

Disclaimer: *This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.*

**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)

### 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

KSHV LANA = Kaposi's sarcoma-associated herpesvirus latency-associated nuclear antigen

FISH = florescence in situ hybridization

FNA = fine needle aspiration

HIV = human immunodeficiency virus

<sup>1</sup> See [Physical Activity](#), [Nutrition](#), and [Tobacco Cessation](#) 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, 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)
- 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 or MUGA (multigated acquisition) scan
  - Lumbar puncture with cytology evaluation
- Consultation to Infectious Diseases
  - Antiretrovirals often can be administered safely with chemotherapy
- Lifestyle risk assessment<sup>1</sup>

### OF USE IN SELECTED CASES:

- Upper GI/barium enema/endoscopy
- MRI of brain with gadolinium or CT of brain
- Pregnancy test in women of childbearing potential
- Discussion of fertility issues and sperm banking

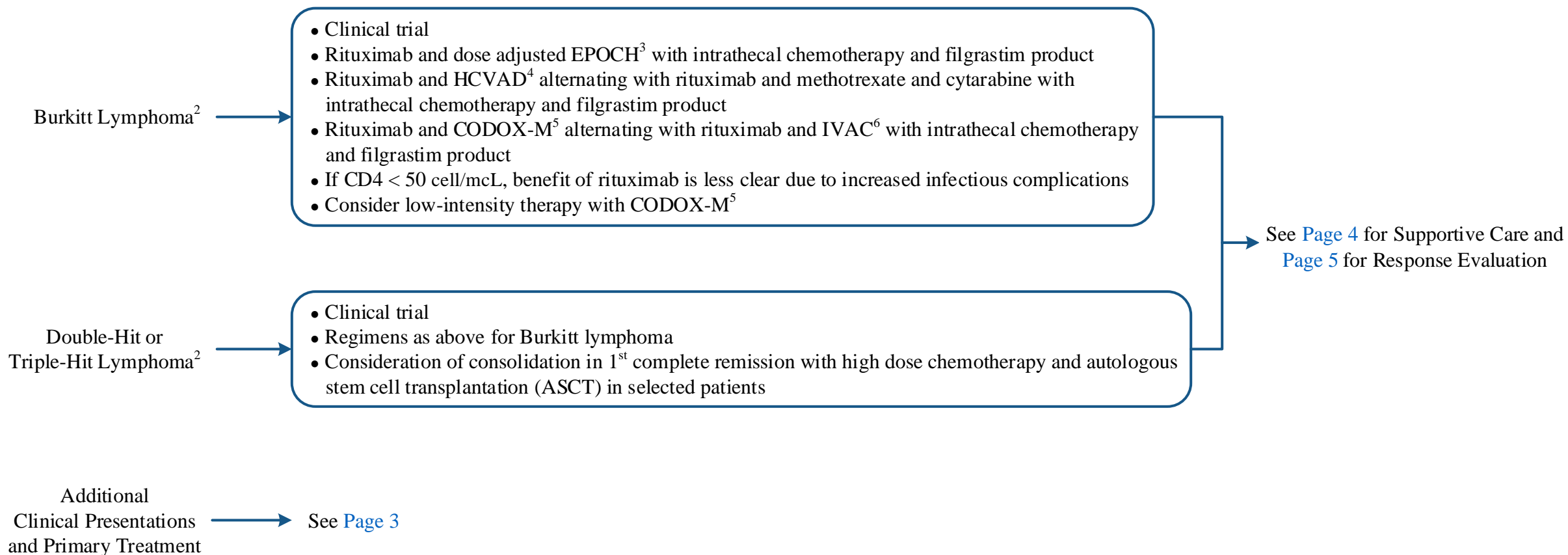
See [Page 2](#) for Clinical Presentations and Primary Treatment

