Sabati Ematologici della Romagna

Meldola, 24 settembre 2016

Nuovi obiettivi clinici nell'impiego del brentuximab vedotin

I LINFOMI PRIMITIVI DELLA CUTE DI DERIVAZIONE T

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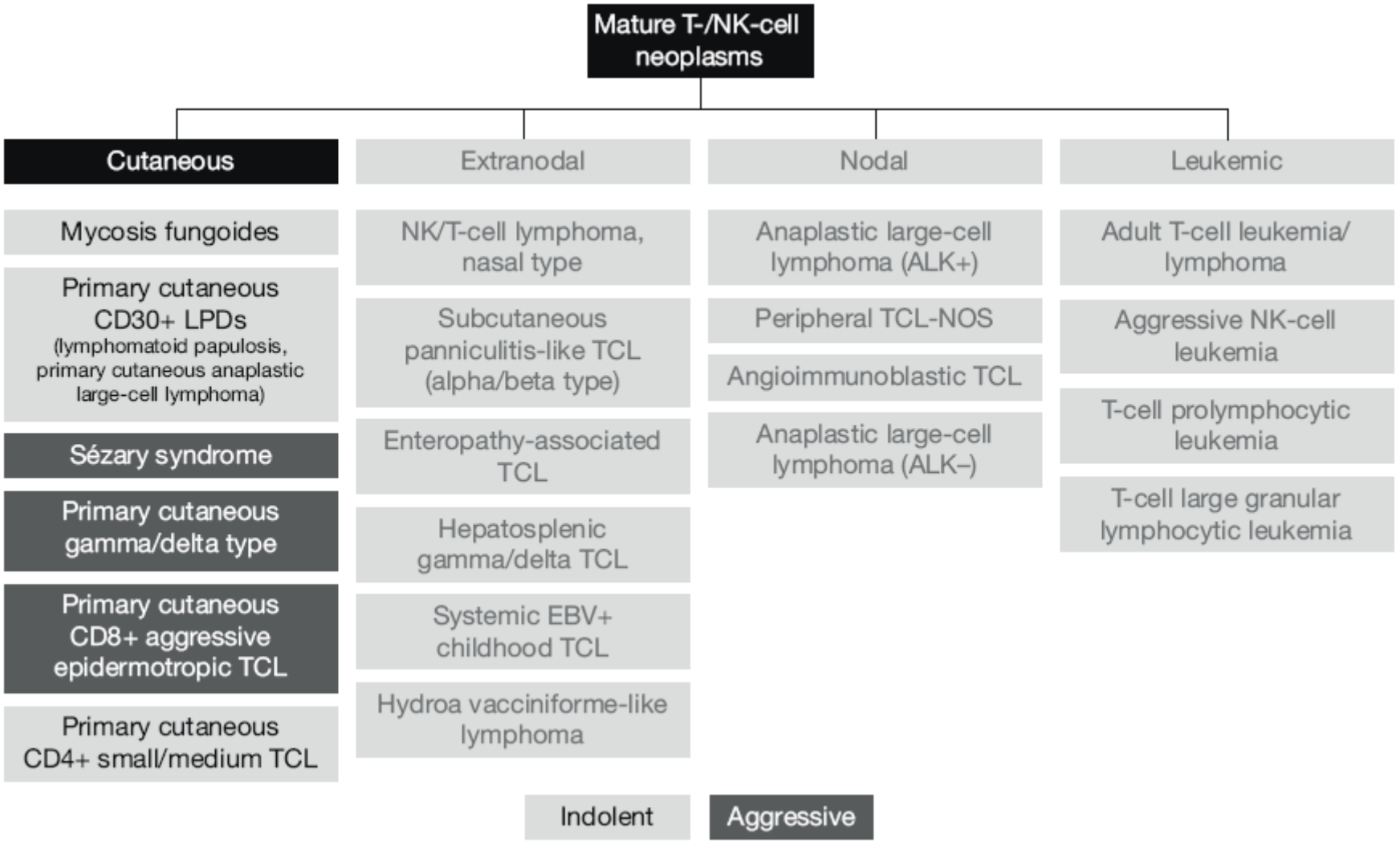
LINFOMI CUTANEI T-LINFOCITARI

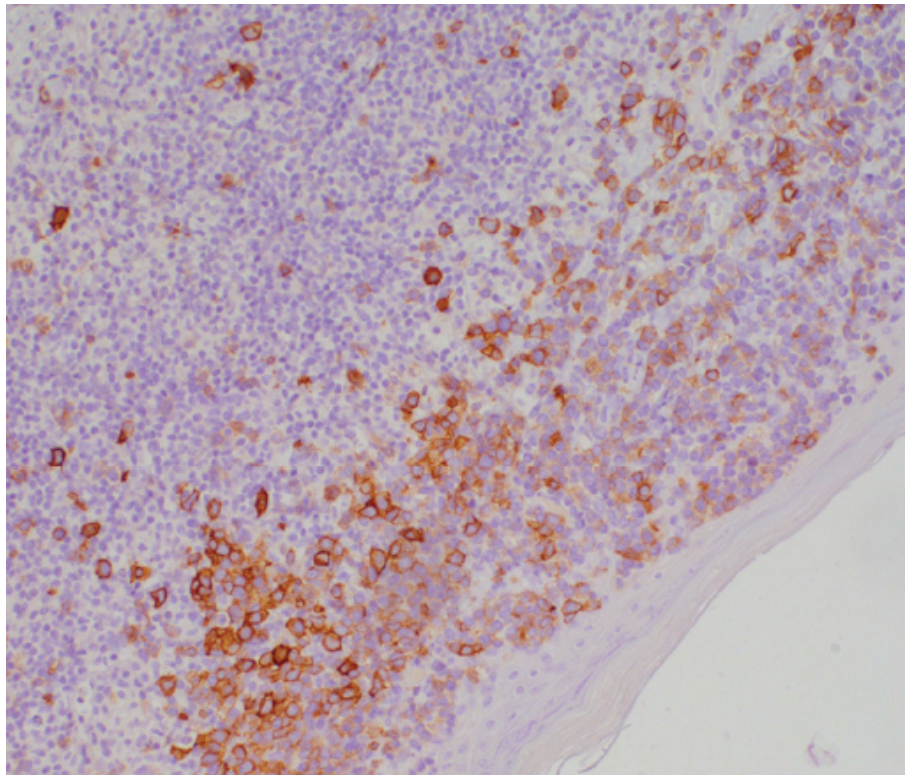


Zinzani PL. *Crit Rev Oncol Hematol*, 2016; 99: 228-240

LINFOMI CUTANEI T-LINFOCITARI CD30+

- Mycosis fungoides
- Mycosis fungoides, variants and subtypes
  - Folliculotropic mycosis fungoides
  - Pagetoid reticulosis
  - Granulomatous slack skin
- Sézary syndrome
- Adult T-cell leukaemia/lymphoma
- Primary cutaneous CD30+ lymphoproliferative disorders
  - Primary cutaneous anaplastic large cell lymphoma
  - Lymphomatoid papulosis
- Subcutaneous panniculitis-like T-cell lymphoma
- Extranodal NK/T-cell lymphoma, nasal type
- Primary cutaneous peripheral T-cell lymphoma, unspecified
  - Primary cutaneous aggressive epidermotropic $CD8^+$ T-cell lymphoma*
  - Cutaneous γ/δ T-cell lymphoma*
  - Primary cutaneous $CD4^+$ small/medium-sized pleomorphic T-cell lymphoma*

*provisional entity.



Prince HM. *J Clin Oncol*, 2015; 33: 3691-3696
Zinzani PL. Broccoli A. *Postgraduate Hematology*, 7th ed. 2016; 524-536

MICOSI FUNGOIDE

- È il più frequente linfoma cutaneo a cellule T (Alibert e Bazin, 1806).
- Il decorso è indolente, con lenta ma progressiva evoluzione temporale in differenti stadi: chiazze (*patches*), placche (*plaques*), tumori.
- La stadiazione clinica correla direttamente con la prognosi ed è funzionale all'impostazione del trattamento.
- La triade: eritrodermia, linfoadenopatia generalizzata, presenza di linfociti atipici circolanti (≥ 1000/mmc) viene definita **sindrome di Sézary** (Sézary e Bouvrain, 1938).

Zinzani PL. Broccoli A. *Postgraduate Hematology*, 7th ed. 2016; 524-536

ESPRESSIONE DEL CD30

	CD30 IHC SCORE					
	0	1+	2+	3+	4	Score ≥2+
PTCL, NOS (87 cases)	31 (35.63%)	11 (12.64%)	18 (20.69%)	11 (12.64%)	16 (18.39%)	45/87 (51.72%)
AITL (42 cases)	24 (51.14%)	9 (21.42%)	5 (11.90%)	4 (9.52%)	-	9/42 (21.42%)
ENTL (10 cases)	2 (20.00%)	1 (10.00%)	3 (30.00%)	1 (10.00%)	3 (30.00%)	7/10 (70.00%)
MF (32 cases)	13* (40.63%)	15** (46.88%)	2§ (6.25%)	-	2§§ (6.25%)	4/32 (12.50%)
Transformed MF (9 cases)	-	-	3 (33.33%)	6 (66.67%)	-	9/9 100%
EATL type 1 (9 cases)	-	-	2 (22.22%)	-	7 (77,78%)	9/9 (100,00%)
EATL type 2 (3 cases)	3 (100%)	-	-	-	-	-
All types (192 cases)	73 (38.02%)	36 (18.75%)	33 (17.18%)	17 (8.85%)	28 (14.58%)	83/192 (43.22%)

(*) 2 casi in stadio tumorale; (**) 1 caso in stadio tumorale; (§) variante follicolotropa; (§§) reticulosi pagetoide

Sabattini E. *Haematologica*, 2013; 98: e81-82

PROCEDURE DI STADIAZIONE

Recommended evaluation/initial staging
Complete physical examination including
Determination of type(s) of skin lesions.
If only patch/plaque disease or erythroderma, then estimate percentage of BSA involved and note any ulceration of lesions.
If tumors are present, determine total number of lesions, aggregate volume, largest size lesion, and regions of the body involved.
Identification of any palpable lymph node, especially those ≥1.5 cm in largest diameter or firm, irregular, clustered, or fixed.
Identification of any organomegaly.
Skin biopsy
Most indurated area if only 1 biopsy.
Immunophenotyping to include at least the following markers: CD2, CD3, CD4, CD5, CD7, CD8, and a B-cell marker such as CD20. CD30 should be considered especially in cases where lymphomatoid papulosis, anaplastic lymphoma, or large-cell transformation is considered. CCR4 if mogamulizumab available.
Evaluation for clonality of TCR gene rearrangement.
Blood tests
CBC with manual differential, liver function tests, LDH, comprehensive chemistries.
TCR gene rearrangement and relatedness to any clone in skin.
Analysis for abnormal lymphocytes by either Sézary cell count with determination absolute number of Sézary cells and/or flow cytometry (including $CD4^+/CD7^-$ or $CD4^+/CD26^-$).
Radiologic tests
In patients with $T_1N_0B_0$ stage disease who are otherwise healthy and without complaints directed to a specific organ system, and in selected patients with $T_2N_0B_0$ disease with limited skin involvement, radiologic studies may be limited to a chest radiograph or ultrasound of the peripheral nodal groups to corroborate absence of adenopathy.
In all patients with other than presumed stage IA disease, or selected patients with limited T_2 disease and the absence of adenopathy or blood involvement, CT scans of chest, abdomen, and pelvis alone ± FDG-PET scan are recommended to further evaluate any potential lymphadenopathy, visceral involvement, or abnormal laboratory tests. In patients unable to safely undergo CT scans, MRI may be substituted.
Lymph node biopsy
Excisional biopsy is indicated in those patients with a node that is either ≥1.5 cm in diameter and/or is firm, irregular, clustered, or fixed.
Site of biopsy: Preference is given to the largest lymph node draining an involved area of the skin or if FDG-PET scan data are available, the node with highest SUV. If there is no additional imaging information and multiple nodes are enlarged and otherwise equal in size or consistency, the order of preference is cervical, axillary, and inguinal areas.
Analysis: pathologic assessment by light microscopy, flow cytometry, and TCR gene rearrangement.

Whittaker S. *Blood*, 2016; 127: 3142-3153

STADIAZIONE TNMB (1)

TNMB	Stadiazione TNMB	
Cute	T1	Chiazze, papule o placche limitate, con interessamento di meno del 10% della superficie cutanea. Ulteriore stratificazione: T1a (solo chiazze), T1b (placche ± chiazze)
	T2	Chiazze, papule o placche diffuse, con interessamento di almeno il 10% della superficie cutanea. Ulteriore stratificazione: T2a (solo chiazze), T2b (placche ± chiazze)
	T3	Una o più lesioni tumorali di diametro ≥ 1 cm
	T4	Eritema confluente, con interessamento di almeno l'80% della superficie cutanea
Linfonodi	N0	Assenza di linfonodi clinicamente patologici
	N1	Linfonodi clinicamente patologici (Dutch grado 1 o NCI LN_{0-2})
	N2	Linfonodi clinicamente patologici (Dutch grado 2 o NCI LN_3)
	N3	Linfonodi clinicamente patologici (Dutch grado 3 o NCI LN_4)
	N_X	Linfonodi clinicamente patologici (assente conferma istologica)
Visceri	M0	Assenza di interessamento viscerale
	M1	Interessamento viscerale (richiesta conferma istologica; l'organo interessato va specificato)
Sangue	B0	Assenza di interessamento del sangue periferico ≤ 5% di linfociti atipici in periferia (cellule di Sézary)
	B1	Interessamento del sangue periferico, oltre il 5% di linfociti atipici in periferia (cellule di Sézary); non soddisfatti i criteri per lo stadio B2
	B2	Interessamento del sangue periferico con almeno 1.000 cellule di Sézary/mmc nel sangue periferico, con conferma immunofenotipica

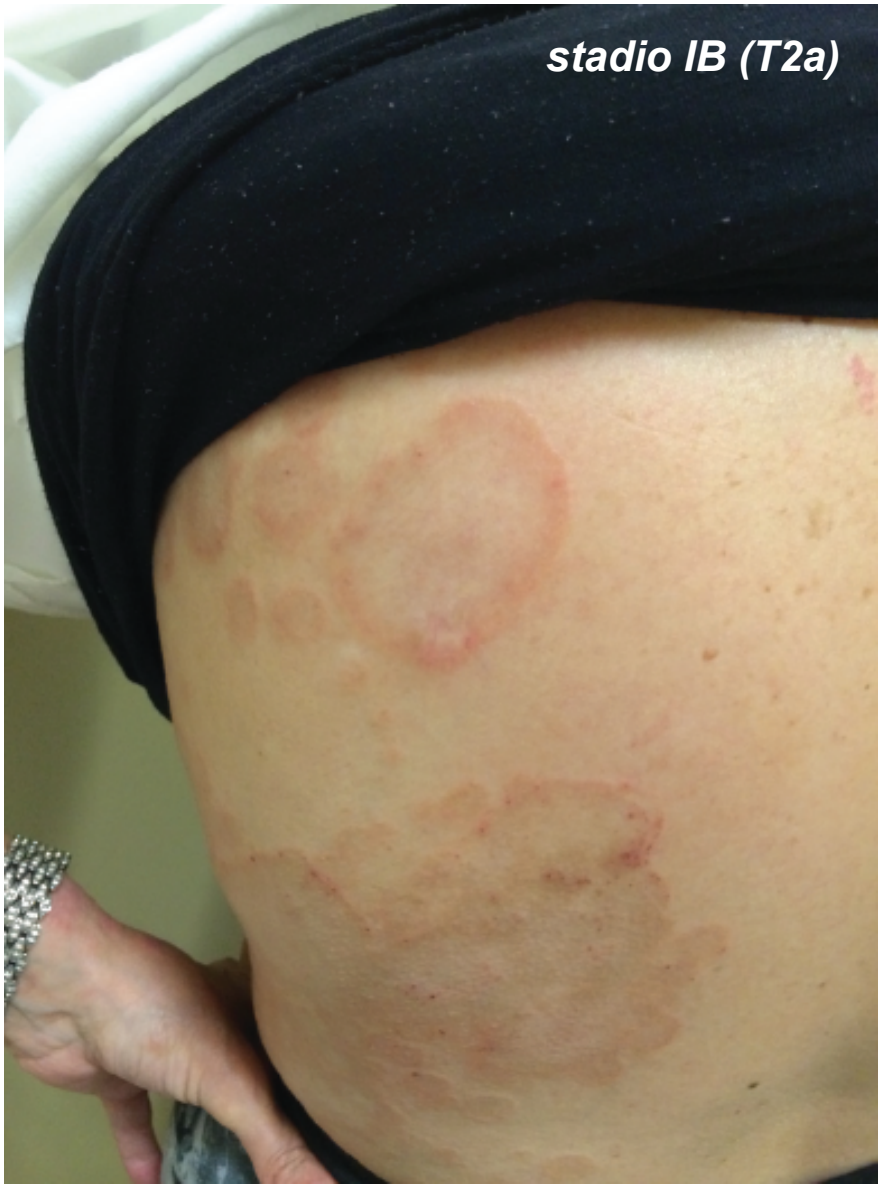
Olsen E. *Blood*, 2007; 110: 1713-1722

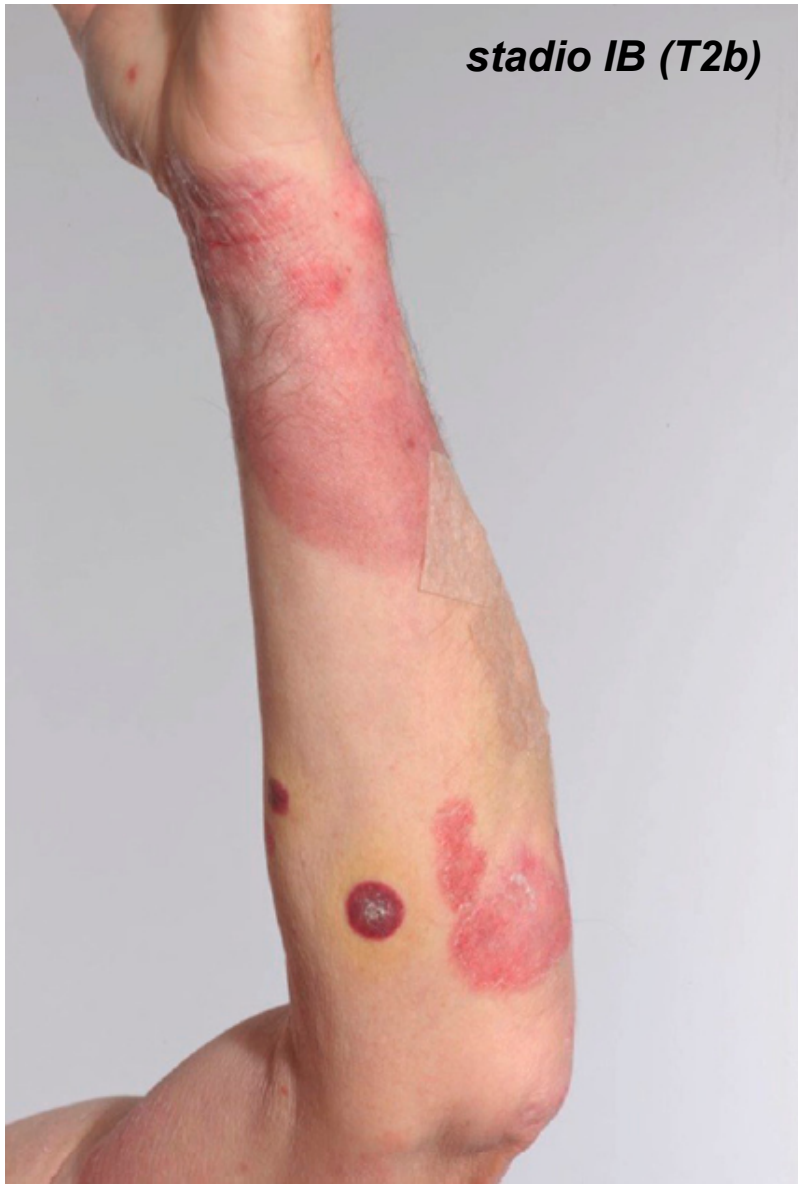
STADIAZIONE TNMB (2)

