LINFOMI PRIMITIVI CUTANEI DI DERIVAZIONE T-LINFOCITARIA:

la multidisciplinarità ottimizza il risultato

29 OTTOBRE 2021

NAPOLI Hotel Royal Continental

MALATTIA «EARLY STAGE»: IL DERMATOLOGO

Nicola Pimpinelli

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Dipartimento Scienze della Salute – sez. Dermatologia, *Università degli Studi di Firenze*
SS.CC. Dermatologia Firenze, *Azienda USL Toscana Centro*

Dichiarazione conflitto di interessi

Nicola Pimpinelli dichiara di aver intrattenuto rapporti con le seguenti aziende farmaceutiche negli ultimi 2 anni:

ALMIRALL, HELSINN, KYOWA KIRIN, MSD, NOVARTIS, PIERRE FABRE, RECORDATI RARE DISEASES, SANOFI, TAKEDA

CME Article

The 2018 update of the WHO-EORTC classification for primary cutaneous lymphomas

Rein Willemze,[1] Lorenzo Cerroni,[2] Werner Kempf,[3] Emilio Berti,[4] Fabio Facchetti,[5] Steven H. Swerdlow,[6] and Elaine S. Jaffe[7]

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Primary cutaneous lymphomas are a heterogeneous group of T- and B-cell lymphomas that present in the skin with no evidence of extracutaneous disease at the time of diagnosis. The 2005 World Health Organization–European Organization for Research and Treatment of Cancer (WHO-EORTC) consensus classification has served as a golden standard for the diagnosis and classification of these conditions. In September 2018, an updated version of the WHO-EORTC was published in the fourth edition of the WHO Classification of Skin Tumours Blue Book. In this classification, primary cutaneous acral CD8$^+$ T-cell lymphoma and Epstein-Barr virus positive (EBV$^+$) mucocutaneous ulcer are included as new provisional entities, and a new section on cutaneous forms of chronic active EBV disease has been added. The term "primary cutaneous CD4$^+$ small/medium T-cell lymphoma" was modified to "primary cutaneous CD4$^+$ small/medium T-cell lymphoproliferative disorder" because of its indolent clinical behavior and uncertain malignant potential. Modifications have also been made in the sections on lymphomatoid papulosis, increasing the spectrum of histologic and genetic types, and primary cutaneous marginal zone lymphomas recognizing 2 different subtypes. Herein, the characteristic features of these new and modified entities as well as the results of recent molecular studies with diagnostic, prognostic, and/or therapeutic significance for the different types of primary cutaneous lymphomas are reviewed. An update of the frequency and survival of the different types of primary cutaneous lymphomas is provided. (*Blood*. 2019;133(16):1703-1714)

Review article

WHO-EORTC classification for cutaneous lymphomas

Rein Willemze, Elaine S. Jaffe, Günter Burg, Lorenzo Cerroni, Emilio Berti, Steven H. Swerdlow, Elisabeth Ralfkiaer, Sergio Chimenti, José L. Diaz-Perez, Lyn M. Duncan, Florent Grange, Nancy Lee Harris, Werner Kempf, Helmut Kerl, Michael Kurrer, Robert Knobler, Nicola Pimpinelli, Christian Sander, Marco Santucci, Wolfram Sterry, Maarten H. Vermeer, Janine Wechsler, Sean Whittaker, and Chris J. L. M. Meijer

Primary cutaneous lymphomas are currently classified by the European Organization for Research and Treatment of Cancer (EORTC) classification or the World Health Organization (WHO) classification, but both systems have shortcomings. In particular, differences in the classification of cutaneous T-cell lymphomas other than mycosis fungoides, Sézary syndrome, and the group of primary cutaneous CD30$^+$ lymphoproliferative disorders and the classification and terminology of different types of cutaneous B-cell lymphomas have resulted in considerable debate and confusion. During recent consensus meetings representatives of both systems reached agreement on a new classification, which is now called the WHO-EORTC classification. In this paper we describe the characteristic features of the different primary cutaneous lymphomas and other hematologic neoplasms frequently presenting in the skin, and discuss differences with the previous classification schemes. In addition, the relative frequency and survival data of 1905 patients with primary cutaneous lymphomas derived from Dutch and Austrian registries for primary cutaneous lymphomas are presented to illustrate the clinical significance of this new classification. (Blood. 2005;105:3768-3785)

Table 1. Relative frequency and prognosis of primary cutaneous lymphomas included in the 2018 update of the WHO-EORTC classification

WHO-EORTC Classification 2018	Frequency, %*	5-y DSS, %*
CTCL		
MF	39	88
MF variants		
Folliculotropic MF	5	75
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PCMZL	9	99
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PCDLBLC, LT	4	56
EBV⁺ mucocutaneous ulcer (provisional)	<1	100
Intravascular large B-cell lymphoma	<1	72

CD8⁺ AECTCL, primary cutaneous aggressive epidermotropic CD8⁺ cytotoxic T-cell lymphoma; DSS, disease-specific survival; NDA, no data available; NOS, not otherwise specified.
*Based on data included in Dutch and Austrian cutaneous lymphoma registries between 2002 and 2017.

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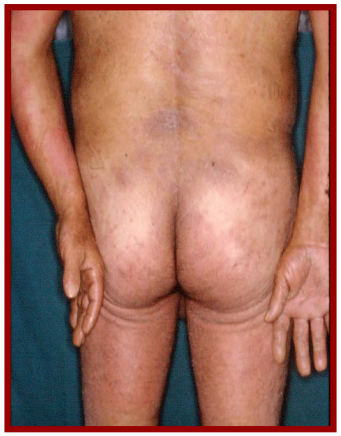
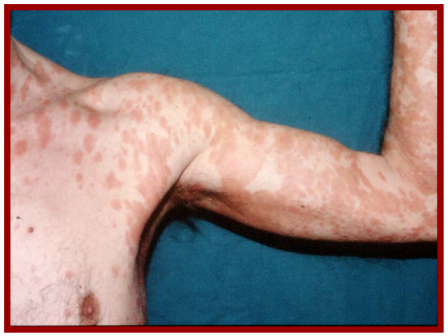
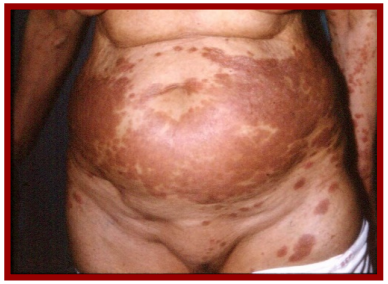
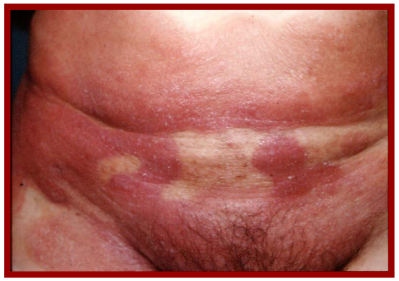




PLAQUE STAGE





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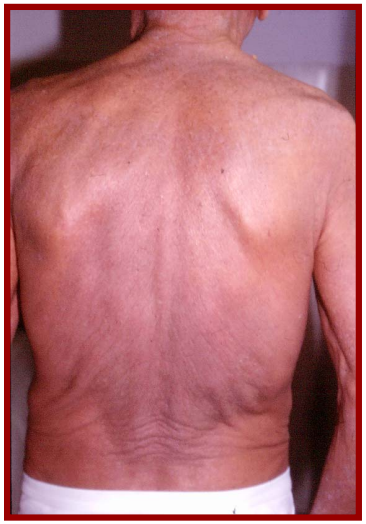
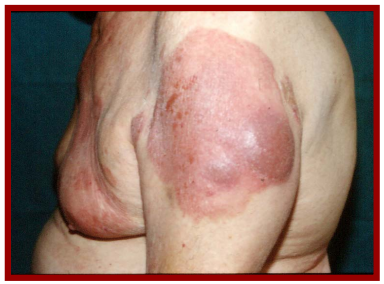
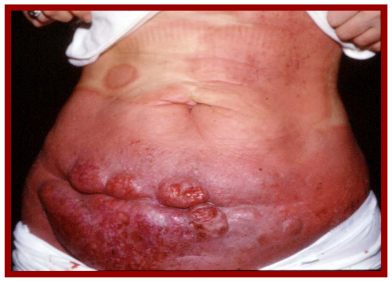


TUMOR STAGE





Defining early mycosis fungoides

Nicola Pimpinelli, MD,[a] Elise A. Olsen, MD,[c] Marco Santucci, MD,[b] Eric Vonderheid, MD,[d] Andreas C. Haeffner, MD,[e] Seth Stevens, MD,[f] Guenter Burg, MD,[e] Lorenzo Cerroni, MD,[g] Brigitte Dreno, MD,[h] Earl Glusac, MD,[i] Joan Guitart, MD,[j] Peter W. Heald, MD,[i] Werner Kempf, MD,[e] Robert Knobler, MD,[k] Stuart Lessin, MD,[l] Christian Sander, MD,[m] Bruce S. Smoller, MD,[n] Gladys Telang, MD,[o] Sean Whittaker, MD,[p] Keiji Iwatsuki, MD, PhD,[q] Erik Obitz, MD,[r] Masahiro Takigawa, MD,[s] Maria L. Turner, MD,[t] and Gary S. Wood, MD,[u] for the International Society for Cutaneous Lymphoma

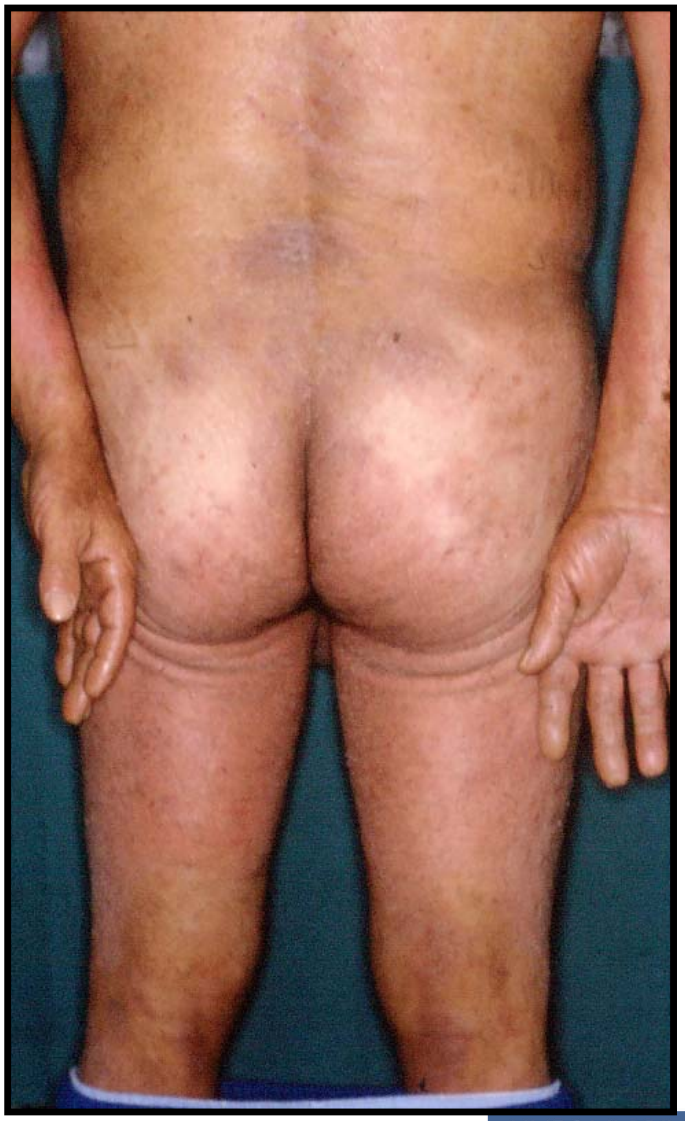
Florence, Italy; Durham, North Carolina; Baltimore, Maryland; Zurich, Switzerland; Thousand Oaks, California; Cleveland, Ohio; Graz and Vienna, Austria; Nantes, France; New Haven, Connecticut; Chicago, Illinois; Philadelphia, Pennsylvania; Munich, Germany; Little Rock, Arkansas; Providence, Rhode Island; London, United Kingdom; Okayama and Hamamatsu, Japan; Aarhus, Denmark; Bethesda, Maryland; and Madison, Wisconsin

