Oncology Clinical Pathways
Plasma Cell Disorders

December 2022 – V1.2022

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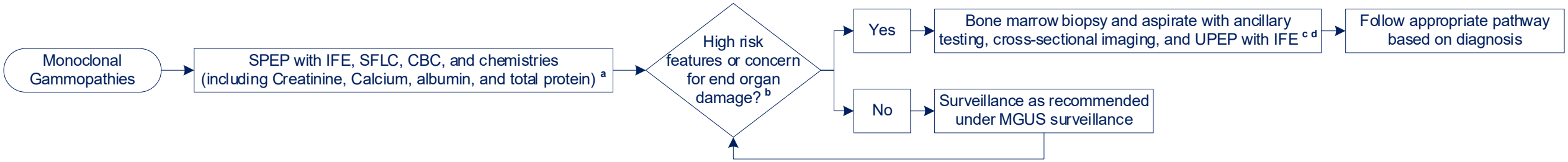
Plasma Cell Disorders – Monoclonal Gammopathies



Clinical trial(s) always considered on pathway.

[a] **Consider Additional Lab Tests** including quantitative immunoglobulins, UPEP with IFE depending on the clinical scenario; **consider cross-sectional imaging** for IgM monoclonal gammopathy

[b] **High Risk** based on risk stratification models that incorporate M-spike level and involved immunoglobulin

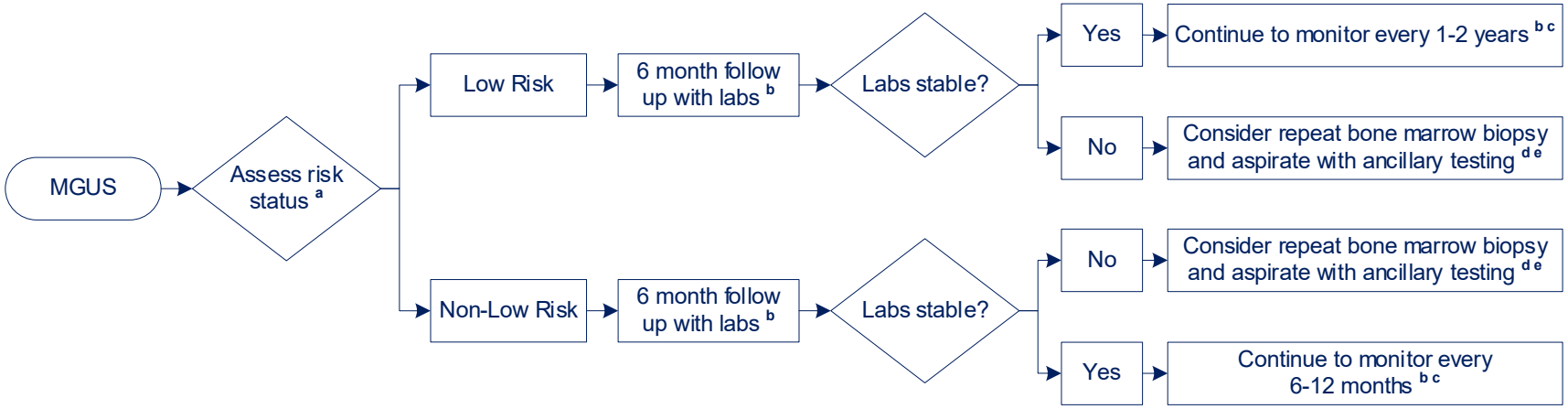
[c] **Ancillary Testing** includes myeloma FISH panel, karyotype, and flow cytometry; myeloma FISH panel should include at minimum: 17p (TP53), del 13, 1q21, 1p, and t(11;14); also either upfront or reflex testing for t(4;14), t(14;16), and t(14;20)

[d] **Imaging** PET/CT vertex to toes, whole body MRI, or whole body low-dose non-contrast CT

IFE Immunofixation Electrophoresis
MGUS Monoclonal Gammopathy of Undetermined Significance
SPEP Serum Protein Electrophoresis
SFLC Serum Free Light Chain
UPEP Urine Protein Electrophoresis

Clinical Trial Resources https://clinicaltrials.gov/ and https://lls-forms.careboxhealth.com/?IRC=HCP

Plasma Cell Disorders – MGUS



Clinical trial(s) always considered on pathway.

