NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Peripheral T-Cell Lymphoma (Part 1 of 3)

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 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 National Comprehensive Cancer Network 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.

Systemic Therapy for Peripheral T-Cell

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

First-Line Therapy ALCL, ALK+ histology ¹				
REGIMEN	DOSING			
CHOP-21 ²⁻⁴	Day 1: Cyclophosphamide 750mg/m ² IV, doxorubicin 50mg/m ² IV, and vincristine 2mg IV Days 1-5: Prednisone 100mg PO. Repeat every 3 weeks for 6 cycles.			
CH0EP-21 ^{3,4}	Day 1: Cyclophosphamide 750mg/m ² IV, doxorubicin 50mg/m ² IV, and vincristine 2mg IV Days 1-3: Etoposide 100mg/m ² IV Days 1-5: Prednisone 100mg PO. Repeat every 3 weeks for 6 cycles.			
First-Line Therapy Other Histologies (ALCL, ALK, PTCL, NOS, AITL, EATL) ¹				
CHOEP (preferred) ^{3,4}	Day 1: Cyclophosphamide 750mg/m ² IV, doxorubicin 50mg/m ² IV, and vincristine 2mg IV Days 1-3: Etoposide 100mg/m ² IV Days 1-5: Prednisone 100mg PO. Repeat every 3 weeks for 6 cycles.			
CHOP-14 (preferred) ²⁻⁴	Day 1: Cyclophosphamide 750mg/m ² IV, doxorubicin 50mg/m ² IV, and vincristine 2mg IV Days 1–5: Prednisone 100mg PO. Repeat every 2 weeks for 6 cycles.			
CHOP-21 (preferred) ^{3,4}	Day 1: Cyclophosphamide 750mg/m ² IV, doxorubicin 50mg/m ² IV, and vincristine 2mg IV Days 1-5: Prednisone 100mg PO. Repeat every 3 weeks for 6 cycles.			
CHOP followed by IVE alternating with intermediate- dose methotrexate ^{5,6*}	Day 1: Cyclophosphamide 750mg/m² IV, doxorubicin 50mg/m² IV, vincristine 1.4mg/m² (max dose 2mg), and prednisone 100mg PO daily for 1 cycle. Repeat every 3 weeks for 6-8 cycles. Followed by Days 1-3: Ifosfamide 3000mg/m² IV, etoposide 200mg/m² IV, epirubicin 50mg/m² IV, and methotrexate 1500mg/m² IV. Repeat every 3 weeks for 3 cycles.			
Dose-adjusted EPOCH ⁷⁻⁹	Days 1-4, via continuous infusion for 96 hours: Etoposide 50mg/m ² IV, vincristine 0.4mg/m ² IV, and doxorubicin 10mg/m ² IV Days 1-6: Prednisone 60mg PO Day 6: Cyclophosphamide 750mg/m ² IV. Repeat every 21 days until complete response.			
HyperCVAD alternating with high-dose methotrexate and cytarabine ¹⁰⁻¹²	 Days 1-2: Methotrexate 200mg/m² IV bolus followed by methotrexate 800mg/m² IV over 24 hours Days 1-3: Cyclophosphamide 300mg/m² IV every 12 hours for 6 doses with mesna 600mg/m²/day Days 1-4 and Days 11-14: Dexamethasone 40mg PO Day 3: Cytarabine 3000mg/m² IV every 12 hours for 4 doses. OR Day 3: Cytarabine 1000mg/m² IV for patients >60 years or serum creatinine >1.5mg/dL and folic acid 50mg PO 24 hours after the end of methotrexate followed by folic acid 15mg PO every 6 hours for 8 doses. Days 4-5: Doxorubicin 25mg/m² IV via continuous infusion over 24 hours; G-CSF 5mcg/kg 24 hours after the end of doxorubicin until granulocyte count >4500/uL followed by methotrexate and cytarabine (begins immediately after clinical and hematologic recovery from HyperCVAD course) Days 4 and 11: Vincristine 2mg/m² IV (first dose 12 hours after last dose of cyclophosphamide). Repeat every 3 weeks for 4 cycles. 			
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NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Peripheral T-Cell Lymphoma (Part 2 of 3)

Systemic Therapy for Peripheral T-Cell (continued)