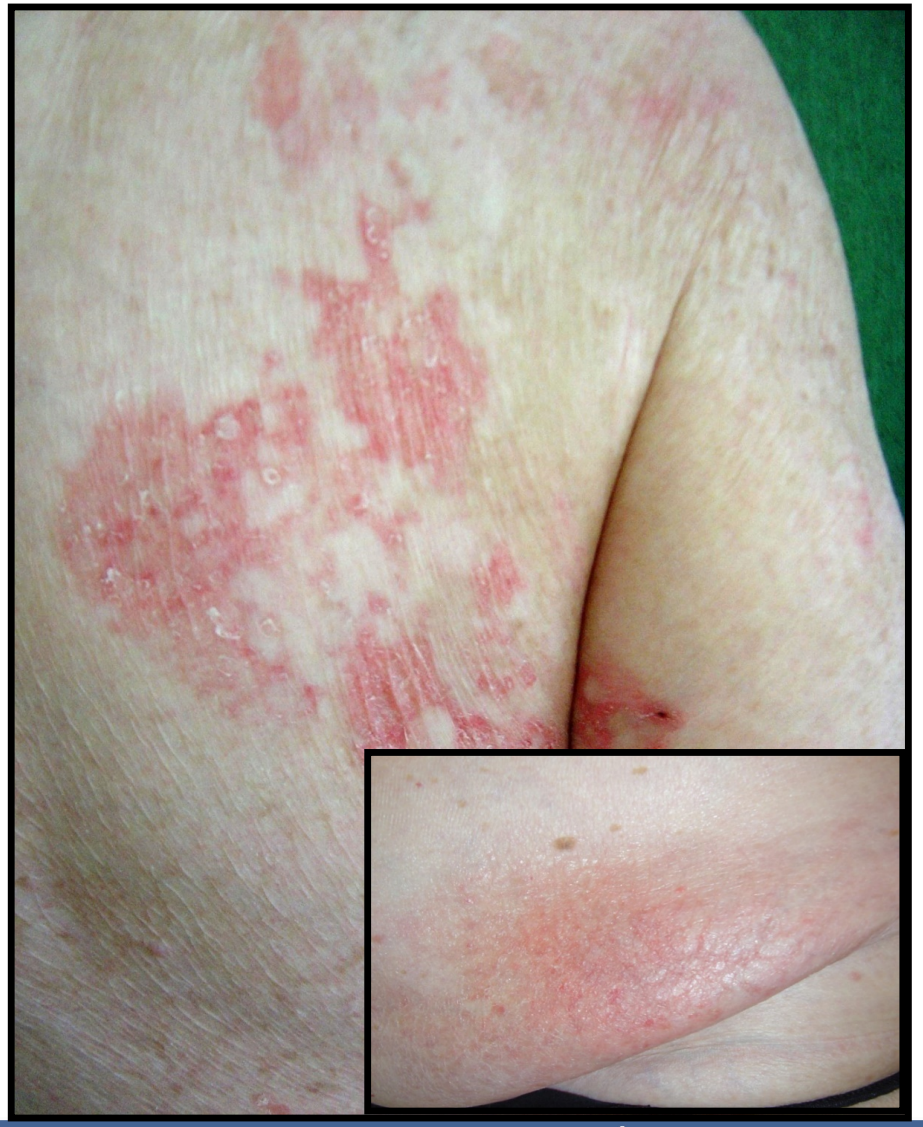
This editorial review summarizes the results of 5 meetings sponsored by the International Society for Cutaneous Lymphoma at which the clinicopathologic and ancillary features of early mycosis fungoides were critically examined. Based on this analysis, an algorithm was developed for the diagnosis of early mycosis fungoides involving a holistic integration of clinical, histopathologic, immunopathologic, and molecular biological characteristics. A novel aspect of this algorithm is that it relies on multiple types of criteria rather than just one, for example, histopathology. Before its finalization, the proposed diagnostic algorithm will require validation and possibly further refinement at multiple centers during the next several years. It is anticipated that a more standardized approach to the diagnosis of early mycosis fungoides will have a beneficial impact on the epidemiology, prognostication, treatment, and analysis of clinical trials pertaining to this most common type of cutaneous lymphoma. (J Am Acad Dermatol 2005;53:1053-63.)

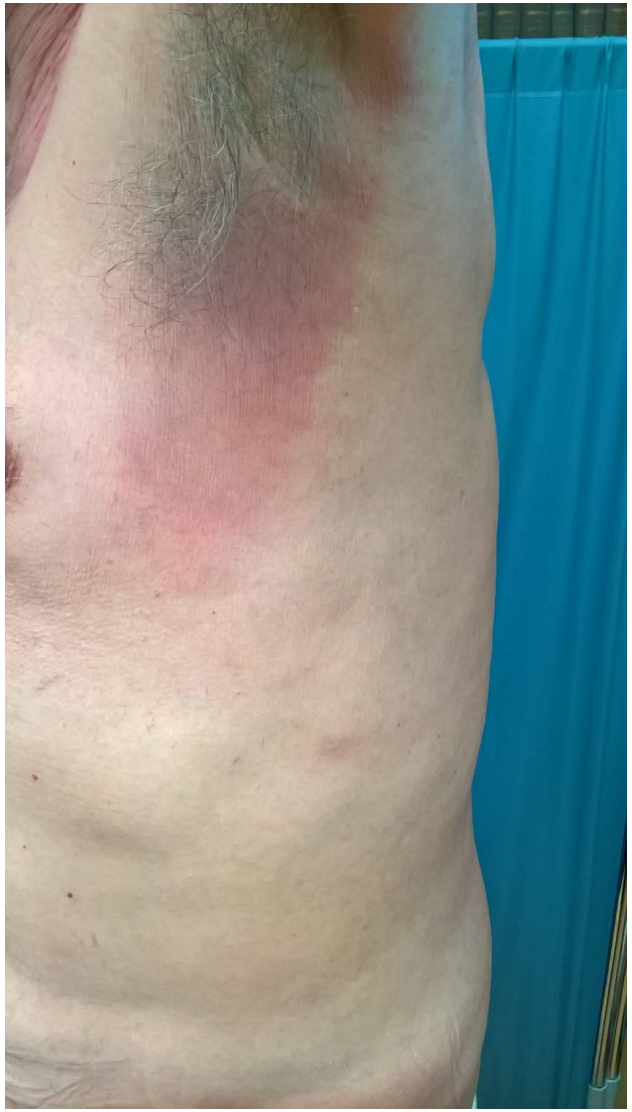
Table I. Algorithm for diagnosis of early MF*

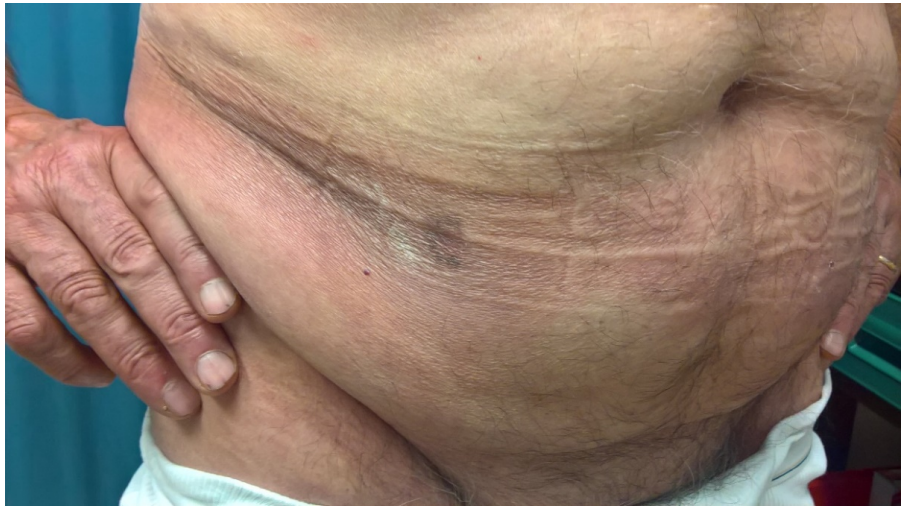
Criteria	Scoring system
Clinical	
Basic	2 points for basic criteria and two additional criteria
Persistent and/or progressive patches/thin plaques	1 point for basic criteria and one additional criterion
Additional	
1) Non-sun exposed location	
2) Size/shape variation	
3) Poikiloderma	
Histopathologic	
Basic	2 points for basic criteria and two additional criteria
Superficial lymphoid infiltrate	1 point for basic criteria and one additional criterion
Additional	
1) Epidermotropism without spongiosis	
2) Lymphoid atypia†	
Molecular biological	
1) Clonal TCR gene rearrangement	1 point for clonality
Immunopathologic	
1) <50% CD2+, CD3+, and/or CD5+ T cells	1 point for one or more criteria
2) <10% CD7+ T cells	
3) Epidermal/dermal discordance of CD2, CD3, CD5, or CD7‡	

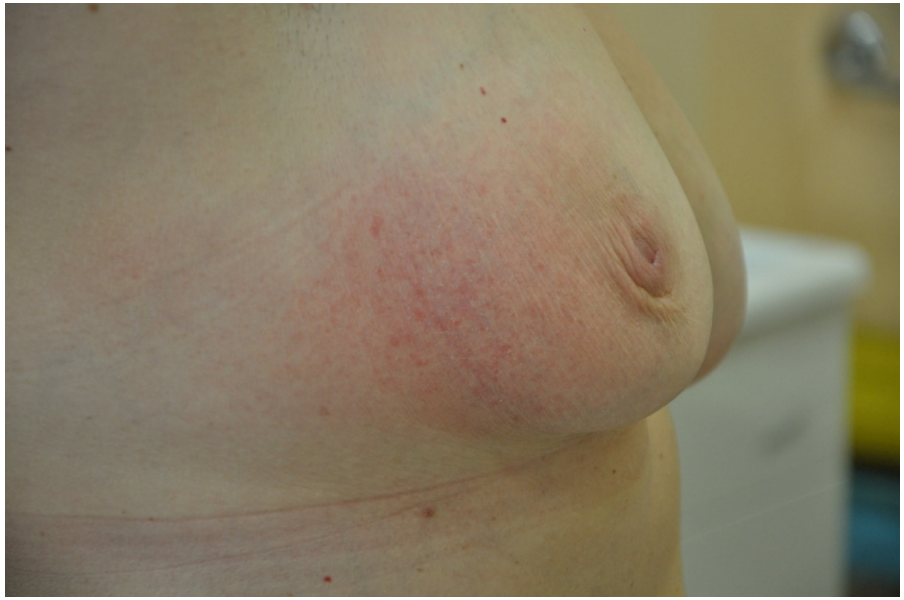
MF, Mycosis fungoides; *TCR*, T-cell receptor.
*A total of 4 points is required for the diagnosis of MF based on any combination of points from the clinical, histopathologic, molecular biological, and immunopathologic criteria.
†Lymphoid atypia is defined as cells with enlarged hyperchromatic nuclei and irregular or cerebriform nuclear contours.
‡T-cell antigen deficiency confined to the epidermis.

