Oncology Clinical Pathways
Marginal Zone Lymphoma

May 2024 – V2.2024

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Marginal Zone Lymphoma – Presumptive Conditions

VA automatically presumes that certain disabilities were caused by military service. This is because of the unique circumstances of a specific Veteran's military service. If a presumed condition is diagnosed in a Veteran within a certain group, they can be awarded disability compensation.

Atomic Veterans – Exposure to Ionizing Radiation

- Lymphomas, other than Hodgkin's disease

Vietnam Veterans – Agent Orange Exposure or Specified Locations

- Non-Hodgkin's lymphoma

Gulf War and Post 9/11 Veterans

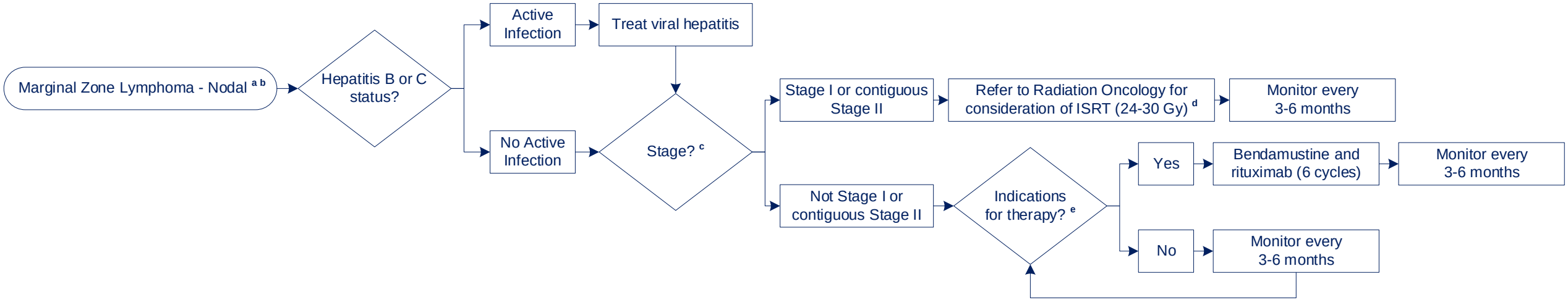
If the patient served on or after Sept. 11, 2001, in Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen or if the patient served in the *Southwest Asia theater of operations, or Somalia, on or after Aug. 2, 1990, specific conditions include:

- Lymphoma of any type

* The Southwest Asia theater of operations refers to Iraq, Kuwait, Saudi Arabia, the neutral zone between Iraq and Saudi Arabia, Bahrain, Qatar, the United Arab Emirates, Oman, the Gulf of Aden, the Gulf of Oman, the Persian Gulf, the Arabian Sea, the Red Sea, and the airspace above these locations.

For more information, please visit U.S. Department of Veterans Affairs - Presumptive Disability Benefits (va.gov)

Marginal Zone Lymphoma – Nodal



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Supportive Care and Pre-Therapy Considerations** include Hepatitis B serologies prior to starting anti-CD20 antibody therapy (e.g. rituximab); consider HBV DNA if HBsAg or HBcAb positive; consider entecavir if HBsAg or HBcAb positive; COVID and pneumococcal vaccinations recommended; consider VZV/HSV and PJP prophylaxis with any bendamustine-regimen

[b] **Pathology Workup** includes sufficient flow cytometry or IHC workup to exclude other small B-cell lymphomas (e.g. CD5, CD10, CD103, CD200, CD11c, CD25, CD23, BCL2, BCL6, cyclin D1, KI-67, etc.); some molecular testing may be diagnostically useful in certain circumstances

