Malattia «Early Stage»: l'Ematologo

Francesco Onida

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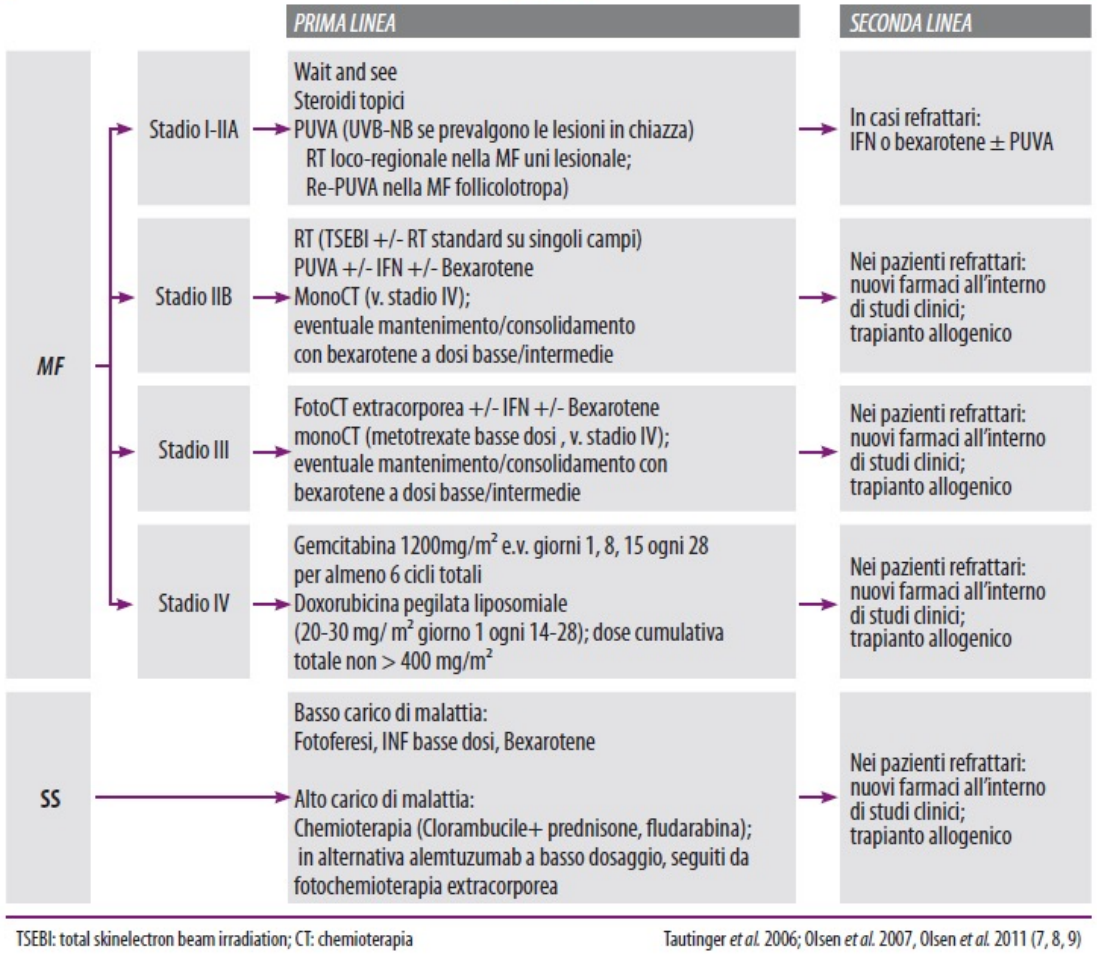
MF/SS linee guida di terapia Commissione Linfomi cutanei - FIL



Coordinate da Nicola Pimpinelli; Autori: Paolo Fava, Silvia Alberti Violetti, Chiara Delfino

MF/SS THERAPY AT A GLANCE: FIRST LINE

European Organisation for Research and Treatment of Cancer consensus recommendations for the treatment of mycosis fungoides/Sézary syndrome - Update 2017.

F. Trautinger, J. Eder, C. Assaf, M. Bagot, A. Cozzio, R. Dummer, R. Gniadecki, C.D. Klemke, P.L. Ortiz-Romero, E. Papadavid, N. Pimpinelli, P Quaglino, A. Ranki, J. Scarisbrick, R. Stadler, L. Väkevä, M.H. Vermeer, S. Whittaker, R. Willemze, R. Knobler

European Journal of Cancer (2017) 77: pp57-74

EORTC
European Organisation for Research and Treatment of Cancer

	Wait & see	Topical steroids	Photo therapy	Local RT	TSET	Interferon	Bexarotene	Mono-CT	MTX	PoliCT	ECP
IA	■	■	■	■							
IB	■	■	■	■							
IIA		■	■	■							
IIB				■	■	■	■	■	■		
III					■	■	■		■		■
SS						■	■	■	■		■
IVA - IVB								■		■	

MF/SS THERAPY AT A GLANCE: SECOND LINE

European Organisation for Research and Treatment of Cancer consensus recommendations for the treatment of mycosis fungoides/Sézary syndrome - Update 2017.

F. Trautinger, J. Eder, C. Assaf, M. Bagot, A. Cozzio, R. Dummer, R. Gniadecki, C.D. Klemke, P.L. Ortiz-Romero, E. Papadavid, N. Pimpinelli, P Quaglino, A. Ranki, J. Scarisbrick, R. Stadler, L. Väkevä, M.H. Vermeer, S. Whittaker, R. Willemze, R. Knobler

European Journal of Cancer (2017) 77: pp57-74

EORTC
European Organisation for Research and Treatment of Cancer

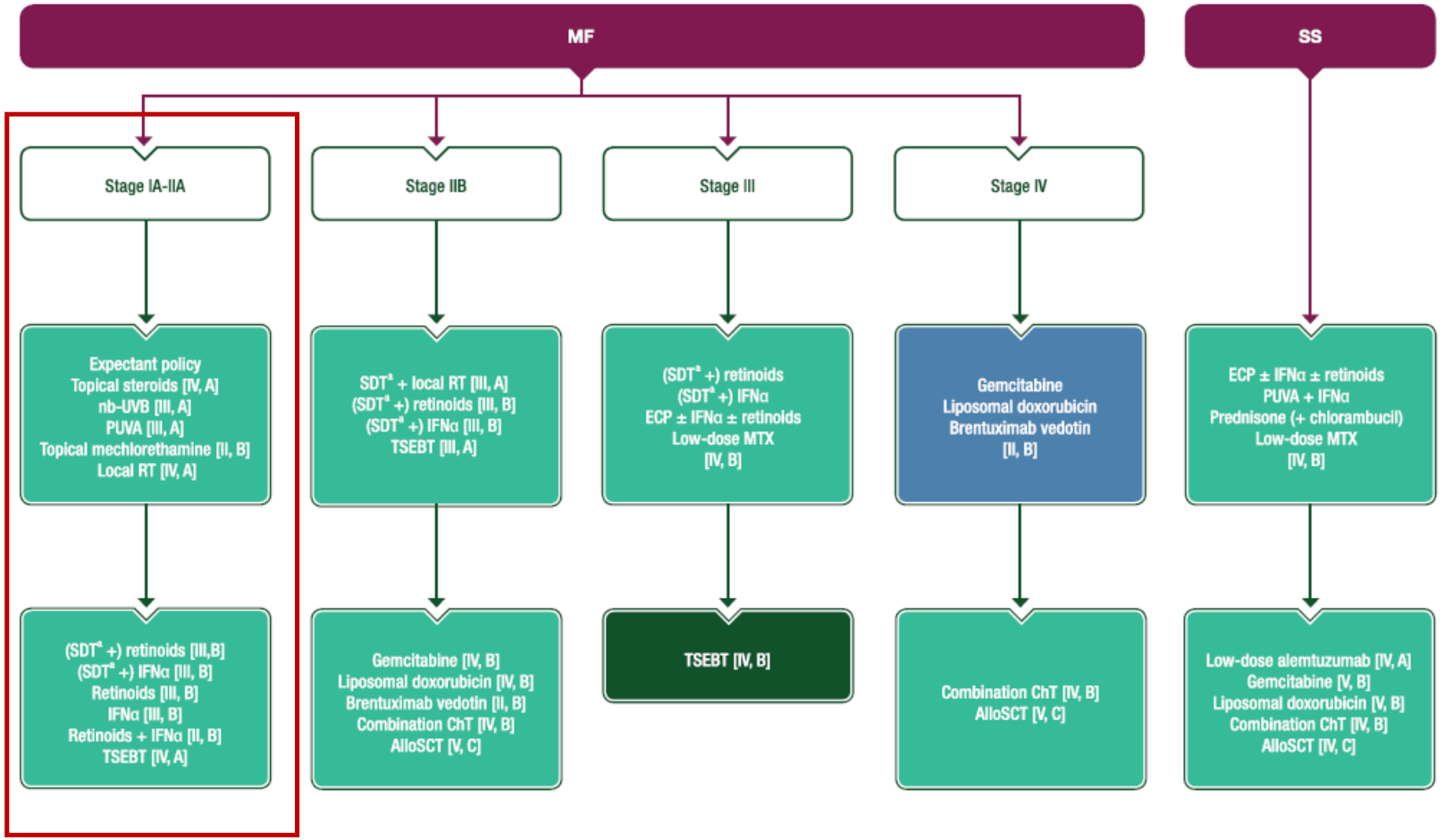
	Topical steroids	Photo therapy	Local RT	TSET	Interferon	Bexarotene	Mono-CT	MTX	PoliCT	ECP	HSCT
IA											
IB											
IIA											
IIB											
III											
SS											
IVA - IVB											

