

AIDS-Related B-Cell Lymphomas

Clinical Trials: The NCCN 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 healthcare 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 only provided to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The National Comprehensive Cancer Network 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.

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

► Burkitt Lymphoma^{1,2,a,n}

REGIMEN	DOSING
Low-Risk Disease	
Preferred Regimens	
CODOX-M (Modified) (Cyclophosphamide + Vincristine + Doxorubicin + High-Dose Methotrexate) + Rituximab ^{3-5,b-i}	<p>Days 1-2: Cyclophosphamide 800mg/m² IV over 30 minutes daily</p> <p>Days 1,8: Vincristine 1.4mg/m² (maximum 2 mg) IV over 5-10 minutes</p> <p>Day 1: Doxorubicin 50mg/m² IV push</p> <p>Day 15: Methotrexate 3,000mg/m² IV over 4 hours</p> <p>Leucovorin: 200mg/m² IV over 30 minutes starting 24 hours from the initiation of Methotrexate infusion, followed by:</p> <p>Leucovorin: 25mg/m² IV over 15 minutes OR orally every 6 hours (until Methotrexate serum concentration is <0.05 micromol/L)</p> <p>Day 1: Rituximab 375mg/m² IV</p> <p>Day 1: Cytarabine 50mg intrathecal OR intraventricular</p> <p>Day 1: Methotrexate 12mg intrathecal OR intraventricular.</p> <p>Repeat cycle every 3 weeks (or when post-nadir ANC is ≥1000 cells/mm³) for 3 cycles.</p>
SC-EPOCH-RR (Short-Course-Etoposide + Prednisone + Vincristine + Cyclophosphamide + Doxorubicin) + Dose-Dense Rituximab ^{3,4,6-8,b-g,j}	<p>Days 1-4 (Cycle 1): Etoposide 50mg/m² IV continuous infusion over 24 hours daily, followed by:</p> <p>Days 1-4 (Cycle 2 and Beyond): Etoposide IV continuous infusion over 24 hour daily (dosing based on absolute neutrophil count and platelet nadir measurements during the previous cycle), with:</p> <p>Days 1-4: Vincristine 0.4mg/m² IV continuous infusion over 24 hours daily, with:</p> <p>Days 1-4 (Cycle 1): Doxorubicin 10 mg/m² IV continuous infusion over 24 hours daily, followed by:</p> <p>Days 1-4 (Cycle 2 and Beyond): Doxorubicin IV continuous infusion over 24 hours daily (dosing based on absolute neutrophil count and platelet nadir measurements during the previous cycle)</p> <p>Day 5 (Cycle 1): Cyclophosphamide 750mg/m² IV over 30 minutes, followed by:</p> <p>Day 5 (Cycle 2 and Beyond): Cyclophosphamide IV over 30 minutes (dosing based on absolute neutrophil count and platelet nadir measurements during the previous cycle)</p> <p>Days 1-5: Prednisone 60mg/m² orally twice daily</p> <p>Day 1,5 (Cycles 1-3): Rituximab 375mg/m² IV.</p> <p>Repeat cycle every 3 weeks for 3 cycles (if interim PET scan after 2 cycles is negative).</p>
Other Recommended Regimens	
R-Hyper CVAD ^{3,4,9,b,i,k}	<p>Cycle A</p> <p>Days 1-3: Cyclophosphamide 300mg/m² IV over 2 hours every 12 hours for 6 doses</p> <p>Days 1-3: Mesna 600mg/m² IV continuous infusion over 24 hours daily starting 1 hour before the first dose of Cyclophosphamide and completing 12 hours after the last dose of Cyclophosphamide</p> <p>Days 4,11: Vincristine 2mg IV over 5-10 minutes</p> <p>Day 4: Doxorubicin 50mg/m² IV continuous infusion over 24 hours</p> <p>Days 1-4,11-14: Dexamethasone 40mg IV OR orally daily</p> <p>Day 1: Rituximab 375mg/m² IV</p> <p>Day 2: Methotrexate 12mg intrathecal OR intraventricular</p> <p>Day 7: Cytarabine 100mg intrathecal OR intraventricular.</p> <p>Repeat cycle A every 3 weeks (or earlier if count recovery occurs: maximum of 14 days) for 4 cycles alternating with cycle B.</p> <p>Cycle B</p> <p>Day 1: Methotrexate 200mg/m² IV over 2 hours, immediately followed by:</p> <p>Day 1: Methotrexate 800mg/m² IV continuous infusion over 22 hours</p> <p>Leucovorin 50mg IV over 15 minutes OR orally starting 12 hours after the completion of Methotrexate, followed by:</p> <p>Leucovorin 15mg IV over 15 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is <0.05 micromol/L)</p> <p>Days 2-3: Cytarabine (age <60 years) 3,000mg/m² IV over 3 hours for 4 doses OR Cytarabine (age ≥60 years) 1,000mg/m² IV over 3 hours for 4 doses</p> <p>Day 1: Rituximab 375mg/m² IV</p> <p>Day 2: Methotrexate 12mg intrathecal OR intraventricular</p> <p>Day 7: Methotrexate 100mg intrathecal OR intraventricular.</p> <p>Repeat cycle every 3 weeks (or earlier if count recovery occurs: minimum of 14 days) for 4 cycles alternating with cycle A (A1,B1,A2,B2,A3,B3,A4,A4).</p>