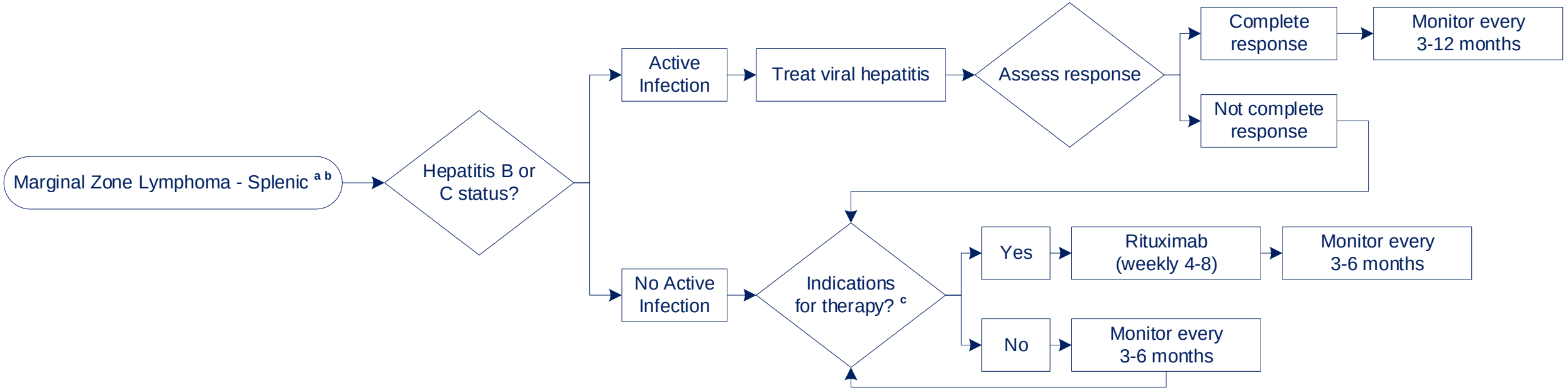
[c] **Stage** if clinically limited stage, perform bone marrow biopsy and PET/CT to confirm

[d] **Radiation** ISRT recommended

[e] **Indications for Therapy** local symptoms due to nodal disease, reduced organ function due to nodal disease, B-symptoms (fever, weight loss, night sweats), cytopenia attributable to disease (Hgb < 10 g/dL, platelets <100,000/mm3), or an increase in disease tempo

IHC Immunohistochemistry
ISRT Involved Site Radiation Therapy

Marginal Zone Lymphoma – Splenic



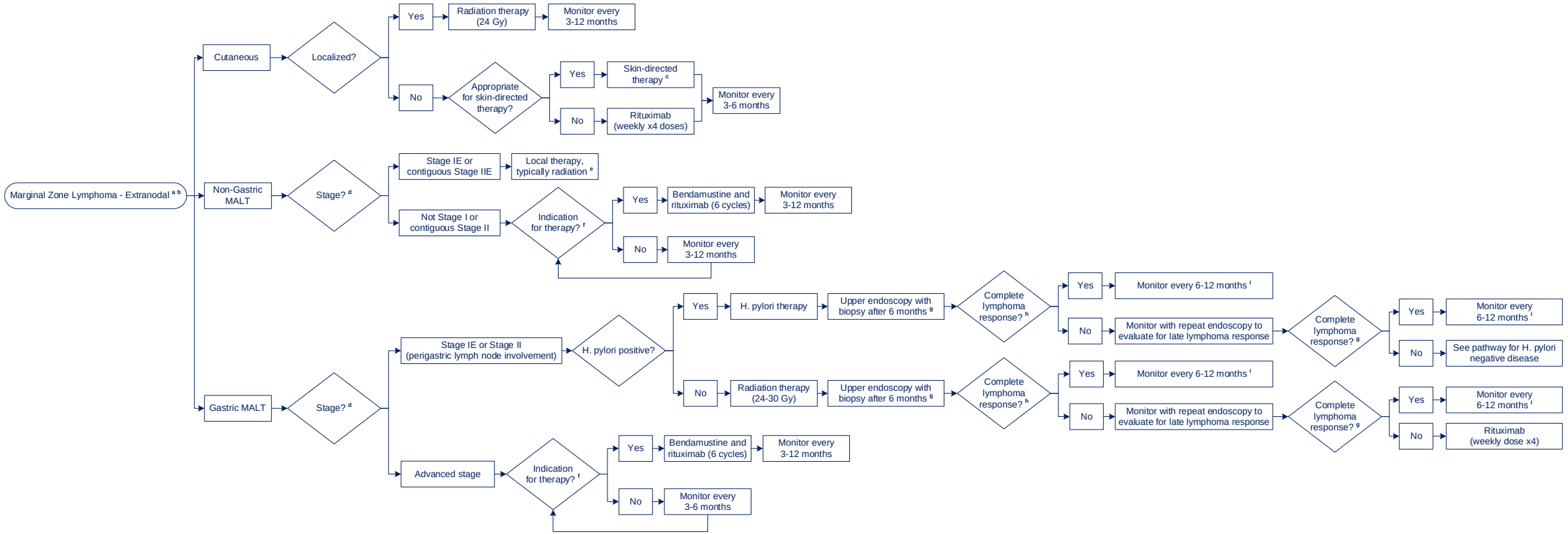
Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Supportive Care and Pre-Therapy Considerations** include Hepatitis B serologies prior to starting anti-CD20 antibody therapy (e.g. rituximab); consider HBV DNA if HBsAg or HBcAb positive; consider entecavir if HBsAg or HBcAb positive; COVID and pneumococcal vaccinations recommended

