

Cutaneous lymphomas: tests, treatment by setting, systemic options and problems during treatment

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A. Diagnosis and staging tests and what they change

Staging mycosis fungoides and Sézary syndrome: TNMB, then the stage

Clinical stage	
T1	<10% BSA patches/plaques
T2	≥10% BSA patches/plaques
T3	One or more tumours ≥1 cm
T4	Erythema ≥80% BSA
NO–N2	Nodes normal or not effaced
N3	Node effaced (Dutch 3–4)
M1	Visceral (M1a marrow only)
BO	<250/μL abnormal CD4 cells
B1	Between BO and B2
B2	≥1000/μL + skin-matched clone
IA	T1 NO MO BO–1
IB	T2 NO MO BO–1
IIA	T1–2 N1–2 MO BO–1
IIB	T3 NO–2 MO BO–1
IIIA	T4 NO–2 MO BO
IIIB	T4 NO–2 MO B1
IVA1	Any T NO–2 MO B2
IVA2	Any T N3 MO BO–2
IVB	Any T any N M1

Early = IA–IIA (skin-directed treatment); advanced = IIB–IV. Image (CT or PET–CT) only for T2b, T3, T4, nodes >1.5 cm, large cell transformation or B2. Biopsy enlarged nodes by excision (FNA is not enough). Marrow only for unexplained cytopenias. Other cutaneous lymphomas use a separate TNM (T1 solitary, T2 regional, T3 generalised).

MF/SS staging (Olsen 2007 and 2022; Kim 2007 for non-MF cutaneous lymphomas; UpToDate staging review).

Table A. Diagnosis and staging tests and what they change

Test	When	What it changes	Pitfalls
Skin punch biopsy ≥4 mm (most indurated lesion); often several over time	Every suspected MF	ISCL/EORTC score; variant (folliculotropic, LCT)	Topicals in the last 2–4 weeks blur the picture
Excisional or deep incisional biopsy including fat	Nodules, SPTCL, B-cell lymphomas, LyP (2 fresh lesions)	Entity	Shave biopsies are inadequate

Test	When	What it changes	Pitfalls
IHC: CD2, CD3, CD4, CD5, CD7, CD8, CD30, ALK, TCRβF1/γδ, CD56, cytotoxic markers; B-cell panel with BCL2, BCL6, MUM1, CD10, light chains	Every biopsy	Names the entity; CD30 → BV option	Read with the clinical picture: pseudolymphomas mimic all of these
TCR (or IgH) clonality, skin and blood	Equivocal histology; erythroderma; staging B and N	1 ISCL point; B2 needs a skin-matched clone	Clones occur in benign disease and with age
Blood flow cytometry (CD4+CD7-, CD4+CD26-; TRBC1)	Every MF/SS staging	BO/B1/B2; Sézary syndrome	Lymphopenia: use percentages
CBC, chemistry, LDH; HTLV-1 serology if from an endemic area or flower cells/high calcium	Baseline	CLIP1; ATLL excluded	ATLL was 17% of cutaneous T-cell lymphomas in one South Indian series
CT or PET-CT	MF with T2b, T3, T4, nodes >1.5 cm, LCT or B2; all non-MF cutaneous lymphomas	N and M stage; primary vs secondary skin lymphoma	Chest X-ray if no CT/PET in limited MF
Node excision; marrow biopsy only if cytopenias or equivocal PET	Enlarged node; suspected systemic disease	N3 (IVA2); M1	FNA cannot grade nodal involvement

B. Treatment by setting

Early-stage MF (IA–IIA): skin-directed treatments and what they achieve

Reported response rates (%), different studies and endpoints



Stage IA: topical steroid first; then mechlorethamine, bexarotene gel, imiquimod or local RT. IB–IIA thin plaques: steroid, mechlorethamine, NBUVB or PUVA. Thick, widespread, symptomatic plaques: TSEBT (low dose 10–12 Gy, repeatable). Folliculotropic MF needs deeper treatment (PUVA, RT); NBUVB alone is usually not enough.

Early aggressive chemotherapy plus electron beam did not improve survival over sequential topical treatment (Kaye 1989). Rotate skin-directed options before systemic drugs.

Skin-directed therapy (Zackheim 1998; Lessin 2013; Phan 2019; Thomas 2013; Hoppe 2015; Kaye 1989; UpToDate early-stage MF review). Mechlorethamine bar = midpoint of 70–80%.

