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This algorithm contains the following subtypes: mycosis fungoides, Sezary syndrome, and primary cutaneous anaplastic large-cell lymphoma (pcALCL).

See Peripheral T-cell Lymphomas (PTCL) algorithm for 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).
INITIAL EVALUATION

ESSENTIAL:
- Physical exam: attention to node-bearing areas, including Waldeyer's ring, and to liver and spleen
  - Dermatology consult for comprehensive skin assessment including possible skin infections especially at sites of erosions and ulcerations
  - Performance status
  - B symptoms (Unexplained fever > 38°C during the previous month; Recurrent drenching night sweats during the previous month; Weight loss > 10% of body weight ≤ 6 months of diagnosis)
  - Calculation of Cutaneous Lymphoma International Prognostic Index if indicated
- 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
- Chest x-ray (AP & LAT)
- PET/CT if palpable nodes
- Lifestyle risk assessment

OF USE IN SELECTED CASES:
- CT head or MRI brain with contrast
- Pregnancy test
- Unilateral or bilateral bone marrow biopsy with aspirate
- MUGA scan or echocardiogram
- Lumbar puncture, if paranasal sinus, testicular, parameningeal, orbit, CNS, paravertebral, bone marrow or HIV lymphoma
- Other work-up for patients at risk for hemophagocytic lymphohistiocytosis (HLH) including EBV by PCR, ferritin, fibrinogen, triglycerides, and cytokine 12 profile including IL-2sR
- Serum immunoelectrophoresis (SIEP)
- Discuss fertility options and sperm banking for patients of child bearing potential

STRONGLY RECOMMENDED:
- Molecular studies to detect clonality of the TCR genes
- NGS studies (end lymphoma panel) to assess the mutational landscape
- Fine needle aspiration (FNA) or core biopsy for tissue array/banking by protocol

PATHOLOGIC DIAGNOSIS

ESSENTIAL:
- Pathology (dermatopathology or hematopathology) review of all slides with at least one paraffin block or 15 unstained slides representative of the tumor. Fresh punch biopsy if consult material is nondiagnostic or unavailable.
- Adequate morphology and immunophenotyping to establish diagnosis
  - Immunohistochemistry on formalin fixed paraffin embedded tissue: CD3, CD4, CD8, CD7, CD30

OF USE IN CERTAIN CIRCUMSTANCES TO DETERMINE SUBGROUP:
- Other IHC stains to consider in selected cases: CD5, CD2, TCRB, TCRD, TIA-1, Granzyme B, PD1, ICOS

STONGLY RECOMMENDED:
- Molecular studies to detect clonality of the TCR genes
- NGS studies (end lymphoma panel) to assess the mutational landscape
- Fine needle aspiration (FNA) or core biopsy for tissue array/banking by protocol

1 Review MD Anderson approved biomarkers
2 See Appendix A for Supportive Therapies
4 See Physical Activity, Nutrition, and Tobacco Cessation algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice
Myeloid Fungoides (MF)/Sezary Syndrome (SS)

Skin-directed therapy (SDT) may be used alone or in combination of multiple SDTs.1,2

- SDT alone or combination of multiple SDTs1,2
- Consider systemic therapy

EVALUATION AND TREATMENT

- Complete or partial response3
- Inadequate response3 after radiation or after multiple SDTs

- Continue therapy as maintenance until progression or taper to optimize response duration
- If disease progression or relapse, treat based on clinical stage

A

Systemic therapy plus SDT1,2

- Bexarotene (preferred)
- Brentuximab vedotin for CD30 positive disease; preferred if unable to tolerate or unfavorable cost benefit from bexarotene or acitretin5
- Romidepsin preferred if unable to tolerate or does not qualify for interferon5
- Vorinostat
- Mogamulizumab preferred if blood involvement6
- Extracorporeal photopheresis (ECP) preferred if SS
- Acitretin5
- Interferons; IFN alpha-2b, IFN gamma-1b, or pegylated IFN; preferred if unable to tolerate or does not qualify for bexarotene or actretin and CD30 negative disease
- Consider methotrexate (dose ≤ 50 mg every week) if predominant symptom is pruritus
- Isotretinoin (13-cis-retinoic acid)

Inadequate response3 after multiple SDT and systemic therapy

- Continue therapy as maintenance until progression or taper to optimize response duration
- If disease progression or relapse, treat based on clinical stage

- Clinical trial or
- Total skin electron beam therapy (TSEBT)2 or
- Focal radiation therapy in combination with systemic or other topicals1,2