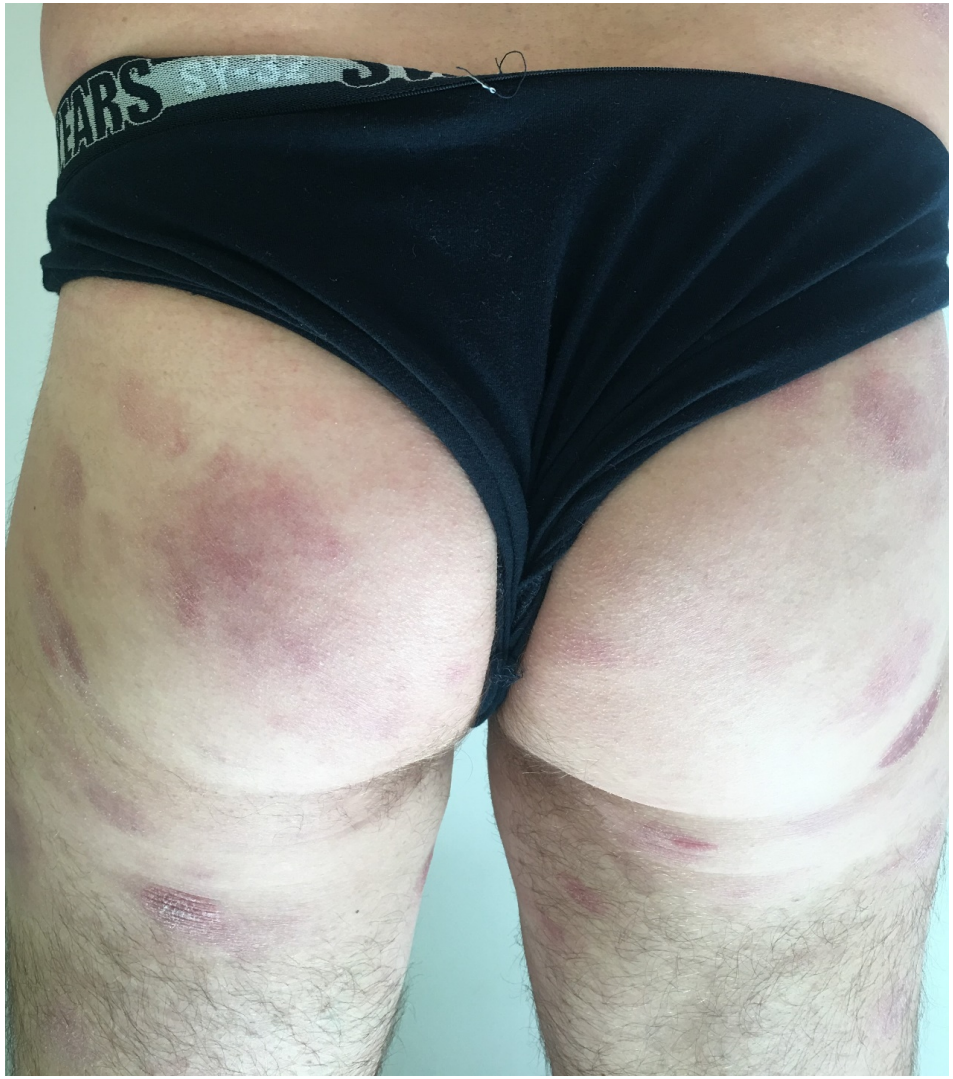


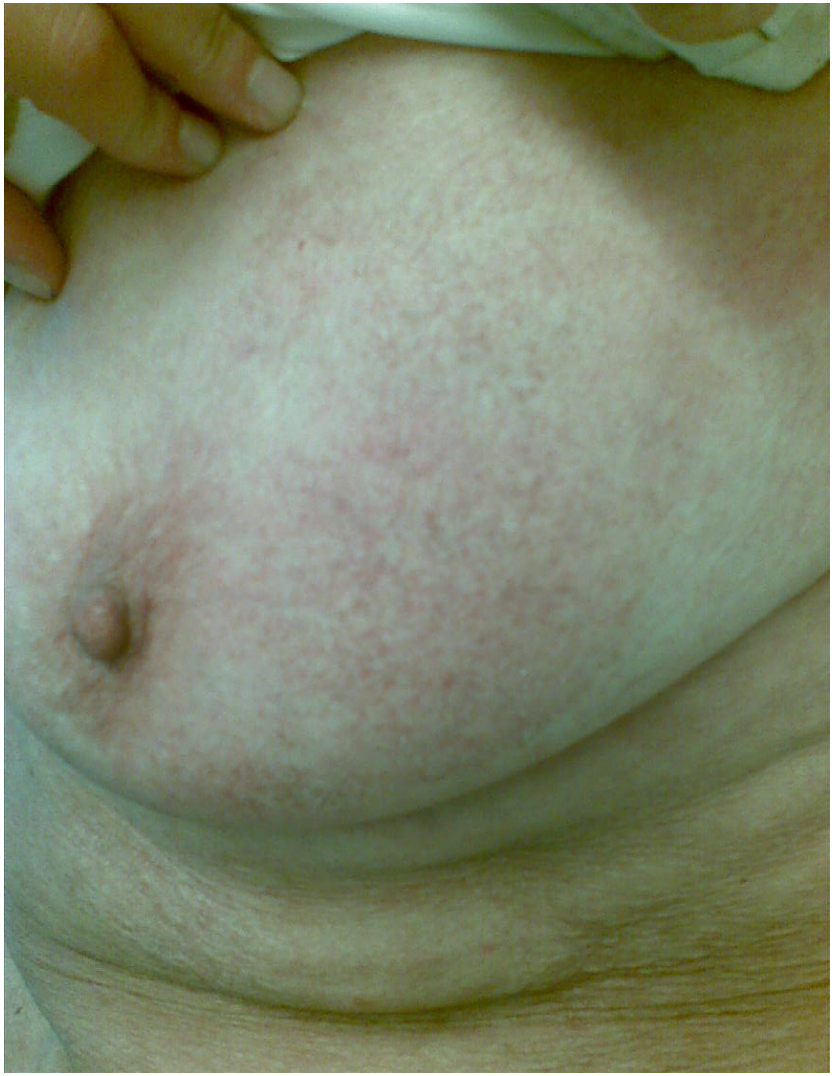


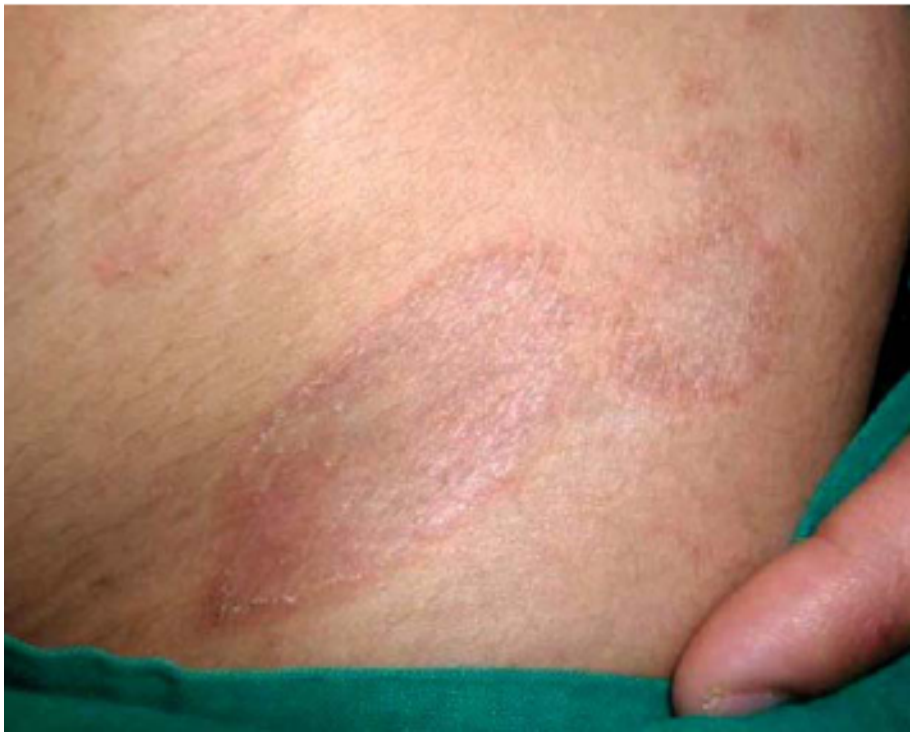


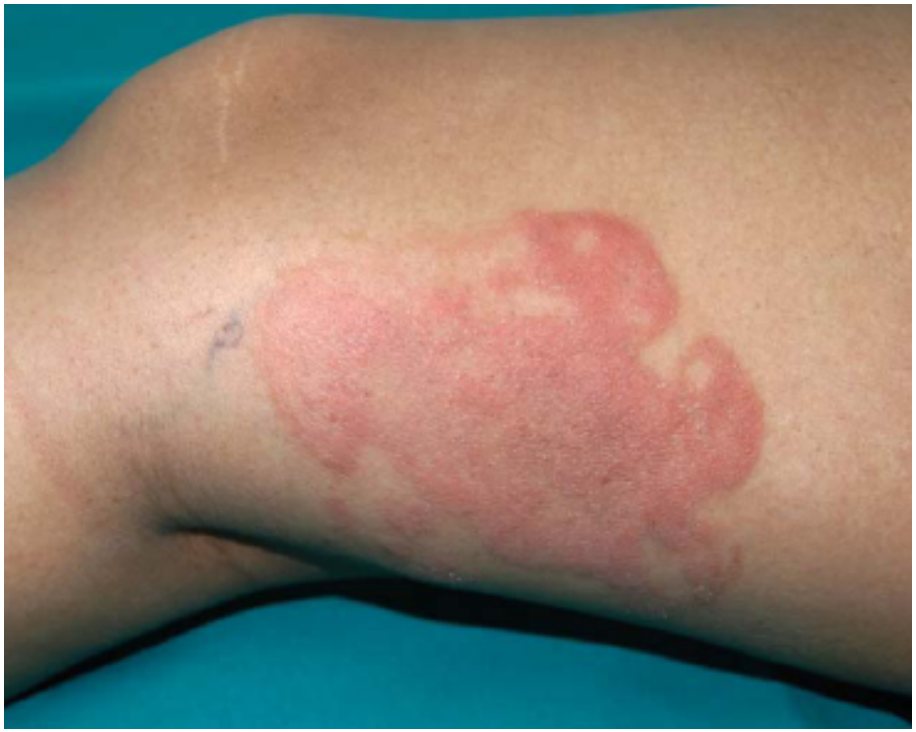












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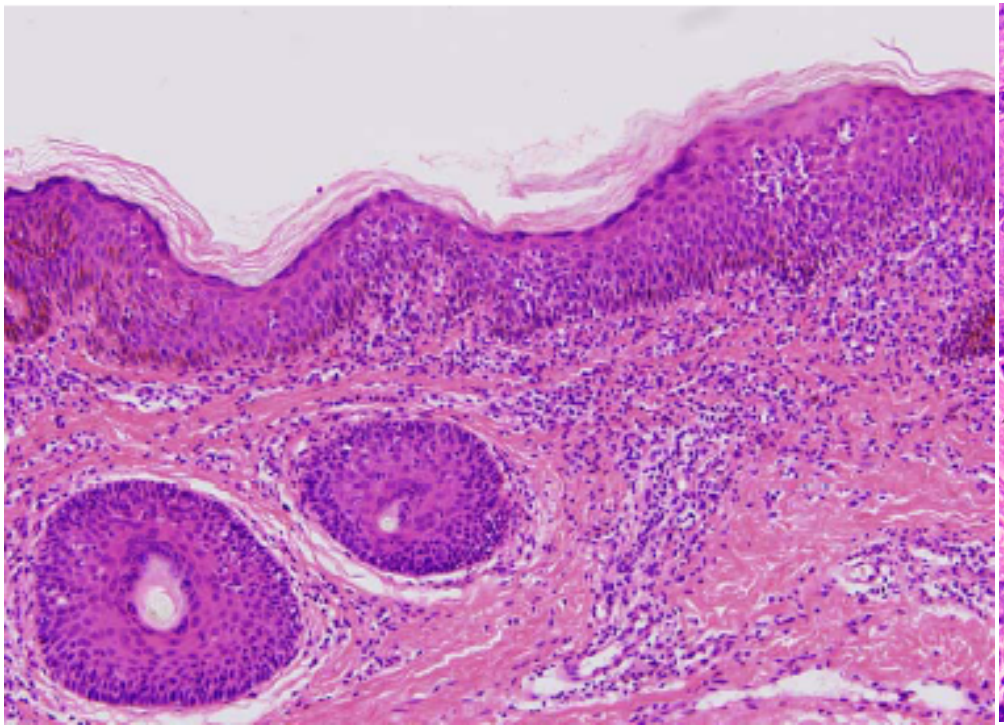