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First-Line Consolidation ¹				
REGIMEN	DOSING			
Consider consolidation with high- dose therapy and stem cell rescue	ALCL, ALK+ is a subtype with good prognosis and does not need consolidative transplant if in remission			
Second-Line Therapy (candidate for transplant) ¹				
Bendamustine ¹³	Days 1 and 2: Bendamustine 120mg/m ² /day IV. Repeat every 3 weeks for 6 cycles.			
Belinostat (Category 2B) ¹⁴	Days 1–5: Belinostat 1,000mg/m ² IV over 30 minutes. Repeat every 3 weeks until disease progression or unacceptable toxicity.			
Brentuximab vedotin for systemic ALCL excluding primary cutaneous ALCL ¹⁵	Day 1: Brentuximab vedotin 1.8mg/kg IV over 30 minutes. Repeat every 3 weeks for 16 doses.			
Brentuximab vedotin for systemic CD30+ PTCL (Category 2B) ¹⁶	Day 1: Brentuximab vedotin 1.8mg/kg IV over 30 minutes. Repeat every 3 weeks until disease progression.			
DHAP ^{17,18}	Day 1: Cisplatin 100mg/m ² IV via continuous infusion over 24 hours <u>followed by</u> Day 2: Cytosine arabinoside in 2 pulses each at a 2g/m ² given 12 hours apart Days 1–4: Dexamethasone 40mg PO or IV. Repeat every 3–4 weeks for 6–10 cycles.			
ESHAP ¹⁹	 Days 1-4: Etoposide 40mg/m² and cisplatin 25mg/m² IV via 24-hour continuous infusion Days 1-5: Methylprednisolone 500mg IV Day 5: Cytarabine 2g/m² IV over 2-3 hours. Repeat every 3-4 weeks for 6-8 cycles. 			
Dose-adjusted EPOCH ⁷⁻⁹	 Days 1-4: Etoposide 50mg/m² IV, vincristine 0.4mg/m² IV, and doxorubicin 10mg/m² IV via continuous infusion for 96 hours Days 1-6: Prednisone 60mg P0 Day 6: Cyclophosphamide 750mg/m² IV. Repeat every 21 days until complete response. 			
GDP ^{20,21}	Day 1: Cisplatin 75mg/m ² IV over 1 hour Days 1 and 8: Gemcitabine 100mg/m ² IV over 30 minutes Days 1-4: Dexamethasone 40mg PO divided dose. Repeat every 21 days for 6 cycles.			
Gem0x ²²	Gemcitabine 1000mg/m ² Oxaliplatin 100mg/m ² . Repeat every 15–21 days for 4 cycles.			
ICE ²³	Day 1: Ifosfamide 5g/m ² via 24-hour continuous infusion Days 1-3: Etoposide 100mg/m ² IV bolus Day 2: Carboplatin 5 × AUC. Repeat every 2 weeks for 3 cycles.			
Pralatrexate ^{24†}	Day 1: Pralatrexate 30mg/m ² /week starting for 6 weeks followed by 1 week of rest. Repeat every 7 weeks until disease progression or unacceptable toxicity.			
Romidepsin ²⁵	Days 1, 8, and 15: Romidepsin 14mg/m ² IV infusion over 4 hours. Repeat every 28 days for up to 6 cycles.			
Second-Line Therapy (non-candidates for transplant) ¹				
Alemtuzumab ²⁶	Day 1: Alemtuzumab 3mg Day 3: Alemtuzumab 10mg, followed by 30mg three times a week. Repeat every week for a max of 12 weeks.			
Bendamustine ¹³	Days 1 and 2: Bendamustine 120mg/m2/day IV. Repeat every 3 weeks for 6 cycles.			
Belinostat (Category 2B) ¹⁴	Days 1-5: Belinostat 1,000mg/m2 IV over 30 minutes. Repeat every 3 weeks until disease progression or unacceptable toxicity.			
Bortezomib (Category 2B) ²⁷	Days 1, 4, 8, and 11: Bortezomib 1.3mg/m ² followed by a 1-week rest period. Repeat every 21 days for 6 cycles.			
Brentuximab vedotin for systemic ALCL excluding primary cutaneous ALCL ¹⁵	Day 1: Brentuximab vedotin 1.8mg/kg IV over 30 minutes. Repeat every 3 weeks for 16 doses.			
Brentuximab vedotin for systemic CD30+ PTCL ¹⁶	Day 1: Brentuximab vedotin 1.8mg/kg IV over 30 minutes. Repeat every 3 weeks until disease progression.			
Cyclosporine for AITL only ²⁸	Cyclosporine 3–5mg/kg PO for 6–8 weeks; taper by 50mg every 1–3 weeks. Responding patients received maintenance dose of 50–100mg with gradual taper after maximal response was achieved.			

