

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

The selection, dosing, and administration of anticancer agents and the management of associated toxicities are complex. Drug dose modifications and schedule and initiation of supportive care interventions are often necessary because of expected toxicities and because of individual patient variability, prior treatment, and comorbidities. Thus, the optimal delivery of anticancer agents requires a healthcare delivery team experienced in the use of such agents and the management of associated toxicities in patients with cancer. The cancer treatment regimens below may include both FDA-approved and unapproved uses/regimens and are provided as references only to the latest treatment strategies. Clinicians must choose and verify treatment options based on the individual patient.

REGIMEN	DOSING
<b>Burkitt Lymphoma</b>	
Administer granulocyte colony-stimulating factor (G-CSF) for all patients. If CD4 <100, consider eliminating rituximab. <sup>1</sup>	
<b>CODOX-M/IVAC modified</b> (cyclophosphamide [Cytosan] + vincristine [Oncovin] + doxorubicin [Adriamycin] + high-dose methotrexate [MTX] alternating with ifosfamide [Ifex] + etoposide [VP-16; Etopophos] + high-dose cytarabine [ARA-C; Cytosar-U] ± rituximab [Rituxan]) <sup>1,2,3</sup>	<b>Day 1:</b> Cyclophosphamide 800mg/m <sup>2</sup> IV, <b>followed by</b> <b>Days 2-5:</b> Cyclophosphamide 200mg/m <sup>2</sup> IV. <b>Day 1:</b> Doxorubicin 40mg/m <sup>2</sup> IV. <b>Days 1 and 8: Cycle 1:</b> Vincristine 1.5mg/m <sup>2</sup> IV; <b>Cycle 2:</b> Days 1, 8, and 15. <b>Day 1:</b> MTX 1,200mg/m <sup>2</sup> IV over 1 hr, <b>followed by</b> 240mg/m <sup>2</sup> /hr over 23 hrs. <b>Days 1 and 3:</b> Intrathecal cytarabine 70mg. <b>Day 1:</b> Rituximab 375mg/m <sup>2</sup> IV. <b>Day 15:</b> Intrathecal MTX 12mg.  <b>Alternate with:</b> <b>Days 1-5:</b> Ifosfamide 1,500mg/m <sup>2</sup> IV. <b>Days 1-5:</b> Etoposide 60mg/m <sup>2</sup> IV. <b>Days 1 and 2:</b> Cytarabine 2,000mg/m <sup>2</sup> IV every 12 hrs for 4 doses. <b>Day 1:</b> Rituximab 375mg/m <sup>2</sup> IV. <b>Day 15:</b> Intrathecal MTX 12mg.
<b>Dose-adjusted EPOCH</b> (etoposide + prednisone + vincristine + cyclophosphamide + doxorubicin) ± rituximab <sup>1,3,4</sup>	<b>Days 1-4:</b> Etoposide 50mg/m <sup>2</sup> IV + prednisone 60mg/m <sup>2</sup> orally + vincristine 0.4mg/m <sup>2</sup> IV + doxorubicin 10mg/m <sup>2</sup> IV. <b>Day 1:</b> Rituximab 375mg/m <sup>2</sup> IV. <b>Day 5:</b> Prednisone 60mg/m <sup>2</sup> orally. <b>Day 5: Cycle 1:</b> Cyclophosphamide 375mg/m <sup>2</sup> IV if CD4 cells ≥100/mm <sup>3</sup> , <b>OR</b> 187mg/m <sup>2</sup> IV if CD4 cells <100/mm <sup>3</sup> . 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.
<b>CDE</b> (cyclophosphamide + doxorubicin + etoposide) <sup>1,5</sup> ± rituximab <sup>1,3,6,7</sup>	<b>Days 1-4:</b> Cyclophosphamide 187.5-200mg/m <sup>2</sup> IV + doxorubicin 12.5mg/m <sup>2</sup> IV infusion + etoposide 60mg/m <sup>2</sup> IV. <b>Day 1:</b> Rituximab 375mg/m <sup>2</sup> IV just before CDE regimen. Repeat cycle every 4 weeks for a maximum of 6 cycles.
<b>Hyper-CVAD</b> (cyclophosphamide + vincristine + doxorubicin + dexamethasone) <b>alternating with high-dose MTX and cytarabine</b> ± rituximab <sup>1,3,8-10</sup>	<b>Cycles 1, 3, 5, 7—HyperCVAD</b> <b>Days 1-3:</b> Cyclophosphamide 300mg/m <sup>2</sup> IV every 12 hrs for 6 doses, <b>plus</b> mesna 600mg/m <sup>2</sup> continuous IV. <b>Days 4 and 11:</b> Vincristine 2mg IV. <b>Day 4:</b> Doxorubicin 50mg/m <sup>2</sup> IV. <b>Days 1-4 and 11-14:</b> Dexamethasone 40mg daily. <b>Days 1 and 11</b> (of Cycles 1 and 3): Rituximab 375mg/m <sup>2</sup> IV.  <b>Cycles 2, 4, 6, 8—high-dose MTX and cytarabine</b> <b>Day 1:</b> MTX 1g/m <sup>2</sup> IV over 24 hrs. <b>Days 2 and 3:</b> Cytarabine 3g/m <sup>2</sup> IV every 12 hrs for 4 doses. <b>Days 1 and 8</b> (of Cycles 2 and 4): Rituximab 375mg/m <sup>2</sup> IV. Repeat every 3 weeks for 8 cycles.

