HIV-Related B-Cell Lymphomas[1]

Note: Consider Clinical Trials as treatment options for eligible patients.

DIAGNOSIS

ESSENTIAL:

- Hematopathology review of all slides with at least one tumor paraffin block. Rebiopsy if consult material is non-diagnostic.
- Adequate immunophenotyping to confirm diagnosis
  - Paraffin panel: CD3, CD10, CD20, CD45 (LCA), BCL2, BCL6, Ki-67, CD 138, kappa/lambda light chains, HHV8
  - Flow cytometry immunophenotyping (optional if paraffin IHC has been performed): kappa/lambda light chains, CD3, CD5, CD10, CD19, CD20, CD45
- In situ hybridization: Epstein-Barr virus encoded RNA (EBER)
- EBV PCR

OF USE IN CERTAIN CIRCUMSTANCES:

- Additional immunohistochemical studies to establish lymphoma subtype
  - Diffuse large B-cell, Burkitt, plasmablastic, primary effusion lymphoma: CD10, BCL2, Ki-67, BCL6, CD138, CD30 for PEL, KSHV LANA-1
- Molecular genetic analysis
  - FISH test to detect *MYC*, BCL2 and BCL6 gene rearrangements

STRONGLY RECOMMENDED:

- FNA or core biopsy for tissue banking by protocol
- Perform gene mutation panel if available

EBV PCR = Epstein-Barr virus polymerase chain reaction
KSHV LANA = Kaposi's sarcoma-associated herpesvirus latency-associated nuclear antigen
FISH = florescence in situ hybridization
FNA = fine needle aspiration
HIV = human immunodeficiency virus

[1] Patients should be co-managed by an oncologist and HIV specialist
[2] See Physical Activity, Nutrition, Obesity Screening and Management, and Tobacco Cessation Treatment algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

INITIAL EVALUATION

ESSENTIAL:

- Physical exam:
  - Performance status (ECOG)
  - B symptoms (Unexplained fever > 38°C during the previous month; Recurrent drenching night sweats during the previous month; Weight loss > 10 percent of body weight ≤ 6 months of diagnosis)
- Laboratory Tests:
  - CBC with differential, BUN, creatinine, AST, ALT, albumin, total bilirubin, alkaline phosphatase, serum calcium, phosphorus, magnesium, LDH, and uric acid
  - HIV-1 and HIV-2 ○ CD4 count ○ HIV viral load
  - Screening for hepatitis B and C (HBcAb, HBsAg, HCV Ab)
  - Beta-2 microglobulin
  - Quantitative immunoglobulin levels
- Imaging:
  - Chest X-ray, PA and lateral
  - CT with contrast of neck, chest, abdomen and pelvis
  - PET/CT scan
- Other tests:
  - Bilateral bone marrow biopsy with aspirate
  - Echocardiogram with strain/speckle tracking or MUGA (multigated acquisition) scan
  - EKG
  - Lumbar puncture with cytology evaluation and flow cytometry
- Consultation to Infectious Diseases
  - Antiretrovirals often can be administered safely with chemotherapy
- Lifestyle risk assessment[2]

OF USE IN SELECTED CASES:

- Upper GI/barium enema/endoscopy
- MRI of brain with gadolinium or CT of brain
- Plain bone radiographs
- HHV-8 PCR
- Pregnancy test in women of childbearing potential
- Consider fertility consultation (refer to Fertility Preservation Prior to Cancer Treatment algorithm)

See Page 2 For Clinical Presentations and Primary Treatment

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HIV-Related B-Cell Lymphomas

Note: Consider Clinical Trials as treatment options for eligible patients.

CLINICAL PRESENTATION	PRIMARY TREATMENT[1]	RESPONSE EVALUATION
Burkitt Lymphoma[2]	• Clinical trial **or** • Rituximab and dose adjusted EPOCH with intrathecal chemotherapy and filgrastim product **or** • Rituximab and HCVAD alternating with rituximab and methotrexate and cytarabine with intrathecal chemotherapy and filgrastim product **or** • Rituximab and CODOX-M[3] alternating with rituximab and IVAC with intrathecal chemotherapy and filgrastim product • If CD4 < 50 cell/mcL, benefit of rituximab is less clear due to increased infectious complications • Supportive Care, see Page 4	See Page 5 for Response Evaluation