Stadio	T	N	M	B	
I A	1	0	0	0-1	Malattia cutanea limitata
I B	2	0	0	0-1	Malattia cutanea generalizzata
II A	1-2	1-2	0	0-1	Malattia cutanea generalizzata
II B	3	0-2	0	0-1	Stadio dei tumori
III A	4	0-2	0	0	Stadio dell'eritrodermia
III B	4	0-2	0	1	
IV A_1	1-4	0-2	0	2	Stadio nodale-viscerale e Sindrome di Sézary
IV A_2	1-4	3	0	0-2	
IV B	1-4	0-3	1	0-2	

Olsen E. *Blood*, 2007; 110: 1713-1722

CLINICA (1)





Zinzani PL. Broccoli A. *Postgraduate Hematology*, 7th ed. 2016; 524-536

Whittaker S. *Blood*, 2016; 127: 3142-3153

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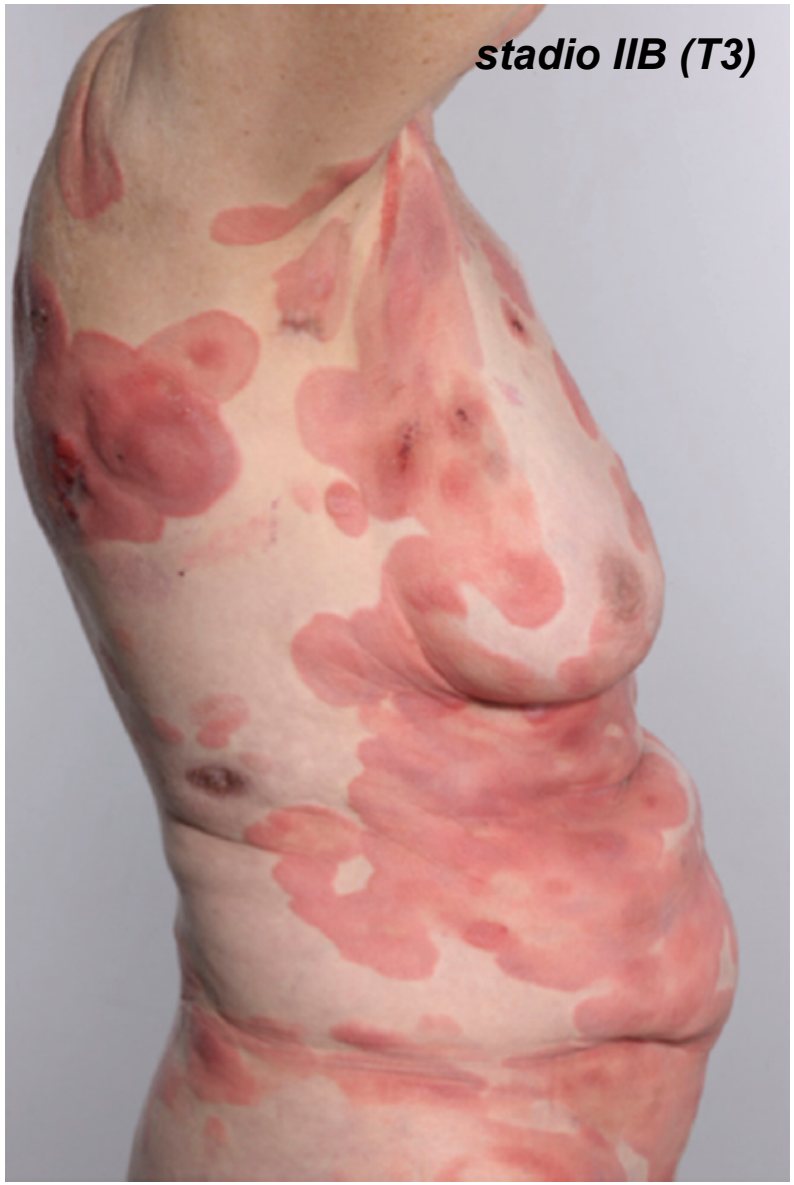
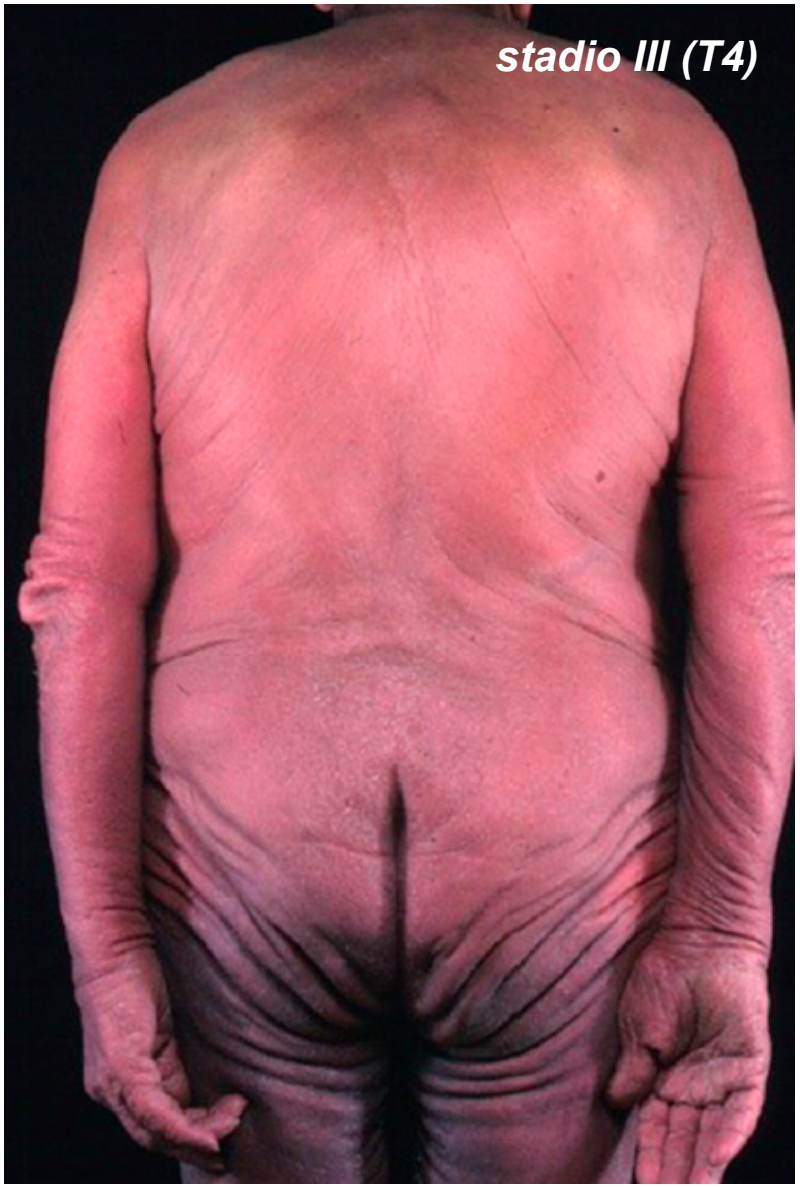
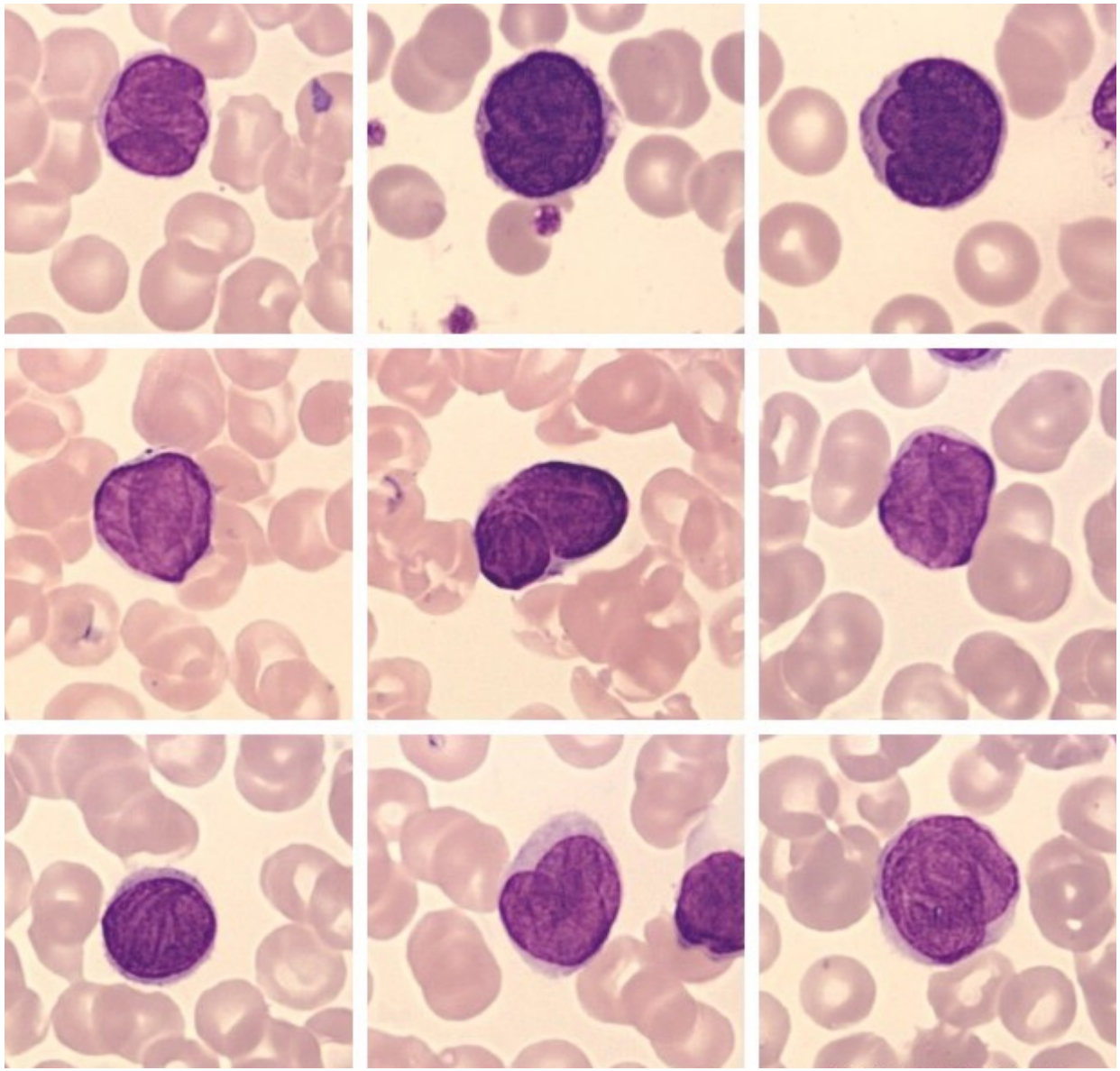
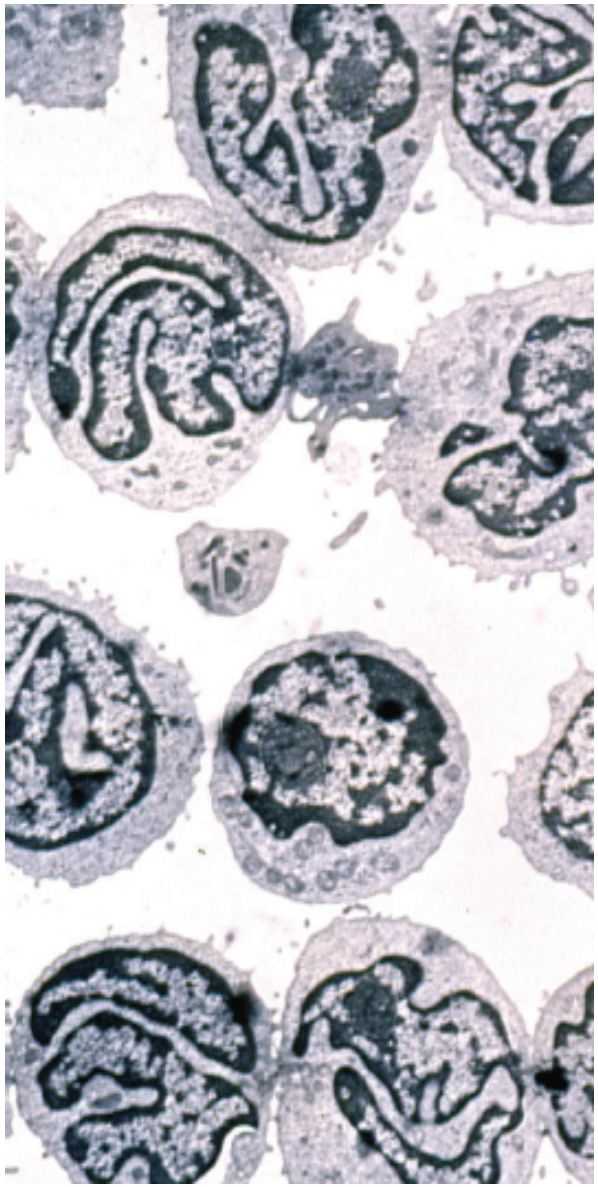




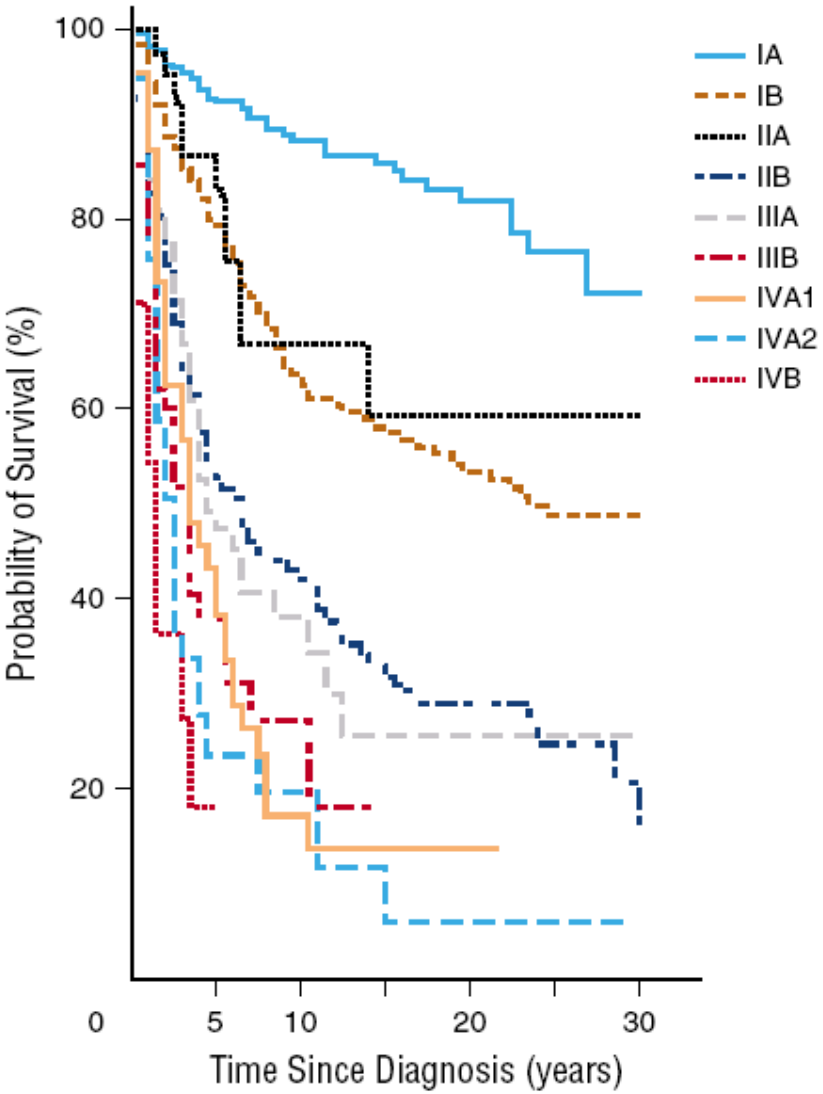
Whittaker S. *Blood*, 2016; 127: 3142-3153

