DIAGNOSIS

ESSENTIAL:

- **Biopsy of suspicious skin sites**
  - **Multiple biopsies may be necessary to capture the pathologic variability of disease at diagnosis**
- **Dermatopathology review of slides[a]**

USEFUL UNDER CERTAIN CIRCUMSTANCES:

- **IHC panel of skin biopsy[b,c,d]**
  - **CD2, CD3, CD4, CD5, CD7, CD8, CD20, CD30, CD25, CD56, TIA1, granzyme B, ßF1, TCR-CγM1**
- **Molecular analysis of skin biopsy: TCR gene rearrangements (assessment of clonality)[b] by PCR methods[e]**
- **Assessment of peripheral blood for Sezary cells (in cases where skin is not diagnostic, especially T4) including:**
  - **Sezary cell prep**
  - **Flow cytometry (CD3, CD4, CD7, CD8, CD26 to assess for expanded CD4+ cells with increased CD4/CD8 ratio or with abnormal immunophenotype, including loss of CD7 or CD26) and**
  - **PCR for TCR gene rearrangement**
- **Biopsy of suspicious lymph nodes (in absence of definitive skin diagnosis)**
- **Assessment of HTLV-1[f] serology in at-risk populations. HTLV-1 PCR if serology is indeterminate**

→ **Workup (MFSS-2)**

[a]Presence of transformation or areas of folliculotropism may have important implications for selection of therapy and outcome and should be included in pathology reports

[b]Clinically or histologically non-diagnostic cases. Pimpinelli N, Olsen EA, Santucci M, et al, for the International Society for Cutaneous Lymphoma. Defining early mycosis fungoides. J Am Acad Dermatol 2005;53:1053-1063.

[c]See Use of Immunophenotyping/Genetic Testing in Differential Diagnosis of Mature B-Cell and NK/T-Cell Neoplasms (NHODG-A).

[d]Typical immunophenotype: CD2+ CD3+ CD5+ CD7- CD4+ CD8- (rarely CD8+) CD30-/+ cytotoxic granule proteins negative.

[e]TCR gene rearrangement results should be interpreted with caution. TCR clonal rearrangement can be seen in non-malignant conditions or may not be demonstrated in all cases of MF/SS. Demonstration of identical clones in skin, blood, and/or lymph node may be helpful in selected cases.

[f]See map for prevalence of HTLV-1 by geographic region.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

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Mycosis Fungoides/Sezary Syndrome

WORKUP

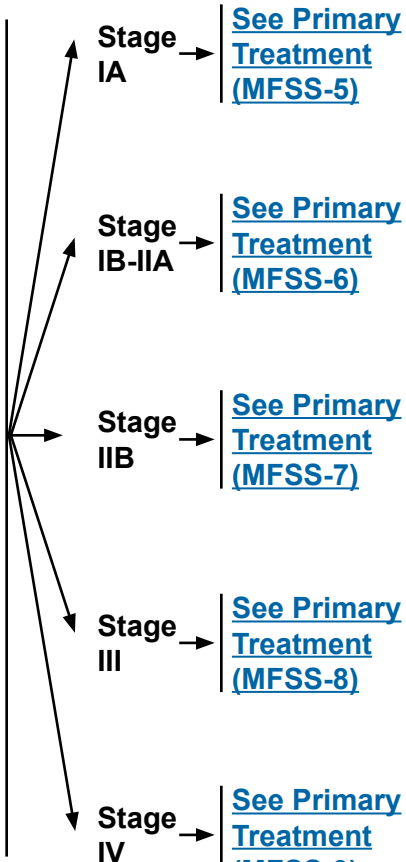
ESSENTIAL:

- Complete physical examination:
  - Examination of entire skin: assessment of % BSA (palm plus digits ≈1% BSA) and type of skin lesion (patch/plaque, tumor, erythroderma)
  - Palpation of peripheral lymph node regions
  - Palpation for organomegaly/masses
- Laboratory studies:[g]
  - CBC with Sezary screen (manual slide review, "Sezary cell prep")
  - Sezary flow cytometric study (optional for T1[h]);
  - TCR gene rearrangement of peripheral blood lymphocytes if blood involvement suspected
  - Comprehensive metabolic panel
  - LDH
- Imaging studies:
  - Chest/abdominal/pelvic contrast-enhanced CT or integrated whole body PET-CT (≥T2 or large cell transformed or folliculotropic MF, or with palpable adenopathy or abnormal laboratory studies)
- Pregnancy testing in women of child-bearing age[i]

USEFUL IN SELECTED CASES:

- Bone marrow biopsy in patients with unexplained hematologic abnormality
- Biopsy (FNA is often inadequate) of suspicious lymph nodes or suspected extracutaneous sites
- Rebiopsy skin if suspicious of large-cell transformation
- Neck CT

STAGE (MFSS-3 and MFSS-4)



[g]Sezary syndrome (B2) is as defined on MFSS-3.
[h]See Discussion for when Sezary flow cytometric study is appropriate in T1 disease.
[i]Many skin-directed and systemic therapies are contraindicated or of unknown safety in pregnancy. Refer to individual drug information.