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

REGIMEN	DOSING
<b>Lymphoma associated with Castleman's disease, Diffuse large-B cell lymphoma, Primary effusion lymphoma</b>	
Administer G-CSF for all patients. If CD4 <100, consider eliminating rituximab. If CD20, rituximab not indicated. <sup>1</sup>	
<b>Dose-adjusted EPOCH</b> (etoposide + prednisone + vincristine + cyclophosphamide + doxorubicin) + <b>rituximab</b> <sup>1,3,4</sup>	<p><b>Days 1-4:</b> Etoposide 50mg/m<sup>2</sup> IV + prednisone 60mg/m<sup>2</sup> orally + vincristine 0.4mg/m<sup>2</sup> IV + doxorubicin 10mg/m<sup>2</sup> IV.</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p><b>Day 5:</b> Prednisone 60mg/m<sup>2</sup> orally.</p> <p><b>Day 5: Cycle 1:</b> Cyclophosphamide 375mg/m<sup>2</sup> IV if CD4 cells ≥100/mm<sup>3</sup>, <b>OR</b> 187mg/m<sup>2</sup> IV if CD4 cells &lt;100/mm<sup>3</sup>.</p> <p>Cyclophosphamide dose-adjustment (after Cycle 1): If nadir ANC &gt;500/mcL, then increase by 187mg above previous cycle. If nadir ANC &lt;500/mcL, or platelets &lt;25,000/mcL, then decrease by 187mg below previous cycle.</p> <p>Repeat cycle every 3 weeks.</p>
<b>CDE</b> (cyclophosphamide + doxorubicin + etoposide) <sup>1,5,7</sup> + <b>rituximab</b> <sup>1,3,6,7</sup>	<p><b>Days 1-4:</b> Cyclophosphamide 187.5-200mg/m<sup>2</sup> IV + doxorubicin 12.5mg/m<sup>2</sup> IV infusion + etoposide 60mg/m<sup>2</sup> IV.</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV just before CDE regimen.</p> <p>Repeat cycle every 4 weeks for a maximum of 6 cycles.</p>
<b>CHOP + rituximab</b> <sup>1,3,11</sup>	<p><b>Option 1—Modified CHOP</b></p> <p><b>Day 1:</b> Cyclophosphamide 375mg/m<sup>2</sup> IV + doxorubicin 25mg/m<sup>2</sup> IV + vincristine 1.4mg/m<sup>2</sup> IV (max dose 2mg).</p> <p><b>Days 1-5:</b> Prednisone 100mg orally.</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p>Repeat cycle every 3 weeks for at least 4 cycles, or for 2 cycles after complete response.</p> <p><b>Option 2—Standard dose CHOP</b></p> <p><b>Day 1:</b> Cyclophosphamide 750mg/m<sup>2</sup> IV + doxorubicin 50mg/m<sup>2</sup> IV + vincristine 1.4mg/m<sup>2</sup> IV (max dose 2mg).</p> <p><b>Days 1-5:</b> Prednisone 100mg orally.</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p>Repeat cycle every 3 weeks for at least 4 cycles, or for 2 cycles after complete response.</p>
<b>CDOP</b> (cyclophosphamide + liposomal doxorubicin + vincristine + prednisone) + <b>rituximab</b> <sup>1,3,12</sup>	<p><b>Day 1:</b> Cyclophosphamide 750g/m<sup>2</sup> 30 min IV infusion + liposomal doxorubicin 30mg/m<sup>2</sup> IV over 1 hr + vincristine 2mg IV over 15 mins.</p> <p><b>Days 1-5:</b> Prednisone 60mg/m<sup>2</sup> IV.</p> <p>Repeat cycle every 3 weeks for 6-8 cycles.</p>
<b>Plasmablastic Lymphoma</b>	
Standard CHOP is not adequate therapy. <sup>1</sup>	
<b>CODOX-M/IVAC modified</b> <sup>1,2</sup>	<p><b>Day 1:</b> Cyclophosphamide 800mg/m<sup>2</sup> IV, <b>followed by</b></p> <p><b>Days 2-5:</b> Cyclophosphamide 200mg/m<sup>2</sup> IV.</p> <p><b>Day 1:</b> Doxorubicin 40mg/m<sup>2</sup> IV.</p> <p><b>Days 1 and 8: Cycle 1:</b> Vincristine 1.5mg/m<sup>2</sup> IV; <b>Cycle 2:</b> Days 1, 8, and 15.</p> <p><b>Day 1:</b> MTX 1,200mg/m<sup>2</sup> IV over 1 hr, <b>followed by</b> 240mg/m<sup>2</sup>/hr over 23 hrs.</p> <p><b>Days 1 and 3:</b> Intrathecal cytarabine 70mg.</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p><b>Day 15:</b> Intrathecal MTX 12mg.</p> <p><b>Alternate with</b></p> <p><b>Days 1-5:</b> Ifosfamide 1,500mg/m<sup>2</sup> IV.</p> <p><b>Days 1-5:</b> Etoposide 60mg/m<sup>2</sup> IV.</p> <p><b>Days 1 and 2:</b> Cytarabine 2,000mg/m<sup>2</sup> IV every 12 hrs for 4 doses.</p> <p><b>Day 1:</b> Rituximab 375mg/m<sup>2</sup> IV.</p> <p><b>Day 15:</b> Intrathecal MTX 12mg.</p>

