AIDS -Related B-Cell Lymphomas

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

**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, and CD45
- In situ hybridization: EBER

**OF USE IN CERTAIN CIRCUMSTANCES:**
- Additional immunohistochemical studies to establish lymphoma subtype
  - Diffuse Large B-Cell, Burkitt, Plasmablastic, Primary effusion lymphoma (PEL): CD10, BCL2, Ki-67, BCL6, CD138, CD30 for PEL, KSHV LANA-1
- Molecular genetic analysis
  - FISH 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

**INITIAL EVALUATION**
- Physical exam:
  - Performance status (ECOG)
  - B symptoms (fever, sweats, weight loss)
- CBC with differential, BUN, creatinine, AST, ALT, albumin, bilirubin, alkaline phosphatase, serum calcium, phosphorus, magnesium, LDH, Uric Acid
- HIV 1 and HIV 2
- Chest X-ray, PA and Lateral
- CT with contrast of neck, chest, abdomen and pelvis
- PET/ CT scan
- Bilateral bone marrow biopsy with aspirate
- Echo or MUGA
- CD4 count
- HIV viral load
- Lumbar Puncture with cytology evaluation
- Screening for hepatitis B and C (HBcAb, HBsAg, HCVAb)
- Consultation to infectious disease physician
  - Antiretrovirals often can be administered safely with chemotherapy

**Useful in selected cases:**
- UGI/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 Pages 2-3 for Clinical Presentations and Primary Treatment
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CLINICAL PRESENTATION

Burkitt Lymphoma\(^2\)

- Clinical trial
- Dose adjusted rituximab and EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) with intrathecal chemotherapy and GCSF
- Rituximab and HCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone) alternating with rituximab and methotrexate and cytarabine with intrathecal chemotherapy and GCSF
- Rituximab and CODOX-M/ rituximab and IVAC (cyclophosphamide, vincristine, doxorubicin, high-dose methotrexate alternating with ifosfamide, etoposide, high-dose cytarabine) with intrathecal chemotherapy and GCSF
- If CD4 less than 50, benefit of rituximab less clear due to increased infectious complications

Double- Hit or Triple- Hit Lymphoma\(^2\)

- 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\(^1\)

G-CSF: Granulocyte Colony-Stimulating Factor, Filgrastim

1 Continue Highly Active AntiRetroviral Therapy (HAART) throughout treatment
2 CHOP: Cyclophosphamide, Doxorubicin, Vincristine, Prednisone is not adequate therapy.

See Page 5 for response evaluation

Clinical presentations continued on the next page
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### CLINICAL PRESENTATION

- Lymphomas associated with Castleman’s disease
  - Diffuse large B-cell lymphoma (DLBCL)
  - Primary effusion lymphomas
- Plasmablastic lymphoma
- Primary Central Nervous System Diffuse large B-cell lymphoma (DLBCL)

### PRIMARY TREATMENT¹

1. **Clinical trial**
2. Dose-adjusted R-EPOCH
3. R-HCVAD/R-methotrexate and cytarabine
4. R-CHOP
5. G-CSF in all patients
6. Intrathecal chemotherapy
7. If CD4 less than 50, benefit of rituximab less clear due to increased infectious complications
8. If CD20 negative, rituximab is not indicated

**See Page 4 for supportive care and Page 5 for response evaluation**
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SUPPORTIVE CARE

- Increased risk of infectious complications mitigated with improved HIV control and aggressive infection prophylaxis:
  - Patients not on highly active antiretroviral therapy (HAART) at diagnosis may initiate HAART during staging period, or alternately initiate after first cycle of chemotherapy. All HAART initiation or changes should be done in consultation with an HIV specialist.
  - AZT 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 of each cycle
  - Pneumocystis pneumonia (PCP): continue until CD4 recovered to greater than 200 post completion of chemotherapy
  - Gram-negative rods: quinolone prophylaxis or equivalent during period of neutropenia
  - Fungal: azole antifungals should be held 24 hours prior to through 24 hours post chemotherapy with CYP3A4 metabolism
  - Mycobacterium avium complex (MAC) prophylaxis for CD4 less than 100

- Strongly consider varicella zoster virus (VZV)/herpes simplex virus (HSV) prophylaxis
- Strongly encourage consult with infectious disease for febrile neutropenia in context of extensive prophylaxis as well as for refractory diarrhea.
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**RESPONSE EVALUATION**

<table>
<thead>
<tr>
<th>Complete Response (CR)</th>
<th>Partial response (PR), Stable Disease, Progressive Disease and recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommend to continue:</td>
<td></td>
</tr>
<tr>
<td>• Routine follow-up and management with Infectious Disease Specialists</td>
<td>• Clinical trial</td>
</tr>
<tr>
<td>• Routine cancer screening tests with Primary Cancer Physician</td>
<td>• Consider non-overlapping chemotherapy option per DLBCL guidelines</td>
</tr>
<tr>
<td>• For primary CNS lymphoma: consider consolidative whole brain radiation therapy 23.4 Gy fractions</td>
<td>• Consider high dose chemotherapy plus autologous stem cell transplant (ASCT) for patients who enter into second remission with good performance status and well controlled concomitant medical issues</td>
</tr>
<tr>
<td>• For limited stage DLBCL consider consolidative radiation to 30.6 Gy in 1.8 Gy fractions</td>
<td>• For patients with CNS lymphoma who have already received high-dose methotrexate can consider for whole brain radiation treatment (WBRT), 23.4-30 Gy with or without boost to gross disease, or temozolomide</td>
</tr>
<tr>
<td>Follow-up:</td>
<td></td>
</tr>
<tr>
<td>• Year 1 - Every 3-4 months</td>
<td>• Year 5 and beyond</td>
</tr>
<tr>
<td>Physical exam and labs</td>
<td>Physical exam and labs</td>
</tr>
<tr>
<td>Repeat CT’s with contrast</td>
<td></td>
</tr>
<tr>
<td>• Years 2-5 – Every 6 months</td>
<td></td>
</tr>
<tr>
<td>Physical exam and labs</td>
<td></td>
</tr>
<tr>
<td>Repeat CT’s with contrast</td>
<td></td>
</tr>
</tbody>
</table>

**Revised Response Criteria for Malignant Lymphoma** (see suggested readings)

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1By Revised Response Criteria for Malignant Lymphoma (see suggested readings)
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**SUGGESTED READINGS**


Suggested Readings continued on next page
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**SUGGESTED READINGS**


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DEVELOPMENT CREDITS

This practice guideline 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 medical oncologists, radiation oncologists, surgical oncologists, and interventional radiologists:

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