Peripheral T-cell Lymphomas (PTCL) 1

This practice algorithm has been specifically developed for MD Anderson using a multidisciplinary approach and taking into consideration circumstances particular to MD Anderson, including the following: MD Anderson’s specific patient population; MD Anderson’s services and structure; and MD Anderson’s clinical information. Moreover, this algorithm is not intended to replace the independent medical or professional judgment of physicians or other health care providers. This algorithm should not be used to treat pregnant women.

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 or
  - 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 (angioimmunoblastic 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, HBeAg, 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

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 lymphomas.

2 See Appendix A for International Prognostic Index

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**Peripheral T-cell Lymphomas (PTCL)**

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### 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

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### INTERIM RESPONSE

- Complete or Partial Response
- No response or Progression

See therapy for relapse on Page 3

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### INITIAL RESPONSE

- Complete Response
- Partial Response
- No response or Progressive disease

- Consider autologous transplant if clinically indicated
- Follow-up every 3 to 4 months for 2 years, then every 6 years

See therapy for relapse on Page 3

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

### RELAPSE #1

**ADDITIONAL THERAPY**

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

**ICE** = ifosfamide, carboplatin, etoposide

**ESHAP** = etoposide, methylprednisolone, high dose cytarabine, cisplatin

**GemOx** = gemcitabine and oxaliplatin

**GDP** = gemcitabine, dexamethasone, and cisplatin

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

**CONSOLIDATION/ADDITIONAL THERAPY**

- Complete Response¹ or Partial Response¹
- **Clinical trial²**
- **Individual approach** (e.g., romidepsin, belinostat, pralatrexate, brentuximab vedotin, gemcitabine, bendamustine)

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**RELAPSE #2 OR GREATER**

- **Clinical trial²**
- **Best supportive care**

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

**No Response**

- **Clinical trial²**
- **Best supportive care**

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

² See Response Criteria for Lymphoma (Appendix B)

² Clinical trials or individual regimens: Patients who progress after three successive regimens are unlikely to derive additional benefit from currently utilized combination chemotherapy regimens, except for patients with a long disease-free interval.

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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>
### 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>
</table>
| **CR** (Complete Response: disappearance of all evidence of disease) | a. FDG-avid or PET positive prior to therapy; mass of any size permitted if PET negative  
b. Variably FDG-avid or PET negative; regression to normal size on CT | Not palpable, nodules disappeared | Infiltrate cleared on repeat biopsy; if indeterminate by morphology, immunohistochemistry should be negative |
| **PR** (Partial Response) | Greater than or equal to 50% decrease in SPD of up to 6 largest dominant masses; no increase in size of other nodes  
a. FDG-avid or PET positive prior to therapy; one or more PET positive at previously involved site  
b. Variably FDG-avid or PET negative; regression on CT | 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 | Irrelevant if positive prior to therapy; cell type should be specified |
| **SD** (Stable Disease: failure to attain CR/PR or PD) | a. FDG-avid or PET positive prior to therapy; PET positive at prior sites of disease and no new sites on CT or PET  
b. Variably FDG-avid or PET negative; no change in size of previous lesions on CT | Greater than 50% increase from nadir in the SPD of any previous lesions | New or recurrent involvement |
| Relapse or Progressive Disease (PD) | 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  
b. New foci of FDG-avidity if FDG-avid lymphoma or PET positive prior to therapy | Greater than 50% increase from nadir in the SPD of any previous lesions | New or recurrent involvement |

FDG [18F] = fluorodeoxy glucose  
SDP = sum of the product of the diameters

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SUGGESTED READINGS


Peripheral T-cell Lymphomas (PTCL) ¹

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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