Additional Clinical Presentations and Primary Treatment → See Page 3

EPOCH = etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin
HCVAD = cyclophosphamide, vincristine, doxorubicin, and dexamethasone
CODOX-M = cyclophosphamide, vincristine, doxorubicin, and high-dose methotrexate
IVAC = ifosfamide, etoposide, and high-dose cytarabine

[1] Continue anti-retroviral therapy (ART) throughout treatment
[2] CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) is not adequate therapy
[3] Consider using modified regimen for older or frail patients

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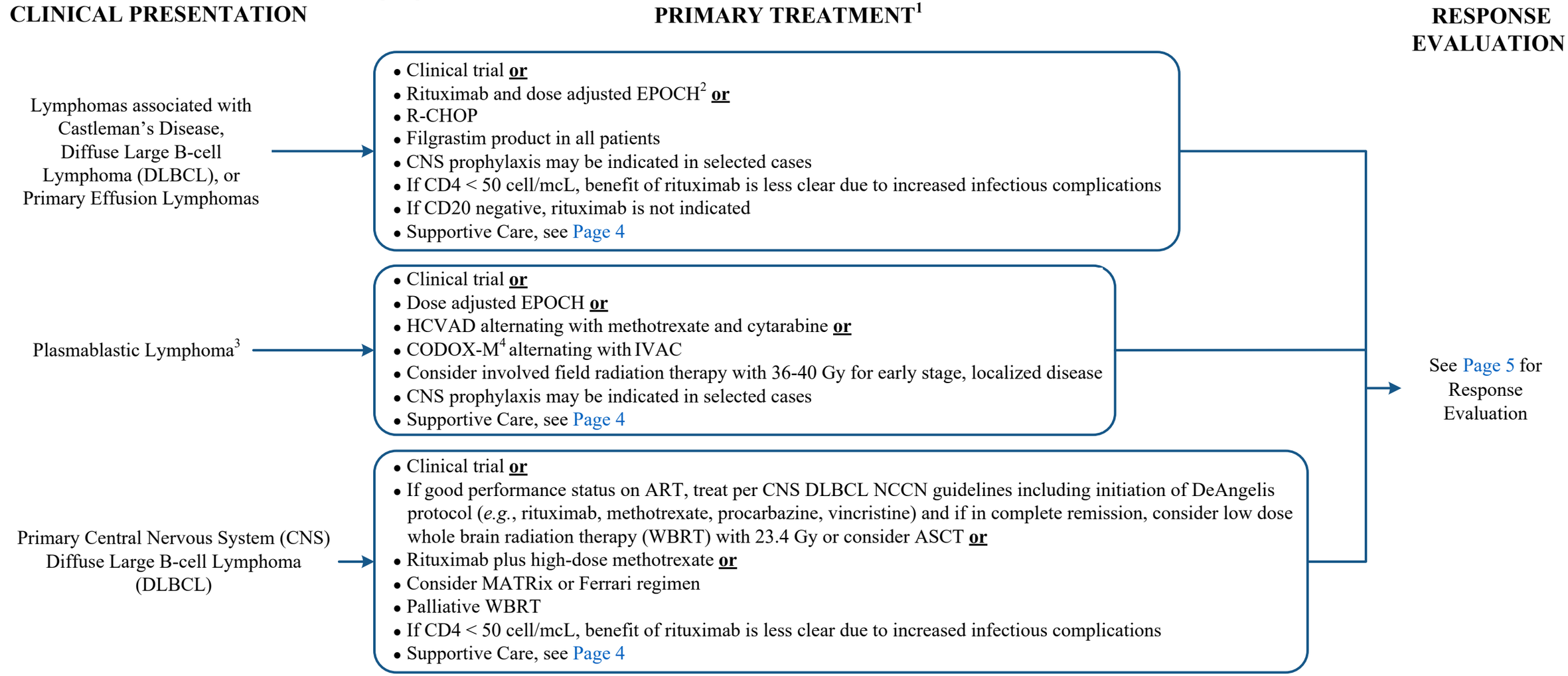
HIV-Related B-Cell Lymphomas

Note: Consider Clinical Trials as treatment options for eligible patients.



