Oncology Clinical Pathways

Diffuse Large B-Cell Lymphoma

September 2024 – V4.2024

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Diffuse Large B-Cell 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

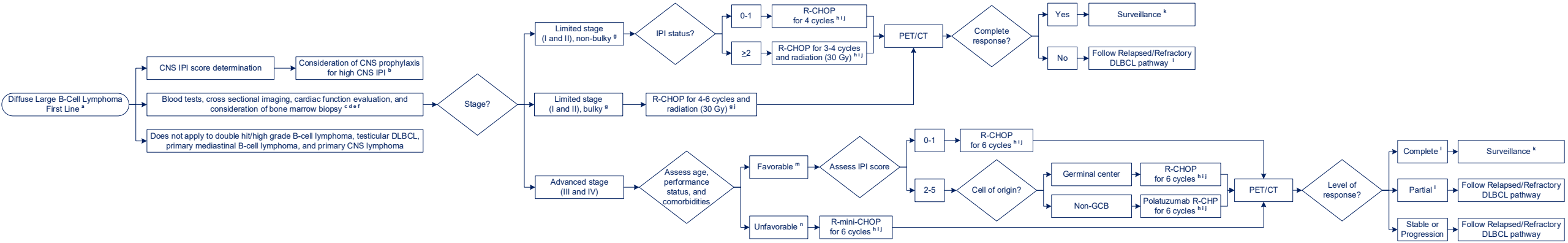
If the patient served on or after Sept. 11, 2001, in Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen or if the patient served in the *Southwest Asia theater of operations, or Somalia, on or after Aug. 2, 1990, specific conditions include:

- 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)

Diffuse Large B-Cell Lymphoma – First Line



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

[a] **Diffuse Large B-Cell Lymphoma** confirmation by biopsy should be excisional; core needle biopsy may be sufficient depending on the sample obtained; confirm pathology evaluation included Cell of Origin testing (CD10, MUM1, and BCL6 IHC) and evaluation for double hit +/- double expressor status (MYC, BCL2, and BCL6 break apart FISH; MYC and BCL2 IHC); consider additional pathology evaluation including cyclin D1, Ki67, and EBER stain based on clinical situation after discussion with your pathologist; second review by a hematopathologist may be helpful

[b] **CNS Prophylaxis** can include either high dose methotrexate or intrathecal methotrexate depending on clinical scenario; the degree of benefit of CNS prophylaxis to overcome high risk of CNS relapse is unclear; risks include infections and cytopenias; discussion with patient and shared decision making is recommended

[c] **Blood Tests** include CBC, CMP, LDH, uric acid, Phos, Hep C Ab, Hep B sAg, Hep B sAb, Hep B cAb, HIV

[d] **Cross Sectional Imaging** PET/CT recommended

[e] **Cardiac Function** should be evaluated by echocardiogram or MUGA; good cardiac function defined as EF >50%; poor cardiac function defined as EF ≤ 50%

[f] **Bone Marrow Biopsy** required to confirm limited stage if combined modality therapy or abbreviated course of chemotherapy is being considered

[g] **Bulky Disease** defined as ≥7cm

[h] **Supportive Care** empiric GCSF support should be used if age >65 years, cytopenias at diagnosis, bone marrow involvement; GCSF should be added if not already used if infections or febrile neutropenia occurs during therapy; anti-infection prophylaxis: VZV/HSV recommended; stimulant laxatives and anti-emetics recommended; consider inpatient monitoring and management for tumor lysis syndrome at cycle 1 in patients with high burden of disease, renal dysfunction, rapidly growing lymphoma; use allopurinol, intravenous fluids, and rasburicase as needed; consider inpatient monitoring for patients with intestinal involvement in cycle 1 due to risk of perforation; consider referral for fertility preservation for appropriate and interested patients; immunizations with pneumococcal and COVID vaccines recommended after chemotherapy; referral to Registered Dietitian for medical nutrition therapy

[i] **Interim Cross-Sectional Imaging** is helpful to confirm initial response

[j] **R-CEOP** is an acceptable alternative in patients with cardiac function that is inadequate for anthracycline therapy

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

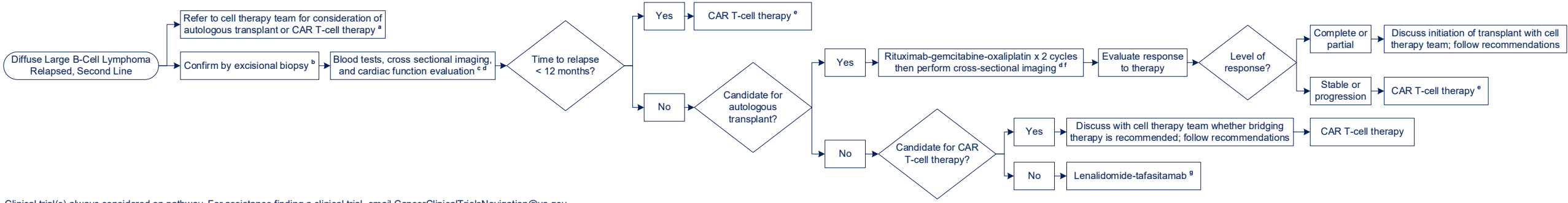
[l] **Consolidation Radiation** Therapy may be considered in patients with bulky disease (30 Gy) or with a single site of persistent FDG-avid disease (36-45 Gy)

