

T-Cell Lymphomas: Adult T-Cell Leukemia/Lymphoma (ATLL) Treatment Regimens

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.

► Initial Therapy

REGIMEN	DOSING
Preferred Regimens	
Chemotherapy	
Brentuximab Vedotin + CHP ² (Cyclophosphamide/ Doxorubicin/Prednisone) (CD30+ cases)	Day 1: Cyclophosphamide 750mg/m ² IV. Day 1: Doxorubicin 50mg/m ² IV. Days 1-5: Prednisone 100mg orally once daily, followed by: Day 1: Brentuximab vedotin 1.8mg/kg IV. Repeat cycle every 3 weeks for 6 or 8 cycles.
Dose-Adjusted EPOCH ³⁻⁴ (Etoposide/Prednisone/ Vincristine/Cyclophosphamide/ Doxorubicin)	Days 1-4: Etoposide 50mg/m ² IV continuous infusion daily. Days 1-4: Vincristine 0.4mg/m ² IV continuous infusion daily. Days 1-4: Doxorubicin 10mg/m ² IV continuous infusion daily. Days 1-5: Prednisone 60mg/m ² orally once daily. Day 5: Cyclophosphamide 750mg/m ² IV. Repeat cycle every 3-4 weeks for a minimum of 2 cycles beyond best response and a maximum of 6 cycles.
Zidovudine + Interferon	
Zidovudine + Interferon ⁵⁻⁹ (acute and chronic/smoldering subtypes)	Zidovudine 1 g orally daily. Interferon-alpha 9 million units subcutaneously daily. Repeat daily treatment for a minimum of 2 months, followed by maintenance therapy with: Zidovudine 600mg orally daily. Interferon-alpha 4.5 million units subcutaneously daily.
Other Recommended Regimens	
CHOEP (Cyclophosphamide/ Doxorubicin/Vincristine/ Etoposide/Prednisone) ¹	See NCCN T-cell Lymphomas Guidelines
HyperCVAD ¹⁻¹⁰ (Cyclophosphamide/Vincristine/ Doxorubicin/Dexamethasone) Alternating with High-Dose Methotrexate/Cytarabine	See NCCN T-cell Lymphomas Guidelines
Useful in Certain Circumstances	
CHOP ¹¹⁻¹² (Cyclophosphamide/Doxorubicin/ Vincristine/Prednisone) (unable to tolerate intensive regimen or non-CD30 expressing ATLL)	Day 1: Cyclophosphamide 750mg/m ² IV Day 1: Doxorubicin 50mg/m ² IV Day 1: Vincristine 1.4mg/m ² IV (maximum dose of 2mg) Days 1-5: Prednisone 100mg orally once daily. Repeat cycle every 2 weeks for 8 cycles.

► Second-Line Therapy or Subsequent Therapy

Preferred Regimens	
Single agents	
Brentuximab vedotin ¹³ (CD30+ cases)	Day 1: Brentuximab vedotin 1.8mg/kg IV. Repeat cycle every 3 weeks.

continued

T-Cell Lymphomas: Adult T-Cell Leukemia/Lymphoma (ATLL) Treatment Regimens

► Second-Line Therapy or Subsequent Therapy (continued)

