Peripheral T-cell Lymphomas (PTCL)\textsuperscript{1}

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

**Initial Evaluation**

**Pathologic Diagnosis**

**Essential:**
- Hematopathology review of all slides with at least one paraffin block or 15 unstained slides representative of the tumor. Re-biopsy if consult material is nondiagnostic.
- Adequate morphology and immunophenotyping to establish diagnosis
  - Paraaffin Panel: CD20, CD4, CD8, CD3 and/or other 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 (angiogenenoblastic 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

**Essential:**
- Physical exam: attention to node-bearing areas, including Waldeyer’s ring, and to size of liver and spleen
- Consider Dermatology consult for comprehensive skin assessment if cutaneous involvement is present or suspected
- Performance status
- B symptoms (Unexplained fever >38°C during the previous month; Recurrent drenching night sweats during the previous month; Weight loss >10 percent of body weight ≤ 6 months of diagnosis)
- CBC with differential, BUN, creatinine, albumin, AST, bilirubin, serum calcium, alkaline phosphatase, uric acid, LDH
- Chest x-ray (AP & LAT)
- Lymphoma screening
- Unilateral or bilateral bone marrow biopsy with aspirate
- Calculation of International Prognostic Index\textsuperscript{2}
- Muga scan or echocardiogram
- PET/CT
- Beta-2-microglobulin
- Screening for HIV 1 and 2, hepatitis B and C (HBcAb, HBAg, HCVAb)
- HTLV 1/2 serology
- HLH work-up including EBV by PCR, ferritin, fibrinogen, triglycerides, and cytokine 12 profile including IL-2sR

**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

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\textsuperscript{1}This algorithm contains the following subtypes: PTCL - not otherwise specified, angioimmunoblastic T-cell lymphoma (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.

\textsuperscript{2}See Appendix A for International Prognostic Index

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Peripheral T-cell Lymphomas (PTCL)

INDUCTION THERAPY

<table>
<thead>
<tr>
<th>Stages I - IV</th>
<th>CD30-positive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>○ CHP-Bv or</td>
</tr>
<tr>
<td></td>
<td>○ Clinical trial</td>
</tr>
<tr>
<td>CD30-negative</td>
<td>○ EPOCH or</td>
</tr>
<tr>
<td></td>
<td>○ CHOP or</td>
</tr>
<tr>
<td></td>
<td>○ Clinical trial</td>
</tr>
<tr>
<td>NK/T cell lymphoma</td>
<td>○ DevIC with radiation therapy</td>
</tr>
<tr>
<td></td>
<td>○ Stage I/II: DevIC or SMILE</td>
</tr>
<tr>
<td>CTL</td>
<td>○ Skin directed therapies: clobetasol, bexarotene, infectious prophylaxis</td>
</tr>
<tr>
<td>Large cell transformation CTLC</td>
<td>○ Brentuximab (if CD30-positive) or</td>
</tr>
<tr>
<td></td>
<td>○ Denileukin diftitox or</td>
</tr>
<tr>
<td></td>
<td>○ Romidepsin or</td>
</tr>
<tr>
<td></td>
<td>○ Pralatrexate</td>
</tr>
<tr>
<td>Hepatosplenic T-cell lymphoma</td>
<td>○ HCVAD or</td>
</tr>
<tr>
<td></td>
<td>○ EPOCH</td>
</tr>
<tr>
<td>Anaplastic lymphoma kinase (ALK) and anaplastic large-cell lymphoma limited disease</td>
<td>○ CHOP or CHOP plus radiation therapy</td>
</tr>
</tbody>
</table>

After 2-4 cycles, repeat all positive studies

Complete or partial response

No response or progressive disease

Complete current treatment

See Page 3: Response, treatment and follow-up

Refractory or relapse therapy

CHOP = cyclophosphamide, doxorubicin, vincristine, prednisone
CHOEP = cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone
CHP-Bv = cyclophosphamide, doxorubicin, prednisone, brentuximab veidotin
EPOCH = etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin
HCVAD = hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone
DeVIC = dexamethasone, etoposide, ifosfamide, carboplatin
SMILE = steroid, methotrexate, ifosfamide, L-asparaginase, etoposide

1 PET scans should be used to assess residual abnormalities on CT scan, especially if done pretreatment
2 Partial Response includes a biological measure of disease: positive PET scan, or ideally positive biopsy
3 See Appendix B for Response Criteria for Lymphoma

