**Burkitt and Double-Hit or Triple-Hit Lymphomas**

DIAGNOSIS

**ESSENTIAL:**
- Hematopathology review of all slides with at least one paraffin block representative of the tumor. Rebiopsy if consult material is non-diagnostic. FNAs are generally inadequate. Recommend core or excisional biopsy.
- Adequate immunophenotyping to establish diagnosis
  - Paraffin Panel: CD3, CD10, CD20, CD45 (LCA), Ki-67, BCL2, BCL6, TdT
  - Flow cytometry immunophenotyping (optional if paraffin IHC has been performed): kappa/lambda light chains, IgM, CD3, CD5, CD10, CD19, CD20, CD45, TdT
  - In situ hybridization: Epstein-Barr virus encoded RNA (EBER)
- Molecular genetic analysis
  - For Burkitt lymphoma: Conventional cytogenetics helpful if available; FISH test to detect MYC gene rearrangements
  - For Double-hit or Triple-hit lymphoma: FISH test to detect MYC gene rearrangements. If positive, then check BCL2 and BCL6 gene rearrangements.

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

**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, albumin, AST, ALT, total bilirubin, alkaline phosphorus, serum calcium, uric acid, phosphate, magnesium, BUN, creatinine, and LDH
  - Screening for HIV-1 and HIV-2
  - 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
- 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

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See Page 2, Clinical Presentation and Primary Treatment

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FNA = fine needle aspiration
FISH = fluorescence in situ hybridization
HIV = human immunodeficiency virus

See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

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

CLINICAL PRESENTATION

Burkitt Lymphoma\(^1\)

- Clinical trial
- Rituximab and dose adjusted EPOCH\(^2\) with intrathecal chemotherapy and filgrastim product
- Rituximab and HCVAD\(^3\) alternating with rituximab, methotrexate and cytarabine with intrathecal chemotherapy and filgrastim product
- Rituximab and CODOX-M\(^4\) alternating with rituximab and IVAC\(^5\) with intrathecal chemotherapy and filgrastim product
- Consider low-intensity therapy for low risk, early stage disease

Double-Hit or Triple-Hit Lymphoma\(^1,6\)

- Clinical trial
- Regimens as above for Burkitt lymphoma

See Page 3, for Response Evaluation

\(^1\) CHOP: cyclophosphamide, doxorubicin, vincristine, and prednisone is not adequate therapy
\(^2\) EPOCH: etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin
\(^3\) HCVAD: cyclophosphamide, vincristine, doxorubicin, and dexamethasone
\(^4\) CODOX-M: cyclophosphamide, vincristine, doxorubicin, high-dose methotrexate and leucovorin
\(^5\) IVAC: ifosfamide, etoposide, and high-dose cytarabine
\(^6\) Also known as high grade B-cell lymphoma with \(MYC\) and/or \(BCL2\) or \(BCL6\) gene rearrangements
Complete response (CR)

**Recommend to continue:**
- Routine cancer screening tests with Primary Cancer physician
- Year 1: every 3-4 months
  - Physical exam and labs
  - Repeat CT with contrast
- Year 2: every 6 months
  - Physical exam and labs
  - Repeat CT with contrast
- Years 3-5: every 12 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 Diffuse Large B-Cell Lymphoma guidelines
- Consider high dose chemotherapy plus autologous stem cell transplant for patients who enter into second remission with good performance status and well controlled concomitant medical issues


**SUGGESTED READINGS**
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:

Olga N. Fleckenstein, BS*
Sandy Horowitz, PharmD (Pharmacy Clinical Programs)
Harjeet Kaur, MSN, RN, CNL*
L. Jeffrey Medeiros, MD (Hematopathology Administration)
Chelsea Pinnix, MD (Radiation Oncology)
Raphael Steiner, MD (Lymphoma/Myeloma)
Jason Westin, MD (Lymphoma/Myeloma)†

† Core Development Team Lead
* Clinical Effectiveness Development Team