



LINFOMI PRIMITIVI  
CUTANEI DI DERIVAZIONE  
T-LINFOCITARIA:  
la multidisciplinarietà ottimizza il risultato

4 OTTOBRE 2021

MILANO Hilton Milan Hotel

## MALATTIA «EARLY STAGE»: IL DERMATOLOGO

Nicola Pimpinelli



UNIVERSITÀ  
DEGLI STUDI  
FIRENZE



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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,<sup>1</sup> Lorenzo Cerroni,<sup>2</sup> Werner Kempf,<sup>3</sup> Emilio Berti,<sup>4</sup> Fabio Facchetti,<sup>5</sup> Steven H. Swerdlow,<sup>6</sup> and Elaine S. Jaffe<sup>7</sup>

<sup>1</sup>Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; <sup>2</sup>Department of Dermatology, Medical University of Graz, Graz, Austria; <sup>3</sup>Kempf und Pfaltz Histologische Diagnostik and Department of Dermatology, University Hospital Zurich, Zurich, Switzerland; <sup>4</sup>Department of Dermatology, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy; <sup>5</sup>Department of Pathology, University of Brescia, Brescia, Italy; <sup>6</sup>Division of Hematopathology, University of Pittsburgh School of Medicine, Pittsburgh, PA; and <sup>7</sup>Hematopathology Section, Laboratory of Pathology, National Cancer Institute, National Institutes of Health, Bethesda, MD

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<sup>+</sup> T-cell lymphoma and Epstein-Barr virus positive (EBV<sup>+</sup>) 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<sup>+</sup> small/medium T-cell lymphoma” was modified to “primary cutaneous CD4<sup>+</sup> 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<sup>+</sup> lymphoproliferative disorders and the classification and terminol-

ogy 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)

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**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, %*
<b>CTCL</b>		
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 <sup>+</sup> 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 $\gamma/\delta$ T-cell lymphoma	<1	11
CD8 <sup>+</sup> AECTCL (provisional)	<1	31
Primary cutaneous CD4 <sup>+</sup> small/medium T-cell lymphoproliferative disorder (provisional)	6	100
Primary cutaneous acral CD8 <sup>+</sup> T-cell lymphoma (provisional)	<1	100
Primary cutaneous peripheral T-cell lymphoma, NOS	2	15
<b>CBCL</b>		
PCMZL	9	99
PCFCL	12	95
PCDLBCL, LT	4	56
EBV <sup>+</sup> mucocutaneous ulcer (provisional)	<1	100
Intravascular large B-cell lymphoma	<1	72

CD8<sup>+</sup> AECTCL, primary cutaneous aggressive epidermotropic CD8<sup>+</sup> 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.





PATCH STAGE



PLAQUE STAGE



ERYTHRODERMA



TUMOR STAGE



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## Defining early mycosis fungoides

Nicola Pimpinelli, MD,<sup>a</sup> Elise A. Olsen, MD,<sup>c</sup> Marco Santucci, MD,<sup>b</sup> Eric Vonderheid, MD,<sup>d</sup>  
Andreas C. Haeffner, MD,<sup>e</sup> Seth Stevens, MD,<sup>f</sup> Guenter Burg, MD,<sup>e</sup> Lorenzo Cerroni, MD,<sup>g</sup>  
Brigitte Dreno, MD,<sup>h</sup> Earl Glusac, MD,<sup>i</sup> Joan Guitart, MD,<sup>j</sup> Peter W. Heald, MD,<sup>i</sup>  
Werner Kempf, MD,<sup>e</sup> Robert Knobler, MD,<sup>k</sup> Stuart Lessin, MD,<sup>l</sup> Christian Sander, MD,<sup>m</sup>  
Bruce S. Smoller, MD,<sup>n</sup> Gladys Telang, MD,<sup>o</sup> Sean Whittaker, MD,<sup>p</sup> Keiji Iwatsuki, MD, PhD,<sup>q</sup>  
Erik Obitz, MD,<sup>r</sup> Masahiro Takigawa, MD,<sup>s</sup> Maria L. Turner, MD,<sup>t</sup> and Gary S. Wood, MD,<sup>u</sup>  
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
<b>Clinical</b>	
<i>Basic</i>	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
<i>Additional</i>	
1) Non-sun exposed location	
2) Size/shape variation	
3) Poikiloderma	
<b>Histopathologic</b>	
<i>Basic</i>	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<sup>†</sup>

**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 <sup>‡</sup> |                                  |

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.