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TNMB		TNMB Classification and Staging of Mycosis Fungoides and Sezary Syndrome[j,k]
Skin	T1	Limited patches,[l] papules, and/or plaques[m] covering <10% of the skin surface
	T2	Patches,[l] papules, and/or plaques[m] covering ≥10% of the skin surface
	T2a	Patch only
	T2b	Plaque ± patch
	T3	One or more tumors[n] (≥1 cm in diameter)
	T4	Confluence of erythema ≥80% body surface area
Node	N0	No abnormal lymph nodes; biopsy not required
	N1	Abnormal lymph nodes; histopathology Dutch Gr 1 or NCI LN 0-2
	N2	Abnormal lymph nodes; histopathology Dutch Gr 2 or NCI LN 3
	N3	Abnormal lymph nodes; histopathology Dutch Gr 3-4 or NCI LN 4
	NX	Abnormal lymph nodes; no histologic confirmation
Visceral	M0	No visceral organ involvement
	M1	Visceral involvement (must have pathology confirmation and organ involved should be specified)
	MX	Abnormal visceral site; no histologic confirmation
Blood	B0	Absence of significant blood involvement: ≤5% of peripheral blood lymphocytes or <250/mcL are atypical (Sezary) cells or <15% CD4+/CD26- or CD4+/CD7- cells
	B1	Low blood tumor burden: >5% of peripheral blood lymphocytes are atypical (Sezary) cells but do not meet the criteria of B2
	B2	High blood tumor burden: ≥1000/mcL Sezary cells[k] or CD4/CD8 ≥10 or ≥40% CD4+/CD7- or ≥30% CD4+/CD26- cells

[j]Adapted from Olsen E, Vonderheid E, Pimpinelli N, et al. Blood 2007;110:1713-1722.
[k]Sezary syndrome (B2) is defined as a clonal rearrangement of the TCR in the blood (clones should be relevant to clone in the skin) and either ≥1000/mcL or increased CD4 or CD3 cells with CD4/CD8 of ≥10 or increase in CD4 cells with an abnormal phenotype (≥40% CD4+/CD7- or ≥30% CD4+/CD26- of the total lymphocyte count).
[l]Patch = Any size skin lesion without significant elevation or induration.
Presence/absence of hypo- or hyperpigmentation, scale, crusting, and/or poikiloderma should be noted.
[m]Plaque = Any size skin lesion that is elevated or indurated. Presence or absence of scale, crusting, and/or poikiloderma should be noted. Histologic features such as folliculotropism or large-cell transformation (≥25% large cells), CD30+ or CD30-, and clinical features such as ulceration are important to document.
[n]Tumor = at least one >1 cm diameter solid or nodular lesion with evidence of depth and/or vertical growth. Note total number of lesions, total volume of lesions, largest size lesion, and region of body involved. Also note if histologic evidence of large-cell transformation has occurred. Phenotyping for CD30 is encouraged.

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Clinical Staging of MF and SS[j]

	T	N	M	B
IA	1	0	0	0,1
IB	2	0	0	0,1
IIA	1–2	1,2	0	0,1
IIB	3	0–2	0	0,1
IIIA	4	0–2	0	0
IIIB	4	0–2	0	1
IVA_1	1–4	0–2	0	2
IVA_2	1–4	3	0	0–2
IVB	1–4	0–3	1	0–2

[j]Olsen E, Vonderheid E, Pimpinelli N, et al. Blood 2007;110:1713-1722.

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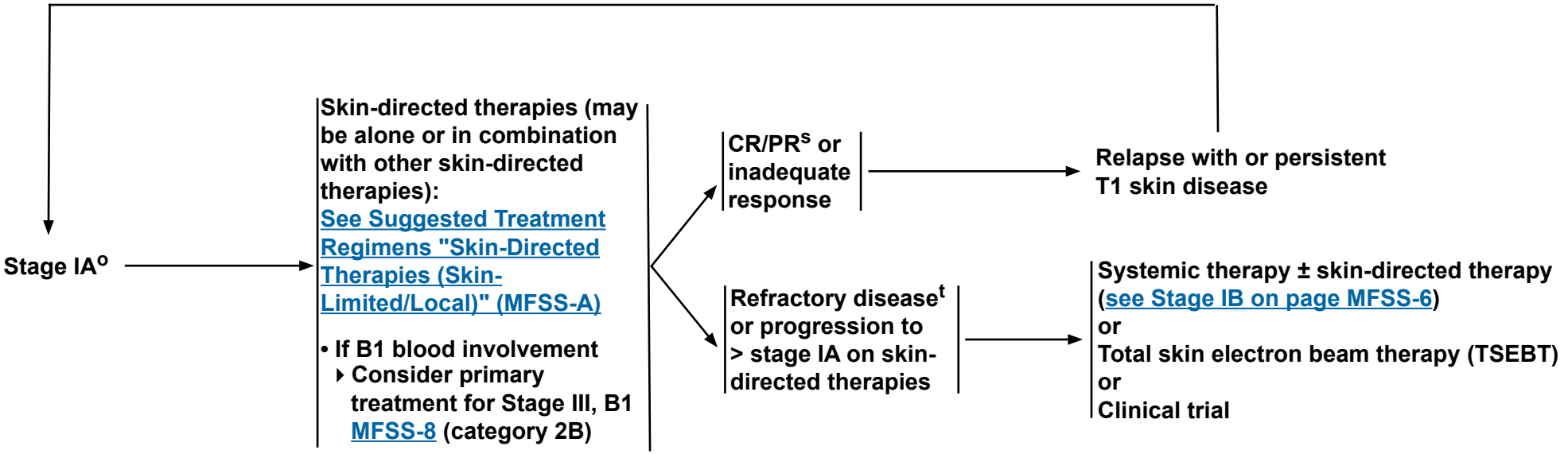
STAGE (MFSS-3 and MFSS-4)

PRIMARY TREATMENT[p,q]

