

NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Lymphoblastic 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
Standard BFM (Berlin–Frankfurt–Munster) Regimen^{1,2}	
Induction Phase	
Vincristine (Oncovin) + daunomycin (DaunoXome) + prednisone + L-asparaginase (Elspar) + cytarabine (Cytosar) + methotrexate (MTX)	Day 0: Intrathecal cytarabine. Day 1: Vincristine 1.5mg/m ² IV + Daunomycin 25mg/m ² IV weekly for 4 weeks. Day 1: L-asparaginase 6,000 IU/m ² IM 3 times a week for 9 doses. Days 1–28: Prednisone 60mg/m ² orally. Day 14: Intrathecal MTX.
Consolidation Phase (5 weeks)	
Prednisone + cyclophosphamide (Cytoxan) + mercaptopurine (Purinethol; 6-MP) + vincristine + cytarabine + MTX + Radiotherapy (RT)	Day 0: Prednisone 7.5mg/m ² orally. Days 0 and 14: Cyclophosphamide 1,000mg/m ² IV. Days 0–27: Mercaptopurine 60mg/m ² orally. Days 1 and 2: Prednisone 3.75mg/m ² orally. Days 1–4, 8–11, 15–18, and 22–25: Cytarabine 75mg/m ² IV. Days 1, 8, 15, and 22: Intrathecal MTX 12mg. Days 14, 21, 42, and 49: Vincristine 1.5mg/m ² IV.
Interim Maintenance Phase (8 weeks)	
Mercaptopurine + MTX	Days 0–41: Mercaptopurine 60mg/m ² orally. Days 0, 7, 14, 21, 28, and 35: MTX 15mg/m ² orally.
Delayed Intensification (7 weeks)	
Reinduction Phase (4 weeks) Dexamethasone + vincristine + doxorubicin (Adriamycin)	Days 0–20: Dexamethasone 10mg/m ² orally, then taper for 7 days. Days 0, 7, and 14: Doxorubicin 25mg/m ² . Days 0, 14, and 21: Vincristine 1.5mg/m ² IV.
Reconsolidation Phase (3 weeks) L-asparaginase + vincristine + cyclophosphamide + thioguanine + cytarabine + MTX	Days 3, 5, 7, 10, 12, and 14: L-asparaginase 6,000 IU/m ² IM. Day 28: Cyclophosphamide 1,000mg/m ² IV. Days 28–41: Thioguanine 60mg/m ² orally. Days 29–32 and 36–39: Cytarabine 75mg/m ² SC or IV. Days 29 and 36: Intrathecal MTX 12mg. Days 42 and 49: Vincristine 1.5mg/m ² IV.
Long-term Maintenance (12 weeks)	
Vincristine + prednisone + mercaptopurine + MTX	Day 0: Intrathecal MTX 12mg. Days 0–83: Mercaptopurine 75mg/m ² orally. Days 0–4, 28–32, and 56–60: Prednisone 40mg/m ² orally. Days 0, 28, and 56: Vincristine 1.5mg/m ² IV. Days 7, 14, 21, 28, 35, 42, 49, 56, 63, 70, and 77: MTX 20mg/m ² orally.
Augmented BFM Regimen^{1,3}	
Induction I	
Prednisone + vincristine + daunorubicin + L-asparaginase + MTX	Day 1: Intrathecal MTX 15mg. Days 1–28: Prednisone 60mg/m ² orally, then taper dose. Days 1, 8, 15, and 22: Vincristine 2mg IV + daunorubicin 45mg/m ² IV. Days 15–28: L-asparaginase 5,000 IU/m ² IV every other day.
Induction II	
Cyclophosphamide + cytarabine + mercaptopurine + MTX	Days 29–57: Mercaptopurine 60mg/m ² orally. Days 29, 43, and 57: Cyclophosphamide 1,000mg/m ² IV. Days 31–34, 38–41, 45–48, and 52–55: Cytarabine 75mg/m ² IV. Days 31, 38, 45, and 52: Intrathecal MTX 15mg.
Consolidation I	
Cytarabine , mitoxantrone (Novantrone) + MTX , L-asparaginase + mercaptopurine	Days 1–4: Cytarabine x 1,000mg/m ² IV every 12 hrs. Days 1–5 and 15–19: Mercaptopurine 25mg/m ² . Days 1 and 15: MTX 1,500mg/m ² continuous IV. Days 2 and 16: L-asparaginase 10,000 IU/m ² IV. Days 3–5: Mitoxantrone 10mg/m ² IV.