<sup>†</sup>Lymphoid atypia is defined as cells with enlarged hyperchromatic nuclei and irregular or cerebriform nuclear contours.

<sup>‡</sup>T-cell antigen deficiency confined to the epidermis.





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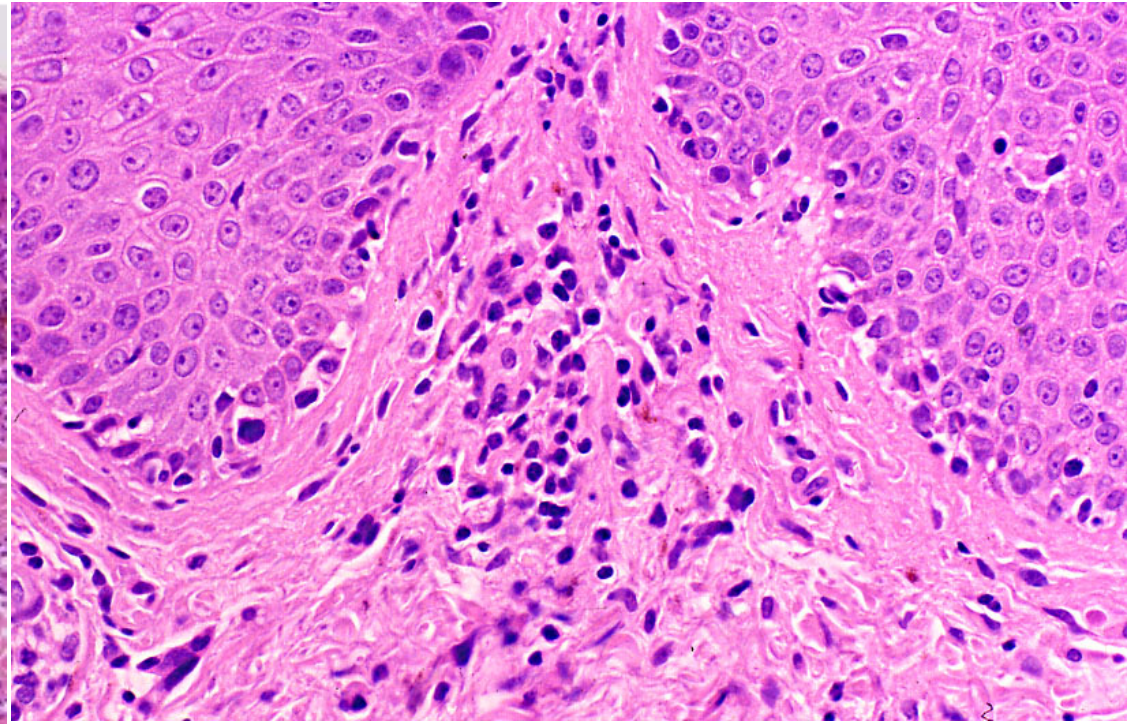
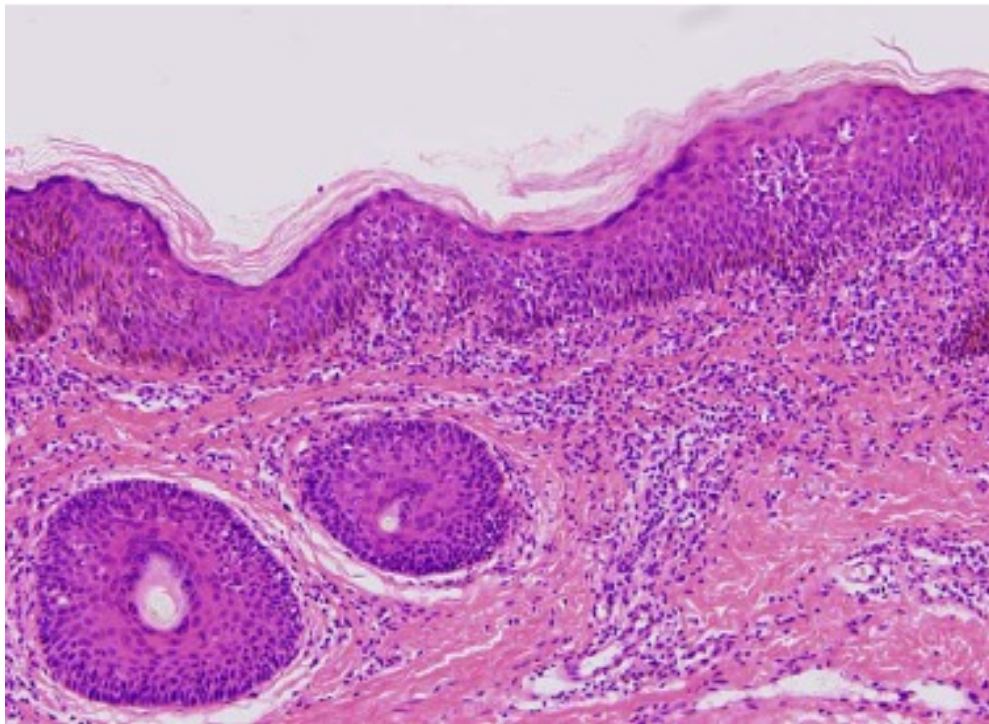
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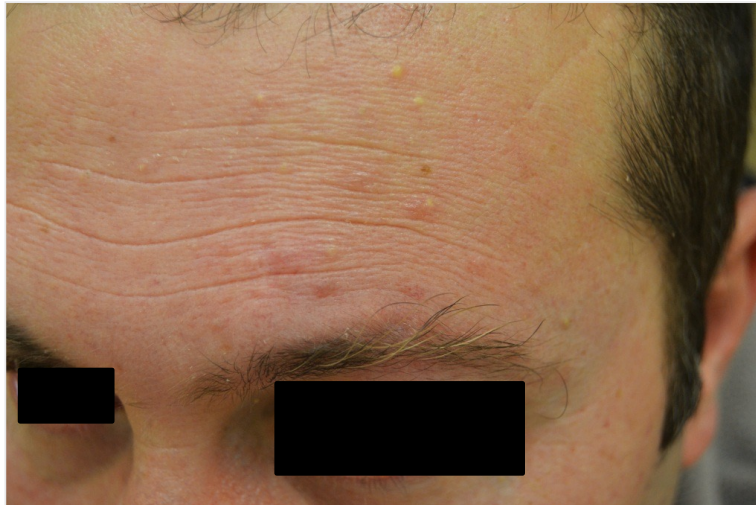