RESPONSE TO THERAPY[r]

See Supportive Care for MF/SS (MFSS-B)



[o]In rare cases of confirmed unilesional MF, RT has been shown to provide long-term remission.
[p]It is preferred that treatment occur at centers with expertise in the management of the disease.
[q]In patients with folliculotropism or histologic large-cell transformed MF, skin disease may be less responsive to topical therapies.
[r]Unlike other NHL subtypes, response criteria for MF/SS has not been demonstrated to correlate with prognosis. Often decisions to continue or switch therapy are on a clinical basis. However, a proposal for detailed response criteria has been published (Olsen E, Whittaker S, Kim YH, et al. J Clin Oncol 2011;29:2598-2607).
[s]Patients achieving a response and/or a clinical benefit should be considered for maintenance or taper regimens to optimize response duration. Patients who relapse often respond well to the same treatment. Patients with a PR should be treated with the other options in the primary treatment list to improve response before moving onto treatment for refractory disease. Patients with relapse or persistent disease after initial primary treatment may be candidates for clinical trials.
[t]Refractory or intolerant to multiple previous therapies.

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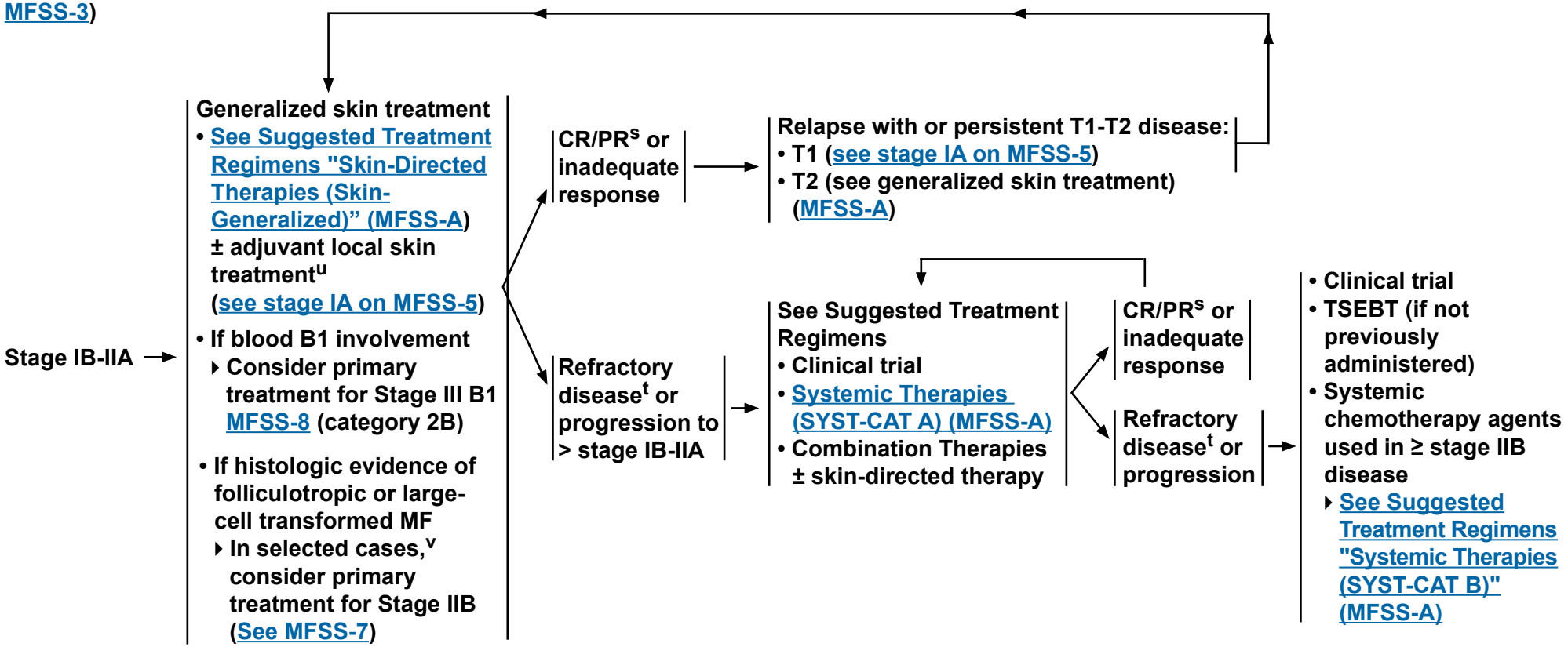
STAGE (MFSS-2 and MFSS-3)

PRIMARY TREATMENT[p]

RESPONSE TO THERAPY[r]

See Supportive Care for MF/SS (MFSS-B)



[p]It is preferred that treatment occur at centers with expertise in the management of the disease.
[r]Unlike other NHL subtypes, response criteria for MF/SS has not been demonstrated to correlate with prognosis. Often decisions to continue or switch therapy are on a clinical basis. However, a proposal for detailed response criteria has been published (Olsen E, Whittaker S, Kim YH, et al. J Clin Oncol 2011;29:2598-2607).
[s]Patients achieving a response and/or a clinical benefit should be considered for maintenance or taper regimens to optimize response duration. Patients who relapse often respond well to the same treatment. Patients with a PR should be treated with the other options in the primary treatment list to improve response before moving onto treatment for refractory disease. Patients with relapse or persistent disease after initial primary treatment may be candidates for clinical trials.
[t]Refractory or intolerant to multiple previous therapies.
[u]For patients with recalcitrant sites after generalized skin treatment, additional local treatment may be needed.
[v]Histologic evidence of folliculotropic or large-cell transformed MF is associated with higher risk of disease progression.