continued

AIDS-Related B-Cell Lymphomas

► Burkitt Lymphoma^{1,2,a,n} (continued)

REGIMEN	DOSING
High-Risk, CNS-Negative Disease	
Preferred Regimens	
CODOX-M (Modified) + R (Cyclophosphamide + Vinristine + Doxorubicin + High-Dose Methotrexate) + Rituximab (Regimen A) alternating with IVAC (Ifosfamide + Etoposide + High-dose Cytarabine; Regimen B) + Rituximab ^{3,4,b,g,l,m}	<p>Regimen A Days 1-2: Cyclophosphamide 800mg/m² IV over 30 minutes daily Days 1,8: Vincristine 1.4mg/m² (maximum 2 mg) IV over 5-10 minutes Day 1: Doxorubicin 50mg/m² IV push Day 15: Methotrexate 3,000mg/m² IV over 4 hours Leucovorin: 200mg/m² IV over 30 minutes starting 24 hours from the initiation of Methotrexate infusion, followed by: Leucovorin: 25mg/m² IV over 15 minutes OR orally every 6 hours (until Methotrexate serum concentration <0.05 micromol/L) Day 1: Rituximab 375mg/m² IV Day 1: Methotrexate 12mg intrathecal OR intraventricular, with: Day 1: Cytarabine 50mg intrathecal OR intraventricular, with: Day 1: Hydrocortisone 50mg intrathecal OR intraventricular, followed by: Day 3: Cytarabine 50mg intrathecal OR intraventricular. Repeat cycle every 3 weeks (or when post-nadir ANC is ≥1000 cells/mm³) for 2 cycles (Cycles 1 and 3) alternating with (Regimen B; Cycles 2 and 4).</p> <p>Regimen B Days 1-5: Ifosfamide 1,500mg/m² IV continuous infusion over 24 hours daily, with: Days 1-5: Mesna 1,500mg/m² IV continuous infusion over 24 hours daily Days 1-5: Etoposide 60mg/m² IV over 60 minutes daily Days 1-2: Cytarabine 2,000mg/m² IV over 3 hours every 12 hours for 4 doses Day 1: Rituximab 375mg/m² IV Day 5: Methotrexate 12mg intrathecal OR intraventricular. Repeat cycle every 3 weeks (or when post-nadir ANC is ≥1000 cells/mm³) for 2 cycles (Cycles 2 + 4) alternating with CODOX-M+ R (Regimen A).</p>
Other Recommended Regimens	
R-Hyper CVAD ^{3,4,9,b+i,k}	<p>Cycle A Days 1-3: Cyclophosphamide 300mg/m² IV over 2 hours every 12 hours for 6 doses Days 1-3: Mesna 600mg/m² IV continuous infusion over 24 hours daily starting 1 hour before the first dose of Cyclophosphamide and completing 12 hours after the last dose of Cyclophosphamide Days 4,11: Vincristine 2mg IV over 5-10 minutes Day 4: Doxorubicin 50mg/m² IV continuous infusion over 24 hours Days 1-4,11-14: Dexamethasone 40mg IV OR orally daily Day 1: Rituximab 375mg/m² IV Day 2: Methotrexate 12mg intrathecal OR intraventricular Day 7: Cytarabine 100mg intrathecal OR intraventricular. Repeat cycle A every 3 weeks (or earlier if count recovery occurs: maximum of 14 days) for 4 cycles alternating with cycle B.</p> <p>Cycle B Day 1: Methotrexate 200mg/m² IV over 2 hours, immediately followed by: Day 1: Methotrexate 800mg/m² IV continuous infusion over 22 hours Leucovorin 50mg IV over 15 minutes OR orally starting 12 hours after the completion of Methotrexate, followed by: Leucovorin 15mg IV over 15 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is <0.05 micromol/L) Days 2-3: Cytarabine (age <60 years) 3,000mg/m² IV over 3 hours for 4 doses OR Cytarabine (age ≥60 years) 1,000mg/m² IV over 3 hours for 4 doses Day 1: Rituximab 375mg/m² IV Day 2: Methotrexate 12mg intrathecal OR intraventricular Day 7: Methotrexate 100mg intrathecal OR intraventricular. Repeat cycle every 3 weeks (or earlier if count recovery occurs: minimum of 14 days) for 4 cycles alternating with cycle A (A1,B1,A2,B2,A3,B3,A4,A4) for a total of 8 cycles.</p>

