Leids Universitair
Medisch Centrum

Multidisciplinaire Werkgroep Cutane Lymfomen

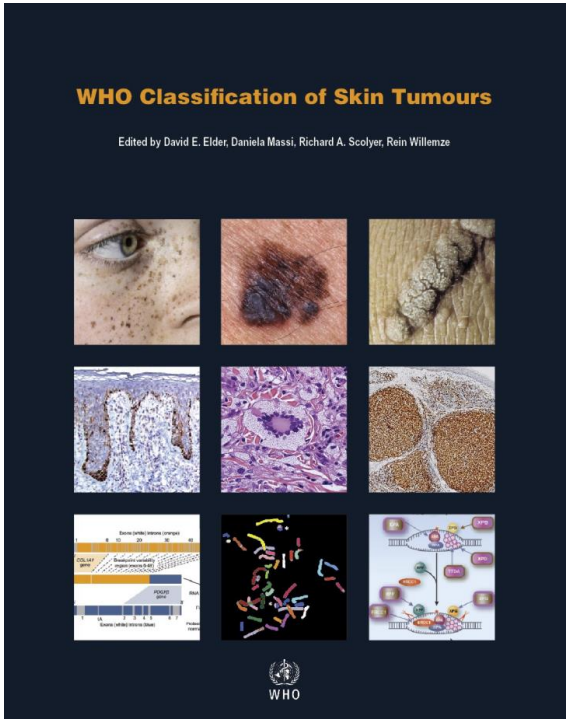
Groep A: onderbouwing kliniek en Pathologie

Patty Jansen

Primaire Diagnostiek Cutane Lymfomen

- Onderzoek nodig om de diagnose te stellen omvat:
  - Klinisch onderzoek door dermatoloog met fotografisch vastleggen van efflorescenties
  - histologisch onderzoek door patholoog
  - immuunfenotypering/immuunhistochemie
  - evt. Moleculair/cytogenetisch onderzoek
- Diagnose in principe nooit zonder clinicopathologische correlatie
- Nieuwe patienten: inbrengen in Landelijke Werkgroep Cutane Lymfomen
- Volgens criteria van WHO-EORTC classificatie/Blue Book

2018 revision of the WHO-EORTC classification



1996 ESDR classification

2001 WHO classification (3rd edition)

2005 WHO-EORTC classification

2008 WHO classification (4th edition)

2017 WHO classification (revised 4th ed.)

2018 Revised WHO-EORTC classification

WHO-EORTC classificatie 2005

Cutaneous T-cell and NK-cell lymphomas

Mycosis fungoides

Mycosis fungoides variants and subtypes
- Folliculotropic MF
- Pagetoid reticulosis
- Granulomatous slack skin

Sézary syndrome

Adult T-cell leukemia/lymphoma

Primary cutaneous CD30-positive 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-positive T-cell lymphoma (provisional)
- Cutaneous γ/δ T-cell lymphoma (provisional)
- Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoma (provisional)

Cutaneous B-cell lymphomas

Primary cutaneous marginal zone B-cell lymphoma

Primary cutaneous follicle center lymphoma

Primary cutaneous diffuse large B-cell lymphoma, leg type

Primary cutaneous diffuse large B-cell lymphoma, other
- intravascular large B-cell lymphoma

Precursor hematologic neoplasm

CD4+/CD56+ hematodermic neoplasm (formerly blastic NK cell lymphoma)

2017 revisie van de WHO-EORTC classificatie

Cutaneous T-cell lymphomas

- Mycosis fungoides & variants of MF
  - Folliculotropic MF
  - Granulomatous slack skin
  - Pagetoid reticulosis
- Sezary syndrome
- Spectrum cutaneous CD30+ LPD
- Subcutaneous panniculitis-like T-cell lymphoma
- Extranodal NK/T-cell lymphoma
- Hydroa vacciniforme-like LPD (CAEBVI)
- Primary cutaneous peripheral T-cell lymphoma, NOS + rare subtypes
  - Primary cutaneous γ/δ T-cell lymphoma
  - Aggressive cytotoxic epidermotropic CD8+ CTCL
  - Primary cutaneous CD4+ small/medium T-cell LPD
  - Primary cutaneous acral CD8+ T-cell lymphoma

Cutaneous B-cell lymphomas

- Extranodal marginal zone lymphoma/ primary cutaneous MZL.
- Primary cutaneous follicle center lymphoma
- Primary cutaneous DLBCL, leg type
- EBV-positive mucocutaneous ulcer
- Intravascular large B-cell lymphoma

2017 revisie van de WHO-EORTC classificatie

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  - Aggressive cytotoxic epidermotropic CD8+ CTCL
  - Primary cutaneous CD4+ small/medium T-cell LPD
  - Primary cutaneous acral CD8+ T-cell lymphoma

New variants

Cutaneous B-cell lymphomas

- Extranodal marginal zone lymphoma/ primary cutaneous MZL.
- Primary cutaneous follicle center lymphoma
- Primary cutaneous DLBCL, leg type
- EBV-positive mucocutaneous ulcer
- Intravascular large B-cell lymphoma

LyP: histologie

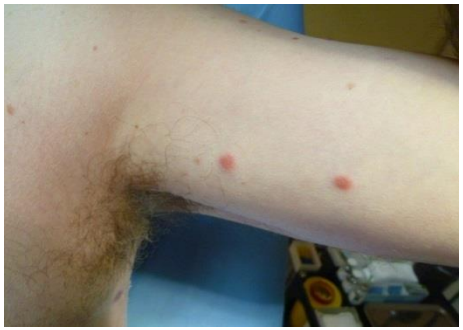
Subtype	Histologic features	
LyP, type A	Scattered CD30+ cells	Willemze, 1982
Lyp, type B	Mimicks MF	Willemze, 1982
LyP, type C	Mimicks ALCL (diffuse CD30)	Willemze, 1994
LyP, type D	Mimicks CD8+ CTCL	Cerroni, 2010
LyP, type E	Angioinvasive	Kempf, 2013
LyP, type F	Follicular	Kempf, 2013
LyP with 6p25.3 rearrangement		Karai, 2013

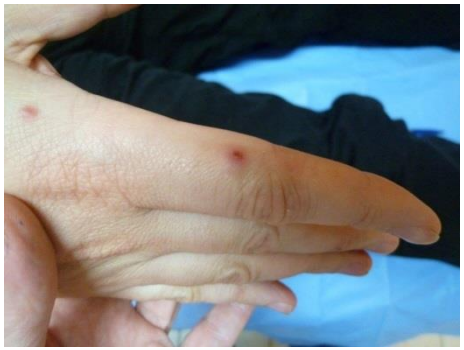
Subtypes LyP

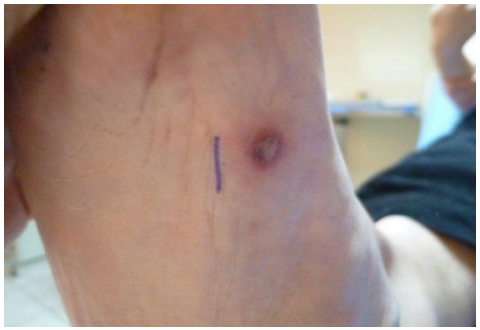
Table 4.3 Histological subtypes and differential diagnosis of lymphomatoid papulosis (LyP) {2545}

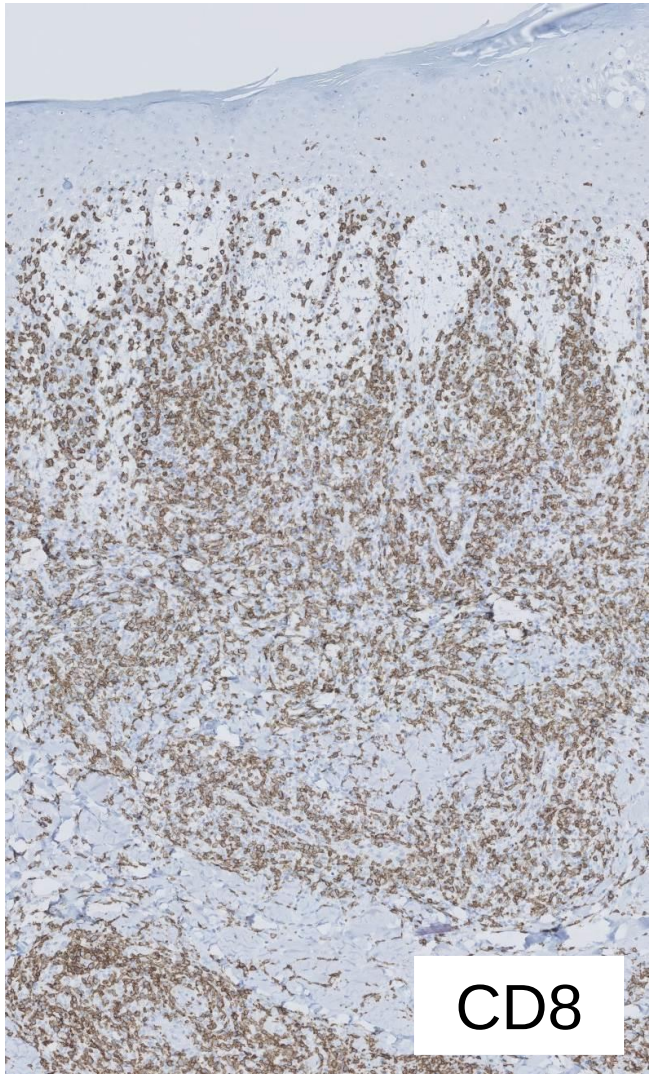
Histological subtype (relative frequency)	Predominant phenotype	Main differential diagnoses
LyP type A (> 80%)	CD4+, CD8−	Cutaneous anaplastic large cell lymphoma, tumour-stage mycosis fungoides, and Hodgkin lymphoma
LyP type B (< 5%)	CD4+, CD8−	Early-stage (plaque-stage) mycosis fungoides
LyP type C (~10%)	CD4+, CD8−	Cutaneous anaplastic large cell lymphoma and transformed (CD30+) mycosis fungoides
LyP type D (< 5%)	CD4−, CD8+	Primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma
LyP type E (< 5%)	CD4−, CD8+	Extranodal NK/T-cell lymphoma
LyP with *DUSP22-IRF4* rearrangement (< 5%)	CD4−, CD8+ or CD4−, CD8−	Transformed mycosis fungoides