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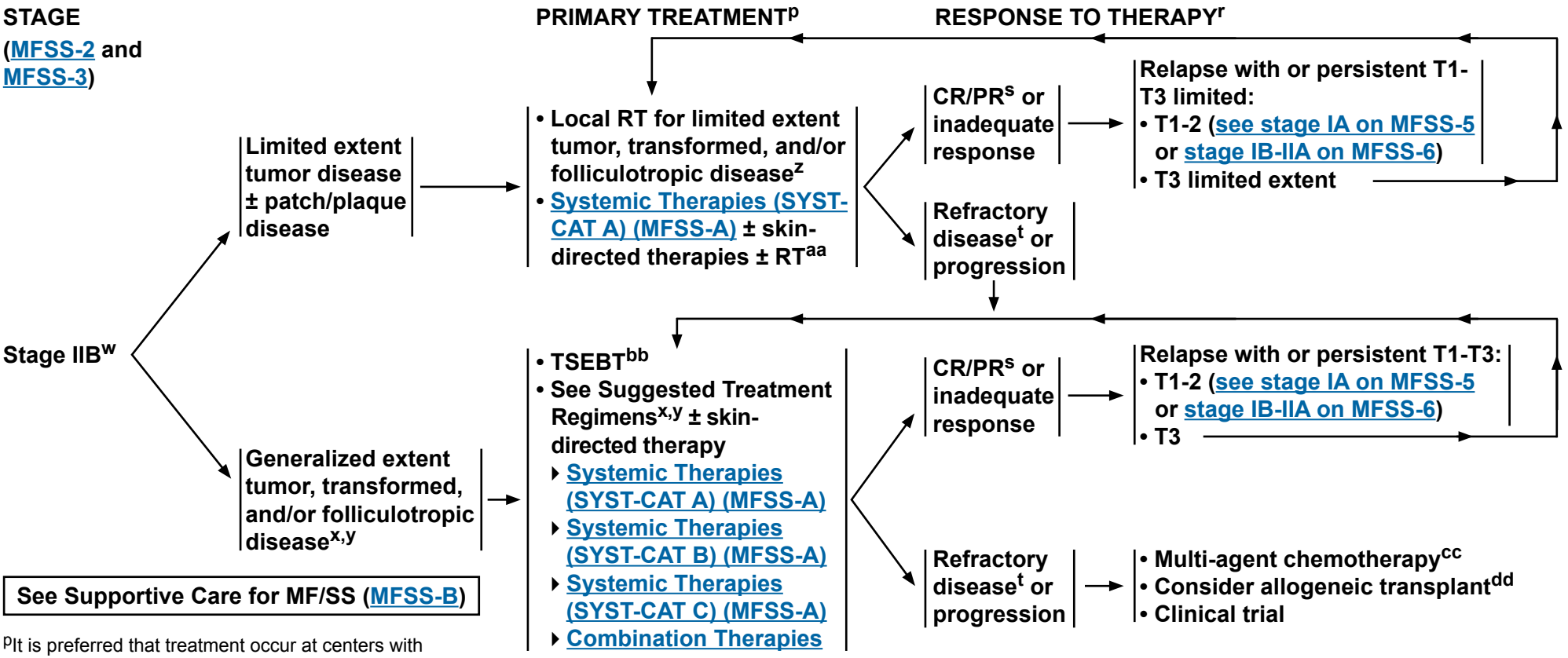

See Supportive Care for MF/SS (MFSS-B)

[p]It is preferred that treatment occur at centers with expertise in the management of the disease.

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[s]Patients achieving a response and/or a clinical benefit should be considered for maintenance or taper regimens to optimize response duration. Patients who relapse often respond well to the same treatment. Patients with a PR should be treated with the other options in the primary treatment list to improve response before moving onto treatment for refractory disease. Patients with relapse or persistent disease after initial primary treatment may be candidates for clinical trials.

[t]Refractory or intolerant to multiple previous therapies.

[w]Rebiopsy if suspect large-cell transformation.

[x]Histologic evidence of LCT often, but not always corresponds to a more aggressive growth rate. If there is no evidence of more aggressive growth, choosing systemic therapies from SYST-CAT A or SYST-CAT B are appropriate. If aggressive growth is seen, then agents listed in SYST-CAT C are preferred.

[y]Patients with indolent/plaque folliculotropic MF (without evidence of LCT) should first be considered for therapies under SYST-CAT A before resorting to treatments listed in SYST-CAT B or SYST-CAT C.

[z]For non-radiated sites, see Stage I-IIA. After patient is rendered disease free by RT, may consider adjuvant systemic biologic therapy (SYST-CAT A) after RT to improve response duration.

[aa]RT is preferred for tumor lesions.

[bb]May consider adjuvant systemic biologic therapy (SYST-CAT A) after TSEBT to improve response duration.

[cc]Most patients are treated with multiple SYST-CAT A/B or combination therapies before receiving multiagent chemotherapy.

[dd]The role of allogeneic HSCT is controversial. See Discussion for further details.

