**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: EBER
- Molecular genetic analysis
  - For Burkitt lymphoma: Conventional cytogenetics helpful if available; FISH to detect MYC gene rearrangements
  - For Double-hit or Triple-hit lymphoma: FISH 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)
- CBC with differential, albumin, AST, ALT, total bilirubin, alkaline phosphorus, serum calcium, uric acid, phosphate, magnesium, BUN, creatinine, LDH
- Screening for HIV-1 and HIV-2, hepatitis B and C (HBcAb, HBsAg, HCV Ab)
- Chest X-ray, PA and lateral
- CT with contrast of neck, chest, abdomen and pelvis
- PET/CT Scan
- Lifestyle risk assessment¹

**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

¹See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

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

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CLINICAL PRESENTATION

Burkitt Lymphoma

• Clinical trial
• Rituximab and dose adjusted EPOCH with intrathecal chemotherapy and filgrastim product
• Rituximab and HCVAD alternating with rituximab, methotrexate and cytarabine with intrathecal chemotherapy and filgrastim product
• Rituximab and CODOX-M alternating with rituximab and IVAC with intrathecal chemotherapy and filgrastim product
• Consider low-intensity therapy for low risk, early stage disease

Double-Hit or Triple-Hit Lymphoma

• Clinical trial
• Regimens as above for Burkitt lymphoma

PRIMARY TREATMENT

CHOP: cyclophosphamide, doxorubicin, vincristine, and prednisone is not adequate therapy
EPOCH: etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin
HCVAD: cyclophosphamide, vincristine, doxorubicin, and dexamethasone
CODOX-M: cyclophosphamide, vincristine, doxorubicin, high-dose methotrexate and leucovorin
IVAC: ifosfamide, etoposide, and high-dose cytarabine

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

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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
RESPONSE EVALUATION

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
Burkitt and Double-Hit or Triple-Hit Lymphomas

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SUGGESTED READINGS


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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