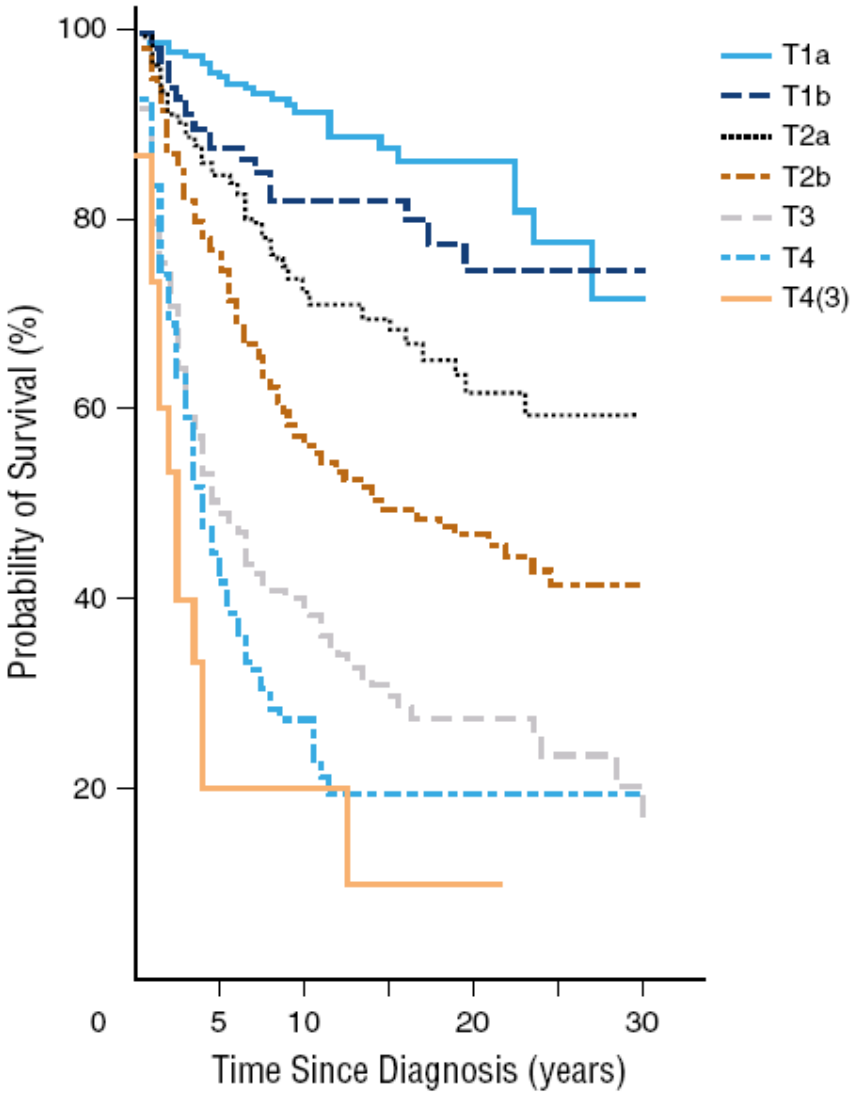
CELLULE DI SÉZARY





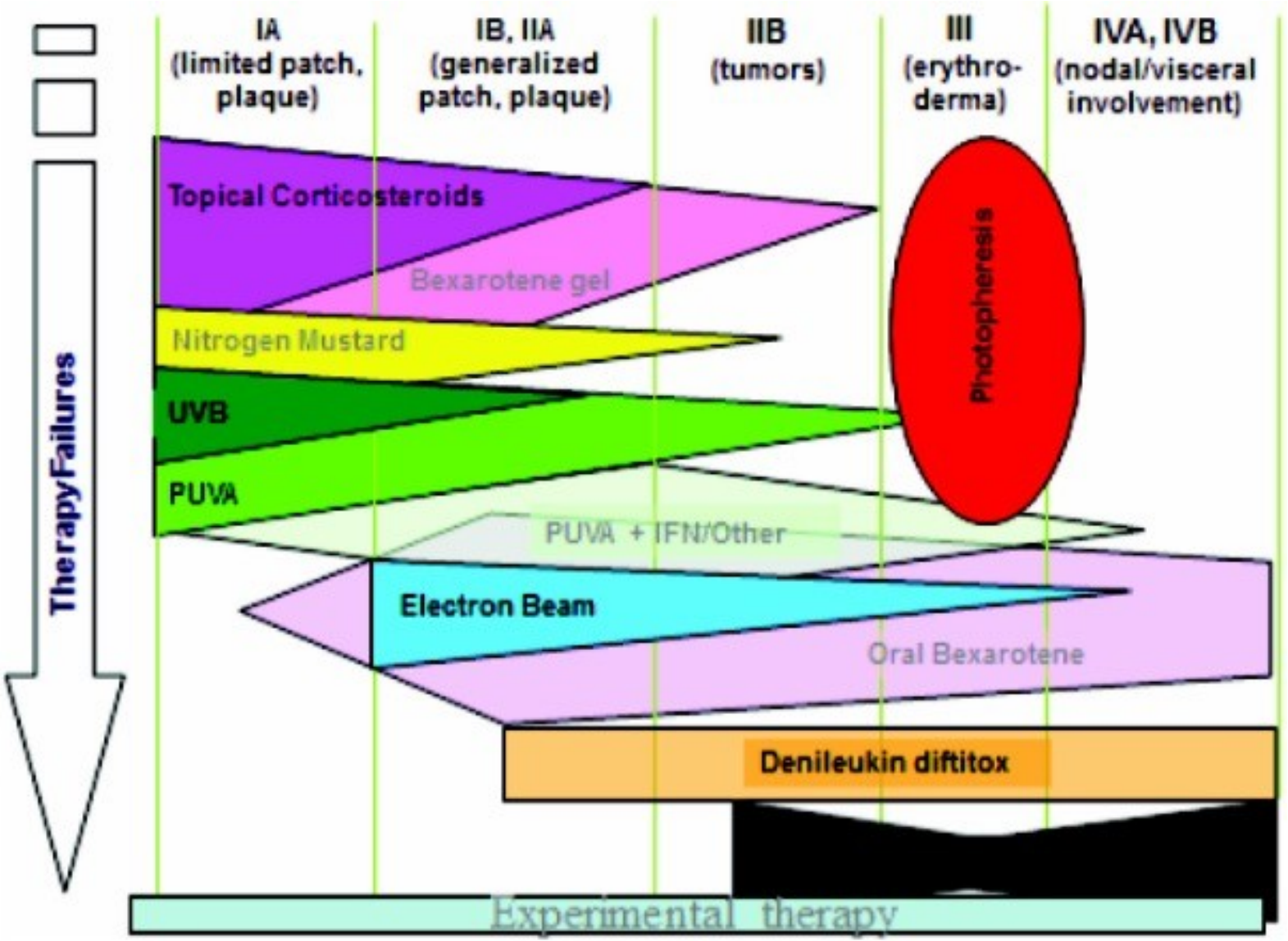
PROGNOSI





Whittaker S. *Blood*, 2016; 127: 3142-3153

PRINCIPI DI TERAPIA

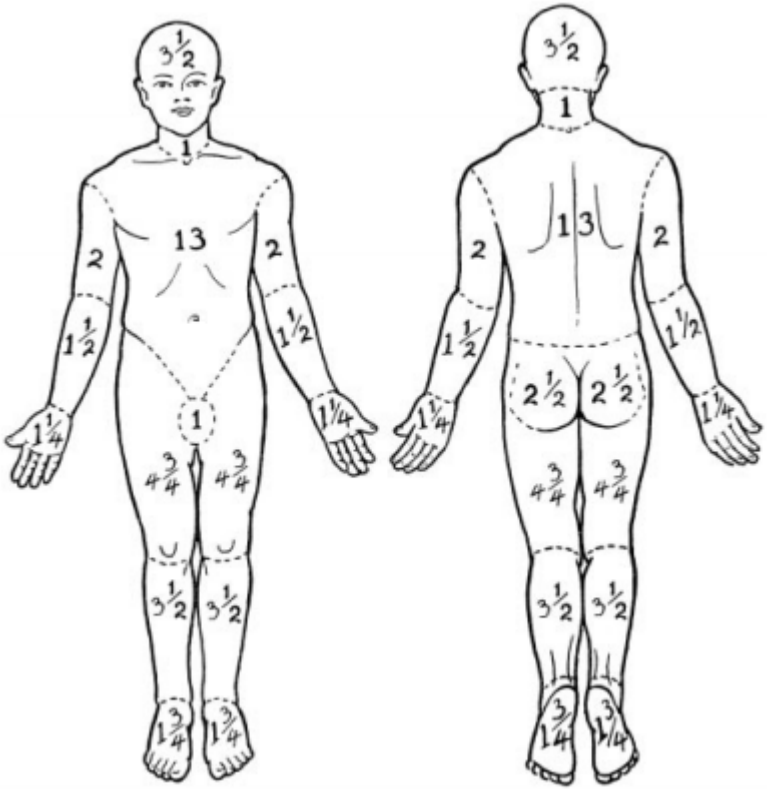


Duvic M. *Hematology Am Soc Hematol Educ Program*, 2015; 2015: 529-544

COINVOLGIMENTO CUTANEO E CRITERI DI RISPOSTA (1)

Body Region	% BSA in Body Region	Assessment of Involvement in Patient's Skin		
		Patch*	Plaque†	Tumor‡
Head	7			
Neck	2			
Anterior trunk	13			
Arms	8			
Forearms	6			
Hands	5			
Posterior trunk	13			
Buttocks	5			
Thighs	19			
Legs	14			
Feet	7			
Groin	1			
Subtotal of lesion BSA				
Weighting factor		×1	×2	×4
Subtotal lesion BSA × weighting factor				

NOTE. mSWAT score equals summation of each column line.
Abbreviations: BSA, body surface area; mSWAT, modified Severity Weighted Assessment Tool.
*Any size lesion without induration or significant elevation above the surrounding uninvolved skin; poikiloderma may be present.
†Any size lesion that is elevated or indurated; crusting, ulceration, or poikiloderma may be present.
‡Any solid or nodular lesion ≥ 1 cm in diameter with evidence of deep infiltration in the skin and/or vertical growth.



mSWAT: modified severity-weighted assessment tool

Olsen E. *Blood*, 2007; 110: 1713-1722
Olsen EA. *J Clin Oncol*, 2011; 29: 2598-2607

COINVOLGIMENTO CUTANEO E CRITERI DI RISPOSTA (2)

Global Score	Definition	Skin	Nodes	Blood	Viscera
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	CR/NI, PR, SD in any category and no category has a PD		
PD	Progressive disease		PD in any category		
Relapse	Recurrence disease in prior CR		Relapse in any category		

Olsen EA. *J Clin Oncol*, 2011; 29: 2598-2607

PAPULOSI LINFOMATOIDE (LyP)

- Eruzione cutanea a carattere cronico e ricorrente (***a "va e vieni"***), con lesioni a carattere papulare o papulo-necrotico, prevalentemente diffuse al tronco e agli arti.

- Il decorso è **indolente** e **autolimitantesi** nell'arco di 4-12 settimane. Le lesioni che regrediscono lasciano una piccola cicatrice superficiale.

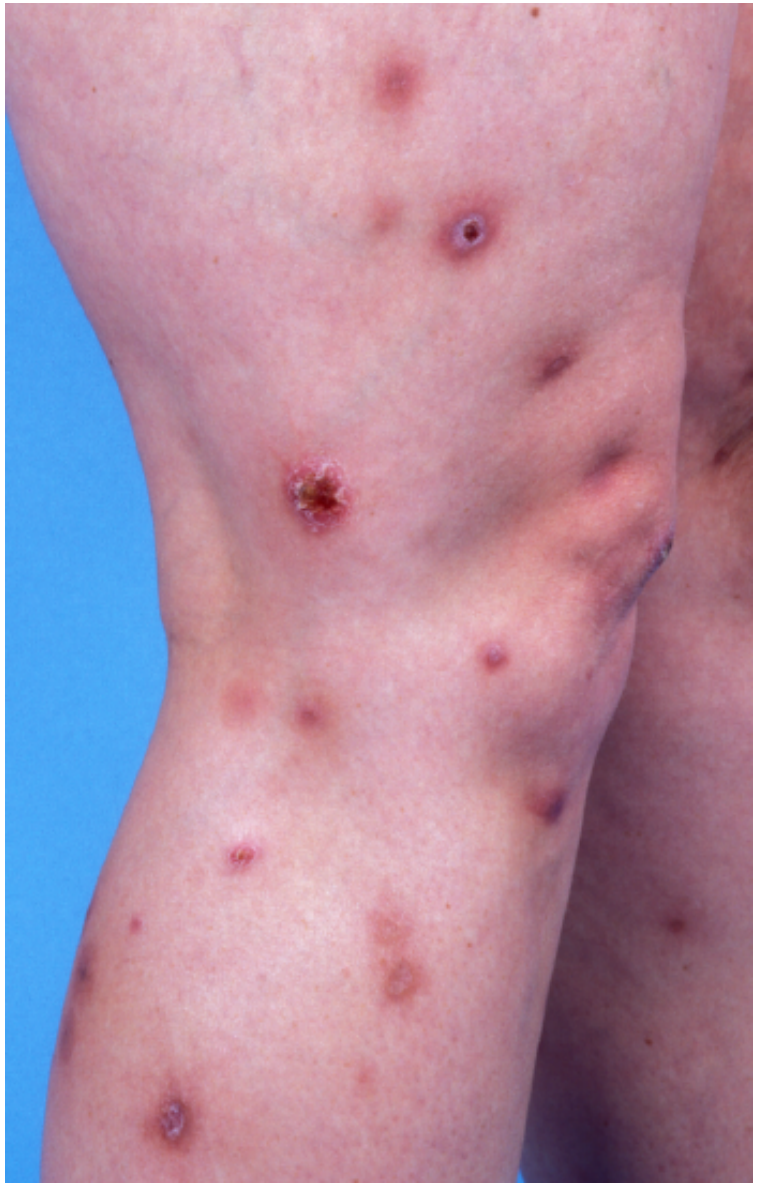
- Istologicamente, ricordano la morfologia di un linfoma T cutaneo (pc-ALCL, MF), con **intensa espressione dell'antigene CD30**.

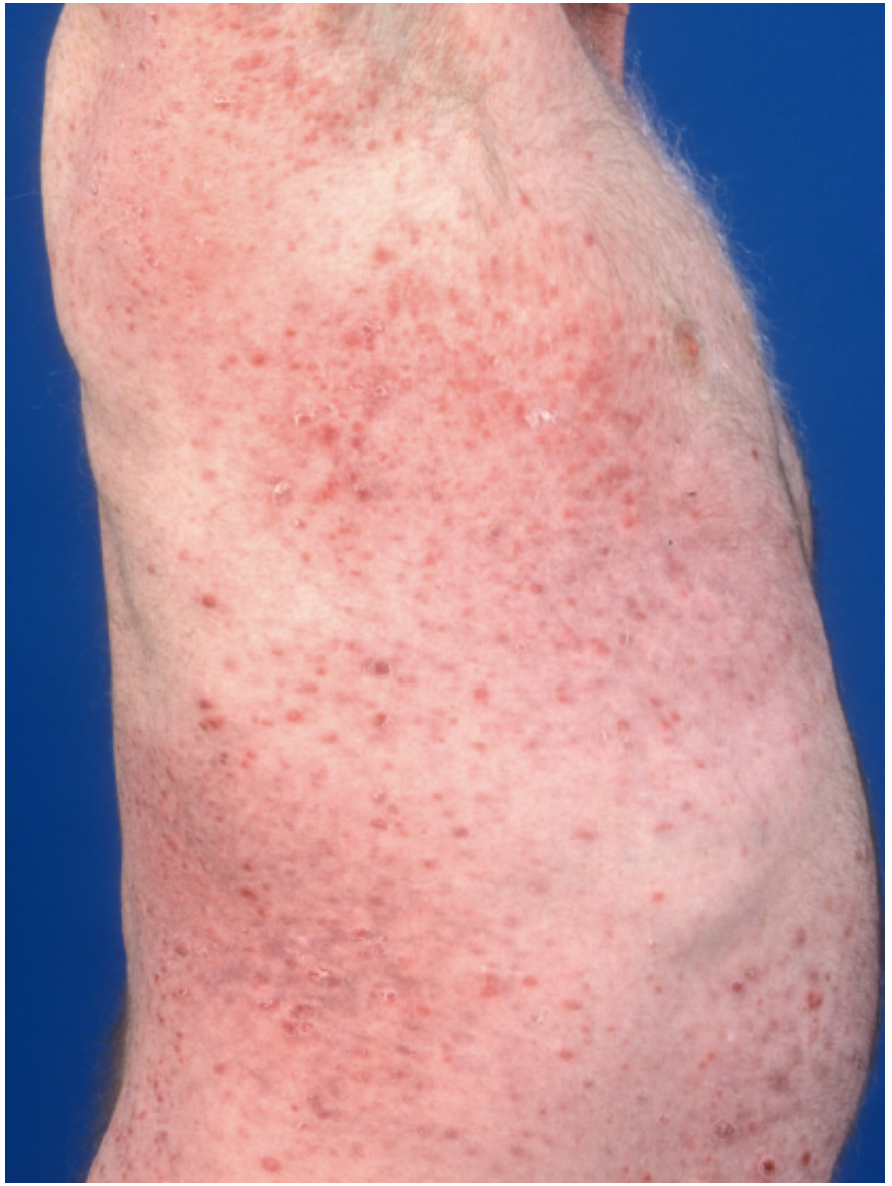
- L'**associazione con neoplasie linfoidi** maligne (pc-ALCL, MF, linfoma di Hodgkin) si ha nel 15-20% dei casi, anche in compresenza.

- **La prognosi è eccellente** senza terapia. Un trattamento (topico) è richiesto in presenza di malattia disseminata.

Zinzani PL. Broccoli A. *Postgraduate Hematology*, 7th ed. 2016; 524-536

PAPULOSI LINFOMATOIDE (LyP)





LINFOMA ANAPLASTICO PRIMITIVO CUTANEO (pc-ALCL)

- È il secondo più frequente linfoma cutaneo a cellule T mature. Colpisce gli individui adulti; è raro nella popolazione pediatrica e adolescente.

- Le lesioni sono generalmente **solitarie**, a carattere papulare, nodulare o tumorale, con frequente tendenza all'**ulcerazione**.

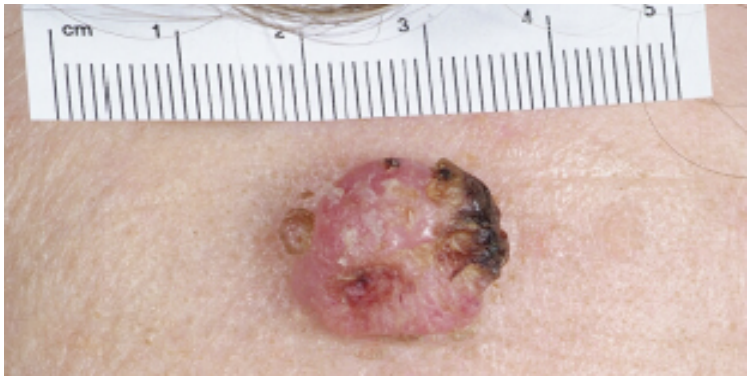
- Le sedi più colpite sono il tronco, il volto, le estremità e i glutei. Sono assai rari sia l'interessamento multifocale sia l'estensione extracutanea e nodale della malattia. Un esteso interessamento degli arti inferiori è correlato ad una prognosi peggiore.

