Peripheral T-cell Lymphomas (PTCL)¹

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TABLE OF CONTENTS

Pathologic Diagnosis/Initial Evaluation ................................................................. Page 2
Peripheral T-Cell Lymphoma Stage I-IV ................................................................. Pages 3-4
Peripheral T-Cell Lymphoma Refractory or Relapse ........................................ Page 5
APPENDIX A: International Prognostic Index for PTCL-U .................................. Page 6
Suggested Readings ............................................................................................... Pages 7-8
Development Credits ............................................................................................ Page 9

¹This algorithm contains the following subtypes: PTCL - not otherwise specified, angioimmunoblastic T-cell lymphoma (AITL), anaplastic large cell lymphoma, anaplastic lymphoma kinase (ALK) positive and ALK negative and enteropatic associated T-cell lymphoma (EATL). The following subtypes are not included in this algorithm: T-cell prolymphocytic leukemia (T-PLL), T-cell large granular lymphocytic leukemia (T-LGL), primary cutaneous anaplastic large-cell lymphoma (ALCL), breast implant-associated (BIA)-ALCL and all other cutaneous T-cell lymphoma [see Cutaneous T-cell Lymphoma (CTCL) algorithm].
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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. Re-biopsy if consult material is nondiagnostic.
- Adequate morphology and immunophenotyping to establish diagnosis
  - Flow cytometry immunophenotypic studies: CD2, CD3, CD4, CD5, CD7, CD8, CD10, CD16, CD25, CD26, CD41, CD45, CD52, CD56, CD57, CD94, TCRbeta, TCRgamma, CD30, and TRCB1
  - Paraffin Panel: CD20, CD4, CD8, CD3, CD30 and/or other pan-T-cell markers (CD2, CD5, CD7, CD43), Ki-67, EBER

**Of Use in Certain Circumstances to Determine Subgroup:**
- TBX21/CXCR3/GATA3 and CCR4 to assess PTCL-TBX21 and PTCL-GATA3 plus ICOS and PD1 to exclude lymphomas with follicular helper phenotype (in cases of PTCL-NOS)
- BetaF1, TCR delta (gamma/delta T-cell lymphomas and subcutaneous panniculitis-like T-cell lymphoma)
- CD10, BCL-6, PD1, CXCL13, CD21, ICOS, and IDH2 R172K (AITL)
- CD15, ALK1, EMA (anaplastic T-cell lymphoma)
- CD103, CD56 (EATL)
- CD1a, CD34, TdT (T lymphoblastic lymphoma)
- TCL-1, FOXP3, CD25 (T-cell prolymphocytic leukemia and adult T-cell leukemia/lymphoma)
- FISH studies to detect DUSP22 and TP63 (ALK negative ALCCL)
- Molecular studies to detect clonality of the TCR genes
- NGS studies (end lymphoma panel) to assess the mutational landscape

**Strongly Recommended:**
- Fine needle aspiration (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
  - 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)
  - Calculation of International Prog nostic Index (see Appendix A)
- CBC with differential, BUN, creatinine, albumin, AST, bilirubin, serum calcium, alkaline phosphatase, uric acid, LDH
- Beta-2-microglobulin
- Screening for HIV 1 and 2, hepatitis B and C (HBcAb, HBaAg, HCVAb)
- HTLV 1/2 serology
- HLH work-up including EBV by PCR, ferritin, fibrinogen, triglycerides, and cytokine 12 profile including IL-2sR (sCD25)
- Chest x-ray (AP & LAT)
- Unilateral or bilateral bone marrow biopsy with aspirate
- MUGA scan or echocardiogram
- PET/CT
- Lifestyle risk assessment

**Of Use in Selected Cases:**
- CT head or MRI with contrast
- EBV with PCR
- Pregnancy test
- Stool guaiac, if anemic
- Lumbar puncture, if parasinal 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 [refer to Fertility Preservation Prior to Cancer Treatment (Women) algorithm]
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Note: Consider Clinical Trials as treatment options for eligible patients.

**INDUCTION THERAPY**

- CD30-positive
  - CHP-Bv

- CD30-negative
  - EPOCH or CHOEP or CHOP
  - NK/T cell lymphoma
    - Stage I/II: DeVIC with ISRT¹
    - Stage III/IV: SMILE or DDGP or P-GEMOX
  - CTCL: Refer to Cutaneous T-cell Lymphoma (CTCL) algorithm
  - Large cell transformation CTCL²
    - Brentuximab vedotin (if CD30-positive) or
    - Romidepsin or
    - Pralatrexate or
    - Gemcitabine or
    - Liposomal doxorubicin
    - Consideration for ISRT³ in limited cutaneous lesions with LCT
  - Multiagent chemotherapy as for PTCL

- Hepatosplenic T-cell lymphoma and EATL
  - HCVAD or
  - Dose adjusted EPOCH
  - ALK positive and negative anaplastic large-cell lymphoma (ALCL)
    - Limited stage CHP-Bv plus with or without ISRT¹
    - Other options: CHOE or CHOEP or with or without ISRT¹
  - Special circumstances: limited stage ALK positive ALCL or ALK negative DUSP22 positive ALCL

- Abbreviated course chemotherapy with ISRT¹

**INTERIM RESPONSE**

- Complete or partial response⁴,⁵
- No response or progressive disease⁴,⁵

- After 2-4 cycles, repeat all positive studies³

- See Page 4 for evaluation, response, treatment and follow up

- Complete current treatment
- See Page 5 for refractory or relapse therapy

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1. Radiation therapy can be considered for limited stage patients with abbreviated systemic therapy, or to sites of bulk or incomplete response after systemic therapy completion

2. Refer to Cutaneous T-cell Lymphoma (CTCL) algorithm

3. PET scans should be used to assess residual abnormalities on CT scan, especially if done pretreatment

4. Partial response includes a biological measure of disease: fluorodeoxyglucose (FDG)-avid disease with reduced uptake compared to baseline PET/CT scan. A positive PET/CT at the end of treatment proved to be lymphoma on biopsy is considered to be residual/refractory disease.


