Supplementary Table 1. List of suggested biomarkers for MF and SS.

Category	Biomarkers
Serum biomarkers	LDH [1] Beta2 microglobulin [2] Soluble IL-2 receptor [3] IL-13 [4], IL-31 [5], IL-12 [3] CCR4 [6] TNFR1/2 [3] HSP60/75/A5 [7]
Cell population changes	Elevated WBC, ALC, eosihophil count [8-10] CD4/CD8 ratio [11] Large cell transformation [12]
Cell surface markers	CD26 [13], $CD3^{dim}$ [14], CD27 [15], CD52 [16], CTLA-4 [17], CD45R0 [18] KIR3DL2 [19, 20] NKp46 [21] PD-1 [22]
Gene and epigenetic markers	Gene expression; TOX [23], T-plastin [24-26], JUNB [25], GATA3 [25], SATB1 [27], STAT4 [25, 28], Twist [26, 29], Fas [30] Non-coding RNAs; miRNAs; miR-21, miR-155, miR-214, miR-486, miR-42-5p, miT-146a [31-34] Long non-coding RNAs [35] Chromosomal changes; Altered 17p11.2–q25.3, 8q24.1–8q24.3, and 10p12.1–q26.3 [36-38] Gains of *TCRB, TCRG, TNFR2*, and *cMYC* [38-40] Loss of *BCL2*, cMYC antagonists [38, 41] Genetic mutations; NFKB2 truncations, TNFAIP3, PLCG1, PRKCQ and TNFAIP3 [42, 43] ZEB1 [44] PDGFR, ERK, JAK/STAT, and MAPK [43, 45] DNMT3A, ASLX3, TET1-3 [46] RAD51C, BRCA2, POLD1 [43] TP53 [44, 46]

Supplementary Table 1 References

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Supplementary Table 2. Response criteria for MF and SS (modified from Olsen EA *et al.* Blood. 2022;140:419-37).

Response in specific tissues				
Sites	Response	Definition		
Skin	CR*	100% clearance of skin lesions[b]		
	PR	50 to <100% clearance of skin disease[b] from baseline without advancement in stage. May designate subset of Very Good PR based on 90 to <100% clearing of total body involvement. Without new tumors (T3) in MF/SS patients with T1, T2, or T4 only skin disease		
	SD	<25% increase or <50% clearance in skin disease from baseline[b] Without new tumors (T3) in MF/SS patients with T1, T2, or T4 only skin disease		
	PD[a]	1. ≥25% increase in skin disease from baseline[b] OR 2. Loss of response: in those with CR or PR, increase of skin score of greater than the sum of nadir plus 50% baseline score. New tumors (T3) in MF/SS patients with T1, T2, or T4 only skin disease Additional suggestions for confirming PD in T1 MF and T1 non-MF/non-SS PCLs may be considered depending on the aims of the study[c]		
Lymph nodes**	CR	Complete metabolic response. Score 1, 2, or 3[d] with or without a residual mass on 5PS.	Target LNs[e]/nodal masses must regress to ≤1.5 cm LDi	All target LNs or nodal masses that previously were >1.5 cm are now ≤1.5 cm LDi by method used to assess size of LNs at baseline/screening or biopsy negative for lymphoma
	PR	Partial metabolic response. Score of 4 or 5[d] with reduced uptake compared with baseline.	≥50% decrease in SPD of up to 6 target measurable LNs. No clear increase in nonmeasured LNs or new LN1.5 cm LDi.	Cumulative reduction >50% of the SPD of up to 6 target LNs and no new LN >1.5 cm LDi unless proven pathologically negative for lymphoma
	SD	No metabolic response. Score of 4 or 5[d] with no significant change in FDG uptake from baseline.	<50% decrease from screening/ baseline in SPD of up to 6 target measurable LNs. Criteria for PD not met.	Fails to meet criteria for CR, PR or PD
	PD	Progressive metabolic disease. Score of 4 or 5[d] with an increase in intensity of uptake.	1. Any LN of LDi 1.5 cm which has increased by ≥50% from PPD nadir 2. New LN 1.5 cm any axis 3. New or clear progression of preexisting nonmeasured LNs	1. Any LN >1.5 cm LDi which has increased by ≥50% from PPD nadir 2. Any prior LN <1.5 cm LDi, which has increased by >50% from PPD nadir to >1.5 cm LDi
Viscera**	CR	Complete metabolic response. Score of 1, 2, or 3[d] with or without a residual mass on 5PS. No evidence of FDG-avid disease.	No extralymphatic sites of disease. Any abnormal size of organ at screening/baseline has returned to normal size. BM normal by morphology.	
	PR	Partial metabolic response. Score of 4 or 5[d]with reduced uptake compared with baseline and residual mass(es) of any size. Residual uptake in BM higher than normal but less than baseline.	1. ≥50% decrease in SPD from baseline of any measurable extranodal site 2. Spleen 50% regression in length beyond normal (≤13 cm) 3. No new lesions 4. No increase in nonmeasured lesions	
	SD	No metabolic response. Score of 4 or 5[d] with no significant change in FDG uptake from baseline. BM no change from BL.	Fails to attain criteria CR, PR, or PD. No clear progression or improvement.	
	PD	1. Progressive metabolic disease 2. New FDG-avid foci consistent with lymphoma	1. New extranodal site >1 cm any axis or if <1 cm, must be attributable to lymphoma 2. An increase in LDi or SDi from nadir of 0.5 cm for lesions ≤2 cm or 1 cm for lesions >2 cm 3. Regrowth of previously resolved lesions 4. In the setting of splenomegaly at BL, an increase in splenic length by >50% from BL or if no splenomegaly at BL, new increase length >2 cm from BL 5. New or clear progression of preexisting nonmeasured lesions	
Blood	CR	B0[f], ***		
	PR	>50% decrease in quantitative measurements of blood tumor burden from baseline in those with B2 classification[f,g], ***		
	SD	Fails to attain criteria for CR, PR, or PD		
	PD[h]	B0 to B2[f], *** OR >50% increase from baseline and ≥5,000 neoplastic cells/μL[i] OR Loss of response in those with PR who were originally B2 at baseline, >50% increase from nadir and ≥5,000 neoplastic cells/μL[i]		

