Peripheral T-cell Lymphomas (PTCL) 1

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Note: Consider Clinical Trials as treatment options for eligible patients.

PATHOLOGIC DIAGNOSIS

**ESSENTIAL:**
- Hematopathology review of all slides with at least one paraffin block or 15 unstained slides representative of the tumor. Rebiopsy if consult material is nondiagnostic.
- Adequate morphology and immunophenotyping to establish diagnosis
  - Paraffin Panel: CD20, CD4, CD8, CD3 and/or another pan-T-cell markers (CD2, CD5, CD7, CD43) and Ki-67
  - Flow cytometry immunophenotypic studies: CD2, CD3, CD4, CD5, CD7, CD8, CD10, CD16, CD25, CD26, CD14, CD45, CD52, CD56, CD57, CD94, TCRbeta and TCRgamma

**OF USE IN CERTAIN CIRCUMSTANCES TO DETERMINE SUBGROUP:**
- EBER *in situ* hybridization, CD56, CD57, cytotoxic proteins (TIA-1, granzyme B or perforin), (extranodal T/NK cell lymphomas, T-cell large granular lymphocytic leukemia)
- BetaF1, TCR gamma (gamma delta T-cell lymphomas and subcutaneous panniculitis-like T-cell lymphoma)
- CD10, BCL-6, PD1, CXCL13 (angiioimmunoblastic T-cell lymphoma)
- CD30, CD15, ALK1, EMA (anaplastic T-cell lymphoma)
- CD103 (enteropathy-associated T cell lymphoma)
- CD1a, CD34, TdT (T lymphoblastic lymphoma)
- TCL-1, FOXP3, CD25 (T-cell prolymphocytic leukemia and adult T-cell leukemia/lymphoma)
- Molecular studies to detect clonality of the TCR genes

**STRONGLY RECOMMENDED:**
- FNA or core biopsy for tissue array/banking by protocol

INITIAL EVALUATION

**ESSENTIAL:**
- Physical exam: attention to node-bearing areas, including Waldeyer's ring, and to size of liver and spleen
- Performance status
- B symptoms (fever, sweats, weight loss)
- CBC, differential, platelets, BUN, creatinine, albumin, AST, bilirubin, alkaline phosphatase, serum calcium, uric acid, LDH
- Chest x-ray, PA and LAT
- Lymphoma screening
- Unilateral or bilateral bone marrow biopsy with aspirate
- Calculation of International Prognostic Index2
- Muga scan or echocardiogram
- PET/CT
- Beta-2-microglobulin
- Screening for HIV 1 and 2, hepatitis B and C (HBcAb, HBaAg, HCVAb)

**OF USE IN SELECTED CASES:**
- CT head or MRI
- Pregnancy test
- Stool guaiac, if anemic
- Lumbar puncture, if paranasal sinus, testicular, parameningeal, orbit, CNS, paravertebral, bone marrow or HIV lymphoma
- Serum Immunoelectrophoresis (SIEP)
- Discuss fertility options and sperm banking for patients of child bearing potential

See Induction Therapy (Page 2)

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1 This algorithm contains the following subtypes: PTCL-NOS, AITL, anaplastic large cell lymphoma, ALK+ and ALK- and enteropatic associated T-cell lymphoma (EATL). The following subtypes are not included in this algorithm: Primary cutaneous anaplastic large-cell lymphoma (ALCL) and all other cutaneous T-cell lymphoma.

2 See Appendix A for International Prognostic Index

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Peripheral T-cell Lymphomas (PTCL)  

**INDUCTION THERAPY**

- Clinical trial
- CHOEP (for age less than or equal to 65 years)
- CHOP (for age greater than 65 years)

**Stages I-IV**

- After 2-4 cycles, repeat all positive studies

**INTERIM RESPONSE**

- Complete or Partial Response
  - Complete current treatment
  - No response or Progressive disease
    - See therapy for relapse on Page 3

**INITIAL RESPONSE**

- Complete Response
  - At completion of treatment, repeat all positive studies. If residual disease, consider rebiopsy.

- Partial Response
  - No response or Progressive disease
    - See therapy for relapse on Page 3

**Note:** Consider Clinical Trials as treatment options for eligible patients.

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CHOP = cyclophosphamide, doxorubicin, vincristine, prednisone
CHOEP = cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone
HCVAD = hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone
DeVIC = dexamethasone, etoposide, ifosfamide, carboplatin
SMILE = steroid, methotrexate, ifosfamide, L-asparaginase, etoposide
ICE = ifosfamide, carboplatin, etoposide

1 Consider other options for rare specific types of T-cell lymphoma:
   - NK/T-cell lymphoma - DeVIC plus radiation or SMILE
   - Hepatosplenic T-cell lymphoma - HCVAD or ICE
   - Anaplastic Lymphoma Kinase (ALK) and Anaplastic Large-Cell Lymphoma limited disease - CHOP for 3 cycles plus radiotherapy
2 PET scans should be used to assess residual abnormalities on CT scan, especially if done pretreatment
3 Partial Response includes a biological measure of disease: positive PET scan, or ideally positive biopsy
4 See Response Criteria for Lymphoma (Appendix B)
Peripheral T-cell Lymphomas (PTCL) ¹

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RELAPSE #1

ADDITIONAL THERAPY

Note: If available, clinical trials should be considered as preferred treatment options for eligible patients.