continued

AIDS-Related B-Cell Lymphomas

► Burkitt Lymphoma^{1,2,a,n} (continued)

REGIMEN	DOSING
High-Risk, CNS Disease at Baseline	
Preferred Regimens	
CODOX-M (Modified) + R (Cyclophosphamide + Vinristine + Doxorubicin + High-Dose Methotrexate) + Rituximab (Regimen A) alternating with IVAC (Ifosfamide + Etoposide + High-dose Cytarabine; Regimen B) + Rituximab ^{3,5,c-1,1,m}	<p>Regimen A</p> <p>Days 1-2: Cyclophosphamide 800mg/m² IV over 30 minutes daily</p> <p>Days 1,8: Vincristine 1.4mg/m² (maximum 2 mg) IV over 5-10 minutes</p> <p>Day 1: Doxorubicin 50mg/m² IV push</p> <p>Day 15: Methotrexate 3,000mg/m² IV over 4 hours</p> <p>Leucovorin: 200mg/m² IV over 30 minutes starting 24 hours from the initiation of Methotrexate infusion, followed by:</p> <p>Leucovorin: 25mg/m² IV over 15 minutes OR orally every 6 hours (until Methotrexate serum concentration <0.05 micromol/L)</p> <p>Day 1: Rituximab 375mg/m² IV</p> <p>Day 1: Methotrexate 12mg intrathecal OR intraventricular, with:</p> <p>Day 1: Cytarabine 50mg intrathecal OR intraventricular, with:</p> <p>Day 1: Hydrocortisone 50mg intrathecal OR intraventricular, followed by:</p> <p>Day 3: Cytarabine 50mg intrathecal OR intraventricular.</p> <p>Repeat cycle every 3 weeks (or when post-nadir ANC is ≥1000 cells/mm³) for 2 cycles (Cycles 1 and 3) alternating with (Regimen B; Cycles 2 and 4).</p> <p>Regimen B</p> <p>Days 1-5: Ifosfamide 1,500mg/m² IV continuous infusion over 24 hours daily, with:</p> <p>Days 1-5: Mesna 1,500mg/m² IV continuous infusion over 24 hours daily</p> <p>Days 1-5: Etoposide 60mg/m² IV over 60 minutes daily</p> <p>Days 1-2: Cytarabine 2,000mg/m² IV over 3 hours every 12 hours for 4 doses</p> <p>Day 1: Rituximab 375mg/m² IV</p> <p>Day 5: Methotrexate 12mg intrathecal OR intraventricular, with:</p> <p>Day 1: Cytarabine 50mg intrathecal or intraventricular, with:</p> <p>Day 1: Hydrocortisone 50mg intrathecal or intraventricular, followed by:</p> <p>Days 3,5: Cytarabine 50mg intrathecal OR intraventricular, with:</p> <p>Days 3,5: Hydrocortisone 50mg intrathecal OR intraventricular.</p> <p>Repeat cycle every 3 weeks (or when post-nadir ANC is ≥1000 cells/mm³) for 2 cycles (Cycles 2 and 4) alternating with Regimen A (Cycles 1 and 3).</p>
Other Recommended Regimens	
R-Hyper CVAD ^{3,4,9,c-1,k}	<p>Cycle A</p> <p>Days 1-3: Cyclophosphamide 300mg/m² IV over 2 hours every 12 hours for 6 doses</p> <p>Days 1-3: Mesna 600mg/m² IV continuous infusion over 24 hours daily starting 1 hour before the first dose of Cyclophosphamide and completing 12 hours after the last dose of Cyclophosphamide</p> <p>Days 4,11: Vincristine 2mg IV over 5-10 minutes</p> <p>Day 4: Doxorubicin 50mg/m² IV continuous infusion over 24 hours</p> <p>Days 1-4,11-14: Dexamethasone 40mg IV OR orally daily</p> <p>Day 1: Rituximab 375mg/m² IV</p> <p>Day 2: Methotrexate 12mg intrathecal OR intraventricular</p> <p>Day 7: Cytarabine 100mg intrathecal OR intraventricular.</p> <p>Repeat cycle A every 3 weeks (or earlier if count recovery occurs: maximum of 14 days) for 4 cycles alternating with cycle B.</p> <p>Cycle B</p> <p>Day 1: Methotrexate 200mg/m² IV over 2 hours, immediately followed by:</p> <p>Day 1: Methotrexate 800mg/m² IV continuous infusion over 22 hours</p> <p>Leucovorin 50mg IV over 15 minutes OR orally starting 12 hours after the completion of Methotrexate, followed by:</p> <p>Leucovorin 15mg IV over 15 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is <0.05 micromol/L)</p> <p>Days 2-3: Cytarabine (age <60 years) 3,000mg/m² IV over 3 hours for 4 doses OR Cytarabine (age ≥60 years) 1,000mg/m² IV over 3 hours for 4 doses</p> <p>Day 1: Rituximab 375mg/m² IV</p> <p>Day 2: Methotrexate 12mg intrathecal OR intraventricular</p> <p>Day 7: Methotrexate 100mg intrathecal OR intraventricular.</p> <p>Repeat cycle every 3 weeks (or earlier if count recovery occurs: minimum of 14 days) for 4 cycles alternating with cycle A (A1,B1,A2,B2,A3,B3,A4,A4) for a total of 8 cycles.</p>

