NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: AIDS-Related B-Cell Lymphomas (Part 1 of 3)

Clinical Trials: The National Comprehensive Cancer Network recommends cancer patient participation in clinical trials as the gold standard for treatment.

Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced health care team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are provided only to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data become available. The NCCN Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The NCCN makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

Burkitt Lymphoma[1,a,b,c]

Note: All recommendations are Category 2A unless otherwise indicated.

Preferred Regimens

REGIMEN	DOSING
CODOX-M/IVAC (modified) (cyclophosphamide + vincristine + doxorubicin + high-dose methotrexate alternating with ifosfamide + etoposide + high-dose cytarabine)[2–4]	**Day 1:** Cyclophosphamide 800mg/m² IV, **followed by** **Days 2–5:** Cyclophosphamide 200mg/m² IV **Day 1:** Doxorubicin 40mg/m² IV **Days 1 and 8: Cycle 1:** Vincristine 1.5mg/m² IV; **Cycle 2:** Days 1, 8, and 15. **Day 1:** MTX 1,200mg/m² IV over 1 hour, followed by 240mg/m²/hour over 23 hours. **Days 1 and 3:** Cytarabine 70mg intrathecally. **Day 1:** Rituximab 375mg/m² IV. **Day 15:** MTX 12mg intrathecally. **Alternate with:** **Days 1–5:** Ifosfamide 1,500mg/m² IV + etoposide 60mg/m² IV **Days 1 and 2:** Cytarabine 2,000mg/m² IV every 12 hours for 4 doses **Day 1:** Rituximab 375mg/m² IV **Day 15:** MTX 12mg intrathecally.
Dose-adjusted EPOCH (etoposide + prednisone + vincristine + cyclophosphamide + doxorubicin) + rituximab[6–8]	**Days 1–4:** Etoposide 50mg/m² IV + prednisone 60mg/m² orally + vincristine 0.4mg/m² IV + doxorubicin 10mg/m² IV **Day 1:** Rituximab 375mg/m² IV **Day 5:** Prednisone 60mg/m² orally **Day 5: Cycle 1:** Cyclophosphamide 375mg/m² IV if CD4 cells ≥100/mm³ **OR** 187mg/m² IV if CD4 cells <100/mm³. **Cyclophosphamide dose-adjustment (after Cycle 1):** If nadir ANC >500/mcL, then increase by 187mg above previous cycle. If nadir ANC <500/mcL, or platelets <25,000/mcL, then decrease by 187mg below previous cycle. Repeat cycle every 3 weeks.

Other Recommended Regimens

HyperCVAD (cyclophosphamide + vincristine + doxorubicin + dexamethasone alternating with high-dose methotrexate and cytarabine + rituximab)[9–11]	**Cycles 1, 3, 5, and 7—HyperCVAD** **Days 1–3:** Cyclophosphamide 300mg/m² IV every 12 hours for 6 doses, **plus** mesna 600mg/m² continuous IV **Days 4 and 11:** Vincristine 2mg IV **Day 4:** Doxorubicin 50mg/m² IV. **Days 1 and 11:** Rituximab 375mg/m² IV **Days 1–4 and Days 11–14:** Dexamethasone 40mg daily. **Cycles 2, 4, 6, 8—High-dose MTX and Cytarabine** **Day 1:** MTX 1g/m² IV over 24 hours **Days 2 and 3:** Cytarabine 3g/m² IV every 12 hours for 4 doses. **Days 1 and 8:** Rituximab 375mg/m² IV Repeat every 3 weeks for 8 cycles.

continued

NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: AIDS-Related B-Cell Lymphomas (Part 2 of 3)

Diffuse large B-cell lymphoma (DLBCL), HHV8-positive DLBCL, NOS, and Primary Effusion Lymphoma[1,a,b,c,d]

REGIMEN	DOSING
Dose-adjusted EPOCH (etoposide + prednisone + vincristine + cyclophosphamide + doxorubicin) + rituximab (preferred)[6–8]	**Days 1–4:** Etoposide 50mg/m² IV + prednisone 60mg/m² orally + vincristine 0.4mg/m² IV + doxorubicin 10mg/m² IV **Day 1:** Rituximab 375mg/m² IV **Day 5:** Prednisone 60mg/m² orally **Day 5: Cycle 1:** Cyclophosphamide 375mg/m² IV if CD4 cells ≥100/mm³ **OR** 187mg/m² IV if CD4 cells <100/mm³. **Cyclophosphamide dose-adjustment (after Cycle 1):** If nadir ANC >500/mcL, then increase by 187mg above previous cycle. If nadir ANC <500/mcL, or platelets <25,000/mcL, then decrease by 187mg below previous cycle. Repeat cycle every 3 weeks.
CHOP + rituximab[12,13]	**Option 1—Modified CHOP** **Day 1:** Cyclophosphamide 375mg/m² IV + doxorubicin 25mg/m² IV + vincristine 1.4mg/m² IV (2mg maximum) **Days 1–5:** Prednisone 100mg orally **Day 1:** Rituximab 375mg/m² IV. Repeat cycle every 3 weeks for at least 4 cycles, or for 2 cycles after complete response. **Option 2—Standard-dose CHOP** **Day 1:** Cyclophosphamide 750mg/m² IV + doxorubicin 50mg/m² IV + vincristine 1.4mg/m² IV (2mg maximum) **Days 1–5:** Prednisone 100mg orally **Day 1:** Rituximab 375mg/m² IV. Repeat cycle every 3 weeks for at least 4 cycles, or for 2 cycles after complete response.

