

Joint British Association of Dermatologists and U.K. Cutaneous Lymphoma Group guidelines for the management of primary cutaneous T-cell lymphomas

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MAJOR RECOMMENDATIONS

Initial Assessment

- Repeated skin biopsies (ellipse rather than punch) are often required to confirm a diagnosis of cutaneous T-cell lymphoma (CTCL).
- Histology, immunophenotypic, and preferably T-cell receptor (TCR) gene analysis should be performed on all tissue samples (ideally molecular studies require fresh tissue).
- All patients (with the possible exception of early stage mycosis fungoides [stage IA] and lymphomatoid papulosis) should ideally be reviewed by an appropriate multidisciplinary team (MDT) for confirmation of the diagnosis and to establish a management strategy.
- Initial staging computed tomography (CT) scans are required in all patients with the exception of those with early stages of mycosis fungoides (stage IA/IB) and lymphomatoid papulosis.
- At diagnosis peripheral blood samples should be analysed for total white cell, lymphocyte, and Sézary cell counts, serum lactate dehydrogenase (LDH), liver and renal function, lymphocyte subsets, CD4/CD8 ratios, human T-cell lymphotropic virus (HTLV)-I serology and, preferably, TCR gene analysis.
- Bone marrow aspirate or trephine biopsies are required for CTCL variants (with the exception of lymphomatoid papulosis) and may also be appropriate for those with late stages of mycosis fungoides (stage IIB or above). (**Grade A/Level III**)

Staging

TNM classification

T1: Patches or plaques < 10% body surface area

T2: Patches or plaques > 10% body surface area

T3: Tumours

T4: Erythroderma

N0: No palpable nodes

N1: Palpable nodes without histological involvement (dermatopathic)

N2: Non-palpable nodes with histological involvement

N3: Palpable nodes with histological involvement

N4: M0: No visceral disease

M1: Visceral disease

B0: No haematological involvement

B1: Sezary count > 5% of total peripheral blood lymphocytes

Bunn & Lambert clinical staging system

- Stage IA: T1 N0
- Stage IB: T2 N0
- Stage IIA: T1-2 N1
- Stage IIB: T3 N0-1
- Stage III: T4 N0-1
- Stage IVA: T-any N2- 3
- Stage IVB: T-any N-any M1

Histology

- The presence or absence of epidermotropism should be documented.
- The depth of the infiltrate should be noted.
- The morphology or cytology of the atypical cells and presence of large cell transformation, folliculotropism, syringotropism, granuloma formation, angiocentricity, and subcutaneous infiltration should be mentioned.
- Immunophenotypic studies should be performed on paraffin-embedded sections and include the T-cell markers CD2, CD3, CD4, CD8, B-cell marker CD20, and the activation marker CD30. Additional markers such as p53 may have prognostic significance in mycosis fungoides. Markers of cytotoxic function such as TIA-I, the monocyte/macrophage marker CD68 and natural killer (NK) cell marker CD56 may be useful for specific CTCL variants.
- Ideally all pathology results should be reviewed by a central panel (usually within cancer centres) as recommended for specialized pathology services.
- The histology, after correlation with the clinical features, should be classified according to the World Health Organization (WHO) European Organization for Research and Treatment of Cancer (EORTC) classification of cutaneous lymphomas Blood 2005; 105: 3768-3785. (**Grade A/Level III**)

Prognosis

- Prognosis in mycosis fungoides (and clinical variants) is related to age at presentation (worse if >60 years), to the stage of the disease, and possibly to the presence of a peripheral blood T-cell clone; some mycosis fungoides clinical variants may have a better prognosis.
- In Sézary syndrome the median survival is 32 months from diagnosis.
- Primary cutaneous CD30+ lymphoproliferative disorders without peripheral nodal disease have an excellent prognosis (range 96-100% 5-year survival).
- The prognosis of other types of CTCL is generally poor with the frequent development of systemic disease. (**Grade A/Level Iii**)

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Treatment of Mycosis Fungoides and Sézary Syndrome

- Skin-directed therapy (topical therapy, superficial radiotherapy, and phototherapy) is appropriate treatment for patients with early stages of mycosis fungoides (stages IA-IIA) with the choice of therapy dependent on the extent of cutaneous disease and plaque thickness. **(Grade A/Level I)**
- Combined psoralen + ultraviolet A (PUVA) and alpha-interferon therapy can be effective for patients with resistant early-stage disease (stage IB-IIA). **(Grade A/Level Iii)**
- Patients with later stages of mycosis fungoides (stage IIB or higher) will require some form of systemic therapy. **(Grade A/Level Iiii)**
- CTCL is a very radiosensitive malignancy and several fractions (2-3) of low energy (80-120 kV) superficial radiotherapy are appropriate for many patients. **(Grade A/Level Iiii)**
- Chemotherapy regimens in advanced stages of mycosis fungoides generally achieve complete responses in the region of 30% but these are short-lived. **(Grade B/Level Iiii)**
- Erythrodermic CTCL patients should be considered for immunotherapy and extracorporeal photopheresis (ECP), as responses to chemotherapy are generally poor. **(Grade A/Level Iiii)**
- Total skin electron beam (TSEB) therapy is an effective treatment for stage IB and stage III mycosis fungoides but is not sufficient alone for stage IIB disease or those with significant haematological involvement. **(Grade A/Level Iiii)**
- New agents such as bexarotene and denileukin diftitox offer important therapeutic alternatives which are currently being evaluated. **(Grade A/Level Iiii)**
- In treatment-resistant cases of late stage disease, palliative radiotherapy and/or chemotherapy may produce a significant short-term benefit but the patient's quality of life should always be given priority. **(Grade B/Level III)**
- All patients and especially those with late stages of disease (>IIA) should be considered for entry into well designed randomized controlled clinical trials.

Treatment of mycosis fungoides/Sézary syndrome

Stage	First line	Second line	Experimental	Not suitable
IA	SDT or no therapy	SDT or no therapy	Bexarotene gel	Chemotherapy
IB	SDT	alpha-interferon + PUVA, TSEB	Denileukin diftitox, bexarotene	Chemotherapy
IIA	SDT	alpha-interferon + PUVA, TSEB	Denileukin diftitox, bexarotene	Chemotherapy
IIB	Radiotherapy or TSEB, chemotherapy	alpha-interferon, denileukin diftitox*, bexarotene	Autologous PBSCT, mini-allograft	Ciclosporin
III	PUVA ± alpha-interferon, ECP ± alpha-interferon, methotrexate	TSEB, bexarotene, denileukin diftitox,* chemotherapy, alemtuzumab	Autologous PBSCT, mini-allograft	Ciclosporin
IVA	Radiotherapy or TSEB, chemotherapy	alpha-interferon, denileukin diftitox,* alemtuzumab bexarotene	Autologous PBSCT, mini-allograft	Ciclosporin
IVB	Radiotherapy, chemotherapy	Palliative therapy	Mini-allograft	

PBSCT, peripheral blood stem cell transplant; ECP, extracorporeal photopheresis; TSEB, total skin electron beam; PUVA, psoralen + ultraviolet A; SDT, skin-directed therapy including topical emollients, steroids, mechlorethamine, carmustine, bexarotene gel, UVB/PUVA, superficial radiotherapy. Stage III includes Sézary syndrome, although some cases of Sézary syndrome will be stage IVA. ECP is ideal for those patients with peripheral blood involvement.

***Not yet licensed in Europe.**

Reference:

Br J Dermatol 2003 Dec;149(6):1095-1107

Production of this guideline summary was kindly sponsored by the British National Formulary