EPOCH = etoposide, prednisone, vincristine, cyclophosphamide and doxorubicin
R-CHOP = rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone
HCVAD = cyclophosphamide, mesna, doxorubicin, and vincristine
CODOX-M = cyclophosphamide, vincristine, doxorubicin, high-dose methotrexate and leucovorin
IVAC = ifosfamide, etoposide, and cytarabine
MATRix = methotrexate, cytarabine, thiotepa, rituximab
Ferrari regimen = cytarabine, methotrexate

[1] Continue anti-retroviral therapy (ART) throughout treatment
[2] Consider NCCN dosing guidelines for HIV-Related B-Cell Lymphomas
[3] CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) is not adequate therapy
[4] Consider using modified regimen for older or frail patients

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HIV-Related B-Cell Lymphomas

Note: Consider Clinical Trials as treatment options for eligible patients.

SUPPORTIVE CARE

All diagnoses →

Increased risk of infectious complications mitigated with improved HIV control and aggressive infection prophylaxis:

- Patients not on ART at diagnosis may initiate ART during staging period, or alternately initiate after first cycle of chemotherapy. All ART initiation or changes should be done in consultation with an HIV specialist.
- Zidovudine (AZT), cobicistat, and non-boosted doses of ritonavir should not be administered concurrently due to myelosuppression
- While feasible to administer most protease inhibitors concurrently with chemotherapy, consideration of changing to non-protease inhibitor based regimens is helpful to avoid potential interactions affecting either chemotherapy or antiretroviral metabolism

Required for all:

- Growth factor support: begin 24-48 hours after chemotherapy and continue past nadir recovery of blood counts for each cycle
- Pneumocystis jiroveci pneumonia (PJP): continue antipneumocystis prophylaxis until CD4 recovery ≥ 200 cell/mcL for ≥ 3 months after completion of chemotherapy
- Gram-negative rods: quinolone prophylaxis or equivalent during period of neutropenia[1]
- Fungal[1]: azole antifungals should be held 24 hours prior to and through 24 hours post chemotherapy with CYP3A4 metabolism
- Mycobacterium avium complex (MAC) prophylaxis for CD4 < 100 cell/mcL
- Strongly consider varicella zoster virus (VZV)/herpes simplex virus (HSV) prophylaxis

Optional:

- Strongly encourage consult with Infectious Diseases for febrile neutropenia in context of extensive prophylaxis as well as for refractory diarrhea

[1] Not required with R-EPOCH

HIV-Related B-Cell Lymphomas

Note: Consider Clinical Trials as treatment options for eligible patients.

RESPONSE EVALUATION

FOLLOW UP/SURVEILLANCE

Complete response (CR) →

Recommend to continue:
- Routine follow-up and management with Infectious Diseases
- Routine cancer screening tests with Primary Cancer physician
- For primary CNS lymphoma, consider consolidative WBRT with 23.4 Gy
- For limited stage DLBCL, consider consolidative radiation with 30.6 Gy in 1.8 Gy fractions

Follow-up:
- Year 1: every 3-4 months
  - Physical exam and labs
  - Repeat CT of neck, chest, abdomen and pelvis with contrast
- Years 2-5: every 6 months
  - Physical exam and labs
  - Repeat CT of neck, chest, abdomen and pelvis with contrast
  - Consider transitioning to Survivorship clinic (except Plasmablastic or Primary CNS Lymphomas)
- Year 5 and beyond: every 12 months
  - Physical exam and labs
  - Consider transitioning to Survivorship clinic for Plasmablastic or Primary CNS Lymphomas

Partial response (PR), stable disease, progressive disease and recurrence →

CNS lymphoma →
- Discuss Goal Concordant Care (GCC) with patient or if clinically indicated, with Patient Representative[1]
- Clinical trial
- Patients with CNS lymphoma who have already received high-dose methotrexate regimen can be considered for consolidation with WBRT (23.4-30 Gy with or without boost to gross disease) **or** high dose cytarabine if not previously given **or** high dose chemotherapy with stem cell transplant
- Consider treatment options per NCCN guidelines for Primary CNS Lymphoma

All other HIV-Related B-Cell lymphomas →
- Discuss Goal Concordant Care (GCC) with patient or if clinically indicated, with Patient Representative[1]
- Clinical trial
- Consider non-overlapping chemotherapy option per High Grade B-Cell Lymphoma NCCN guidelines if not previously given and as clinically indicated
- Consider high dose chemotherapy plus ASCT for patients who enter into second remission with good performance status and well controlled concomitant medical issues

→ Re-evaluate and treat based on response

[1] GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients, or if clinically indicated, the Patient Representative should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).

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DEVELOPMENT CREDITS

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