Stage IA (skin only, < 10% BSA)

Predominantly patch

Stage IB (skin only, ≥ 10% BSA)/Stage IIA

Predominantly plaque

BSA = body surface area

1 See Appendix B for Skin Directed Therapies
2 See Appendix C for Principles of Radiation Therapy

5 Excludes SS
6 Not FDA approved

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


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

**Mycosis Fungoides (MF)/Sezary Syndrome (SS)**

<table>
<thead>
<tr>
<th>STAGE</th>
<th>TREATMENT</th>
<th>EVALUATION AND TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage IIB (presence of tumor, ( \geq 1 ) tumor measuring 1 cm)</td>
<td>1. Local radiation therapy plus/minus skin-directed therapy (SDT)(^{1,2} ) or 2. Local radiation therapy(^{2} ) plus/minus systemic therapy</td>
<td>Complete or partial response(^{3} )</td>
</tr>
</tbody>
</table>
| Generalized tumor lesions | 3. TSEBT\(^{2} \) or 4. Systemic therapy plus/minus SDT\(^{1} \)  
  - Brentuximab vedotin if CD30 positive disease\(^{4} \)  
  - Gemcitabine (if CD30 negative disease)  
  - Romidepsin  
  - Subsequent options:  
    - Pralatrexate (low-dose or standard dose) alone or in combination with Bexarotene (preferred combination therapy)  
    - Liposomal doxorubicin\(^{5} \)  
  - Consider combination of systemic, SDT\(^{1} \) and TSEBT\(^{2,6} \)  
  - Consult Stem Cell Transplantation | Inadequate response\(^{3} \) after radiation, SDT and systemic therapy |

TSEBT = total skin electron beam therapy

1 See Appendix B for Skin Directed Therapies  
2 See Appendix C for Principles of Radiation Therapy  
4 Excludes SS  
5 Final results of phase II trial did not benefit when bexarotene was added  
6 Limited data exists on the safety of these combinations. Institutional experience on the safety of drugs and combination with radiation:  
  - Therapies that appear safe: brentuximab vedotin, romidepsin, bexarotene, extracorporeal photopheresis (ECP)  
  - Concern for toxicity including radiation sensitization and/or radiation recall: gemcitabine, doxorubicin, pralatrexate, methotrexate

● Continue therapy as maintenance until progression or taper to optimize response duration  
  ● If disease progression or relapse, treat based on clinical stage

● Clinical trial or  
  ● Consider repeat biopsy if concerns for large cell transformation (LCL)  
  ○ See Page 8 for LCL if indicated

STAGE TREATMENT EVALUATION AND TREATMENT

Department of Clinical Effectiveness V1 rev  
Approved by the Executive Committee of the Medical Staff on 07/19/2022
# Cutaneous T-cell Lymphomas (CTCL)

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

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<th>EVALUATION AND TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mycosis Fungoides (MF)/Sezary Syndrome (SS)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>● Frontline options:</td>
<td>● Continue therapy as maintenance&lt;sup&gt;6&lt;/sup&gt; until progression or taper to optimize response duration</td>
</tr>
<tr>
<td></td>
<td>● Low symptom burden (responses expected 2-3 months after initiation)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>○ Phototherapy plus interferon (IFN alfa-2bmor, IFN gamma-1b)</td>
<td>● If disease progression or relapse, treat based on clinical stage</td>
</tr>
<tr>
<td></td>
<td>○ Phototherapy plus retinoid</td>
<td>● Stem cell transplant consolidation</td>
</tr>
<tr>
<td></td>
<td>○ Phototherapy plus ECP if blood involvement</td>
<td></td>
</tr>
<tr>
<td></td>
<td>○ High symptom burden (need for immediate response)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>● Subsequent options: Combinations of phototherapy plus:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>○ Brentuximab vedotin for CD30 positive disease&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>○ Gemcitabine (if CD30 negative disease)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>○ Romidepsin (preferred if unable to tolerate or not qualify for interferon)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>○ Pralatrexate (low-dose or standard dose) alone or in combination with Bexarotene (preferred combination therapy)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>○ Mogamulizumab preferred if blood involvement&lt;sup&gt;3&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>○ Liposomal doxorubicin&lt;sup&gt;4&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>● ECP plus interferon (IFN alfa-2b, IFN gamma-1b, or pegylated IFN)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>● ECP plus retinoid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>● ECP plus retinoid plus interferon (IFN alfa-2b, IFN gamma-1b, or pegylated IFN)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>● Retinoid plus interferon (IFN alfa-2b, IFN gamma-1b, or pegylated IFN)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Complete or partial response&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inadequate response&lt;sup&gt;5&lt;/sup&gt; after therapy</td>
</tr>
</tbody>
</table>

---

**Note:** Patients with extensive skin lesions (e.g., erythrodermic disease, ulcerative lesions) are at increased risk for secondary infection with skin pathogens; systemic antibiotic therapy should be considered.