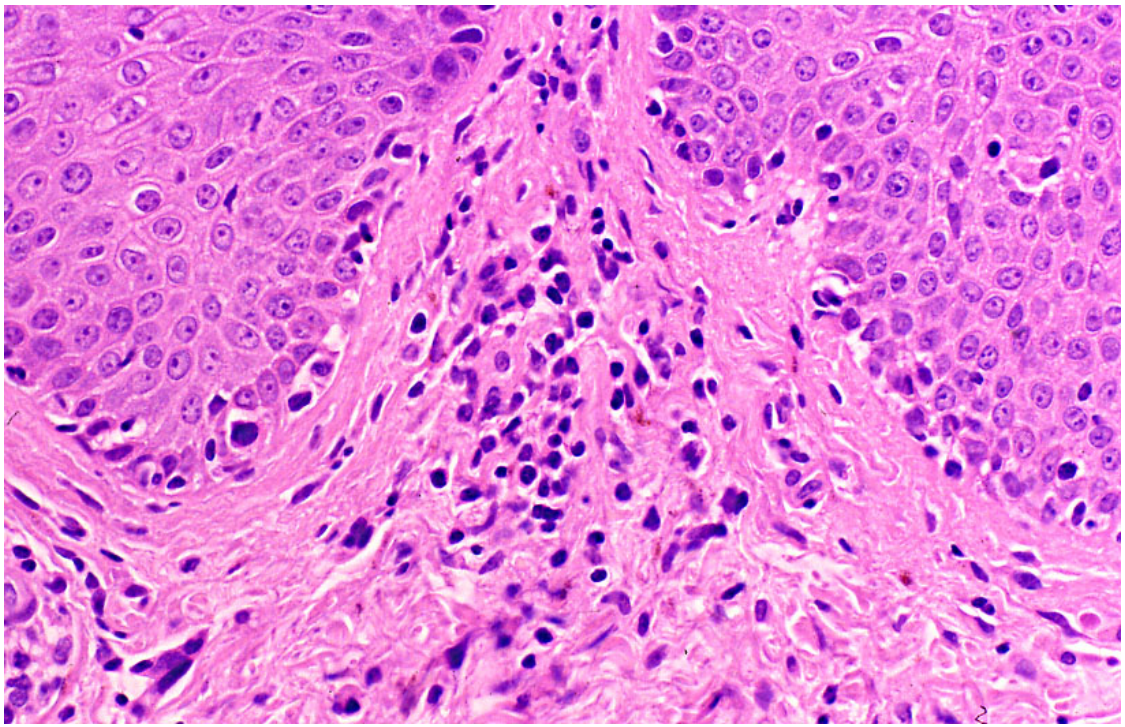

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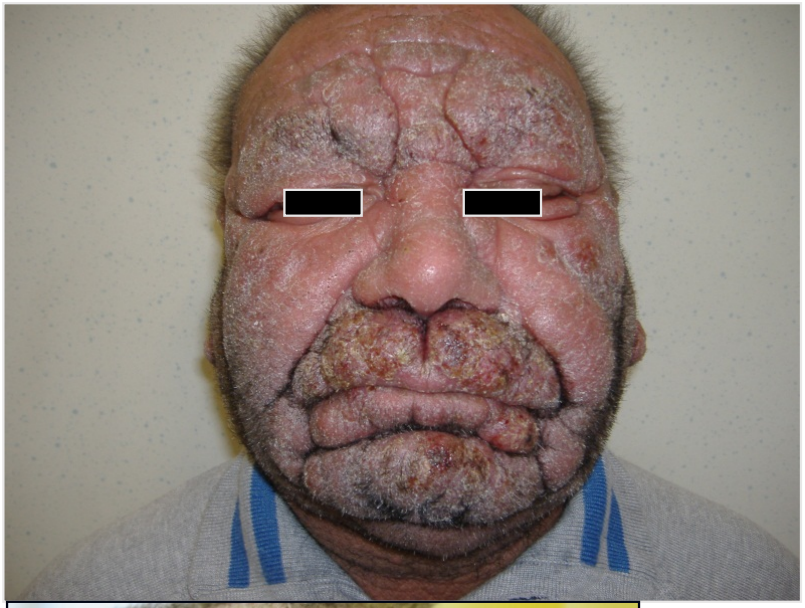
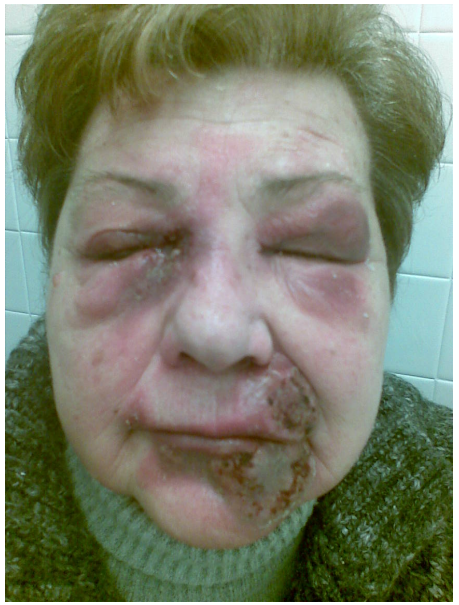
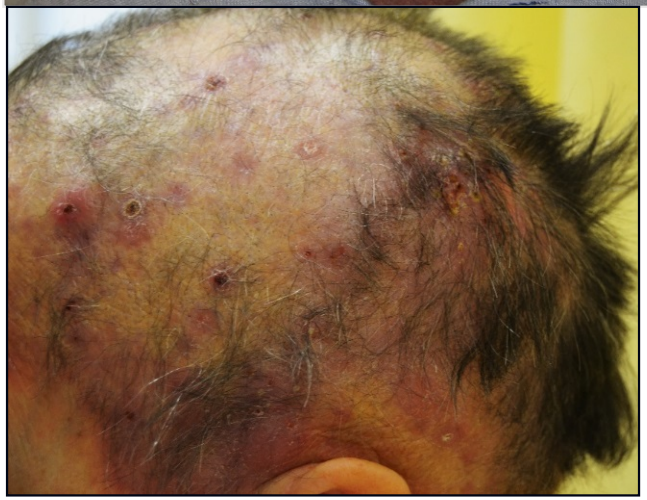
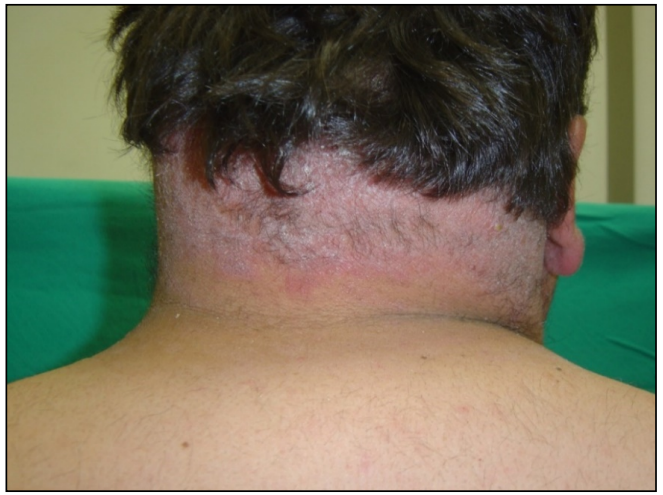
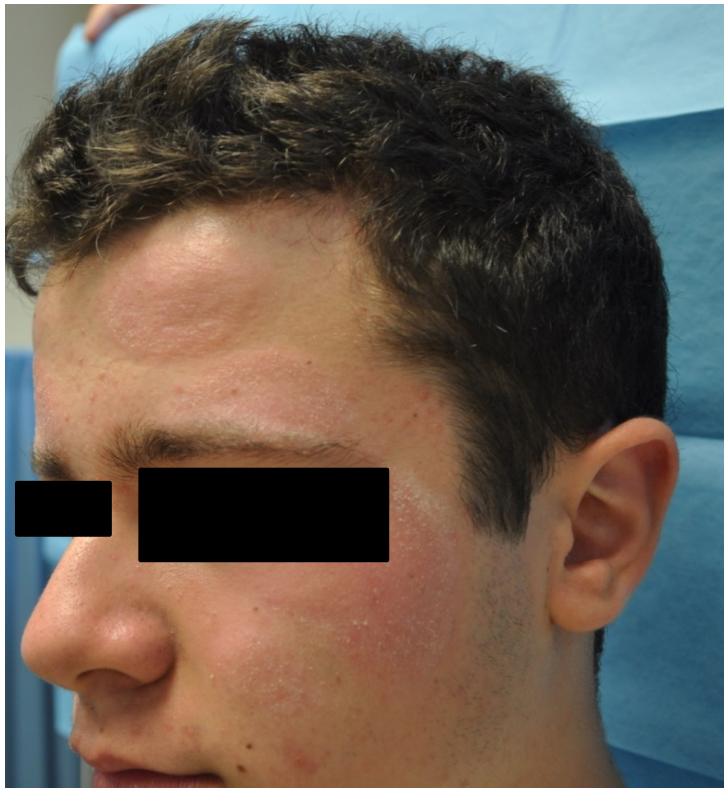
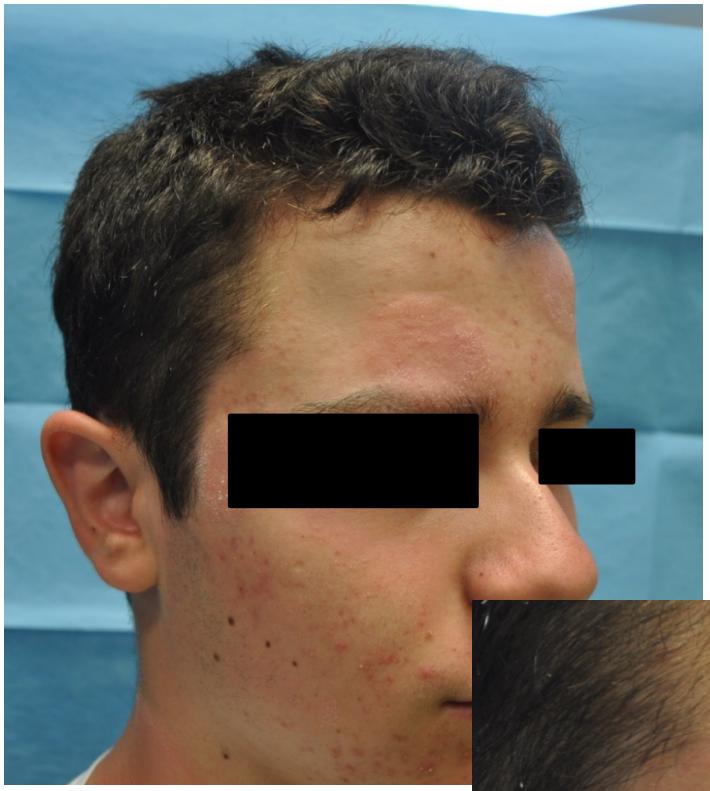


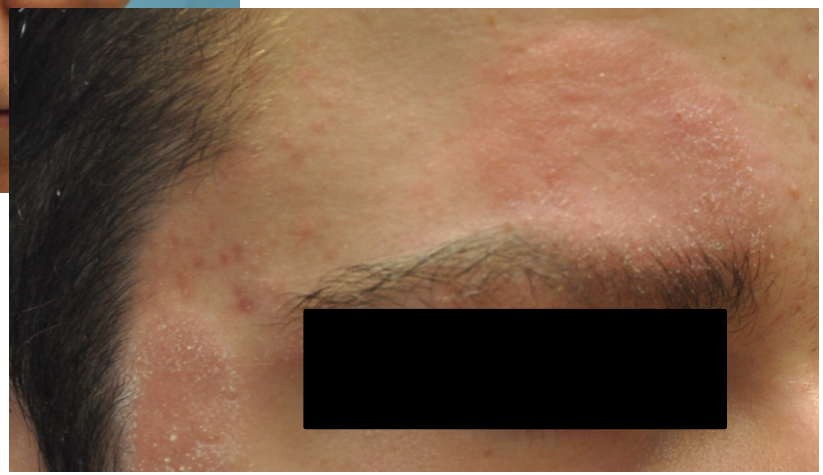


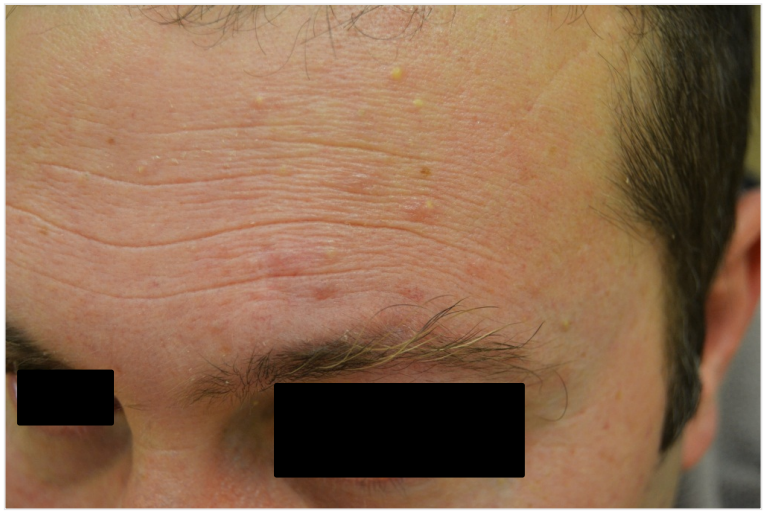


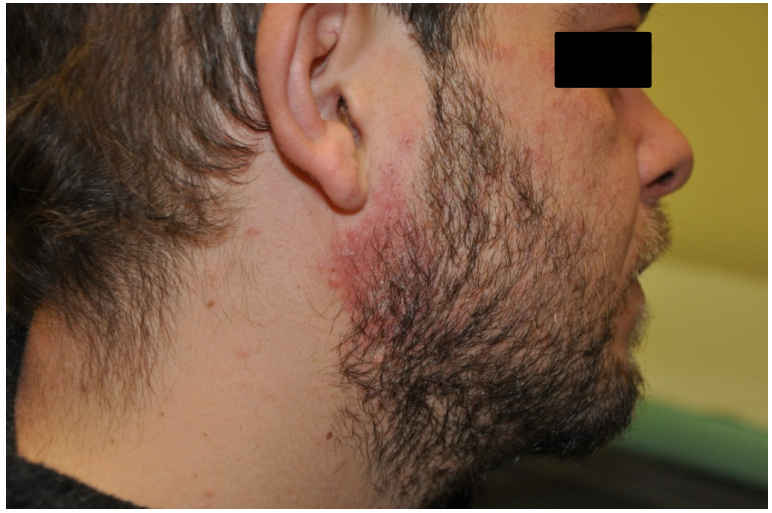


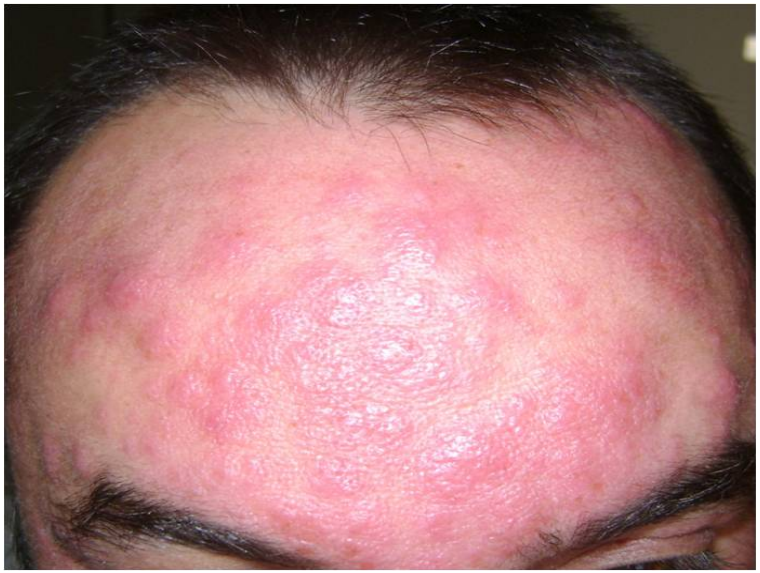


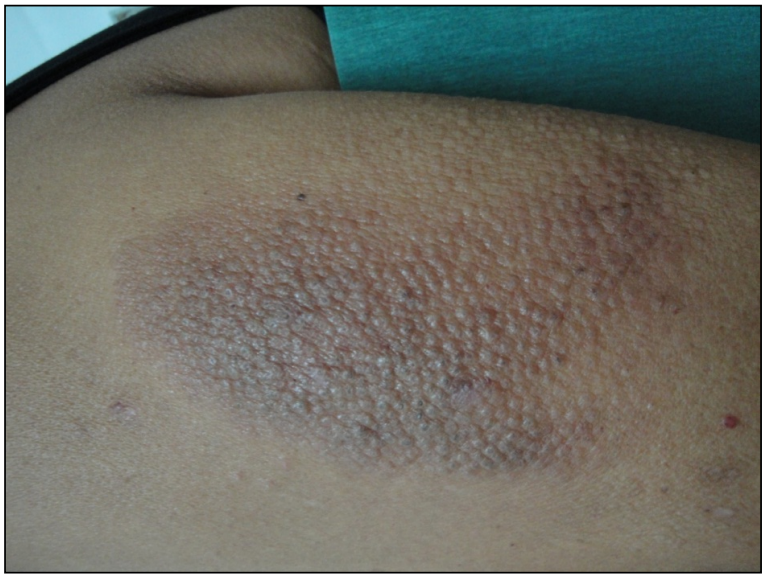












Revisions to the staging and classification of mycosis fungoides and Sézary syndrome: a proposal of the International Society for Cutaneous Lymphomas (ISCL) and the cutaneous lymphoma task force of the European Organization of Research and Treatment of Cancer (EORTC)