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

REGIMEN	DOSING
<b>Plasmablastic Lymphoma (continued)</b>	
<p><b>Dose-adjusted EPOCH</b> (etoposide + prednisone + vincristine + cyclophosphamide + doxorubicin)<sup>1,4</sup></p>	<p><b>Days 1–4:</b> Etoposide 50mg/m<sup>2</sup> IV + prednisone 60mg/m<sup>2</sup> orally + vincristine 0.4mg/m<sup>2</sup> IV + doxorubicin 10mg/m<sup>2</sup> IV.  <b>Day 5:</b> Prednisone 60mg/m<sup>2</sup> orally.  <b>Day 5: Cycle 1:</b> Cyclophosphamide 375mg/m<sup>2</sup> IV if CD4 cells ≥100/mm<sup>3</sup>, <b>OR</b> 187mg/m<sup>2</sup> IV if CD4 cells &lt;100/mm<sup>3</sup>.                      Cyclophosphamide dose-adjustment (after Cycle 1): If nadir ANC &gt;500/mcL, then increase by 187mg above previous cycle. If nadir ANC &lt;500/mcL, or platelets &lt;25,000/mcL, then decrease by 187mg below previous cycle.                      Repeat cycle every 3 weeks.</p>
<p><b>Hyper-CVAD</b> (cyclophosphamide + vincristine + doxorubicin + dexamethasone) <b>alternating with high-dose MTX and cytarabine</b><sup>1,8-10</sup></p>	<p><b>Cycles 1, 3, 5, 7—HyperCVAD</b>  <b>Days 1–3:</b> Cyclophosphamide 300mg/m<sup>2</sup> IV every 12 hrs for 6 doses, <u>plus</u> mesna 600mg/m<sup>2</sup> continuous IV.  <b>Days 4 and 11:</b> Vincristine 2mg IV.  <b>Day 4:</b> Doxorubicin 50mg/m<sup>2</sup> IV.  <b>Days 1–4 and 11–14:</b> Dexamethasone 40mg daily.</p> <p><b>Cycles 2, 4, 6, 8—high-dose MTX and cytarabine</b>  <b>Day 1:</b> MTX 1g/m<sup>2</sup> IV over 24 hrs.  <b>Days 2 and 3:</b> Cytarabine 3g/m<sup>2</sup> IV every 12 hrs for 4 doses.                      Repeat every 3 weeks for 8 cycles.</p>
<b>Primary CNS Lymphoma</b>	
Consider high-dose MTX. Consider RT alone. Best supportive care. <sup>1</sup>	
<b>References</b>	
<ol style="list-style-type: none"> <li>1. NCCN Clinical Practice Guidelines in Oncology™. Non-Hodgkin's Lymphomas. v 2.2012. Available at: <a href="http://www.nccn.org/professionals/physician_gls/pdf/nhl.pdf">http://www.nccn.org/professionals/physician_gls/pdf/nhl.pdf</a>. Accessed June 18, 2012.</li> <li>2. Wang ES, Straus DJ, Teruya-Feldstein J, et al. Intensive chemotherapy with cyclophosphamide, doxorubicin, high-dose methotrexate/ifosfamide, etoposide, and high-dose cytarabine (CODOX-M/IVAC) for human immunodeficiency virus-associated Burkitt lymphoma. <i>Cancer</i>. 2003;98:1196–1205.</li> <li>3. Rituxan [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2011.