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# Revisions to the staging and classification of mycosis fungoides and Sézary syndrome: a proposal of the International Society for Cutaneous Lymphomas (ISCL) and the cutaneous lymphoma task force of the European Organization of Research and Treatment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

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

<sup>1</sup>Department of Medicine, Divisions of Dermatology and Oncology, Duke University Medical Center, Durham, NC; <sup>2</sup>Department of Dermatology, Johns Hopkins University, Baltimore, MD; <sup>3</sup>Department of Dermatological Sciences, University of Florence, Florence, Italy; <sup>4</sup>Department of Dermatology, Leliden University Medical Center, Leliden, The Netherlands; <sup>5</sup>Department of Dermatology, Stanford University Medical Center, Stanford, CA; <sup>6</sup>Department of Dermatology, University of Vienna, Vienna, Austria; <sup>7</sup>Department of Dermatology, University of California at San Francisco; <sup>8</sup>Department of Dermatology, University of Texas at Houston; <sup>9</sup>Department of Dermatology, University of Barcelona, Barcelona, Spain; <sup>10</sup>Department of Dermatology, University of Wisconsin, Madison; <sup>11</sup>Department of Dermatology, University Hospital Zurich, Zurich, Switzerland; <sup>12</sup>Department of Dermatology and Venereal Diseases, Helsinki University Hospital, Helsinki, Finland; <sup>13</sup>Department of Dermatology, Yale University, New Haven, CT; <sup>14</sup>Department of Dermatology, Mayo Clinic, Rochester, MN; <sup>15</sup>Department of Dermatology, University of Turin, Turin, Italy; <sup>16</sup>Department of Dermatology, Charité, Humboldt University, Berlin, Germany; <sup>17</sup>Department of Immuno-Dermatology, Hospital Avicenne-University of Paris XIII, Paris, France; <sup>18</sup>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 per-