continued

AIDS-Related B-Cell Lymphomas

▶ Primary CNS Lymphoma (see NCCN Central Nervous System Guidelines)^{1,2,10,a,o-q}

For select patients with good performance status, see NCCN Guidelines for CNS – Primary CNS Lymphoma.¹⁰

▶ Diffuse Large B-Cell Lymphoma, HHV8-positive DLBCL, NOS, or Primary Effusion Lymphoma^{1,2,a,b}

REGIMEN	DOSING
CD20-Positive Disease: First-Line Therapy	
Preferred Regimens	
Dose-Adjusted EPOCH (Etoposide, Prednisone, Vincristine, Cyclophosphamide, Doxorubicin) + Rituximab ^{3-5,11,12,c,e-g}	<p>Days 1-4 (Cycle 1): Etoposide 50mg/m² IV continuous infusion over 24 hours daily, followed by:</p> <p>Days 1-4 (Cycle 2 and Beyond): Etoposide IV continuous infusion over 24 hour daily (dosing for Cycle 2 and beyond based on absolute neutrophil count and platelet nadir measurements during the previous cycle), with:</p> <p>Days 1-4: Vincristine 0.4mg/m² IV continuous infusion over 24 hours daily, with:</p> <p>Days 1-4 (Cycle 1): Doxorubicin 10mg/m² IV continuous infusion over 24 hours daily, followed by:</p> <p>Days 1-4 (Cycle 2 and Beyond): Doxorubicin IV continuous infusion over 24 hours daily (dosing for Cycle 2 and beyond based on absolute neutrophil count and platelet nadir measurements during the previous cycle), with:</p> <p>Day 5 (Cycle 1): Cyclophosphamide 750mg/m² (if baseline CD4 is >200 cells/mm³) IV over 30 minutes OR Cyclophosphamide 375mg/m² (if baseline CD4 is 50-200 cells/mm³) IV over 30 minutes, OR Cyclophosphamide consider a starting dose of 187.5mg/m² (if baseline CD4 is <50 cells/mm³) IV over 30 minutes, followed by:</p> <p>Day 5 (Cycle 2 and Beyond): Cyclophosphamide IV over 30 minutes (dosing for Cycle 2 and beyond based on absolute neutrophil count and platelet nadir measurements during the previous cycle)</p> <p>Day 1: Rituximab 375mg/m² IV</p> <p>Days 1-5: Prednisone 60mg/m² orally daily</p> <p>Day 1: Methotrexate 12mg intrathecal OR intraventricular (a total of 4 to 8 doses is recommended over the 6 cycles of treatment).</p> <p>Repeat cycle every 3 weeks for 6 cycles.</p>
Other Recommended Regimens	
CHOP (Cyclophosphamide, Doxorubicin, Vincristine/Prednisone) + Rituximab ^{3,4,13,14,c,e-g}	<p>Day 1: Cyclophosphamide 750mg/m² IV over 30 minutes</p> <p>Day 1: Doxorubicin 50mg/m² IV push</p> <p>Day 1: Vincristine 1.4mg/m² (maximum 2mg) IV over 5-10 minutes</p> <p>Day 1-5: Prednisone 100mg orally daily</p> <p>Day 1: Rituximab 375mg/m² IV</p> <p>Day 1: Methotrexate 12mg intrathecal OR intraventricular, with:</p> <p>Day 1: Cytarabine 50mg intrathecal OR intraventricular, with:</p> <p>Day 1: Hydrocortisone 50mg intrathecal OR intraventricular.</p> <p>Repeat cycle every 3 weeks for 6 cycles.</p>