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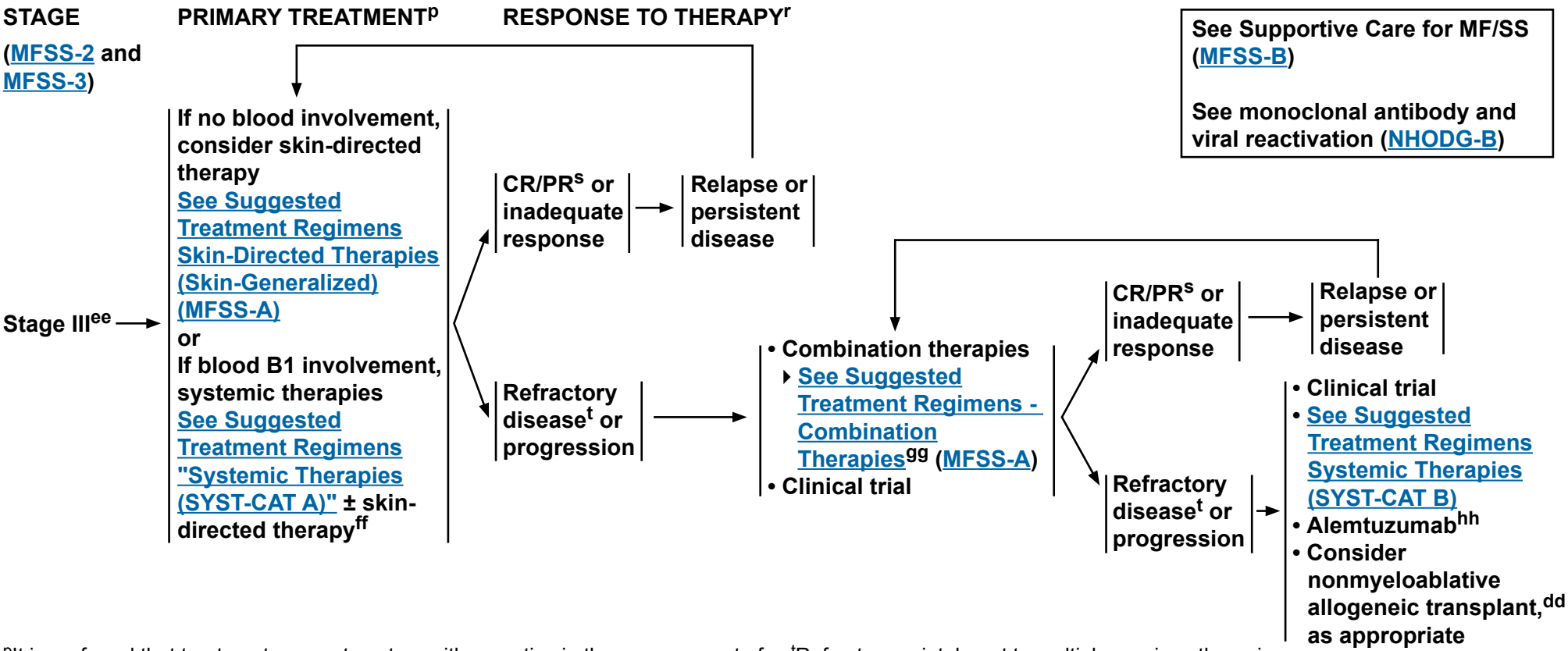

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[r]Unlike other NHL subtypes, response criteria for MF/SS has not been demonstrated to correlate with prognosis. Often decisions to continue or switch therapy are on a clinical basis. However, a proposal for detailed response criteria has been published (Olsen E, Whittaker S, Kim YH, et al. J Clin Oncol 2011;29:2598-2607).

[s]Patients achieving a response and/or a clinical benefit should be considered for maintenance or taper regimens to optimize response duration. Patients who relapse often respond well to the same treatment. Patients with a PR should be treated with the other options in the primary treatment list to improve response before moving onto treatment for refractory disease. Patients with relapse or persistent disease after initial primary treatment may be candidates for clinical trials.

[t]Refractory or intolerant to multiple previous therapies.

[dd]The role of allogeneic HSCT is controversial. See Discussion for further details.

[ee]Generalized skin-directed therapies (other than topical steroids) may not be well-tolerated in stage III and should be used with caution. Phototherapy (PUVA or UVB) or TSEBT can be used successfully.

[ff]Mid-potency topical steroids should be included (± occlusive modality) with any of the primary treatment modalities to reduce skin symptoms. Erythrodermic patients are at increased risk for secondary infection with skin pathogens and systemic antibiotic therapy should be considered.

[gg]Combination therapy options can be considered earlier (primary treatment) depending on treatment availability or symptom severity.

[hh]Lower doses of alemtuzumab administered subcutaneously have shown lower incidence of infectious complications.

