

PROGNOSTIC FACTORS

Mycosis Fungoides and Sézary Syndrome

Prognostic Factors Required for Stage Grouping

Factor	Definition	Clinical significance	Level of evidence
Blood	Extent involvement B1: >5% B2: >1,000/ μ L (flow cytometry)	Overall survival	I

Additional Factors Recommended for Clinical Care

Factor	Definition	Clinical significance	Level of evidence
Skin	Patch, plaque, tumor, erythroderma, extent involvement (i.e., <10%)	Therapy consideration, overall survival	I
Nodes	Extent involvement (pathology)	Overall survival	I
Visceral	Location (pathology)	Overall survival	I
Folliculotropic MF	Pathology	Therapy consideration, overall survival	I
Large cell transformation	Pathology	Overall survival, treatment selection (a subset expresses CD30 and is responsive to brentuximab vedotin)	I

Primary Cutaneous B-Cell/T-Cell Lymphoma (Non-MF/SS) Lymphoma

Prognostic Factors Required for Stage Grouping

Beyond the factors used to assign T, N, or M categories, no additional prognostic factors are required for stage grouping.²

Additional Factors Recommended for Clinical Care

The Lugano classification includes no prognostic variable for determination of stage. A separate TNM staging system is used for non-MF/SS lymphomas.

Factor	Definition	Clinical significance	Level of evidence
Skin	Extent involvement; solitary, regional, generalized (clinical)	Therapy consideration, overall survival	I
Nodes	Involvement of draining lymph node, nondraining or central (pathology)	Overall survival	I
Metastases	Visceral organ (pathology)	Overall survival	I
Pathology	Histologic type, immunophenotype	Affects choice of therapy and overall survival	I

DEFINITIONS OF AJCC TNM

Mycosis Fungoides and Sézary Syndrome

Definition of Primary Tumor (T)

ISCL/EORTC revision to the classification of mycosis fungoides and Sézary Syndrome