CD20-Negative Disease: First-Line Therapy	
Dose-Adjusted EPOCH (Etoposide + Prednisone + Vincristine + Cyclophosphamide + Doxorubicin) ^{11,12,c,f,g}	<p>Days 1-4 (Cycle 1): Etoposide 50mg/m² IV continuous infusion over 24 hours daily, followed by:</p> <p>Days 1-4 (Cycle 2 and Beyond): Etoposide IV continuous infusion over 24 hour daily (dosing for Cycle 2 and beyond based on absolute neutrophil count and platelet nadir measurements during the previous cycle), with:</p> <p>Days 1-4: Vincristine 0.4mg/m² IV continuous infusion over 24 hours daily, with:</p> <p>Days 1-4 (Cycle 1): Doxorubicin 10mg/m² IV continuous infusion over 24 hours daily, followed by:</p> <p>Days 1-4 (Cycle 2 and Beyond): Doxorubicin IV continuous infusion over 24 hours daily (dosing for Cycle 2 and beyond based on absolute neutrophil count and platelet nadir measurements during the previous cycle)</p> <p>Day 5 (Cycle 1): Cyclophosphamide 750mg/m² (if baseline CD4 is >200 cells/mm³) IV over 30 minutes OR Cyclophosphamide 375mg/m² (if baseline CD4 is 50-200 cells/mm³) IV over 30 minutes, OR Cyclophosphamide consider a starting dose of 187.5mg/m² (if baseline CD4 is <50 cells/mm³) IV over 30 minutes, followed by:</p> <p>Day 5 (Cycle 2 and Beyond): Cyclophosphamide IV over 30 minutes (dosing for Cycle 2 and beyond based on absolute neutrophil count and platelet nadir measurements during the previous cycle)</p> <p>Days 1-5: Prednisone 60mg/m² orally daily</p> <p>Day 1: Methotrexate 12mg intrathecal OR intraventricular (a total of 4 to 8 doses is recommended over the 6 cycles of treatment).</p> <p>Repeat cycle every 3 weeks for 6 cycles.</p>
CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) ^{13-15,c,f,g}	<p>Day 1: Cyclophosphamide 750 mg/m² IV over 30 minutes</p> <p>Day 1: Doxorubicin 50 mg/m² IV push</p> <p>Day 1: Vincristine 1.4mg/m² (maximum 2mg) IV over 5-10 minutes.</p> <p>Days 1-5: Prednisone 100mg orally daily</p> <p>Day 1: Methotrexate 12mg intrathecal OR intraventricular, with:</p> <p>Day 1: Cytarabine 50mg intrathecal OR intraventricular, with:</p> <p>Day 1: Hydrocortisone 50mg intrathecal OR intraventricular</p> <p>Repeat cycle every 3 weeks for 6 cycles.</p>

continued

AIDS-Related B-Cell Lymphomas

► Primary CNS Lymphoma (see NCCN Central Nervous System Guidelines)^{1,2,10,a,o-q}