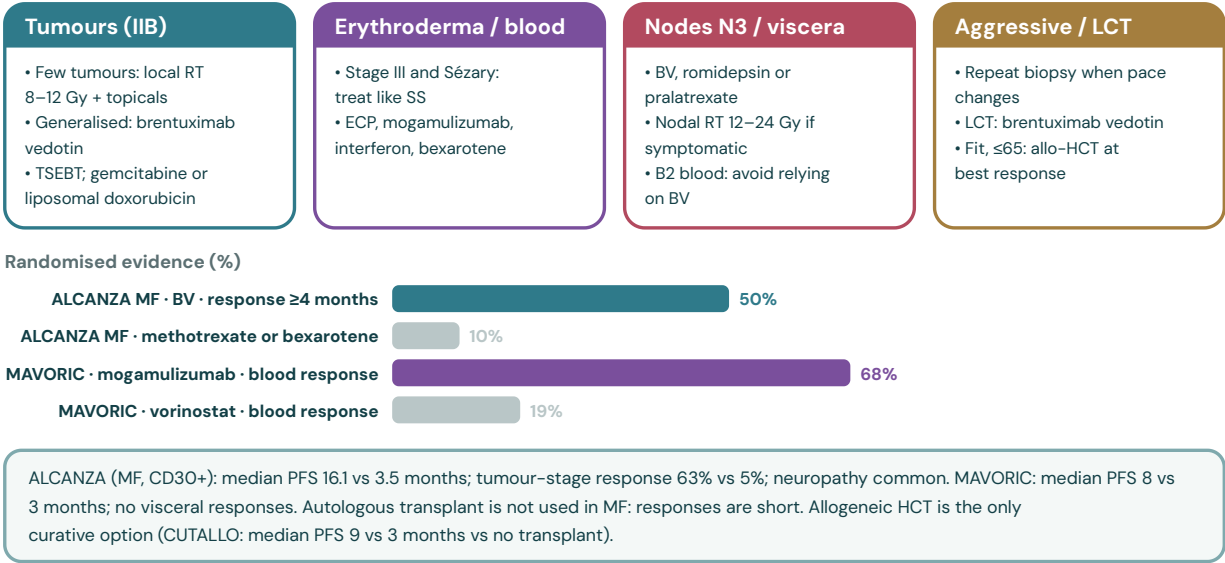
Table B. Treatment by setting

Setting	Standard choice	Key evidence	Notes
MF IA	Potent topical steroid; then mechlorethamine, bexarotene gel, imiquimod, local RT	Zackheim 1998	Rotate skin-directed options before systemic drugs
MF IB–IIA, thin plaques	Steroid, mechlorethamine, NBUVB or PUVA	Phan 2019	PUVA: more CR; both need maintenance tapering
MF IB–IIA, thick widespread plaques	TSEBT (low dose 10–12 Gy), then adjuvant topical, light or retinoid	Hoppe 2015	Add systemic agent if B1, folliculotropic or LCT
MF IIB, few tumours	Local RT 8–12 Gy + topicals	Thomas 2013	Electrons or low-energy x-rays
MF IIB, generalised tumours; LCT	Brentuximab vedotin	ALCANZA	Neuropathy; TSEBT after response
MF III and Sézary IVA	ECP ± interferon, or mogamulizumab	MAVORIC	Treat itch and Staphylococcus too
MF IVB; SS with M1b, LCT or bulky nodes	BV, romidepsin or pralatrexate (MF); gemcitabine or liposomal doxorubicin (SS)	Zinzani 2000, EORTC 21012	RT 12–24 Gy to symptomatic nodes
Advanced MF/SS, fit, ≤65	Allogeneic HCT at best response	CUTALLO	No autologous HCT
LyP	Observe or topical steroid; low-dose methotrexate; PUVA	Kempf 2011	No multiagent chemotherapy
PCFCL or PCMZL, localised	RT (PCFCL 4 Gy response-adapted to 24 Gy; PCMZL 24 Gy) or excision	ILROG 2026	Leg site PCFCL: worse outlook

Setting	Standard choice	Key evidence	Notes
PCFCL extensive; PCMZL multifocal	PCFCL: rituximab; PCMZL: observe, intralesional steroid, low-dose RT	Senff 2008	Chemotherapy rarely
Acral CD8+ or CD4+ small/medium T-LPD	Excision, RT or intralesional steroid	Kempf 2022	Behave like pseudolymphoma
Primary cutaneous ALCL, localised	Excision or involved-site RT (≤ 20 Gy appears enough)	Million 2016	No added RT after excision; no chemotherapy
C-ALCL, multifocal with nodes or symptoms	Brentuximab vedotin (methotrexate if neuropathy)	ALCANZA	Asymptomatic multifocal: observe first
SPTCL	Not yet covered in this module	—	Plan with the lymphoma team; HLH is urgent

C. Systemic options: evidence and best fit

Advanced MF (IIB–IV): choose by compartment



Advanced MF (Prince 2017 and Horwitz 2021, ALCANZA; Kim 2018, MAVORIC; de Masson 2023, CUTALLO; UpToDate advanced MF review).