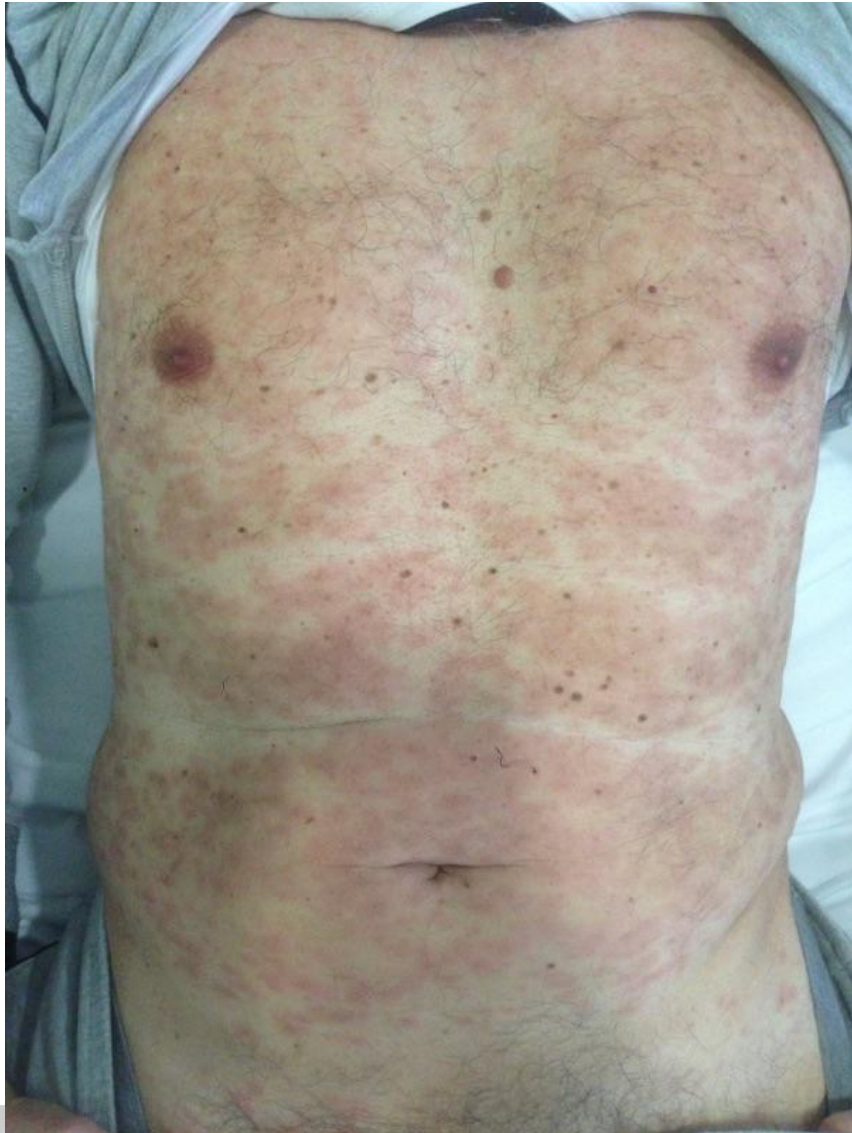
tains specifically to MF and SS. The evidence supporting the revisions is discussed as well as recommendations for evaluation and staging procedures based on these revisions. (Blood. 2007;110:1713-1722)

