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**AIDS-Related B-Cell Lymphomas**

**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
- Lifestyle risk assessment

**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

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**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: 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

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1See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice
AIDS-Related B-Cell Lymphomas

CLINICAL PRESENTATION

Bburkitt Lymphoma

- Clinical trial
- Dose adjusted rituximab and EPOCH\(^1\) with intrathecal chemotherapy and GCSF\(^4\)
- Rituximab and HCVAD\(^5\) alternating with rituximab and methotrexate and cytarabine with intrathecal chemotherapy and GCSF\(^4\)
- Rituximab and CODOX-M\(^6\) alternating with rituximab and IVAC\(^7\) with intrathecal chemotherapy and GCSF\(^8\)
- If CD4 less than 50 cell/\(\mu\)L, benefit of rituximab is less clear due to increased infectious complications

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 Highly Active AntiRetroviral Therapy (HAART) throughout treatment
- CHOP: cyclophosphamide, doxorubicin, vincristine, and prednisone is not adequate therapy
- EPOCH: etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin
- G-CSF: granulocyte colony stimulating factor (filgrastim)
- HCVAD: cyclophosphamide, vincristine, doxorubicin, and dexamethasone
- CODOX-M: cyclophosphamide, vincristine, doxorubicin, and high-dose methotrexate
- IVAC: ifosfamide, etoposide, and high-dose cytarabine

Clinical presentations continued on the next page

\(^1\)Continue Highly Active AntiRetroviral Therapy (HAART) throughout treatment
\(^2\)CHOP: cyclophosphamide, doxorubicin, vincristine, and prednisone is not adequate therapy
\(^3\)EPOCH: etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin
\(^4\)G-CSF: granulocyte colony stimulating factor (filgrastim)
\(^5\)HCVAD: cyclophosphamide, vincristine, doxorubicin, and dexamethasone
\(^6\)CODOX-M: cyclophosphamide, vincristine, doxorubicin, and high-dose methotrexate
\(^7\)IVAC: ifosfamide, etoposide, and high-dose cytarabine
AIDS-Related B-Cell Lymphomas

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

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 TREATMENT

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

- Clinical trial
- HCVAD alternating with methotrexate and cytarabine
- Dose-adjusted EPOCH
- CODOX-M alternating with IVAC
- Consider involved field radiation therapy, 36-40 Gy for early stage, localized disease

- Clinical trial
- If good performance status on HAART, 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 23.4 Gy or consider an ASCT
- Rituximab plus high-dose methotrexate
- Palliative whole brain radiation treatment (WBRT)
- If CD4 less than 50 cell/mcL, benefit of rituximab is less clear due to increased infectious complications

1. Continue Highly Active AntiRetroviral Therapy (HAART) 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. G-CSF: granulocyte colony stimulating factor (filgrastim or pegfilgrastim)
6. CHOP: cyclophosphamide, doxorubicin, vincristine, and prednisone is not adequate therapy
7. CODOX-M: cyclophosphamide, vincristine, doxorubicin, high-dose methotrexate and leucovorin
8. IVAC: ifosfamide, etoposide, and cytarabine

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

Department of Clinical Effectiveness V5
Approved by the Executive Committee of the Medical Staff on 11/28/2017

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SUPPORTIVE CARE

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

- Patients not on 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.
- Zidovudine (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 recovery to greater than 200 cell/mcL 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 cell/mcL

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.

All diagnoses
AIDS-Related B-Cell Lymphomas

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RESPONSE EVALUATION

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

Follow-up:
- Year 1: Every 3-4 months
  - Physical exam and labs
  - Repeat CTs with contrast
- Years 2-5: Every 6 months
  - Physical exam and labs
  - Repeat CT with contrast
- Year 5 and beyond:
  - Physical exam and labs

1By Revised Response Criteria for Malignant Lymphoma (see suggested readings)
AIDS-Related B-Cell Lymphomas

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SUGGESTED READINGS


Suggested Readings continued on next page
SUGGESTED READINGS - continued


Readings continued on next page
SUGGESTED READINGS - continued


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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AIDS-Related B-Cell Lymphomas

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