[b] **Pathology Workup** includes sufficient flow cytometry or IHC workup to exclude other small B-cell lymphomas (e.g. CD5, CD10, CD103, CD200, CD11c, CD25, CD23, BCL2, BCL6, cyclin D1, KI-67, etc.); some molecular testing may be diagnostically useful in certain circumstances

[c] **Indications for Therapy** local symptoms related to splenomegaly or cytopenias due to hypersplenism or bone marrow involvement; autoimmune cytopenias should be treated with specific therapies for these situations

Marginal Zone Lymphoma – Extranodal



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Supportive Care and Pre-Therapy Considerations** include Hepatitis B serologies prior to starting anti-CD20 antibody therapy (e.g. rituximab); consider HBV DNA if HBsAg or HBcAb positive; consider entecavir if HBsAg or HBcAb positive; COVID and pneumococcal vaccinations recommended; consider VZV/HSV and PJP prophylaxis with any bendamustine-regimen; if biopsy is negative for H pylori, stool antigen testing should also be pursued to rule out active infection

[b] **Pathology Workup** includes sufficient flow cytometry or IHC workup to exclude other small B-cell lymphomas (e.g. CD5, CD10, CD103, CD200, CD11c, CD25, CD23, BCL2, BCL6, cyclin D1, KI-67, etc.); some molecular testing may be diagnostically useful in certain circumstances; the presence of t(11;18) is associated with inferior response to H. pylori antibiotic therapy

[c] **Skin Directed Therapy** (appropriate for patients with multifocal low volume disease) examples include palliative radiation therapy (2 Gy x2), intralesional steroids, topical steroids, topical imiquimod

[d] **Stage** if clinically limited stage, perform bone marrow biopsy and PET/CT to confirm

[e] **Local Therapy** in certain situations, surgery is used; decision between surgery and radiation therapy should take into consideration the site involved and the risks of either intervention (surgery vs radiation therapy); if the risks of local therapy are excessive, observation may be appropriate, especially in asymptomatic patients; if radiation is being pursued for localized orbital malt lymphoma, 2 Gy x2 is recommended with higher doses (20-24 Gy) reserved for patients with progressive disease

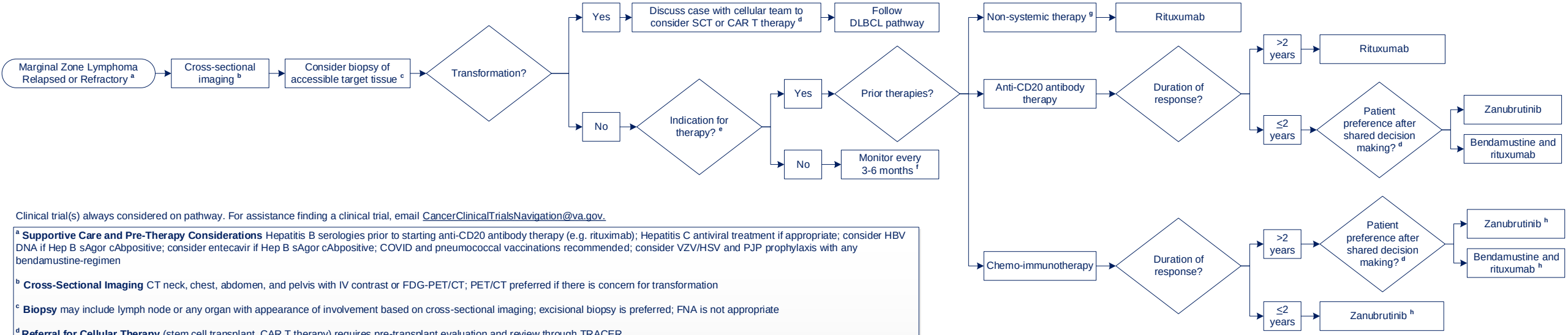
[f] **Indications for Therapy** include cytopenias felt to be due bone marrow involvement by lymphoma; symptomatic adenopathy or splenomegaly, impaired organ function felt to be due to lymphoma