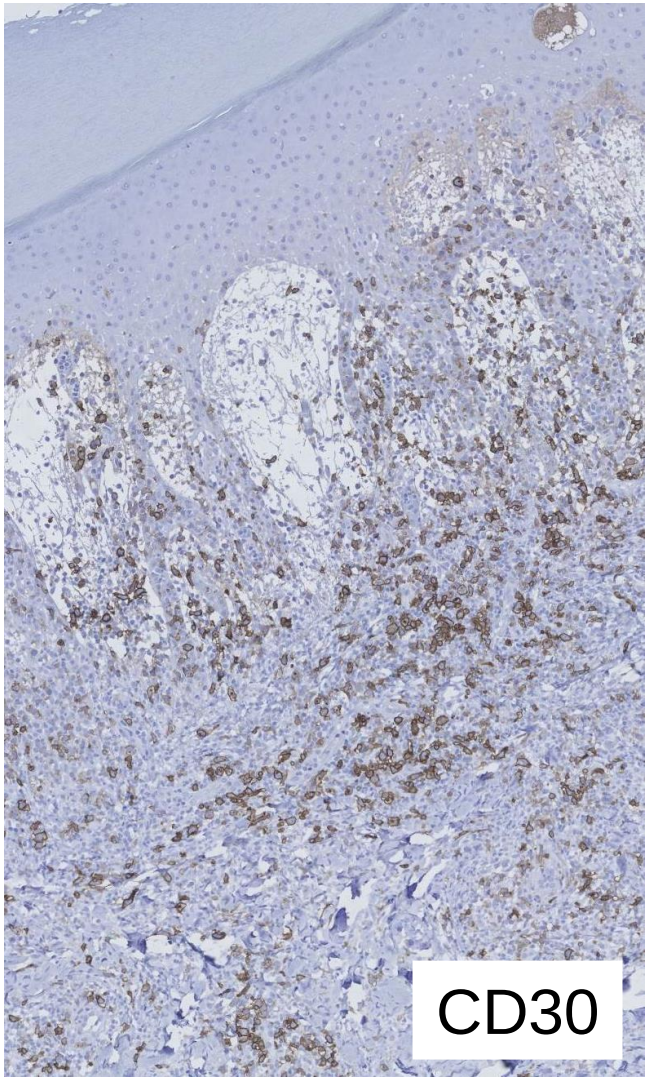
LyP type D (H14-1348)











LyP type E en F

E

Angioinvasive Lymphomatoid Papulosis
A New Variant Simulating Aggressive Lymphomas

Werner Kempf, MD,† Dmitry V. Kazakov, MD, PhD,‡ Leo Schärer, MD,§ Arno Rütten, MD,§ Thomas Mentzel, MD,§ Bruno E. Paredes, MD,§ Gabriele Palmedo, PhD,§ Renato G. Panizzon, MD,‖ and Heinz Kutzner, MD§*

(*Am J Surg Pathol* 2013;37:1–13)

DERMATOPATHOLOGY

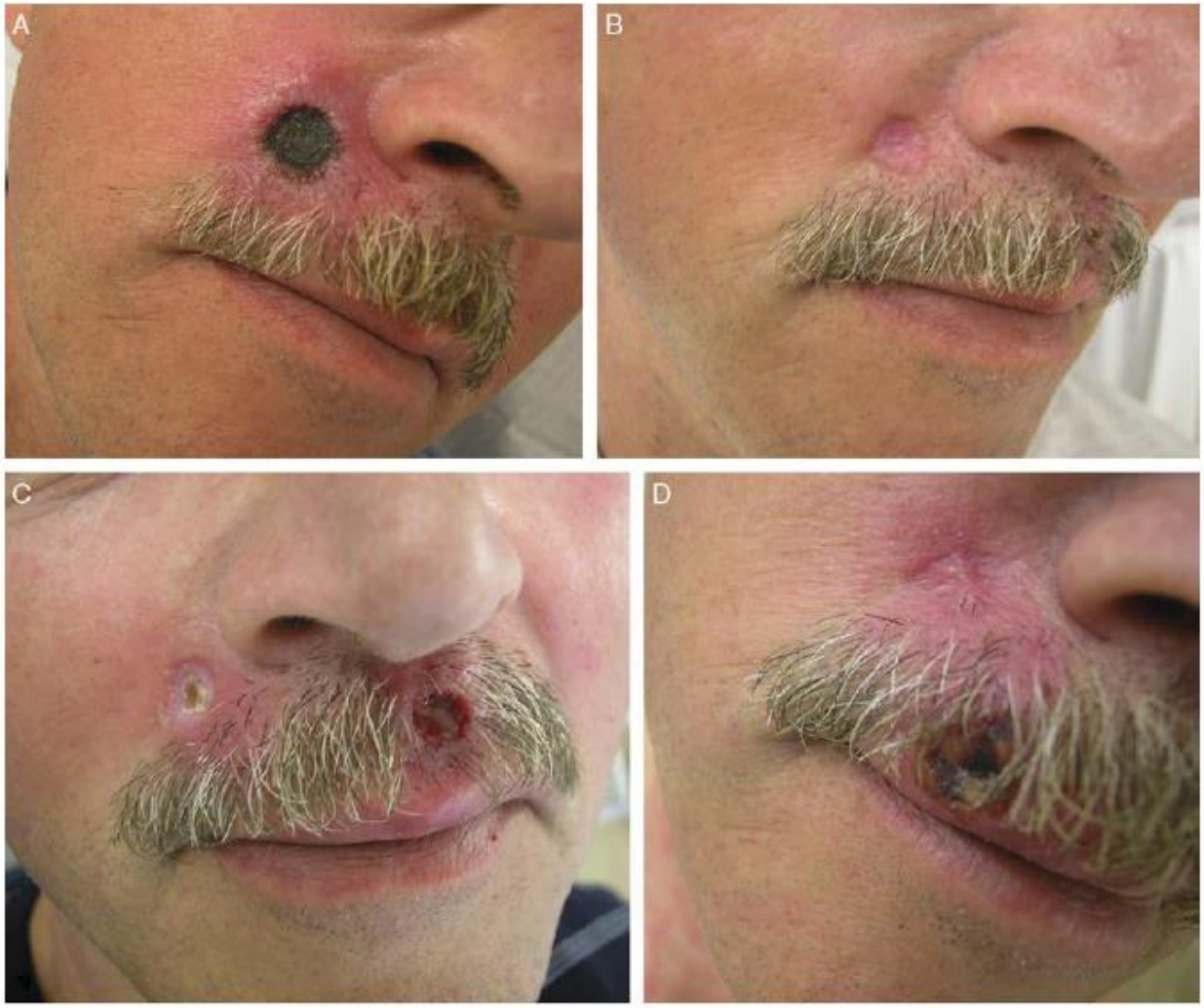
F

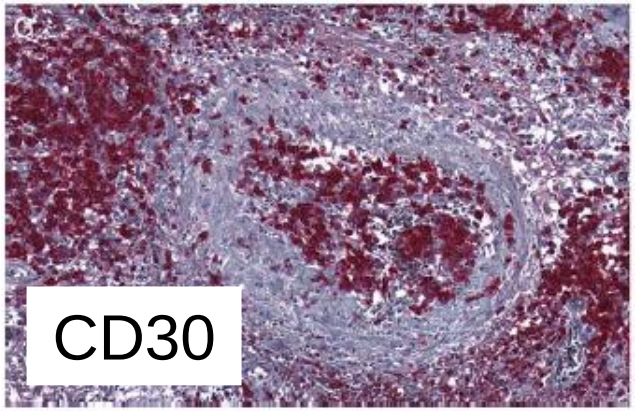
Follicular lymphomatoid papulosis revisited: A study of 11 cases, with new histopathological findings

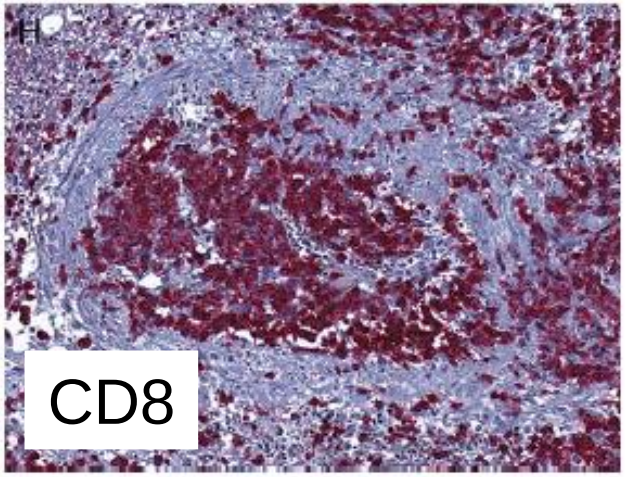
Werner Kempf, MD,[a] Dmitry V. Kazakov, MD, PhD,[b] Hans-Peter Baumgartner, MD,[c] and Heinz Kutzner, MD[d]
Zürich and Zug, Switzerland; Pilsen and Prague, Czech Republic; and Friedrichshafen, Germany

(J Am Acad Dermatol 2013;68:809-16.)

Angioinvasieve LyP (type E)