ESMO

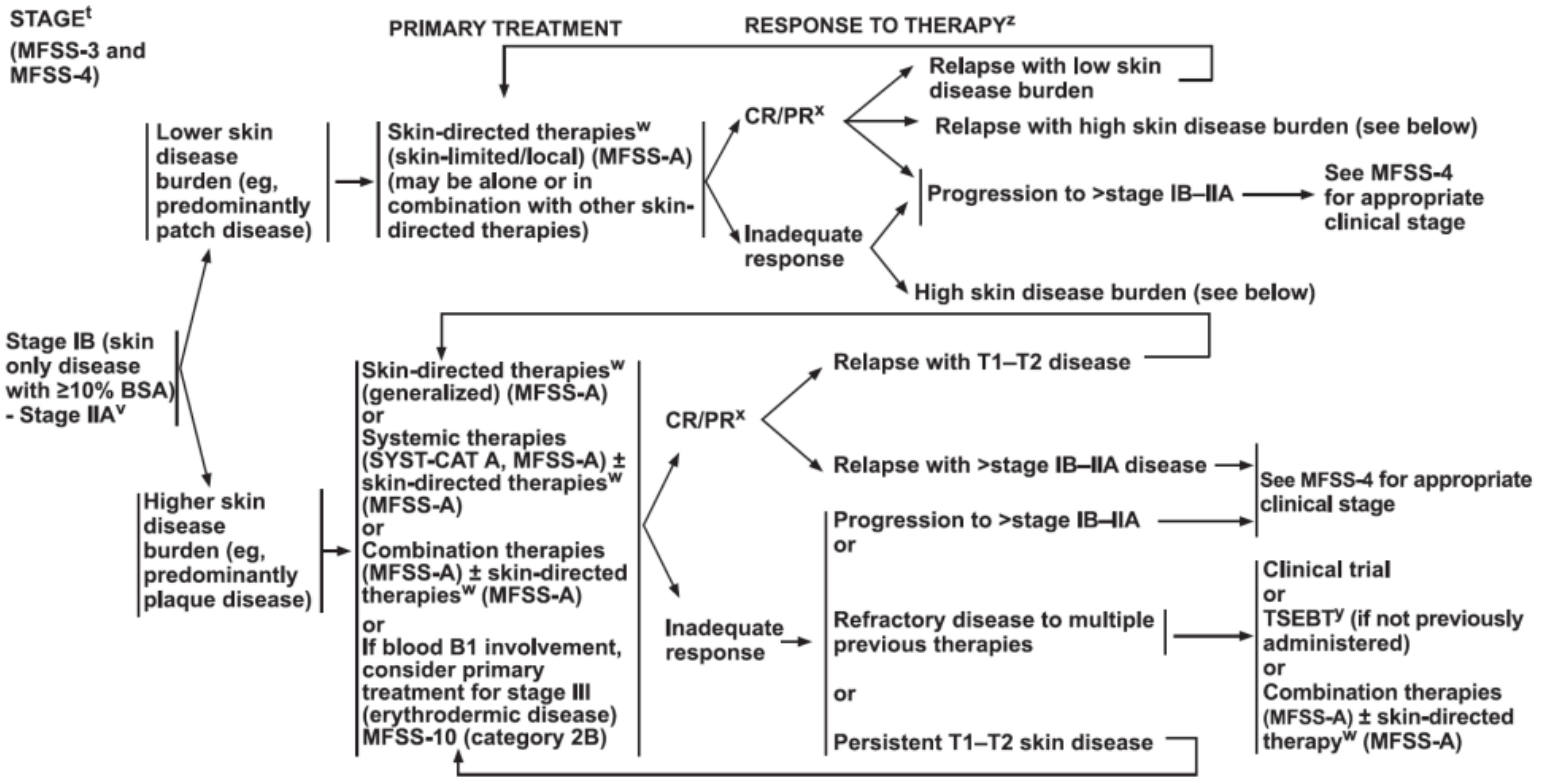
CLINICAL PRACTICE GUIDELINES

Primary cutaneous lymphomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

R. Willemze[1], E. Hodak[2], P. L. Zinzani[3], L. Specht[4] & M. Ladetto[5], on behalf of the ESMO Guidelines Committee*



Willemze R et al. Annals of Oncol 2018



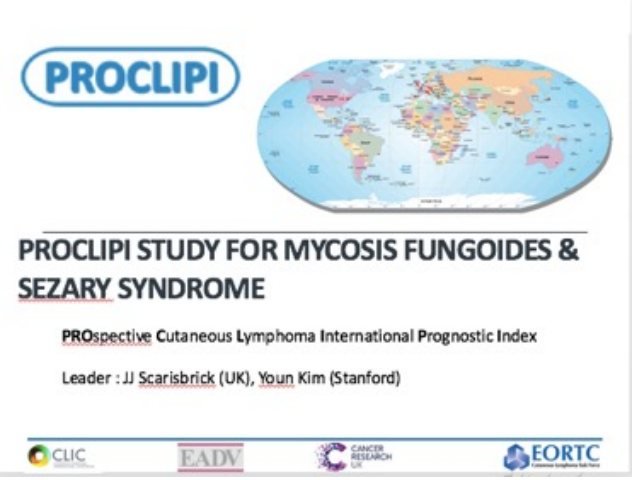
[t] See Principles for Mycosis Fungoides/Sézary Syndrome (MFSS/INTRO-1).
[v] Rebiopsy if suspect LCT; if histologic evidence of LCT, see MFSS-12.
[w] In patients with histologic evidence of folliculotropic MF, skin disease may be less responsive to topical therapies.
[x] Patients with disease achieving a clinical benefit and/or those with disease responding to primary treatment should be considered for maintenance or tapering of regimens to optimize response duration.
[y] See Principles of Radiation Therapy (LYMP-A).
[z] Imaging indicated when suspicious of clinical extracutaneous disease with modalities used in workup.

See Supportive Care for MF/SS (MFSS-B)

SUGGESTED TREATMENT REGIMENS[a,b]

SYSTEMIC THERAPIES			
	Preferred Regimens (alphabetical order)	**Other Recommended Regimens**	**Useful Under Certain Circumstances**
SYST-CAT A	• Brentuximab vedotin[i,j,k] • Bexarotene[h] • Extracorporeal photopheresis (ECP)[l] • Interferons (IFN-alfa-2b[m] or IFN-gamma 1b) • Methotrexate (≤50 mg q week) • Mogamulizumab[n] • Romidepsin[h] • Vorinostat[h]	• Acitretin[h] • All-trans retinoic acid[h] • Isotretinoin [13-cis-retinoic acid][h]	
SYST-CAT B	• Brentuximab vedotin[i,j,k] • Gemcitabine • Liposomal doxorubicin • Pralatrexate (low-dose or standard dose)		• Relapsed/refractory disease requiring systemic therapy; alphabetical order by category) ▸ Alemtuzumab[k,p] ▸ Chlorambucil ▸ Cyclophosphamide ▸ Etoposide ▸ Pentostatin ▸ Temozolomide for CNS involvement ▸ Bortezomib (category 2B) ▸ Pembrolizumab (category 2B)[q,r] ▸ See TCEL-B 2 of 5 for regimens listed for PTCL-NOS[o]
Large-cell transformation (LCT)	• Brentuximab vedotin[i,j,k] • Gemcitabine • Liposomal doxorubicin • Pralatrexate (low-dose or standard dose) • Romidepsin • See TCEL-B 2 of 5 for regimens listed for PTCL-NOS[o]		

PROCLIPI is an international prospective database in which all the new cases of mycosis fungoides(MF)/Sézary syndrome are registered after central clinico-pathological review to confirm diagnosis.



GENERAL DERMATOLOGY — BJD British Journal of Dermatology

The PROCLIPI international registry of early-stage mycosis fungoides identifies substantial diagnostic delay in most patients

J.J. Scarisbrick,[1,2,3,4] P. Quaglino,[2,3] H.M. Prince,[3] E. Papadavid,[2,3] E. Hodak,[2,3] M. Bagot,[2,3] O. Servitje,[2,3] E. Berti,[2,3] P. Ortiz-Romero,[2,3] R. Stadler,[2,3] A. Patsatsi,[2,3] R. Knobler,[2,3] E. Guenova,[2,3] F. Child,[2,4] S. Whittaker,[2,3,4] V. Nikolaou,[2,3] C. Tomasini,[2] I. Amitay,[2,3] H. Prag Naveh,[2,3] C. Ram-Wolff,[2] M Battistella,[2,3] S. Alberti-Violetti,[2] R. Stranzenbach,[2,3] V. Gargallo,[2] C. Muniesa,[2] T. Koletsa,[2] C. Jonak,[2,3] S. Porkert,[2] C. Mitteldorf,[2] T. Estrach,[2] A. Comballa,[2] M. Marschalko,[2] J. Csomor,[2] A. Szepesi,[2] A. Cozzio,[2,3] R. Dummer,[2] N. Pimpinelli,[2] V. Grandi,[2] M. Beylot-Barry,[2] A. Pham-Ledard,[2] M. Wobser,[2] E. Geissinger,[2] U. Wehkamp,[2,3] M. Weichenthal,[2] R. Cowan,[2,4] E. Parry,[2,4] J. Harris,[4] R. Wachsmuth,[2,4] D. Turner,[4] A. Bates,[4] E. Healy,[4] F. Trautinger,[2,3] J. Latzka,[2] J. Yoo,[1,2] B. Vydianath,[5] R. Amel-Kashipaz,[5] L. Marinos,[2] A. Oikonomidi,[2] A. Stratigos,[2] M.-D. Vignon-Pennamen,[2] M. Battistella,[2] F. Climent,[2] E. Gonzalez-Barca,[2] E. Georgiou,[2] R. Senetta,[2] P. Zinzani,[2] L. Vakeva,[2] A. Ranki,[2] A.-M. Busschots,[2] E. Hauben,[2] A. Bervoets,[2] F.J.S.H. Woei-A-jin,[2] R. Matin,[4] G. Collins,[4] S. Weatherhead,[4] J. Frew,[4] M. Bayne,[4] G. Dunnill,[4] P. McKay,[4] A. Arumainathan,[4] R. Azurdia,[4] K. Benstead,[4] R. Twigger,[3] K. Rieger,[3] R. Brown,[3] J.A. Sanches,[3] D. Miyashiro,[3] O. Akilov,[3] S. McCann,[3] H. Sahl,[3] F.M. Damasco,[3] C. Querfeld,[3] A. Folkes,[3] C. Bur,[3] C.-D. Klemke,[2] P. Enz,[3] R. Pujol,[2,3] K. Quint,[2] L. Geskin,[3] E. Hong,[3] F. Evison,[1] M. Vermeer,[2,3] L. Cerroni,[2] W. Kempf,[2] Y. Kim[3] and R. Willemze[2]

[1]European Co-ordinating PROCLIPI Centre for PROCLIPI, University Hospitals Birmingham, Birmingham, U.K.
[2]Member of the European Organisation of Research and Treatment of Cancer (EORTC), Cutaneous Lymphoma Task Force
[3]Member of the Cutaneous Lymphoma International Consortium (CLIC)
[4]Member of the UK Cutaneous Lymphoma Group

the PROCLIPI (PROspective InternationalCutaneous Lymphoma Prognostic Index) study for early-stage MF is a prototype study for international collaborations in rare disease and present our initial findings and central review process.