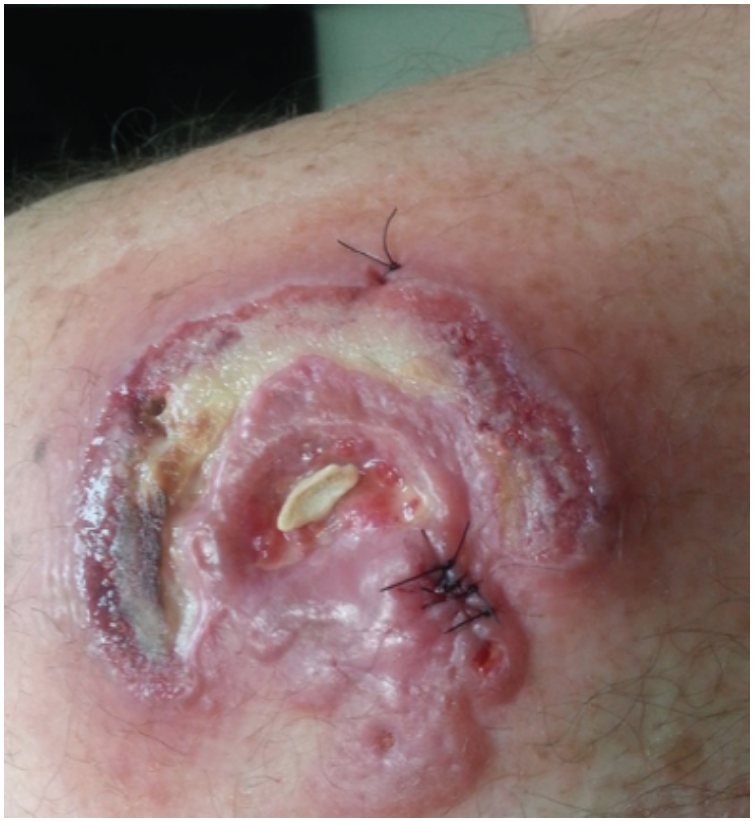
- Le lesioni possono mostrare una **regressione spontanea** completa o parziale, tuttavia la **ricaduta cutanea** rappresenta la regola.

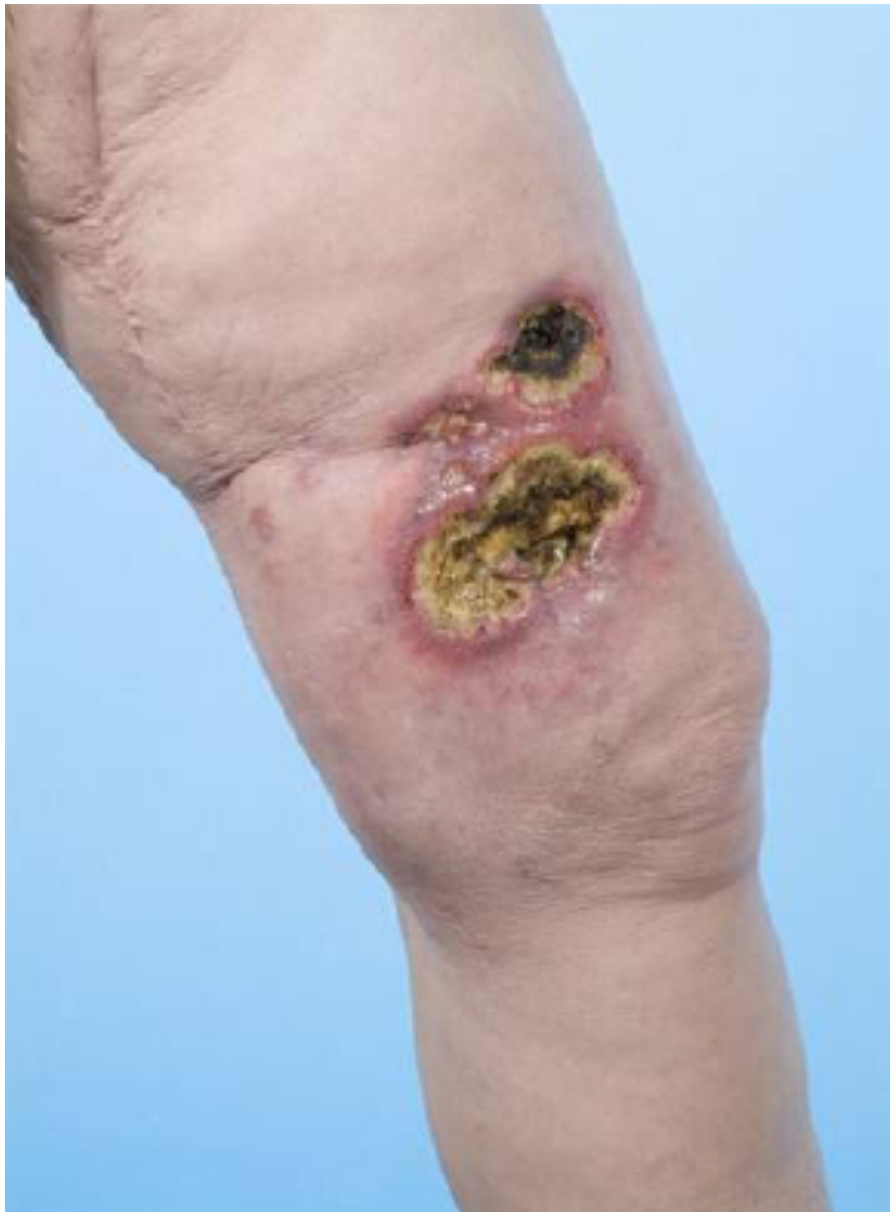
- **La prognosi è eccellente**. La terapia è loco-regionale (chirurgia, radioterapia) o sistemica in caso di interessamento esteso, multifocale, o alla ricaduta.

Zinzani PL. Broccoli A. *Postgraduate Hematology*, 7th ed. 2016; 524-536

LINFOMA ANAPLASTICO PRIMITIVO CUTANEO (pc-ALCL)







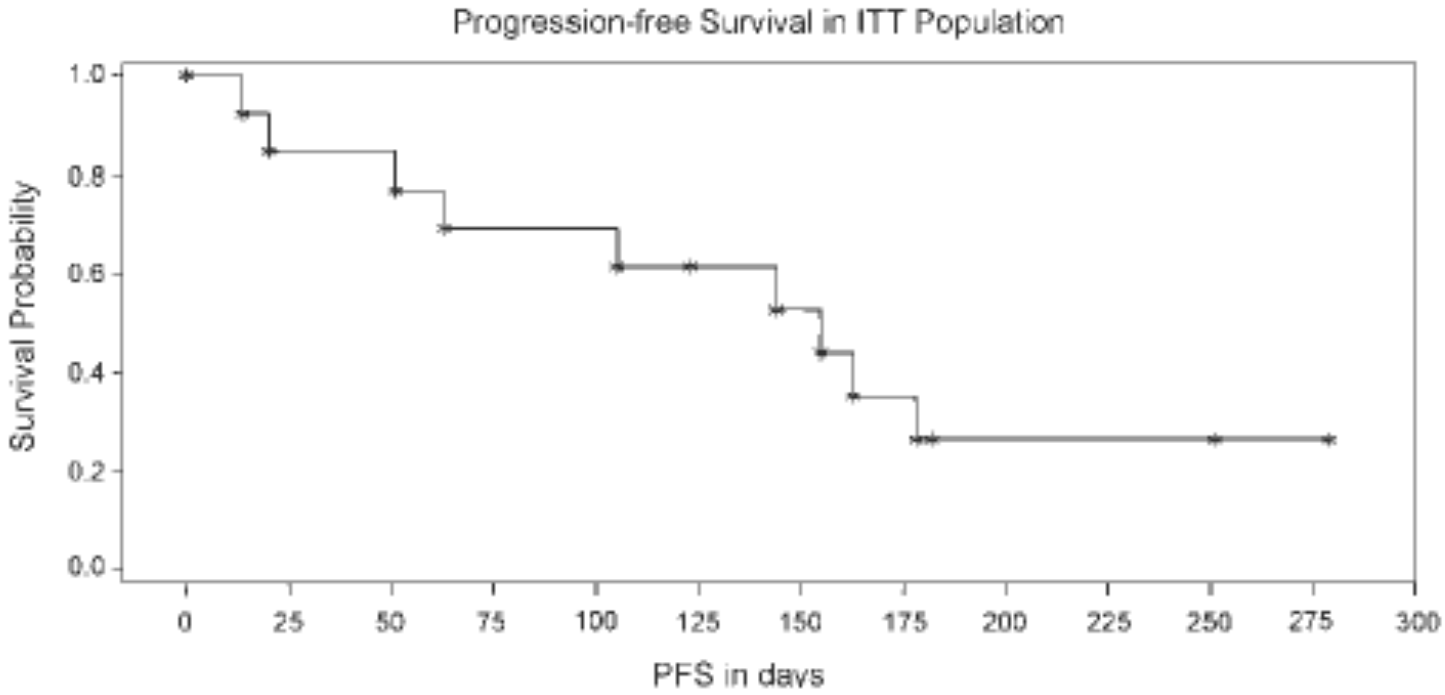
A Phase II Study of SGN-30 in Cutaneous Anaplastic Large Cell Lymphoma and Related Lymphoproliferative Disorders

	SGN-30 initial dose level		All patients (*N* = 23)
	4 mg/kg (*n* = 6)	12 mg/kg (*n* = 17)	
Age, y (median)	66.0	55.0	63.0
Range	42-79	32-78	32-79
Age category (y), *n* (%)			
<60	1 (17%)	9 (53%)	10 (43%)
≥60	5 (83%)	8 (47%)	13 (57%)
Gender, *n* (%)			
Male	5 (83%)	10 (59%)	15 (65%)
Female	1 (17%)	7 (41%)	8 (35%)
Race, *n* (%)			
Caucasian	5 (83%)	15 (88%)	20 (87%)
Black	0	1 (6%)	1 (4%)
Asian/Pacific Islander	1 (17%)	1 (6%)	2 (9%)
Weight (kg), median (range)	83 (61-147)	82 (45-128)	82 (45-147)
Electrocardiogram, *n* (%)*			
Normal	3 (50%)	8 (47%)	11 (48%)
Abnormal	3 (50%)	8 (47%)	11 (48%)
Primary diagnosis, *n* (%)			
pc-ALCL	5 (83%)	6 (35%)	11 (48%)
LyP	0	3 (18%)	3 (13%)
T-MF	0	3 (18%)	3 (13%)
Multiple diagnoses†	1 (17%)	5 (29%)	6 (26%)
Prior surgery			
Yes	1 (17%)	8 (47%)	9 (39%)
No	5 (83%)	9 (53%)	14 (61%)
Prior radiotherapy			
Yes	4 (67%)	9 (53%)	13 (57%)
No	2 (33%)	8 (47%)	10 (43%)
Prior systemic therapy			
Yes	6 (100%)	16 (94%)	22 (96%)
No	0	1 (6%)	1 (4%)
No. prior regimens of chemotherapy/systemic therapies			
Median	2.5	6.0	4.0
Range	2-4	0-19	0-19

Duvic M. *Clin Cancer Res*, 2009; 15: 6217-6224

A Phase II Study of SGN-30 in Cutaneous Anaplastic Large Cell Lymphoma and Related Lymphoproliferative Disorders

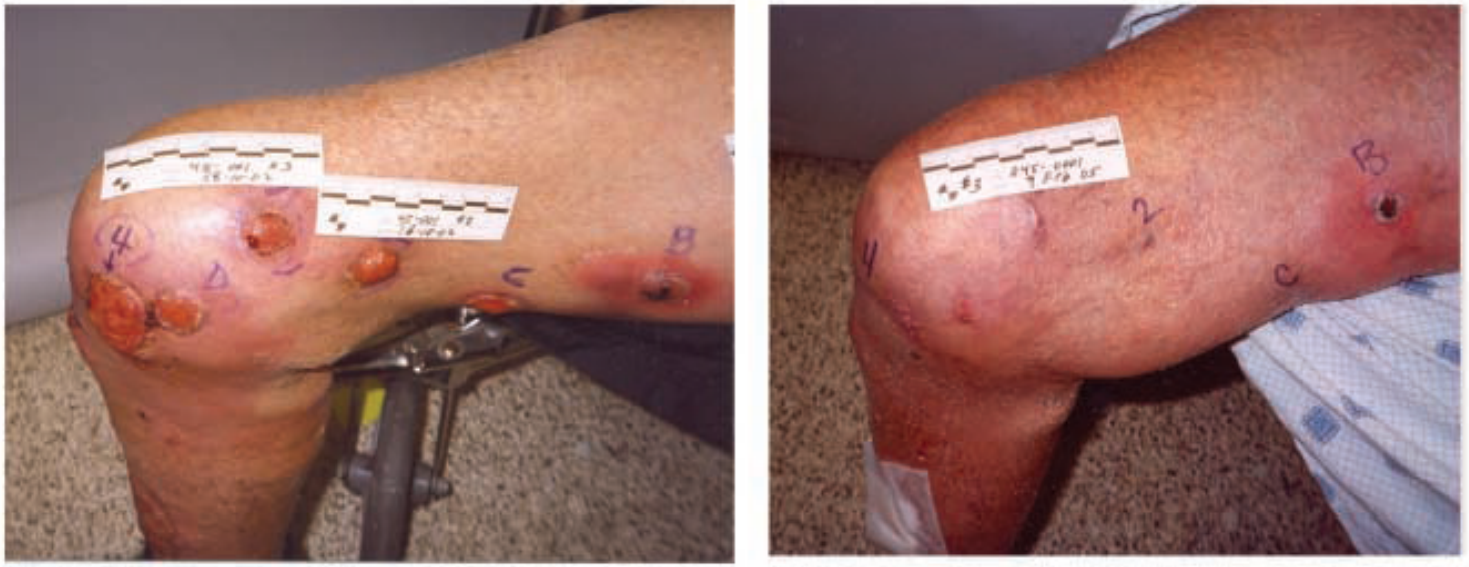
	Diagnosis				Total (*N* = 23), *n* (%)
	pc-ALCL (*n* = 11), *n* (%)	LyP (*n* = 3), *n* (%)	T-MF (*n* = 3), *n* (%)	Multiple (*n* = 6), *n* (%)	
CR	6 (55%)	1 (33%)	0	3 (50%)	10 (43%)
PR	3 (27%)	1 (33%)	1 (33%)	1 (17%)	6 (26%)
CR or PR	9 (82%)	2 (67%)	1 (33%)	4 (67%)	16 (70%)
SD	2 (18%)	1 (33%)	1 (33%)	0	4 (17%)
Progressive disease	0	0	1 (33%)	2 (33%)	3 (13%)



Duvic M. *Clin Cancer Res*, 2009; 15: 6217-6224

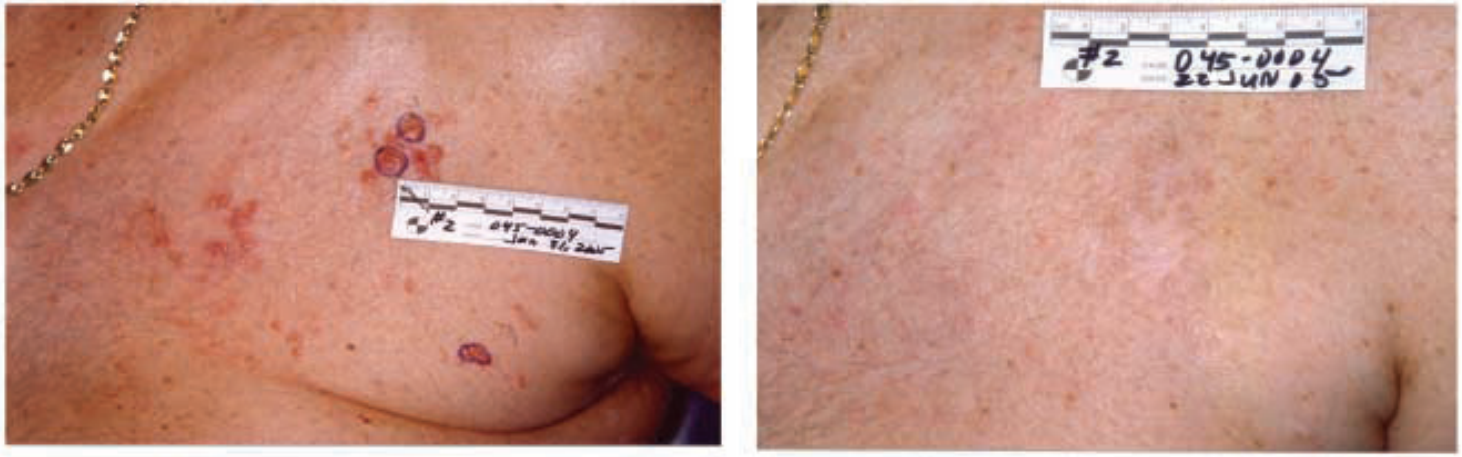
A Phase II Study of SGN-30 in Cutaneous Anaplastic Large Cell Lymphoma and Related Lymphoproliferative Disorders

A



pc-ALCL
18 mesi

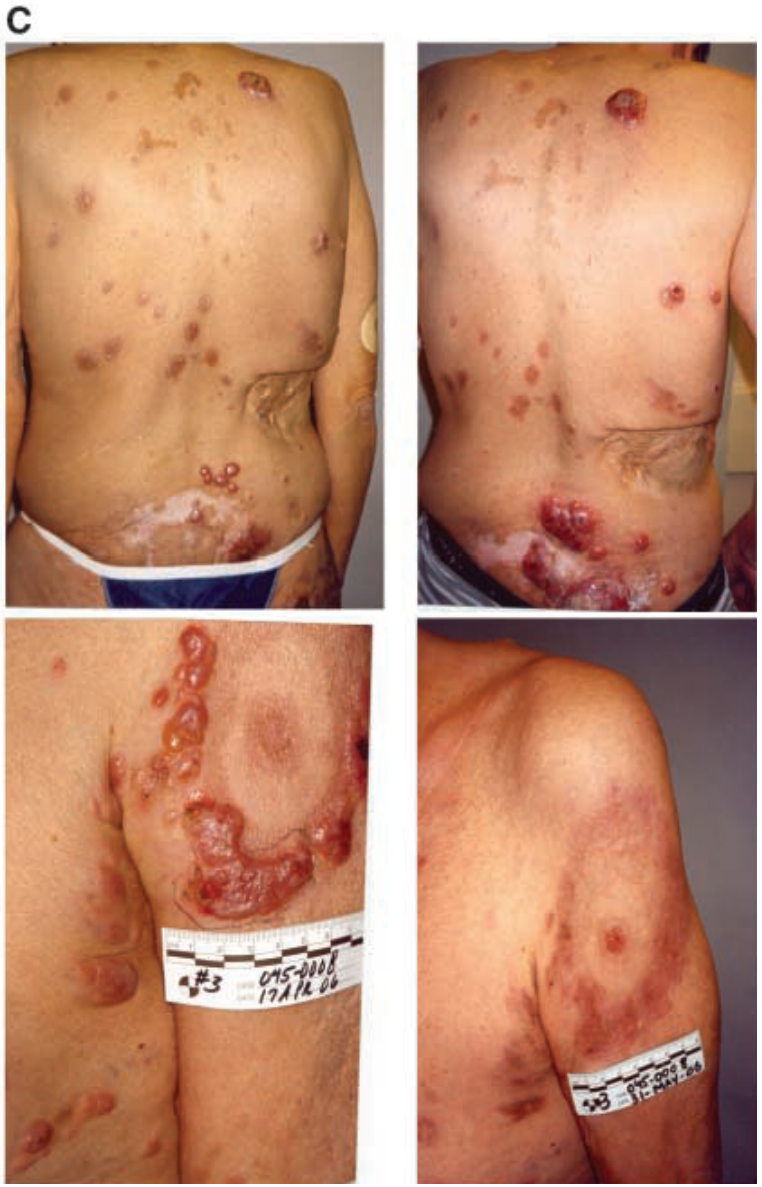
B



t-MF
6 mesi

Duvic M. *Clin Cancer Res*, 2009; 15: 6217-6224

A Phase II Study of SGN-30 in Cutaneous Anaplastic Large Cell Lymphoma and Related Lymphoproliferative Disorders