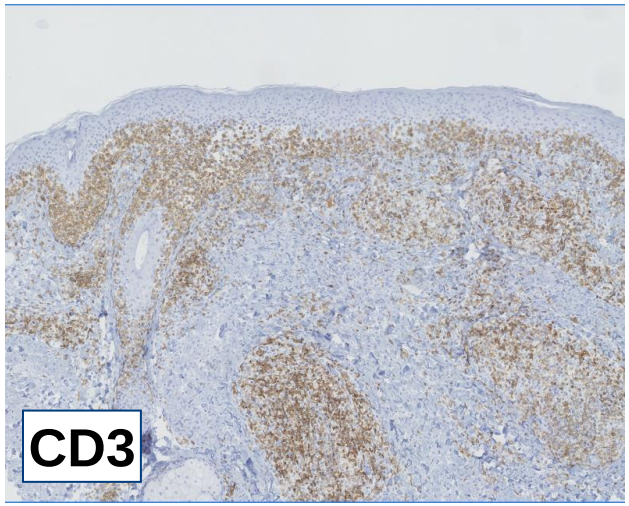


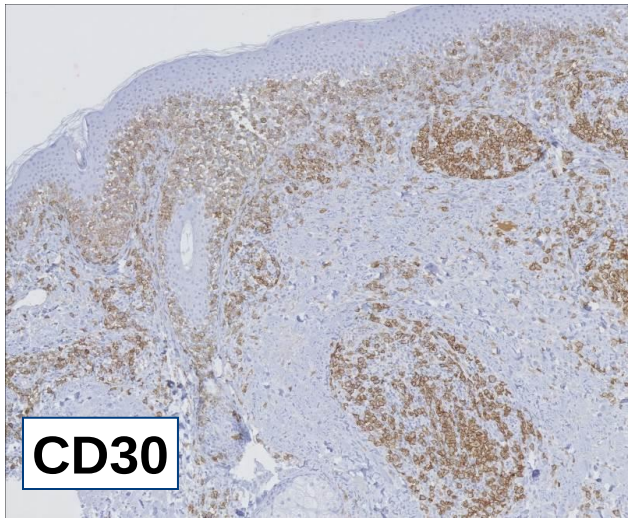


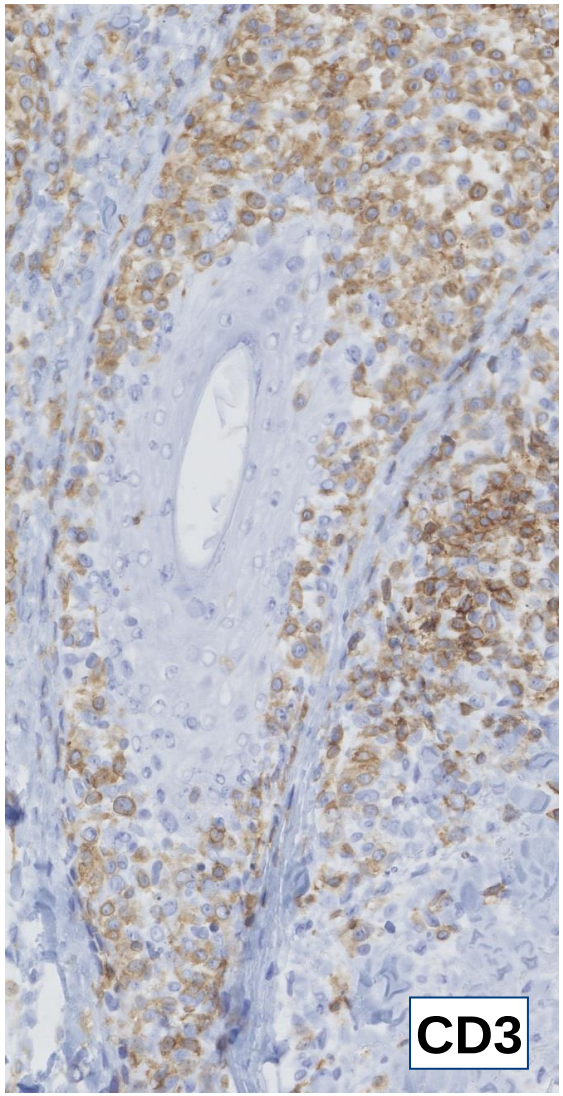


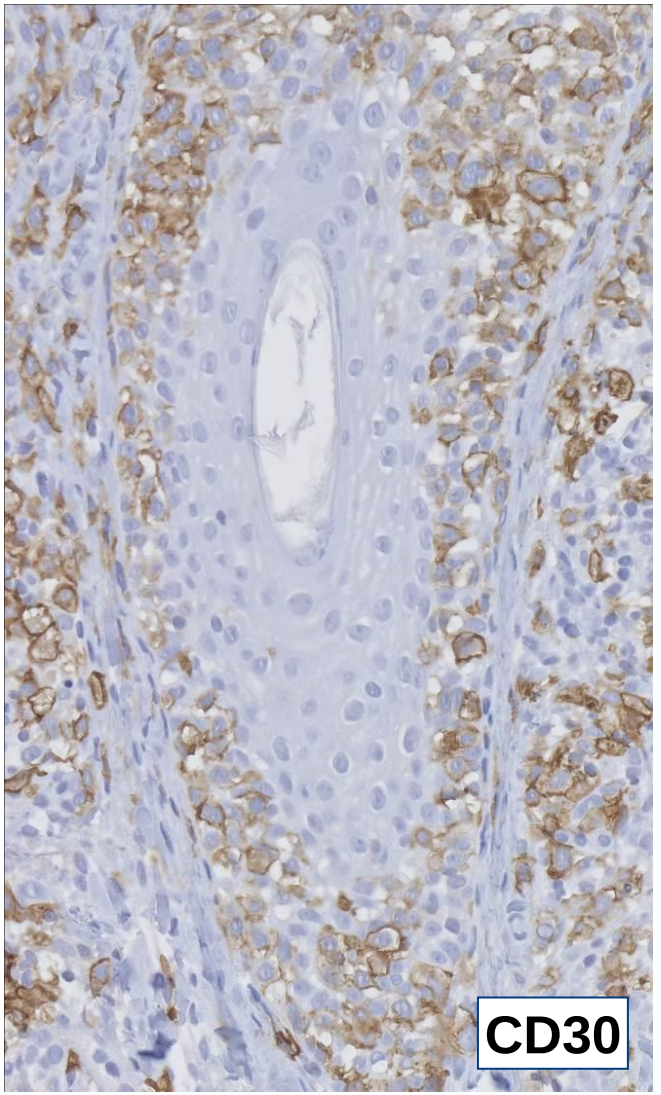
Kempf W et al; Am J Surg Pathol 2012

LyP type D + F (R11-80706)









LyP with DUSP22-IRF4 rearrangement

ORIGINAL ARTICLE

Chromosomal Rearrangements of 6p25.3 Define a New Subtype of Lymphomatoid Papulosis

Laszlo J. Karai, MD,† Marshall E. Kadin, MD,‡ Eric D. Hsi, MD,§ Jason C. Sluzevich, MD,‖ Rhett P. Ketterling, MD,¶ Ryan A. Knudson, BS,¶ and Andrew L. Feldman, MD¶*

(*Am J Surg Pathol* 2013;37:1173–1181)

LyP with 6p25.3 rearrangement

- Chromosomal rearrangement of DUSP22-IRF4 locus on 6p25.3
- Older adults
- Localized skin lesions.
- Small cerebriform cells in the epidermis (weak CD30) and blast cells in dermis (strong CD30) simulating transformed MF.
- Variably CD4 and/or CD8 positive or CD4-/CD8-

LyP with DUSP22/IRF4 rearrangement

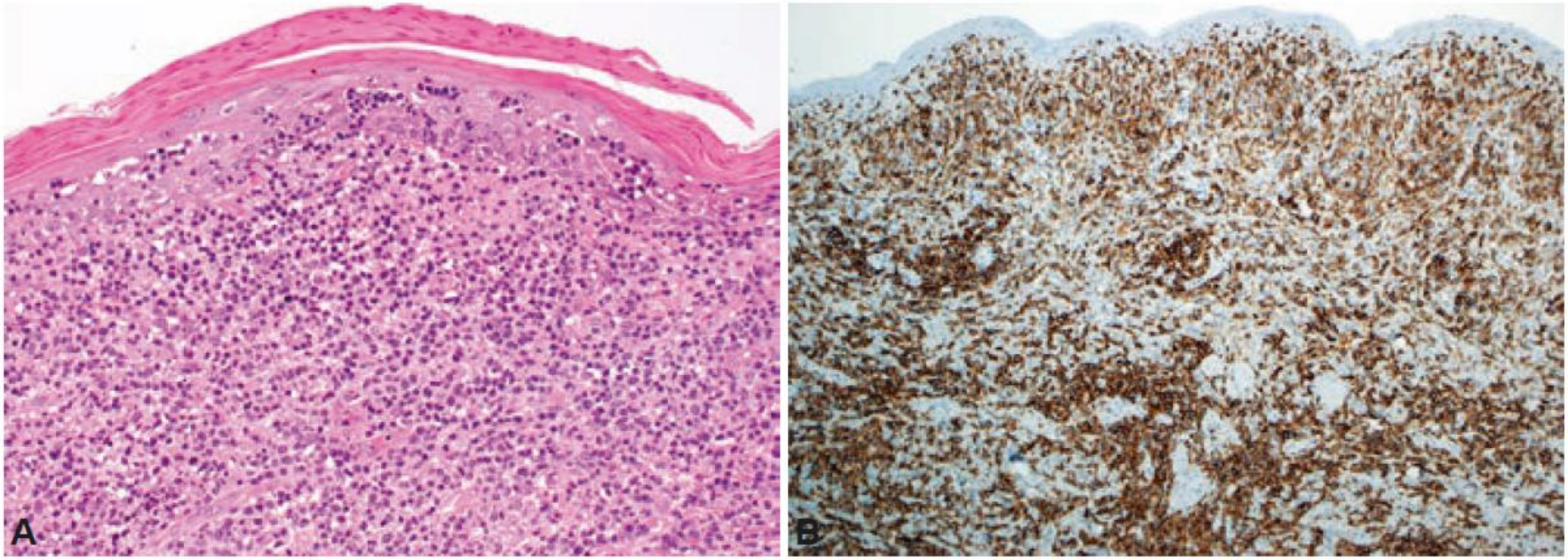
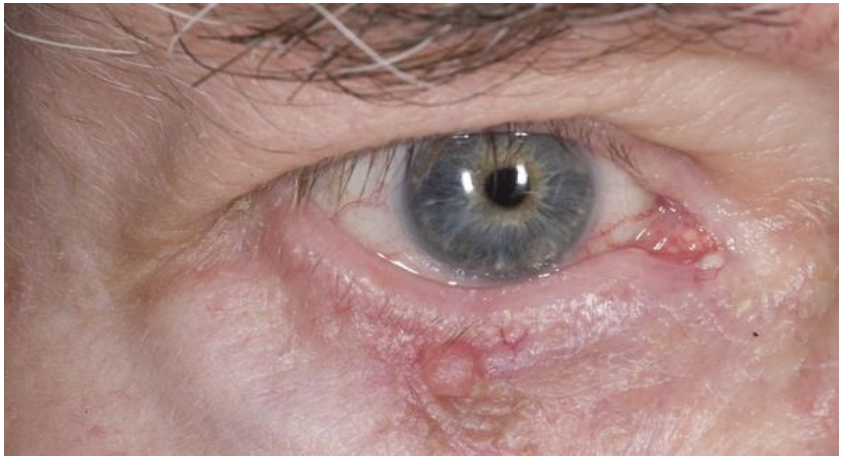
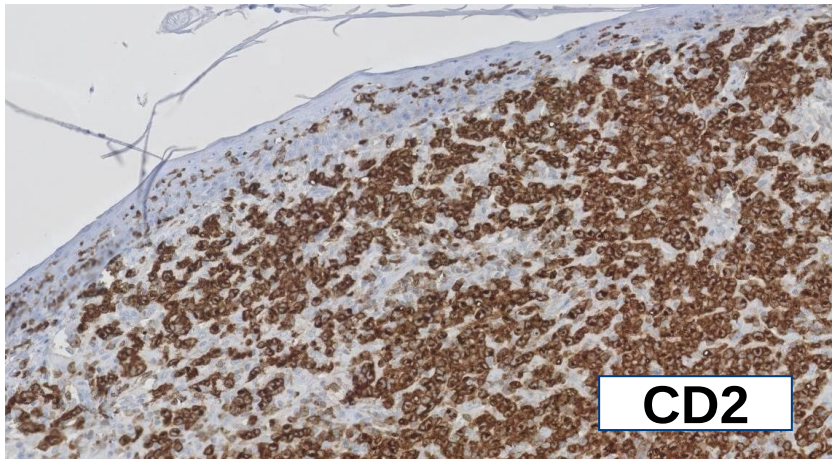
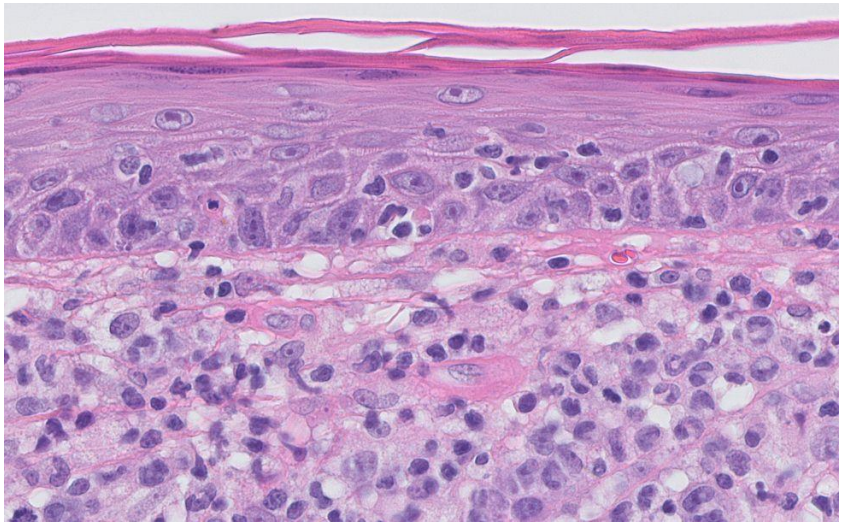


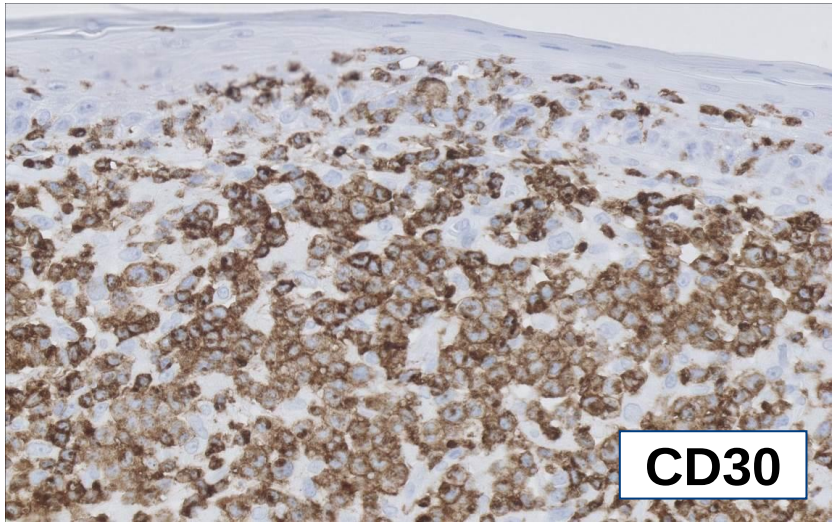
Fig. 4.28 Lymphomatoid papulosis with *DUSP22-IRF4* rearrangement. **A** Intraepidermal mycosis fungoides–like small cells and dermal large blastic cells. **B** CD30 staining is diffusely positive and is stronger in dermal cells with blastic cytology.