For select patients with good performance status, see NCCN Guidelines for CNS – Primary CNS Lymphoma.¹⁰

► Diffuse Large B-Cell Lymphoma, HHV8-positive DLBCL, NOS, or Primary Effusion Lymphoma^{1,2,a,b} (continued)

REGIMEN	DOSING
Relapsed CD20-Positive Disease^a	
Bortezomib/ICE + R (Ifosfamide + Carboplatin + Etoposide) + Rituximab (Category 2B) ^{3,4,16,17,e-g,l}	<p>Days 1,8: Bortezomib 1.5mg/m² subcutaneous OR IV push Day 9: Ifosfamide 5,000mg/m² IV continuous infusion over 24 hours, with: Day 9: Mesna 5,000mg/m² IV continuous infusion over 24 hours Day 9: Carboplatin AUC 5 (maximum 750mg) IV over 30 minutes Days 8-10: Etoposide 100mg/m² IV over 60 minutes daily. Administer for one 4-week cycle, followed by: Days 1,8: Bortezomib 1.5mg/m² subcutaneous or IV push over 3 – 5 seconds Day 2: Ifosfamide 5,000mg/m² IV continuous infusion over 24 hours, with: Day 2: Mesna 5,000mg/m² IV continuous infusion over 24 hours Day 2: Carboplatin AUC 5 IV over 30 minutes Days 1-3: Etoposide 100mg/m² IV over 60 minutes daily Day 1: Rituximab 375mg/m² IV. Repeat cycle every 3 weeks for 5 cycles.</p>
Relapsed CD20-Negative Disease^a	
Bortezomib/ICE (Ifosfamide + Carboplatin + Etoposide) (Category 2B) ^{16,17,f,g,l}	<p>Days 1,8: Bortezomib 1.5mg/m² subcutaneous OR IV push over 3-5 seconds Day 9: Ifosfamide 5,000mg/m² IV continuous infusion over 24 hours, with: Day 9: Mesna 5,000mg/m² IV continuous infusion over 24 hours Day 9: Carboplatin AUC 5 (maximum 750 mg) IV over 30 minutes Days 8-10: Etoposide 100mg/m² IV over 60 minutes daily Administer for one 4-week cycle, followed by: Days 1,8: Bortezomib 1.5mg/m² subcutaneous or IV push over 3-5 seconds Day 2: Ifosfamide 5,000mg/m² IV continuous infusion over 24 hours, with: Day 2: Mesna 5,000mg/m² IV continuous infusion over 24 hours Day 2: Carboplatin AUC 5 (maximum 750mg) IV over 30 minutes Days 1-3: Etoposide 100mg/m² IV over 60 minutes daily. Repeat cycle every 3 weeks for 5 cycles.</p>

► Plasmablastic Lymphoma^{1,2,a,s,t}

Preferred Regimens	
Dose-Adjusted EPOCH (Etoposide + Prednisone + Vincristine + Cyclophosphamide + Doxorubicin) ^{11,12,c,f,g}	<p>Days 1-4 (Cycle 1): Etoposide 50mg/m² IV continuous infusion over 24 hours daily, followed by: Days 1-4 (Cycle 2 and Beyond): Etoposide IV continuous infusion over 24 hour daily (dosing for Cycle 2 and beyond based on absolute neutrophil count and platelet nadir measurements during the previous cycle), with: Days 1-4: Vincristine 0.4mg/m² IV continuous infusion over 24 hours daily, with: Days 1-4 (Cycle 1): Doxorubicin 10mg/m² IV continuous infusion over 24 hours daily, followed by: Days 1-4 (Cycle 2 and Beyond): Doxorubicin IV continuous infusion over 24 hours daily (dosing for Cycle 2 and beyond based on absolute neutrophil count and platelet nadir measurements during the previous cycle) Day 5 (Cycle 1): Cyclophosphamide 750mg/m² (if baseline CD4 is >200 cells/mm³) IV over 30 minutes OR Cyclophosphamide 375mg/m² (if baseline CD4 is 50-200 cells/mm³ IV over 30 minutes). OR Cyclophosphamide consider a starting dose of 187.5 mg/m² (if baseline CD4 is <50 cells/mm³) IV over 30 minutes, followed by: Day 5 (Cycle 2 and Beyond): Cyclophosphamide IV over 30 minutes (dosing for Cycle 2 and beyond based on absolute neutrophil count and platelet nadir measurements during the previous cycle) Days 1-5: Prednisone 60mg/m² orally daily Day 1: Methotrexate 12mg intrathecal OR intraventricular (a total of 4 to 8 doses is recommended over the 6 cycles of treatment) Repeat cycle every 3 weeks for 6 cycles.</p>