MEDICAL DERMATOLOGY

BJD
British Journal of Dermatology

Treatment of early-stage mycosis fungoides: results from the PROspective Cutaneous Lymphoma International Prognostic Index (PROCLIPI) study*

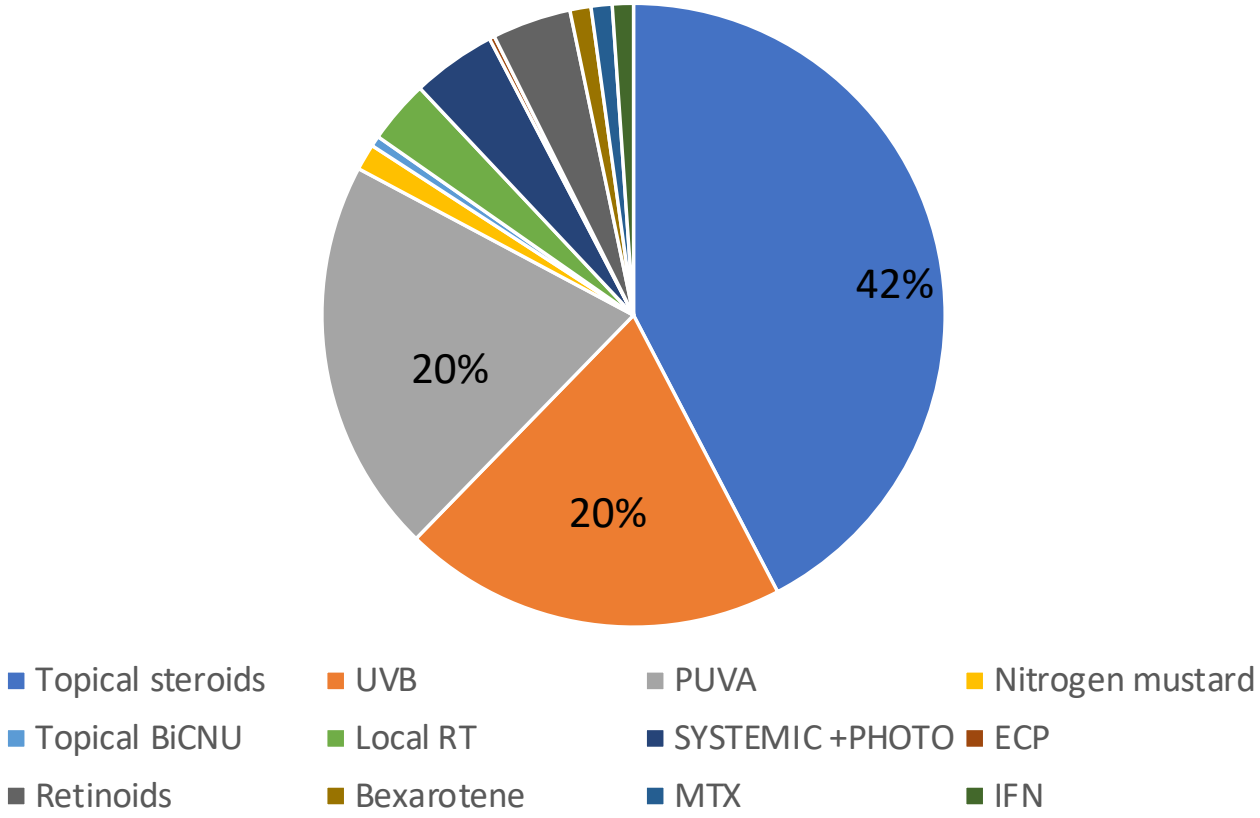
P. Quaglino,[1] H.M. Prince,[2] R. Cowan,[3] M. Vermeer,[4] E. Papadavid,[5] M. Bagot,[6] O. Servitjie,[7] E. Berti,[8] E. Guenova,[9] R. Stadler,[10] C. Querfeld,[11] A.M. Busschots,[12] E. Hodak,[13] A. Patsatsi,[14] J. Sanches,[15] M. Maule,[16] J. Yoo,[17] M. Kevin,[17] P. Fava,[1] S. Ribero,[1] L. Zocchi,[1] M. Rubatto,[1] M.T. Fierro,[1] U. Wehkamp,[18] M. Marshalko,[19] C. Mitteldorf,[20] O. Akilov,[21] P. Ortiz-Romero,[22] T. Estrach,[23] L. Vakeva,[24] P.A. Enz,[25] M. Wobser,[26] M. Bayne,[27] C. Jonak,[28] M. Rubeta,[29] A. Forbes,[30] A. Bates,[31] M. Battistella,[6] R. Amel-Kashipaz,[17] B. Vydianath,[17] A. Combalia,[23] E. Georgiou,[14] E. Hauben,[12] E.K. Hong,[32] M. Jost,[18] R. Knobler,[28] I. Amitay-Laish,[13] D. Miyashiro,[15] J. Cury-Martins,[15] X. Martinez,[11] C. Muniesa,[7] H. Prag-Naveh,[13] A. Stratigos,[5] V. Nikolaou,[5] K. Quint,[4] C. Ram-Wolff,[6] K. Rieger,[32] R. Stranzenbach,[10] Á. Szepesi,[19] S. Alberti-Violetti,[8] E. Felicity,[17] L. Cerroni,[33] W. Kempf,[34] S. Whittaker,[35] R. Willemze,[4] Y. Kim[32] and J.J. Scarisbrick[17,36]

395 “early stage MF” (stage IA, IB, IIA) included in the database after passing central review process from 01/2015 to 2/2018

Parameter	Number	%
Male	243	62%
Female	152	38
Age median (range)	56 (5-97)	
mSWAT median (range)	10 (0.3-120)	
Europe	349	88%
Outside Europe	46	12%
Stage IA	198	50%
Stage IB	164	42%
Stage IIA	33	8%
T1a	113	29%
T1b	96	24%
T2a	80	20%
T2b	106	27%
Patches only T1a+T2a	193	49%
Patches + plaques T1b + T2b	202	51%
FMF	71	18%

Quaglino P et al. BJD 2021

Summary of treatments registered at first visit (first-line therapies)



Quaglino P et al. BJD 2021

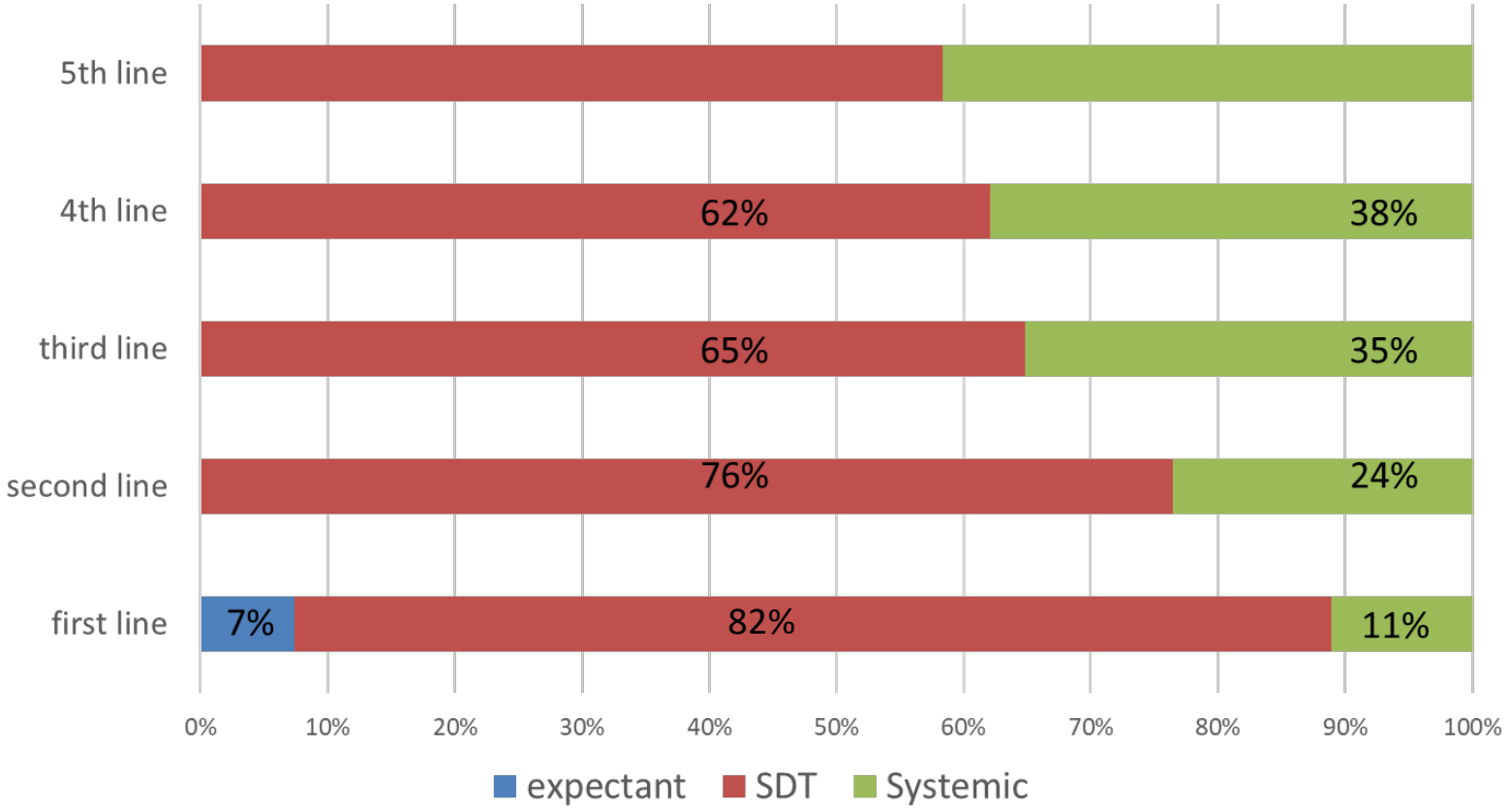
La terapia nel paziente ricaduto/refrattario con CTCL

Further treatment lines according to stage

	2nd line (n; %)	3rd line (n; %)	4th line (n; %)	>4 lines (n; %)
IA (n=207)	72; 35%	24; 12%	4; 2%	5; 2%
IB (n=188)	65; 35%	28; 15%	10; 5%	15; 8%
IIA (n=29)	28; 96%	5; 17%	3; 10%	5; 17%
ALL (n=424)	165; 39%	57; 13%	17; 4%	25; 6%
FMF (n=82)	32; 39%	10; 12%	6; 7%	9; 11%

Quaglino P et al. BJD 2021

Summary of treatments according to the therapy line



1st vs 2nd line Chi square: P<0.001

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First-line therapies according to the stage

Treatment	All (n; %) N=395	IA (n; %) N=198	IB (n;%) N=164	IIA (n;%) N=33
Expectant	29 (7%)	17 (9%)	9 (5%)	3 (10%)
SKIN-DIRECTED	322 (82%)	168 (85%)	131 (80%)	23 (70%)
SYSTEMIC	44 (11%)	14 (6%)	23 (14%)	7 (20%)

The percentage of patients undergoing a first-line systemic approach increased from stage IA to IB to IIA paralleling a decrease in skin-directed therapies (SDT)(particularly in stage IIA. The difference between stage IA-IB and IIA was statistically significant (chi square:15.398; $p<0.0001$).