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NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Peripheral T-Cell Lymphoma (Part 3 of 3)

Systemic Inerapy for Peripheral I-Cell (continued)				
Second-Line Inerapy (non-ca	ndidates for transpla	ant)* (continued)		
REGIMEN	DOSING			
Dose-adjusted EPOCH ⁷⁻⁹	Days 1-4: Etoposide 50mg/m ² IV, vincristine 0.4mg/m ² IV, and doxorubicin 10mg/m ² IV via continuous infusion for 96 hours Days 1-6: Prednisone 60mg PO Day 6: Cyclophosphamide 750mg/m ² IV. Repeat every 21 days until complete response.			
Gemcitabine ^{29,30}	Days 1, 8, and 15: Gemcitabine 1200mg/m ² . Repeat every 28 days for 3 cycles.			
Pralatrexate ^{24†}	Day 1: Pralatrexate 30r Repeat every 7 weeks u	ng/m ² /week for 6 weeks followed by 1 week of rest. until disease progression or unacceptable toxicity.		
Romidepsin ²⁵	Days 1, 8, and 15: Rom Repeat every 28 days f	nidepsin 14mg/m² IV infusion over 4 hours. For up to 6 cycles.		
* Studied only in patients with EATL.	[†] Limited activity in AITL.			
References				
 Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Hodgkin's Lymphomas V2.2015. Available at: http://www.nccn.org/ Accessed April 6, 2015. Savage KJ, Chhanabhai M, Gascoyne RD, Connors JM. Char- acterization of peripheral T-cell lymphomas in a single North American institution by the WHO classification. Ann Oncol. 		 Pro B, Advani R, Brice P et al. Brentuximab vedotin (SGN-35) in patients with relapsed or refractory systemic anaplastic large-cell lymphoma: Results of a phase II study. <i>J Clin Oncol.</i> 2012;30:2190–2196. Horwitz SM, Advani RH, Bartlett NL, et al. Objective responses in relapsed T-cell lymphomas with single-agent brentuximab vedotin. <i>Blood.</i> 2014;123:3095–3100. Velasquez WS, Cabanillas F, Salvador P, et al. Effective salvage therapy for lymphoma with cisplatin in combination with high-dose Ara-C and dexamethasone (DHAP). <i>Blood.</i> 1988;71:117–122. Mey UJ, Orlopp KS, Flieger D, et al. Dexamethasone, high-dose cytarabine, and cisplatin in combination with rituximab a salvage treatment for patients with relapsed or refractory aggressive non-Hodgkin's lymphoma. <i>Cancer Invest.</i> 2006;24:593–600. Velasquez WS, McLaughlin P, Tucker S, et al. ESHAP—an effective chemotherapy regimen in refractory and relapsing lymphoma: a 4-year follow-up study. <i>J Clin Oncol.</i> 1994;12:1169–1176. Crump M, Baetz T, Couban S, et al. Gemcitabine, dexamethasone, and cisplatin in patients with recurrent or refractory aggressive histology B-cell non-Hodgkin lymphoma: a Phase II study by the National Cancer .2004;101:1835–1842. Dong M, He XH, Liu P, et al. Gemcitabine-based combination regimen in patients with peripheral T-cell lymphoma. <i>Med Oncol.</i> 2013;30:351. Lopez A, Gutierrez A, Palacios A, et al. GEMOX-R regimen is a highly effective salvage regimen in patients with refractory/ relapsing diffuse large-cell lymphoma: A phase II study. <i>Lur J Haematol.</i> 2008;80:127–132. Zelenetz AD, Hamlin P, Kewalramani T, et al. Ifosfamide, carboplatin, etoposide (ICE)-based second-line chemotherapy for the management of relapsed and refractory aggressive non-Hodgkin's lymphoma. <i>Ann Oncol.</i> 2011;29:1182–1189. Coiffier B, Pro B, Pinter-Brown L, et al. Pralatexate in patients with relapsed or refractory peripheral T-cell lymp		