1. See Appendix C for Principles of Radiation Therapy
2. Excludes SS
3. Excludes large cell transformation
4. Final results of phase II trial did not benefit when Bexarotene was added
6. For patients treated with TSEBT, maintenance options may include phototherapy with or without oral regimens

---

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**Cutaneous T-cell Lymphomas (CTCL)**

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

---

**STAGE**

<table>
<thead>
<tr>
<th>Stage IVA1 or any stage with blood involvement with aberrant cell count &gt; 1000</th>
<th>Mycosis Fungoides (MF)/Sezary Syndrome (SS)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>TREATMENT</strong></td>
</tr>
<tr>
<td></td>
<td>● ECP plus retinoid plus/minus interferon</td>
</tr>
<tr>
<td></td>
<td>● Mogamulizumab preferred if significant symptomatic leukocytosis for ECP not feasible</td>
</tr>
<tr>
<td></td>
<td>● For high symptom burden (need for immediate response), TSEBT1 alone plus systemic therapy options</td>
</tr>
<tr>
<td></td>
<td>● Subsequent options: Combinations of skin directed therapy2 plus:</td>
</tr>
<tr>
<td></td>
<td>○ Brentuximab vedotin for CD30 positive disease3</td>
</tr>
<tr>
<td></td>
<td>○ Gemcitabine (if CD30 negative disease)</td>
</tr>
<tr>
<td></td>
<td>○ Romidepsin (preferred if unable to tolerate or not qualify for interferon)</td>
</tr>
<tr>
<td></td>
<td>○ Pralatrexate (low-dose or standard dose) alone or in combination with Bexarotene (preferred combination therapy)</td>
</tr>
<tr>
<td></td>
<td>○ Liposomal doxorubicin4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage IVA2 and IVB</th>
<th><strong>EVALUATION AND TREATMENT</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systemic therapy plus or minus skin directed therapy is the preferred treatment option (see Page 8 for large cell transformation (LCT))</td>
</tr>
<tr>
<td>Complete or partial response5 after therapy</td>
<td>● Continue therapy as maintenance until progression or taper to optimize response duration</td>
</tr>
<tr>
<td>Inadequate response5 after therapy</td>
<td>● Stem cell transplant consolidation</td>
</tr>
</tbody>
</table>

---

1 See Appendix C for Principles of Radiation Therapy
2 See Appendix B for Skin Directed Therapies
3 Excludes SS
4 Final results of phase II trial did not benefit when bexarotene was added
6 GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients or if clinically indicated, the SDM should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).

---

ECP = extracorporeal photopheresis
TSEBT = total skin electron beam therapy

---

Stage IVA1 or any stage with blood (B2) involvement with aberrant cell count > 1000

Stage IVA2 and IVB Systemic therapy plus or minus skin directed therapy is the preferred treatment option [see Page 8 for large cell transformation (LCT)]
Cutaneous T-cell Lymphomas (CTCL)

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

STAGE

Clinically aggressive / relapsed and refractory MF/SS requiring systemic therapy

Mycosis Fungoides (MF)/Sezary Syndrome (SS)

TREATMENT

- Clinical trial preferred
- **Outside of a trial, institutional practice:**
  - Mogamulizumab preferred if blood involvement¹
  - Regimens for Peripheral T-cell lymphoma not otherwise specified (PTCL-NOS) if intention is for transplant (see Page 8 for LCT)
  - Alemtuzumab
  - Pembrolizumab
  - Discuss GCC with patient or if clinically indicated, with SDM²

---

¹ Concern for increased risk for acute GVHD in patients receiving therapy approximately 80 days prior to transplant
² GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients or if clinically indicated, the SDM should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).
**Cutaneous T-cell Lymphomas (CTCL)**

**Preparation**

- Consider radiation therapy to lesions with LCT along with management of co-existing disease.