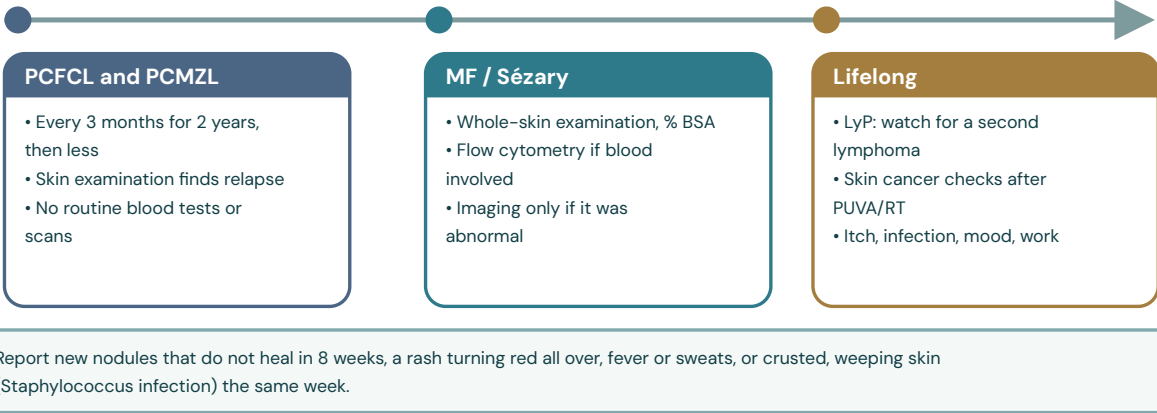
Table C. Systemic options: evidence and best fit

Option	Best for	Evidence	Watch for
Brentuximab vedotin	CD30+ MF (tumours, LCT, nodes); multifocal C–ALCL	ALCANZA : MF response ≥4 months 50% vs 10%; C–ALCL 75% vs 20%, PFS 28 vs 5 months	Peripheral neuropathy; not relied on for B2 blood
Mogamulizumab	Blood and erythrodermic skin (SS, stage III)	MAVORIC : PFS 8 vs 3 months; blood response 68% vs 19%	Avoid in autoimmune disease; caution before allo-HCT
Extracorporeal photopheresis	Erythroderma, blood involvement; combine with interferon or bexarotene	Observational series (response in skin common, CR uncommon)	Specialised centres; slow responses; venous access
Bexarotene, methotrexate, interferon	Patch/plaque and itch in advanced MF; add-on to skin-directed therapy	Less active than BV in ALCANZA	Bexarotene: triglycerides, thyroid
Romidepsin, pralatrexate	Tumours, nodes; MF IVB	Phase 2 (romidepsin 34% overall, 57% blood response)	Romidepsin hard for frail patients

Option	Best for	Evidence	Watch for
Gemcitabine, liposomal doxorubicin	Aggressive or visceral MF/SS	Zinzani 2000 (71%); EORTC 21012 (41%)	Myelosuppression
Rituximab (single agent)	Extensive PCFCL; in-field relapse of PCFCL/PCMZL	Small series; responses often transient	Skin relapse is common
Allogeneic HCT	Advanced MF/SS, fit, best response	CUTALLO ; EBMT (7-year OS 44%)	Non-relapse mortality about 20%

D. Managing problems during treatment

A simple follow-up rhythm for cutaneous lymphomas



Follow-up rhythm (Terhorst 2012; UpToDate PCFCL, PCMZL, LyP and MF reviews). Individualise.

Table D. Managing problems during treatment

Problem	What to do	Notes
Itch (MF, SS)	Emollients after bathing, topical steroid, antihistamines; doxepin at night, gabapentin or pregabalin; mirtazapine, aprepitant or naltrexone if refractory	Itch tracks stage; a new infection worsens it
Staphylococcus aureus colonisation or infection	Culture crusted or weeping erosions; dilute bleach baths or chlorhexidine plus topical antibiotic; systemic antibiotics (consider MRSA) for real infection	Clearing infection often improves the lymphoma skin signs
Herpes simplex or zoster in erythroderma	Recognise and treat promptly	Risk of disseminated infection
Topical steroid side effects	Watch for atrophy and striae; care near the eyes	Response by 3 months, or change
Phototherapy and RT late effects	Skin cancer and cataract surveillance after PUVA; RT dermatitis, alopecia	Avoid PUVA after many skin cancers
Brentuximab neuropathy	Dose delay, reduction or stop (half needed a change in ALCANZA)	41% still had grade ≤2 neuropathy at long follow-up
HLH (SPTCL, γδ TCL)	Ferritin, triglycerides, fibrinogen in a febrile cytopenic patient; urgent haematology	Main adverse factor in SPTCL