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ALK = anaplastic lymphoma kinase
CHOP = cyclophosphamide, doxorubicin, vincristine, prednisone
CHOEP = cyclophosphamide, doxorubicin, vincristine, etoposide, prednisone
CHP-Bv = cyclophosphamide, doxorubicin, prednisone, brentuximab vedotin
DeVIC = dexamethasone, etoposide, ifosfamide, carboplatin
DDGP = cisplatin, dexamethasone, gemcitabine, pegaspargase
DMILE = steroid, methotrexate, ifosfamide, L-asparaginase, etoposide
EPOCH = etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin
P-GEMOX = pegaspargase, gemcitabine, oxaliplatin
HCVAD = hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone
ISRT = involved site radiation therapy
<table>
<thead>
<tr>
<th>EVALUATION</th>
<th>RESPONSE</th>
<th>TREATMENT AND FOLLOW-UP</th>
</tr>
</thead>
</table>
| - At completion of treatment, repeat all positive studies\(^1\)  
- If residual disease, consider biopsy | Complete response\(^2\) | - Consider autologous stem cell transplant if clinically indicated  
- Consider allogeneic peripheral blood stem cell transplant for young patients with aggressive disease [e.g., ATLL, all gamma/delta phenotypes (HSGDTL, PCGDTL, MEITL, etc.)]  
- Consider clinical trial with maintenance  
- Follow-up every 3 to 6 months for 2 years with PET-CT. Further follow up with imaging as clinically indicated. After 5 years, refer to Survivorship - Peripheral T-Cell Lymphoma algorithm |
| | Partial response\(^2,3\) | See Page 5 for refractory or relapse therapy |
| | No response or progressive disease\(^2,3\) | |

\(^1\) 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: fluorodeoxyglucose (FDG)-avid disease with reduced uptake compared to baseline PET/CT scan. A positive PET/CT at the end of treatment proved to be lymphoma on biopsy is considered to be residual/refractory disease.
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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 (CD30 positive PTCL), romidepsin, belinostat, bendamustine with or without brentuximab vedotin)

ADDITIONAL THERAPY

- Candidate for high dose therapy
  - Complete or partial response\(^2\)
  - High-dose therapy plus autologous stem cell transplant or Allogeneic stem cell transplant

- Refractory or Relapse
  - Non candidate for high dose therapy
  - No response\(^3\)
    - Clinical trial
    - Consider radiation for palliation
    - Best supportive care

CONSOLIDATION/
ADDITIONAL THERAPY

- If disease progression
  - Clinical trial
  - Other individual approach [e.g., romidepsin, belinostat, pralatrexate, brentuximab vedotin (CD30 positive PTCL), gemcitabine, bendamustine] or
  - Consider lenalidomide

RELAPSE #2 OR GREATER

- Clinical trial
- Other individual approach [e.g., romidepsin, belinostat, pralatrexate, brentuximab vedotin, gemcitabine, bendamustine]

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 Partial response includes a biological measure of disease: fluorodeoxyglucose (FDG)-avid disease with reduced uptake compared to baseline PET/CT scan. A positive PET/CT at the end of treatment proved to be lymphoma on biopsy is considered to be residual/refractory disease.
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 &gt; 60 years</td>
<td>Group 1</td>
<td>0</td>
</tr>
<tr>
<td>Serum LDH &gt; 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>

1 Other prognostic scoring systems have been proposed and validated, but none are currently used to impact PTCL treatment algorithm
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SUGGESTED READINGS


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SUGGESTED READINGS - continued


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DEVELOPMENT CREDITS

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:

Core Development Team Leads
Swaminathan P. Iyer, MD (Lymphoma/Myeloma)
Ranjit Nair, MD (Lymphoma/Myeloma)

Workgroup Members
Tharakeswara K. Bathala, MD (Abdominal Imaging Department)  Hun Lee, MD (Lymphoma/Myeloma)
Luis Malpica Castillo, MD (Lymphoma/Myeloma)  Jeffrey Medeiros, MD (Hematopathology Administration)
Sheree E. Chen, PharmD (Pharmacy Clinical Programs)  Loretta Nastoupil, MD (Lymphoma/Myeloma)
Bouthaina S. Dabaja, MD (Radiation Oncology)  Sattva Neelapu, MD (Lymphoma/Myeloma)
Bryan Do, PharmD (Pharmacy Clinical Programs)  Felipe Samaniego, MD (Lymphoma/Myeloma)
Luis E. Fayad, MD (Lymphoma/Myeloma)  Samer Srour, MBCHB (Stem Cell Transplantation)
Olga N. Fleckenstein, BS*  Carlos A. Torres-Cabala, MD (Pathology, Anatomical)
Chistopher Flowers, MD (Lymphoma/Myeloma)  Francisco Vega, MD, PhD (Hematopathology Administration)
Nathan Fowler, MD (Lymphoma/Myeloma)  Michael Wang, MD (Lymphoma/Myeloma)
Jillian Gunther, MD (Radiation Oncology)  Mary Lou Warren, DNP, APRN, CNS-CC*
Fredrick Hagemeister, MD (Lymphoma/Myeloma)  Jason Westin, MD (Lymphoma/Myeloma)
Chitra Hosing, MD (Stem Cell Transplantation)  

* Clinical Effectiveness Development Team

Department of Clinical Effectiveness V5
Approved by the Executive Committee of the Medical Staff on 07/19/2022