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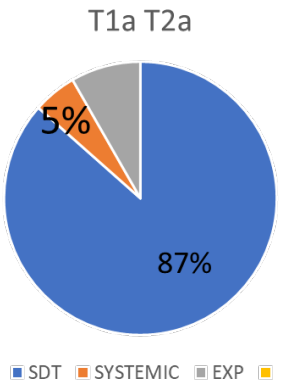
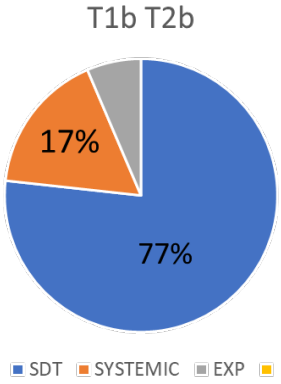
First-line therapies according to T score

Treatment	T1a (n; %) N=113	T1b (n;%) N=96	T2a (n;%) N=80	T2b (n; %) N=106
Expectant	8 (7%)	9 (9%)	8 (10%)	4 (3%)
SKIN-DIRECTED	100 (89%)	76 (79%)	67 (84%)	79 (75%)
SYSTEMIC	5 (4%)	11 (12%)	5 (6%)	23 (22%)





Chi square: P<0.001

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Multivariate analysis of parameters associated with a more frequent first systemic approach

Variable	Coefficient	Standard error	p	O.R	95% CI low	95% CI high
Geographical	0.7711	0.4636	0.0962	2.1622	0.8715	5.3643
Age	-0.0011	0.0103	0.9146	0.9989	0.9790	1.0192
Gender	-0.0219	0.3543	0.9508	0.9784	0.4886	1.9593
mSWAT	0.1683	0.4283	0.6943	1.1833	0.5111	2.7395
TNM stage	0.4363	0.3003	0.1463	1.5470	0.8587	2.7871
Plaques	1.1221	0.4186	0.0074	3.0712	1.3521	6.9761
FMF	1.0391	0.3641	0.0043	2.8268	1.3846	5.7709

O.R. odds ratio
CI Confidence Interval
FMF: Follicolotropic mycosis fungoides

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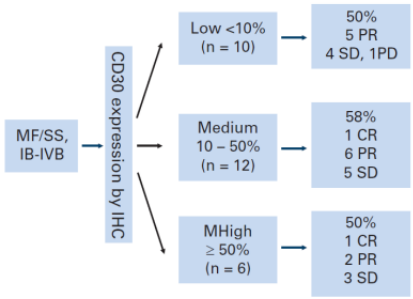
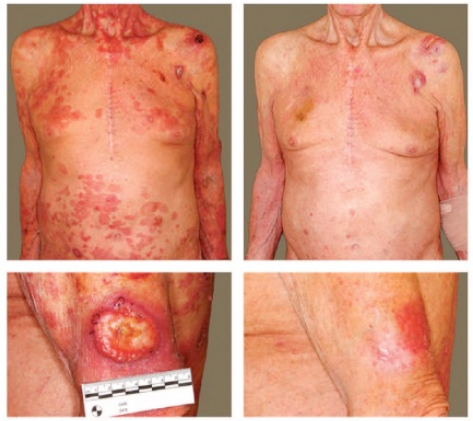
Brentuximab vedotin

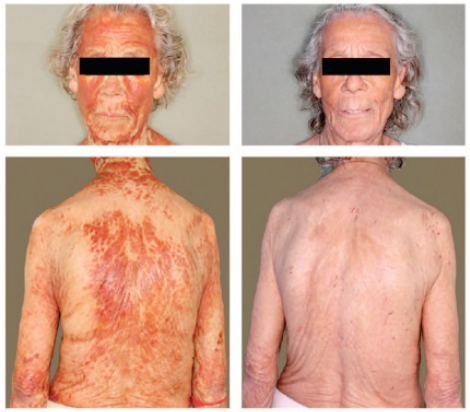
Table 2. Response in Evaluable Patients

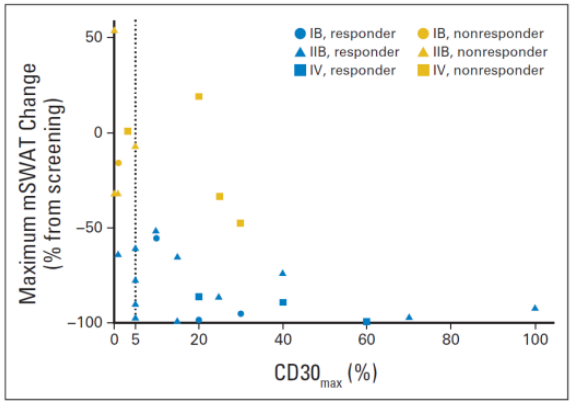
Diagnosis	Total No. of Patients (N = 48)	Response		Secondary Response (No.)
		No.	%	
All patients	48	35	73	
MF	28	13 PR, 2 CR	54	
LyP	9	5 CR, 4 PR	100	
pc-ALCL	2	2 CR	100	
LyP/MF	7	6 LyP CR, 1 LyP PR	100	6 MF PR, 1 MF SD
pc-ALCL/LyP	1	CR	100	1 LyP PD
pc-ALCL/MF	1	CR	100	1 MF PR

Abbreviations: ALCL, anaplastic large-cell lymphoma; CR, complete response; LyP, lymphomatoid papulosis; MF, mycosis fungoides; pc, primary cutaneous; PD, progressive disease; PR, partial response; SD, stable disease.



