Burkitt Lymphoma

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 IHC panel: CD3, CD5, CD10, CD20, CD45 (LCA), Ki-67, BCL2, BCL6, TdT, MYC
  - Flow cytometry immunophenotyping (optional if paraffin IHC has been performed): kappa/lambda light chains, IgM, CD3, CD5, CD10, CD19, CD20, CD38, 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

ECOG = Eastern Cooperative Oncology Group
FNA = fine needle aspiration
FISH = florescence in situ hybridization
HIV = human immunodeficiency virus
IHC = immunohistochemistry

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:
  - Echocardiogram or MUGA (multigated acquisition) scan
  - Lumbar puncture with cytology evaluation and flow cytometry
- Lifestyle risk assessment[1]

OF USE IN SELECTED CASES:

- Bilateral or unilateral bone marrow biopsy with aspirate
- Upper GI/barium enema/endoscopy
- MRI of brain with gadolinium or CT of brain
- Pregnancy test in women of childbearing potential
- Discussion of fertility options and sperm banking for patients of child bearing potential (refer to Fertility Preservation Prior to Cancer Treatment algorithm)

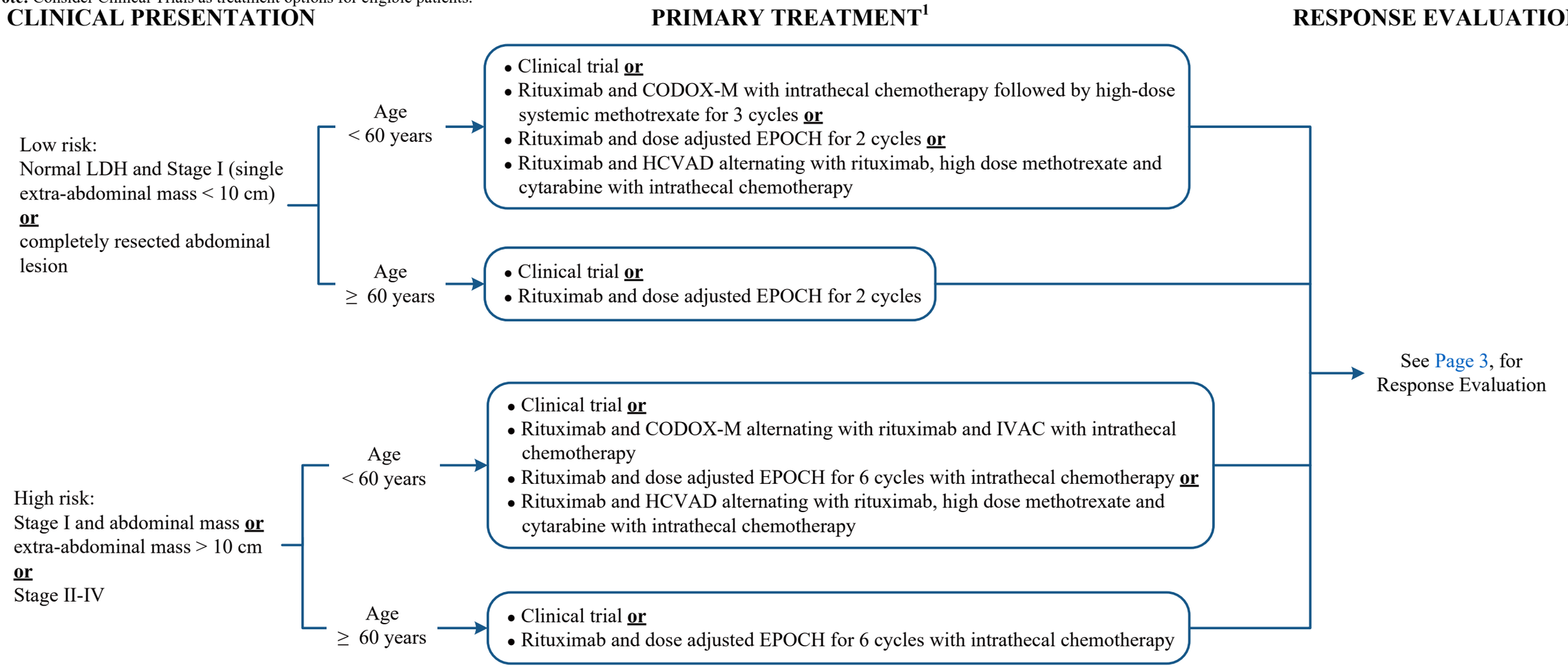
See Page 2, Clinical Presentation and Primary Treatment