[a] **Risk Stratification** based on involved immunoglobulin and level of monoclonal protein

[b] **Follow Up with Labs** measurement of monoclonal protein (e.g. SPEP, SFLC, quantitative immunoglobulins), CBC, and chemistries (including SCr and Ca)

[c] **Monitoring** if expected life expectancy is <5 years, consider discontinuing monitoring

[d] **Ancillary Testing** includes myeloma FISH panel, karyotype, and flow cytometry; myeloma FISH panel should include at minimum: 17p (TP53), del 13, 1q21, 1p, and t(11;14); also either upfront or reflex testing for t(4;14), t(14;16), and t(14;20)

[e] **Imaging** PET/CT vertex to toes, whole body MRI, or whole body low-dose non-contrast CT

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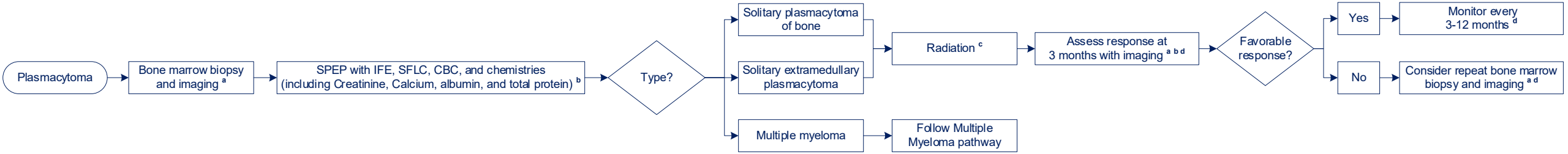
Plasma Cell Disorders – Plasmacytoma



Clinical trial(s) always considered on pathway.

[a] **Imaging** PET/CT, whole body MRI, or whole body non-contrast CT

[b] **Consider Additional Lab Tests** including quantitative immunoglobulins, UPEP, and IFE depending on the clinical scenario

[c] **Radiation** if solitary plasmacytoma of bone is less ≤ 5cm dose with 35-40Gy; if > 5cm 40-50Gy; if solitary extramedullary plasmacytoma dose 40-50Gy regardless of size

[d] **Monitoring** assess response with imaging after completion of radiation; SPEP with IFE, SFLC, CBC, and chemistries (including Creatinine, Calcium, albumin, and total protein)

IFE Immunofixation Electrophoresis
SPEP Serum Protein Electrophoresis
SFLC Serum Free Light Chain
UPEP Urine Protein Electrophoresis

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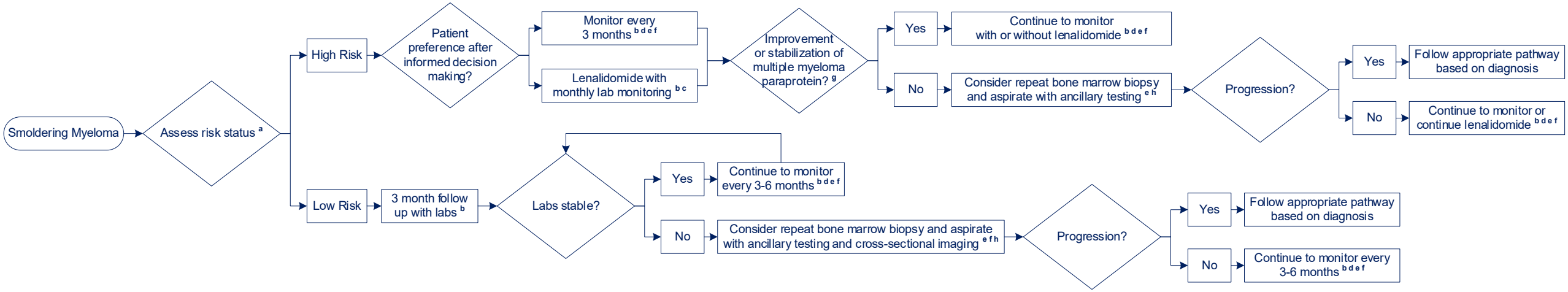
Plasma Cell Disorders – Smoldering Myeloma