C-ALCL (R13-83444)









LyP 2018

- Increasing number of histologic subtypes.
- Different types in one patient or in one lesion (mixed types)

- **Relevance for dermatologist: none**
  - All subtypes have in common a combination of waxing and waning skin lesions and histology of CTCL.
  - No therapeutic or prognostic significance (clinically not useful)

- **Relevance for pathologist**
  - Illustrate the heterogeneous histology of LyP.
  - Important information for differential diagnosis

Hydroa-vacciniforme-like LPD

Cutaneous manifestations of chronic active EBV infection

- Hydroa-vacciniforme (HV)-like LPD (cytotoxic T-cell)
- Severe mosquito bite hypersensitivity (NK cell derivation)

Both condition may either run an indolent clinical course or progress to frank lymphoma

Primary cutaneous PTCL-NOS, rare subtypes

WHO-EORTC 2018 Revision

- Primary cutanous gamma/delta-T-cell lymphoma
- Aggressive epidermotropic cytotoxic CD8+ CTCL
- Primary cutaneous CD4+ small/medium T-cell LPD (provisional entity).
- Primary cutaneous acral CD8+ T-cell lymphoma or T-cell LPD (provisional entity).

PCSM-TCLPD

Definition:

- Clonal proliferation of small/medium CD4+ pleomorphic T-cells.
- Presentation with a solitary lesion.
- No signs or history of MF or SS.

WHO- EORTC and WHO 2008:

- Primary cutaneous CD4+ small/medium pleomorphic T-cell lymphoma

WHO 2017 and WHO-EORTC 2018: genuine malignancy ?

- Primary cutaneous CD4+ small/medium pleomorphic T-cell lymphoproliferative disorder

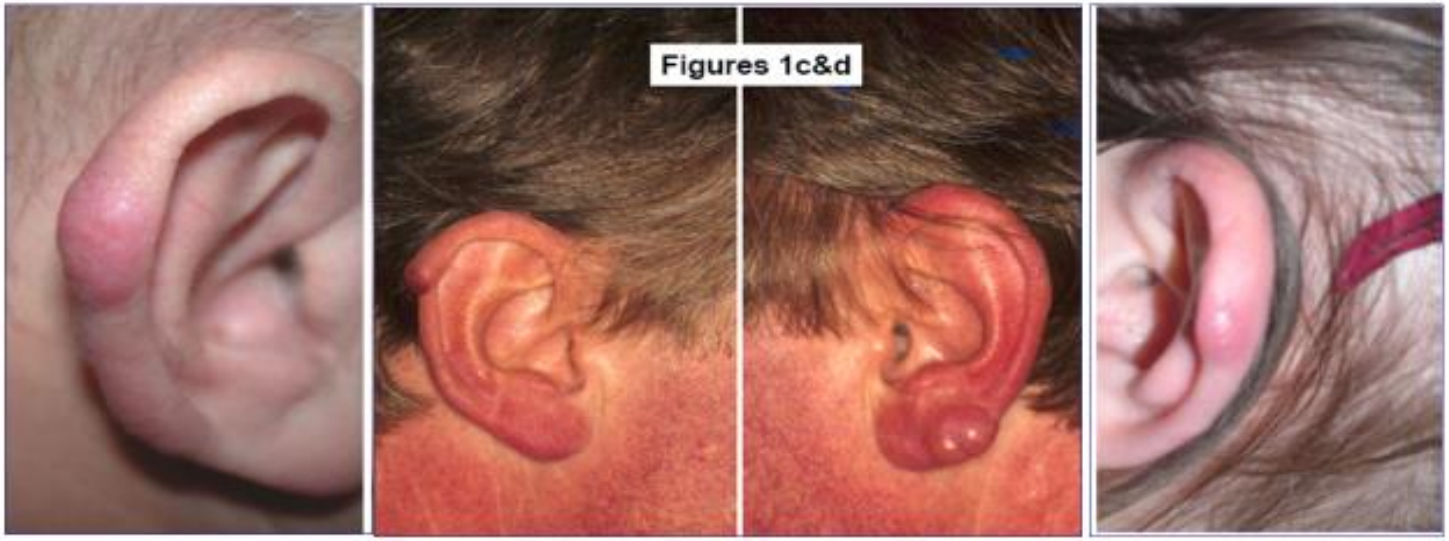
Primary Cutaneous acral CD8+ T-cell lymphoma

Indolent CD8-positive Lymphoid Proliferation of the Ear

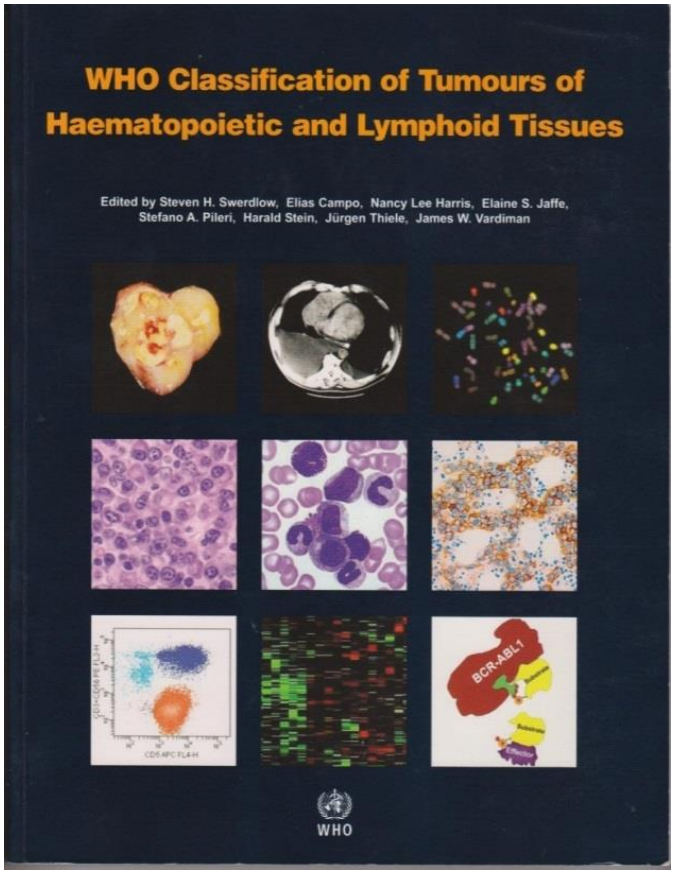
A Distinct Primary Cutaneous T-cell Lymphoma?

Tony Petrella, MD, Eve Maubec, MD,† Pascale Cornillet-Lefebvre, MD,‡ Rein Willemze, MD,§ Michel Pluot, MD,‖ Anne Durlach, MD, PhD,¶ Eduardo Marinho, MD,# Jean-Luc Benhamou, MD,** Patty Jansen, MD, PhD,†† Alistair Robson, MRCPath, DipRCPath,‡‡ and Florent Grange, MD, PhD§§*

Petrella T. et al; Am J Surg Pathol 2007;31:1887-1892



Revised WHO-EORTC classification CBCL



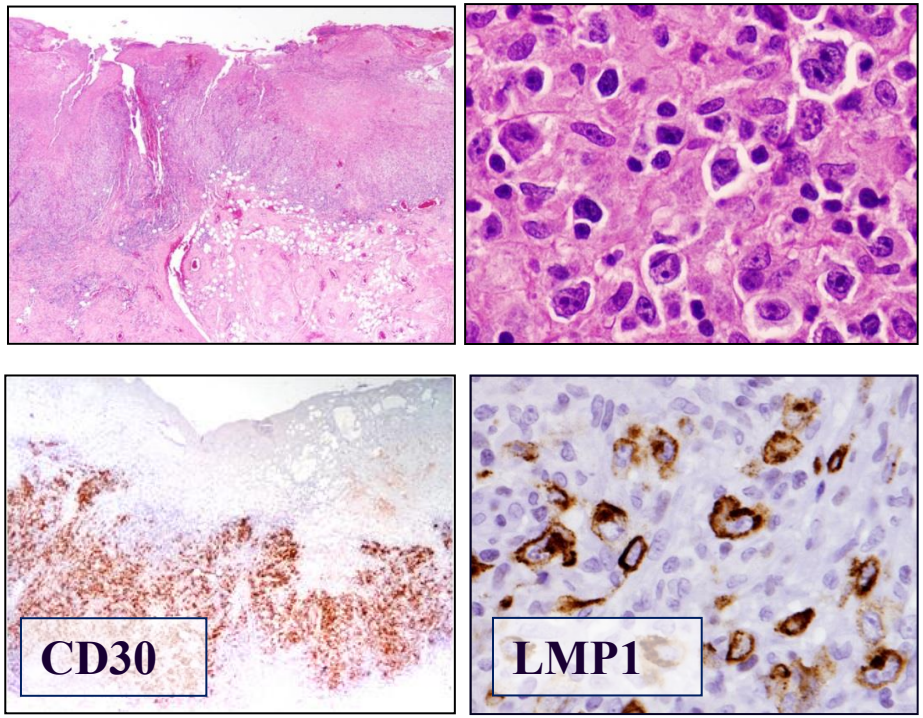
Cutaneous B-cell lymphomas

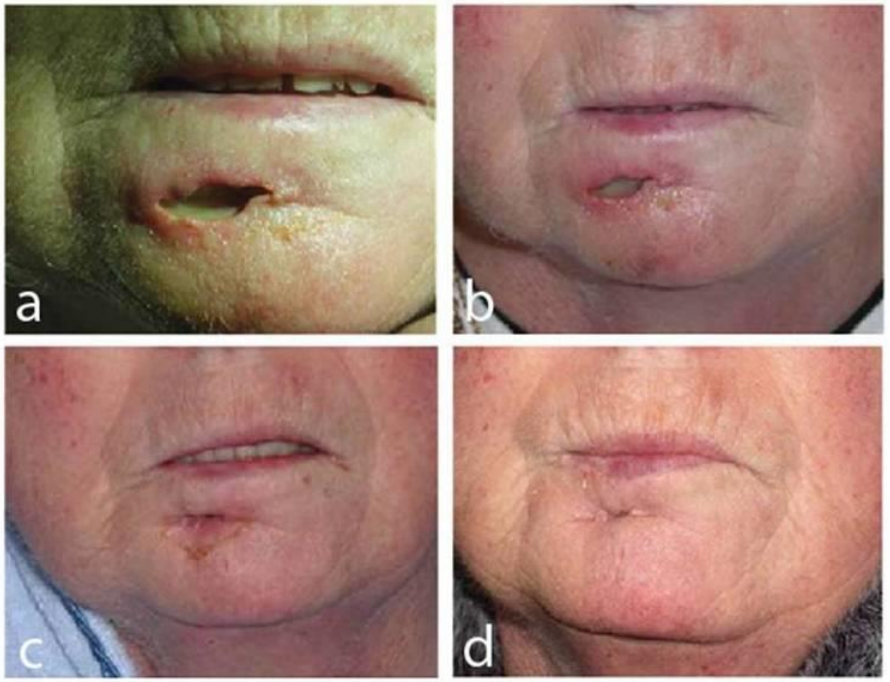
- Extranodal marginal zone lymphoma (PCMZL)
- Primary cutaneous follicle center lymphoma
- Primary cutaneous diffuse large B-cell lymphoma, leg type
- Intravascular large B-cell lymphoma
- EBV-positive mucocutaneous ulcer