[1] See Physical Activity, Nutrition, Obesity Screening and Management, and Tobacco Cessation Treatment algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

Department of Clinical Effectiveness V7
Approved by the Executive Committee of the Medical Staff on 3/17/2026

Burkitt Lymphoma

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



EPOCH = etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin
HCVAD = cyclophosphamide, vincristine, doxorubicin, and dexamethasone
CODOX-M = cyclophosphamide, vincristine, doxorubicin, intrathecal methotrexate and cytarabine followed by high-dose systemic methotrexate
IVAC = ifosfamide, etoposide, and high-dose cytarabine
[1] CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) is not adequate therapy

Department of Clinical Effectiveness V7
Approved by the Executive Committee of the Medical Staff on 3/17/2026

Burkitt Lymphoma

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

RESPONSE EVALUATION

FOLLOW UP/SURVEILLANCE

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 of neck, chest, abdomen and pelvis with contrast
- Year 2: every 4-6 months
  - Physical exam and labs
  - Repeat CT of neck, chest, abdomen and pelvis with contrast
  - Consider transitioning to Survivorship clinic
- Years 3-5: every 12 months
  - Physical exam and labs
  - Repeat CT of neck, chest, abdomen and pelvis with contrast

Note: PET scan can be useful for follow up in certain circumstances

EPOCH = etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin
DHAP = dexamethasone, cisplatin, and cytarabine
ICE = ifosfamide, carboplatin, and etoposide
IVAC = ifosfamide, etoposide, and high-dose cytarabine
GDP = gemcitabine, dexamethasone, and cisplatin

Partial response (PR), stable disease, progressive disease and recurrence →

- Discuss Goal Concordant Care (GCC) with patient or if clinically indicated, with Patient Representative[1]
- Clinical trial **or**
- Consider one of the following non-overlapping chemotherapy option per High Grade B-Cell Lymphoma NCCN guidelines if not previously given:
  - Rituximab and dose adjusted EPOCH
  - Rituximab and DHAP
  - Rituximab and ICE with intrathecal chemotherapy
  - Rituximab and IVAC with intrathecal chemotherapy
  - Useful in certain circumstance: Rituximab and GDP; high dose cytarabine and rituximab
- For recurrence, consider intrathecal chemotherapy
- Consider high dose chemotherapy plus stem cell transplant for patients who enter into second remission with good performance status and well controlled concomitant medical issues

→ Re-evaluate and treat based on response

[1] GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients, or if clinically indicated, the Patient Representative should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).

Department of Clinical Effectiveness V7
Approved by the Executive Committee of the Medical Staff on 3/17/2026

SUGGESTED READINGS

Aukema, S. M., Siebert, R., Schuuring, E., van Imhoff, G. W., Kluin-Nelemans, H. C., Boerma, E., & Kluin, P. M. (2011). Double-hit B-cell lymphomas. *Blood, 117*(8), 2319-2331. doi:10.1182/blood-2010-09-297879

Barnes, J. A., LaCasce, A. S., Feng, Y., Toomey, C. E., Neuberg, D., Michaelson, J. S., … Abramson, J. S. (2011). Evaluation of the addition of rituximab to CODOX-M/IVAC for burkitt's lymphoma: A retrospective analysis. *Annals of Oncology, 22*(8), 1859-1864. doi:10.1093/annonc/mdq677

Blum, K. A., Lozanski, G., & Byrd, J. C. (2004). Adult burkitt leukemia and lymphoma. *Blood, 104*(10), 3009-3020. doi:10.1182/blood-2004-02-0405

Cheson, B. D., Pfistner, B., Juweid, M. E., Gascoyne, R. D., Specht, L., Horning, S. J., … International Harmonization Project on Lymphoma. (2007). Revised response criteria for malignant lymphoma. *Journal of Clinical Oncology, 25*(5), 579-586. doi:10.1200/JCO.2006.09.2403

Dunleavy, K., Little, R., Pittaluga, S., Grant, N., Shovlin, M., Steinberg, S., … Wilson, W. (2008). A prospective study of dose-adjusted (DA) epoch with rituximab in adults with newly diagnosed burkitt lymphoma: A regimen with high efficacy and low toxicity. *Annals of Oncology, 19*, 83-84. Retrieved from https://academic.oup.com/annonc