Clinical trial(s) always considered on pathway.

[a] **Risk Stratification** high risk defined as bone marrow plasma cells >20%, monoclonal protein >2 g/dL, and SFLC ratio >20 (involved/uninvolved light chain)

[b] **Follow Up with Labs** measurement of monoclonal protein (e.g. SPEP, SFLC, quantitative immunoglobulins), CBC, and chemistries (including SCr and Ca)

[c] **Lenalidomide** thromboembolism prophylaxis required; monitor for toxicity and response; reduce dose based on kidney function

[d] **Consider Additional Lab Tests** including quantitative immunoglobulins, UPEP, and IFE depending on the clinical scenario; **consider yearly cross-sectional imaging** (e.g. PET/CT vertex to toes, whole body MRI, or whole body low-dose non-contrast CT)

[e] **Monitoring** if expected life expectancy is <5 years, consider discontinuing monitoring

[f] **Imaging** PET/CT vertex to toes, whole body MRI, or whole body low-dose non-contrast CT

[g] **Improvement or Stabilization of Multiple Myeloma Paraprotein** based on SPEP, SFLC, UPEP, quantitative immunoglobulins

[h] **Ancillary Testing** includes myeloma FISH panel, karyotype, and flow cytometry; myeloma FISH panel should include at minimum: 17p (TP53), del 13, 1q21, 1p, and t(11;14); also either upfront or reflex testing for t(4;14), t(14;16), and t(14;20)

SPEP Serum Protein Electrophoresis
SFLC Serum Free Light Chain
IFE Immunofixation Electrophoresis

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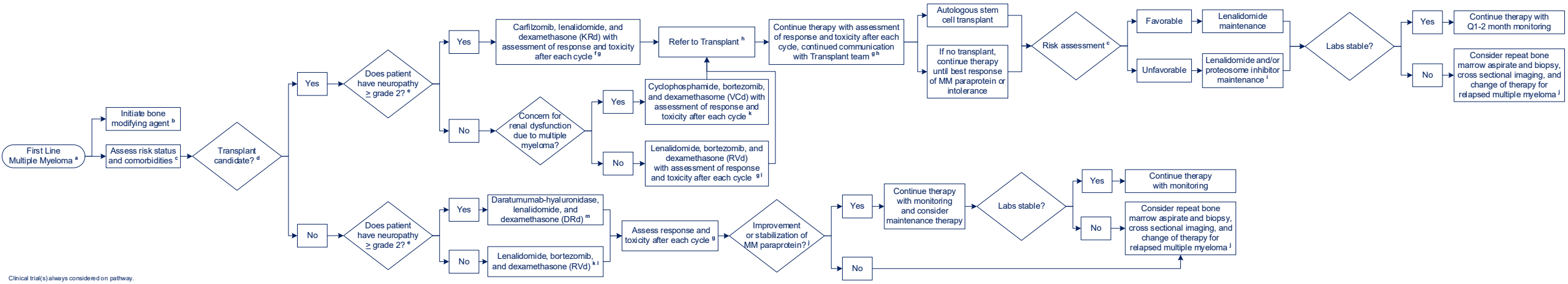
Plasma Cell Disorders – Multiple Myeloma, First Line



Clinical trial(s) always considered on pathway.