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## CLINICAL PRESENTATION

## PRIMARY TREATMENT<sup>1</sup>



<sup>1</sup> Continue anti-retroviral therapy (ART) throughout treatment

<sup>2</sup> CHOP: cyclophosphamide, doxorubicin, vincristine, and prednisone is not adequate therapy

<sup>3</sup> EPOCH: etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin

<sup>4</sup> HCVAD: cyclophosphamide, vincristine, doxorubicin, and dexamethasone

<sup>5</sup> CODOX-M: cyclophosphamide, vincristine, doxorubicin, and high-dose methotrexate

<sup>6</sup> IVAC: ifosfamide, etoposide, and high-dose cytarabine

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## CLINICAL PRESENTATION

## PRIMARY TREATMENT<sup>1</sup>

Lymphomas associated with Castleman's Disease, Diffuse Large B-cell Lymphoma (DLBCL), or Primary Effusion Lymphomas

- Clinical trial
- Rituximab and dose adjusted EPOCH<sup>2</sup>
- Rituximab and HCVAD<sup>3</sup> alternating with rituximab, methotrexate and cytarabine
- R-CHOP<sup>4</sup>
- Filgrastim product in all patients
- Intrathecal chemotherapy
- If CD4 < 50 cell/microliter, benefit of rituximab is less clear due to increased infectious complications
- If CD20 negative, rituximab is not indicated

Plasmablastic Lymphoma<sup>5</sup>

- Clinical trial
- HCVAD<sup>3</sup> alternating with methotrexate and cytarabine
- Dose adjusted EPOCH<sup>2</sup>
- CODOX-M<sup>6</sup> alternating with IVAC<sup>7</sup>
- Consider involved field radiation therapy with 36-40 Gy for early stage, localized disease

Primary Central Nervous System (CNS) Diffuse Large B-cell Lymphoma (DLBCL)

- Clinical trial
- If good performance status on ART, treat per CNS Diffuse Large B-Cell Lymphoma guideline including initiation of DeAngelis protocol and if in complete remission consider low dose whole brain radiation therapy (WBRT) with 23.4 Gy or consider an ASCT
- Rituximab plus high-dose methotrexate
- Palliative WBRT
- If CD4 < 50 cell/microliter, benefit of rituximab is less clear due to increased infectious complications

See Page 4 for Supportive Care and Page 5 for Response Evaluation

<sup>1</sup> Continue anti-retroviral therapy (ART) throughout treatment

<sup>2</sup> EPOCH: etoposide, prednisone, vincristine, cyclophosphamide and doxorubicin

<sup>3</sup> HCVAD: cyclophosphamide, mesna, doxorubicin, and vincristine

<sup>4</sup> R-CHOP: rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone

<sup>5</sup> CHOP: cyclophosphamide, doxorubicin, vincristine, and prednisone is not adequate therapy

<sup>6</sup> CODOX-M: cyclophosphamide, vincristine, doxorubicin, high-dose methotrexate and leucovorin

<sup>7</sup> IVAC: ifosfamide, etoposide, and cytarabine

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## SUPPORTIVE CARE

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  $\geq 200$  cell/microliter for  $\geq 3$  months after completion of chemotherapy
- Gram-negative rods: quinolone prophylaxis or equivalent during period of neutropenia
- Fungal: 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/microliter
- 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

All diagnoses →

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## RESPONSE EVALUATION

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 with contrast
- Years 2-5: every 6 months
  - Physical exam and labs
  - Repeat CT with contrast
- Year 5 and beyond: every 12 months
  - Physical exam and labs

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

- Clinical trial
- Consider non-overlapping chemotherapy option per DLBCL guidelines
- Consider high dose chemotherapy plus ASCT for patients who enter into second remission with good performance status and well controlled concomitant medical issues
- Patients with CNS lymphoma who have already received high-dose methotrexate can be considered for WBRT (23.4-30 Gy with or without boost to gross disease) or temozolomide

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## DEVELOPMENT CREDITS

This practice algorithm is based on majority expert opinion of the Lymphoma Center Faculty at the University of Texas MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following:

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