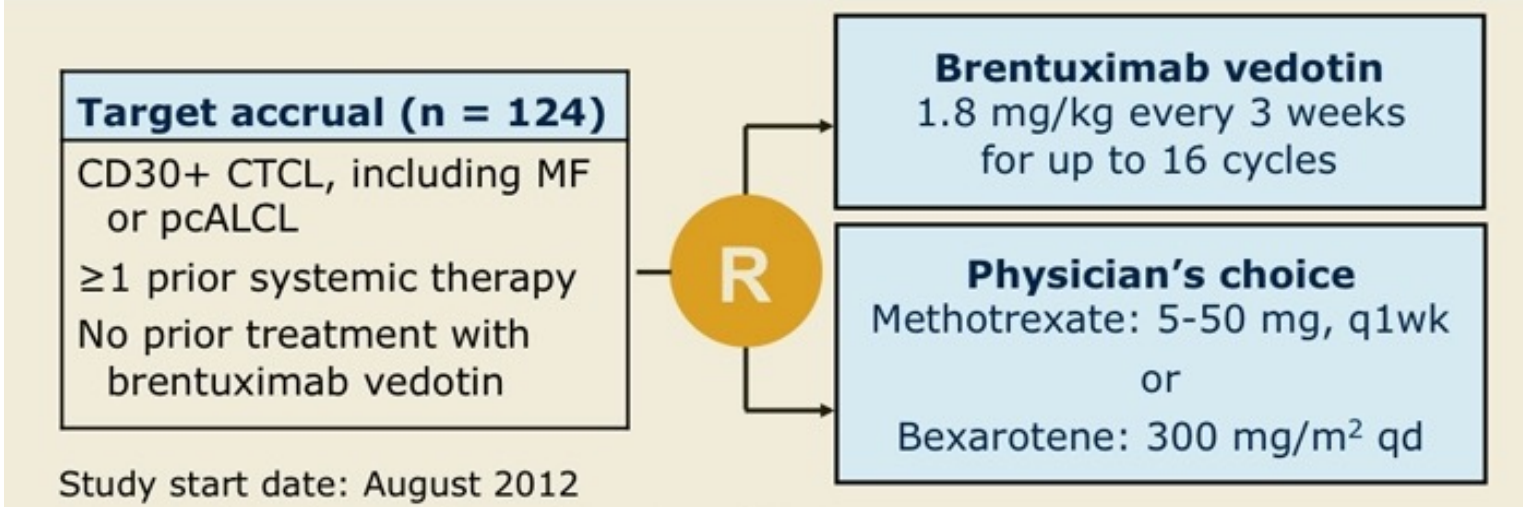






Duvic M et al JCO 2015; Kim Y et al. JCO 2015

Phase III ALCANZA Trial



Study start date: August 2012

Estimated study completion date: June 2015

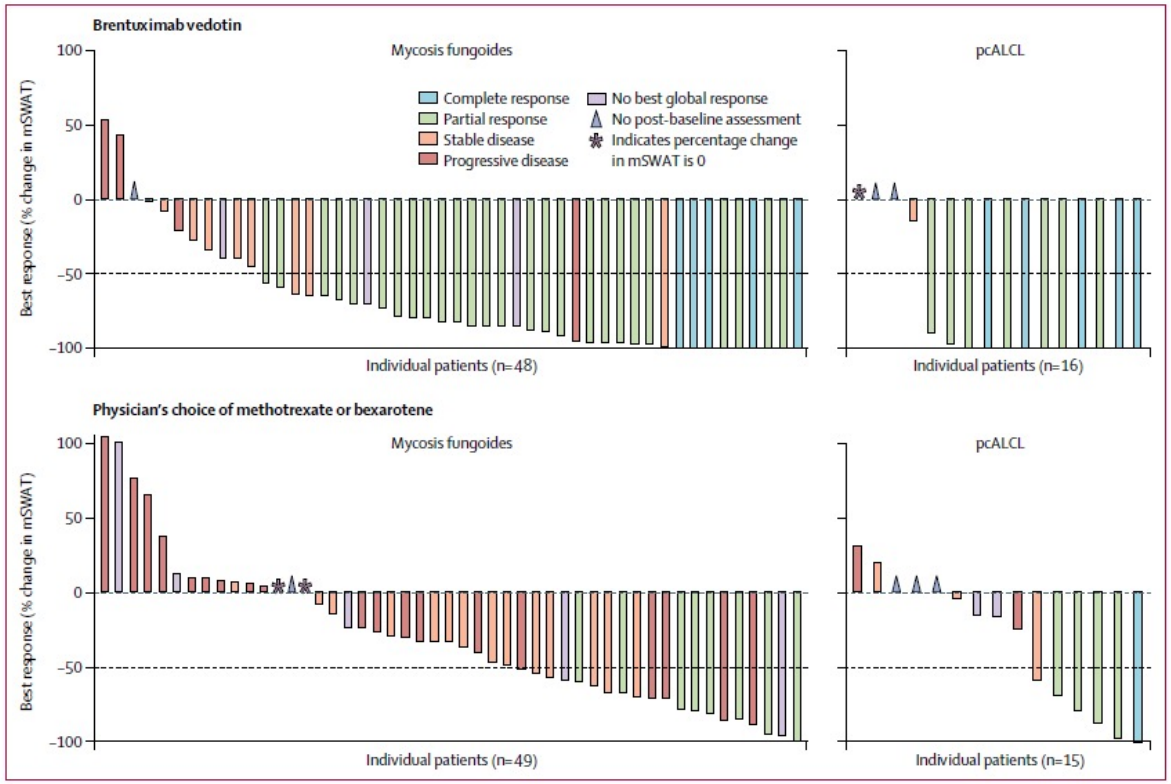
MF = mycosis fungoides; pcALCL = primary cutaneous anaplastic large-cell lymphoma

- **Primary endpoint:** ORR lasting ≥4 months
- **Secondary endpoints include:** Complete response, progression-free survival and changes in burden of symptom domain per Skindex-29 questionnaire

Kim YH et al. *Proc ICML* 2013;Abstract 572.

Brentuximab vedotin or physician's choice in CD30-positive cutaneous T-cell lymphoma (ALCANZA): an international, open-label, randomised, phase 3, multicentre trial

H Miles Prince*, Youn H Kim*, Steven M Horwitz, Reinhard Dummer, Julia Scarisbrick, Pietro Quaglino, Pier Luigi Zinzani, Pascal Wolter, Jose A Sanches, Pablo L Ortiz-Romero, Oleg E Akilov, Larisa Geskin, Judith Trotman, Kerry Taylor, Stephane Dalle, Michael Weichenthal, Jan Walewski, David Fisher, Brigitte Dréno, Rudolf Stadler, Tatyana Feldman, Timothy M Kuzel, Yinghui Wang, Maria Corinna Palanca-Wessels, Erin Zagadailov, William L Trepicchio, Wenwen Zhang, Hui-Min Lin, Yi Liu, Dirk Huebner, Meredith Little, Sean Whittaker†, Madeleine Duvic†, on behalf of the ALCANZA study group†



	Brentuximab vedotin, n/N (%)	Physician's choice of methotrexate or bexarotene, n/N (%)	Difference in percentages (95% CI)
Mycosis fungoides	24/48 (50·0%)	5/49 (10·2%)	39·8 (19·9 to 56·2)
pcALCL	12/16 (75·0%)	3/15 (20·0%)	55·0 (19·7 to 80·4)
Baseline ECOG PS=0	29/43 (67·4%)	6/46 (13·0%)	54·4 (37·3 to 71·5)
Baseline ECOG PS≥1	7/21 (33·3%)	2/18 (11·1%)	22·2 (−10·2 to 51·2)
Men	19/33 (57·6%)	5/37 (13·5%)	44·1 (21·3 to 63·3)
Women	17/31 (54·8%)	3/27 (11·1%)	43·7 (18·5 to 64·7)
Age <65 years	20/36 (55·6%)	2/40 (5·0%)	50·6 (29·3 to 68·3)
Age ≥65 years	16/28 (57·1%)	6/24 (25·0%)	32·1 (6·9 to 57·4)
Europe	23/37 (62·2%)	3/35 (8·6%)	53·6 (32·7 to 71·3)
Non-Europe	13/27 (48·1%)	5/29 (17·2%)	30·9 (4·2 to 53·5)
Bexarotene	36/64 (56·3%)	6/38 (15·8%)	40·5 (23·7 to 57·3)
Methotrexate	36/64 (56·3%)	2/26 (7·7%)	48·6 (26·7 to 67·7)
Skin only	21/31 (67·7%)	5/30 (16·7%)	51·1 (27·3 to 71·0)
Skin and other involvement	15/33 (45·5%)	3/34 (8·8%)	36·6 (12·3 to 56·3)
Baseline skin tumour score>0	26/41 (63·4%)	2/38 (5·3%)	58·2 (38·1 to 74·1)
Baseline skin tumour score=0	10/23 (43·5%)	6/26 (23·1%)	20·4 (−5·5 to 46·3)
Overall	**36/64 (56·3%)**	**8/64 (12·5%)**	**43·8 (29·1 to 58·4)**

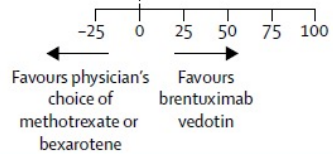
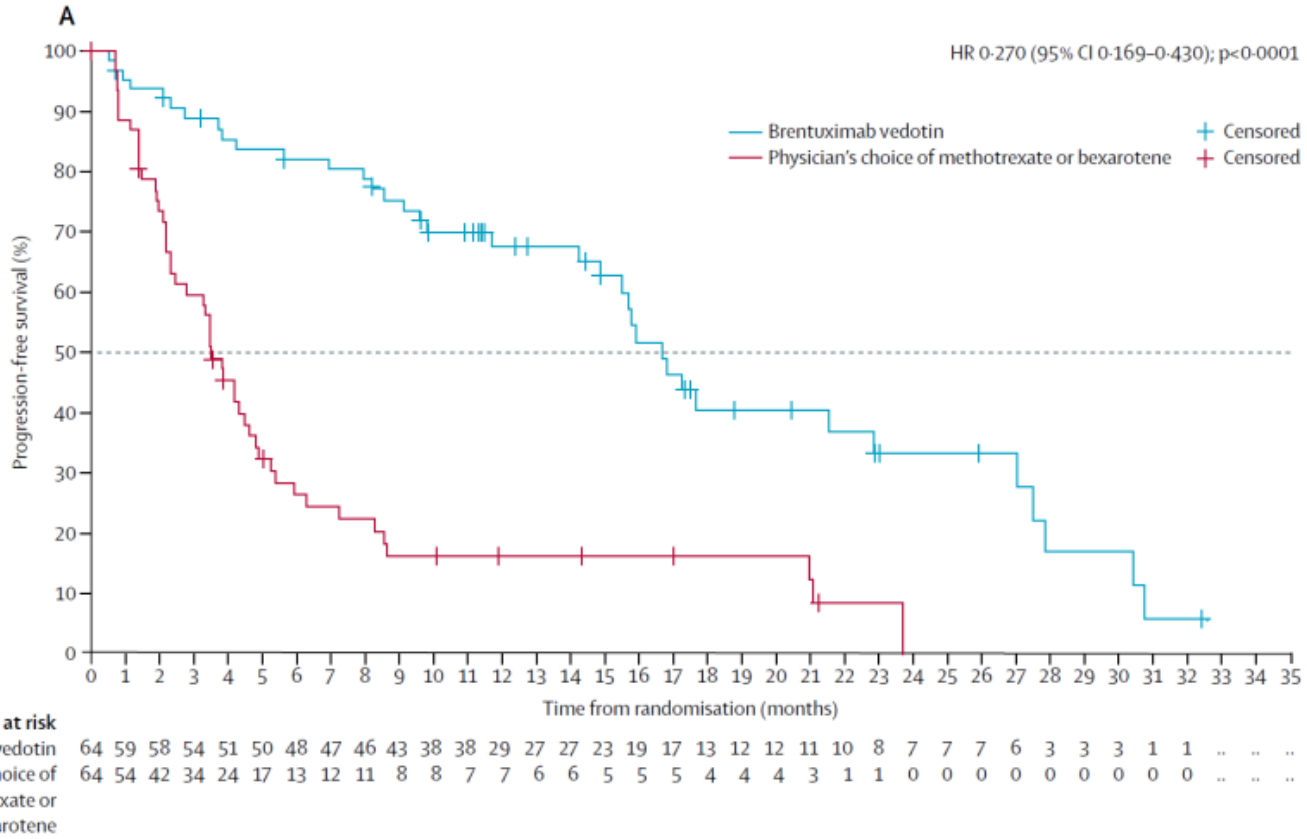


Figure 3: **Maximum percent change in skin mSWAT score**
mSWAT=modified severity weighted assessment tool. pcALCL=primary cutaneous anaplastic large-cell lymphoma.