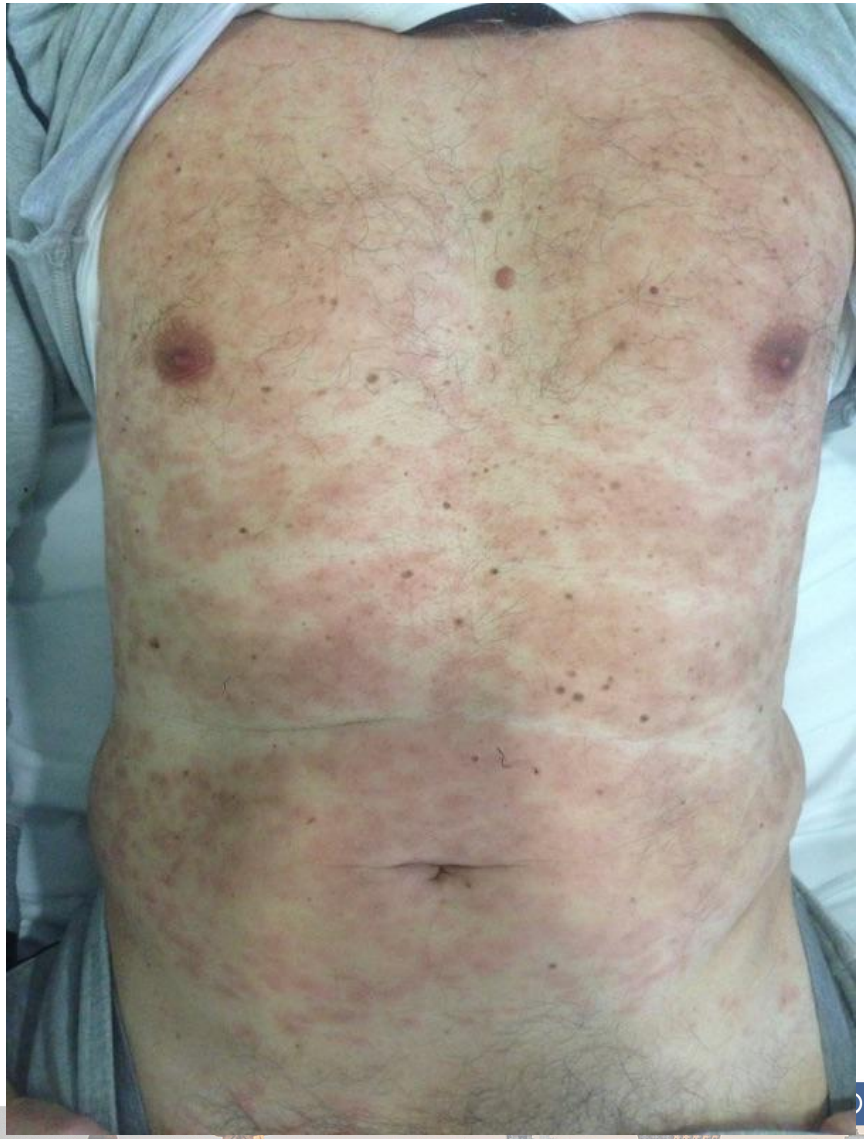
Elise Olsen,[1] Eric Vonderheid,[2] Nicola Pimpinelli,[3] Rein Willemze,[4] Youn Kim,[5] Robert Knobler,[6] Herschel Zackheim,[7] Madeleine Duvic,[8] Teresa Estrach,[9] Stanford Lamberg,[2] Gary Wood,[10] Reinhard Dummer,[11] Annamari Ranki,[12] Gunter Burg,[11] Peter Heald,[13] Mark Pittelkow,[14] Maria-Grazia Bernengo,[15] Wolfram Sterry,[16] Liliane Laroche,[17] Franz Trautinger,[6] and Sean Whittaker,[18] for the ISCL/EORTC

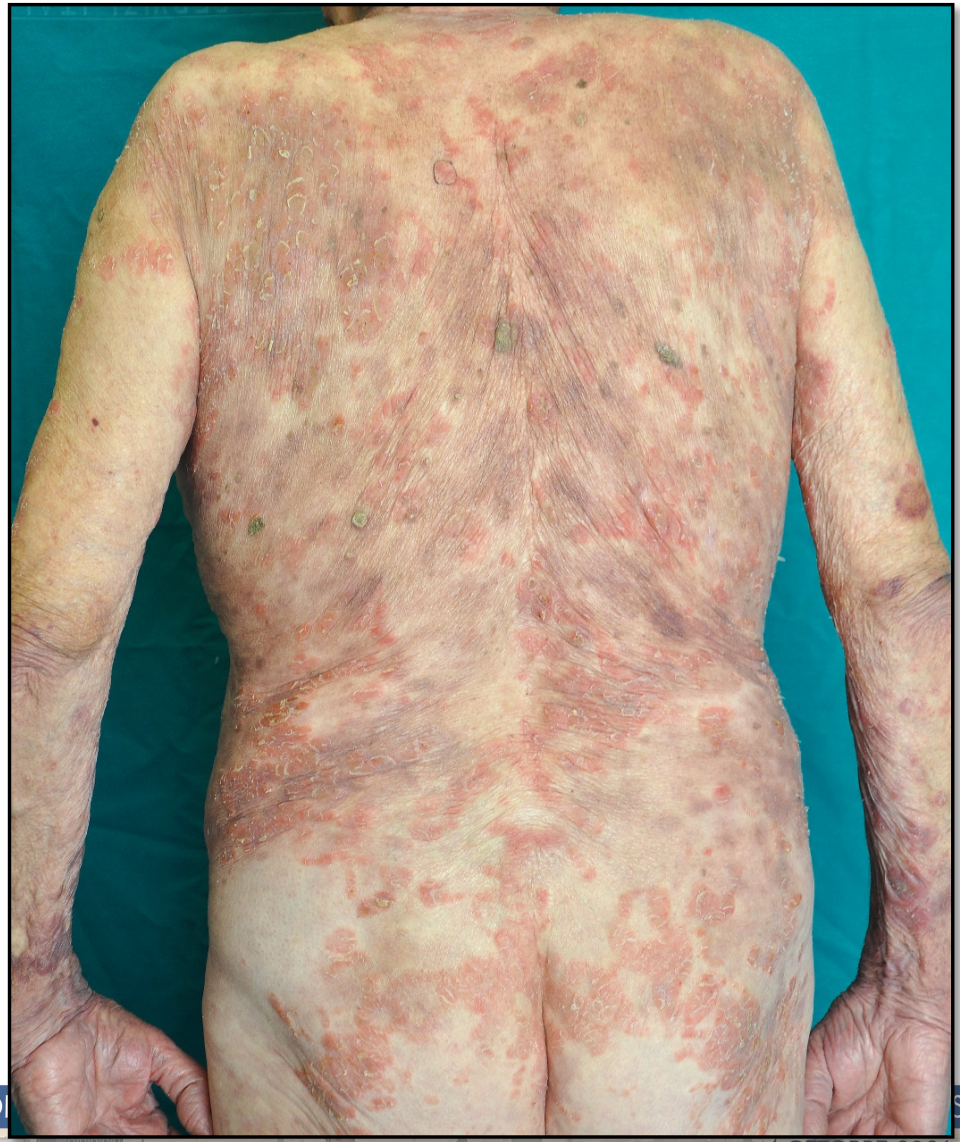
[1]Department of Medicine, Divisions of Dermatology and Oncology, Duke University Medical Center, Durham, NC; [2]Department of Dermatology, Johns Hopkins University, Baltimore, MD; [3]Department of Dermatological Sciences, University of Florence, Florence, Italy; [4]Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; [5]Department of Dermatology, Stanford University Medical Center, Stanford, CA; [6]Department of Dermatology, University of Vienna, Vienna, Austria; [7]Department of Dermatology, University of California at San Francisco; [8]Department of Dermatology, University of Texas at Houston; [9]Department of Dermatology, University of Barcelona, Barcelona, Spain; [10]Department of Dermatology, University of Wisconsin, Madison; [11]Department of Dermatology, University Hospital Zurich, Zurich, Switzerland; [12]Department of Dermatology and Venereal Diseases, Helsinki University Hospital, Helsinki, Finland; [13]Department of Dermatology, Yale University, New Haven, CT; [14]Department of Dermatology, Mayo Clinic, Rochester, MN; [15]Department of Dermatology, University of Turin, Turin, Italy; [16]Department of Dermatology, Charité, Humboldt University, Berlin, Germany; [17]Department of Immuno-Dermatology, Hospital Avicenne–University of Paris XIII, Paris, France; [18]St John's Institute of Dermatology, Skin Tumour Unit, St Thomas' Hospital, London, United Kingdom

The ISCL/EORTC recommends revisions to the Mycosis Fungoides Cooperative Group classification and staging system for cutaneous T-cell lymphoma (CTCL). These revisions are made to incorporate advances related to tumor cell biology and diagnostic techniques as pertains to mycosis fungoides (MF) and Sézary syndrome (SS) since the 1979 publication of the original guidelines, to clarify certain variables that currently impede effective interinstitution and interinvestigator communication and/or the development of standardized clinical trials in MF and SS, and to provide a platform for tracking other variables of potential prognostic significance. Moreover, given the difference in prognosis and clinical characteristics of the non-MF/non-SS subtypes of cutaneous lymphoma, this revision pertains specifically to MF and SS. The evidence supporting the revisions is discussed as well as recommendations for evaluation and staging procedures based on these revisions. (Blood. 2007;110: 1713-1722)

Table 4. ISCL/EORTC revision to the classification of mycosis fungoides and Sézary syndrome

TNMB stages	
Skin	
T_1	Limited patches,* papules, and/or plaques† covering < 10% of the skin surface. May further stratify into T_{1a} (patch only) vs T_{1b} (plaque ± patch).
T_2	Patches, papules or plaques covering ≥ 10% of the skin surface. May further stratify into T_{2a} (patch only) vs T_{2b} (plaque ± patch).
T_3	One or more tumors‡ (≥ 1-cm diameter)
T_4	Confluence of erythema covering ≥ 80% body surface area
Node	
N_0	No clinically abnormal peripheral lymph nodes§; biopsy not required
N_1	Clinically abnormal peripheral lymph nodes; histopathology Dutch grade 1 or NCI LN_{0-2}
N_{1a}	Clone negative#
N_{1b}	Clone positive#
N_2	Clinically abnormal peripheral lymph nodes; histopathology Dutch grade 2 or NCI LN_3
N_{2a}	Clone negative#
N_{2b}	Clone positive#
N_3	Clinically abnormal peripheral lymph nodes; histopathology Dutch grades 3-4 or NCI LN_4; clone positive or negative
N_x	Clinically abnormal peripheral lymph nodes; no histologic confirmation
Visceral	
M_0	No visceral organ involvement
M_1	Visceral involvement (must have pathology confirmation¶ and organ involved should be specified)
Blood	
B0	Absence of significant blood involvement: ≤ 5% of peripheral blood lymphocytes are atypical (Sézary) cells‖
B_{0a}	Clone negative#
B_{0b}	Clone positive#
B1	Low blood tumor burden: > 5% of peripheral blood lymphocytes are atypical (Sézary) cells but does not meet the criteria of B_2
B_{1a}	Clone negative#
B_{1b}	Clone positive#
B2	High blood tumor burden: ≥ 1000/μL Sézary cells‖ with positive clone#





Available online at www.sciencedirect.com

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journal homepage: www.ejcancer.com

Review

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

Franz Trautinger [a,b,*], Johanna Eder [a,b], Chalid Assaf [c], Martine Bagot [d], Antonio Cozzio [e], Reinhard Dummer [f], Robert Gniadecki [g,h], Claus-Detlev Klemke [i], Pablo L. Ortiz-Romero [j], Evangelia Papadavid [k], Nicola Pimpinelli [l], Pietro Quaglino [m], Annamari Ranki [n], Julia Scarisbrick [o], Rudolf Stadler [p], Liisa Väkevä [n], Maarten H. Vermeer [q], Sean Whittaker [r], Rein Willemze [q], Robert Knobler [s]

Table 4a
Recommendations for first-line treatment of MF stages IA, IB, and IIA.