**Treatment**

**Prefered front line regimen**

- Brentuximab vedotin (Bv) if CD30 positive disease.
- Romidepsin.
- Gemcitabine.
- Regimens for PTCL-NOS if intention is for transplant:
  - EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin).
  - DHAP (dexamethasone, cytarabine, cisplatin).
  - ICE (ifosfamide, carboplatin, etoposide).
  - DHAX (dexamethasone, cytarabine, oxaliplatin).
  - ESHAP (etoposide, methylprednisolone, cytarabine) + platinum (cisplatin or oxaliplatin).
  - GDP (gemcitabine, dexamethasone, cisplatin).
  - GemOx (gemcitabine, oxaliplatin).

**Subsequent options**

- Pralatrexate (low-dose or standard dose) alone.
- Liposomal doxorubicin.

**Evaluation and Treatment**

- Complete or partial response.
  - Continue therapy as maintenance until progression or taper to optimize response duration.
  - If disease progression or relapse, treat based on clinical stage.
  - Stem cell transplant consolidation.

- Inadequate response.
  - Clinical trial.
  - Consider allo-stem cell transplant if disease is controlled.
  - Discuss GCC with patient or if clinically indicated, with SDM.

---

1 See Appendix C for Principles of Radiation Therapy


3 If intention is for transplant, institutional practice is Bv + CHP.

4 Non-CHOP preferred over CHOP-like regimens; however, overall data is limited to guide optimal therapy.

5 Final results of phase II trial did not benefit when bexarotene was added.

6 GCC should be initiated by the Primary Oncologist. If Primary Oncologist is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Oncologist. Patients or if clinically indicated, the SDM should be informed of therapeutic and/or palliative options. GCC discussion should be consistent, timely, and re-evaluated as clinically indicated. The Advance Care Planning (ACP) note should be used to document GCC discussion. Refer to GCC home page (for internal use only).
APPENDIX A: Supportive Therapies

- Wound care assessment by Dermatology
- Whirlpool Therapy consultation for extensive wounds
- Infections
  - Swab and culture
  - Topical and oral treatment as indicated
    - Empiric therapy with anti-staphylococcus aureus coverage if erythrodermic
    - Gram negative coverage for tumors
  - Infectious Diseases consult for multi-drug resistant lesions
  - Assess erosions for herpes simplex virus (HSV) and varicella zoster virus (VZV) reactivation
  - For colonization, diluted bleach baths and hibiclens wash at least weekly
- Physical Therapy and Occupational Consult, as indicated
- Pruritis: consider gabapentin, pregabalin, antihistamines, and/or mirtazapine
- Supportive Care consult and/or Psychiatry consult, as indicated (e.g., depression, anxiety)

APPENDIX B: Skin-Directed Therapies (SDT)

- Radiation Therapy (See Appendix B: Principles of Radiation Therapy)
- Phototherapy (UVB, NB-UVB for patch/thin plaques; PUVA/UVA1 for thicker plaques)
  - Preferred in widespread lesions
  - Localized therapy if thicker plaques or tumors, followed by radiation
- Topical management
  - First-line: high-potency corticosteroids
  - Second-line: topical mechlorethamine (nitrogen mustard)
  - Third-line: topical imiquimod
  - Less preferred
    - Topical carmustine (concern for toxicity)
    - Topical retinoids (bexarotene, tazarotene) (unfavorable cost:benefit ratio)

APPENDIX C: Principles of Radiation Therapy

- Dosing
  - Patch/plaque disease is typically treated with 4-8Gy in 2-4 fractions
  - Plaque/tumor disease is typically treated with 8-12 Gy in 3-6 fractions
  - Refractory disease resistant to prior radiation therapy courses may require higher dose
  - Treatment is typically delivered with superficial electrons
- Focal versus total skin electron beam therapy (TSEBT)
  - Focal therapy can be given for individual lesions or groups of lesions when TSEBT is not indicated
  - Decision for TSEBT should be made based on multidisciplinary discussion and is typically reserved for patients with higher BSA involvement
  - TSEBT is typically given as 12 Gy delivered over 2-3 weeks. Boost dose is given to shielded areas (e.g., axillae, perianal region, perineum)
  - Patients intended to undergo allogeneic stem cell transplant often receive pre-transplant TSEBT to a dose of 28-32 Gy over 6-8 weeks

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SUGGESTED READINGS


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MD Anderson Institutional Policy #CLN1202 - Advance Care Planning Policy

Advance Care Planning (ACP) Conversation Workflow (ATT1925)


**SUGGESTED READINGS - continued**

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SUGGESTED READINGS - continued


Cutaneous T-cell Lymphomas (CTCL)

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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:

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