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¹ This algorithm contains the following subtypes: mycosis fungoides and Sezary syndrome. Refer to the [Peripheral T-cell Lymphomas \(PTCL\) algorithm](#) for other T-cell related lymphomas.

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

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
- Flow cytometry for MF/SS - Blood

OF USE IN CERTAIN CIRCUMSTANCES TO DETERMINE SUBGROUP:

- Other IHC stains to consider in selected cases: CD5, CD20, TCRB, TCRD, TIA-1, Granzyme B, PD1, ICOS, EBER

STRONGLY RECOMMENDED:

- Molecular studies to detect clonality of the *TCR* genes; consider TCR HTS if available
- Next generation sequencing (NGS) studies (end lymphoma panel) to assess the mutational landscape
- Fine needle aspiration (FNA) or core biopsy for tissue array/banking by protocol

MF = mycosis fungoides SS = Sezary syndrome
TCR = T cell receptor HTS = high throughput sequencing

¹ See [Appendix A](#) for Supportive Therapies

² Refer to Benton, E. C., Crichton, S., Talpur, R., Agar, N. S., Fields, P. A., Wedgeworth, E., ... Whittaker, S. J. (2013). A cutaneous lymphoma international prognostic index (CLIPi) for mycosis fungoides and Sezary syndrome. *European Journal of Cancer*, 49(13), 2859–2868. doi:10.1016/j.ejca.2013.04.018

³ See [Physical Activity](#), [Nutrition](#), [Obesity Screening and Management](#), and [Tobacco Cessation Treatment](#) algorithms; ongoing reassessment of lifestyle risks should be a part of routine clinical practice

⁴ GCC should be initiated by the Primary Treating Physician. If Primary Treating Physician is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Treating Physician. Patients or if clinically indicated, the Patient Representative 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).
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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 ulcerations¹, body surface area (BSA) and Modified Severity-Weighted Assessment Tool (mSWAT)
 - 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 indicated²
- CBC with differential, BUN, creatinine, albumin, AST, bilirubin, calcium, uric acid, alkaline phosphatase, LDH
- Beta-2-microglobulin • HTLV 1/2 serology
- Screening for HIV 1 and 2, hepatitis B and C (HBcAb, HBaAg, HCVAb)
- Autoimmune screening: ANA and rheumatoid factor if clinically indicated
- Lifestyle risk assessment³
- Discuss Goal Concordant Care (GCC) with patient or if clinically indicated, with Patient Representative⁴

OF USE IN SELECTED CASES:

- Baseline PET/CT or CT chest/abdomen/pelvis with contrast if palpable lymphadenopathy or aggressive clinical behavior
- Pregnancy test • Unilateral or bilateral bone marrow biopsy with aspirate
- Multigated acquisition (MUGA) scan or echocardiogram if needed for systemic therapy
- Other work-up for patients at risk for hemophagocytic lymphohistiocytosis (HLH) including EBV by PCR, ferritin, fibrinogen, triglycerides, CRP, natural killer (NK) subset panel, T-NK flow cytometry and cytokine panel which includes IL-2sR (sCD25)
- Serum immunoelectrophoresis (SIEP)
- Discuss fertility options and sperm banking for patients of child bearing potential (refer to [Fertility Preservation Prior to Cancer Treatment algorithm](#))

TREATMENT

- MF/SS: Stage IA, IB, IIA → [Page 3](#)
- MF/SS: Stage IIB → [Page 4](#)
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- Large Cell Transformation (LCT) → [Page 8](#)