Prince HM et al. Lancet 2017

Phase III ALCANZA Trial



Median PFS 16.7 vs 3.5 months
(HR 0.270, p>0.0001)

Prince HM et al. Lancet 2017

Brentuximab vedotin or physician's choice in CD30-positive cutaneous T-cell lymphoma (ALCANZA): an international, open-label, randomised, phase 3, multicentre trial

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	Brentuximab vedotin				Physician's choice of methotrexate or bexarotene			
	Total (n=64)	ORR4	ORR	CR	Total (n=64)	ORR4	ORR	CR
ITT population	64 (100%)	36 (56%)*	43 (67%)	10 (16%)	64 (100%)	8 (13%)†	13 (20%)	1 (2%)
Mycosis fungoides	48 (75%)	24 (50%)	31 (65%)	5 (10%)	49 (77%)	5 (10%)	8 (16%)	0
Stage‡§								
IA–IIA	15 (31%)	6 (40%)	8 (53%)	1 (7%)	18 (37%)	4 (22%)	5 (28%)	0
IIB	19 (40%)	12 (63%)	13 (68%)	3 (16%)	19 (39%)	1 (5%)	3 (16%)	0
IIIA–IIIB	4 (8%)	2 (50%)	3 (75%)	0	2 (4%)	0	0	0
IVA	2 (4%)	2 (100%)	2 (100%)	1 (50%)	9 (18%)	0	0	0
IVB	7 (15%)	2 (29%)	4 (57%)	0	0	NA	NA	NA
pcALCL	16 (25%)	12 (75%)	12 (75%)	5 (31%)	15 (23%)	3 (20%)	5 (33%)	1 (7%)
Disease involvement‡								
Skin only	9 (56%)	8 (89%)	8 (89%)	4 (44%)	11 (73%)	3 (27%)	5 (45%)	1 (9%)
Extracutaneous disease	7 (44%)	4 (57%)	4 (57%)	1 (14%)	4 (27%)	0	0	0

Data are n (%). ORR4, ORR, and CR percentages are based on the number of patients in the total column. ORR4=achieved an objective response lasting at least 4 months. ORR=achieved an objective response. CR=achieved a complete response. ITT=intent to treat. NA=not applicable. pcALCL=primary cutaneous anaplastic large-cell lymphoma. *One patient with mycosis fungoides in the brentuximab vedotin group achieved a partial response after C1, C2, and C3, and discontinued because of an adverse event. About 4·3 months later the patient received chemotherapy (gemcitabine) before end-of-treatment visit. Total duration of response, including after receipt of gemcitabine, was 4·8 months. †One patient with pcALCL in the bexarotene group who achieved partial response after C2 and sustained it at C5 chose to withdraw from treatment. The patient received subsequent therapy (methotrexate) about 3·5 months into the response to bexarotene but before end-of-treatment visit. Total duration of response, including after receipt of methotrexate, was 4·4 months. ‡Percentage in each subcategory in the total column is based on the number of patients in each disease subtype. §One patient in each group had incomplete staging data and are not included in the table: one patient in the brentuximab vedotin group had partial response and one patient in the physician's choice group had no response.

Table 2: **Patient responses by clinical stage at baseline**

	Brentuximab vedotin (n=64)	Physician's choice of methotrexate or bexarotene (n=64)	Overall (N=128)
Age (years)	62 (51–70)	59 (48–67)	60 (48–69)
Sex			
Male	33 (52%)	37 (58%)	70 (55%)
Female	31 (48%)	27 (42%)	58 (45%)
Race			
White	56 (88%)	53 (83%)	109 (85%)
Other	5 (8%)	10 (16%)	15 (12%)
Not reported	3 (5%)	1 (2%)	4 (3%)
ECOG PS			
0	43 (67%)	46 (72%)	89 (70%)
1	18 (28%)	16 (25%)	34 (27%)
2	3 (5%)	2 (3%)	5 (4%)
Median CD30 expression*	32·5% (12·5–67·5)	31·3% (12·0–47·5)	31·3% (12·5–60·0)
Time since initial diagnosis (months)	42·2 (12·8–87·4)	37·0 (12·3–102·7)	40·9 (12·7–96·8)
Time since progression on last therapy† (months)	2·4 (1·4–7·9)	1·3 (0·9–3·7)	1·9 (1·1–3·8)
Lines of previous therapy			
Total	4·0 (2·0–7·0)	3·5 (2·0–5·5)	4·0 (2·0–6·0)
Skin-directed	1·0 (1·0–2·0)	1·0 (1·0–2·0)	1·0 (1·0–2·0)
Systemic	2·0 (1·0–4·0)	2·0 (1·0–3·0)	2·0 (1·0–4·0)
Mycosis fungoides	48 (75%)	49 (77%)	97 (76%)
Disease stage‡§			
IA–IIA	15/48 (31%)	18/49 (37%)	33/97 (34%)
IIB	19/48 (40%)	19/49 (39%)	38/97 (39%)
IIIA–IIIB	4/48 (8%)	2/49 (4%)	6/97 (6%)
IVA1	0	1/49 (2%)	1/97 (1%)
IVA2	2/48 (4%)	8/49 (16%)	10/97 (10%)
IVB	7/48 (15%)	0	7/97 (7%)
pcALCL	16 (25%)	15 (23%)	31 (24%)

Prince HM et al. Lancet 2017

Mogamolizumab

- Mogamulizumab a first-in-class defucosylated humanised IgG1κ moAb, selectively binds to C-C chemokine receptor 4 (CCR4) with enhanced antibody-dependent cellular cytotoxicity activity

- CCR4, which is involved in cell trafficking of lymphocytes to skin, is consistently expressed on the surface of tumour cells in T-cell malignancies, such as cutaneous T-cell lymphoma (including mycosis fungoides and Sezary syndrome), adult T-cell leukaemia-lymphoma, and peripheral T-cell lymphoma

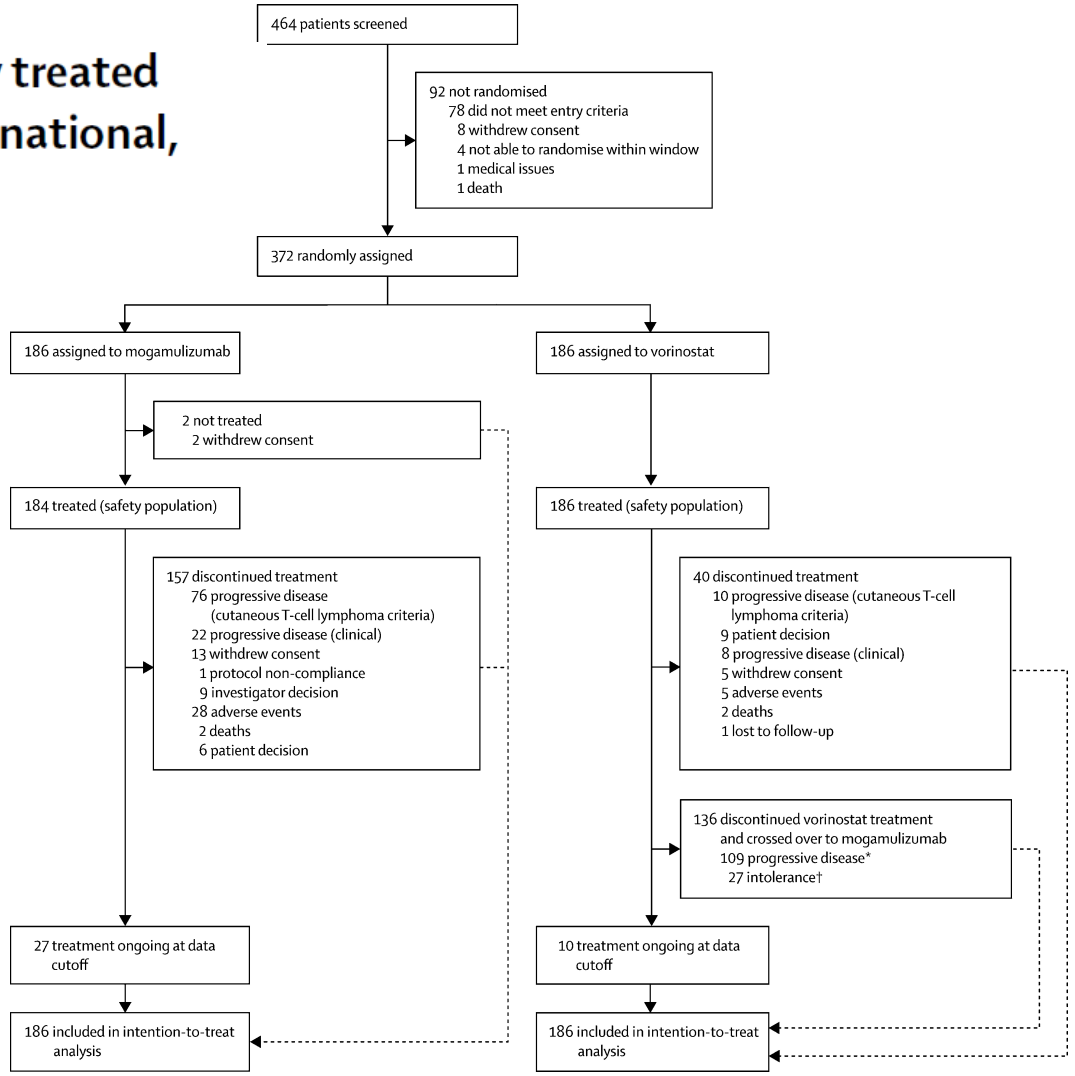
- In phase I/II Trials ORR 38%-42%

Mogamulizumab versus vorinostat in previously treated cutaneous T-cell lymphoma (MAVORIC): an international, open-label, randomised, controlled phase 3 trial

R/R MF or SS (61 centres)