Expectant policy (mainly T1a)		Level 4
SDT	Topical corticosteroids (mainly T1a and T2a)	Level 3
	UVB[a] (mainly T1a and T2a)	Level 2
	PUVA[b]	Level 2
	Localised RT (for localised MF including pagetoid reticulosis)	Level 4
	Mechlorethamine[c]	Level 2

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DOI: 10.1111/phpp.12658

ORIGINAL ARTICLE

Photodermatology, Photoimmunology & Photomedicine WILEY

Italian expert-based recommendations on the use of photo(chemo)therapy in the management of mycosis fungoides: Results of an e-Delphi consensus

Vieri Grandi[1,2] | Antonello Baldo[3] | Emilio Berti[4,5] | Pietro Quaglino[6] | Serena Rupoli[7] | Mauro Alaibac[8] | Silvia Alberti-Violetti[4,5] | Paolo Amerio[9] | Valeria Brazzelli[10] | Pier Luigi Bruni[11] | Piergiacomo Calzavara-Pinton[12] | Aurora Parodi[13] | Emanuele Cozzani[13] | Martina Burlando[13] | Maria Concetta Fargnoli[14] | Daniele Gambini[15] | Paolo Iacovelli[16] | Alessia Pacifico[16] | Caterina Longo[17,18] | Giuseppe Monfrecola[19] | Alberico Motolese[20] | Giorgio Mozzicafreddo[21] | Carlo Cota[21] | Paolo Pigatto[22] | Alessandro Pileri[23] | Paola Savoia[24] | Marco Simonacci[25] | Marina Venturini[12] | Annamaria Offidani[26] | Elisa Molinelli[26] | Michele Pellegrino[27] | Emanuele Trovato[28] | Roberta Piccinno[29] | Karl Lawrence[30] | Nicola Pimpinelli[1]

Abstract

Background: Phototherapy is a mainstay for the treatment of MF. However, there is scarce evidence for its use, mostly due to the lack of a unified schedule.

Aims: The primary aim of this study was to establish the first structured, expert-based consensus regarding the indications and technical schedules of NB-UVB and PUVA for MF. The secondary aim was to determine the consensus level for each specific item.

Materials & Methods: E-delphi study. Item-specific expert consensus was defined as the number of "Totally Agree" results to ≥80% of the panelists. Cronbach alpha index ≥0.7 was used as a measure of homogeneity in the responses among questions related to the same topic.

Results: Overall, there was a high homogeneity among responders (0.78). On specific topics, the highest grade was observed for technical items (0.8) followed by indications for early (0.73) and advanced stages (0.7).

Conclusions: Items related to the most canonical indications of phototherapy and to treatment schedules showed the highest agreements rates. There is consensus about the use of standardized treatment schedules for the induction and consolidation phases for NB-UVB and PUVA in MF.

KEYWORDS

delphi study, evidence-based medicine, guideline, mycosis fungoides, phototherapy

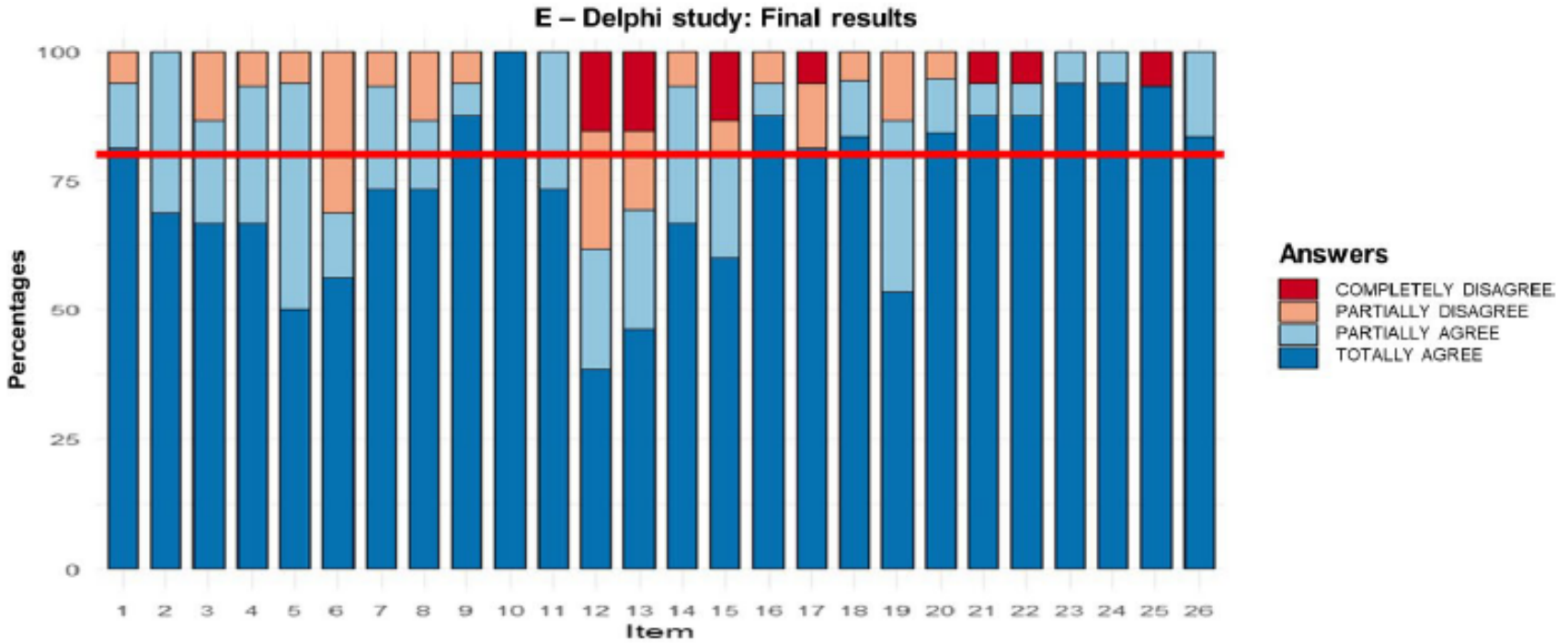


FIGURE 3 Barplot chart showing rates of agreement/disagreement per each questionnaire item. Cutoff value used to define a consensus is depicted as a red horizontal bar set at 80% «TOTALLY AGREE»

TABLE 2 a (top) and b (bottom): recommended schedules for initiation and consolidation phases for NB-UVB and PUVA

a) Narrow-band UVB

Skin phototype	Starting dose[a]	Dose increase per treatment[a]
I	130 mJ/cm^2	15 mJ/cm^2
II	220 mJ/cm^2	25 mJ/cm^2
III	260 mJ/cm^2	40 mJ/cm^2
IV	330 mJ/cm^2	45 mJ/cm^2
V	350 mJ/cm^2	60 mJ/cm^2
VI	400 mJ/cm^2	65 mJ/cm^2
Consolidation[b]	Dose and frequency held steady for 1-3 months	

b) PUVA

Skin phototype	Starting dose	Dose increase per treatment[c]
I	500 mJ/cm^2	500 mJ/cm^2
II	1000 mJ/cm^2	500 mJ/cm^2
III	1500 mJ/cm^2	1000 mJ/cm^2
IV	2000 mJ/cm^2	1000 mJ/cm^2
V	2500 mJ/cm^2	1500 mJ/cm^2
VI	3000 mJ/cm^2	1500 mJ/cm^2
Consolidation[b]	Dose and frequency held steady for 1-3 months	

[a]Starting dose can be calculated alternatively as 70% of MED, and dose increase of 20% per session (10% if photoreaction).

[b]Consolidation phase should not be used routinely. A case by case approach is recommended.

[c]If poorly tolerate, consider increase the dose every two treatments.

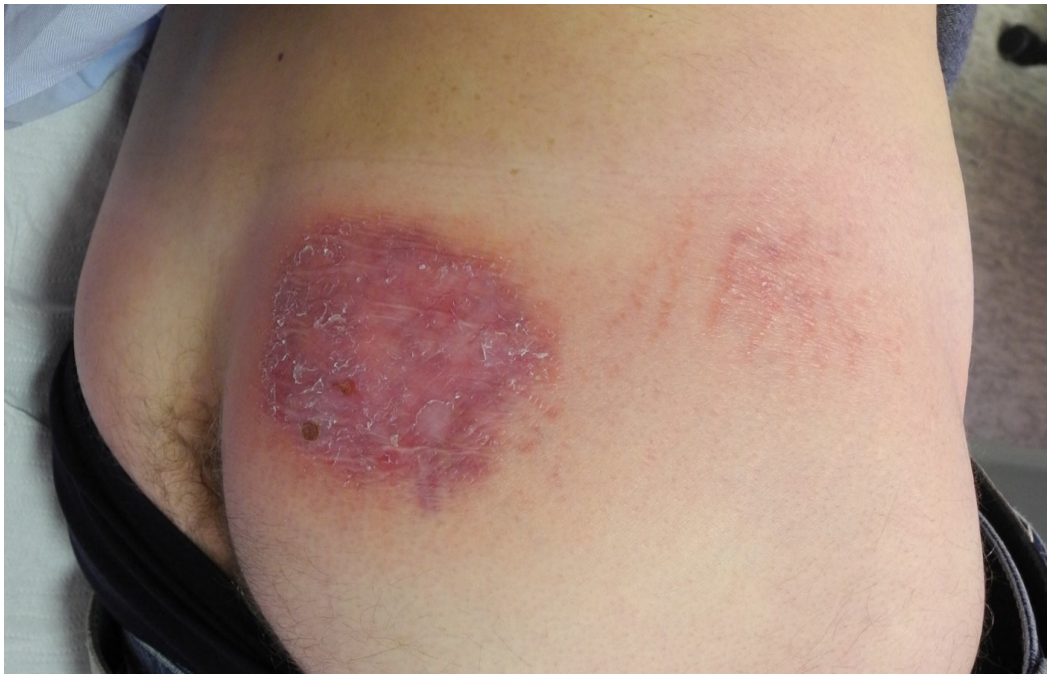
UNILESIONAL/LOCALIZED MF

➔ Radiotherapy in first line

➔ 20- 24 Gy (conventional fractioning)

➔ “curative” treatment with ≥ 2 cm margins

Micaily, IJROBP 2008
Wilson, IJROBP 2008
Specht, IJROBP 2015



Dermatology

Research Article

Dermatology
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Post hoc Analysis of a Randomized, Controlled, Phase 2 Study to Assess Response Rates with Chlormethine/Mechlorethamine Gel in Patients with Stage IA–IIA Mycosis Fungoides

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Emmanuella Guenova[e, f] Martine Bagot[g] Pablo Luis Ortiz-Romero[h]
Pietro Quaglino[i] Erminio Bonizzoni[j] Emmilia Hodak[k]

Table 2. Clinical response (≥50% improvement in skin score) by MF stage in the original and post hoc analyses of the 201 study data

	ITT population			EE population		
	CL gel	CL ointment	*p* value	CL gel	CL ointment	*p* value
CAILS, %						
Original analysis*						
Stage IA	59.2	40.0	N/A	79.6	56.1	N/A
Stage IB–IIA	57.4	55.4	N/A	73.2	61.1	N/A
Post hoc analysis						
Stage IA	79.8	49.2	0.0014	82.3	51.4	0.0036
Stage IB–IIA	77.0	59.6	0.0785	79.5	61.5	0.0697
mSWAT, %						
Original analysis*						
Stage IA	40.8	36.9	N/A	57.1	48.8	N/A
Stage IB–IIA	55.6	55.4	N/A	70.7	61. 1	N/A
Post hoc analysis						
Stage IA	48.9	36.9	0.2422	54.3	38.2	0.1384
Stage IB–IIA	55.2	55.8	0.9554	58.9	57.3	0.8766
BSA, %						
Post hoc analysis						
Stage IA	49.5	33.2	0.0934	56.4	35.2	0.0488
Stage IB–IIA	47.2	50.3	0.7648	49.4	51.6	0.8368

* The original study 201 analysis was based on noninferiority. BSA, body surface area; CAILS, Composite Assessment of Index Lesion Severity; CL, chlormethine; EE, efficacy-evaluable; ITT, intent-to-treat; MF, mycosis fungoides; mSWAT, Modified Severity-Weighted Assessment Tool; N/A, not available.