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

TNMB stages	
<b>Skin</b>	
T <sub>1</sub>	Limited patches,* papules, and/or plaques† covering < 10% of the skin surface. May further stratify into T <sub>1a</sub> (patch only) vs T <sub>1b</sub> (plaque ± patch).
T <sub>2</sub>	Patches, papules or plaques covering ≥ 10% of the skin surface. May further stratify into T <sub>2a</sub> (patch only) vs T <sub>2b</sub> (plaque ± patch).
T <sub>3</sub>	One or more tumors‡ (≥ 1-cm diameter)
T <sub>4</sub>	Confluence of erythema covering ≥ 80% body surface area
<b>Node</b>	
N <sub>0</sub>	No clinically abnormal peripheral lymph nodes§; biopsy not required
N <sub>1</sub>	Clinically abnormal peripheral lymph nodes; histopathology Dutch grade 1 or NCI LN <sub>0,2</sub>
N <sub>1a</sub>	Clone negative#
N <sub>1b</sub>	Clone positive#
N <sub>2</sub>	Clinically abnormal peripheral lymph nodes; histopathology Dutch grade 2 or NCI LN <sub>3</sub>
N <sub>2a</sub>	Clone negative#
N <sub>2b</sub>	Clone positive#
N <sub>3</sub>	Clinically abnormal peripheral lymph nodes; histopathology Dutch grades 3-4 or NCI LN <sub>4</sub> ; clone positive or negative
N <sub>x</sub>	Clinically abnormal peripheral lymph nodes; no histologic confirmation
<b>Visceral</b>	
M <sub>0</sub>	No visceral organ involvement
M <sub>1</sub>	Visceral involvement (must have pathology confirmation¶ and organ involved should be specified)
<b>Blood</b>	
B <sub>0</sub>	Absence of significant blood involvement: ≤ 5% of peripheral blood lymphocytes are atypical (Sézary) cells
B <sub>0a</sub>	Clone negative#
B <sub>0b</sub>	Clone positive#
B <sub>1</sub>	Low blood tumor burden: > 5% of peripheral blood lymphocytes are atypical (Sézary) cells but does not meet the criteria of B <sub>2</sub>
B <sub>1a</sub>	Clone negative#
B <sub>1b</sub>	Clone positive#
B <sub>2</sub>	High blood tumor burden: ≥ 1000/μL Sézary cells   with positive clone#







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Review

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



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

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Table 4a

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


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

---



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

## 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  $\geq 80\%$  of the panelists. Cronbach alpha index  $\geq 0.7$  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





