3% per year	Light chain myeloma, amyloidosis
Low risk MGUS (IgG, <15 g/L, normal FLC)	2% lifetime risk	

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What is multiple myeloma?

- 1% of all cancers and 15% of hematologic malignancies
  - ~2,700 new cases in Canada in 2015
    - (estimated 80 new cases per year in Manitoba)
  - Prevalence of ~7,500 across Canada
- Median age at diagnosis of 69 years
- Incurable malignancy characterized by multiple relapse
- Risk factors: first degree relative with MM, nuclear radiation exposure, occupational exposure to petroleum and pesticides

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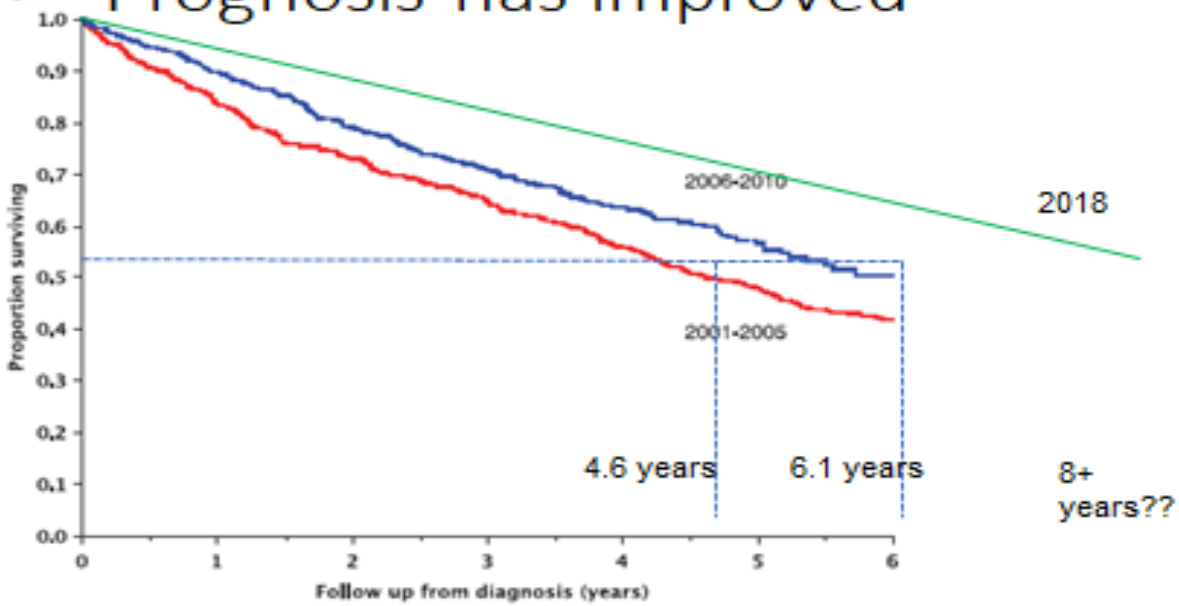
a Prognosis has improved



- Mayo clinic study of 1038 patients diagnosed with myeloma between 2001 and 2010 with a median follow up of 5.9 years
- Current estimated OS is 6-8 years

Kumar et al. Leukemia 2014;1122-28

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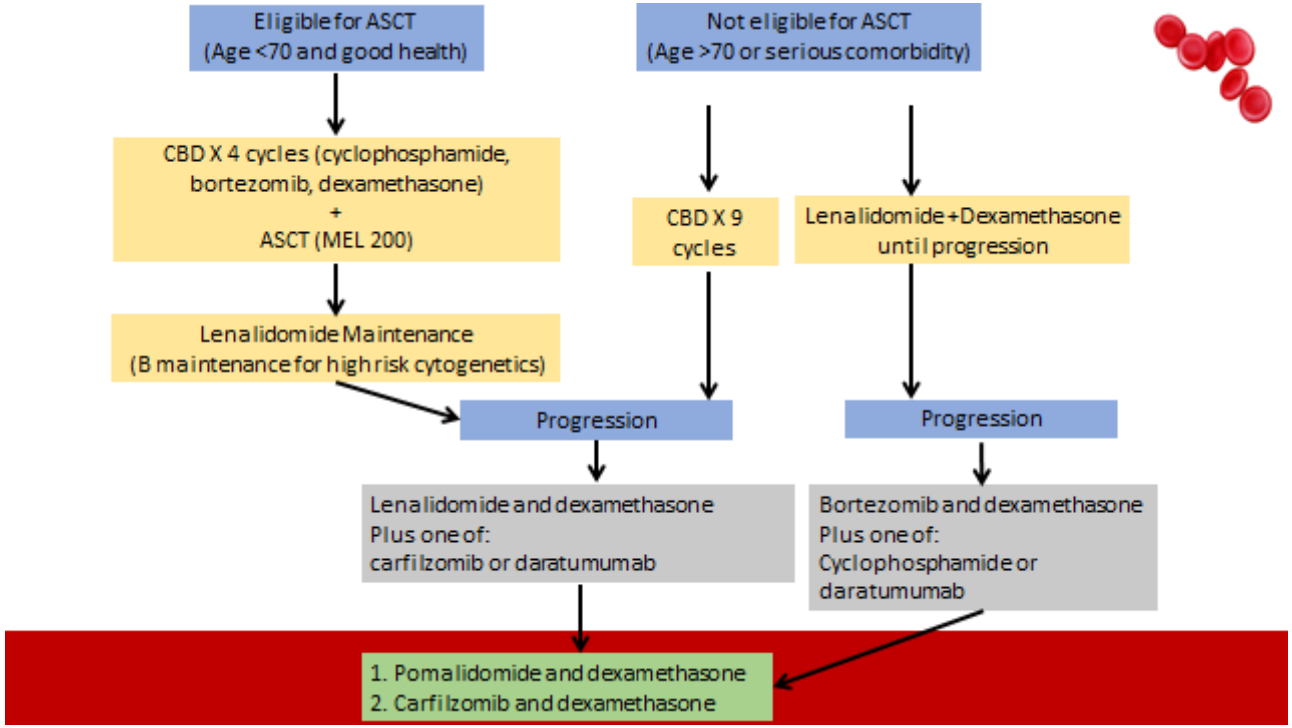
Treatment for multiple myeloma



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Supportive care for patients with myeloma

- Bone disease:
  - pain control (analgesia/radiation/surgical stabilization)
  - bisphosphonate (also treat hypercalcemia)
- Renal insufficiency: avoid nephrotoxins, good hydration
- Low counts (Hb, platelet) – transfusion support
- Venous thromboembolism (ASA or LMWH or DOAC)
- Infection: yearly influenza + consider recombinant VZV vaccine
- Screening for:
  - Neuropathy
  - Hypothyroidism
  - Hyperglycemia
  - Secondary malignancies: skin, GI, hematologic, Gyne/GU, breast, lung, thyroid

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Take home messages

- MGUS and multiple myeloma are on the same spectrum of plasma cell disorders
- Patients with MGUS can be monitored and do not require treatment unless progressive into multiple myeloma
- Overall prognosis of multiple myeloma has improved but it is still an incurable malignancy that requires long term management