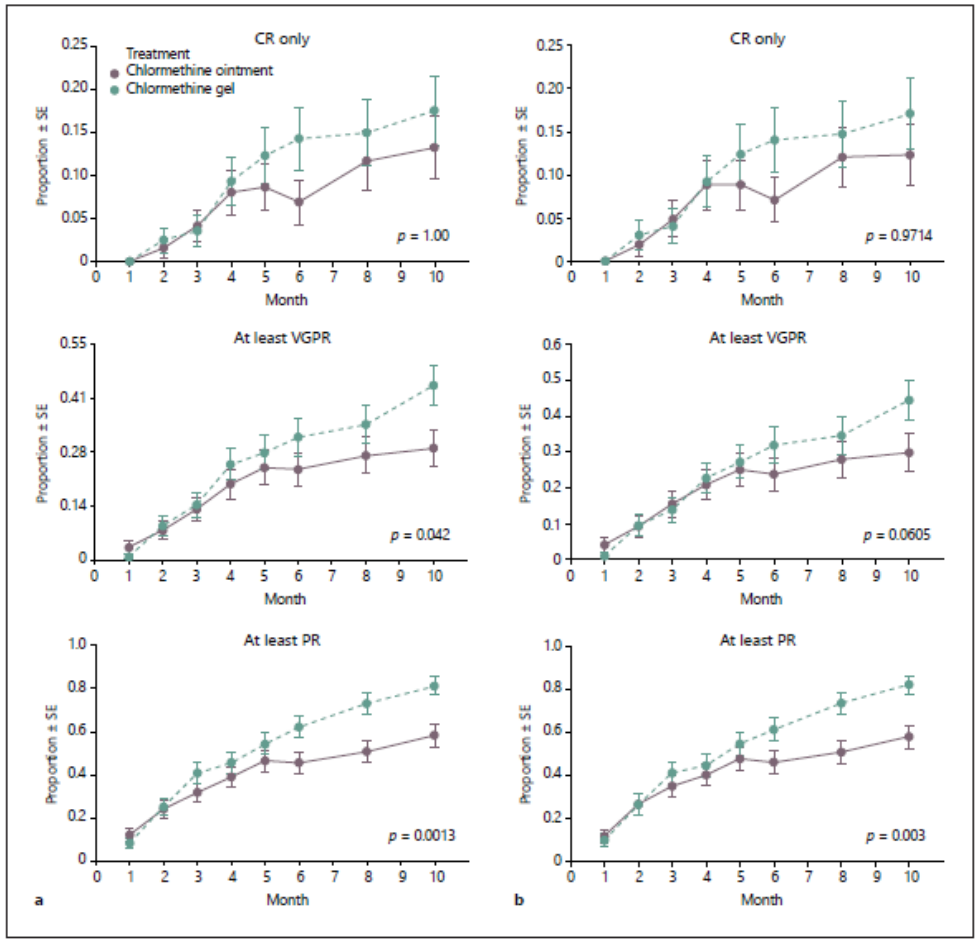


Fig. 2. Composite Assessment of Index Lesion Severity (CAILS) response trends for patients treated with chlormethine gel (dashed line) or ointment (solid line) in the intent-to-treat (**a**) or efficacy-evaluable populations (**b**). CR, complete response; VGPR, very good partial response; PR, partial response; SE, standard error.

CLORMETINE gel: pros

* relatively easy to manage

* possible alternative to phototherapy, particulary in stage IA (*even more in the COVID era …*)

* possible integration to phototherapy in «sanctuary» or refractory areas

CLORMETINE gel: cons

* cost (currently not refunded by NHS, weight on institutional budget)

* short expiry date

* irritant contact dermatitis (useful association / rotation with topical steroids)

MF/SS THERAPY AT A GLANCE: SECOND LINE

Cortesia Prof. P. Quaglino

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											

Table 4b
Recommendations for second-line treatment of MF stages IA, IB, and IIA.

Systemic therapies[a]	
Retinoids[b]	Level 2
IFN-α	Level 2
TSEB (mainly T2b)	Level 2
Low-dose MTX	Level 4

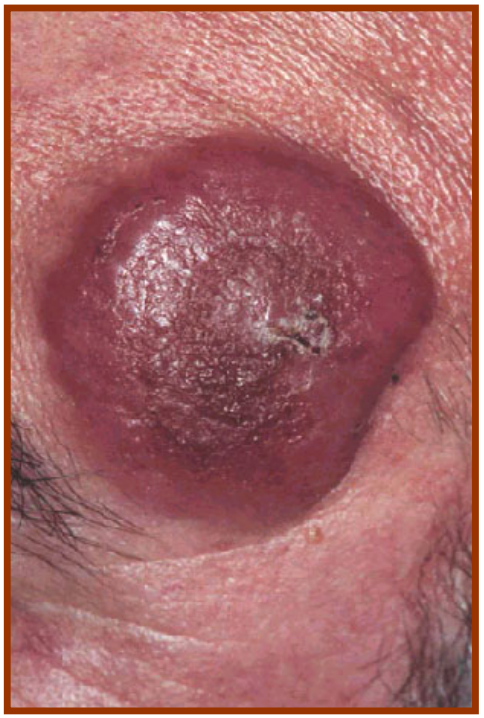
[a] The following agents are most commonly combined with PUVA, combinations with other modalities and with each other are also widely used.

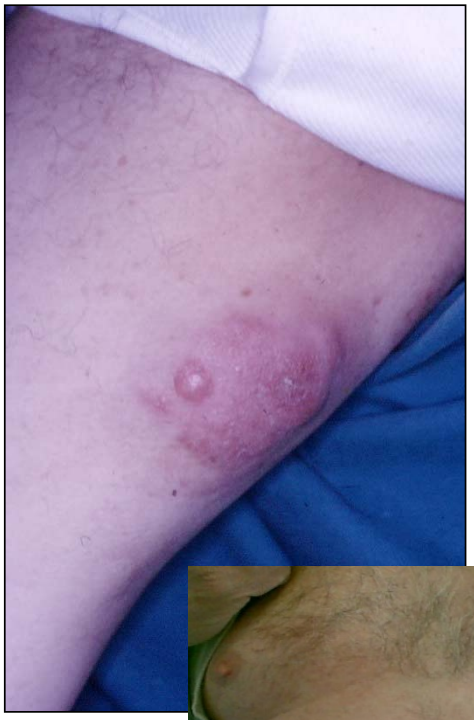
[b] Including RAR and RXR agonists.

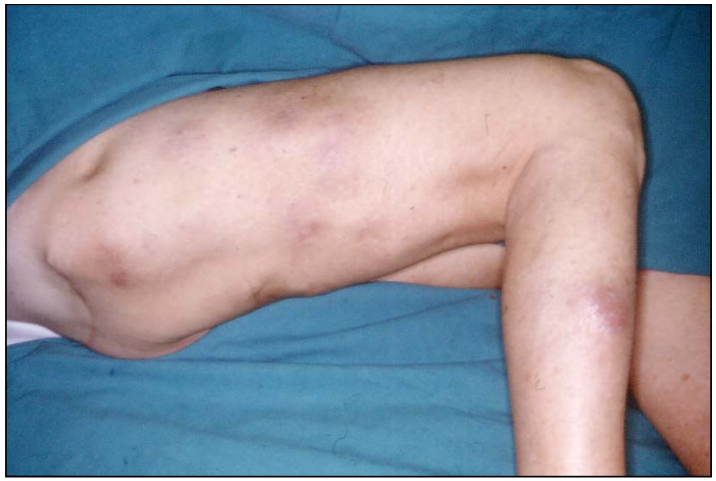
Table 1. Relative frequency and prognosis of primary cutaneous lymphomas included in the 2018 update of the WHO-EORTC classification

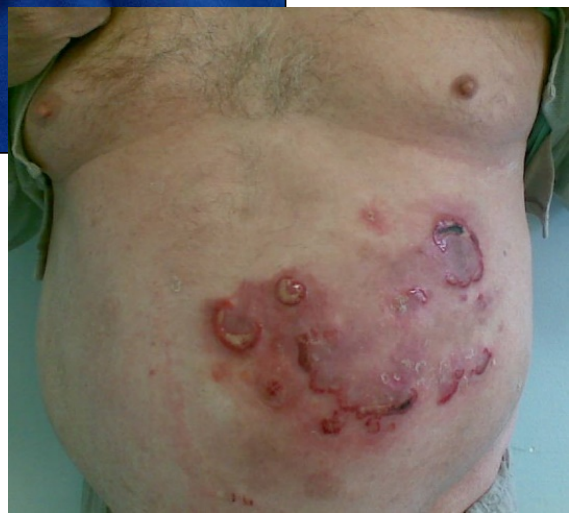
WHO-EORTC Classification 2018	Frequency, %*	5-y DSS, %*
CTCL		
MF	39	88
MF variants		
Folliculotropic MF	5	75
Pagetoid reticulosis	<1	100
Granulomatous slack skin	<1	100
SS	2	36
Adult T-cell leukemia/lymphoma	<1	NDA
Primary cutaneous CD30⁺ LPDs		
C-ALCL	8	95
LyP	12	99
Subcutaneous panniculitis-like T-cell lymphoma	1	87
Extranodal NK/T-cell lymphoma, nasal type	<1	16
Chronic active EBV infection	<1	NDA
Primary cutaneous peripheral T-cell lymphoma, rare subtypes		
Primary cutaneous γ/δ T-cell lymphoma	<1	11
CD8⁺ AECTCL (provisional)	<1	31
Primary cutaneous CD4⁺ small/medium T-cell lymphoproliferative disorder (provisional)	6	100
Primary cutaneous acral CD8⁺ T-cell lymphoma (provisional)	<1	100
Primary cutaneous peripheral T-cell lymphoma, NOS	2	15
CBCL		
PCMZL	9	99
PCFCL	12	95
PCDLBLC, LT	4	56
EBV⁺ mucocutaneous ulcer (provisional)	<1	100
Intravascular large B-cell lymphoma	<1	72

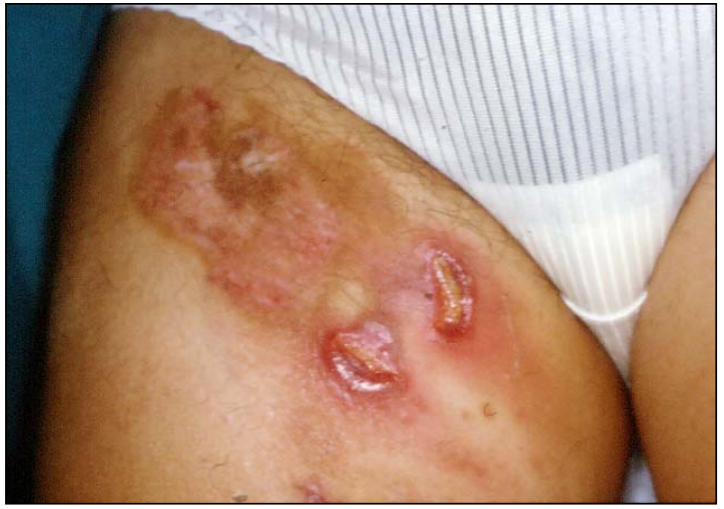
CD8⁺ AECTCL, primary cutaneous aggressive epidermotropic CD8⁺ cytotoxic T-cell lymphoma; DSS, disease-specific survival; NDA, no data available; NOS, not otherwise specified.
*Based on data included in Dutch and Austrian cutaneous lymphoma registries between 2002 and 2017.