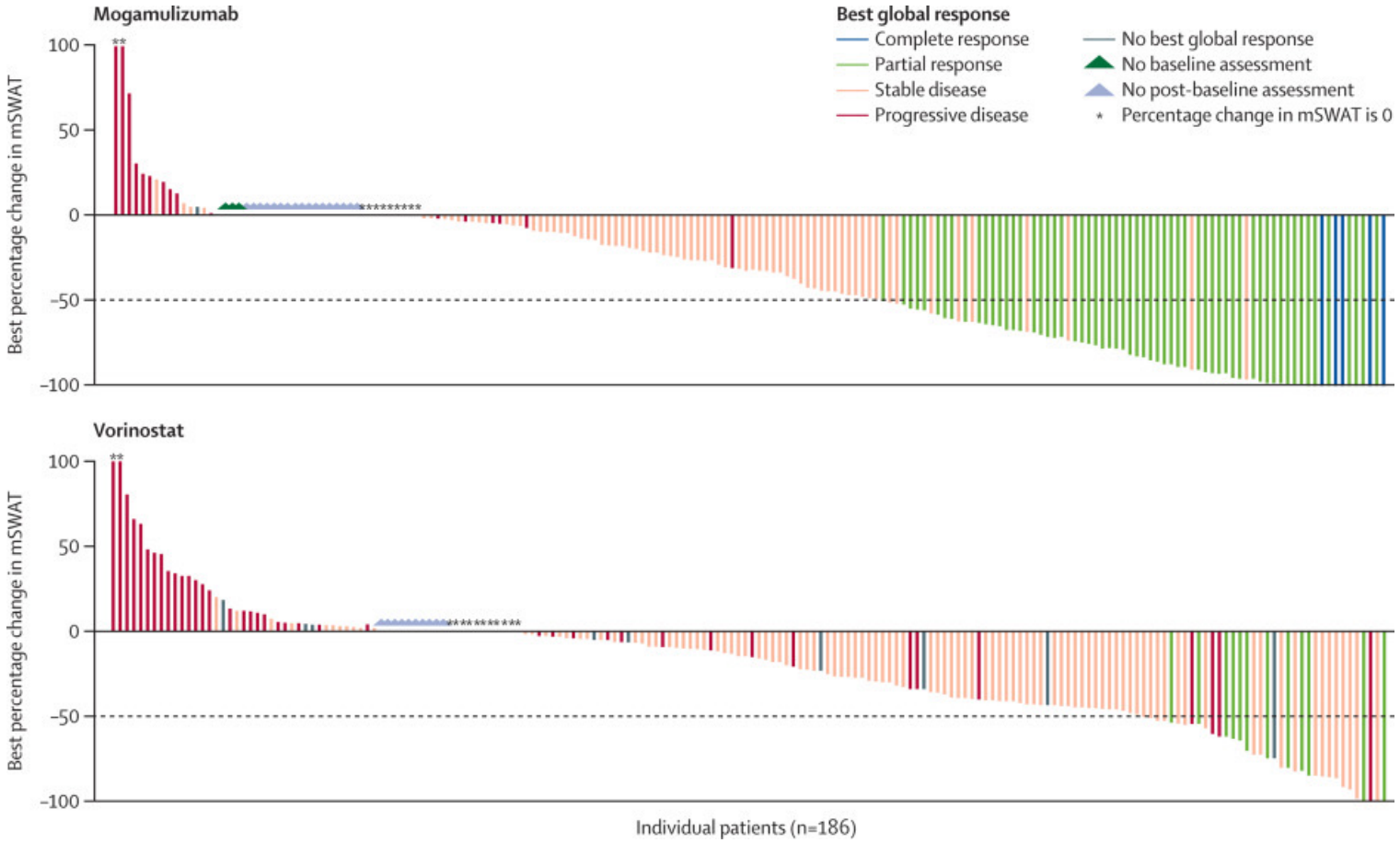
Random Mogamulizumab vs Vorinostat

Stratified by disease subtype and stage



Kim YH et al. Lancet Oncol 2018

Phase III MAVORIC Trial



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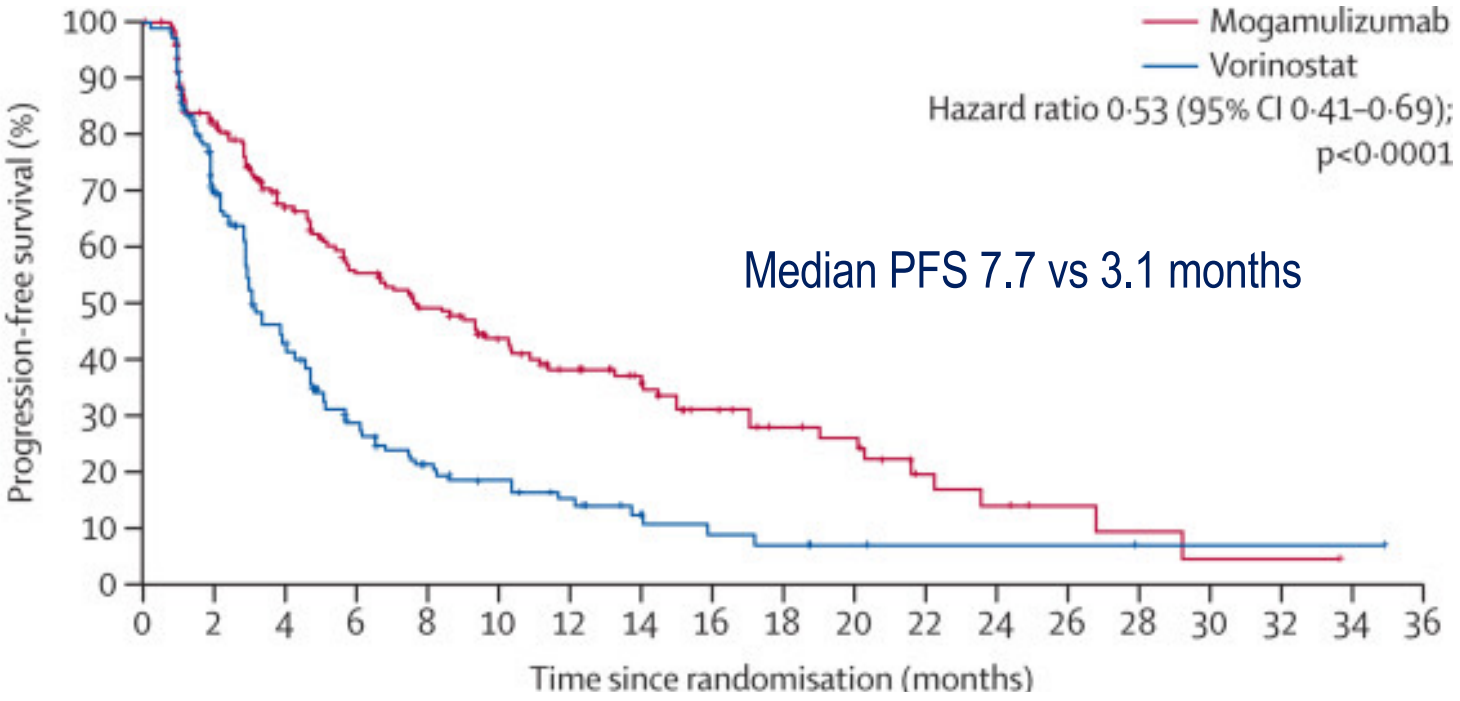
Phase III MAVORIC Trial



Kim YH et al. Lancet Oncol 2018

Phase III MAVORIC Trial

	Mogamulizumab (n=186)	Vorinostat (n=186)
Age, years	64 (54-73)	65 (56-72)
Age group, years		
<65	99 (53%)	89 (48%)
≥65	87 (47%)	97 (52%)
Sex		
Male	109 (59%)	107 (58%)
Female	77 (41%)	79 (42%)
Race		
White	125 (67%)	135 (73%)
Other	37 (20%)	26 (14%)
Not reported*	24 (13%)	25 (13%)
ECOG performance status†		
0	106 (57%)	104 (56%)
1	78 (42%)	82 (44%)
2	2 (1%)	0
Time from initial diagnosis, months‡	41·0 (17·4-78·8)	35·4 (16·2-68·2)
Disease type		
Mycosis fungoides	105 (56%)	99 (53%)
Sézary syndrome	81 (44%)	87 (47%)
Current clinical stage		
IB-IIA	36 (19%)	49 (26%)
IIB	32 (17%)	23 (12%)
IIIA-IIIB	22 (12%)	16 (9%)
IVA1	73 (39%)	82 (44%)
IVA2	19 (10%)	12 (6%)
IVB§	4 (2%)	4 (2%)
Number of previous systemic regimens received	3 (2-5)	3 (2-5)
Previous cutaneous T-cell lymphoma therapies		
Bexarotene	107 (58%)	110 (59%)
Interferon	81 (44%)	94 (51%)
Conventional chemotherapy¶	108 (58%)	94 (51%)
Romidepsin	45 (24%)	32 (17%)
Alemtuzumab	19 (10%)	16 (9%)
Pralatrexate	14 (8%)	13 (7%)
Brentuximab vedotin	16 (9%)	4 (2%)

	Mogamulizumab (n=186)	Vorinostat (n=186)
Proportion of patients with an overall response by global assessment*†	52/186 (28%)	9/186 (5%)
Overall responses in patient subgroups		
Mycosis fungoides	22/105 (21%)	7/99 (7%)
Sézary syndrome	30/81 (37%)	2/87 (2%)
Stage IB or IIA	7/36 (19%)	5/49 (10%)
Stage IIB	5/32 (16%)	1/23 (4%)
Stage III	5/22 (23%)	0/16 (0)
Stage IV	35/96 (36%)	3/98 (3%)
Duration of response, months	14·1 (8·4–19·2)	9·1 (5·6–NE)
Mycosis fungoides	13·1 (4·7–18·0)	9·1 (5·6–NE)
Sézary syndrome	17·3 (9·4–19·9)	6·9 (6·9–6·9)
Compartment response*‡		
Skin	78/186 (42%)	29/186 (16%)
Blood	83/122 (68%)	23/123 (19%)
Lymph nodes	21/124 (17%)	5/122 (4%)
Viscera	0/3 (0%)	0/3 (0%)

Data are n/N (%) or median (IQR). The proportion of patients achieving an overall response is based on the Global Composite Response score. NE=not estimable. *Proportion of patients with an overall response or compartmental response is the percentage of patients with confirmed complete response or confirmed partial response. †p<0·0001. ‡Denominator includes patients with measurable compartmental disease at baseline.