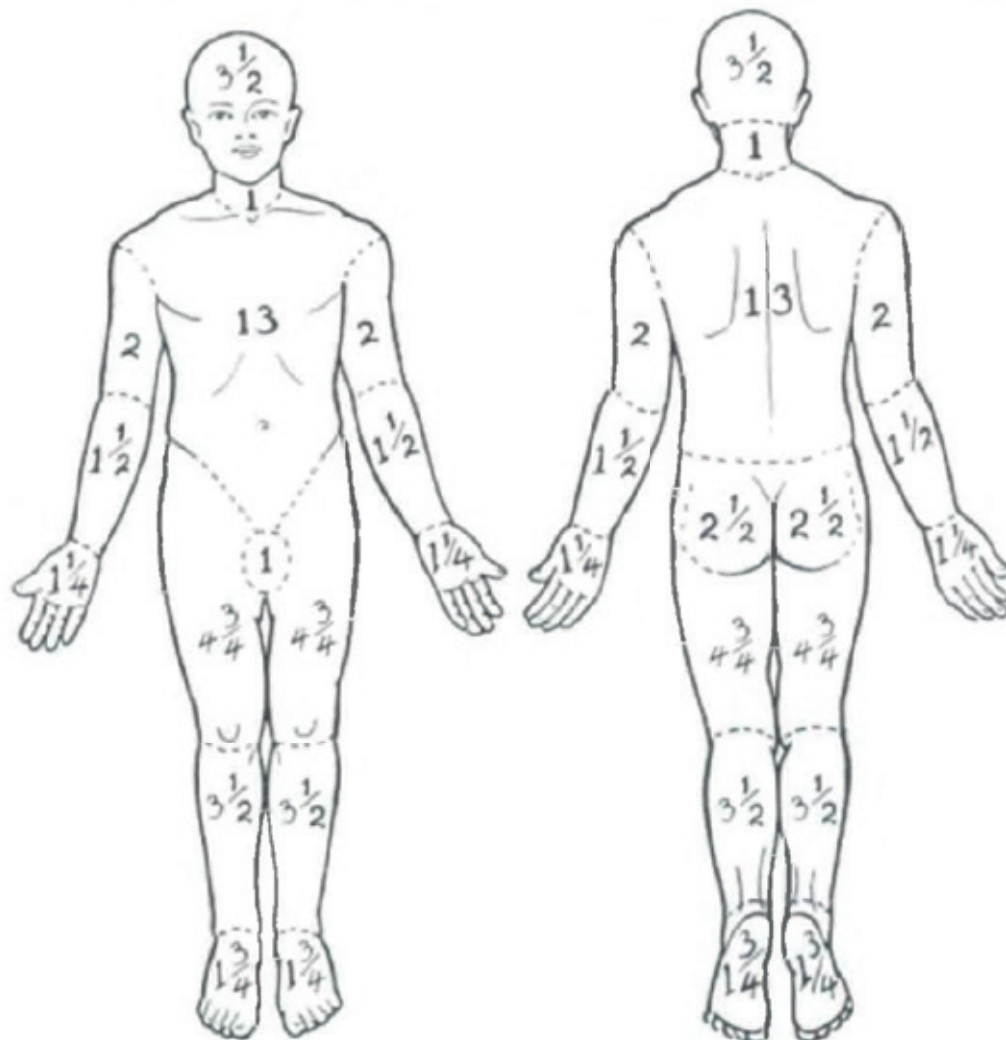
Skin

T Category	T Criteria
T1	Limited patches,* papules, and/or plaques** covering < 10% of the skin surface
T1a	T1a (patch only)
T1b	T1b (plaque $\pm$ patch)
T2	Patches, papules, or plaques covering $\geq$ 10% of the skin surface
T2a	T2a (patch only)
T2b	T2b (plaque $\pm$ patch)
T3	One or more tumors*** ($\geq$ cm in diameter)
T4	Confluence of erythema covering $\geq$ 80% of body surface area

*For skin, *patch* indicates any size skin lesion without significant elevation or induration. Presence/absence of hypo- or hyperpigmentation, scale, crusting, and/or poikiloderma should be noted.

**For skin, *plaque* indicates any size skin lesion that is elevated or indurated. Presence/absence of scale, crusting, and/or poikiloderma should be noted. Histologic features such as folliculotropism, large cell transformation (>25% large cells), and CD30 positivity or negativity, as well as clinical features such as ulceration, are important to document.

***For skin, *tumor* indicates at least one 1-cm diameter solid or nodular lesion with evidence of depth and/or vertical growth. Note the total number of lesions, total volume of lesions, largest size lesion, and region of body involved. Also note whether there is histologic evidence of large cell transformation. Phenotyping for CD30 is encouraged.



Definition of Regional Lymph Node (N)

Node

N Category	N Criteria
NX	Clinically abnormal peripheral lymph nodes; no histologic confirmation
N0	No clinically abnormal peripheral lymph nodes*; biopsy not required
N1	Clinically abnormal peripheral lymph nodes; histopathology Dutch grade 1 or National Cancer Institute (NCI) LN0-2
N1a	Clone negative**
N1b	Clone positive**
N2	Clinically abnormal peripheral lymph nodes; histopathology Dutch grade 2 or NCI LN3
N2a	Clone negative**
N2b	Clone positive**
N3	Clinically abnormal peripheral lymph nodes; Histopathology Dutch grades 3-4 or NCI LN4; clone positive or negative

*For node, *abnormal peripheral lymph node(s)* indicates any palpable peripheral node that on physical examination is firm, irregular, clustered, fixed or ≥ 1.5 cm in diameter. Node groups examined on physical examination include cervical, supraclavicular, epitrochlear, axillary, and inguinal. Central nodes, which generally are not amenable to pathological assessment, currently are not considered in the nodal classification unless used to establish N3 histopathologically.

**A T-cell clone is defined by polymerase chain reaction (PCR) or Southern blot analysis of the TCR gene.

Definition of Distant Metastasis (M)

Visceral

M Category	M Criteria
M0	No visceral organ involvement
M1	Visceral involvement (must have pathology confirmation,* and organ involved should be specified)

*For viscera, spleen and liver may be diagnosed by imaging criteria.