Dunleavy, K., Pittaluga, S., Shovlin, M., Steinberg, S., Cole, D., Grant, C., … Wilson, W. (2013). Low-intensity therapy in adults with burkitt's lymphoma. *New England Journal of Medicine, 369*(20), 1915-1925. doi:10.1056/NEJMoa1308392

Fang, H., Wang, W., & Medeiros, L. J. (2025). Burkitt lymphoma. *Human Pathology, 156,* 105703. doi:10.1016/j.humpath.2024.105703

Griffin, T. C., Weitzman, S., Weinstein, H., Chang, M., Cairo, M., Hutchison, R., … Children's Oncology Group. (2009). A study of rituximab and ifosfamide, carboplatin, and etoposide chemotherapy in children with recurrent/refractory B-cell (CD20+) non-hodgkin lymphoma and mature B-cell acute lymphoblastic leukemia: A report from the children's oncology group. *Pediatric Blood and Cancer, 52*(2), 177-181. doi:10.1002/pbc.21753

Lacasce, A., Howard, O., Li, S., Fisher, D., Weng, A., Neuberg, D., & Shipp, M. (2004). Modified magrath regimens for adults with burkitt and burkitt-like lymphomas: Preserved efficacy with decreased toxicity. *Leukemia & Lymphoma, 45*(4), 761-767. doi:10.1080/1042819031000141301

Magrath, I., Adde, M., Shad, A., Venzon, D., Seibel, N., Gootenberg, J., … Horak, I. D. (1996). Adults and children with small non-cleaved-cell lymphoma have a similar excellent outcome when treated with the same chemotherapy regimen. *Journal of Clinical Oncology, 14*(3), 925-934. doi:10.1200/JCO.1996.14.3.925

National Comprehensive Cancer Network. (2025). *B-cell lymphomas*. (NCCN Guideline Version 3.2025). Retrieved from https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf

Olszewski, A. J., Jakobsen, L. H., Collins, G. P., Cwynarski, K., Bachanova, V., Blum, K. A., … Evens, A. M. (2021). Burkitt lymphoma international prognostic index. *Journal of Clinical Oncology, 39*(10), 1129. doi:10.1200/JCO.20.03288

Continued on next page

SUGGESTED READINGS - continued

Rizzieri, D., Johnson, J., Byrd, J., Lozanski, G., Blum, K., Powell, B., … Alliance Clinical Trials Oncology. (2014). Improved efficacy using rituximab and brief duration, high intensity chemotherapy with filgrastim support for burkitt or aggressive lymphomas: Cancer and leukemia group B study 10002. *British Journal of Hematology, 165*(1), 102-111. doi:10.1111/bjh.12736

Stenning, S. P., Mead, G. M., Wright, D., Sydes, M. R., Walewski, J., Grigg, A., … UKLG LY06 collaborators. (2002). An international evaluation of CODOX-M and CODOX-M alternating with IVAC in adult burkitt's lymphoma: Results of United Kingdom Lymphoma Group LY06 study. *Annals of Oncology, 13*(8), 1264-1274. doi:10.1093/annonc/mdf253

Thomas, D. A., Faderl, S., O'Brien, S., Bueso-Ramos, C., Cortes, J., Garcia-Manero, G., … Kantarjian, H. G. (2006). Chemoimmunotherapy with hyper-CVAD plus rituximab for the treatment of adult burkitt and burkitt-type lymphoma or acute lymphoblastic leukemia. *Cancer, 106*(7), 1569-1580. doi:10.1002/cncr.21776

Thomas, D. A, Kantarjian, H. G., Cortes, J., Faderl, S., Wierda, W. G., Ravandi, F., … O'Brien, S. (2008). Long-term outcome after hyper-CVAD and rituximab chemoimmunotherapy for burkitt (BL) or burkitt-like (BLL) leukemia/lymphoma and mature B-cell acute lymphocytic leukemia (ALL). *Blood, 112*(11), 1929. doi:10.1182/blood.V112.11.1929.1929

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:

Core Development Team Leads

Luis Fayad, MD (Lymphoma/Myeloma)
Sandy Horowitz, PharmD (Pharmacy Clinical Programs)
Jason Westin, MD (Lymphoma/Myeloma)

Workgroup Members

Olga N. Fleckenstein, BS♦
L. Jeffrey Medeiros, MD (Hematopathology Administration)
Ranjit Nair, MD (Lymphoma/Myeloma)
Chelsea Pinnix, MD (Radiation Oncology)
Mary Lou Warren, DNP, APRN, CNS-CC♦

♦Clinical Effectiveness Development Team