***Table 2:* Measures of response by investigator assessment**

Kim YH et al. Lancet Oncol 2018

REVIEW ARTICLE

BJD
British Journal of Dermatology

The importance of assessing blood tumour burden in cutaneous T-cell lymphoma*

M.H. Vermeer[1] J.P. Nicolay[2,3,4] J.J. Scarisbrick[5] and P.L. Zinzani[6,7]

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[2]Department of Dermatology, University Medical Centre Mannheim, University of Heidelberg, Mannheim, Germany
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[4]Section of Clinical and Experimental Dermatology, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany
[5]University Hospital Birmingham, Birmingham, UK
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[7]Istituto di Ematologia 'Seràgnoli', Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale, Università degli Studi, Bologna, Italy

Table 1 Classification of peripheral blood involvement in patients with cutaneous T-cell lymphoma (mycosis fungoides or Sézary syndrome)

Original TNM classification[6]		ISCL/EORTC revised classification[11]		EORTC–CLWG updated blood classification[14]
B0	No Sézary cells circulating in peripheral blood (< 5%)	B0	No significant blood involvement: ≤ 5% of lymphocytes in peripheral blood are atypical	Recommend objective assessment of blood class using flow cytometry to assess absolute lymphocyte counts of either $CD4^+$ $CD7^-$ in $CD26^+$ patients or $CD4^+$ $CD26^-$
		B0a	T-cell clone negative[a]	
		B0b	T-cell clone positive	
B1	Sézary cells present in peripheral blood (> 5%); record the total white blood cell count, total lymphocyte count and number of Sézary cells per 100 lymphocytes	B1	Low blood tumour burden: > 5% peripheral blood lymphocytes are atypical but does not meet criteria for B2 class	B0 is defined as a count of < 250 cells μL^{-1}
		B1a	T-cell clone negative	B1 is defined as a count of > 250 cells μL^{-1} up to 1000 cells μL^{-1}
		B1b	T-cell clone positive	
		B2	High blood tumour burden: ≥ 1000 Sézary cells per µL or increased $CD4^+$ or $CD3^+$ cells with CD4/CD8 ratio of ≥ 10 or increased $CD4^+$ cells with an atypical phenotype (≥ 40% $CD4^+$ $CD7^-$ or ≥ 30% $CD4^+$ $CD26^-$) and a positive T-cell clone	B2 is defined as a count of ≥ 1000 cells μL^{-1} plus a positive T-cell clone

Wermeer MH et al . BJD 2021

- It has been reported that patients in either B1 or B2 stage have a 4 to 6-fold greater risk of disease progression than those in B0
- Furthermore, the median survival of patients with B1 or B2 blood involvement is considerably affected compared with B0, independently of disease stage
- A better understanding of which patients with early-stage disease will go on to develop advanced disease is particularly important in this context, as it will help guide treatment choices
- Improving the methodology and extent of blood testing for patients with early-stage MF to establish the proportion of patients with B1- or B2-level blood involvement in stage I–IIA disease is crucial in determining the risk for disease progression in patients with less advanced disease

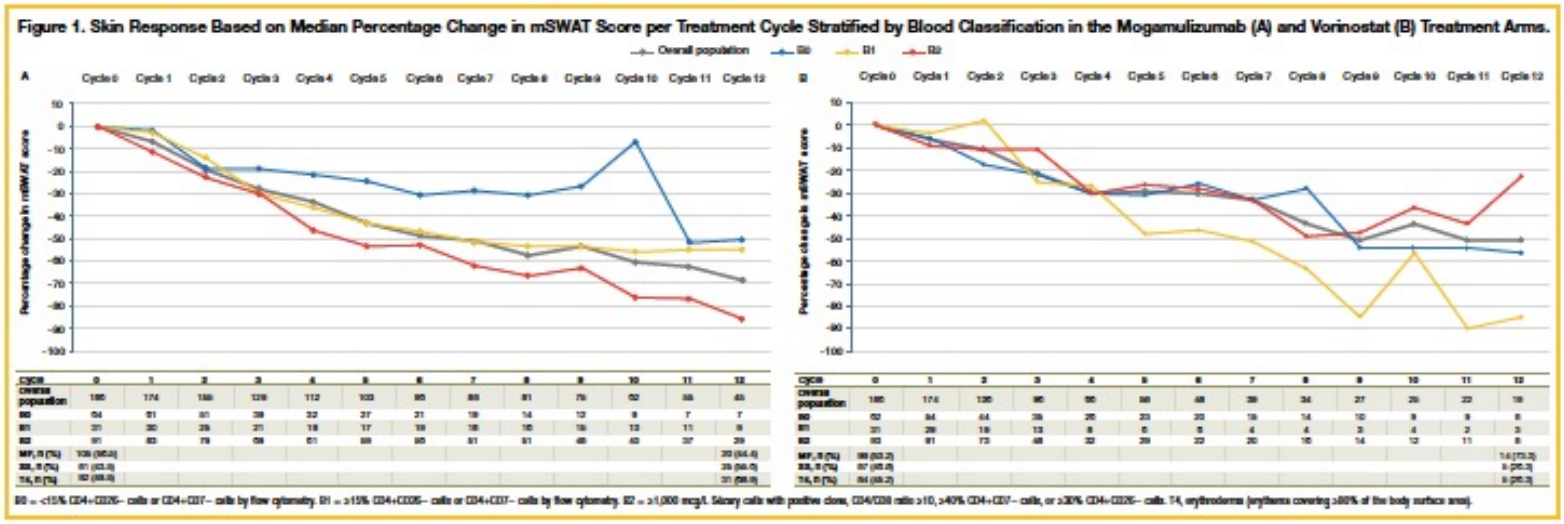
The Correlation Between Skin Response and Blood Involvement with Mogamulizumab

P139

Pietro Quaglino[1], Lars Iversen[2], Reinhard Dummer[3], Amy Musiek[4], Jan-Paul Rosen[5]

[1]University of Turin, Turin, Italy; [2]Department of Dermatology, Aarhus University Hospital, Aarhus, Denmark; [3]University Hospital Zurich, Zurich, Switzerland; [4]Division of Dermatology, Washington University in St. Louis, St. Louis, MO, USA; [5]Kyowa Kirin International, Marlow, UK

OVERALL POPULATION **B0** **B1** **B2**



By courtesy of Pietro Quaglino

The Correlation Between Skin Response and Blood Involvement with Mogamulizumab

P139

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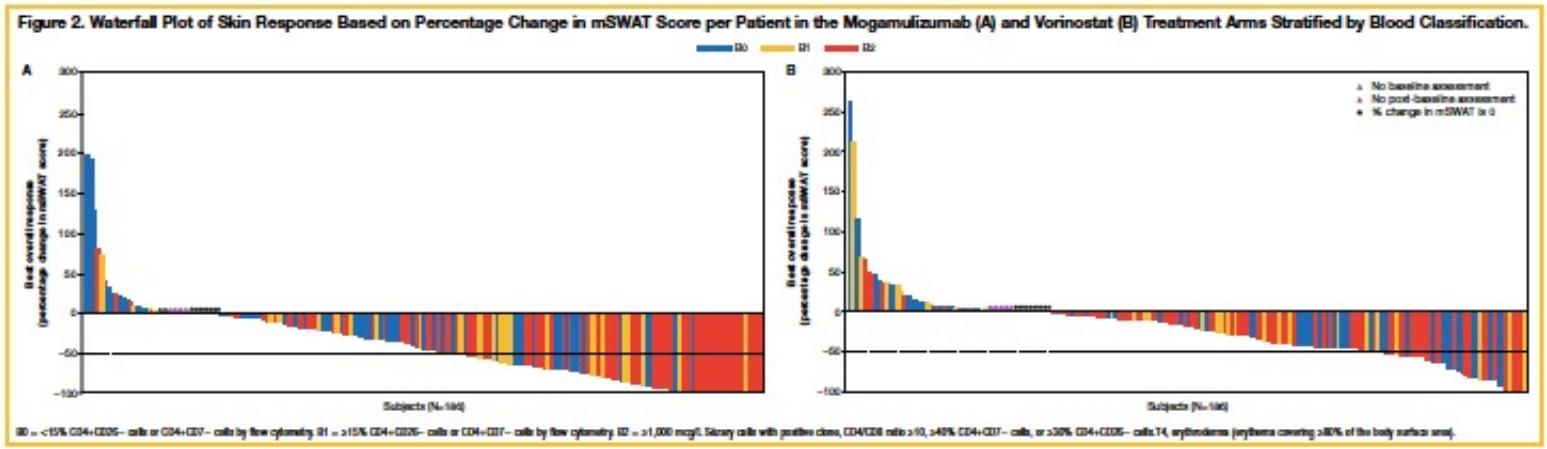
OVERALL POPULATION **B0** **B1** **B2**



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RESEARCH ARTICLE

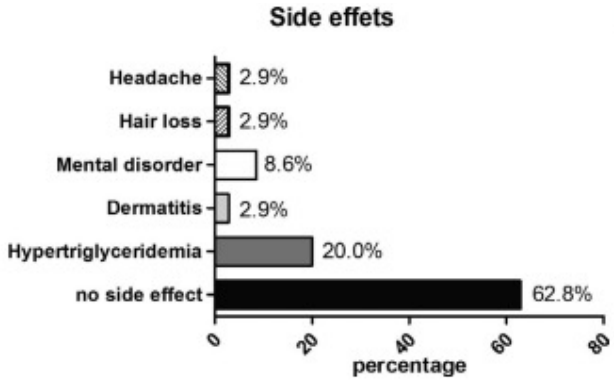
Cancer Medicine Open Access WILEY

Alitretinoin in the treatment of cutaneous T-cell lymphoma

Till Kaemmerer[1] | Pia-Charlotte Stadler[1] | Leonie Helene Frommherz[1] | Anne Guertler[1] | Lars Einar French[1,2] | Markus Reinholz[1]

	Overall	Mycosis fungoides (MF)	Sézary syndrome (SS)
	n = 35	*n* = 28	*n* = 7
Age (years)		56 (26–77)	65 (49–79)
Stages (TNMB)			
I			
IA	5 (14.3%)	5 (17.9%)	0
IB	13 (37.1%)	13 (46.4%)	0
II			
IIA	0	0	0
IIB	6 (17.1%)	6 (21.4%)	0
III			
IIIA	3 (8.6%)	3 (10.7%)	0
IIIB	1 (3%)	1 (3.6%)	0
IV			
IVA1	7 (20%)	0	7 (100%)

	Overall	Mycosis fungoides (MF)	Sézary syndrome (SS)
	n = 35	*n* = 28	*n* = 7
Single-agent alitretinoin	9 (25.7%)	9 (32.1%)	0
Combinations with alitretinoin			
INF-a	3 (8.6%)	3 (10.7%)	0
ECP	11 (31.4%)	8 (13.8%)	3 (42.9%)
PUVA	4 (11.4%)	3 (10.7%)	1 (12.5%)
UVB	3 (8.6%)	2 (7.1%)	1 (12.5%)
PUVA + Radiotherapy	2 (5.7%)	2 (7.1%)	0
PUVA + ECP	3 (8.6%)	1 (3.6%)	2 (28.6%)



	Overall	Mycosis fungoides (MF)	Sézary syndrome (SS)	Duration of alitretinoin
	n = 35	*n* = 28	*n* = 7	
Complete response (CR)	3 (8.6%)	3 (10.7%)	0	29 (16-54)
Partial response (PR)	10 (28.6%)	9 (32.1%)	1 (14.3%)	18 (3-83)
Stable disease (SD)	10 (28.6%)	8 (28.6%)	2 (28.6%)	17 (2-47)
Progressive disease (PD)	12 (34.3%)	8 (28.6%)	4 (57.1%)	27 (2-80)

Kaemmerer T et al. Cancer Med 2021

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