Oncology Clinical Pathways
Follicular Lymphoma

December 2024 – V3.2024

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Follicular 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

Gulf War and Post 9/11 Veterans

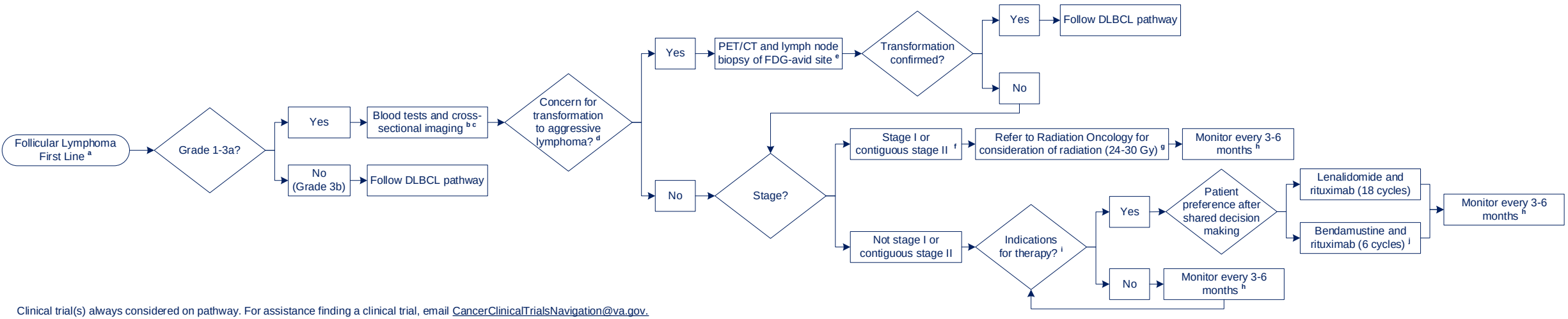
If the patient served on or after Sept. 11, 2001, in Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen or if the patient served in the *Southwest Asia theater of operations, or Somalia, on or after Aug. 2, 1990, specific conditions include:

- 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)

Follicular Lymphoma – First Line



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

[a] **Supportive Care** Hepatitis B serologies prior to starting anti-CD20 antibody therapy (e.g. rituximab); consider HBV DNA if HBsAg or HBcAb positive; prescribe entecavir if HBsAg or HBcAb positive; Hepatitis C antiviral treatment if appropriate; COVID and pneumococcal vaccinations recommended; VTE prophylaxis required with lenalidomide; consider VZV/HSV and PJP prophylaxis with any bendamustine-regimen; consider G-CSF growth factor support for age >70 years, pre-existing leukopenia, recent prior chemotherapy; radiation therapy (2 Gy x 2) can be helpful for symptomatic sites; referral to Registered Dietitian for medical nutrition therapy

[b] **Cross-Sectional Imaging** CT neck, chest, abdomen, and pelvis with IV contrast or FDG-PET/CT; PET/CT preferred if Stage I-II

[c] **Blood Tests** CBC with differential, CMP, uric acid, LDH, HBsAg, HBsAb, HBcAb, HCV antibody, HIV

[d] **Clinical Suspicion for Transformation to Aggressive Lymphoma** may include features such as rapid enlargement of an individual lymph node, PET/CT with high FDG uptake, very elevated LDH, and/or significant B- symptoms/weight loss not attributed to other causes; a pathological diagnosis is needed for confirmation

[e] **Biopsy** of lymph node; excisional preferred; ancillary/molecular test as appropriate based on discussion with hematopathology

[f] **Stage** bone marrow biopsy and PET/CT should be performed to confirm limited stage

[g] **Radiation** risk-benefit consideration should include assessment of side effect profile and goal of therapy (low dose of XRT, low side effects, expected very lengthy duration of response) together with consideration of life expectancy from non-lymphoma causes as survival from limited stage follicular lymphoma is generally excellent

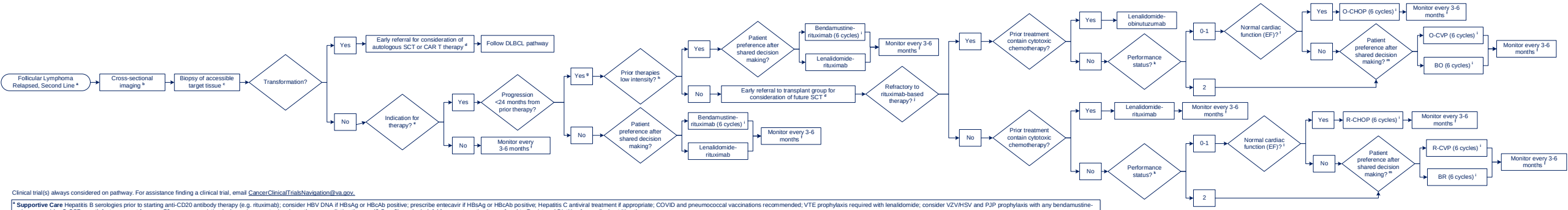
[h] **Surveillance** initially q3 months, then spaced to Q6-12 months, consisting of physical exam and labs; surveillance imaging is not recommended for asymptomatic patients

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

[j] **Maintenance Rituximab** dosed every 8 weeks for a total of 24 months improves progression free survival without improved overall survival and increases the risks of infection including COVID; may be considered but only after weighing risks and benefits with the patient