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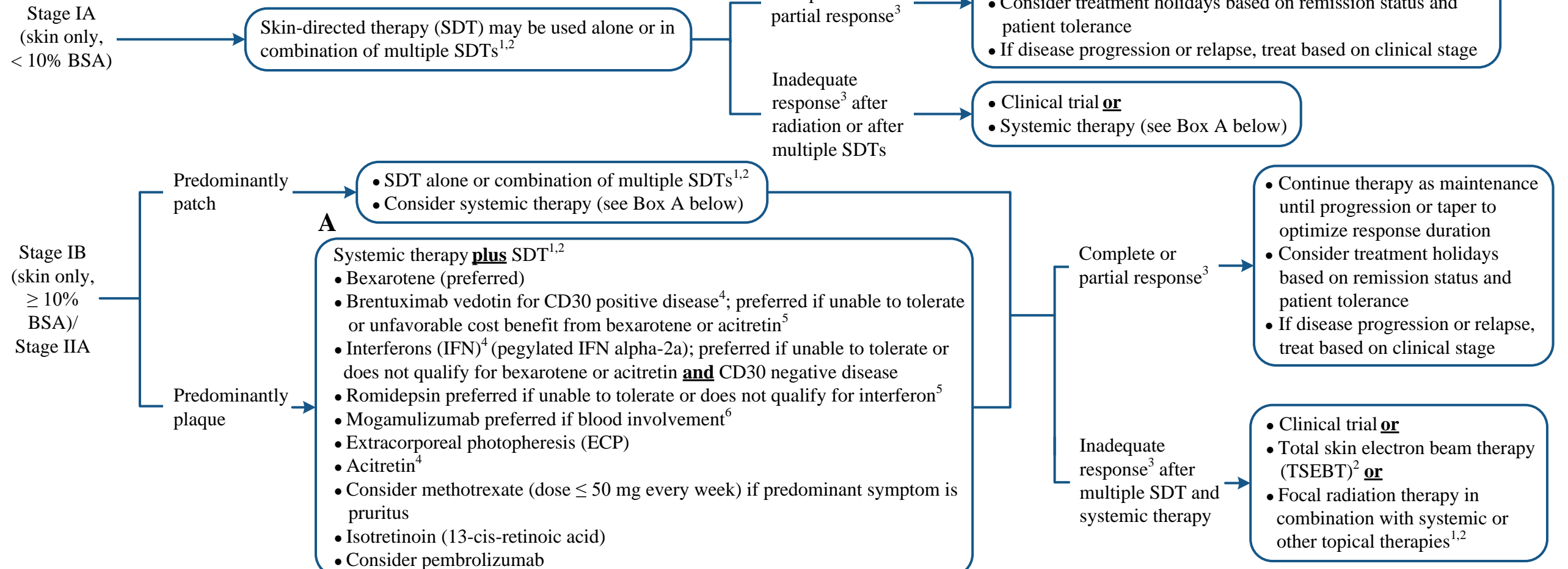
Note: Consider Clinical Trials as treatment options for eligible patients.

Mycosis Fungoides (MF)/Sezary Syndrome (SS)

STAGE

TREATMENT

EVALUATION AND TREATMENT



¹ See [Appendix B](#) for Skin Directed Therapies

² See [Appendix C](#) for Principles of Radiation Therapy

³ For response assessment, refer to: Olsen, E. A., Whittaker, S., Willemze, R., Pinter-Brown, L., Foss, F., Geskin, L., ... Scarisbrick, J. (2022). Primary cutaneous lymphoma: Recommendations for clinical trial design and staging update from the ISCL, USCLC, and EORTC. *Blood*, 140(5), 419-437. doi:10.1182/blood.2021012057

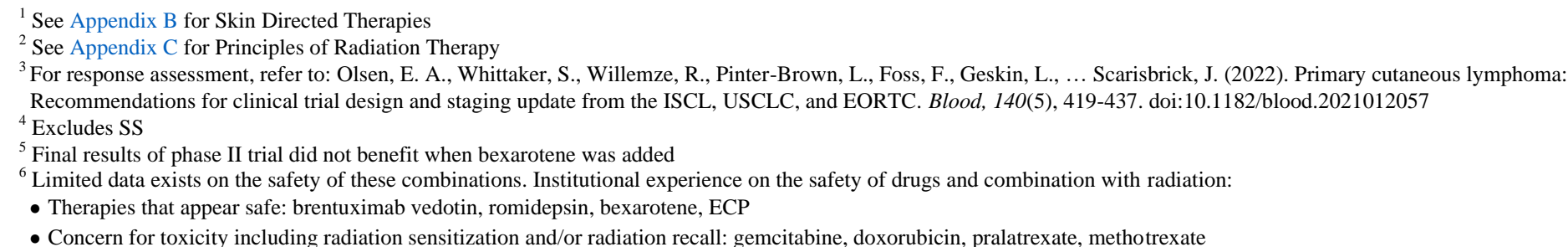
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⁴ Excludes SS

