Primary cutaneous T-cell lymphoma (mycosis fungoides and Sézary syndrome)

Part II. Prognosis, management, and future directions

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Learning Objectives

After completing this learning activity, participants should be able to identify topical and skin-directed therapy for patch, plaque, and tumor stage MF; demonstrate a fundamental understanding of systemic treatment options in tumor stage MF/ erythrodermic MF and SS; and identify treatment options for alleviation of patient symptoms in advanced stage MF/SS.

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Both mycosis fungoides (MF) and Sézary syndrome (SS) have a chronic, relapsing course, with patients frequently undergoing multiple, consecutive therapies. Treatment is aimed at the clearance of skin disease, the minimization of recurrence, the prevention of disease progression, and the preservation of quality of life. Other important considerations are symptom severity, including pruritus and patient age/comorbidities. In general, for limited patch and plaque disease, patients have excellent prognosis on ≥ 1 topical formulations, including topical corticosteroids and nitrogen mustard, with widespread patch/plaque disease often requiring phototherapy. In refractory early stage MF, transformed MF, and folliculotropic MF, a combination of skin-directed therapy plus low-dose immunomodulators (eg, interferon or bexarotene) may be effective. Patients with advanced and erythrodermic MF/SS can have profound immunosuppression, with treatments targeting tumor cells aimed for immune reconstitution. Biologic agents or targeted therapies either alone or in combination—including immunomodulators and histone-deacetylase inhibitors—are tried first, with more immunosuppressive therapies, such as alemtuzumab or chemotherapy, being generally reserved for refractory or rapidly progressive disease or extensive lymph node and metastatic involvement. Recently, an increased understanding of the pathogenesis of MF and SS with identification of important molecular markers has led to the development of new targeted therapies that are currently being explored in clinical trials in advanced MF and SS. (J Am Acad Dermatol 2014;70:223.e1-17.)

Key words: cutaneous T-cell lymphoma; immunomodulators; mycosis fungoides; phototherapy; prognosis; Sézary syndrome; skin-directed treatment; staging; systemic treatment; targeted therapies; topical corticosteroids; topical nitrogen mustard; topical retinoids/rexinoids.

The treatment of mycosis fungoides (MF) and Sézary syndrome (SS) is primarily determined by disease extent and the impact on quality of life, prognostic factors (eg, folliculotropic MF and large cell transformation), and patient age/comorbidities. Early stage MF (stages IA-IIA), with disease primarily confined to the skin, has a favorable prognosis, with skin-directed therapies as first-line treatment. Prolonged complete remissions have been obtained, although disease cure is unclear.

Advanced stage MF/SS (stages IIB-IVB) is often treatment refractory and results in an unfavorable prognosis; treatment is aimed at reducing the tumor burden, delaying disease progression, and preserving quality of life. Current approaches include immunobiologic and targeted therapies, but the duration of clinical response is often short. Single/multiagent chemotherapy should be reserved for cases that are refractory to treatment. The revised guidelines by the International Society for Cutaneous Lymphomas (ISCL), the United States Cutaneous Lymphoma Consortium (USCLC), and the Cutaneous Lymphoma Task Force of the European Organization of Research and Treatment of Cancer (EORTC) include treatment options for MF/SS that match the National Comprehensive

Abbreviations used:

BSA:	body surface area
CR:	complete response
CRR:	complete response rate
CTCL:	cutaneous T-cell lymphoma
ECP:	extracorporeal photopheresis
EORTC:	European Organization of Research and Treatment of Cancer
HDACi:	histone deacetylase inhibitor
IFNα:	interferon-alfa
ISCL:	International Society for Cutaneous Lymphoma
MF:	mycosis fungoides
mSWAT:	modified severity-weighted assessment tool
NBUVB:	narrowband ultraviolet B light
NCCN:	National Comprehensive Cancer Network
NK:	natural killer
NM:	nitrogen mustard
NMSC:	nonmelanoma skin cancer
ORR:	overall response rate
PUVA:	psoralen plus ultraviolet A light phototherapy
RAR:	retinoic acid receptor
RXR:	retinoid X receptor
SS:	Sézary syndrome
TNMB:	tumor, node, metastasis, blood
TSEBT:	total skin electron beam therapy
USCLC:	United States Cutaneous Lymphoma Consortium
UVB:	ultraviolet B light

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