NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Extranodal NK/T-Cell Lymphoma (Part 1 of 2)

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 Extranodal NK/T-cell Lymphomas¹	
Note: All recommendations are Category 2A unless otherwise indicated.	
Combination Chemotherapy Regimens (pegaspargase-based)	
REGIMEN	DOSING
AspaMetDex ^{2*†}	Day 1: Methotrexate 3g/m² IV Days 1-4: Dexamethasone 40mg PO Days 1-4 Days 2, 4, 6, and 8: Pegaspargase 6000 U/m² IM Repeat every 21 days for 3 cycles.
SMILE ^{3,4}	Day 1: Methotrexate 2g/m² IV Day 1 Days 2-4: Dexamethasone 40mg IV or PO, leucovorin 15mg × 4 doses/day IV or PO, ifosfamide 1500mg/m² IV, and etoposide 100mg/m² IV Days 8, 10, 12, 14, 16, 18, and 20: L-asparaginase 6000U/m² IV Repeat every 21 days for 3 cycles.
Concurrent Chemoradiation Therapy (CCRT)	
CCRT ^{5,6}	Radiation 50Gy and 3 courses of DeVIC (dexamethasone, etoposide, ifosfamide, carboplatin) Level 1 (2/3 DeVIC) Day 1: Carboplatin 200mg/m² IV over 30 minutes Days 1-3: Dexamethasone 40mg IV, etoposide 67mg/m² IV over 2 hours, and ifosfamide 1g/m² IV over 3 hours. Level 2 (100% DeVIC)
	Day 1: Carboplatin 300mg/m ² Days 1-3: Dexamethasone 40mg IV, etoposide 100mg/m ² IV, and ifosfamide 1.5mg/m ² Repeat chemotherapy every 3 weeks for 3 cycles.
CCRT ^{6,7}	Radiation 40-52.8Gy and cisplatin 30mg/m² IV for 3-5 weeks followed by 3 cycles of VIPD: Days 1-3: Etoposide 100mg/m² IV over 90 minutes, ifosfamide 1200mg/m² IV over 1 hour, cisplatin 33mg/m² IV over 1 hour, and dexamethasone 40mg PO or IV Repeat chemotherapy every 3 weeks for 3 cycles.
Sequential Chemoradiation	
SMILE followed by RT 45-50.4Gy ⁴	Day 1: Methotrexate 2g/m² IV Days 2-4: Dexamethasone 40mg IV or PO, leucovorin 15mg × 4 IV or PO, ifosfamide 1500mg/m² IV, and etoposide 100mg/m² IV Days 8, 10, 12, 14, 16, 18, and 20: L-asparaginase 6000U/m² Repeat every 21 days for 3 cycles.
VIPD followed by RT 45-50.4Gy ⁷	Days 1–3: Etoposide 100mg/m² IV over 90 minutes, ifosfamide 1200mg/m² IV over 1 hour, cisplatin 33mg/m² IV over 1 hour, and dexamethasone 40mg PO or IV Repeat chemotherapy every 3 weeks for 3 cycles.
Radiotherapy alone	
• Radiotherapy (RT) ⁸	Recommended tumor dose is ≥ 50Gy Early or up-front RT had an essential role in improved overall survival and disease-free survival in patients with localized extranodal NK/T-cell lymphoma, nasal-type, in the upper aerodigestive tract Up-front RT may yield more benefits on survival in patients with stage 1 disease.
* Second-line regimen † In patients older than 70 years old: methotrexate and dexamethasone doses were decreased to 2g/m² and 20mg for 4 days respectively	

continued

NON-HODGKIN LYMPHOMA TREATMENT REGIMENS: Extranodal NK/T-Cell Lymphoma (Part 2 of 2)

References

- Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Hodgkin's Lymphomas V.2.2014. Available at: http://www.nccn.org. Accessed April 10, 2014.
- Jaccard A, Gachard N, Marin B, et al. Efficacy of L-asparaginase with methotrexate and dexamethasone (AspaMetDex regimen) in patients with refractory or relapsing extranodal NK/T-cell lymphoma, a phase 2 study. Blood. 2011;117:1834–1839.
- Yamaguchi M, Suzuki R, Kwong YL, et al. Phase I study of dexamethasone, methotrexate, ifosfamide, L-asparaginase, and etoposide (SMILE) chemotherapy for advanced-stage, relapsed or refractory extranodal natural killer (NK)/T-cell lymphoma and leukemia. Cancer Sci. 2008;99:1016–1020.
- Yamaguchi M, Kwong YL, Kim WS, et al. Phase II study of SMILE chemotherapy for newly diagnosed stage IV, relapsed, or refractory extranodal natural killer (NK)/T-cell lymphoma, nasal type: The NK-Cell Tumor Study Group Study. J Clin Oncol. 2011;29: 4410–4416.

- Yamaguchi M, Tobinai K, Oguchi M, et al. Concurrent chemoradiotherapy for localized nasal natural killer/T-cell lymphoma: an updated analysis of the Japan clinical oncology group study JC06221. J Clin Oncol. 2012;30:4044–4046.
- Yamaguchi M, Tobinai K, Oguchi M, et al. Phase I/II study of concurrent chemoradiotherapy for localized nasal natural killer/T-cell lymphoma: Japan Clinical Oncology Group Study JCOGO211. J Clin Oncol. 2009;27:5594–5600.
- Kim SJ, Kim K, Kim BS, et al. Phase II trial of concurrent radiation and weekly cisplatin followed by VIPD chemotherapy in newly diagnosed, stage IE to IIE, nasal, extranodal NK/T-cell lymphoma: Consortium for Improving Survival of Lymphoma study. J Clin Oncol. 2009;27:6027–6032.
- Huang MJ, Jiang Y, Liu WP, et al. Early or up-front radiotherapy improved survival of localized extranodal NK/T-cell lymphoma, nasal-type in the upper aerodigestive tract. Int J Radiat Oncol Biol Phys. 2008 Jan 1;70(1):166-174.

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