AIDS-Related B-Cell Lymphomas

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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 immunohistochemistry to confirm diagnosis
  - Paraffin panel: CD3, CD10, CD20, CD45 (LCA), BCL2, BCL6, Ki-67, CD 138, kappa/lambda light chains, HHV8
  - Flow cytometry immunohistochemistry (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 = fluorescence in situ hybridization
FNA = fine needle aspiration
HIV = human immunodeficiency virus

1 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

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
**AIDS-Related B-Cell Lymphomas**

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### CLINICAL PRESENTATION

- Burkitt Lymphoma
  - Clinical trial
  - Rituximab and dose adjusted EPOCH\(^1\) with intrathecal chemotherapy and filgrastim product
  - Rituximab and HCVAD\(^2\) alternating with rituximab and methotrexate and cytarabine with intrathecal chemotherapy and filgrastim product
  - Rituximab and CODOX-M\(^3\) alternating with rituximab and IVAC\(^4\) with intrathecal chemotherapy and filgrastim product
  - If CD4 < 50 cell/mcL, benefit of rituximab is less clear due to increased infectious complications
  - Consider low-intensity therapy with CODOX-M\(^5\)

- Double-Hit or Triple-Hit Lymphoma
  - Clinical trial
  - Regimens as above for Burkitt lymphoma
  - Consideration of consolidation in 1\(^{st}\) complete remission with high dose chemotherapy and autologous stem cell transplantation (ASCT) in selected patients

### PRIMARY TREATMENT\(^1\)

- Continue anti-retroviral therapy (ART) throughout treatment

\(^1\) CHOP: cyclophosphamide, doxorubicin, vincristine, and prednisone is not adequate therapy

\(^2\) HCVAD: cyclophosphamide, vincristine, doxorubicin, and dexamethasone

\(^3\) CODOX-M: cyclophosphamide, vincristine, doxorubicin, and high-dose methotrexate

\(^4\) IVAC: ifosfamide, etoposide, and high-dose cytarabine

See Page 4 for Supportive Care and Page 5 for Response Evaluation
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### CLINICAL PRESENTATION

<table>
<thead>
<tr>
<th>Lymphomas associated with Castleman’s Disease, Diffuse Large B-cell Lymphoma (DLBCL), or Primary Effusion Lymphomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasmablastic Lymphoma(^5)</td>
</tr>
<tr>
<td>Primary Central Nervous System (CNS) Diffuse Large B-cell Lymphoma (DLBCL)</td>
</tr>
</tbody>
</table>

### PRIMARY TREATMENT\(^1\)

- **Clinical trial**
- **Rituximab and dose adjusted EPOCH\(^2\)**
- **Rituximab and HCVAD\(^3\) alternating with rituximab, methotrexate and cytarabine**
- **R-CHOP\(^4\)**
- **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

- **Clinical trial**
- HCVAD\(^3\) alternating with methotrexate and cytarabine
- Dose adjusted EPOCH\(^2\)
- CODOX-M\(^6\) alternating with IVAC\(^7\)
- Consider involved field radiation therapy with 36-40 Gy for early stage, localized disease

- **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

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1. Continue anti-retroviral therapy (ART) throughout treatment
2. EPOCH: etoposide, prednisone, vincristine, cyclophosphamide and doxorubicin
3. HCVAD: cyclophosphamide, mesna, doxorubicin, and vincristine
4. R-CHOP: rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone
5. CHOP: cyclophosphamide, doxorubicin, vincristine, and prednisone is not adequate therapy
6. CODOX-M: cyclophosphamide, vincristine, doxorubicin, high-dose methotrexate and leucovorin
7. IVAC: ifosfamide, etoposide, and cytarabine

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

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

Department of Clinical Effectiveness V6
Approved by the Executive Committee of the Medical Staff on 09/21/2021

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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.

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


Continued on next page
SUGGESTED READINGS - continued


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SUGGESTED READINGS - continued


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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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