EBV-positive mucocutaneous ulcer

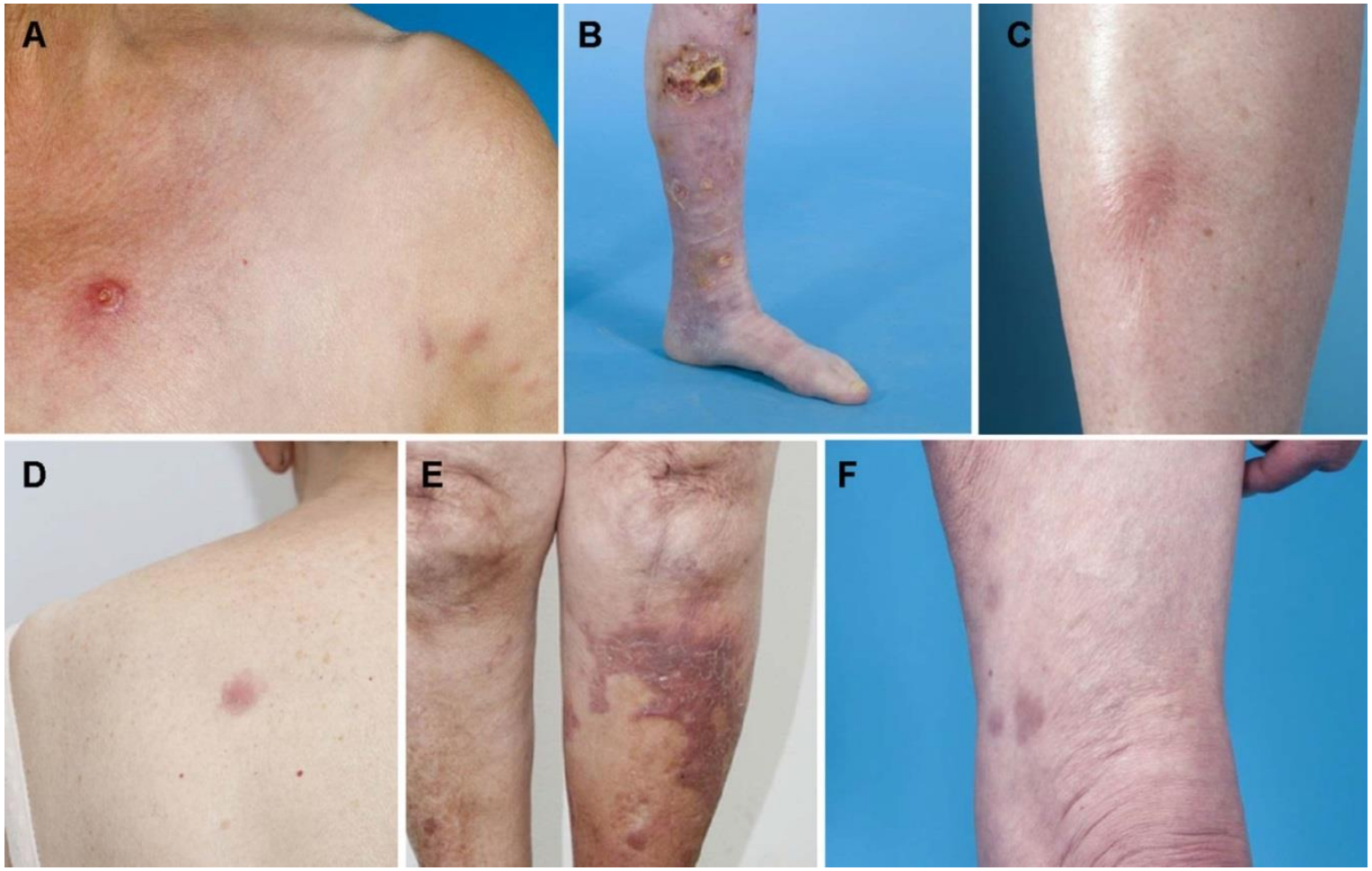
- Mucosal (mostly oropharyngeal) or cutaneous ulcers.
- Age-related or iatrogenic (MTX !) immunosuppression →defective surveillance for EBV.
- At sites of local trauma or inflammation.
- Usually self-limiting clinical course.
- May resolve spontaneously or with limited therapy (withdrawal of immunosuppression; rituximab).

EBV-positive mucocutanous ulcer





Spontaneous resolution of MCU in a patient with RA on MTX over the course of 8 weeks following withdrawal of drug (Dojcinov SD et al. Am J Surg Pathol 2011)



EBV+

EBV -

MTX-associated B-cell lymphoproliferative disorder presenting in the skin: a clinicopathologic and immunophenotypical study of ten cases (Koens L et al; Am J Surg Pathol 2014;38:999-1006)

WHO-EORTC 2005

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Primary cutaneous diffuse large B-cell lymphoma, other
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Precursor hematologic neoplasm

CD4+/CD56+ hematodermic neoplasm (formerly blastic NK cell lymphoma)

Primary DLBCL, other - WHO-EORTC 2018

	WHO Blue Book	WHO-EORTC (Blood)
T-cell rich/histiocyte-rich large B-cell lymphoma	+	+
Plasmablastic lymphoma	+	+
Intravascular large B-cell lymphoma	+	+
PCDLBCL, large transformed cells (BCL2-, BCL6+)	+	-
PCDLBCL, other = non-leg (American Cancer Society)	-	-

Primaire Diagnostiek Cutane Lymfomen

- Onderzoek nodig om de diagnose te stellen omvat:
  - Klinisch onderzoek door dermatoloog met fotografisch vastleggen van efflorescenties
  - histologisch onderzoek door patholoog
  - immuunfenotypering/immuunhistochemie
  - evt. Moleculair/cytogenetisch onderzoek
- Diagnose in principe nooit zonder clinicopathologische correlatie
- Nieuwe patienten: inbrengen in Landelijke Werkgroep Cutane Lymfomen
- Volgens criteria van WHO-EORTC classificatie/Blue Book

Primaire Diagnostiek Cutane Lymfomen

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  - histologisch onderzoek door patholoog
  - immuunfenotypering/immuunhistochemie
  - evt. Moleculair/cytogenetisch onderzoek

1. **Eén biopt of meerdere biopten, wanneer excisie, vriesmateriaal?**
2. **Minimaal standaard panel IHC**
3. **Rol voor klonaliteitsanalyse, NGS, FISH**

Leids Universitair
Medisch Centrum

Multidisciplinaire Werkgroep Cutane Lymfomen

Groep B: onderbouwing kliniek en Pathologie

Ellen de Haas

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

Recommendations for first-line treatment of MF stage IIB.

Systemic therapies[a]	
Retinoids[b]	Level 2
IFN-α	Level 2
TSEB	Level 2
Monochemotherapy (gemcitabine, pegylated liposomal doxorubicine)	Level 4
Low dose MTX	Level 4
Localised RT[c]	Level 4

Table 5b
Recommendations for second-line treatment of MF stage IIB.

Polychemotherapy[a]	level 3
Allogeneic stem cell transplantation[b]	level 3

[a] CHOP is the most widely used regimen with a number of variants and other combinations available.
[b] Should be restricted to exceptional patients, see text for details.

Table 6b
Recommendations for second-line treatment of MF stage IIIA and B.

Monochemotherapy (gemcitabine, pegylated liposomal doxorubicine)	Level 3
Allogeneic stem cell transplantation[a]	Level 3

[a] Should be restricted to exceptional patients, see text for details.

Table 7

Recommendations for treatment of MF stages IVA and IVB.[a]

Chemotherapy (gemcitabine, pegylated liposomal doxorubicine, CHOP and CHOP-like polychemotherapy)[b]	Level 3
Radiotherapy (TSEB and localised)[c]	Level 4
Alemtuzumab (mainly in B2)	Level 4
Allogeneic stem cell transplantation	Level 3

[a] For treatment of MF stage IVA1 recommendations for SS (Table 8a and b) might apply.

[b] Monochemotherapy should be preferentially used.

[c] Used alone or in combination with systemic therapies.

Table 8a
Recommendations for first-line treatment of SS.

ECP[a]	Level 3
Chlorambucil + prednisone	Level 3
Systemic therapies in combination with ECP or PUVA	
Retinoids[b]	Level 3
IFN-α	Level 3
Low dose MTX	Level 4

[a] ECP can be used alone or in combination with skin directed and other systemic therapies.
[b] Including RAR and RXR agonists.

Table 8b
Recommendations for second-line treatment of SS.

