Burkitt and Double-Hit Lymphomas

This practice algorithm has been specifically developed for MD Anderson using a multidisciplinary approach and taking into consideration circumstances particular to MD Anderson, including the following: MD Anderson's specific patient population; MD Anderson's services and structure; and MD Anderson's clinical information. Moreover, this algorithm is not intended to replace the independent medical or professional judgment of physicians or other health care providers. This algorithm should not be used to treat pregnant women.

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

### 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 H&C 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 lymphoma: FISH to detect the 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, albumin, AST, ALT, total bilirubin, alkaline phosphorus, serum calcium, uric acid, phosphate, magnesium, BUN, creatinine, LDH
- Screening for HIV 1 and 2, hepatitis B and C (HBcAb, HBAg, HCVAb)
- Chest X-ray, PA and lateral
- CT with contrast of neck, chest, abdomen and pelvis
- Echo or MUGA
- Lumbar puncture with cytology evaluation
- Bilateral bone marrow biopsy with aspirate
- PET/CT Scan
- 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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1See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice.
INDUCTION THERAPY

**Burkitt Lymphoma**
- Clinical trial
- Dose adjusted rituximab and EPOCH\(^2\) with intrathecal chemotherapy and GCSF\(^3\)
- Rituximab and HCVAD\(^4\) alternating with rituximab, methotrexate and cytarabine with intrathecal chemotherapy and GCSF\(^3\)
- Rituximab and CODOX-M\(^5\) alternating with rituximab and IVAC\(^6\) with intrathecal chemotherapy and GCSF\(^3\)

**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

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\(^1\)R-CHOP: rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone is not adequate therapy
\(^2\)EPOCH: etoposide, prednison, vincristine, cyclophosphamide, and doxorubicin
\(^3\)GCSF: granulocyte colony stimulating factor (filgrastim or pegfilgrastim)
\(^4\)HCVAD: cyclophosphamide, vincristine, doxorubicin, and dexamethasone
\(^5\)CODOX-M: cyclophosphamide, vincristine, doxorubicin, high-dose methotrexate and leucovorin
\(^6\)IVAC: ifosfamide, etoposide, and high-dose cytarabine
Note: Consider Clinical Trials as treatment options for eligible patients.

**RESPONSE EVALUATION**

- Complete Response (CR)
- Partial response (PR), Stable Disease, Progressive Disease and Recurrence

**FOLLOW-UP**

Recommend to continue:
- Routine follow-up and management with infectious disease specialists
- Routine cancer screening tests with primary cancer physician
- Year 1: Every 3-4 months; Year 2: Every 6 months
  - Physical exam and labs
  - Repeat CTs with contrast
- Years 3-5: Every 12 months
  - Physical exam and labs
  - Repeat CTs with contrast
- Year 5 and beyond:
  - Physical exam and labs

- Clinical trial
- Consider non-overlapping chemotherapy option per Diffuse Large B-Cell Lymphoma guidelines
- Consider high dose chemotherapy plus ASCT for patients who enter into second remission with good performance status and well controlled concomitant medical issues

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


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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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Approved by the Executive Committee of the Medical Staff on 11/28/2017

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