[m] **Favorable** defined as age <80 years, ECOG PS 0-2, fewer/compensated comorbidities

[n] **Unfavorable** defined as age ≥ 80 years, ECOG PS 3 not due to lymphoma, more/uncompensated comorbidities

CNS Central Nervous System
DLBCL Diffuse Large B-Cell Lymphoma
IPI International Prognostic Index
GCB Germinal Center B-Cell
PMBCL Primary Mediastinal B-Cell Lymphoma
R-CHOP Rituximab, Cyclophosphamide, Doxorubicin, Vincristine, Prednisone
R-CEOP Rituximab, Cyclophosphamide, Etoposide, Vincristine, Prednisone

Diffuse Large B-Cell Lymphoma – Relapsed, Second Line



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[a] **Refer to Cellular Therapy** (stem cell transplant, CAR T-cell therapy) requires pre-transplant evaluation and review through TRACER

[b] **Confirmation by Excisional Biopsy** preferred; core needle biopsy may be sufficient depending on the sample obtained; confirm pathology evaluation included Cell of Origin testing (CD10, MUM1, and BCL6 IHC) and evaluation for double hit +/- double expressor status (MYC, BCL2, and BCL6 break apart FISH; MYC and BCL2 IHC); consider additional pathology evaluation including cyclin D1, Ki67, and EBER stain based on clinical situation; second review by a hematopathologist may be helpful

[c] **Blood Tests** include CBC, CMP, LDH, uric acid, Phos, Hep C Ab, Hep B sAg, Hep B sAb, Hep B cAb, HIV

[d] **Cross Sectional Imaging** PET/CT

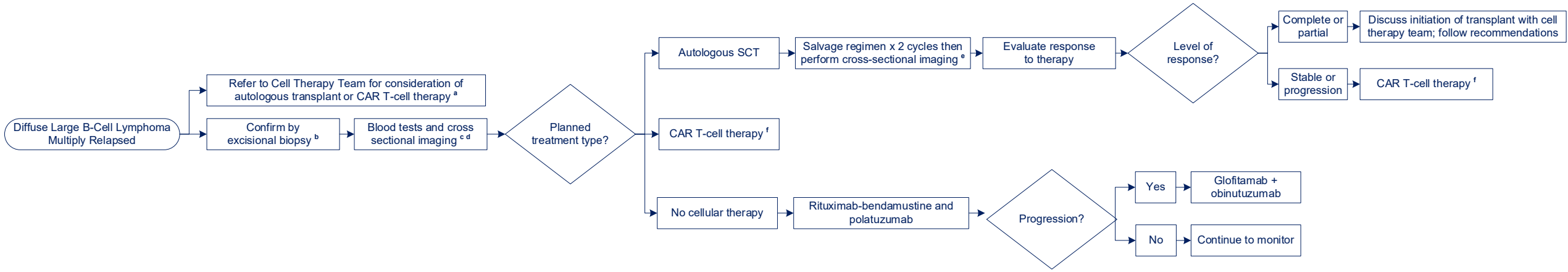
[e] **CAR T-cell Therapy** discuss with cell therapy team whether bridging therapy is recommended; follow recommendations

[f] **Salvage Regimens** various platinum-based salvage regimens are considered equivalent and may be selected based on administration schedule and side effects; rituximab-gemcitabine-oxaliplatin may be administered in outpatient clinic but others are administered via continuous inpatient IV infusion; rituximab-ifosfamide-carboplatin-etoposide should be used with caution in patients with renal impairment or older age due to central neurotoxicity; monitor for peripheral neuropathy with all salvage regimens

[g] **Lenalidomide-Tafasitamab** based therapy requires thromboprophylaxis

CAR Chimeric Antigen Receptor T-cell
DLBCL Diffuse Large B-Cell Lymphoma

Diffuse Large B-Cell Lymphoma – Multiply Relapsed



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Diffuse Large B-Cell Lymphoma – Molecular Testing Table

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Diffuse Large B-Cell Lymphoma, Initial Diagnosis or Relapse	IHC	Hans algorithm testing for cell of origin CD10, MUM1, and BCL6	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	IHC	IHC for BCL2, MYC double expressor status	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	FISH	MYC, BCL2, BCL6 break apart FISH	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	ISH	EBER in-situ hybridization (if morphologically concerning)	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	IHC	Consider Ki67, Cyclin D1 (if pathologist recommended post discussion)	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	IHC	Consider IHC for CD30 (if considering brentuximab therapy)	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	FISH	Consider FISH for IRF4 rearrangement (if pathologist recommended post discussion)	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
Diffuse Large B-Cell Lymphoma: High-Grade Morphologic Features but NOT Double/Triple Hit	IHC	Consider IHC for TdT and CD34 if concerned for lymphoblastic lymphoma	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	IHC	Consider CD5 and cyclin D1 if concerned for pleomorphic/blastoid mantle cell lymphoma	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood
	Array CGH or FISH	Consider 11q abnormalities for Burkitt-like lymphoma	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Lymph Node Biopsy, Blood