[a] **Multiple Myeloma** bone marrow biopsy for diagnosis required; consider Congo Red if amyloidosis is clinically or histologically suspected; consider CD138 immunohistochemistry for suboptimal BM aspirate or apparent discordance between aspirate smear and core biopsy

[b] **Bone Protective Agent** dental evaluation and serum calcium with vitamin D level required before initiation; assess kidney function; preferred agent is zoledronic acid (if CrCl < 30 ml/min, use denosumab or pamidronate)

[c] **Risk Assessment** by R-ISS (B2M, LDH, myeloma FISH, and albumin); if not already complete, obtain CBC, chemistries (including SCr and Ca), cross sectional imaging (PET/CT, whole body MRI, or whole non-contrast CT), measure of monoclonal protein (SPEP, SFLC, Quantitative immunoglobulins, and/or UPEP); myeloma FISH panel should include at minimum: 17p (TP53), del 13, 1q21, 1p, and t(11;14); also either upfront or reflex testing for t(4;14), t(14;16), and t(14;20)

[d] **Transplant Eligibility** refer to Transplant team; discourage use of tobacco, alcohol, or illicit drugs

[e] **Grade 2 Neuropathy** moderate symptoms or limiting instrumental ADLs

[f] **KRd** check transthoracic echocardiogram prior to therapy initiation; do not use for patients with congestive heart failure or active coronary artery disease; consider DOAC for thromboprophylaxis due to higher risk of VTE with Carfilzomib based therapy

[g] **Assessment of Response** includes SPEP, SFLC, and/or UPEP as appropriate; assessment of toxicity includes assessing cytopenias, neuropathy, VTE, infections

[h] **Transplant** early referral recommended; transplant can occur early or delayed based on patient discussion with Transplant team; post-transplant consolidation and/or maintenance timing and selection should occur in consultation with Transplant team; referral for cellular therapy (stem cell transplant, CAR T therapy) requires pre-transplant evaluation and review through TRACER

[i] **Proteosome Inhibitor** preferred agent is bortezomib; monitor for neuropathy and dose reduce or discontinue proteosome inhibitor for worsening neuropathy

[j] **Improvement or Stabilization of Multiple Myeloma Paraprotein** based on SPEP, SFLC, UPEP, quantitative immunoglobulins

[k] **VCd or RVd** consider weekly bortezomib and subcutaneous administration of bortezomib to reduce neuropathy

[l] **RVd or KRd** thromboprophylaxis and VZV prophylaxis required; consider PJP prophylaxis; consider dose reduction of lenalidomide based on renal function; consider dose reduction of dexamethasone based on age

[m] **DRd** thromboprophylaxis and VZV prophylaxis required; consider PJP prophylaxis. Hepatitis B serology, T&S and antibody screen required prior to initiation; consider dose reduction of lenalidomide based on renal function; consider dose reduction of dexamethasone based on age; daratumumab can affect quantification of SPEP M-spike

B2M Serum Beta-2 Microglobulin
DOAC Direct Oral Anticoagulant
MM Multiple Myeloma
SPEP Serum Protein Electrophoresis
SFLC Serum Free Light Chain
T&S Type and Screen
VTE Venous Thromboembolism

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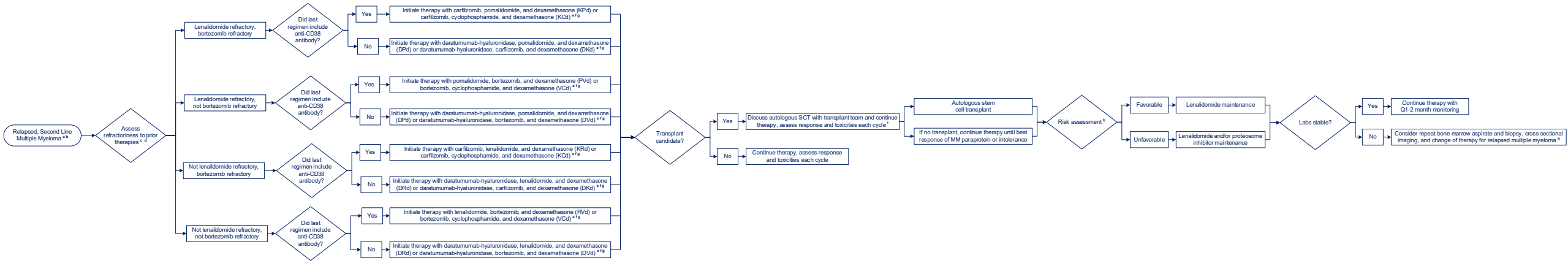
Plasma Cell Disorders – Multiple Myeloma, Second Line Relapsed