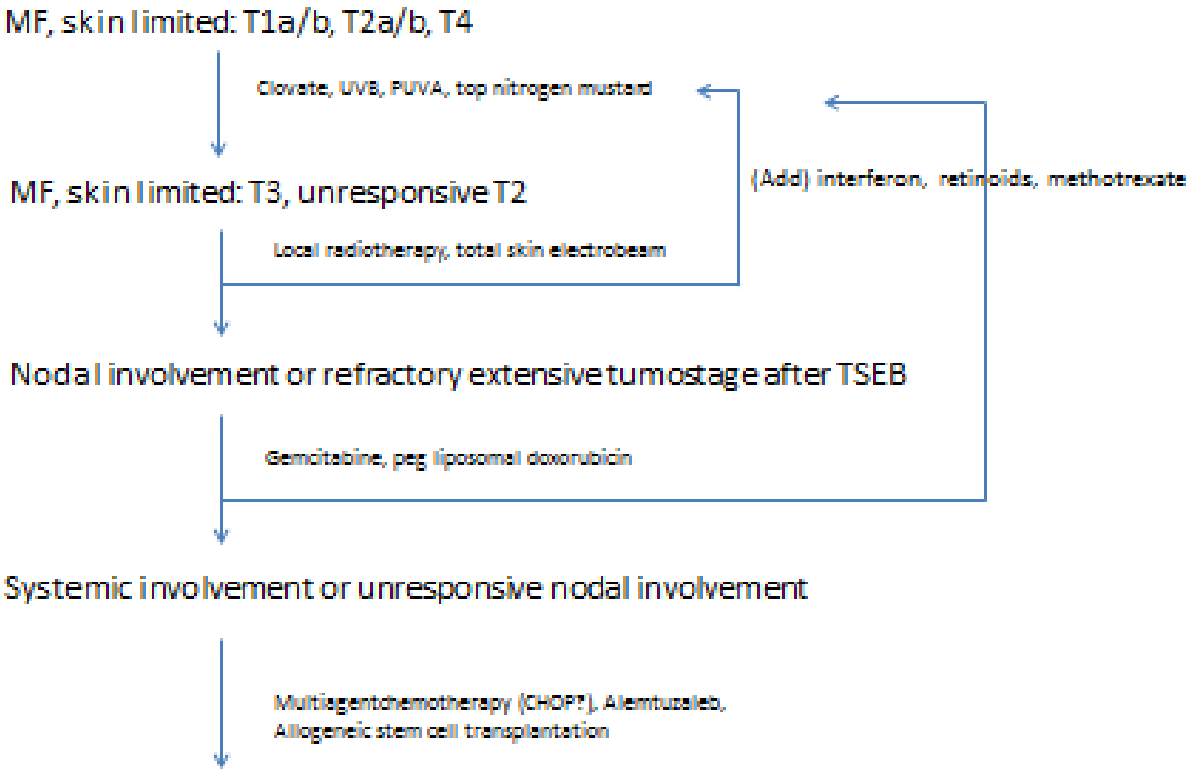
Chemotherapy (gemcitabine, pegylated liposomal doxorubicine, CHOP and CHOP-like polychemotherapy)	Level 3
Alemtuzumab	Level 4
Allogeneic stem cell transplantation[a]	Level 3

[a] Should be restricted to exceptional patients, see text for details.

Table 9
Agents that can be used for maintenance after remission has been achieved in MF and SS.[a]

ECP
IFN-α
Low-dose methotrexate
Mechlorethamine
PUVA
Retinoids
Topical corticosteroids
UVB

[a] Options are listed alphabetically and should be chosen to be effective, tolerable, easy to use, and efficient. OCEBM levels are generally 5.


MF, skin limited: T1a/b, T2a/b, T4
Clovate, UVB, PUVA, top nitrogen mustard
MF, skin limited: T3, unresponsive T2
Local radiotherapy, total skin electrobeam
(Add) interferon, retinoids, methotrexate
Nodal involvement or refractory extensive tumostage after TSEB
Gemcitabine, peg liposomal doxorubicin
Systemic involvement or unresponsive nodal involvement
Multiagentchemotherapy (CHOP?), Alemtuzaleb,
Allogeneic stem cell transplantation

Eenduidige vastlegging

- SWAT = (patch %TBSA × 1) + (plaque %TBSA × 2) + (tumor or ulcer %TBSA × 4).
- The CAILS adding severity score of each of the following categories for up to 5 index lesions: erythema, scaling, plaque elevation, and surface area. Severity was graded from 0 (none) to 8 (severe) for erythema and scaling; 0 to 3 for plaque elevation; and 0 to 9 for surface area
- Fotografische vastlegging
- VAS /Pat Severity Index 0-10

Leids Universitair
Medisch Centrum

Multidisciplinaire Werkgroep Cutane Lymfomen

Groep C: Systemische Therapie

Sherida Woei-a-Jin

Behandelpad systemische therapie voor gevorderde stadia Mycosis Fungoides en Sézary Syndroom

Sherida Woei-A-Jin, An Bervoets en Annemie Busschots

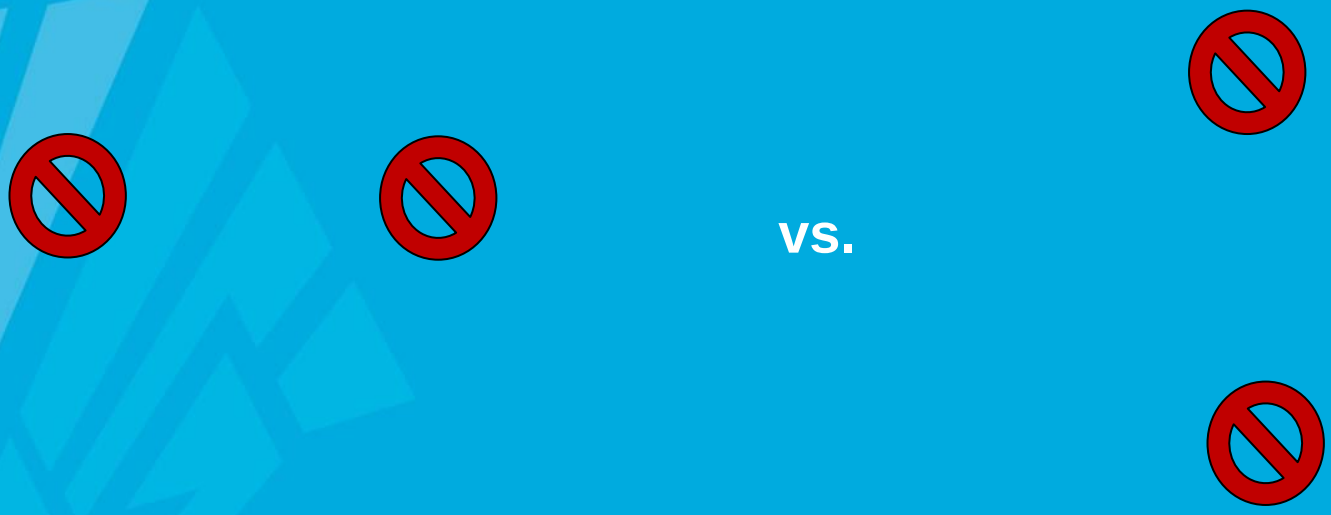
UZ Leuven | Herestraat 49 B - 3000 Leuven | www.uzleuven.be tel. +32 16 33 22 11 | UNIVERSITY HOSPITALS LEUVEN

Dilemma's:

DEFINITIES, STADIËRING EN TNMB CLASSIFICATIE

Definitie “gevorderd / advanced”?

- Formeel vanaf tumor stadium, ofwel stadium IIB



UZ LEUVEN

NIH NATIONAL CANCER INSTITUTE

NCI Dictionary of Cancer Terms

The NCI Dictionary of Cancer Terms features **8,270** terms related to cancer and medicine.

We offer a widget that you can add to your website to let users look up cancer-related terms. Get NCI's Dictionary of Cancer Terms Widget.

◉ Starts with ○ Contains

Enter keywords or phrases **Search**

Browse: A B C D E F G H I J K L M N O P Q R S T U V W X Y Z #

systemic disease (sis-TEH-mik dih-ZEEZ)
Disease that affects the whole body.

Systemische betrokkenheid?

Cutaan Dermatopathisch Visceraal Hyperprogression

Interpretatie bloed betrokkenheid?

- Patiënten met stadium IA, IB en IIA kunnen ook bloed betrokkenheid hebben (B_{0-1})
- *An sich* is bloed betrokkenheid niet altijd een reden voor opstart systemische therapie en kan skin directed therapy volstaan

Definitie bloed betrokkenheid

- B0: absoluut aantal CD4+CD7- óf CD4+CD26- T-cellen <250/µL
- B1: absoluut aantal CD4+CD7- óf CD4+CD26- T-cellen: 250/µL – 1000/µL
- B2: Verhoogd CD4-getal met CD4:CD8 ratio >10, óf CD4+CD7- T-cellen>40%, óf CD4+CD26- T-cellen >30%

Behandellijnen therapie bij MF op basis van global response score, of:

KEUZE THERAPIE BASEREN OP COMPARTIMENT BETROKKENHEID?

Specialismen tijdens behandeltraject

IA

IB

IIA

IIB

III

IV-A1

IV-A2

IV-B

Dermatoloog
- Skin-directed therapie
- Fototherapie
- Systeemtherapie

Radiotherapeut
- Lokale RT
- Total skin
- Concomitant?
- Palliatief?

Hematoloog/oncoloog
- Systeemtherapie
- Management van toxiciteit en infecties

Compartiment response score óf GRS gestuurde therapie?

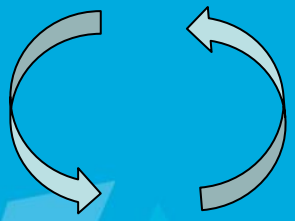
- Huid (T): mSWAT, toename >25% = PD
- Lymfeklier (N): sum of product dimensions (SPD), toename >50% = PD
- “Viscera” (M): SPD, toename >50% = PD
- Bloed (B): flowcytometrie, toename >50% én minstens 5000/µL circulerende CTCL cellen

- GRS = PD zodra 1 compartiment PD toont

Systemische therapie

MYCOSIS FUNGOIDES

Debulking



Maintenance therapie

Indien refractair is de vervolg therapie afhankelijk van:

- Betrokken compartiment
- CD30+ grootcellige transformatie?
- Onderscheid cutane transformatie en nodaal?

Hoe logisch onder te verdelen?

- Lijnen therapie?
- Aangewezen behandeling op basis van betrokken compartimenten?
- Per agens indicatie vermelden?
- Debulkende therapie vs. maintenance?

Inductie of onderhoudstherapie?

- Interferon alfa
  - Na skin-directed therapie
  - Alle stadia CTCL?
- Bexaroteen bij gevorderde CTCL
  - Na interferon alfa?
  - Plaats van andere retinoiden (alleen bij folliculotrope MF)?
- Methotrexaat
  - Alleen inductie gezien toxiciteit? Maximale dosis?
  - Restricties aan dosis in kader van onderhoudstherapie?
- Therapiepauze ja/nee?
- Duur van onderhoudstherapie

Evidence voor combinatie therapie?

- IFNα + bexaroteen of retinoide
- IFNα + MTX
- MTX + bexaroteen of retinoide

- Welke combinaties met radiotherapie?
- Welke combinaties met UVB / PUVA?
- Met name nieuwe compounds?

Brentuximab-vedotin

- Debulking tumor stadium mycosis fungoides met CD30+ grootcellige transformatie
- In ALCANZA studie alle stadia geïncludeerd!
- Ook effect bij CD30 negatieve CTCL
- Knelpunten voor behandeling in niet-tumorale al dan niet vroegere stadia:
  - Vergoeding Brentuximab voor in totaal 16 cycli (geen restricties in Nederland)?
  - Hoeveel cycli zijn echt nodig?
  - Rationale voor rechallenge met Brentuximab?
  - Plaatsbepaling? 1^{e} keus, of ná IFNα en/of bexaroteen?
  - Restricties hogere stadia? Bv. wat als beperkt T3 met B2?

Overige systeemtherapieën

- Lenalidomide
- Romidepsin
- Bortezomib
- Mogamolizumab
- Pembrolizumab?