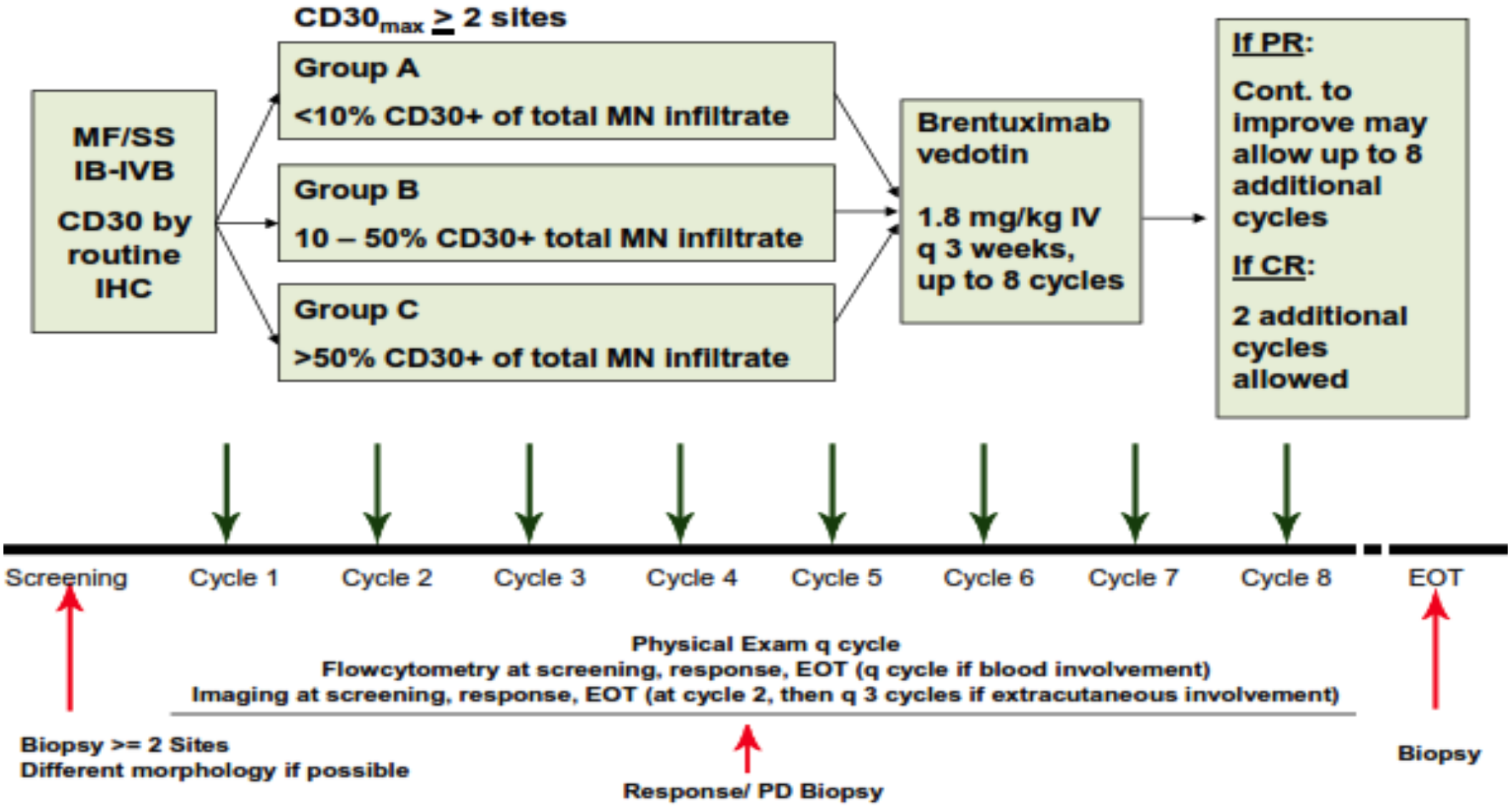
pc-ALCL

Progressione tumorale (dorso) durante trattamento

Regressione delle lesioni tumorali al braccio sinistro

Duvic M. *Clin Cancer Res*, 2009; 15: 6217-6224

Phase II Investigator-Initiated Study of Brentuximab Vedotin in Mycosis Fungoides and Sézary Syndrome With Variable CD30 Expression Level: A Multi-Institution Collaborative Project



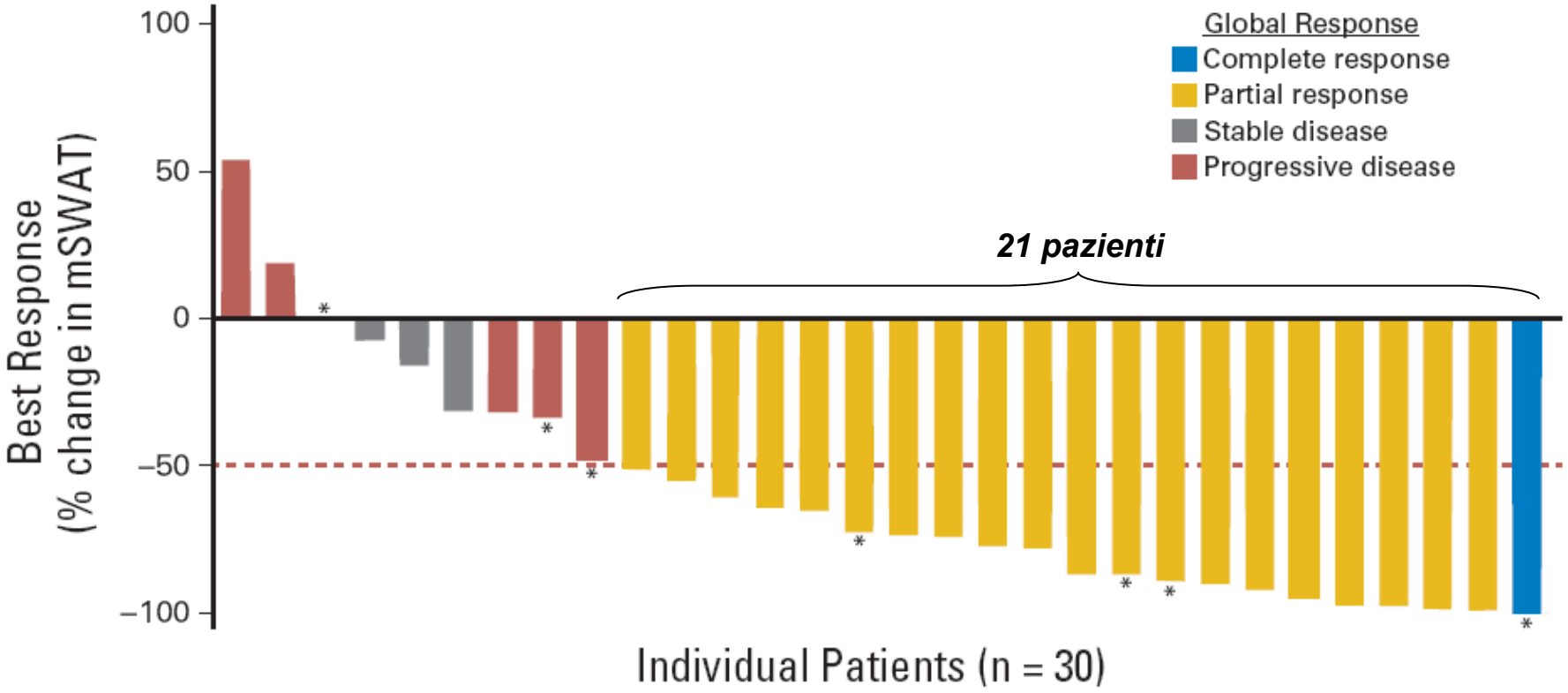
Kim YH. *J Clin Oncol*, 2015; 33: 3750-3758

Phase II Investigator-Initiated Study of Brentuximab Vedotin in Mycosis Fungoides and Sézary Syndrome With Variable CD30 Expression Level: A Multi-Institution Collaborative Project

Characteristics	All Patients, N = 32, n (%)	Evaluable for Response, n = 30					
		CR	PR	SD	PD	NE	ORR, n (%)
Sex							
Male	19 (59)	0	13	1	4	1	13 of 18 (72)
Female	13 (41)	1	7	3	1	1	8 of 12 (67)
Age, years, median (range)	62 (20-87)	78	60 (38-87)	60 (20-82)	64 (57-77)	60 (50-70)	
Clinical stage							
All	32 (100)	1	20	4	5	2	21 of 30 (70)
IB	4 (13)	0	3	1	0	0	3 of 4 (75)
IIB	18 (56)	0	14	2	2	0	14 of 18 (78)
IV/SS	10 (31)	1	3	1	3	2	4 of 8 (50)
Adverse prognostic factors							
LCT or FMF	29 (90)	1	19	3	5	1	20 of 28 (71)
LCT	16 (50)	1	9	2	3	1	10 of 15 (67)
FMF	8 (25)	0	7	1	0	0	7 of 8 (88)
LCT + FMF	5 (16)	0	3	0	2	0	3 of 5 (60)
No. of prior systemic therapies							
< 3	15 (47)	0	8	2	4	1	8 of 14 (57)
≥ 3	17 (53)	1	12	2	1	1	13 of 16 (81)
CD30 grouping at screening							
A (< 10%)	14 (44)	0	7	4	2	1	7 of 13 (54)
B (10% to 50%)	14 (44)	0	11	0	3	0	11 of 14 (79)
C (> 50%)	4 (13)	1	2	0	0	1	3 of 3 (100)

Kim YH. *J Clin Oncol*, 2015; 33: 3750-3758

Phase II Investigator-Initiated Study of Brentuximab Vedotin in Mycosis Fungoides and Sézary Syndrome With Variable CD30 Expression Level: A Multi-Institution Collaborative Project



(*) pazienti con malattia in stadio IV (nodale-viscerale)

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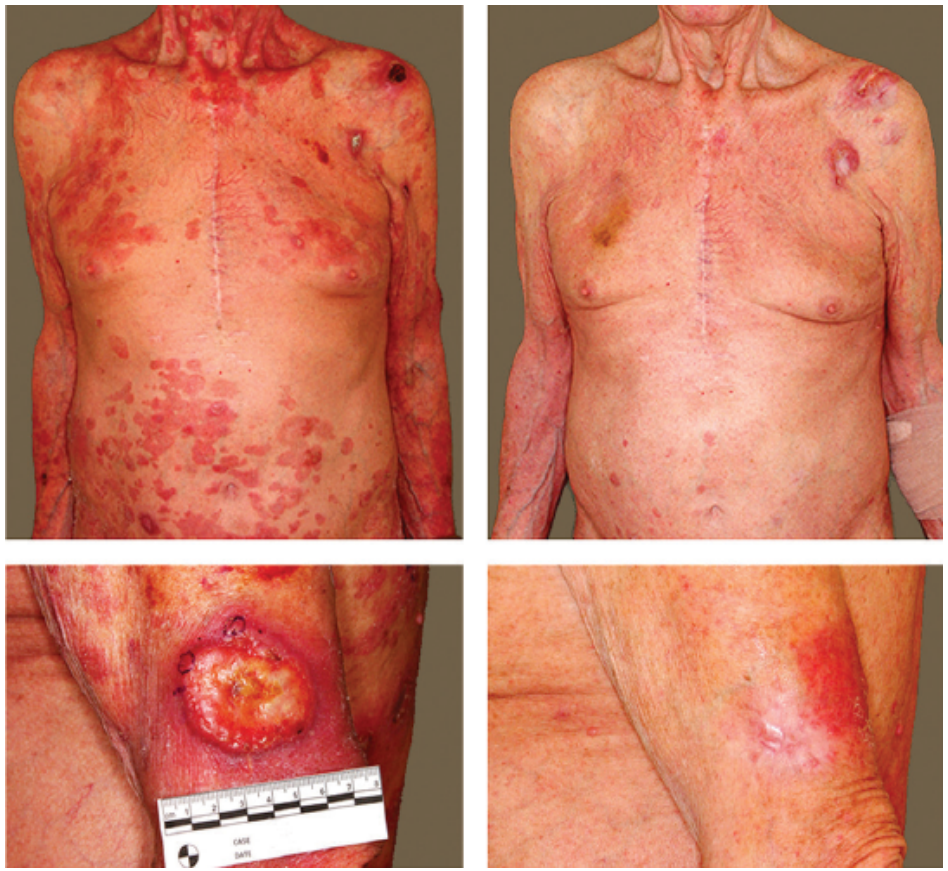
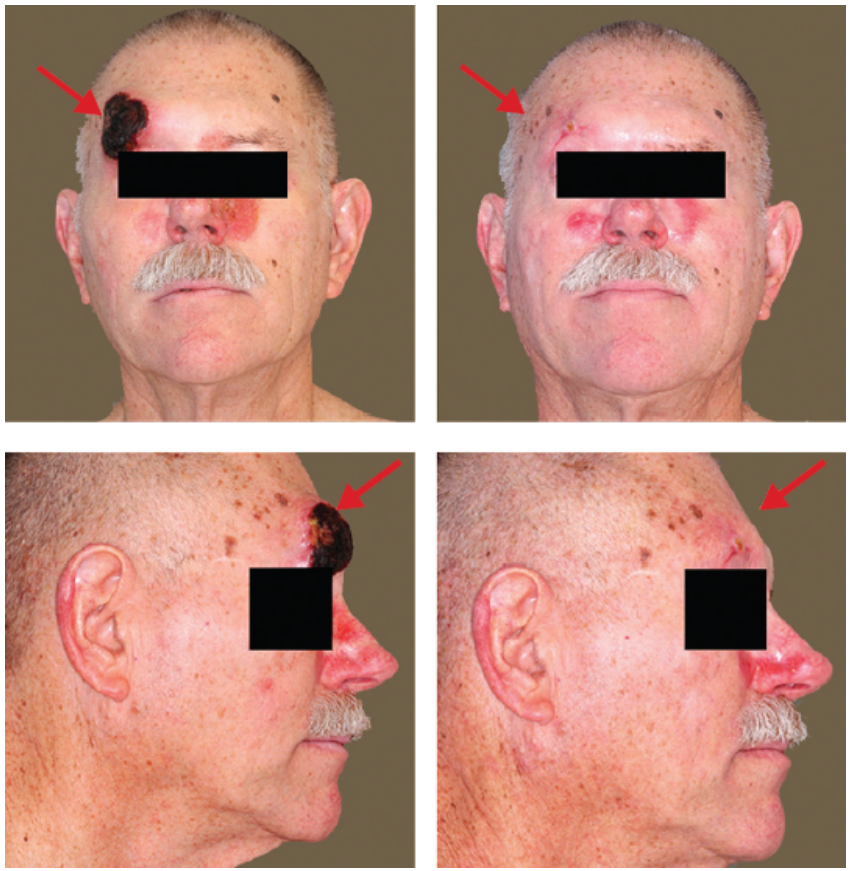


- MF, stadio IIB, regressione della lesione tumorale al braccio e riduzione mSWAT > 90%.



- MF, stadio IIB, regressione completa della lesione tumorale.

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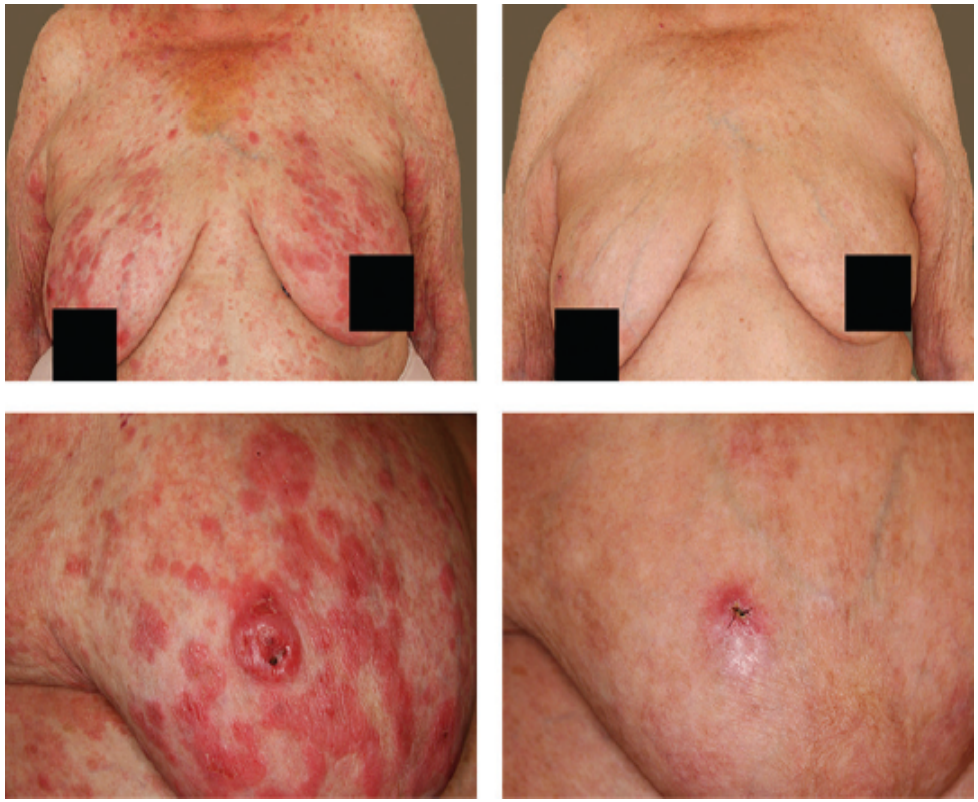
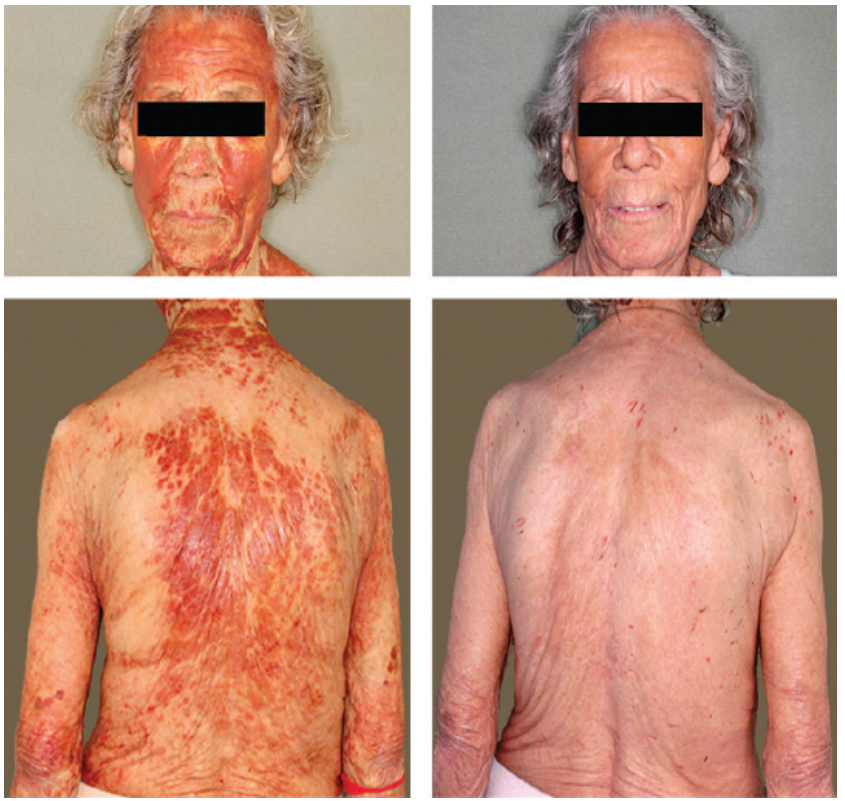


- Sindrome di Sézary, stadio IVA_2, con riduzione mSWAT del 100% e risposta globale completa (TNMB).