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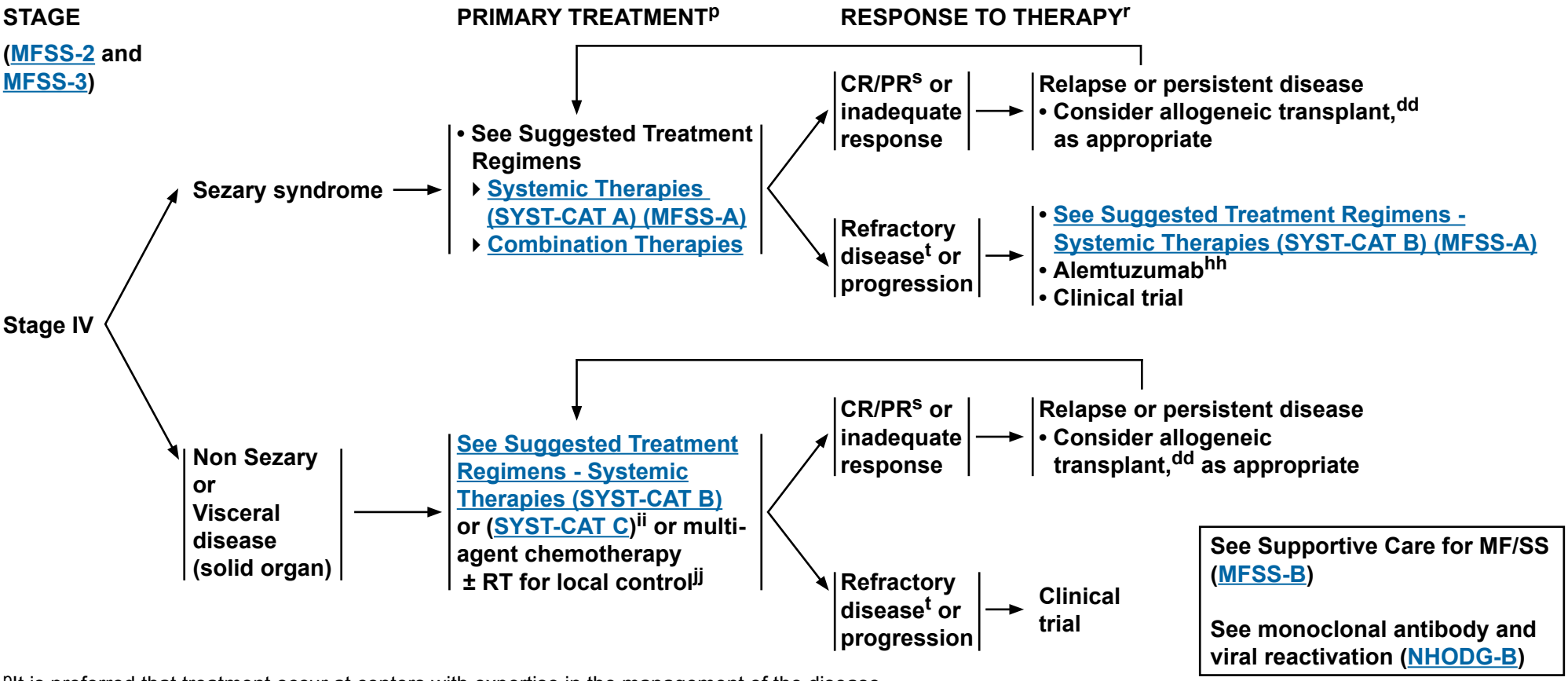

[p]It is preferred that treatment occur at centers with expertise in the management of the disease.
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[s]Patients achieving a response and/or a clinical benefit should be considered for maintenance or taper regimens to optimize response duration. Patients who relapse often respond well to the same treatment. Patients with a PR should be treated with the other options in the primary treatment list to improve response before moving onto treatment for refractory disease. Patients with relapse or persistent disease after initial primary treatment may be candidates for clinical trials.
[t]Refractory or intolerant to multiple previous therapies.
[dd]The role of allogeneic HSCT is controversial. See Discussion for further details.
[hh]Lower doses of alemtuzumab administered subcutaneously have shown lower incidence of infectious complications.
[ii]Patients with stage IV non-Sezary/visceral disease may present with more aggressive growth characteristics. If there is no evidence of more aggressive growth, systemic therapies from SYST-CAT B are appropriate. If aggressive growth is seen, then agents listed in SYST-CAT C are preferred.
[jj]Consider adjuvant systemic biologic therapy (SYST-CAT A) after chemotherapy to improve response duration.

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SUGGESTED TREATMENT REGIMENS[a]

SKIN-DIRECTED THERAPIES

For limited/localized skin involvement (Skin-Limited/Local)
- Topical corticosteroids[b]
- Topical chemotherapy (mechlorethamine [nitrogen mustard])
- Local radiation (8–36 Gy)
- Topical retinoids (bexarotene, tazarotene)
- Phototherapy (UVB, NB-UVB for patch/thin plaques; PUVA for thicker plaques)[c]
- Topical imiquimod

For generalized skin involvement (Skin-Generalized)
- Topical corticosteroids[b]
- Topical chemotherapy (mechlorethamine [nitrogen mustard])
- Phototherapy (UVB, NB-UVB, for patch/thin plaques; PUVA for thicker plaques)[c]
- Total skin electron beam therapy (TSEBT) (12–36 Gy)[d,e] (reserved for those with severe skin symptoms or generalized thick plaque or tumor disease, or poor response to other therapies)

SYSTEMIC THERAPIES

Category A (SYST-CAT A)
- Retinoids (bexarotene, all-trans retinoic acid, isotretinoin [13-cis-retinoic acid], acitretin)[e]
- Interferons (IFN-alpha, IFN-gamma)
- HDAC-inhibitors (vorinostat, romidepsin)[e]
- Extracorporeal photopheresis[f]
- Methotrexate (≤100 mg q week)

Category B (SYST-CAT B)
- First-line therapies (alphabetical order)
  - Brentuximab vedotin
  - Gemcitabine
  - Liposomal doxorubicin
  - Low-dose pralatrexate
- Second-line therapies
  - Chlorambucil
  - Pentostatin
  - Etoposide
  - Cyclophosphamide
  - Temozolomide
  - Methotrexate (>100 mg q week)
  - Bortezomib (category 3)

SYSTEMIC THERAPIES (continued)