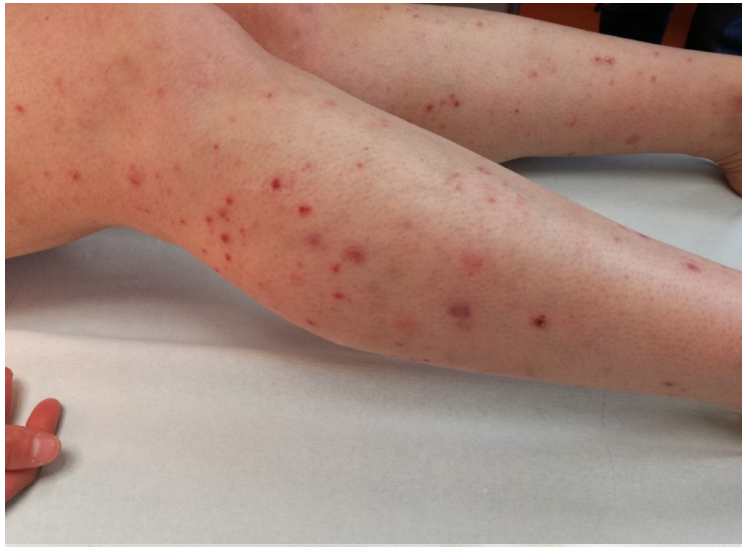


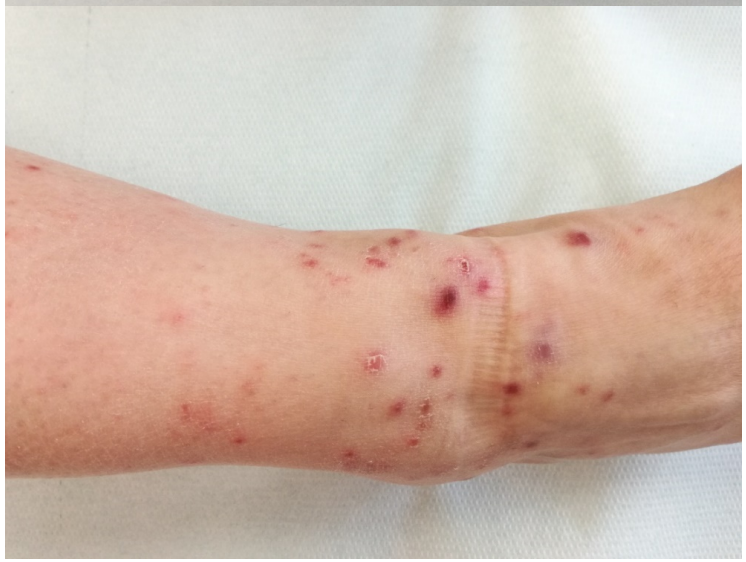


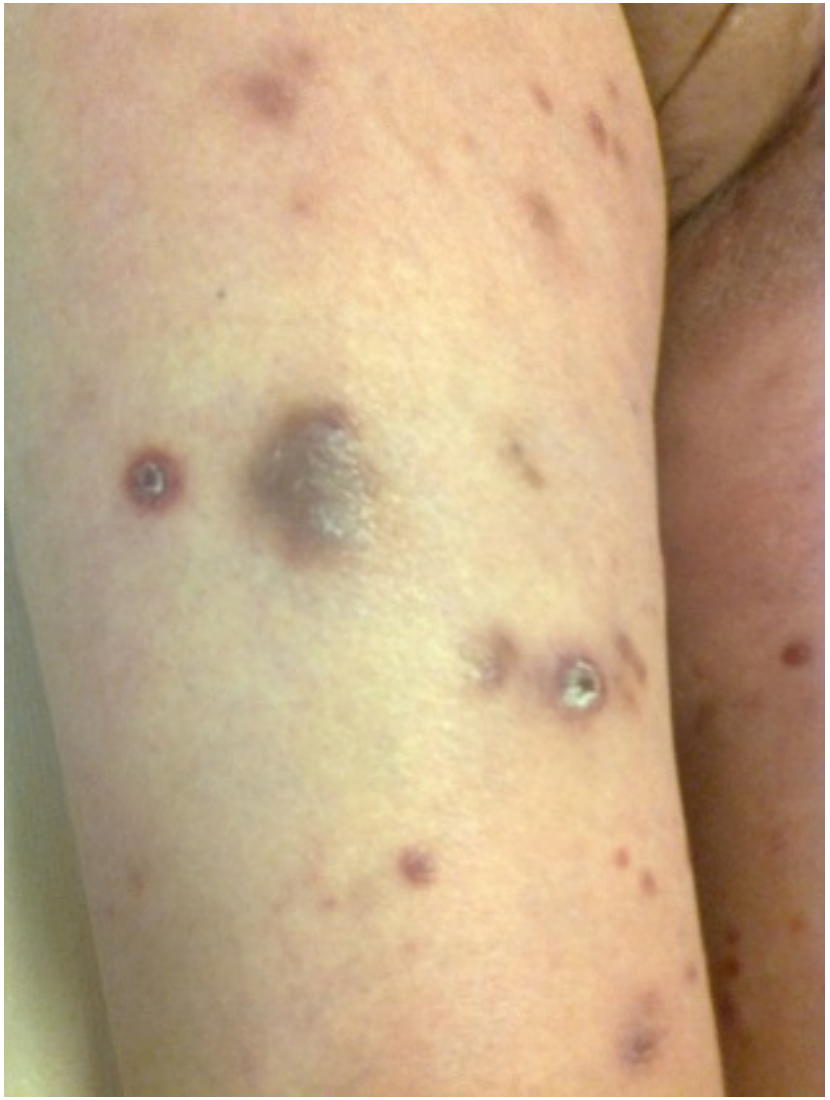


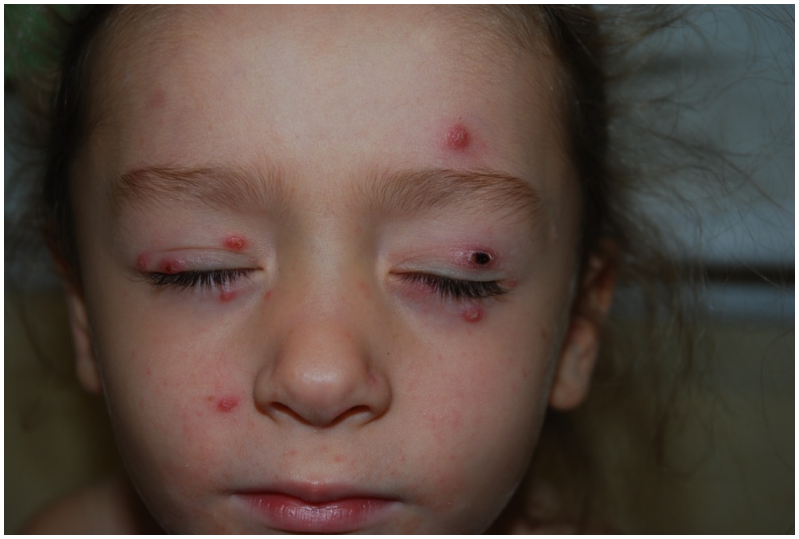


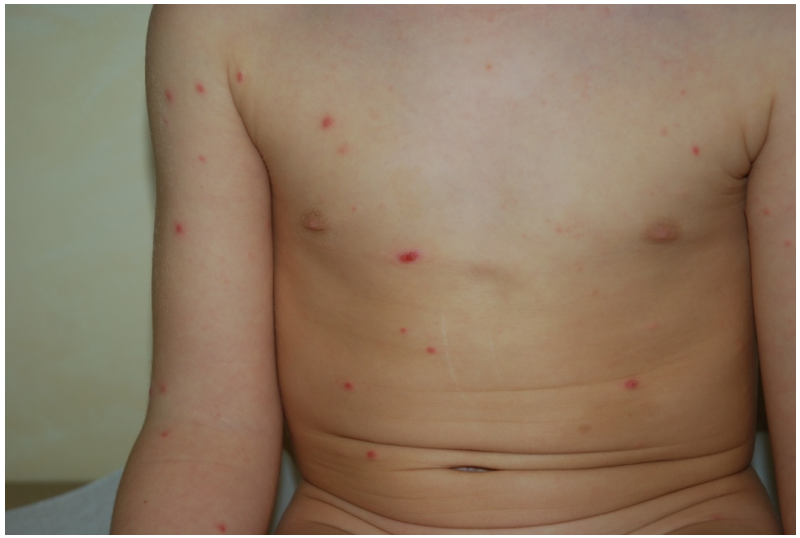


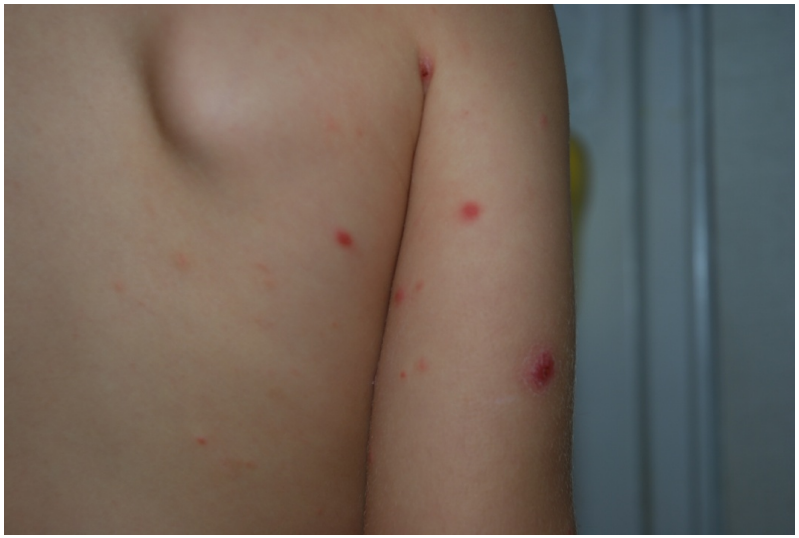


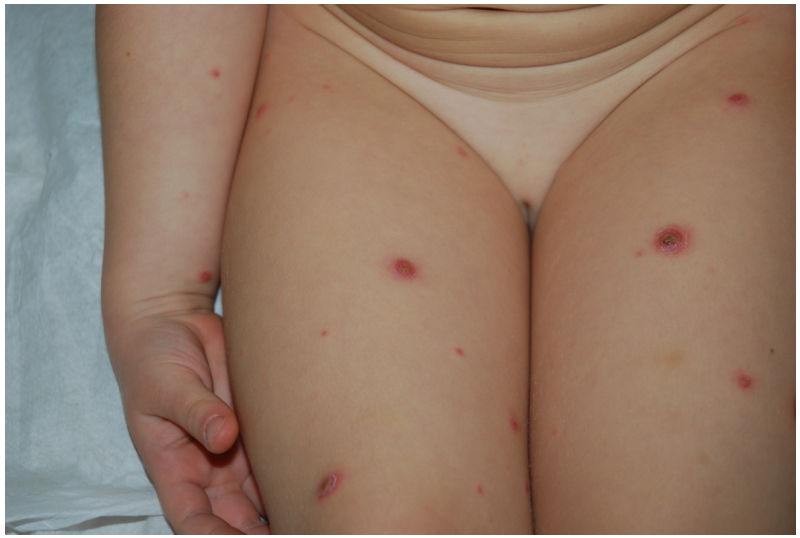












Review article

EORTC, ISCL, and USCLC consensus recommendations for the treatment of primary cutaneous CD30-positive lymphoproliferative disorders: lymphomatoid papulosis and primary cutaneous anaplastic large-cell lymphoma*

Werner Kempf,[1,2] †Katrin Pfaltz,[2] †Maarten H. Vermeer,[3] Antonio Cozzio,[1] Pablo L. Ortiz-Romero,[4] Martine Bagot,[5] Elise Olsen,[6] Youn H. Kim,[7] Reinhard Dummer,[1] Nicola Pimpinelli,[8] Sean Whittaker,[9] Emmilia Hodak,[10] Lorenzo Cerroni,[11] Emilio Berti,[12] Steve Horwitz,[13] H. Miles Prince,[14] Joan Guitart,[15] Teresa Estrach,[16] José A. Sanches,[17] Madeleine Duvic,[18] Annamari Ranki,[19] Brigitte Dreno,[20] Sonja Ostheeren-Michaelis,[2] Robert Knobler,[21] Gary Wood,[22] and Rein Willemze[3]

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Blood **(2011) 118 (15): 4024–4035.**

Table 5. Recommendations for the treatment (standard therapies) of CD30⁺ LPD

PCALCL			LYP	
Solitary or grouped lesion(s)	Multifocal lesions	Extracutaneous spread	Localized/regional or few lesions*	Numerous and/or generalized lesions
SE	Methotrexate	Single or multiagent chemotherapy‡	Observation	Observation
RT	Alternatives: retinoids, interferon†		Phototherapy§	Phototherapy§
			Topical steroids	Methotrexate
				Topical steroids
				Alternatives†: retinoids, interferon

*For larger (defined as > 2 cm in diameter) and persistent (defined as duration of lesion > 12 weeks) lesions, SE or RT may represent alternatives.
†These therapies are of low-level evidence other than expert opinion.
‡In cases of skin and only local node involvement in PCALCL, one could consider addition of local nodal radiation [4]
§PUVA is best documented. Alternatively, treatment with other types of phototherapy (eg, UVB-narrow band) can be tried (evidence level 5).

THERAPY OF AGGRESSIVE non MF/SS CTCLs…

Cortesia Prof. P. Quaglino

	DSS 5-YEAR SURVIVAL %	THERAPY
Primary cutaneous gamma/delta TCL	11%	CHOP/CHOP-like, HSCT
Primary cutaneous aggressive epidermotropic CD8+ T-cell Lymphoma (AECTCL)	31%	
Primary cutaneous peripheral T-cell lymphoma, NOS	15%	

Toro JR, Blood. 2003.
Guitart J, et al. Am J Surg Pathol. 2012.
Geller S, et al. Semin Cut Med Surg, 2018.
Plakhouri KM, et al. JAAD case reports, 2017.

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Webinars Cutaneous Lymphoma
EuroBloodNet Topic on Focus

INTERNATIONAL SOCIETY FOR CUTANEOUS LYMPHOMAS

EORTC European Organisation for Research and Treatment of Cancer

Cutaneous Lymphoma Task Force

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Luca NASSI, Benedetta PUCCINI (Ematologia)

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