Systemische therapie bij erytrodermie en B2

SÉZARY SYNDROOM

Sézary Syndroom en erythroderme MF

- Systemische corticosteroiden (dosis, duur?)
- Interferon alfa
- Bexaroteen
- ECP (Extracorporele photoferese)
- Total skin electron beam therapie
- Lage dosis alemtuzumab (bij B1-2)
- Chloorambucil +/- prednisolon (bij B2)
  - Pulse therapie of continu
- Lage dosis methotrexaat
- Lenalidomide (off label / medical need)
- Romidepsin (named patient program)

Sézary Syndroom (vervolg)

- Brentuximab-vedotin indien CD30+
- Respons op conventionele cytostatica?
  - Liposomaal doxorubicine (Caelyx)
  - Gemcitabine
  - Fludarabine +/- interferon alfa (geen cladribine vanwege immuungecompromitteerde status?)
  - CHOP
- Plaats bortezomib, mogamulizumab en pembrolizumab?

Dilemma’s bij uitgebreide tumorale huidbetrokkenheid

DOSIS RADIOTHERAPIE

Maximale dosis radiotherapie?

- Welke dosis voor tumorale stadia?
- Low dose total skin radiotherapie?
- Recall radiatie dermatitis?
- Maximale huidtolerantie? Cumulatief 70 Gy?

- Concomitante chemoradiotherapie?

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Groep D: alloSCT bij CTCL

Erik Marijt/Maarten Vermeer

LUMC results

(Immuno-)chemotherapy

Allogeneic stem cell transplantation

Proposal new alloSCT protocol

Erik Marijt, 7-Nov-2017

Introductie

CTCL worden naar Hematologie verwezen wanneer lokale of beperkte systemische therapie niet meer werkt:

- Tumoreuze stadia in huid
- Systemische betrokkenheid, meestal lymfadenopathie

Analyze gedaan op een groep van 28 patienten die sinds 2007 naar Hematologie zijn verwezen voor systemische chemotherapie
Deel van de patienten is vervolgens allogeen getransplanteerd

LUMC results chemo for MF/SS

Therapy	N=22	total per chemo group	Results
CHOP	12		
A-CHOP	2		13x PD
CHOEP	1	17	3x CR
BV-CHEP	2		1x SD
liposomal doxo	1	1	1x SD
Alemtuzumab	3	3	1x SD,1x PD, 1x PR
MTX/AraC	1	1	1x CR

Evalueerbaar ivm chemotherapie: 22

14x PD	64%
4xCR	18
3x SD	14
1x PR	5
Median months to PD	5

LUMC results alloSCT for MF/SS

CTL UPN	Diagnosis	Dead	CoD	
8	MF	yes	PD	
9	SS	yes	neurological	
10	MF	yes	PD	
14	MF	no		
15	MF	yes	GVHD	
19	SS	yes	PD	
21	prim aggr cut CD8+ TCL	yes	GVHD	
25	prim aggr cut CD8+ TCL	no		short f-up!
28	MF-HTLV1	no		
		OS 3/9		

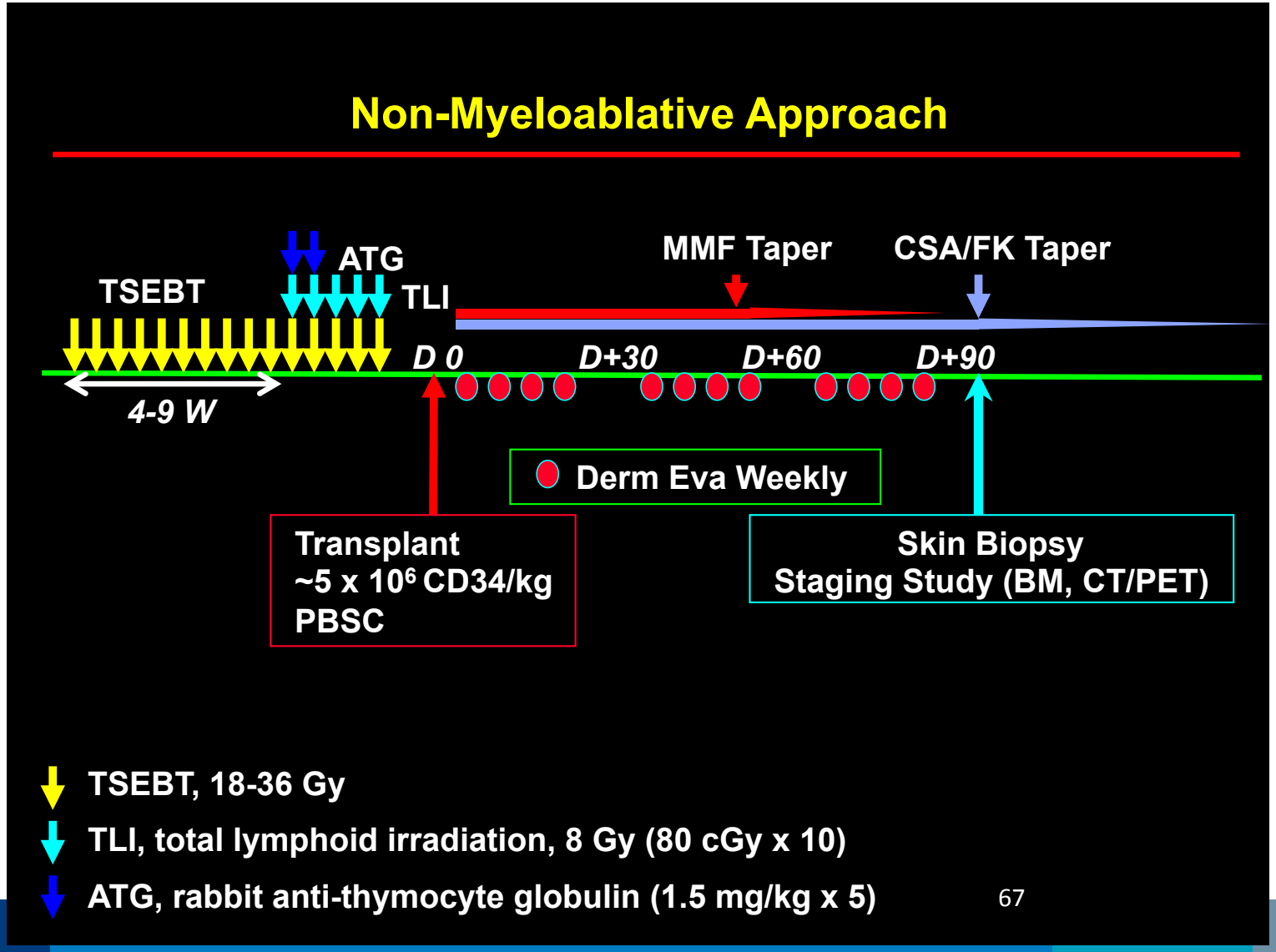
Conclusion-1

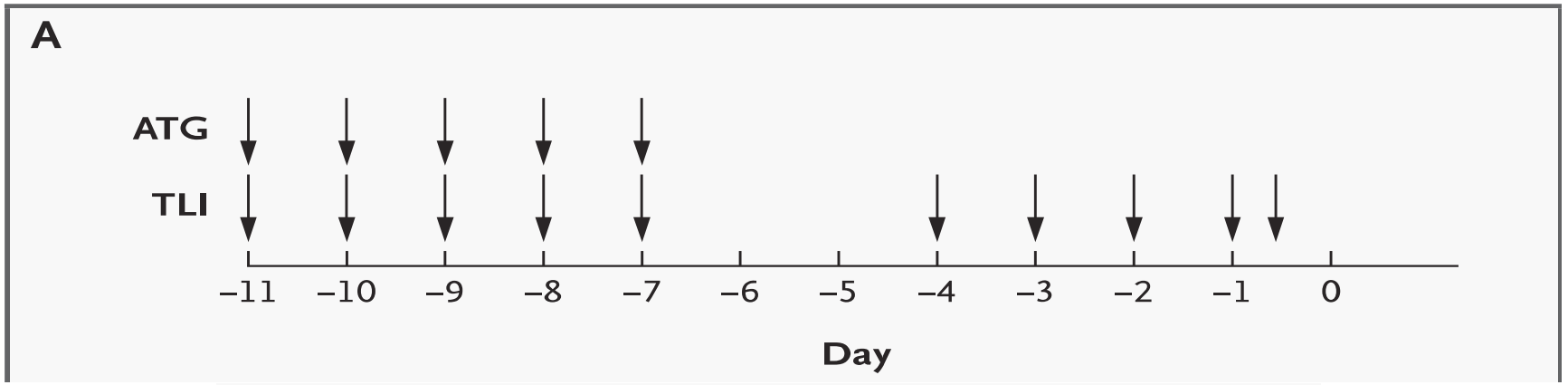
Advanced stage CTCL: slechte resultaten multi-agent CHOP (like) chemotherapie, maar vergelijkbaar met resultaten beschreven in literatuur

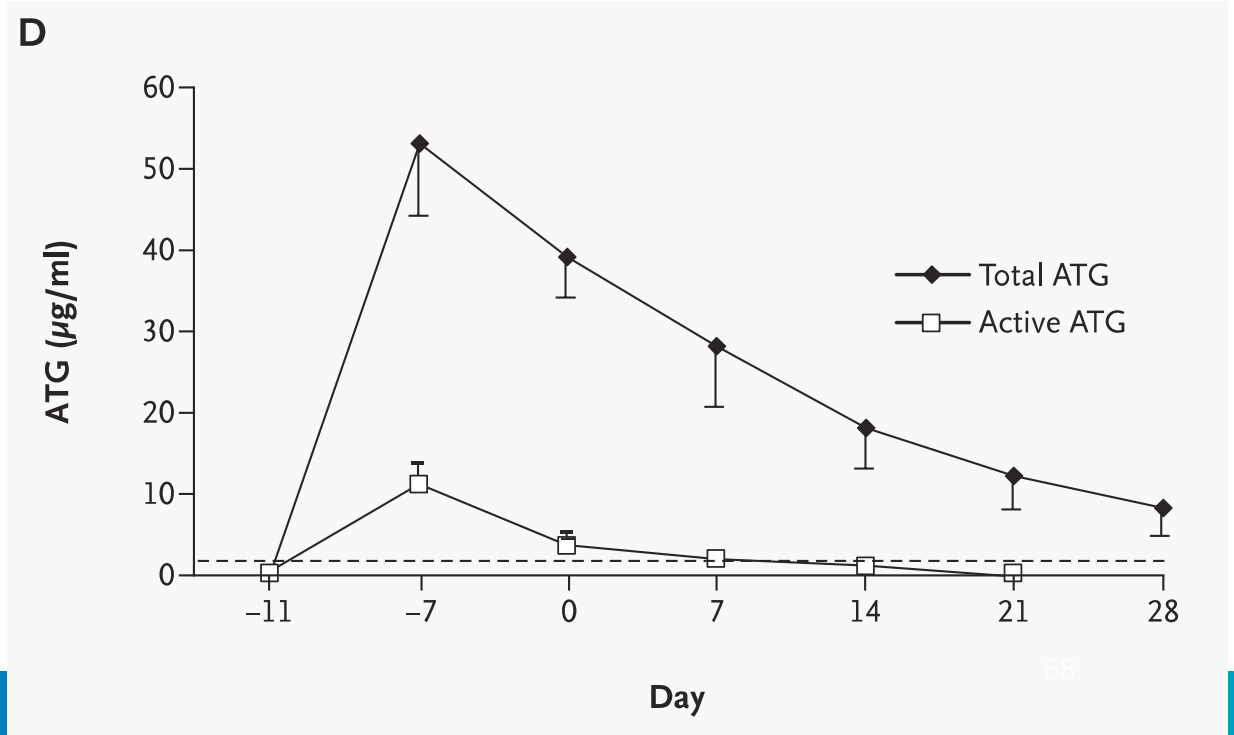
Deel van deze patienten kan echter toch worden getransplanteerd >> 9 patienten:

- 3 overlijden alsnog aan PD
- 2 dood tgv GVHD
- 1x dood door onbegrepen neurologisch beeld
- OS 3/9

TSI+TLI for CTCL (Stanford schema)




A
ATG
TLI
−11
−10
−9
−8
−7
−6
−5
−4
−3
−2
−1
0
Day


D
ATG (μg/ml)
60
50
40
30
20
10
0
Total ATG
Active ATG
−11
−7
0
7
14
21
28
Day

Immunosuppressive therapy after transplantation:

oral cyclosporine: day -3, at a dose of 6.25 mg per kilogram twice per day
MMF, 15 mg per kilogram twice a day, day +1

MRD:

- cyclosporine was tapered to discontinuation from day 56 to day 180
- MMF was stopped on day 28.