</li> <li>4. Little RF, Pittaluga S, Grant N, et al. Highly effective treatment of acquired immunodeficiency syndrome-related lymphoma with dose-adjusted EPOCH: impact of antiretroviral therapy suspension and tumor biology. <i>Blood</i>. 2003;101:4653–4659.</li> <li>5. Sparano JA, Lee S, Chenmg, et al. Phase II trial of infusional cyclophosphamide, doxorubicin, and etoposide in patients with HIV-associated non-Hodgkin's lymphoma: An Eastern Cooperative Oncology Group Trial (E1494). <i>J Clin Oncol</i>. 2004;22:1491–1500.</li> <li>6. Spina M, Chimienti E, Vaccher E, et al. Long-term follow-up of rituximab and infusional cyclophosphamide, doxorubicin, and etoposide in combination with HAART in HIV related Non-Hodgkin's lymphomas. <i>Blood</i>. 2008;112:Abstract 1467.</li> <li>7. Spina M, Jaeger U, Sparano JA, et al. Rituximab plus infusional cyclophosphamide, doxorubicin, and etoposide in HIV-</li> </ol>	<ol style="list-style-type: none"> <li>associated non-Hodgkin lymphoma: pooled results from 3 phase 2 trials. <i>Blood</i>. 2005;105:1891–1897.</li> <li>8. Cortes J, Thomas D, Rios A, et al. Hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone and highly active antiretroviral therapy for patients with acquired immunodeficiency syndrome-related Burkitt lymphoma/leukemia. <i>Cancer</i>. 2002;94:1492–1499.</li> <li>9. Thomas DA, Faderl S, O'Brien S, et al. Chemoimmunotherapy with hyper-CVAD plus rituximab for the treatment of adult Burkitt and Burkitt-type lymphoma or acute lymphoblastic leukemia. <i>Cancer</i>. 2006;106:1569–1580.</li> <li>10. Thomas DA, Kantarjian HM, Cortes J, et al. Long-term outcome after hyper-CVAD and rituximab chemoimmunotherapy for Burkitt (BL) or Burkitt-like (BLL) leukemia/lymphoma and mature B-cell lymphocytic leukemia (ALL). <i>Blood</i>. 2008;112: Abstract 1929.</li> <li>11. Ratner L, Lee J, Tang S, et al. Chemotherapy for human immunodeficiency virus-associated non-Hodgkin's lymphoma in combination with highly active antiretroviral therapy. <i>J Clin Oncol</i>. 2001;19:2171–2178.</li> <li>12. Martino R, Perea G, Caballero MD, et al. Cyclophosphamide, pegylated liposomal doxorubicin (Caelyx), vincristine and prednisone (CCOP) in elderly patients with diffuse large B-cell lymphoma: results from a prospective phase II study. <i>Haematologica</i>. 2002;87:822–827.</li> </ol>
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