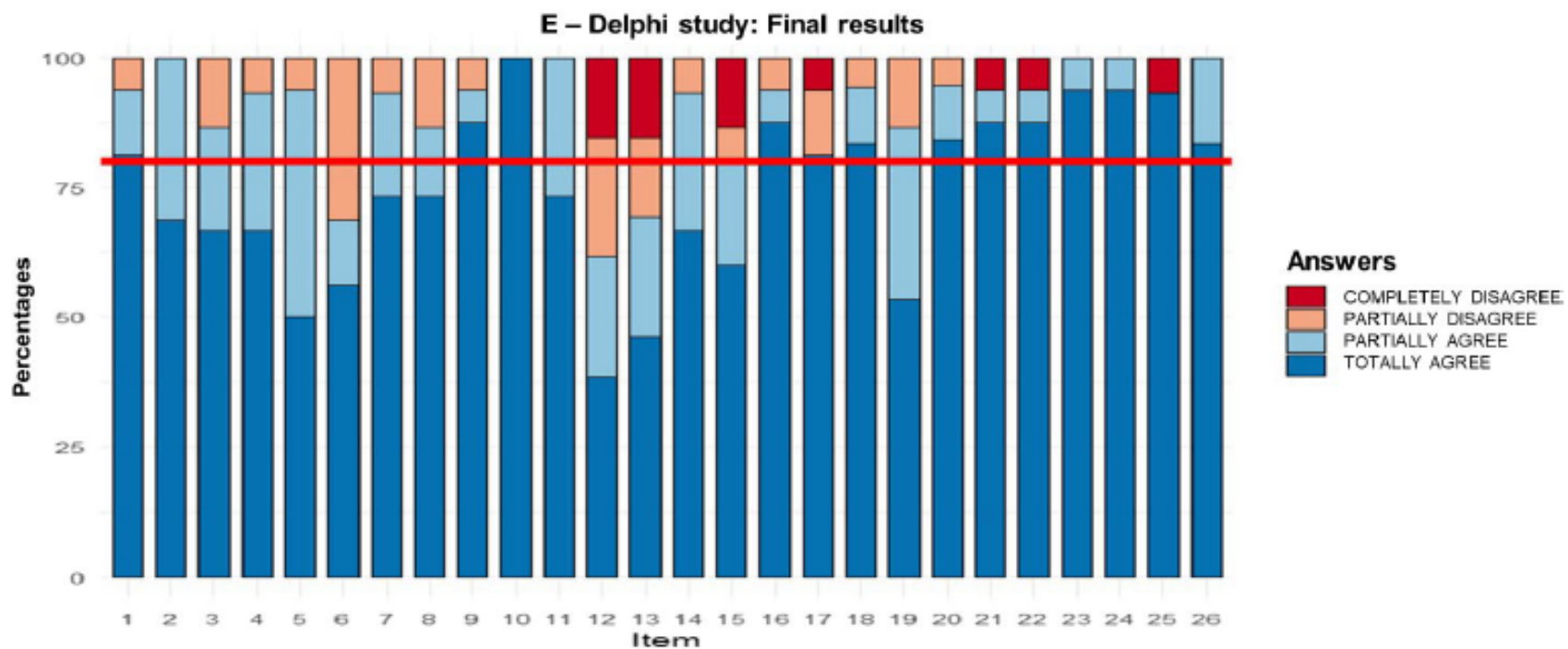


FIGURE 3 Barplot chart showing rates of agreement/disagreement per each questionnaire item. Cutoff value used to define a consensus is depicted as a red horizontal bar set at 80% «TOTALLY AGREE»

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 <sup>a</sup>	Dose increase per treatment <sup>a</sup>
I	130 mJ/cm <sup>2</sup>	15 mJ/cm <sup>2</sup>
II	220 mJ/cm <sup>2</sup>	25 mJ/cm <sup>2</sup>
III	260 mJ/cm <sup>2</sup>	40 mJ/cm <sup>2</sup>
IV	330 mJ/cm <sup>2</sup>	45 mJ/cm <sup>2</sup>
V	350 mJ/cm <sup>2</sup>	60 mJ/cm <sup>2</sup>
VI	400 mJ/cm <sup>2</sup>	65 mJ/cm <sup>2</sup>
Consolidation <sup>b</sup>	Dose and frequency held steady for 1-3 months	
b) PUVA		
Skin phototype	Starting dose	Dose increase per treatment <sup>c</sup>
I	500 mJ/cm <sup>2</sup>	500 mJ/cm <sup>2</sup>
II	1000 mJ/cm <sup>2</sup>	500 mJ/cm <sup>2</sup>
III	1500 mJ/cm <sup>2</sup>	1000 mJ/cm <sup>2</sup>
IV	2000 mJ/cm <sup>2</sup>	1000 mJ/cm <sup>2</sup>
V	2500 mJ/cm <sup>2</sup>	1500 mJ/cm <sup>2</sup>
VI	3000 mJ/cm <sup>2</sup>	1500 mJ/cm <sup>2</sup>
Consolidation <sup>b</sup>	Dose and frequency held steady for 1-3 months	

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

<sup>b</sup>Consolidation phase should not be used routinely. A case by case approach is recommended.

<sup>c</sup>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  $\geq 2$  cm margins

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



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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