⁵ Not FDA approved

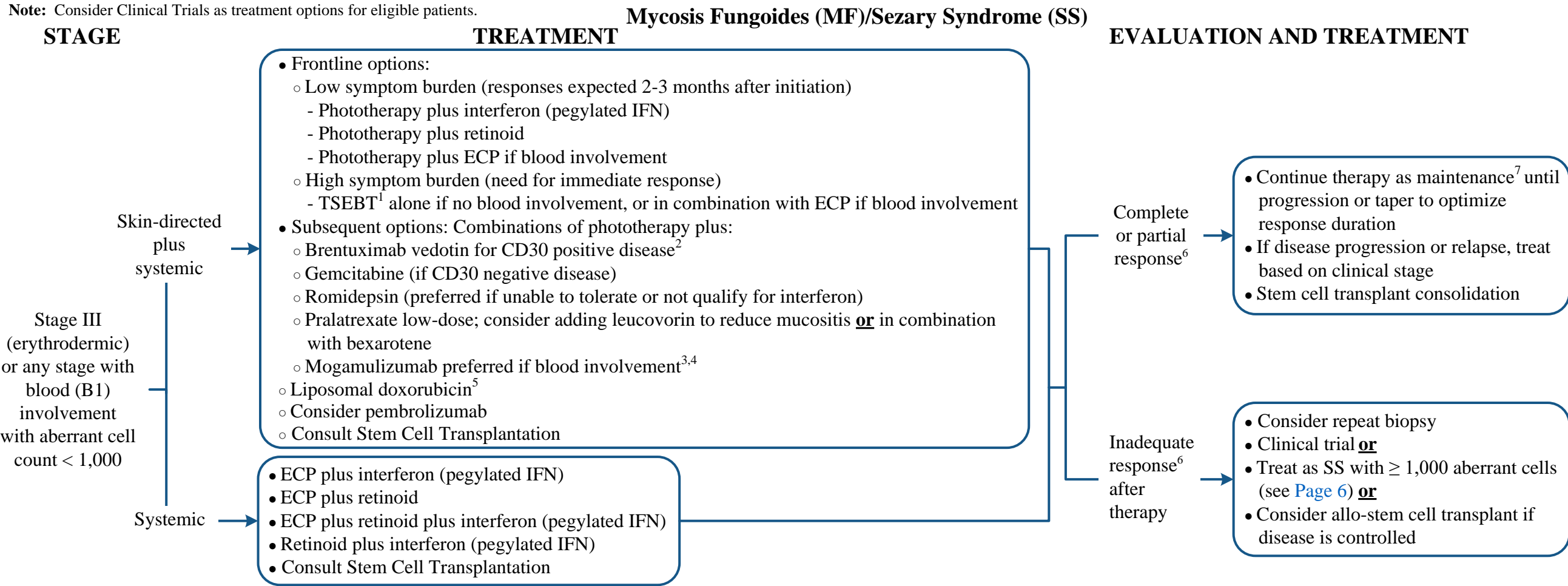
⁶ Excludes LCT

Mycosis Fungoides (MF)/Sezary Syndrome (SS)