- Sindrome di Sézary, stadio IVA_1, con riduzione mSWAT dell'89% e *clearance* delle cellule circolanti.

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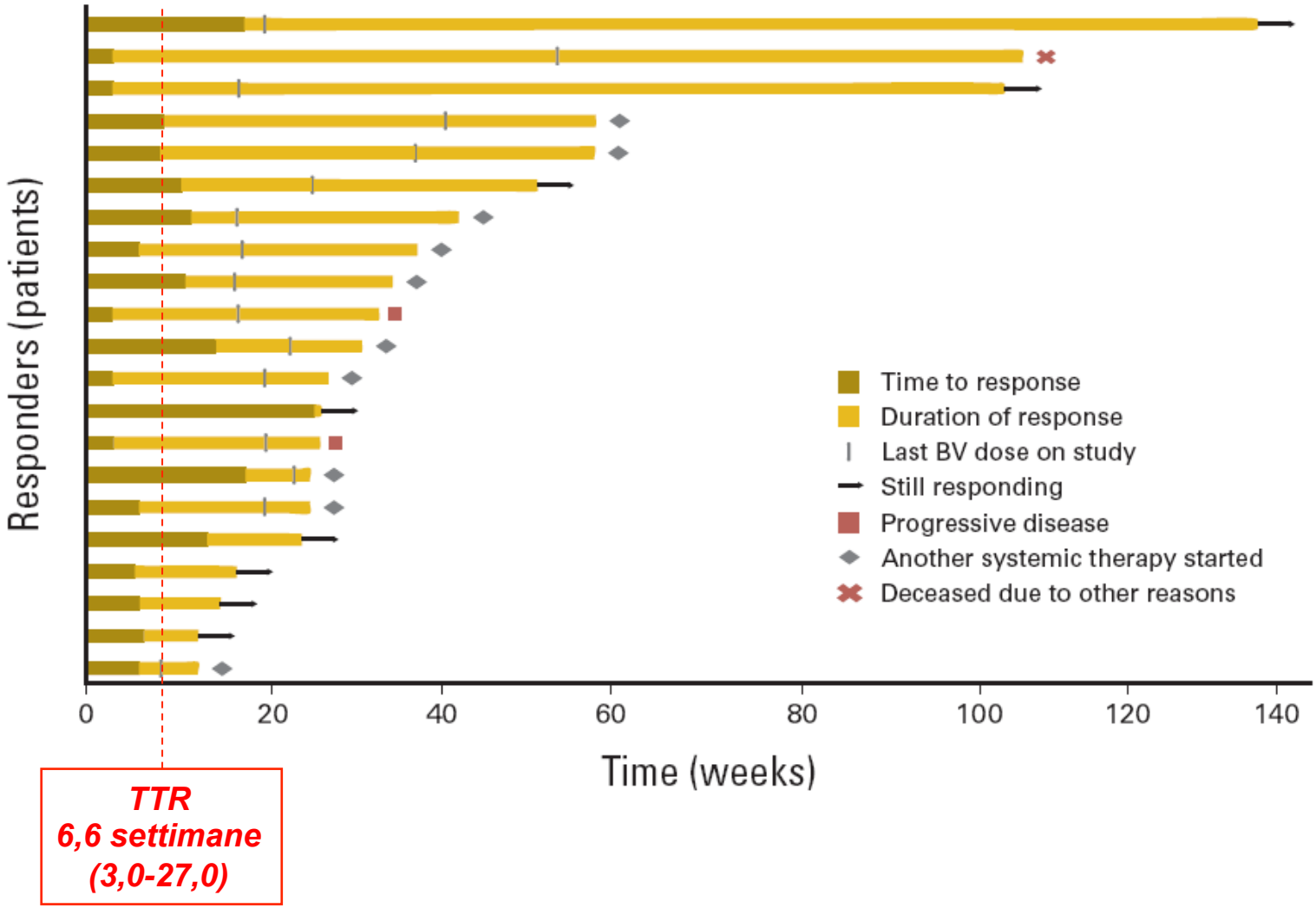

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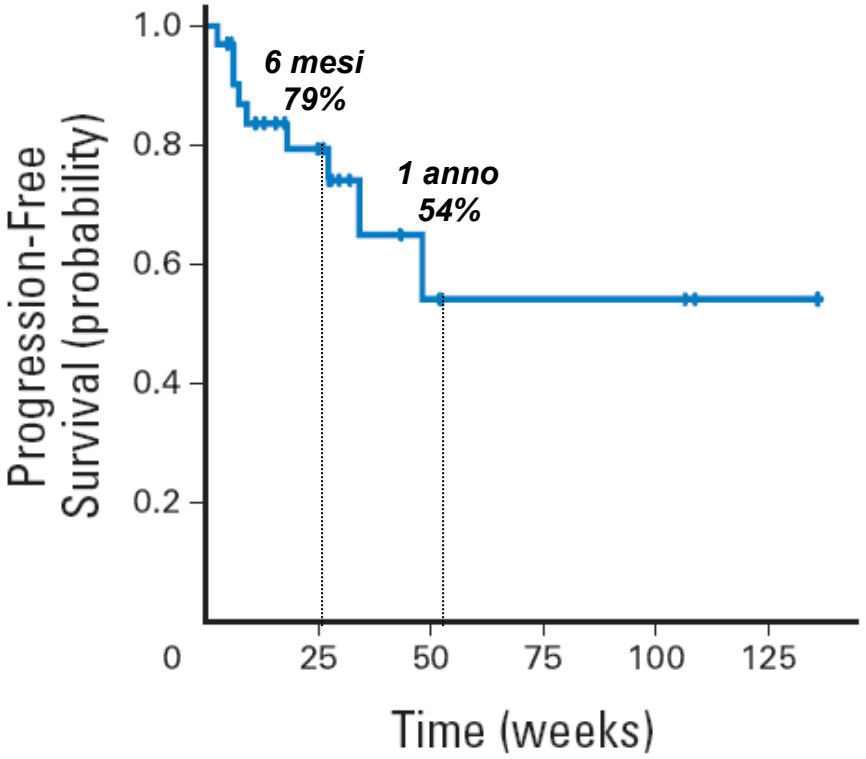

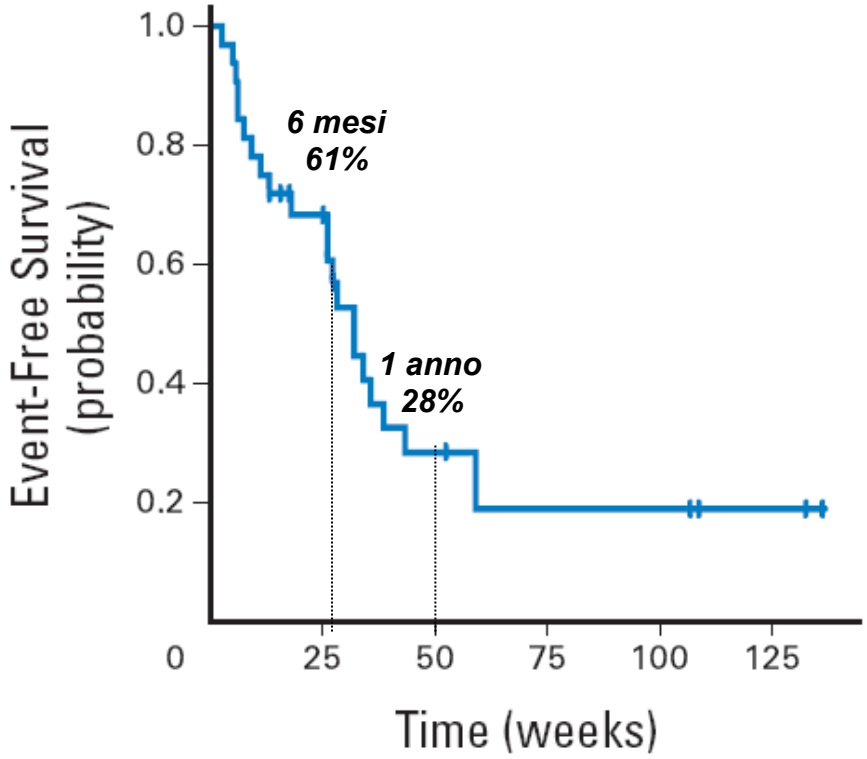

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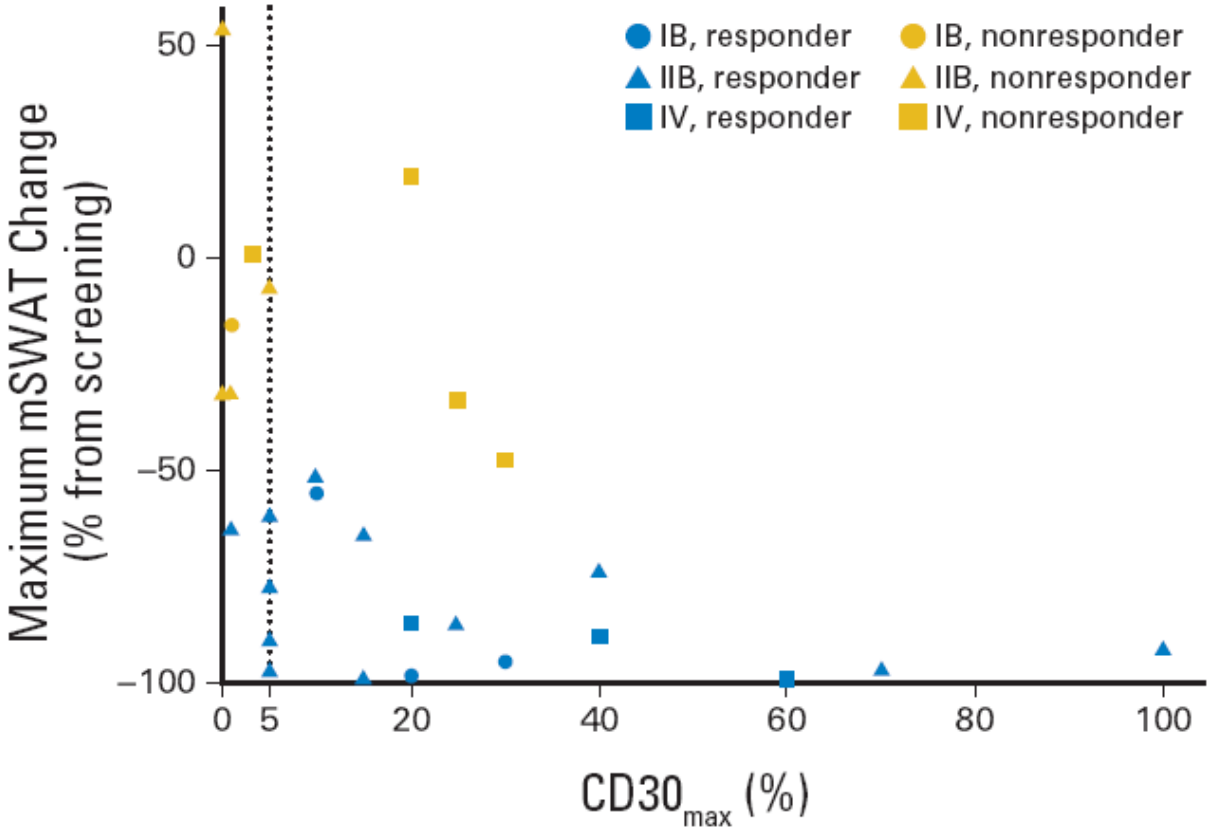
Phase II Investigator-Initiated Study of Brentuximab Vedotin in Mycosis Fungoides and Sézary Syndrome With Variable CD30 Expression Level: A Multi-Institution Collaborative Project

- **Tasso di risposta**: 17% ($CD30_{max}$<5%) *vs* 83% ($CD30_{max}$≥5%) (*P*=0,0046).
- Correlazione tra $CD30_{max}$ e riduzione del punteggio mSWAT (P=0,0031).



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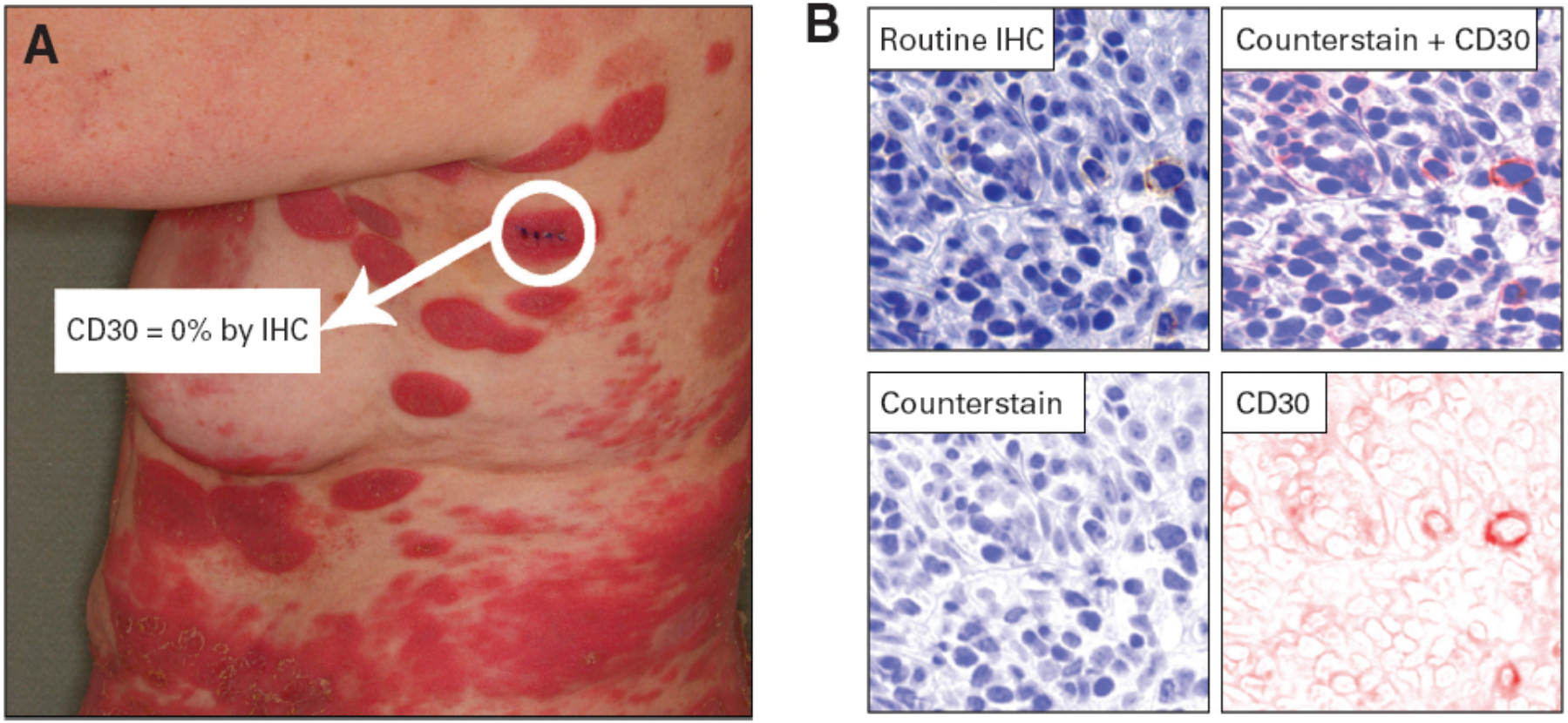

- Il limite di riconoscimento dell'antigene CD30 in immunoistochimica (microscopio ottico) è valicato dall'utilizzo di metodiche multispettrali che evidenziano una CD30-positività anche al disotto della soglia osservabile.

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Results of a Phase II Trial of Brentuximab Vedotin for CD30$^+$ Cutaneous T-Cell Lymphoma and Lymphomatoid Papulosis

Characteristic	No. (%) All Patients (N = 54)	No. (%) All Eligible Patients (n = 48)
Age, years		
Median	59.5	
Range	31-77	
Sex		
Male	27 (50)	26 (54)
Female	27 (50)	22 (46)
Race		
White	31 (57)	30 (63)
African American	15 (28)	13 (27)
Hispanic	8 (15)	5 (11)
Diagnosis		
MF	31	28
pc-ALCL	3	2
LyP	10	9
LyP and MF	8	7
ALCL/LyP/MF	2	2

Duvic M. *J Clin Oncol*, 2015; 33: 3759-3765

Results of a Phase II Trial of Brentuximab Vedotin for $CD30^+$ Cutaneous T-Cell Lymphoma and Lymphomatoid Papulosis

- **Brentuximab vedotin (1,8 mg/kg)** somministrato per massimo 8 cicli (mediana 7 cicli per pazienti con MF, 7,5 cicli per pazienti con LyP/pc-ALCL).
- Possibilità di estendere il trattamento nei pazienti con risposta parziale; possibilità di ritrattamento nei pazienti in ricaduta.