- New non cross-resistant regimen (e.g., ICE, ESHAP, GemOx, GDP, pralatrexate, brentuximab vedotin, romidepsin, belinostat)

- ICE = ifosfamide, carboplatin, etoposide
- ESHAP = etoposide, methylprednisolone, high dose cytarabine, cisplatin
- GemOx = gemcitabine, dexamethasone, and cisplatin

- Clinical trial²
- Individual approach (e.g., romidepsin, belinostat, pralatrexate, brentuximab vedotin, gemcitabine, bendamustine)

CONSOLIDATION/ADDITIONAL THERAPY

- Complete Response¹ or Partial Response¹
- No Response

- High-dose therapy plus autologous stem cell transplant (category 1 for CR in relapse, category 2A for all others)
- Allogeneic stem cell transplant
- Clinical trial²
- Best supportive care

RELAPSE #2 OR GREATER

If disease progression, clinical trial² or consider lenalidomide or other individual approach (e.g., romidepsin, belinostat, pralatrexate, brentuximab vedotin, gemcitabine, bendamustine)

Note: Consider Clinical Trials as treatment options for eligible patients.
### APPENDIX A: International Prognostic Index for PTCL-U

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Prognostic Risk</th>
<th>Number of Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age greater than 60 years</td>
<td>Group 1</td>
<td>0</td>
</tr>
<tr>
<td>Serum LDH greater than 1 times normal</td>
<td>Group 2</td>
<td>1</td>
</tr>
<tr>
<td>Performance status 2 – 4</td>
<td>Group 3</td>
<td>2</td>
</tr>
<tr>
<td>Bone marrow involvement</td>
<td>Group 4</td>
<td>3 or 4</td>
</tr>
</tbody>
</table>

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APPENDIX B: Response Criteria for Malignant Lymphoma

<table>
<thead>
<tr>
<th>Response Category</th>
<th>Nodal Masses</th>
<th>Spleen, Liver</th>
<th>Bone Marrow</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR (Complete Response: disappearance of all evidence of disease)</td>
<td>a. FDG-avid or PET positive prior to therapy; mass of any size permitted if PET negative &lt;br&gt;b. Variably FDG-avid or PET negative; regression to normal size on CT</td>
<td>Not palpable, nodules disappeared</td>
<td>Infiltrate cleared on repeat biopsy; if indeterminate by morphology, immunohistochemistry should be negative</td>
</tr>
<tr>
<td>PR (Partial Response)</td>
<td>Greater than or equal to 50% decrease in SPD of up to 6 largest dominant masses; no increase in size of other nodes &lt;br&gt;a. FDG-avid or PET positive prior to therapy; one or more PET positive at previously involved site &lt;br&gt;b. Variably FDG-avid or PET negative; regression on CT</td>
<td>Greater than or equal to 50% decrease in SPD of nodules (for single nodule in greatest transverse diameter); no increase in size of liver or spleen</td>
<td>Irrelevant if positive prior to therapy; cell type should be specified</td>
</tr>
<tr>
<td>SD (Stable Disease: failure to attain CR/PR or PD)</td>
<td>a. FDG-avid or PET positive prior to therapy; PET positive at prior sites of disease and no new sites on CT or PET &lt;br&gt;b. Variably FDG-avid or PET negative; no change in size of previous lesions on CT</td>
<td>Greater than or equal to 50% decrease in SPD of nodules (for single nodule in greatest transverse diameter); no increase in size of liver or spleen</td>
<td>Greater than 50% increase from nadir in the SPD of any previous lesions</td>
</tr>
<tr>
<td>Relapse or Progressive Disease (PD) (Any new lesion or increase by greater than or equal to 50% of previously involved sites from nadir)</td>
<td>a. Appearance of a new lesion(s) greater than 1.5 cm in any axis, greater than or equal to 50% increase in SPD of more than one node, or greater than or equal to 50% increase in longest diameter of a previously identified node greater than 1 cm in short axis &lt;br&gt;b. New foci of FDG-avidity if FDG-avid lymphoma or PET positive prior to therapy</td>
<td>Greater than 50% increase from nadir in the SPD of any previous lesions</td>
<td>New or recurrent involvement</td>
</tr>
</tbody>
</table>

FDG \[^{18}\text{F}] = \text{fluorodeoxy glucose}
SDP = \text{sum of the product of the diameters}

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SUGGESTED READINGS


Peripheral T-cell Lymphomas (PTCL) ¹

DEVELOPMENT CREDITS

This practice guideline is based on majority expert opinion of the Lymphoma Center Faculty at the University of Texas, MD Anderson Cancer Center. It was developed using a multidisciplinary approach that included input from the following medical oncologists, radiation oncologists, surgical oncologists, and hematopathologists:

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