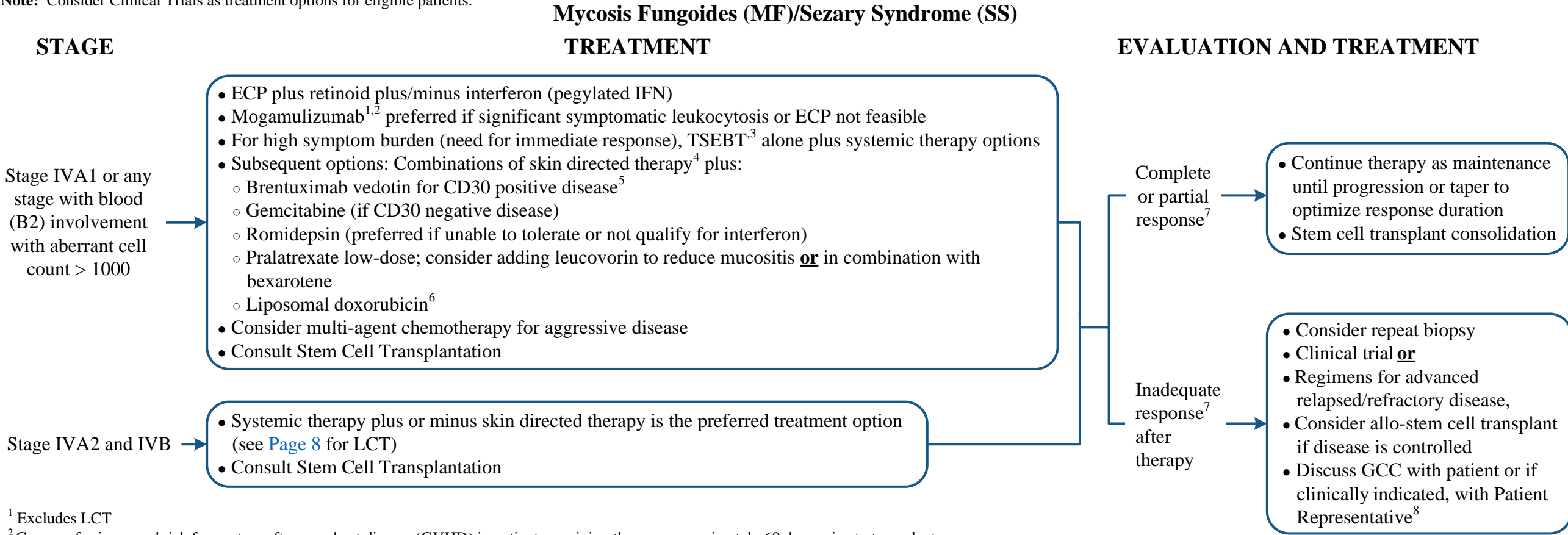
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Note: Consider Clinical Trials as treatment options for eligible patients.



¹ Excludes LCT

² Concern for increased risk for acute graft versus host disease (GVHD) in patients receiving therapy approximately 60 days prior to transplant

³ See [Appendix C](#) for Principles of Radiation Therapy

⁴ See [Appendix B](#) for Skin Directed Therapies

⁵ Excludes SS

⁶ Final results of phase II trial did not benefit when bexarotene was added

⁷ For response assessment, refer to: Olsen, E. A., Whittaker, S., Willemze, R., Pinter-Brown, L., Foss, F., Geskin, L., ... Scarisbrick, J. (2022). Primary cutaneous lymphoma: Recommendations for clinical trial design and staging update from the ISCL, USCLC, and EORTC. *Blood*, 140(5), 419-437. doi:10.1182/blood.2021012057

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Mycosis Fungoides (MF)/Sezary Syndrome (SS)

STAGE

TREATMENT

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



- Clinical trial preferred
- **Outside of a trial, institutional practice:**
 - Mogamulizumab preferred if blood involvement^{1,2}
- Regimens for peripheral T-cell lymphoma not otherwise specified (PTCL-NOS) if intention is for transplant; see [Page 8](#) for LCT
- Alemtuzumab
- Pembrolizumab
- Consider multi-agent chemotherapy for aggressive disease
- Discuss GCC with patient or if clinically indicated, with Patient Representative³

¹ Excludes LCT

² Concern for increased risk for acute graft versus host disease (GVHD) in patients receiving therapy approximately 80 days prior to transplant

³ GCC should be initiated by the Primary Treating Physician. If Primary Treating Physician is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Treating Physician. Patients or if clinically indicated, the Patient Representative 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).