DLBCL Diffuse Large B-Cell Lymphoma

Follicular Lymphoma – Relapsed, Second Line



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[a] **Supportive Care** Hepatitis B serologies prior to starting anti-CD20 antibody therapy (e.g. rituximab); consider HBV DNA if HBsAg or HBcAb positive; prescribe entecavir if HBsAg or HBcAb positive; Hepatitis C antiviral treatment if appropriate; COVID and pneumococcal vaccinations recommended; VTE prophylaxis required with lenalidomide; consider VZV/HSV and PJP prophylaxis with any bendamustine-regimen; consider G-CSF growth factor support for age >70 years, pre-existing leukopenia, recent prior chemotherapy; radiation therapy (2 Gy x 2) can be helpful for symptomatic sites; referral to Registered Dietitian for medical nutrition therapy

[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** local symptoms due to nodal disease, reduced organ function due to nodal disease, B-symptoms (fever, weight loss, night sweats), cytopenias (Hgb < 10 g/dL, platelets <100,000/mm3), or an increase in disease tempo; discussion with stem cell therapy team as appropriate

[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] **Patients with Progression** may have poor prognosis regardless of prior therapies; a clinical trial is recommended

[h] **Low Intensity Therapies** include XRT, single agent anti-CD20 antibody, and/or chlorambucil

[i] **Maintenance Anti-CD20 Antibody (e.g., rituximab, obinutuzumab)** dosed every 8 weeks for a total of 24 months improves progression free survival without improved overall survival and increases the risks of infection including COVID; may be considered but only after weighing risks and benefits with the patient

[j] **Refractory** defined as relapse within 6 months of therapy completion

[k] **Performance Status** refer to ECOG Performance Status rating

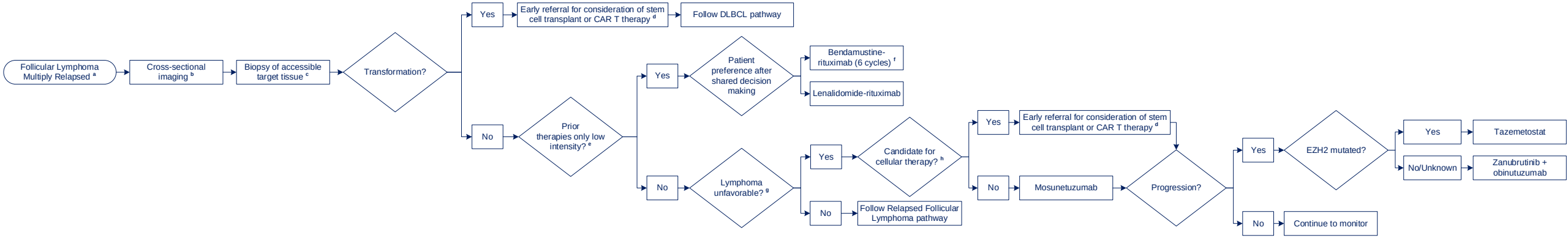
[l] **Normal Cardiac Function** defined as ejection fraction >50% on echocardiogram or MUGA

[m] **Shared Decision Making** selection based on side effect profile; BR and BO associated with more nausea, infusion reactions, lymphopenia, and possibly more secondary malignancies; R-CVP and O-CVP associated with more neuropathy, neutropenia, and alopecia; BO has been associated with a higher risk of infections; VZV and PJP prophylaxis is recommended

[n] **Criteria for Radio-Immunotherapy** includes patient-specific factors (bone marrow involvement by lymphoma is <25%, not having received prior radiation therapy affecting >25% of the bone marrow, platelet count >100,000, ANC >1,500, and no prior stem cell therapy) and facility-specific factors (radio-immunotherapy is not offered at all facilities and there may be delays in referrals to facilities that do offer it)

BO Bendamustine, Obinutuzumuab
BR Bendamustine, Rituximab
DLBCL Diffuse Large B-Cell Lymphoma
EF Ejection Fraction
O-CHOP Obinutuzumab, Cyclophosphamide, Vincristine, Doxorubicin, Prednisone
O-CVP Obinutuzumab, Cyclophosphamide, Vincristine, Prednisone
R-CVP Rituximab, Cyclophosphamide, Vincristine, Prednisone
R-CHOP Rituximab, Cyclophosphamide, Vincristine, Doxorubicin, Prednisone

Follicular Lymphoma – Multiply Relapsed



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[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] **Low Intensity Therapies** include XRT, single agent anti-CD20 antibody, and/or chlorambucil

[f] **Maintenance Rituximab** dosed every 8 weeks for a total of 24 months improves progression free survival without improved overall survival and increases the risks of infection including COVID; may be considered but only after weighing risks and benefits with the patient

[g] **Unfavorable** defined as relapsed after anti-CD20 antibody, cytotoxic chemotherapy, and lenalidomide, or progression <24 months from all prior treatments

[h] **Candidate for Cellular Therapy** defined as ECOG performance status 0-1, few or controlled comorbidities, younger age (typically <70 years), patient and caregiver willing to relocate to cell therapy site if needed

Follicular Lymphoma – Molecular Testing Table

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Clinical or Pathological Features Suspicious for Pediatric-Type Follicular Lymphoma	IHC	IHC for BCL2 and BCL6	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	FISH	FISH for t(14;18), BCL6, IRF4 or IGH rearrangements, 1p36	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
Clinical or Pathological Features Suspicious for Large B-Cell Lymphoma with IRF4 Rearrangement	IHC	IHC for BCL2, BCL6, CD10 and MUM1	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	FISH	FISH for IRF4/MUM1 cryptic rearrangement with IGH	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
Multiply Relapsed Follicular Lymphoma	Molecular	*EZH2* mutation analysis	Tempus Foundation	Yes Yes	Bone Marrow Biopsy, Lymph Node Biopsy, Blood