continued

AIDS-Related B-Cell Lymphomas

► Plasmablastic Lymphoma^{1,2,a,s,t} (continued)

REGIMEN	DOSING
Other Recommended Regimens	
<p>Modified CODOX-M (Cyclophosphamide + Vincristine + Doxorubicin + High-Dose Methotrexate)/IVAC (Ifosfamide + Etoposide + High-Dose Cytarabine)^{9,c,d,f,i,l,m}</p>	<p>Regimen A Days 1-2: Cyclophosphamide 800mg/m² IV over 30 minutes daily Days 1,8: Vincristine 1.4mg/m² (maximum 2 mg) IV over 5-10 minutes Day 1: Doxorubicin 50mg/m² IV push Day 15: Methotrexate 3,000mg/m² IV over 4 hours Leucovorin: 200mg/m² IV over 30 minutes starting 24 hours from the initiation of Methotrexate infusion, followed by: Leucovorin: 25mg/m² IV over 15 minutes OR orally every 6 hours (until Methotrexate serum concentration is <0.05 micromol/L) Day 1: Methotrexate 12mg intrathecal OR intraventricular, with: Day 1: Cytarabine 50 mg intrathecal OR intraventricular, with: Day 1: Hydrocortisone 50mg intrathecal OR intraventricular, followed by: Days 3: Cytarabine 50mg intrathecal OR intraventricular. Repeat cycle every 3 weeks (or when post-nadir ANC is ≥1000 cells/mm³) for 2 cycles (Cycles 1 + 3) alternating with Regimen B (Cycles 2 + 4). Regimen B Days 1-5: Ifosfamide 1,500mg/m² IV continuous infusion over 24 hours daily, with: Days 1-5: Mesna 1,500mg/m² IV continuous infusion over 24 hours daily Days 1-5: Etoposide 80mg/m² IV over 60 minutes daily Days 1-2: Cytarabine 2,000mg/m² IV over 3 hours every 12 hours for 4 doses Day 5: Methotrexate 12mg intrathecal OR intraventricular. Repeat cycle every 3 weeks (or when post-nadir ANC is ≥1000 cells/mm³) for 2 cycles (Cycles 2 + 4) alternating with Regimen A (Cycles 1 + 3).</p>
<p>Hyper CVAD (Cyclophosphamide + Vincristine + Doxorubicin + High-Dose Methotrexate + Cytarabine)^{9,18,c,d,f,i,k}</p>	<p>Cycle A Days 1-3: Cyclophosphamide 300mg/m² IV over 2 hours every 12 hours for 6 doses Days 1-3: Mesna 600mg/m² IV continuous infusion over 24 hours daily starting 1 hour before the first dose of Cyclophosphamide and completing 12 hours after the last dose of Cyclophosphamide Days 4,11: Vincristine 2mg IV over 5-10 minutes Day 4: Doxorubicin 50 mg/m² IV continuous infusion over 24 hours Days 1-4, 11-14: Dexamethasone 40mg orally IV OR orally daily Day 2: Methotrexate 12mg intrathecal OR intraventricular Day 7: Cytarabine 100mg intrathecal OR intraventricular. Repeat cycle every 3 weeks (or earlier if count recovery occurs; minimum of 14 days) for 4 cycles alternating with Cycle B. Cycle B: Day 1: Methotrexate 200mg/m² IV over 2 hours, immediately followed by: Day 1: Methotrexate 800mg/m² IV continuous infusion over 22 hours Leucovorin 50mg IV over 15 minutes OR orally starting 12 hours after completion of Methotrexate, followed by: Leucovorin 15mg over 15 minutes OR orally every 6 hours for at least 8 doses (until Methotrexate serum concentration is <0.05 micromol) Days 2-3: Cytarabine (age <60 years) 3,000mg/m² IV over 3 hours every 12 hours for 4 doses OR Cytarabine (age ≥60 years) 1,000mg/m² IV over 3 hours every 12 hours for 4 doses Day 2: Methotrexate 12mg intrathecal or intraventricular Day 7: Cytarabine 100mg intrathecal OR intraventricular. Repeat cycle every 3 weeks (or earlier if count recovery occurs; minimum of 14 days) for a total of 4 cycles alternating with Cycle A (A1, B1, A2, B2, A2, B3, A4, B4) for a total of 8 cycles.</p>