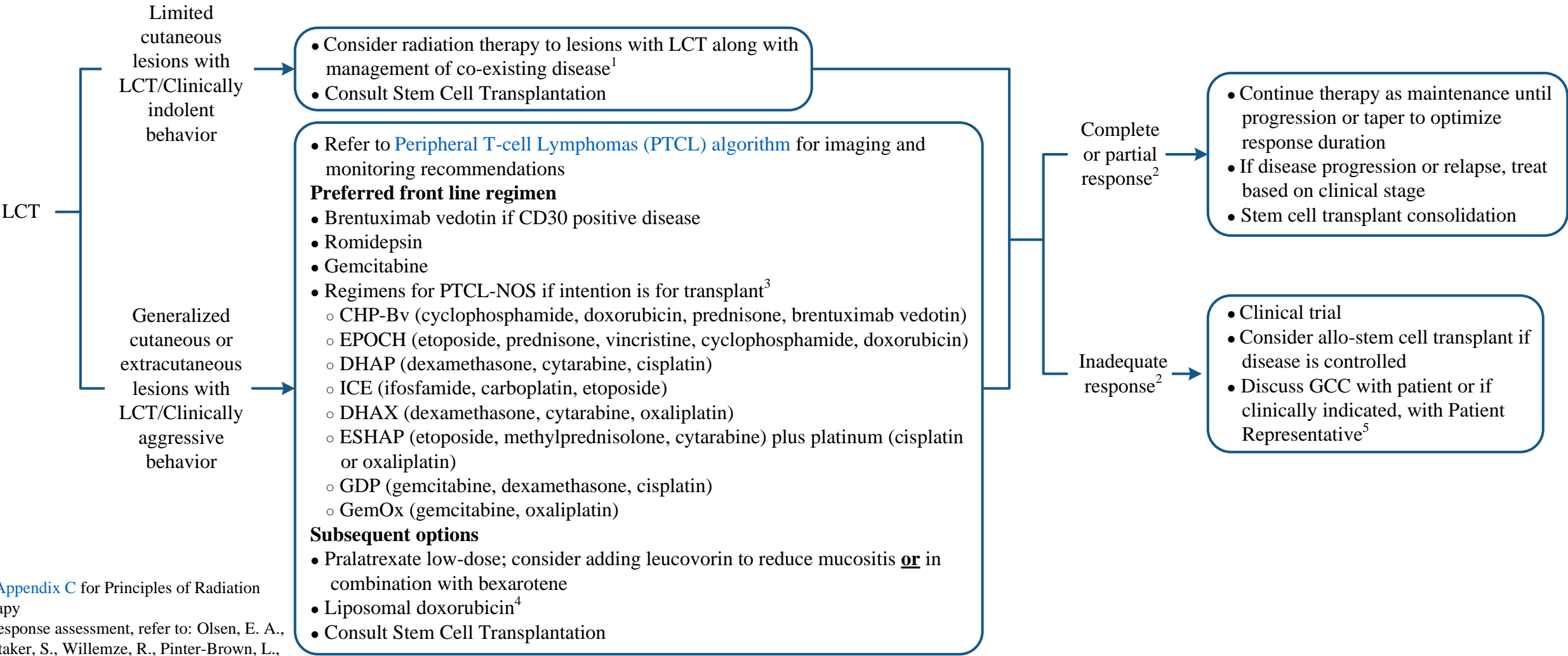
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PRESENTATION

TREATMENT

EVALUATION AND TREATMENT



¹ See [Appendix C](#) for Principles of Radiation Therapy

² For response assessment, refer to: Olsen, E. A., Whittaker, S., Willemze, R., Pinter-Brown, L., Foss, F., Geskin, L., ... Scarisbrick, J. (2022). Primary cutaneous lymphoma: Recommendations for clinical trial design and staging update from the ISCL, USCLC, and EORTC. *Blood*, 140(5), 419-437. doi:10.1182/blood.2021012057

³ Non-CHOP preferred over CHOP-like regimens; however, overall data is limited to guide optimal therapy

⁴ Final results of phase II trial did not benefit when bexarotene was added

⁵ GCC should be initiated by the Primary Treating Physician. If Primary Treating Physician is unavailable, Primary Team/Attending Physician to initiate GCC discussion and notify Primary Treating Physician. Patients or if clinically indicated, the Patient Representative 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).

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APPENDIX A: Supportive Therapies

- Wound care assessment by Dermatology
- Whirlpool Therapy consultation for extensive wounds if available
- 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
- Puritis: 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 C: Principles of Radiation Therapy)
- Phototherapy (UVB, NB-UVB for patch/thin plaques; PUVA/UVA1 for thicker plaques)
 - Preferred in widespread lesions
 - For thicker plaques or tumors, combine phototherapy with localized radiation therapy
- 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 4-8 Gy 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 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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DEVELOPMENT CREDITS

This practice algorithm is based on majority expert opinion of the Lymphoma Center providers 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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