continued

NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Lymphoblastic Lymphoma (Part 2 of 3)

REGIMEN	DOSING
Augmented BFM Regimen^{1,3} (continued)	
Reduction I	
Prednisolone + vincristine + doxorubicin	Days 1–28: Prednisolone 60mg/m ² orally. Days 1, 8, 15, and 22: Vincristine 2mg IV + doxorubicin 25mg/m ² IV.
For Triple Prophylaxis MTX + cytarabine + dexamethasone	Day 1: Intrathecal MTX 15mg + intrathecal cytarabine 40mg + intrathecal dexamethasone 4mg.
Reduction II	
Cyclophosphamide + cytarabine + 6-thioguanine	Day 29: Cyclophosphamide 1,000mg/m ² IV. Days 29–42: 6-thioguanine 60mg/m ² orally. Days 31–34 and 38–41: Cytarabine 75mg/m ² IV.
For Triple Prophylaxis MTX + cytarabine + dexamethasone	Day 29: Intrathecal MTX 15mg + intrathecal cytarabine 40mg + intrathecal dexamethasone 4mg.
Consolidation II	
Etoposide (Etopophos, VP-16) + cytarabine	Days 1–5: Etoposide 100mg/m ² IV + cytarabine 150mg/m ² IV.
Cyclophosphamide + cytarabine	Day 1: Cyclophosphamide 1,000mg/m ² IV + cytarabine 500mg/m ² IV.
CALGB ALL Regimen^{1,4}	
Introduction Therapy (4 weeks)	
Cyclophosphamide + daunorubicin + vincristine + prednisone + L-asparaginase	Day 1: Cyclophosphamide 1,200mg/m ² IV. Days 1–21: Prednisone 60mg/m ² orally or IV. Days 1, 2, and 3: Daunorubicin 45mg/m ² IV. Days 1, 8, 15, and 22: Vincristine 2mg IV. Days 5, 8, 11, 15, 18, and 22: L-asparaginase 6,000 IU/m ² SC. <u>For Patients ≥60 Years</u> Day 1: Cyclophosphamide 800mg/m ² IV. Days 1–3: Daunorubicin 30mg/m ² IV. Day 1–7: Prednisone 60mg/m ² orally or IV.
Early Intensification (4 weeks)	
MTX + cyclophosphamide + mercaptopurine + cytarabine + vincristine + L-asparaginase	Day 1: Intrathecal MTX 15mg + cyclophosphamide 1,000mg/m ² IV. Days 1–14: Mercaptopurine 60mg/m ² orally. Days 1–4 and 8–11: Cytarabine 75mg/m ² SC. Days 15 and 22: Vincristine 2mg IV. Days 15, 18, 22, and 25: L-asparaginase 6,000 IU/m ² SC.
CNS Prophylaxis and Interim Maintenance	
MTX + mercaptopurine + cranial irradiation in select cases	Days 1–70: Mercaptopurine 60mg/m ² orally. Days 1, 8, 15, 22, and 29: Intrathecal MTX 15mg. Days 36, 43, 50, 57, and 64: MTX 20mg/m ² orally.
Late Intensification (8 weeks)	
Doxorubicin + vincristine + dexamethasone + cyclophosphamide + 6-thioguanine + cytarabine	Days 1–14: Dexamethasone 10mg/m ² orally. Days 1, 8, and 15: Doxorubicin 30mg/m ² IV + vincristine 2mg IV. Day 29: Cyclophosphamide 1,000mg/m ² IV. Days 29–42: 6-thioguanine 60mg/m ² orally. Days 29–32 and 36–39: Cytarabine 75mg/m ² SC.
Prolonged Maintenance (until 24 months from diagnosis)	
Vincristine + prednisone + MTX + mercaptopurine	Day 1: Vincristine 2mg IV every 4 weeks. Days 1–5: Prednisone 60mg/m ² orally every 4 weeks. Days 1–28: Mercaptopurine 60mg/m ² orally. Days 1, 8, 15, and 22: MTX 20mg/m ² orally.

continued

NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Lymphoblastic Lymphoma (Part 3 of 3)