- ^a Antiretroviral therapy (ART) can be administered safely with chemotherapy but consultation with an HIV specialist or pharmacist is important to optimize compatibility. With continued development, new ARTs 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 (Barta SK, Xue X, Wang D, et al. *Blood*. 2103;122:3251-3262).
- ^b If CD4 <50, maximize supportive care and monitor closely for cytopenias and infections while administering lymphoma therapy.
- ^c Oral hydration is strongly encouraged with Cyclophosphamide; poorly hydrated patients may need supplemental IV hydration. Patients should attain combined oral and IV hydration of 2,000-3,000mL/day on day of chemotherapy.
- ^d Alkaline hydration is required pre- and post-administration of high-dose Methotrexate.
- ^e Rituximab: Premedication for infusion reactions is required. The recommended dosing is: diphenhydramine 12.5-50mg IV or orally 30-40 minutes pre-Rituximab AND acetaminophen 650mg orally 30-40 minutes pre-Rituximab. An FDA-approved biosimilar is an appropriate substitute for Rituximab.
- ^f This regimen may be associated with a risk of tumor lysis syndrome with the first cycle. Tumor lysis prophylaxis and/or treatment may be indicated.
- ^g Regimen should be administered with myeloid growth factor support.
- ^h Leucovorin dose should be titrated for delayed methotrexate clearance (<10-fold decrement in serum methotrexate levels per day) or increases in serum creatinine
- ⁱ For leucovorin: The dose listed is based on racemic leucovorin product. LEVOleucovorin is not interchangeable and the product doses are not equivalent.
- ^j For R-EPOCH dosing, see Dunleavy K, Pitaluga S, Shovlin M, et al. Low-intensity therapy in adults with Burkitt's lymphoma. *N Engl J Med*. 2013;369:1915-1925; Roschewski M, Dunleavy K, Abramson JS, et al. *Blood*. 2017;130(Suppl_1):Abstract 188.

continued

AIDS-Related B-Cell Lymphomas

- ^k CNS prophylaxis in the form of both intrathecal and intravenous therapy are part of this regimen. If a patient presents with positive CSF or leptomeningeal involvement, intrathecal therapy should be administered twice weekly unit CSF is negative, then weekly x 1 month, then monthly x 6 months. Although the specific regimen may vary, a suggested regimen is Cytarabine 50mg + Methotrexate 12mg + Hydrocortisone 50mg.
- ^l Hydration is required pre- and post-administration of Ifosfamide.
- ^m CNS prophylaxis in the form of both intrathecal and intravenous therapy are part of the regimen. If CNS disease is confirmed, treatment should start with either high-dose Methotrexate or IVAC.
- ⁿ For relapse, see second-line therapy for Burkitt lymphoma.
- ^o Initiate ART, if not already receiving.
- ^p Even with poorly controlled HIV and/or marginal performance status, consider high-dose Methotrexate. (Gupta N, Nolan A, Omuro A, et al. *Neuro Oncol.* 2017;19:99-108.)
- ^q For select patients with good performance status, see NCCN Guidelines for CNS – Primary CNS Lymphoma.¹⁰
- ^r For relapse, also see regimens for relapsed/refractory disease for patients with DLBCL.¹
- ^s Standard CHOP is not adequate therapy.
- ^t For relapse, see second-line therapy without rituximab for patients with DLBCL.¹

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