REGIMEN	DOSING
Preferred Regimens (continued)	
Single agents (continued)	
Lenalidomide ¹⁴	Days 1-28: Lenalidomide 25mg orally once daily. Repeat cycle every 4 weeks.
Mogamulizumab ¹⁵⁻¹⁶ (C-C Chemokine Receptor 4 [CCR4]-positive cases)	Days 1, 8, 15, and 22: Mogamulizumab 1.0mg/kg IV infusion over 1 hour. Administered for one cycle, followed by: Days 1 and 15: Mogamulizumab 1.0mg/kg IV infusion over 1 hour. Repeat cycle every 4 weeks.
Combination regimens	
DHAP (Dexamethasone/Cytarabine/Cisplatin) ^{1,16}	Days 1-4: Dexamethasone 40mg IV daily. Day 1: Cisplatin 100mg/m ² IV over 24 hours, followed by: Day 2: Cytarabine 2000mg/m ² IV over 3 hours every 12 hours for 2 doses. Repeat cycle every 4 weeks.
DHAX (Dexamethasone/Cytarabine/Oxaliplatin) ¹	See NCCN T-cell Lymphomas Guidelines
ESHAP (Etoposide/Methylprednisolone/Cytarabine) + Platinum (Cisplatin or Oxaliplatin) ¹	See NCCN T-cell Lymphomas Guidelines
GDP (Gemcitabine/Dexamethasone/Cisplatin) ¹	See NCCN T-cell Lymphomas Guidelines
GemOx (Gemcitabine/Oxaliplatin) ^{1,16}	Day 1: Gemcitabine 1000mg/m ² IV over 30 minutes, followed by: Day 1: Oxaliplatin 100mg/m ² IV over 2 hours. Repeat cycle every 2 weeks.
GVD (Gemcitabine/Vinorelbine/Liposomal Doxorubicin) ¹	See NCCN T-cell Lymphomas Guidelines
ICE (Ifosfamide/Carboplatin/Etoposide) ¹	See NCCN T-cell Lymphomas Guidelines
Zidovudine + Interferon ⁵⁻⁹ (acute and chronic/smoldering subtypes)	Zidovudine 1 g orally daily. Interferon-alpha 9 million units subcutaneously daily. Repeat daily treatment for a minimum of 2 months, followed by maintenance therapy with: Zidovudine 600mg orally daily. Interferon-alpha 4.5 million units subcutaneously daily.
Alternative Regimens	
Single agents	
Alemtuzumab ¹⁷	Week 1 Day 1: Alemtuzumab 3mg IV. Day 2: Alemtuzumab 10mg IV. Day 3: Alemtuzumab 30mg IV. Weeks 2-12: Alemtuzumab 30mg IV three times weekly Monday, Wednesday, Friday or Tuesday, Thursday, Saturday.
Arsenic Trioxide ¹⁸	Arsenic Trioxide 0.15mg/kg IV once daily.
Belinostat ¹	See NCCN T-cell Lymphomas Guidelines
Bendamustine ¹	See NCCN T-cell Lymphomas Guidelines
Bortezomib ¹⁹	Days 1, 4, 8, and 11: Bortezomib 1.3mg/m ² IV. Repeat cycle every 3 weeks for 8 cycles.
Gemcitabine ¹	See NCCN T-cell Lymphomas Guidelines
Pralatrexate ^{20,21}	Day 1: Pralatrexate: 30mg/m ² IV Push over 3-5 minutes weekly for 6 weeks, followed by 1 week off. Repeat cycle every 7 weeks.

