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 Lymphomas⁴

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

#### Combination Chemotherapy Regimens (pegaspargase-based)

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<th>REGIMEN</th>
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| AspaMetDex²† | Day 1: Methotrexate 3g/m² IV  
Days 1–4: Dexamethasone 40mg PO Days 1–4  
Days 2, 4, 6, and 8: Pegasparagase 6000 U/m² IM  
Repeat every 21 days for 3 cycles. |

| SMILE³⁴ | 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)

| CCRT⁵⁶ | 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/m²  
Days 1–3: Dexamethasone 40mg IV, etoposide 100mg/m² IV, and ifosfamide 1.5mg/m²  
Repeat chemotherapy every 3 weeks for 3 cycles. |

| CCRT⁵⁷ | 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 45-50.4Gy⁴ | 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 IV  
Repeat every 21 days for 3 cycles. |

| VVIPD followed by RT 45–50.4Gy⁷ | 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. |

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* 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.
### References