Supplementary Table 2. Continued.

Global response score[¶]					
Global score[§]	Definition	Skin	Lymph nodes	Viscera	Blood
CR	Complete disappearance of all clinical evidence of disease	CR	All categories have CR/NI.		
PR	Regression of measurable disease	CR	All categories do not have a CR/NI and no category has a PD.		
		PR	No category has a PD and if any category involved at baseline, at least one has a CR or PR.		
SD	Failure to attain CR, PR, or PD representative of all disease	PR	No category has a PD and if any category involved at baseline, no CR or PR in any.		
		SD	R/NI, PR, SD in any category and no category has a PD.		
PD	Progressive disease	PD in any category.			
Relapse	Recurrence of disease in prior CR	Relapse in any category.			

[a)]Whichever criterion occurs first. [b)]One form of assessment of skin disease should be used throughout a given clinical trial. For a global response score and a designation of Very Good PR, a comparison of total body skin assessment based on mSWAT assessment or sum of the product of perpendicular tumor measurements (SLAT score is one example) at baseline is necessary. Regional or lesional skin scoring may also have CR, PR, SD and PD response but may not be representative of the response of skin disease on the entire body skin surface and cannot be used to assess global response. [c)]For patients with limited T1 stage disease, there is a potential for a ≥25% increase inpatch/plaque skin score to lead to a PD despite an insignificant change in total skin lymphoma. This is of particular concern in studies where global response is the primary endpoint and skin the primary determinant of that response. In these cases, study design may elect to add additional requirements for PD in patients with T1 disease at BL, including a T1 to T2 change in skin classification in addition to the ≥25% increase in skin score. [d)]5PS: 1=no FDG uptake >background; 2=FDG uptake ≤mediastinum; 3=FDG uptake >mediastinum but ≤liver; 4=FDG uptake moderately > liver; 5=FDG uptake markedly >liver and/or new lesions. [e)]Target LNs are those >1.5 cm with representative abnormal node positive pathologically for lymphoma. In MF/SS, this is currently the LN classification of N3. [f)]The absolute number of CD4+CD26- and/or CD4+CD7- lymphocytes may be used to assess blood involvement in clinical trials. In the case where more than one aberrant population of lymphocytes is recorded, the population with the highest absolute number at baseline should determine the B classification and the highest absolute number at each assessment should be used to determine the number of aberrant lymphocytes for response purposes. [g)]There is no PR in those with B1 disease at baseline as the difference within the range of neoplastic cells that define B1 is not considered significant and should not affect determination of global objective response. [h)]Whichever occurs first. [i)]The determination of what constitutes a significantly high count of neoplastic cells above 1,000 neoplastic cells/μL and what should be used here to help define PD in MF/SS blood involvement is at present arbitrary and based on expert opinion. We cede modification of this number to published data showing prognostic value for a different number of neoplastic cells per microliter than what is published here.

*A biopsy of normal appearing skin is unnecessary to assign a CR. However, a skin biopsy should be performed of a representative area of the skin if there is any question of residual disease (persistent erythema or pigmentary change) where otherwise a CR would exist. If histologic changes are suspicious or suggestive of PCL, the response should be considered a PR only.

**Based on Cheson *et al.* J Clin Oncol. 2014;32:3059-68.

***As determined by absolute numbers of neoplastic cells/mL by flow cytometry.

[¶]Modified from Olsen *et al.* J Clin Oncol. 2011;29:2598-607 and Kempf *et al.* Blood. 2011;118:4024-35. This table assumes that (1) all patients at baseline have measurable skin disease and (2) in patients with PCL and no extracutaneous disease at baseline, any new nodal or visceral involvement constitutes PD in those compartments.

[§]This assumes that the response (CR, PR, SD, PD, or relapse) has been maintained for at least 4 weeks in any involved category.

Abbreviations: 5PS, 5-point scale; FDG, fluorodeoxyglucose; LDi, longest diameter; LN, lymph node; NI, noninvolved; PD, progressive disease; SD, stable disease; SDi, short axis (longest perpendicular diameter to the LDi); SPD, sum of the products of the perpendicular diameters for multiple lesions.