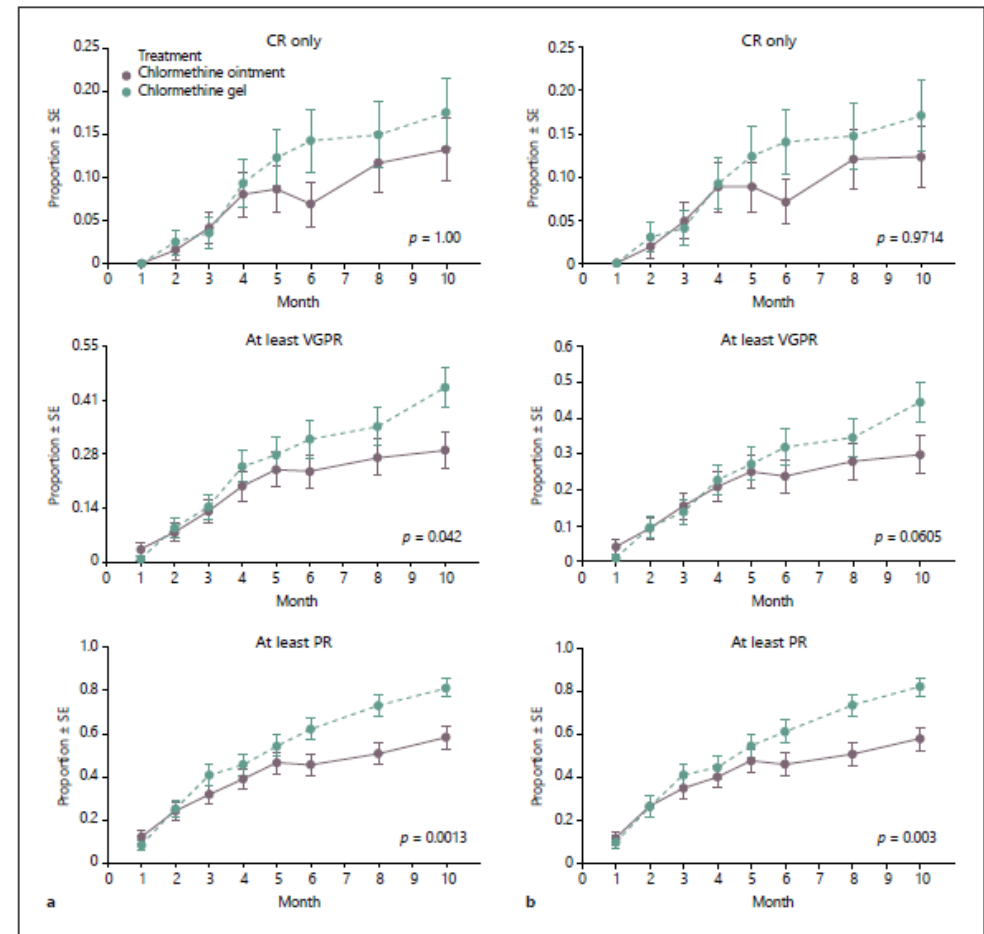
Christiane Querfeld<sup>a</sup> Julia J. Scarisbrick<sup>b</sup> Chalid Assaf<sup>c, d</sup>  
Emmanuella Guenova<sup>e, f</sup> Martine Bagot<sup>g</sup> Pablo Luis Ortiz-Romero<sup>h</sup>  
Pietro Quaglino<sup>i</sup> Erminio Bonizzoni<sup>j</sup> Emilia Hodak<sup>k</sup>



**Table 2.** Clinical response ( $\geq 50\%$  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	<i>p</i> value	CL gel	CL ointment	<i>p</i> value
<b>CAILS, %</b>						
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
<b>mSWAT, %</b>						
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
<b>BSA, %</b>						
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, particularly 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. Väkevā, M.H. Vermeer, S. Whittaker, R. Willemze, R. Knobler

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



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

LINFOMI PRIMITIVI CUTANEI DI DERIVAZIONE T-LINFOCITARIA: LA MULTIDISCIPLINARITÀ OTTIMIZZA IL RISULTATO

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Table 4b

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

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Systemic therapies<sup>a</sup>

Retinoids<sup>b</sup>

Level 2

IFN- $\alpha$

Level 2

TSEB (mainly T2b)

Level 2

Low-dose MTX

Level 4

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<sup>a</sup> The following agents are most commonly combined with PUVA, combinations with other modalities and with each other are also widely used.