[g] **Upper Endoscopy** can be done earlier in patients with persistent symptoms

[h] **Complete Lymphoma Response** assessment for response to H. pylori therapy for gastric MALT should include evaluation for clearance of H. pylori infection and evaluation for resolution of lymphoma (a complete response may take up to 18 months to be achieved); if there is persistent H. pylori infection, additional antibiotic therapy should be given; the presence of t(11;18) is associated with inferior response to H. pylori antibiotic therapy

[i] **Clinical Monitoring** is recommended after gastric MALT therapy and post-treatment endoscopy demonstrating complete response; routine endoscopy for asymptomatic patients is not recommended; the presence of t(11;18) may require closer monitoring in patients treated with antibiotic therapy

Marginal Zone Lymphoma – Relapsed or Refractory



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov.

[a] **Supportive Care and Pre-Therapy Considerations** Hepatitis B serologies prior to starting anti-CD20 antibody therapy (e.g. rituximab); Hepatitis C antiviral treatment if appropriate; consider HBV DNA if Hep B sAgor cAbpositive; consider entecavir if Hep B sAgor cAbpositive; COVID and pneumococcal vaccinations recommended; consider VZV/HSV and PJP prophylaxis with any bendamustine-regimen

[b] **Cross-Sectional Imaging** CT neck, chest, abdomen, and pelvis with IV contrast or FDG-PET/CT; PET/CT preferred if there is concern for transformation

[c] **Biopsy** may include lymph node or any organ with appearance of involvement based on cross-sectional imaging; excisional biopsy is preferred; FNA is not appropriate

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

[e] **Indications for Therapy** local symptoms due to lymphoma, reduced organ function due to lymphoma, B-symptoms (fever, weight loss, night sweats), cytopenias (Hgb < 10 g/dL, platelets <100,000/mm3), or an increase in disease tempo

[f] **Surveillance** initially q3 months, then spaced to Q6-12 months, consisting of physical exam and labs; surveillance imaging is not recommended for asymptomatic patients

[g] **Non-systemic therapy** examples include palliative XRT, intralesional injection, topical steroids, topical imiquimod and surgical resection

[h] **Referral to Cell Therapy Team** for refractory or multiply relapsed disease referral for evaluation for cellular therapies is recommended

DLBCL Diffuse Large B-Cell Lymphoma

Marginal Zone Lymphoma – Molecular Testing

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Suspected Nodal Marginal Zone Lymphoma to Assist with Diagnosis	Consider IHC or Flow Cytometry	IHC for CD5, CD10, CD103, CD200, CD11c, CD25, CD23, BCL2, BCL6, cyclin D1, KI-67	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	Consider FISH	FISH for t(11;14) to differentiate from mantle cell lymphoma	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	Consider Targeted Sequencing	MYD88 mutation testing to differentiate from lymphoblastic lymphoma	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
Suspected Marginal Zone Lymphoma of Mucosa-Associated Lymphoid Tissue (MALT) to Assist with Diagnosis	Consider IHC or Flow Cytometry	IHC for CD5, CD10, CD103, CD200, CD11c, CD25, CD23, BCL2, BCL6, cyclin D1, KI-67	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	Consider FISH	FISH for t(11;14) to differentiate from mantle cell lymphoma	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	Consider Targeted Sequencing	MYD88 mutation testing to differentiate from lymphoplasmacytic lymphoma. Please note that can be found in 5-10% of MALTs.	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	Consider FISH	FISH for MALT1 break apart, t(1;14), t(3;14), t(14;18), t(11;18)	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	Consider FISH	Trisomy 3 and trisomy 18. Please note that they may not be specific	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
Suspected Cutaneous Marginal Zone Lymphoma to Assist with Diagnosis	Consider IHC	IHC for IgM, IgG, IgG4, IgA	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood

***** Routine FISH and molecular testing not required unless required for diagnosis