MUD:

- cyclosporine was tapered to discontinuation from day 100 to day 180
- MMF was tapered to discontinuation from day 42 to day 96.

Sci Trans Med 2013: clinical course after TSI + TLI for CTCL; n=10

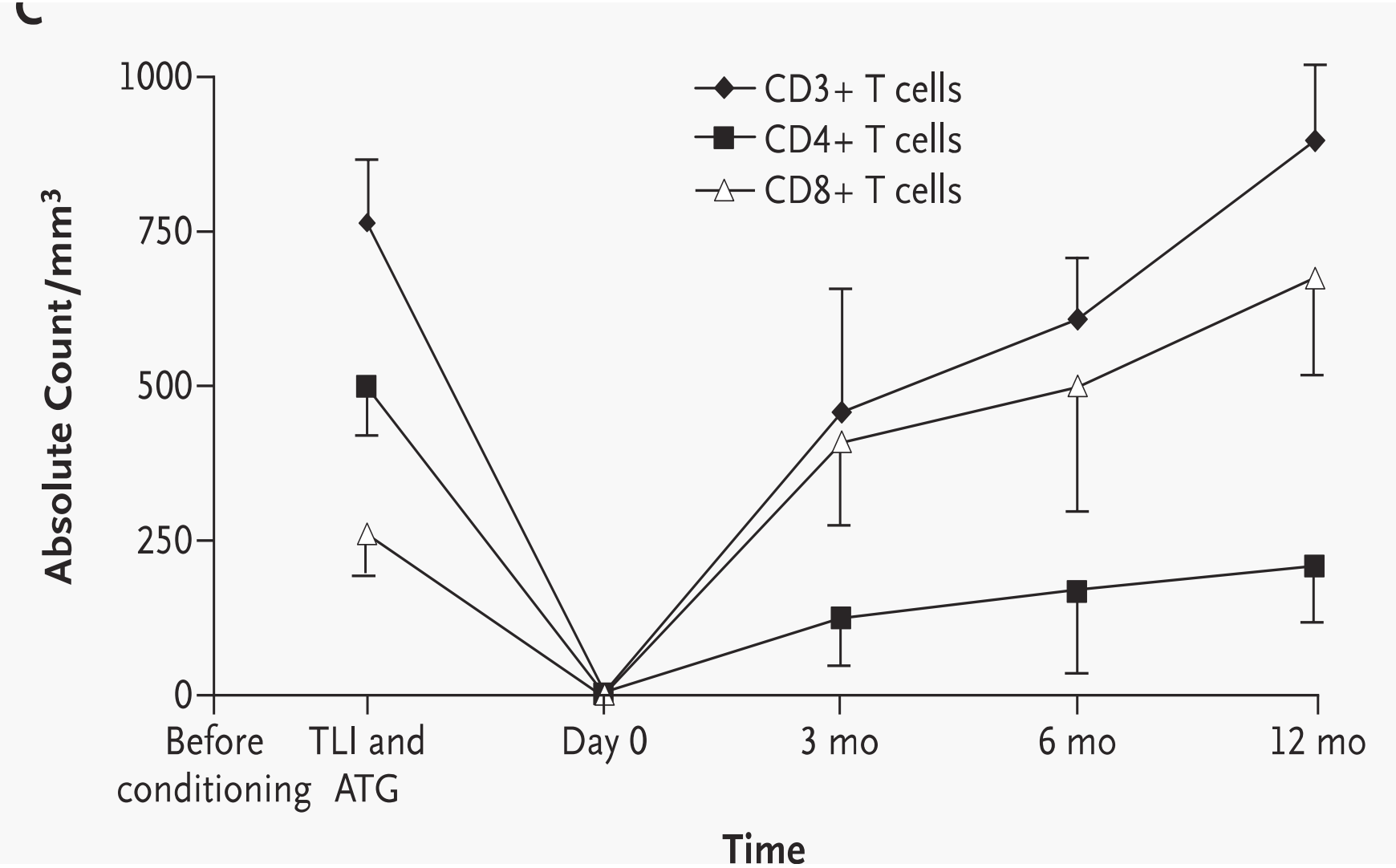
Supplementary Table 1. Clinical Characteristics

Patient	Age	Stage	Large Cell Transformation	Time from Diagnosis to Transplant (Mo)	No. of Prior Systemic Tx	Last Systemic Treatment	Disease Status at Time of Transplant			Clinical Response at Day+90 Post Transplant	Aute GVHD	Chronic GVHD
							Skin*	Blood	Lymph node			
#1	62	IVB	Yes	27.5	4	Vorinostat	+	+	+	CR#	Skin, Grade 2	-
#2	20	IVA	Yes	31.3	2	Doxorubicin Liposome	+	-	-	PR	-	-
#3	73	IVA	no	46.7	9	Romidepsin	-	-	-	CR	-	Oral, Skin, Gut
#4	47	IVA	no	39.6	8	Romidepsin	+	+	+	CR	-	-
#5	63	IVA	Yes	34.8	6	Denileukin Diftitox	+	-	-	CR	-	-
#6	62	IVB	no	60.6	6	Romidepsin	+	+	+	CR	-	-
#7	62	IVA	no	151.7	6	Gemcitabine/ Dexamethasone /Cisplantin	-	-	+	CR	-	-
#8	64	IVA	no	22.3	4	Alemtuzumab	+	-	-	CR	-	-
#9	63	IVA	no	10.2	4	Alemtuzumab	+	-	-	CR	-	-
#10	65	IVA	no	55.6	4	Romidepsin	+	+	+	CR	Skin, Grade 3	Skin

* Skin, + generalized erythroderma/plaque/tumor, confirmed by biopsy
Blood ,+ determined by multi-parameter flow cytometry and pathologist's review
Lymph node, + by computed tomography/positron emission tomography and biopsy confirmation

CR, complete clinical response using criteria in Ref 41
PR, partial clinical response

T cell reconstitution



Inclusie patienten

inclusie van patienten die advanced stage CTCL hebben: stad IIB/IV

bij voorkeur patienten patienten die alleen huidafw. hebben (IIB), maar wel met blastaire transformatie; deze krijgen ook snel LK betrokkenheid (zie studies Vermeer over prognostische factoren voor snelle progressie)

alleen chemotherapeutische voorbehandeling bij LK betrokkenheid?

fungoides: a retrospective analysis of 100 cases

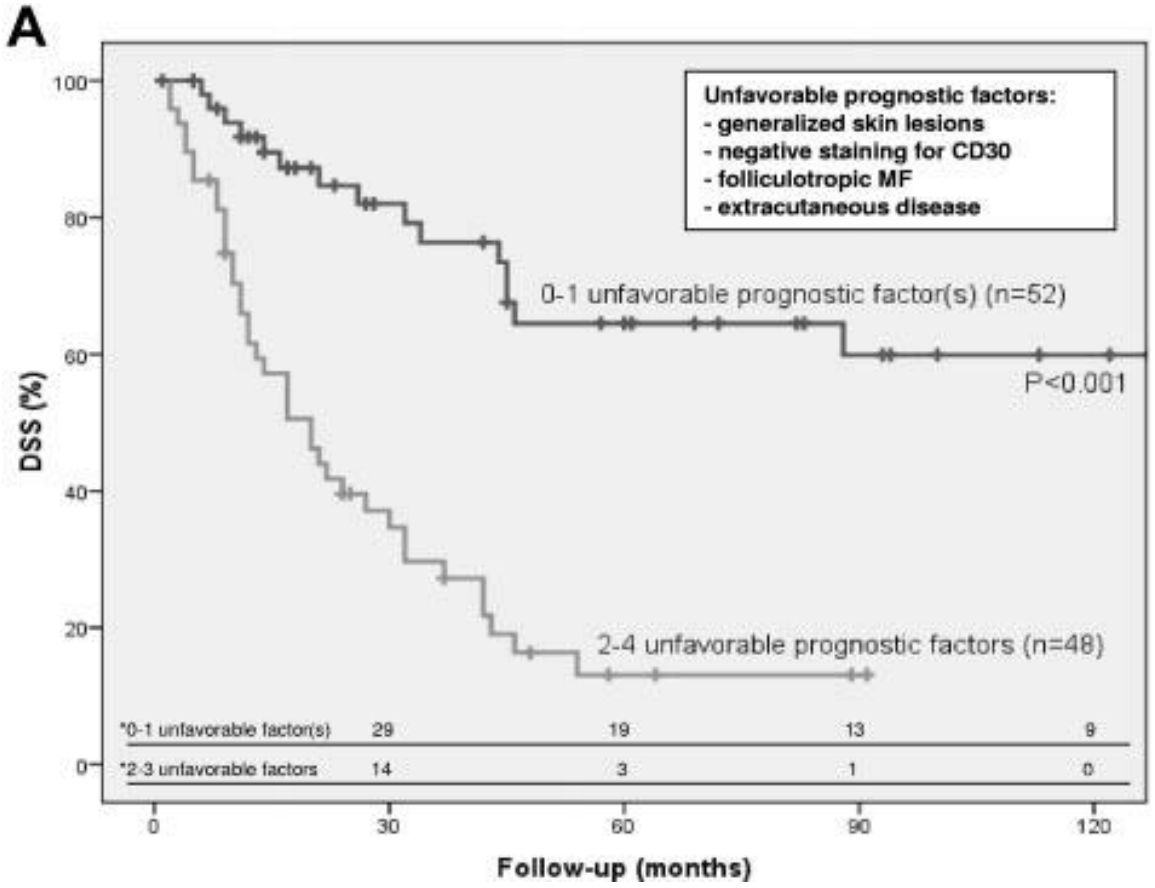


Figure 2. Prognostic index indicating differences in DSS. Prognostic index indicating differences in DSS in total group of patients with transformed MF (n=100; A)

Vragen aSCT

Procedure

- Indicatie: welke patiënten?
- Behandeling: welk protocol?
- Monitoring: hoe, wanneer, welke consequentie?
- Waar: academische centra, STZ, combinatie?

aSCT netwerk voor Cutane Lymfomen

- Indicatiestelling
- Standaard protocol

Database met follow up
Biobanking