<sup>b</sup> 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, %*
<b>CTCL</b>		
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 <sup>+</sup> 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 $\gamma/\delta$ T-cell lymphoma	<1	11
CD8 <sup>+</sup> AECTCL (provisional)	<1	31
Primary cutaneous CD4 <sup>+</sup> small/medium T-cell lymphoproliferative disorder (provisional)	6	100
Primary cutaneous acral CD8 <sup>+</sup> T-cell lymphoma (provisional)	<1	100
Primary cutaneous peripheral T-cell lymphoma, NOS	2	15
<b>CBCL</b>		
PCMZL	9	99
PCFCL	12	95
PCDLBCL, LT	4	56
EBV <sup>+</sup> mucocutaneous ulcer (provisional)	<1	100
Intravascular large B-cell lymphoma	<1	72

CD8<sup>+</sup> AECTCL, primary cutaneous aggressive epidermotropic CD8<sup>+</sup> 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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## 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\*

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<sup>1</sup>Department of Dermatology, University Hospital Zürich, Zürich, Switzerland; <sup>2</sup>Kempf and Pfaltz, Histological Diagnostics, Research Unit, Zürich, Switzerland; <sup>3</sup>Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands; <sup>4</sup>Department of Dermatology, Hospital 12 de Octubre, Madrid, Spain; <sup>5</sup>Department of Dermatology, Hôpital Saint Louis, Paris, France; <sup>6</sup>Department of Medicine, Divisions of Dermatology and Oncology, Duke University Medical Center, Durham, NC; <sup>7</sup>Department of Dermatology, Stanford Comprehensive Cancer Center, Stanford, CA; <sup>8</sup>Department of Dermatological Sciences, University of Florence, Florence, Italy; <sup>9</sup>Skin Tumour Unit, St Thomas' Hospital, London, United Kingdom; <sup>10</sup>Department of Dermatology, Tel Aviv University, Tel Aviv, Israel; <sup>11</sup>Department of Dermatology, Medical University, Graz, Austria; <sup>12</sup>Department of Dermatology, University of Milano-Bicocca, Istituti di Ricovero e Cura a Carattere Scientifico Ospedale Maggiore di Milano, Milano, Italy; <sup>13</sup>Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY; <sup>14</sup>Peter MacCallum Cancer Centre, East Melbourne, Australia; <sup>15</sup>Department of Dermatology, Northwestern University, Chicago, IL; <sup>16</sup>Department of Dermatology, Hospital Clínico, University of Barcelona, Barcelona, Spain; <sup>17</sup>Department of Dermatology, University of São Paulo, São Paulo, Brazil; <sup>18</sup>Department of Dermatology, The University of Texas M. D. Anderson Cancer Center, Houston, TX; <sup>19</sup>Department of Dermatology and Venereal Diseases, Helsinki University Hospital, Helsinki, Finland; <sup>20</sup>Department of Dermatology, University Hospital Nantes, Nantes, France; <sup>21</sup>Department of Dermatology, University of Vienna Medical School, University of Vienna, Vienna, Austria; and <sup>22</sup>Department of Dermatology, University of Wisconsin, Madison, WI

*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§ Topical steroids	Phototherapy§ 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<sup>4</sup>

§PUVA is best documented. Alternatively, treatment with other types of phototherapy (eg, UVEB-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%	

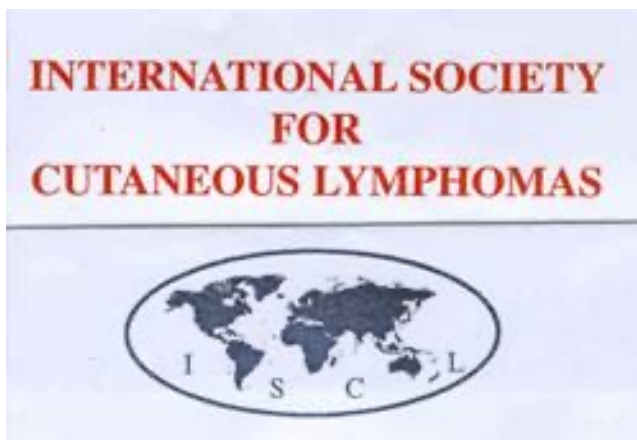
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Cutaneous Lymphoma Task Force

**Gruppo Multidisciplinare LINFOMI CUTANEI Firenze**

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Luca NASSI, Benedetta PUCCINI (Ematologia)

Gabriele SIMONTACCHI, Laura P. Ciccone (Radioterapia)