Category C (SYST-CAT C)[g] **(alphabetical order)**
- Bortezomib (category 3)
- Brentuximab vedotin
- Gemcitabine
- Liposomal doxorubicin
- Low- or standard-dose pralatrexate
- Romidepsin
- See regimens listed on TCEL-B 2 of 5 (PTCL-NOS)[h]

COMBINATION THERAPIES

Skin-directed + Systemic
- Phototherapy + retinoid[e]
- Phototherapy + IFN
- Phototherapy + photopheresis[f]
- Total skin electron beam + photopheresis[f]

Systemic + Systemic
- Retinoid + IFN
- Photopheresis[f] + retinoid
- Photopheresis[f] + IFN
- Photopheresis[f] + retinoid + IFN

[a]See references for regimens MFSS-A 2 of 4, MFSS-A 3 of 4, and MFSS-A 4 of 4.
[b]Long-term use of topical steroid may be associated with skin atrophy and/or striae formation. This risk worsens with increased potency of the steroid. High-potency steroid used on large skin surfaces may lead to systemic absorption.
[c]Cumulative dose of UV is associated with increased risk of UV-associated skin neoplasms; thus, phototherapy may not be appropriate in patients with a history of extensive squamoproliferative skin neoplasms or basal cell carcinomas or who have had melanoma.
[d]It is common practice to follow TSEBT with systemic therapies such as interferon or bexarotene to maintain response.
[e]Safety of combining TSEBT with systemic retinoids or HDAC inhibitors, such as vorinostat or romidepsin, or combining phototherapy with vorinostat or romidepsin is unknown.
[f]Photopheresis may be more appropriate as systemic therapy in patients with some blood involvement (B1 or B2).
[g]Patients with large cell transformed (LCT) MF and stage IV non-Sezary/visceral disease may present with more aggressive growth characteristics. In general, agents listed in SYST-CAT C are preferred in these circumstances.
[h]Combination regimens are generally reserved for patients with relapsed/refractory or extracutaneous disease.

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SUGGESTED TREATMENT REGIMENS
References

Skin-directed Therapies

Topical corticosteroids

Zackheim HS, Kashani Sabet M, Amin S. Topical corticosteroids for mycosis fungoides. Experience in 79 patients. Arch Dermatol 1998;134(8):949-954.

Zackheim HS. Treatment of patch stage mycosis fungoides with topical corticosteroids. Dermatol Ther 2003;16:283-287.

Nitrogen mustard (mechlorethamine hydrochloride)

Kim YH, Martinez G, Varghese A, Hoppe RT. Topical nitrogen mustard in the management of mycosis fungoides: Update of the Stanford experience. Arch Dermatol 2003;139:165-173.

Lessin SR, Duvic M, Guitart J, et al. Topical chemotherapy in cutaneous T-cell lymphoma: positive results of a randomized, controlled, multicenter trial testing the efficacy and safety of a novel mechlorethamine, 0.02%, gel in mycosis fungoides. JAMA Dermatol 2013;149:25-32.

Local radiation

Wilson LD, Kacinski BM, Jones GW. Local superficial radiotherapy in the management of minimal stage IA cutaneous T-cell lymphoma (Mycosis Fungoides). Int J Radiat Oncol Biol Phys 1998;40:109-115.

Neelis KJ, Schimmel EC, Vermeer MH, et al. Low-dose palliative radiotherapy for cutaneous B- and T-cell lymphomas. Int J Radiat Oncol Biol Phys 2009;74:154-158.

Thomas TO, Agrawal P, Guitart J, et al. Outcome of patients treated with a single-fraction dose of palliative radiation for cutaneous T-cell lymphoma. Int J Radiat Oncol Biol Phys 2013;85:747-753

Topical bexarotene

Breneman D, Duvic M, Kuzel T, et al. Phase 1 and 2 trial of bexarotene gel for skin directed treatment of patients with cutaneous T cell lymphoma. Arch Dermatol 2002;138:325-332.

Heald P, Mehlmauer M, Martin AG, et al. Topical bexarotene therapy for patients with refractory or persistent early stage cutaneous T cell lymphoma: results of the phase III clinical trial. J Am Acad Dermatol 2003;49:801-815.

Tazarotene Gel

Apisarnthanarax N, Talpur R, Ward S, Ni X, Kim HW, Duvic M. Tazarotene 0.1% gel for refractory mycosis fungoides lesions: an open-label pilot study. J Am Acad Dermatol 2004;50:600-607.

Topical imiquimod

Deeths MJ, Chapman JT, Dellavalle RP, Zeng C, Aeling JL. Treatment of patch and plaque stage mycosis fungoides with imiquimod 5% cream. J Am Acad Dermatol 2005;52:275-280.

Phototherapy (UVB and PUVA)

Gathers RC, Scherschun L, Malick F, Fivenson DP, Lim HW. Narrowband UVB phototherapy for early stage mycosis fungoides. J Am Acad Dermatol 2002;47:191-197.

Querfeld C, Rosen ST, Kuzel TM, et al. Long term follow up of patients with early stage cutaneous T cell lymphoma who achieved complete remission with psoralen plus UVA monotherapy. Arch Dermatol 2005;141:305-311.

Ponte P, Serrao V, Apetato M. Efficacy of narrowband UVB vs. PUVA in patients with early-stage mycosis fungoides. J Eur Acad Dermatol Venereol 2010;24:716-721.

Total skin electron beam therapy (TSEBT)

Chinn DM, Chow S, Kim YH, Hoppe RT. Total skin electron beam therapy with or without adjuvant topical nitrogen mustard or nitrogen mustard alone as initial treatment of T2 and T3 mycosis fungoides. Int J Radiat Oncol Biol Phys 1999;43:951-958.