continued

T-Cell Lymphomas: Adult T-Cell Leukemia/Lymphoma (ATLL) Treatment Regimens

References

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology® T-Cell Lymphomas v2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed April 9, 2022.
2. Horwitz S, O'Connor OA, Pro B, et al. Brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma (ECHOLON-2): a global, double-blind, randomised, phase 3 trial. *Lancet*. 2019;393:229-240.
3. Ratner L, Harrington W, Feng X, et al. Human T-cell leukemia virus reactivation with progression of adult T-cell leukemia-lymphoma. *PLoS ONE*. 2009;4:e4420.
4. Ratner L, Rauch D, Abel H, et al. Dose-adjusted EPOCH chemotherapy with bortezomib and raltegravir for human T-cell leukemia virus-associated adult T-cell leukemia lymphoma. *Blood Cancer J*. 2016;6:e408.
5. Bazarbachi A, Hermine O. Treatment with a combination of zidovudine and alpha-interferon in naive and pretreated adult T-cell leukemia/lymphoma patients. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1996;13 Suppl 1:S186-190.
6. Bazarbachi A, Plumelle Y, Carlos Ramos J, et al. Meta-analysis on the use of zidovudine and interferon-alfa in adult T-cell leukemia/lymphoma showing improved survival in the leukemic subtypes. *J Clin Oncol*. 2010;28:4177-4183.
7. Hermine O, Allard I, Lévy V, et al. A prospective phase II clinical trial with the use of zidovudine and interferon-alpha in the acute and lymphoma forms of adult T-cell leukemia/lymphoma. *Hematol J*. 2002;3:276-282.
8. Hodson A, Crichton S, Montoto S, et al. Use of zidovudine and interferon alfa with chemotherapy improves survival in both acute and lymphoma subtypes of adult T-cell leukemia/lymphoma. *J Clin Oncol*. 2011;29:4696-4701.
9. White JD, Wharfe G, Stewart DM, et al. The combination of zidovudine and interferon alpha-2B in the treatment of adult T-cell leukemia/lymphoma. *Leuk Lymphoma*. 2001;40:287-294.
10. Alduaij A, Butera JN, Treaba D, Castillo J. Complete remission in two cases of adult T-cell leukemia/lymphoma treated with hyper-CVAD: a case report and review of the literature. *Clin Lymphoma Myeloma Leuk*. 2010;10:480-483.
11. Taguchi H, Kinoshita KI, Takatsuki K, et al. An intensive chemotherapy of adult T-cell leukemia/lymphoma: CHOP followed by etoposide, vindesine, ranimustine, and mitoxantrone with granulocyte colony-stimulating factor support. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1996;12:182-186.
12. Tsukasaki K, Utsunomiya A, Fukuda H, et al. VCAP-AMP-VECP compared with biweekly CHOP for adult T-cell leukemia-lymphoma: Japan Clinical Oncology Group Study JCOG9801. *J Clin Oncol*. 2007;25:5458-5464.
13. Horwitz SM, Advani RH, Bartlett NL, et al. Objective responses in relapsed T-cell lymphomas with single-agent brentuximab vedotin. *Blood*. 2014;123:3095-3100.
14. Ishida T, Fujiwara H, Nosaka K, et al. Multicenter phase II study of lenalidomide in relapsed or recurrent adult T-cell leukemia/lymphoma: ATLL-002. *J Clin Oncol*. 2016;34:4086-4093.
15. Ishida T, Utsunomiya A, Jo T, et al. Mogamulizumab for relapsed adult T-cell leukemia-lymphoma: Updated follow-up analysis of phase I and II studies. *Cancer Sci*. 2017;108:2022-2029.
16. Phillips AA, Fields PA, Hermine O, et al. Mogamulizumab versus investigator's choice of chemotherapy regimen in relapsed/refractory adult T-cell leukemia/lymphoma. *Haematologica*. 2019;104:993-1003.
17. Sharma K, Janik JE, O'Mahony D, et al. Phase II study of alemtuzumab (CAMPATH-1) in patients with HTLV-1-associated adult T-cell leukemia/lymphoma. *Clin Cancer Res*. 2017;23:35-42.
18. Ishitsuka K, Suzumiya J, Aoki M, et al. Therapeutic potential of arsenic trioxide with or without interferon-alpha for relapsed/refractory adult T-cell leukemia/lymphoma. *Haematologica* 2007;92:719-720.
19. Ishitsuka K, Utsunomiya A, Katsuya H, et al. A phase II study of bortezomib in patients with relapsed or refractory aggressive adult T-cell leukemia/lymphoma. *Cancer Sci*. 2015;106:1219-1223.
20. Lunning MA, Gonsky J, Ruan J, et al. Pralatrexate in Relapsed/Refractory HTLV-1 Associated Adult T-Cell Lymphoma/Leukemia [abstract]: A New York City Multi-Institutional Experience. *Blood*. 2012;120:Abstract 2735.
21. O'Connor OA, Pro B, Pinter-Brown L, et al. Pralatrexate in patients with relapsed or refractory peripheral T-cell lymphoma: Results from the pivotal PROPEL study. *J Clin Oncol*. 2011;29:1182-1189.

(Revised 4/2022; NCCN T-Cell Lymphomas Guidelines v2.2022) © 2022 by Haymarket Media, Inc.