Peripheral Blood Involvement (B)

B Category	B Criteria
B0	Absence of significant blood involvement: $\geq 5\%$ of peripheral blood lymphocytes are atypical (Sézary) cells*
B0a	Clone negative**
B0b	Clone positive**
B1	Low blood tumor burden: $>5\%$ of peripheral blood lymphocytes are atypical (Sézary) cells, but does not meet the criteria of B2

(continued)

B Category	B Criteria
B1a	Clone negative**
B1b	Clone positive**
B2	High blood tumor burden: $\geq 1,000/\mu\text{L}$ Sézary cells* with positive clone**

*For blood, Sézary cells are defined as lymphocytes with hyperconvoluted cerebriform nuclei. If Sézary cells cannot be used to determine tumor burden for B2, then one of the following modified ISCL criteria, along with a positive clonal rearrangement of the TCR, may be used instead: (1) expanded CD4+ or CD3+ cells with a CD4/CD8 ratio of ≥ 10 , or (2) expanded CD4+ cells with abnormal immunophenotype, including loss of CD7 or CD26.

**A T-cell clone is defined by PCR or Southern blot analysis of the TCR gene.

From Olsen et al., with permission from the American Society of Hematology.¹

Table 81.1 Histopathologic staging of lymph nodes in mycosis fungoides and Sézary syndrome

EORTC classification	Dutch system	NCI-VA classification
N1	Grade 1: dermatopathic lymphadenopathy (DL)	LN0: no atypical lymphocytes LN1: occasional and isolated atypical lymphocytes (not arranged in clusters) LN2: many atypical lymphocytes or lymphocytes in 3-6-cell clusters
N2	Grade 2: DL; early involvement by MF (presence of cerebriform nuclei $<7.5\ \mu\text{m}$)	LN3: aggregates of atypical lymphocytes; nodal architecture preserved
N3	Grade 3: partial effacement of lymph node architecture; many atypical cerebriform mononuclear cells Grade 4: complete effacement	LN4: partial/complete effacement of nodal architecture by atypical lymphocytes or frankly neoplastic cells

From Olsen et al.,¹ with permission from the American Society of Hematology.

AJCC PROGNOSTIC STAGE GROUPS

Mycosis Fungoides and Sézary Syndrome

ISCL/EORTC revision to the staging of mycosis fungoides and Sézary syndrome

When T is...	And N is...	And M is...	And peripheral blood involvement (B) is...	Then the stage group is...
T1	N0	M0	B0,1	IA
T2	N0	M0	B0,1	IB

(continued)

ISCL/EORTC revision to the staging of mycosis fungoides and Sézary syndrome

When T is...	And N is...	And M is...	And peripheral blood involvement (B) is...	Then the stage group is...
T1,2	N1,2	M0	B0,1	IIA
T3	N0-2	M0	B0,1	IIB
T4	N0-2	M0	B0,1	III
T4	N0-2	M0	B0	IIIA
T4	N0-2	M0	B1	IIIB
T1-4	N0-2	M0	B2	IVA1
T1-4	N3	M0	B0-2	IVA2
T1-4	N0-3	M1	B0-2	IVB

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REGISTRY DATA COLLECTION VARIABLES

Mycosis Fungoides and Sézary Syndrome

1. Peripheral blood involvement

DEFINITIONS OF AJCC TNM

Primary Cutaneous B-Cell/T-Cell Lymphoma (Non-MF/SS) Lymphoma

Definition of Primary Tumor (T)

T Category	T Criteria
T1	Solitary skin involvement
T1a	Solitary lesion $<5\ \text{cm}$
T1b	Solitary lesion $\geq 5\ \text{cm}$
T2	Regional skin involvement: multiple lesions limited to one body region or two contiguous body regions
T2a	All disease encompassing in a $<15\text{-cm}$ circular area
T2b	All disease encompassing in a $\geq 15\text{-cm}$ and $<30\text{-cm}$ circular area
T2c	All disease encompassing in a $\geq 30\text{-cm}$ circular area
T3	Generalized skin involvement

Definition of Regional Lymph Node (N)

N Category	N Criteria
NX	Regional lymph nodes cannot be assessed
N0	No clinical or pathological lymph node involvement
N1	Involvement of one peripheral node region that drains an area of current or prior skin involvement
N2	Involvement of two or more peripheral node regions or involvement of any lymph node region that does not drain an area of current or prior skin involvement
N3	Involvement of cenrowal nodes