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

INTERIM RESPONSE

Complete or partial response

No response or progressive disease

See Page 4: Refractory or relapse therapy

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**RESPONSE**

- Complete response\(^2\)
  - At completion of treatment, repeat all positive studies\(^1\)
  - If residual disease, consider re-biopsy

- Partial response\(^2, 3\)

- No response or progressive disease\(^2\)

**TREATMENT AND FOLLOW-UP**

- Consider autologous transplant if clinically indicated
- Consider allogeneic peripheral blood stem cell transplant for young patients with aggressive disease
- Consider clinical trial with maintenance
- Follow-up every 3 to 4 months for 2 years, then every 6 months

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\(^1\) PET scans should be used to assess residual abnormalities on CT scan, especially if done pretreatment

\(^2\) See Response Criteria for Lymphoma (Appendix B)

\(^3\) Partial Response includes a biological measure of disease: positive PET scan, or ideally positive biopsy

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Peripheral T-cell Lymphomas (PTCL)

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

**RELAPSE #1**

- **Clinical trial**
- New non cross-resistant regimen (e.g., ICE, ESHAP, GemOx, GDP, pralatrexate, brentuximab vedotin, romidepsin, belinostat, bendamustine with or without brentuximab vedotin)

**ADDITIONAL THERAPY**

- Candidate for high dose therapy
- Non candidate for high dose therapy

**CONSOLIDATION/ADDITIONAL THERAPY**

- Complete response or Partial response

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

- No response

- **Clinical trial**
- Other individual approach (e.g., romidepsin, belinostat, pralatrexate, brentuximab vedotin, gemcitabine, belinostat, brentuximab vedotin)

- **Clinical trial**
- Consider radiation for palliation
- Best supportive care

**RELAPSE #2 OR GREATER**

- If disease progression
- Clinical trial or Other individual approach (e.g., romidepsin, belinostat, pralatrexate, brentuximab vedotin, gemcitabine, belinostat) or
- Consider lenalidomide

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

1 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

2 See Response Criteria for Lymphoma (Appendix B)

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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>
<tbody>
<tr>
<td>CR (Complete response; disappearance of all evidence of disease)</td>
<td>• FDG-avid or PET positive prior to therapy; mass of any size permitted if PET negative</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></td>
<td>• Variably FDG-avid or PET negative; regression to normal size on CT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PR (Partial response)</td>
<td>• Decrease of ≥ 50% in SPD of up to 6 largest dominant masses; no increase in size of other nodes</td>
<td>Decrease of ≥ 50% 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></td>
<td>• FDG-avid or PET positive prior to therapy; one or more PET positive at previously involved site</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Variably FDG-avid or PET negative; regression on CT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD (Stable disease; failure to attain CR/PR or PD)</td>
<td>• FDG-avid or PET positive prior to therapy; PET positive at prior sites of disease and no new sites on CT or PET</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Variably FDG-avid or PET negative; no change in size of previous lesions on CT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relapse or progressive disease (PD) (Any new lesion or increase by ≥ 50% of previously involved sites from nadir)</td>
<td>• Appearance of a new lesion(s) &gt; 1.5 cm in any axis, ≥ 50% increase in SPD of more than one node, or ≥ 50% increase in longest diameter of a previously identified node &gt; 1 cm in short axis</td>
<td>Increase of &gt; 50% from nadir in the SPD of any previous lesions</td>
<td>New or recurrent involvement</td>
</tr>
<tr>
<td></td>
<td>• New foci of FDG-avidity if FDG-avid lymphoma or PET positive prior to therapy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

SUGGESTED READINGS


**Continued on next page**
SUGGESTED READINGS - continued


Peripheral T-cell Lymphomas (PTCL)

This practice algorithm 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:

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- Christopher Flowers, MD (Lymphoma/Myeloma)
- Nathan Fowler, MD (Lymphoma/Myeloma)
- Fredrick Hagemeister, MD (Lymphoma/Myeloma)
- Swaminathan P. Iyer, MD (Lymphoma/Myeloma)*
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- Jason Westin, MD (Lymphoma/Myeloma)

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DEVELOPMENT CREDITS

*Core Development Team Lead
*Clinical Effectiveness Development Team