 Preundschuh M, Trümper L, Kloess M, et al. German high- grade non-Hodgkin's Lymphoma Study Group. Two-weekly or 3-weekly CHOP chemotherapy with or without etoposide for the treatment of young patients with good-prognosis (normal LDH) aggressive lymphomas: results of the NHL-B1 trial of the DSHNHL. <i>Blood</i>. 2004;104:626–633. Pfreundschuh M, Trümper L, Kloess M, et al. German high-grade non-Hodgkin's Lymphoma Study Group. Two-weekly or 3-weekly CHOP chemotherapy with or without etoposide for the treatment of elderly patients with aggressive lymphomas: results of the NHL-B2 trial of the DSHNHL. <i>Blood</i>. 2004;104:634–641. Sieniawski M, Lennard J, Millar C, et al. Aggressive primary chemotherapy plus autologous stem cell transplantation improves outcome for peripheral T cell lymphomas compared with CHOP-like regimens. <i>Blood</i>. 2009;114:Abstract1660. Sieniawski M, Angamuthu N, Boyd K, et al. Evaluation of enteropathy-associated T-cell lymphoma comparing standard therapies with a novel regimen including autologous stem cell transplantation. <i>Blood</i>. 2010;115:3664–3670. Dunleavy K, Shovlin M, Pittaluga S, et al. DA-EPOCH Chemo- therapy is highly effective in ALK-positive and ALK-negative ALCL: Results of a prospective study of PTCL subtypes in adults [abstract]. <i>Blood</i>. 2011;118:Abstract 1618. Wilson WH, Bryant G, Bates S, et al. EPOCH chemotherapy: toxicity and efficacy in relapsed and refractory non-Hodgkin's lymphoma. <i>J Clin Oncol</i>. 1993;11:1573–582. Peng YL, Huang HQ, Lin XB, et al. Clinical outcomes of patients with peripheral T-cell lymphoma (PTCL) treated by 				
 Escalon MP, Liu NS, Yang Y, et al. Prog of patients with T-cell non-Hodgkin ly Cancer Center experience. <i>Cancer</i>. Pozadzides JV, Perini G, Hess M, et a of patients with peripheral T-cell lym Cancer Center experience. <i>J Clin Onc</i> Khouri JF, Romaguera J, Kantarjian high-dose methotrexate/cytarabin transplantation: an active regimen hymphoma. <i>(Clin Concel</i> 1092-16) 	nostic factors and treatment mphoma: the M. D. Anderson 2005;103:2091–2098. Il. Prognosis and treatment phoma: The M. D. Anderson ol. 2010;28:Abstract 8051. H, et al. Hyper-CVAD and e followed by stem-cell for aggressive mantle-cell 2903-2800	 Chemicable, Priase in Study of Rolindepsin in RelaySet of Refractory Peripheral T-Cell Lymphoma After Prior Systemic Therapy. J Clin Oncol. 2012;30:631–636. 26. Enblad G, Hagberg H, Erlanson M, et al. A pilot study of alemtuzumab (anti-CD52 monoclonal antibody) therapy for patients with relapsed or chemotherapy-refractory peripheral T-cell lymphomas. <i>Blood</i>. 2004;103:2920–2924. 27. Zinzani P, Musuraca G, Tani M, et al. Phase II trial of proteasome inhibitor bortezomib in patients with relapsed or refractory cuta- neous T-cell lymphoma. <i>J Clin Oncol</i>. 2007;25:4293–4297. 28. Adhenis U, Mawite G, Zalande M, Unaria CO. Machinements. 		
 Damaj G, Gressin R, Bouabdallah K, e spective, open-label, phase II trial of t relapsed T-cell lymphomas: the BENTI 2013;31:104–110. O'Connor O, Masszi T, Savage K, et bistone deactylase inhibitor (HDAC 	 a. Belinostat, a novel pan- i) in relapsed or refractory 	 Zustani N, Horwitz S, Zeiniedz A, Rolliniig SJ. AngouinindinbollaSub T cell lymphoma: treatment experience with cyclosporine. <i>Leuk Lymphoma</i>. 2007;48:521–525. Zinzani PL, Baliva G, Magagnoli M, et al. Gemcitabine treatment in pretreated cutaneous T-cell lymphoma: Experience in 44 patients. <i>J Clin Oncol</i>. 2000;18:2603–2606. Zinzani PL, Magagnoli M, Bendandi M, et al. Therany with 		
peripheral T-cell lymphoma (R/R PTCL): Results from the BELIEF trial [abstract]. J Clin Oncol. 2013;31:Abstract 8507.		 Zinzani FL, Wagagioni W, beridario W, et al. Inerapy With gemcitabine in pretreated peripheral T-cell lymphoma patients. <i>Ann Oncol.</i> 1998;9:1351–1353. 		