Clinical trial(s) always considered on pathway.

[a] **Supportive Care** supportive care should be provided to all myeloma patients receiving therapy

[b] **Subsequent Therapy** consider the following when selecting subsequent therapy:
- Triplet therapy is usually considered more effective than doublet therapy
- CD38 antibody based therapy regimens should be considered if not previously administered
- Alternate combination of drug classes or alternate drugs within a class when selecting a new treatment regimen (i.e., immunomodulatory agents, proteosome inhibitors, CD38 antibodies, alkylator chemotherapy, and others)
- Route and frequency of administration of new treatment regimens to align with patient preferences in therapy
- Dose reduction may be needed to continue therapy in the face of adverse events and prior toxicities

[c] **Consideration of Alternate Treatment** based on duration and/or depth of response to prior therapy and toxicities

[d] **Assessment of Response** includes SPEP, SFLC, and/or UPEP as appropriate; assessment of toxicity includes assessing cytopenias, neuropathy, VTE, infections

[e] **Treat Until Intolerance or Progression** consider reduction or elimination of dexamethasone for patients responding well to therapy after at least six cycles

[f] **Assess patient** comorbidities, multiple myeloma predictive/prognostic factors, and patient preference

[g] **Patient Comorbidities** neuropathy: avoid bortezomib, cardiopulmonary disease: avoid carfilzomib **Multiple Myeloma Predictive/Prognostic Factors:** high risk cytogenetics: favor bortezomib or carfilzomib based regimens, presence of t(11;14): consider venetoclax based regimen; **Patient Preference**: consider regimens that are administered only in clinic depending on patient preference

[h] **Supportive Care and Treatment Modification Considerations**
- Thromboprophylaxis required with IMIDs (e.g., lenalidomide, pomalidomide); options include aspirin, enoxaparin, or DOAC; DOAC preferred when IMID is paired with Carfilzomib due to higher thrombosis risk
- VZV prophylaxis is required with proteosome inhibitors (e.g., bortezomib, carfilzomib) and with CD38 antibodies (e.g., daratumumab)
- PJP prophylaxis recommended due to ongoing/chronic dexamethasone use.
- Lenalidomide requires dose reduction/modification based on renal function
- Dexamethasone should be dose reduced to 20 mg weekly for age >75 years
- Once multiple myeloma response has been reached, dexamethasone dosing frequency should be reduced or even discontinued to reduce risk of infections
- Bortezomib should be administered subcutaneously to reduce risk of neuropathy. Consider weekly bortezomib administration to reduce risk of neuropathy
- Subcutaneous daratumumab-hyaluronidase is preferred over daratumumab due to reduced adverse reactions and faster administration
- T&S and antibody screen and hepatitis B serologies prior to daratumumab or daratumumab-hyaluronidase administration
- Palliative XRT for painful osseous lesions; minimize bone marrow exposure, especially of the pelvis, in patients who are transplant candidates
- Consider IVIG for patients with hypogammaglobulinemia of the uninvolved immunoglobulins and recurrent infections

[i] **Referral for Cellular Therapy** (stem cell transplant, CAR T therapy) requires pre-transplant evaluation and review through TRACER