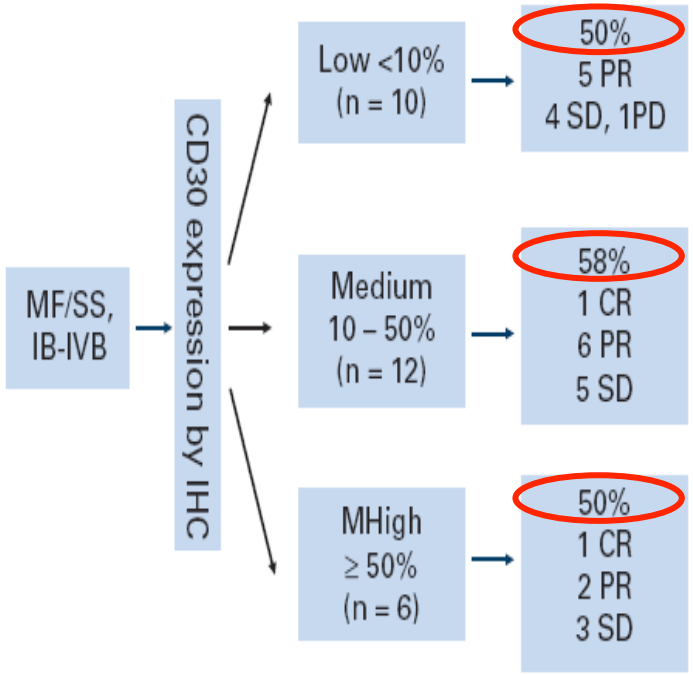
Diagnosis	Total No. of Patients (N = 48)	Response		Secondary Response (No.)
		No.	%	
All patients	48	35	73	
MF	28	13 PR, 2 CR	54	
LyP	9	5 CR, 4 PR	100	
pc-ALCL	2	2 CR	100	
LyP/MF	7	6 LyP CR, 1 LyP PR	100	6 MF PR, 1 MF SD
pc-ALCL/LyP	1	CR	100	1 LyP PD
pc-ALCL/MF	1	CR	100	1 MF PR

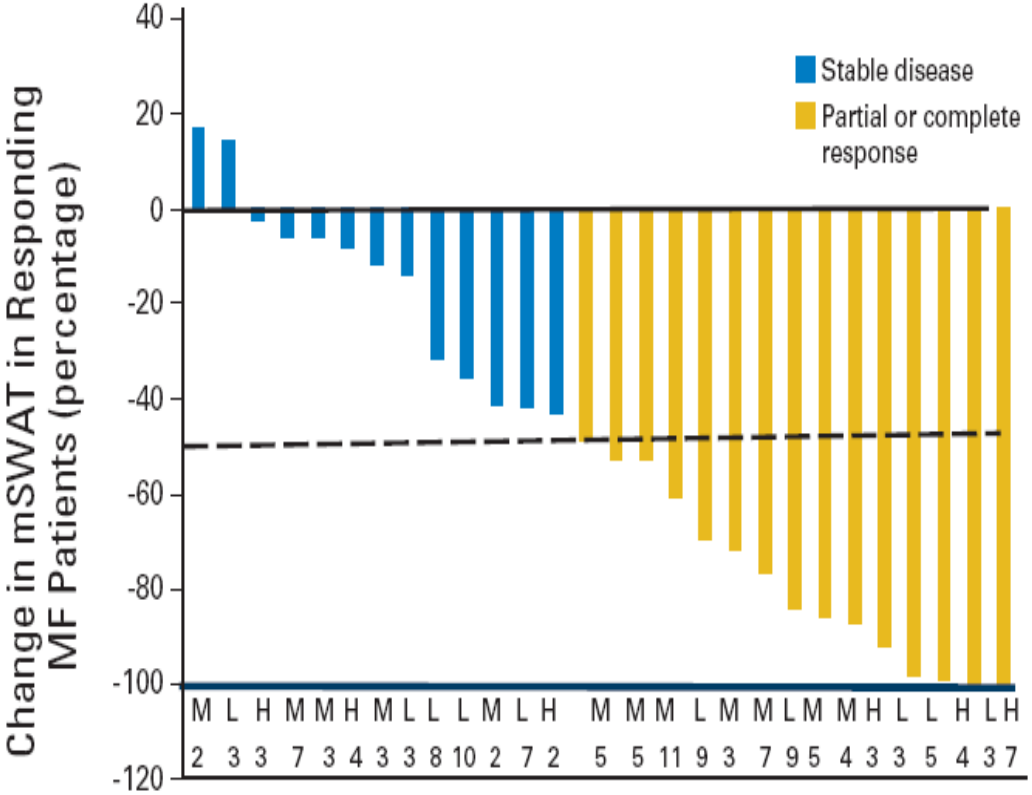
Duvic M. *J Clin Oncol*, 2015; 33: 3759-3765

Results of a Phase II Trial of Brentuximab Vedotin for CD30$^+$ Cutaneous T-Cell Lymphoma and Lymphomatoid Papulosis

MICOSI FUNGOIDE (28 pazienti)

- Tasso di risposta: indipendente dalla categoria di espressione di CD30.
- Profondità della risposta: non influenzata dalla concentrazione di CD30 nel tessuto tumorale.





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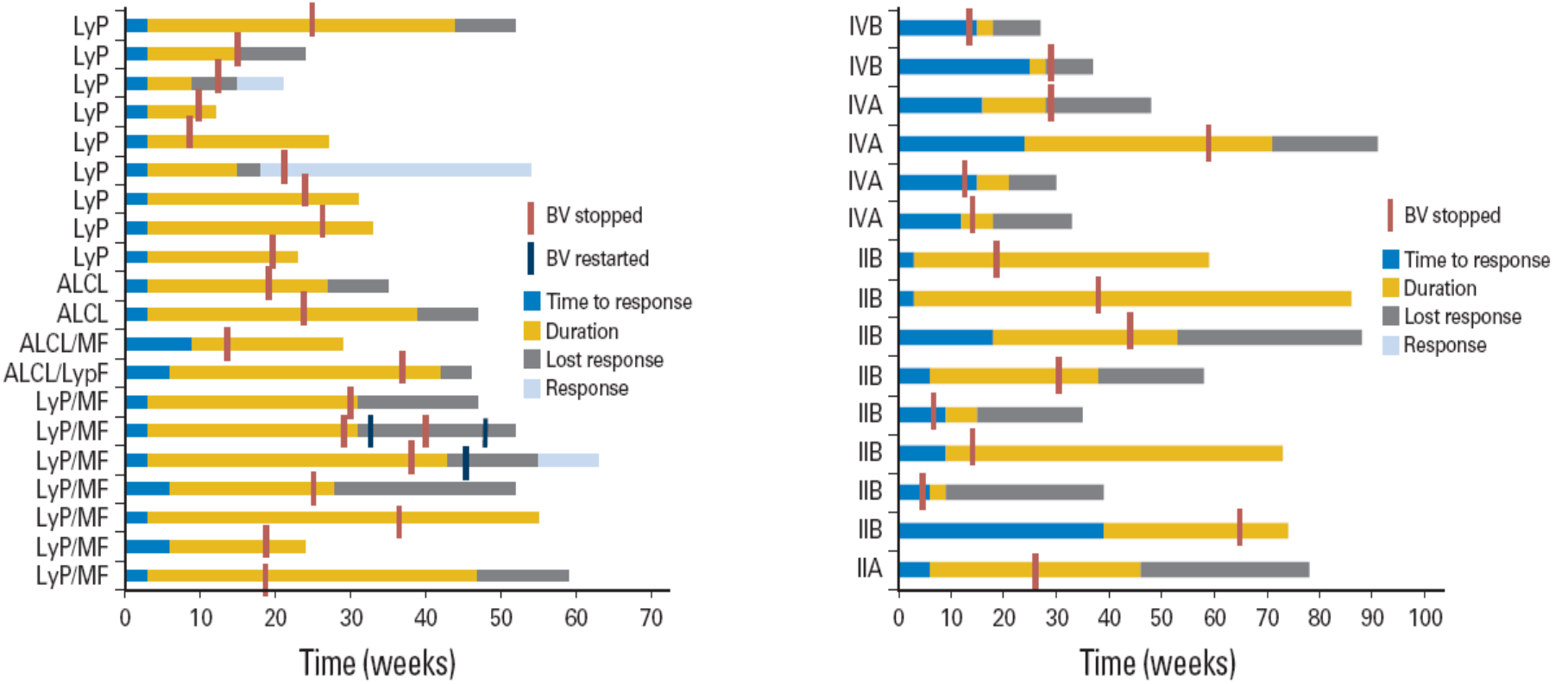
Results of a Phase II Trial of Brentuximab Vedotin for CD30$^+$ Cutaneous T-Cell Lymphoma and Lymphomatoid Papulosis



pc-ALCL, LyP, LyP/pc-ALCL	TTR: 3 (3-9) settimane	DOR: 26 (6-44) settimane
MF	TTR: 12 (3-39) settimane	DOR: 32 (3-93) settimane

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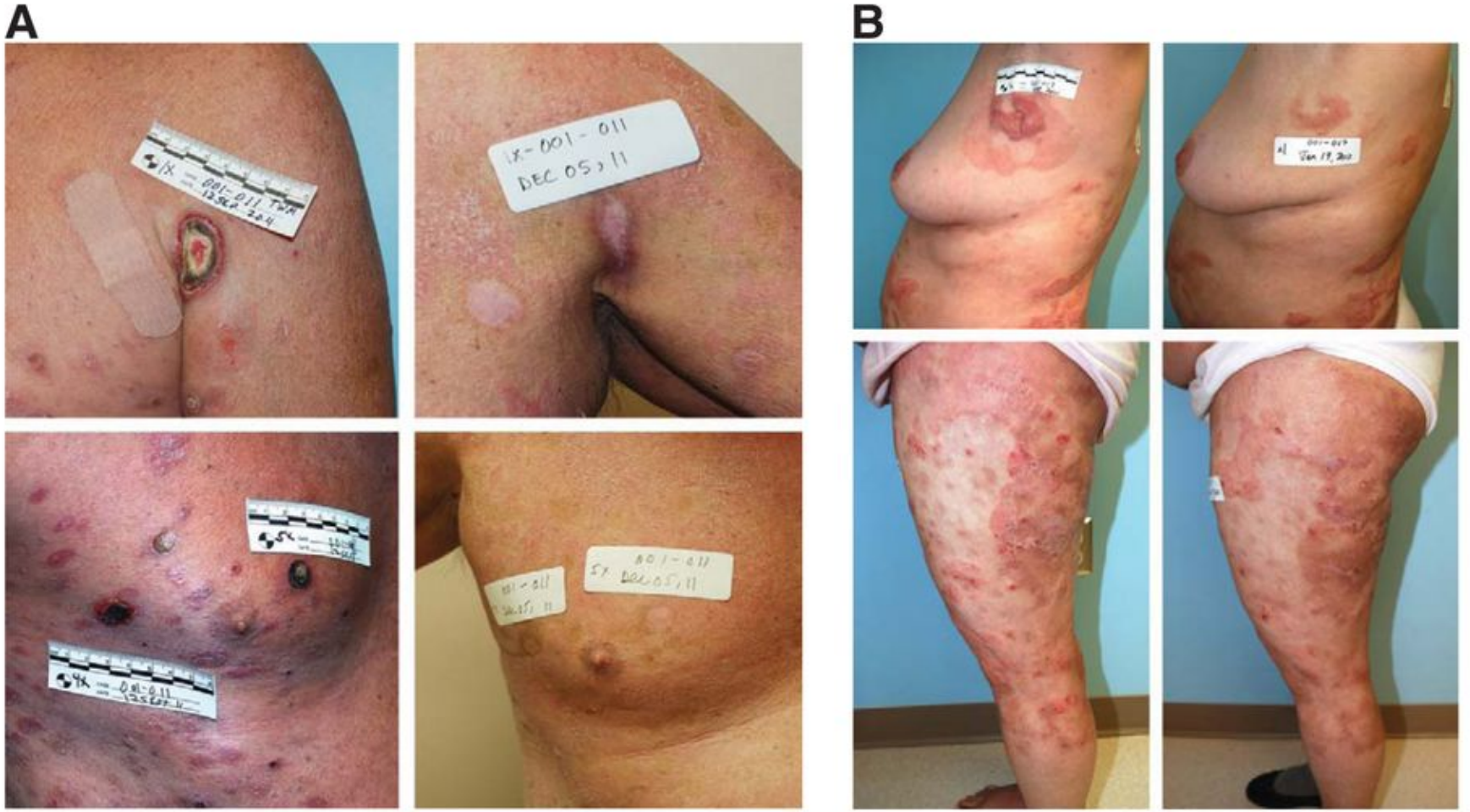
Results of a Phase II Trial of Brentuximab Vedotin for CD30^{+} Cutaneous T-Cell Lymphoma and Lymphomatoid Papulosis



- LyP multifocale + pc-ALCL + MF. Risposta completa per LyP e ALCL, parziale per MF.
- MF, lesione tumorale (risp. completa) + placche (risp. parziale).

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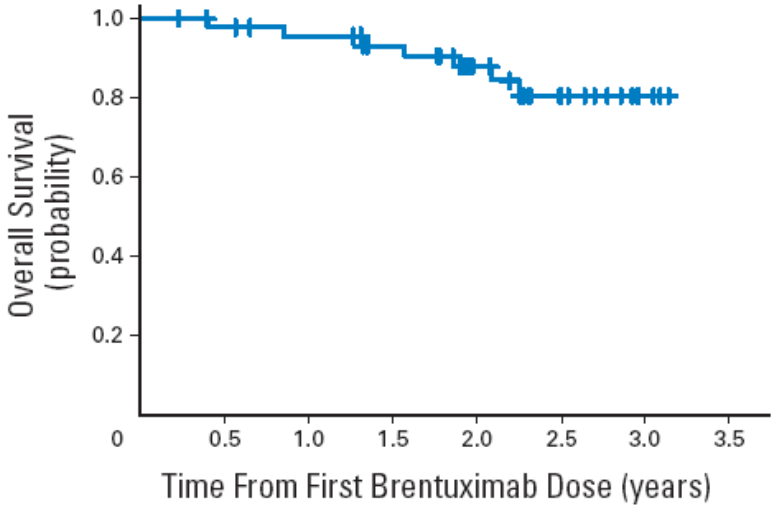
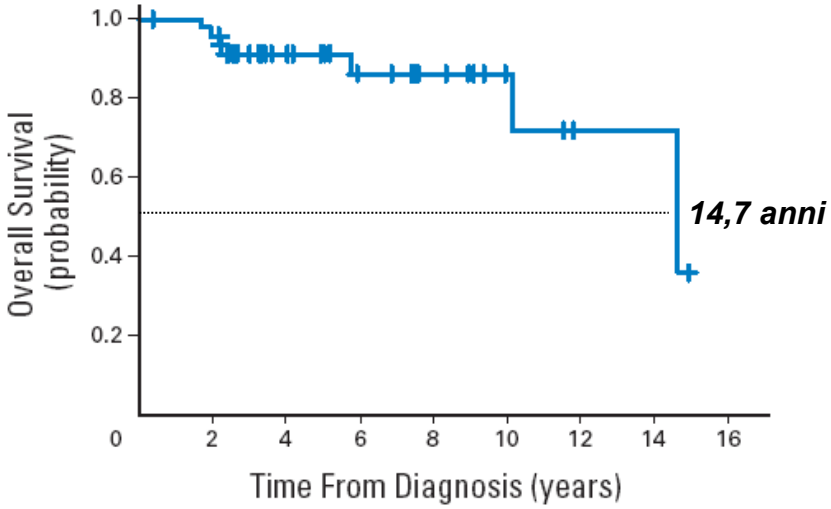
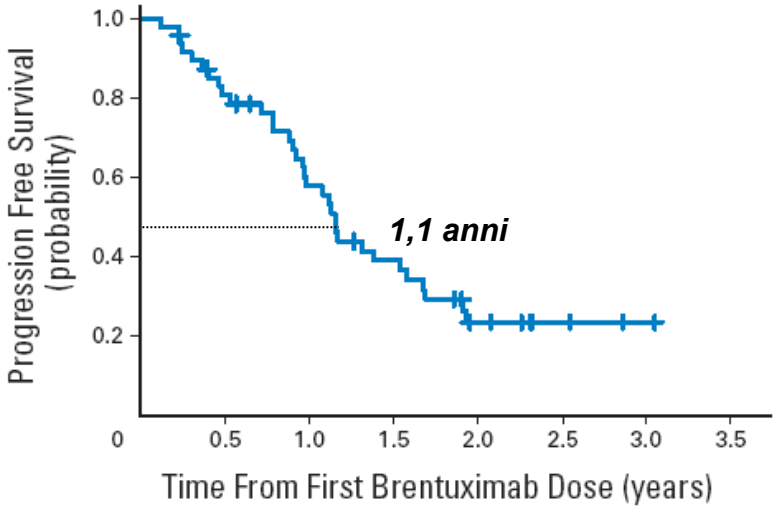
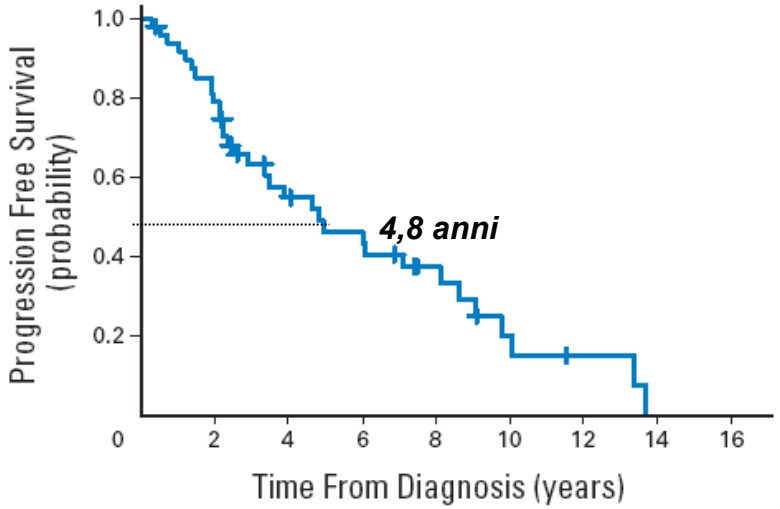
Results of a Phase II Trial of Brentuximab Vedotin for CD30^{+} Cutaneous T-Cell Lymphoma and Lymphomatoid Papulosis