REGIMEN	DOSING
Hyper-CVAD Alternating with MTX + Cytarabine^{1,5,6}	
Hyper-CVAD (cyclophosphamide + vincristine + doxorubicin + dexamethasone) alternating with MTX + cytarabine	<p>Cycles 1, 3, 5, and 7—HyperCVAD Days 1–3: Cyclophosphamide 300mg/m² IV every 12 hrs for 6 doses, plus mesna (same total dose as cyclophosphamide) continuous IV starting with cyclophosphamide and ending 6 hrs after the last dose. Days 1–4 and 11–14: Dexamethasone 40mg. Day 4: Doxorubicin 50mg/m² IV. Days 4 and 11: Vincristine 2mg IV.</p> <p>Cycles 2, 4, 6, and 8 Day 1: MTX 200mg/m² IV over 2 hrs, followed by MTX 800mg/m² IV over 24 hrs. Days 1–3: Methylprednisolone 50mg IV twice daily. Days 2 and 3: Cytarabine 3g/m² IV every 12 hrs for 4 doses.</p>
Maintenance Therapy	
POMP (mercaptopurine + MTX, vincristine + prednisone)	<p>Mercaptopurine 50mg orally 3 times daily. MTX 20mg/m² orally once a week. Vincristine 2mg IV once a month. Prednisone 200mg daily for 5 doses with vincristine.</p> <p style="text-align: center;">OR</p> <p>Mercaptopurine 1g/m² IV for 5 doses monthly. MTX 10mg/m² IV for 5 doses monthly. Vincristine 2mg IV once a month. Prednisone 200mg daily for 5 doses with vincristine.</p> <p>NOTE: <ul style="list-style-type: none"> ■ If CD20 positive (≥20%) ALL, the addition of rituximab (Rituxan) should be considered. ■ If Ph+ ALL, imatinib (Gleevec) should be incorporated into regimen. </p>
LMB-86 Regimen^{1,7}	
Cytoreductive Therapy	
COP (cyclophosphamide + vincristine + prednisone)	<p>Day 1: Vincristine 2mg IV + cyclophosphamide 300mg/m² IV. Day 1–7: Prednisone 60mg/m² orally.</p>
Induction Therapy	
COPADM (cyclophosphamide + vincristine + prednisone + doxorubicin + MTX)	<p>Day 1: Vincristine 2mg IV + MTX 3g/m² IV. Days 1–7: Prednisone 60mg/m² orally. Day 2: Doxorubicin 60mg/m² IV. Days 2–4: Cyclophosphamide 500mg/m² IV.</p>
Consolidation Therapy	
CYVE (cytarabine + etoposide)	<p>Days 1–5: Cytarabine 50mg/m² IV (12 hr infusion before high-dose cytarabine). Days 2–5: Cytarabine 3g/m² IV + etoposide 200mg/m² IV. NOTE: Up to 2 years of maintenance therapy based on the treatment protocol is recommended.</p>
References	
<ol style="list-style-type: none"> 1. NCCN Clinical Practice Guidelines in Oncology™. Non-Hodgkin's Lymphoma. v.3.2012. Available at: http://www.nccn.org/professionals/physician_gls/pdf/nhl.pdf. Accessed July 12, 2012. 2. Stock W, La M, Sanford B, et al. What determines the outcomes for adolescents and young adults with acute lymphoblastic leukemia treated on cooperative group protocols? A comparison of Children's Cancer Group and Cancer and Leukemia Group B studies. <i>Blood</i>. 2008;112:1646–1654. 3. Hoelzer D, Gökbuget N, Digel W, et al. Outcome of adult patients with T-lymphoblastic lymphoma treated according to protocols for acute lymphoblastic leukemia. <i>Blood</i>. 2002;99:4379–4385. 4. Larson RA, Dodge RK, Burns CP, et al. A five-drug remission induction regimen with intensive consolidation for adults with 	<p>acute lymphoblastic leukemia: cancer and leukemia group B study 8811. <i>Blood</i>. 1995;85:2025–2037.</p> <ol style="list-style-type: none"> 5. Kantarjian HM, O'Brien S, Smith TL, et al. Results of treatment with hyper-CVAD, a dose-intensive regimen, in adult acute lymphocytic leukemia. <i>J Clin Oncol</i>. 2000;18:547–561. 6. Thomas DA, O'Brien S, Cortes J, et al. Outcome with the hyper-CVAD regimens in lymphoblastic lymphoma. <i>Blood</i>. 2004;104:1624–1630. 7. Soussain C, Patte C, Ostronoff M, et al. Small noncleaved cell lymphoma and leukemia in adults. A retrospective study of 65 adults treated with the LMB pediatric protocols. <i>Blood</i>. 1995;85:664–674.
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