Ysebaert L, Truc G, Dalac S et al. Ultimate results of radiation therapy for T1-T2 mycosis fungoides. Int J Radiat Oncol Biol Phys 2004;58:1128-1134.

Harrison C, Young J, Navi D, et al. Revisiting low-dose total skin electron beam therapy in mycosis fungoides. Int J Radiat Oncol Biol Phys 2011;81:e651-657.

Hoppe RT, Harrison C, Tavallaee M, et al. Low-dose total skin electron beam therapy as an effective modality to reduce disease burden in patients with mycosis fungoides: results of a pooled analysis from 3 phase-II clinical trials. J Am Acad Dermatol 2015;72:286-292.

Systemic Therapies

Alemtuzumab for Sezary syndrome ± lymph node disease

Lundin J, Hagberg H, Repp R, et al. Phase 2 study of alemtuzumab (anti-CD52 monoclonal antibody) in patients with advanced mycosis fungoides/Sezary syndrome. Blood 2003;101:4267-4272.

Bernengo MG, Quaglino P, Comessatti A, et al. Low-dose intermittent alemtuzumab in the treatment of Sezary syndrome: clinical and immunologic findings in 14 patients. Haematologica 2007;92:784-794.

Gautschi O, Blumenthal N, Streit M, et al. Successful treatment of chemotherapy-refractory Sezary syndrome with alemtuzumab (Campath-1H). Eur J Haematol 2004;72:61-63.

Querfeld C, Mehta N, Rosen ST, et al. Alemtuzumab for relapsed and refractory erythrodermic cutaneous T-cell lymphoma: a single institution experience from the Robert H. Lurie Comprehensive Cancer Center. Leuk Lymphoma 2009;50:1969-1976.

Bortezomib

Zinzani PL, Musuraca G, Tani M, et al. Phase II trial of proteasome inhibitor bortezomib in patients with relapsed or refractory cutaneous T-cell lymphoma. J Clin Oncol 2007;25:4293-4297.

Brentuximab vedotin

Duvic M, Tetzlaff M, Gangar P, et al. Results of a Phase II Trial of Brentuximab Vedotin for CD30+ Cutaneous T-Cell Lymphoma and Lymphomatoid Papulosis. J Clin Oncol 2015.

Kim YH, Tavallaee M, Sundram U, et al. Phase II investigator-initiated study of brentuximab vedotin in mycosis fungoides and Sezary syndrome with variable CD30 expression level: A multi-institution collaborative project. J Clin Oncol 2015.

Retinoids

Zhang C, Duvic M. Treatment of cutaneous T-cell lymphoma with retinoids. Dermatol Ther 2006;19:264-271.

Duvic M, Martin AG, Kim Y, et al. Phase 2 and 3 clinical trial of oral bexarotene (Targretin capsules) for the treatment of refractory or persistent early-stage cutaneous T-cell lymphoma. Arch Dermatol 2001;137:581-593.

Duvic M, Hymes K, Heald P, et al. Bexarotene is effective and safe for treatment of refractory advanced-stage cutaneous T-cell lymphoma: multinational phase II-III trial results. J Clin Oncol 2001;19:2456-2471.

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SUGGESTED TREATMENT REGIMENS
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Systemic Therapies Continued

Interferon

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SUGGESTED TREATMENT REGIMENS
References

Combination Therapies

Skin-directed + Systemic

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SUPPORTIVE CARE FOR MF/SS

Pruritus

- Assessment
  - Pruritus should be assessed at each visit using consistent measurements
  - Generalized pruritus and localized pruritus should be distinguished
  - Correlation between sites of disease and localization of pruritus should be noted
  - Other potential causes for pruritus should be ruled out

- Treatment
  - Moisturizers and emollients
  - Topical steroid (appropriate strength for body region) ± occlusion
  - Optimize skin-directed and systemic therapy
  - Topical preparations - camphor/menthol formulations, pramoxine formulations
  - Systemic agents
    - ◊ First-line
      - – Antihistamines
      - – Doxepin
      - – Gabapentin
    - ◊ Second-line
      - – Aprepitant
      - – Mirtazapine
      - – Selective serotonin reuptake inhibitors
    - ◊ Third-line
      - – Naltrexone

Infections

- Active or Suspected Infections
  - Cutaneous viral infections
    - ◊ High risk for skin dissemination of localized viral infections (HSV/VZV)
  - Erythroderma:
    - ◊ Skin swab and nares cultures for Staphylococcus aureus (S. aureus) infection or colonization
    - ◊ Intranasal mupirocin
    - ◊ Oral dicloxacillin or cephalexin
    - ◊ Sulfamethoxazole/trimethoprim, doxycycline if suspect MRSA
    - ◊ Vancomycin if no improvement or bacteremia
    - ◊ Bleach baths or soaks (if limited area)
  - Ulcerated and necrotic tumors:
    - ◊ Gram-negative rods (GNR) common in necrotic tumors may lead to bacteremia and sepsis
    - ◊ If high suspicion for infection, obtain blood cultures, start antibiotics even if fever absent
    - ◊ Role of wound cultures not clear due to colonization
    - ◊ Empirical therapy for both GNR and gram-positive coccal infections is necessary initially
- Prophylaxis
  - Optimize skin barrier protection
  - Mupirocin for S. aureus colonization
  - Bleach baths or soaks (if limited area)
  - Avoid central lines (especially in erythrodermic patients)
  - For patients receiving alemtuzumab, see NHODG-B.

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