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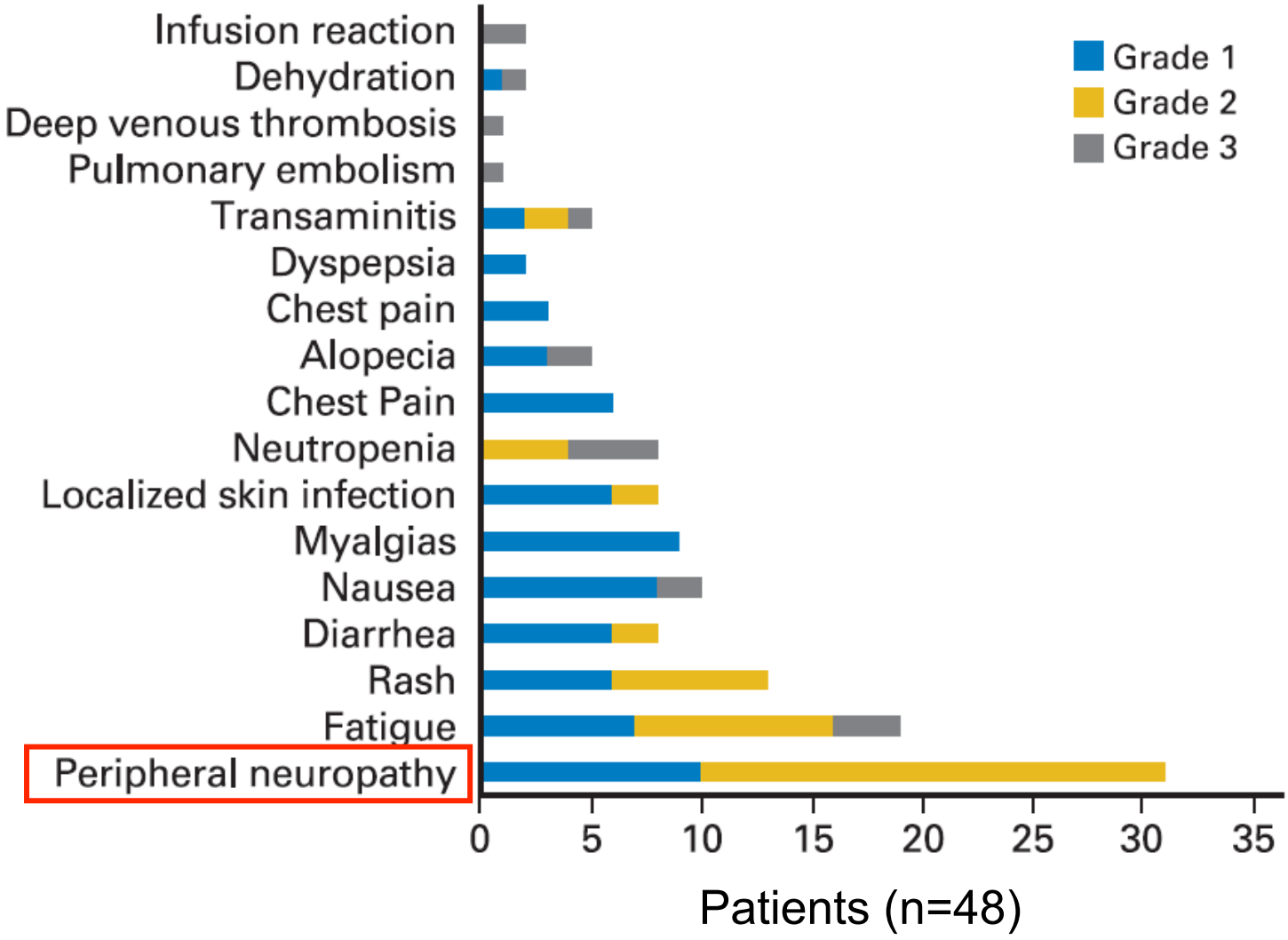

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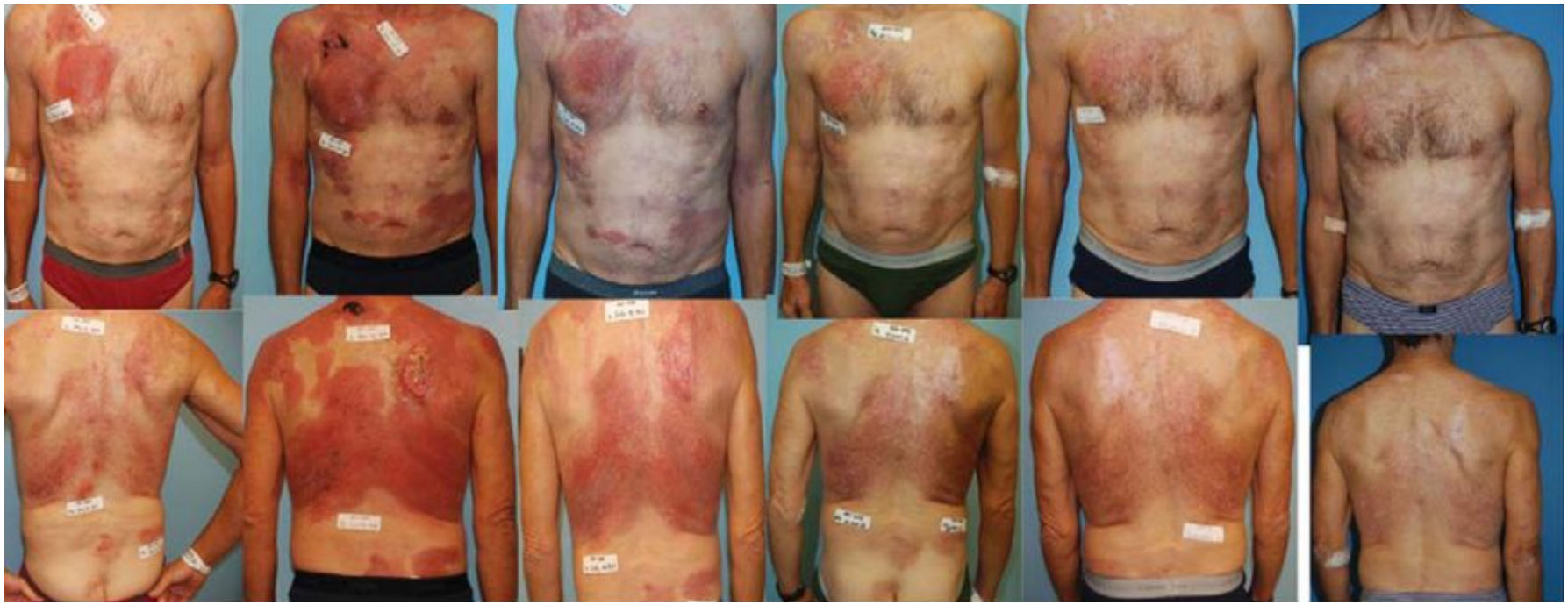

- Paziente in trattamento con brentuximab vedotin per micosi fungoide follicolotropa. Al termine del primo ciclo, marcato aumento dell'estensione delle lesioni cutanee (*tumor flare*), su base infiammatoria/ipersensibilità.
- Risoluzione del quadro con la progressione del trattamento con brentuximab vedotin.
- Ottenimento di una risposta cutanea completa.

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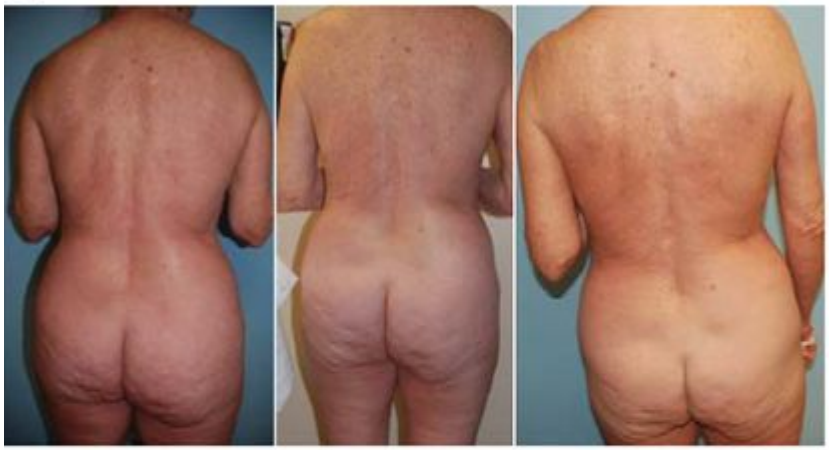
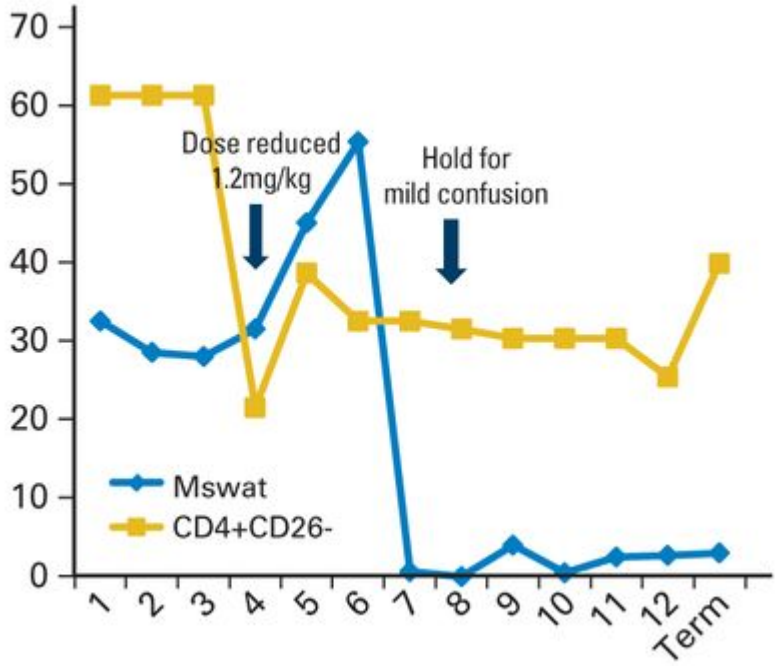
Results of a Phase II Trial of Brentuximab Vedotin for $CD30^+$ Cutaneous T-Cell Lymphoma and Lymphomatoid Papulosis





- Paziente in trattamento con brentuximab vedotin per sindrome di Sézary, pluritrattata.
- Presenta una rapida e duratura riduzione della conta delle cellule di Sézary (CD4+CD26-) circolanti, pur con un aumento iniziale dell'eritrodermia (incremento mSWAT).
- Al 2° ciclo, sviluppa una transitoria reazione da ipersensibilità tipo rash morbilliforme.
- L'eritrodermia si riduce e si risolve a partire dal 7° ciclo di trattamento.

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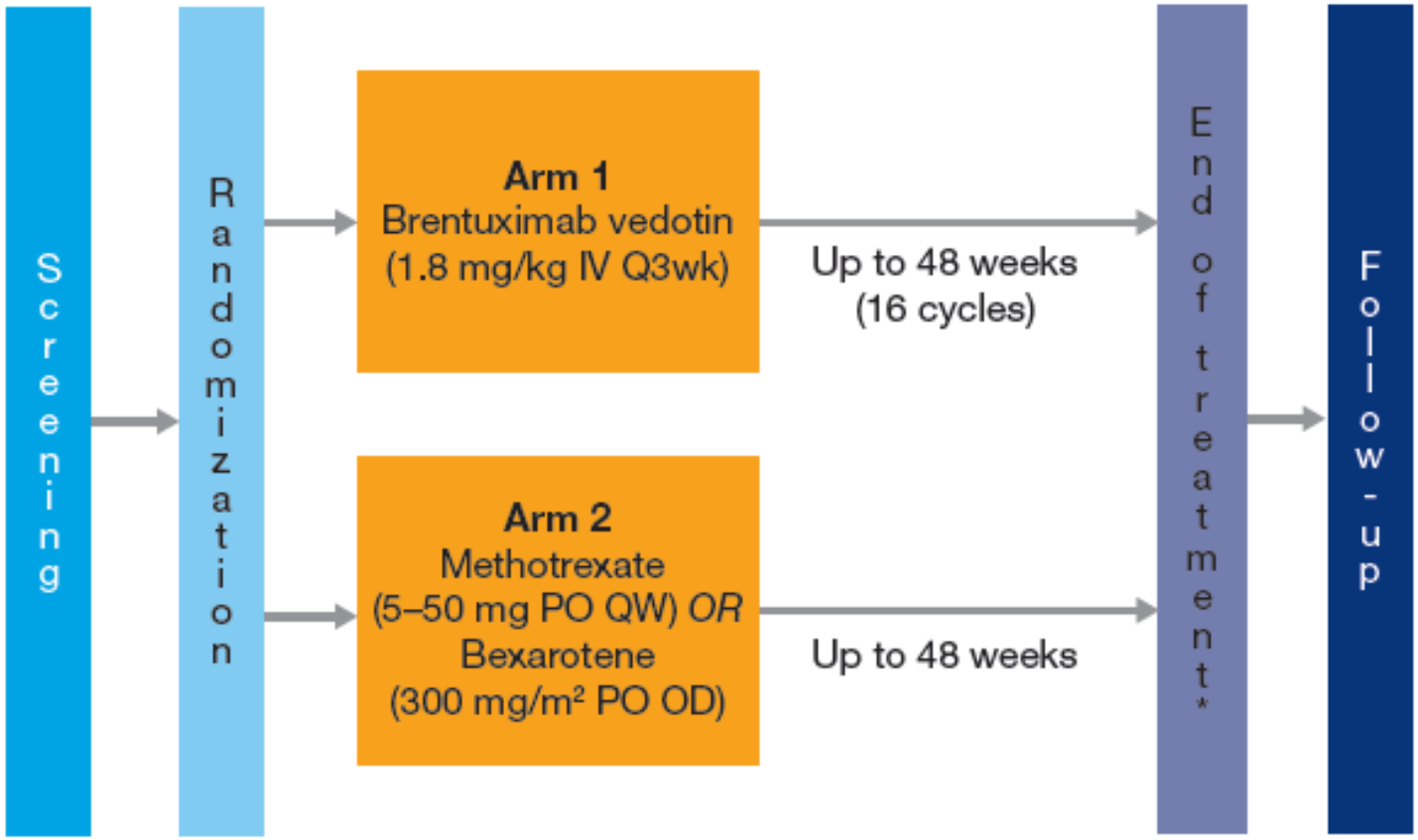
INDIRIZZI FUTURI

Studio ALCANZA: studio randomizzato, di fase 3, con impiego di brentuximab vedotin *versus* terapia standard nei pazienti con linfoma T-linfocitario cutaneo CD30^{+} (NCT01578499).

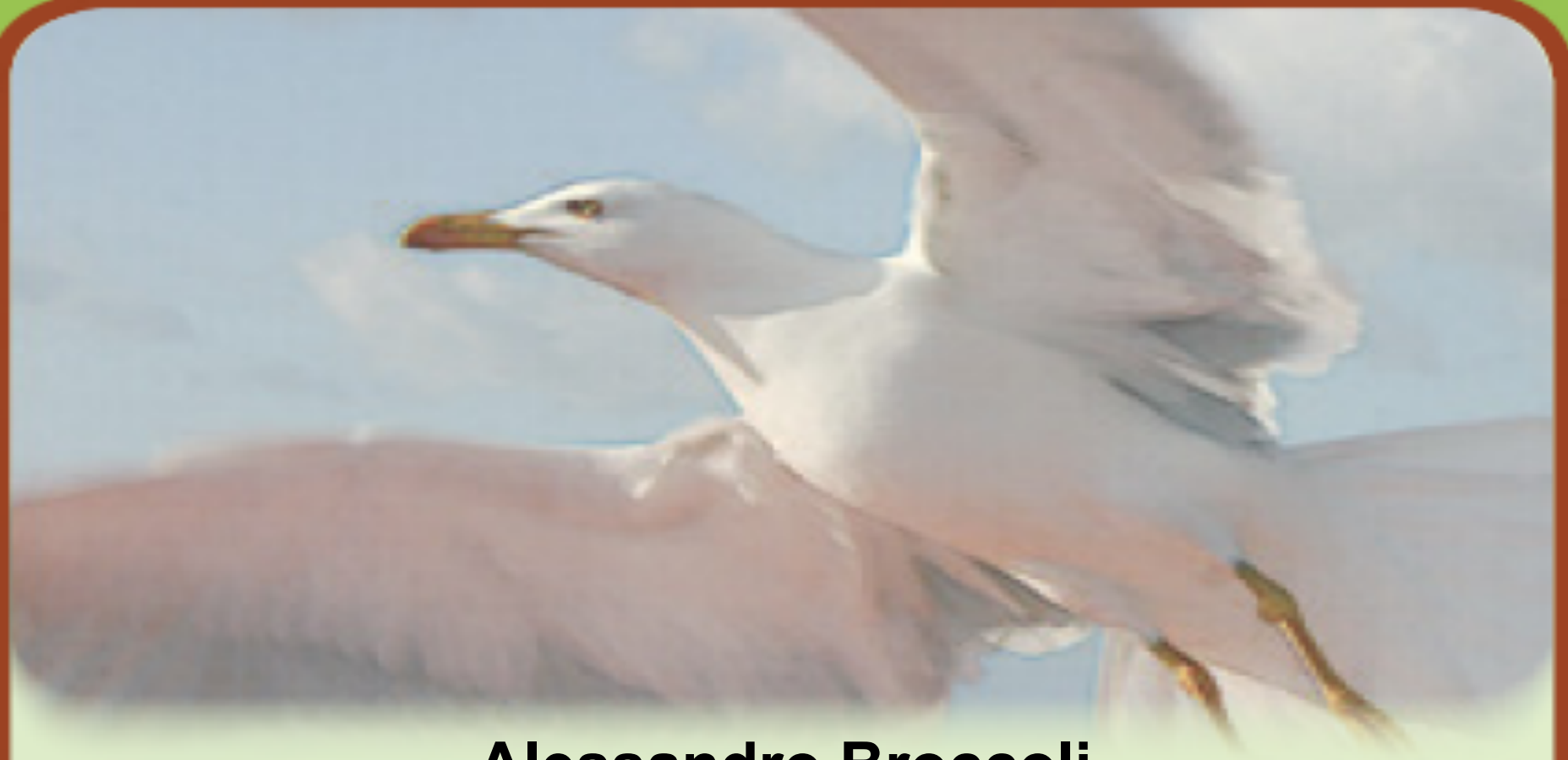


INDIRIZZI FUTURI

- **Endpoint primario**: raggiungimento di una risposta clinica di durata superiore ai 4 mesi (ORR4).
- **Endpoint secondario**: tasso di risposte complete, sopravvivenza libera da progressione, impatto sulla sintomatologia.
- **Criteri di inclusione**: pazienti con linfoma T cutaneo $CD30^+$ (confermato in sede di revisione centralizzata) già sottoposto a precedente trattamento (radioterapia o almeno una linea precedente di trattamento sistemico).
- **Criteri di esclusione**: concomitante neoplasia linfoproliferativa, sindrome di Sézary, s-ALCL.

131 pazienti arruolati, 50 siti attivi (Europa, America, Australia).

Raggiungimento endpoint primario: l'uso di brentuximab vedotin migliora il tasso di risposta clinica con durata di almeno 4 mesi (56,3% *versus* 12,5% nel braccio di controllo, $P < 0{,}0001$).



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