Plasmablastic Lymphoma[1,a,e,f,g]

CODOX-M/IVAC (modified) (cyclophosphamide + vincristine + doxorubicin + high-dose methotrexate alternating with ifosfamide + etoposide + high-dose cytarabine)[2–4]	**Day 1:** Cyclophosphamide 800mg/m² IV, **followed by** **Days 2–5:** Cyclophosphamide 200mg/m² IV **Day 1:** Doxorubicin 40mg/m² IV **Days 1 and 8: Cycle 1:** Vincristine 1.5mg/m² IV; **Cycle 2:** Days 1, 8, and 15. **Day 1:** MTX 1,200mg/m² IV over 1 hour, followed by 240mg/m²/hour over 23 hours. **Days 1 and 3:** Cytarabine 70mg intrathecally. **Day 1:** Rituximab 375mg/m² IV. **Day 15:** MTX 12mg intrathecally. **Alternate with:** **Days 1–5:** Ifosfamide 1,500mg/m² IV + etoposide 60mg/m² IV **Days 1 and 2:** Cytarabine 2,000mg/m² IV every 12 hours for 4 doses **Day 1:** Rituximab 375mg/m² IV **Day 15:** MTX 12mg intrathecally.
Dose-adjusted EPOCH (etoposide + prednisone + vincristine + cyclophosphamide + doxorubicin) (preferred)[5]	**Days 1–4:** Etoposide 50mg/m² IV + prednisone 60mg/m² orally + vincristine 0.4mg/m² IV + doxorubicin 10mg/m² IV **Day 5:** Prednisone 60mg/m² orally **Day 5: Cycle 1:** Cyclophosphamide 375mg/m² IV if CD4 cells ≥100/mm³ **OR** 187mg/m² IV if CD4 cells <100/mm³. **Cyclophosphamide dose-adjustment (after Cycle 1):** If nadir ANC >500/mcL, then increase by 187mg above previous cycle. If nadir ANC <500/mcL, or platelets <25,000/mcL, then decrease by 187mg below previous cycle. Repeat cycle every 3 weeks.

continued

NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: AIDS-Related B-Cell Lymphomas (Part 3 of 3)

Plasmablastic Lymphoma[1,a,e,f,g] (continued)

REGIMEN	DOSING
HyperCVAD (cyclophosphamide + vincristine + doxorubicin + dexamethasone alternating with high-dose methotrexate and cytarabine)[9–11]	**Cycles 1, 3, 5, and 7—HyperCVAD** **Days 1–3:** Cyclophosphamide 300mg/m² IV every 12 hours for 6 doses, **plus** mesna 600mg/m² continuous IV **Days 4 and 11:** Vincristine 2mg IV **Day 4:** Doxorubicin 50mg/m² IV. **Days 1–4 and Days 11–14:** Dexamethasone 40mg daily. **Cycles 2, 4, 6, 8—High-dose MTX and Cytarabine** **Day 1:** MTX 1g/m² IV over 24 hours **Days 2 and 3:** Cytarabine 3g/m² IV every 12 hours for 4 doses. Repeat every 3 weeks for 8 cycles.

Primary CNS Lymphoma[1b]

- Initiate ART (antiretroviral therapy), if not already receiving.
- Even with poorly controlled HIV and/or marginal performance status, consider high-dose methotrexate.
- Consider RT alone for palliation of patients who are not candidates for systemic therapy.
- For select patients with good performance status on ART, see NCCN Guidelines for CNS cancers.
- Best supportive care.

[a] Antiretrovirals (ARVs) can be administered safely with chemotherapy but consultation with an HIV specialist or pharmacist is important to optimize compatibility. With continued development of new ARVs, effective alternatives are often available to patients when the existing ARVs are expected to affect metabolism of or share toxicities with chemotherapy. In general, avoidance of zidovudine, cobicistat, and ritonavir is strongly recommended. Concurrent ART is associated with higher CR rates.[14]

[b] Granulocyte colony-stimulating factor (GCSF) should be given to all patients. If CD4 <50, maximize supportive care.

[c] Rituximab and hyaluronidase human injection for subcutaneous use may be substituted for rituximab after patients have received the first full dose of rituximab by intravenous infusion. This substitution cannot be made for rituximab used in combination with ibritumomab tiuxetan.

[d] If CD20 negative, rituximab is not indicated.

[e] Standard CHOP is not adequate therapy.

[f] Management can also apply to HIV-negative plasmablastic lymphoma.

[g] Consider high-dose therapy with autologous stem cell rescue in first complete remission in select high-risk patients.

References

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