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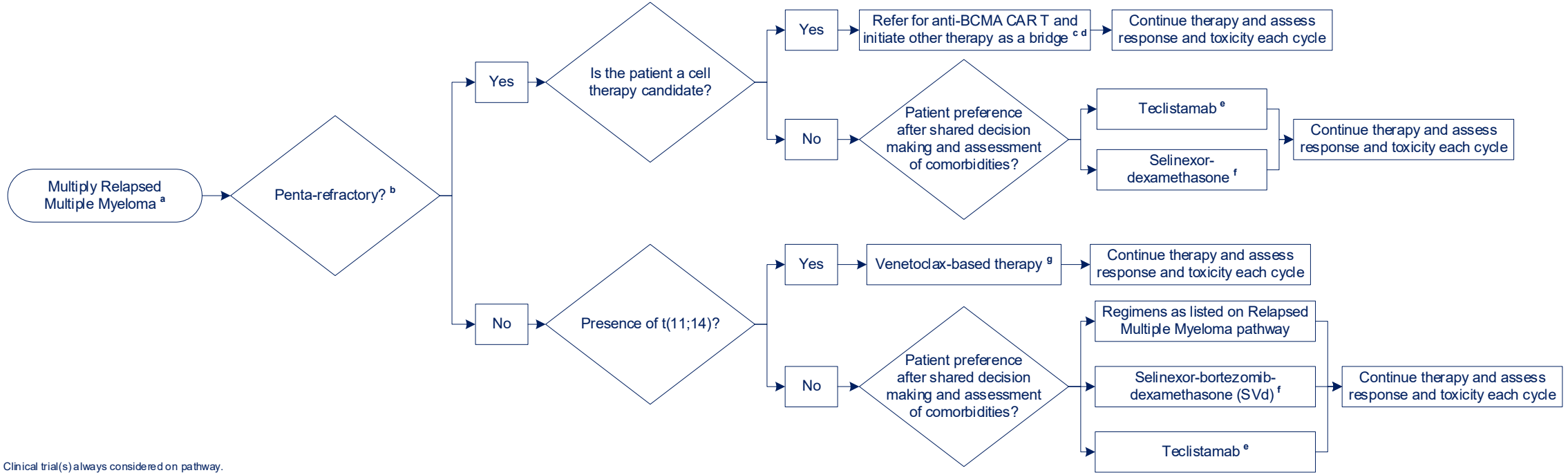
Plasma Cell Disorders – Multiple Myeloma, Multiply Relapsed



Clinical trial(s) always considered on pathway.

[a] **Supportive Care** supportive care should be continued for all myeloma patients receiving therapy; referral to palliative care recommended

[b] **Penta-refractory** progression within 6 months of therapy of each of the following therapies: Lenalidomide, Pomalidomide, Bortezomib, Carfilzomib, and CD38 antibody (e.g. daratumumab)

[c] **CAR T Therapy** is associated with risk of cytokine release syndrome and neurotoxicity, and requires inpatient hospitalization for monitoring

[d] **Referral for Cellular Therapy** (stem cell transplant, CAR T therapy) requires pre-transplant evaluation and review through TRACER

[e] **Teclistamab** requires facility support and protocols for monitoring of and management of cytokine release syndrome and CNS toxicity

[f] **Selinexor** has moderate to high emetogenicity risk, can cause fatigue and hyponatremia; anti-emetic prophylaxis and close monitoring recommended; dose reduction after 1-2 cycles recommended

[g] **Venetoclax** requires TLS monitoring during ramp-up period and is associated with risk of infections; anti-viral prophylaxis is highly recommended; growth factor support may be used for cytopenias

BCMA B-Cell Maturation Antigen
CAR T Chimeric Antigen Receptor T-cell
Clinical Trial Resources https://clinicaltrials.gov/ and https://lls-forms.careboxhealth.com/?IRC=HCP

Questions?

Contact VHAOncologyPathways@va.gov