virtuel | 18.09.2021

Cutaneous T-cell lymphoma

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LEARNING OBJECTIVES

CUTANEOUS T CELL LYMPHOMA

- RECOGNIZE

  the most common entities

- UNDERSTAND

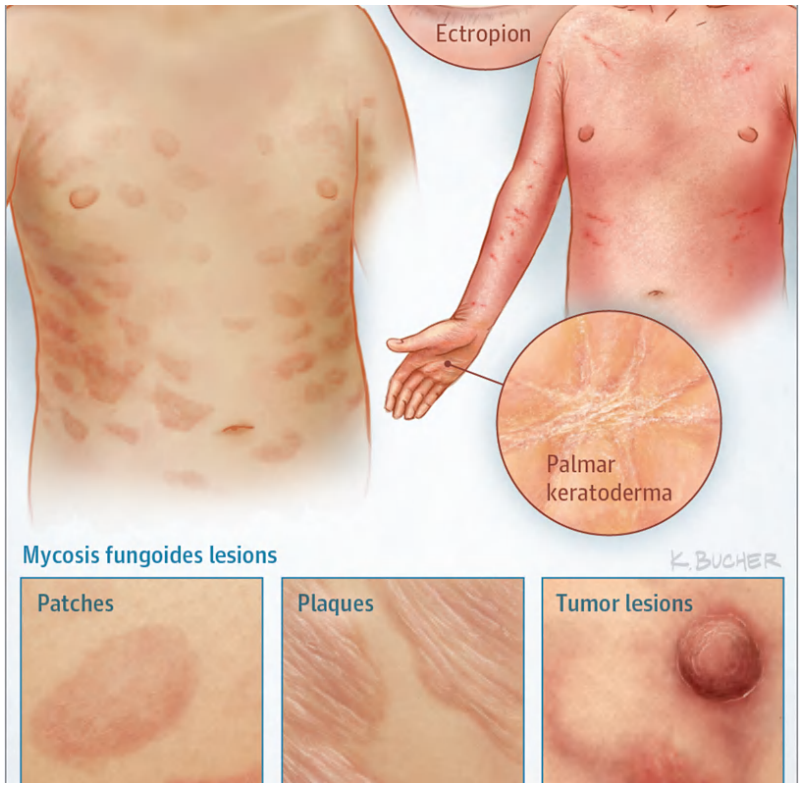
  the current concepts in the treatment of early and advanced disease

- GAIN KNOWLEDGE

  about newly developped treatment modalities

Cutaneous T-cell Lymphoma

DIAGNOSTICS & STAGING

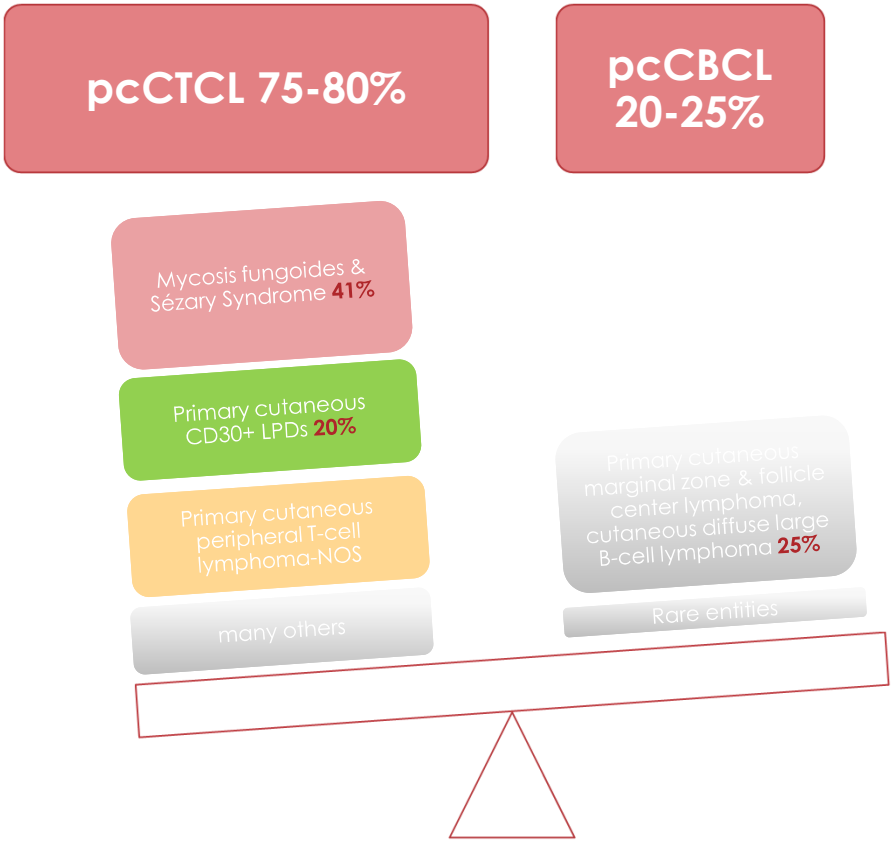


Dai J et al. *JAMA Dermatol.* 2017;153(6):620.

Primary cutaneous lymphoma

Definition

- Group of lymphoid neoplasias
- Initial presentation in the skin
- No extracutaneous involvement at diagnosis
- Epidemiology
  - Incidence, around 1/100.000
  - 75-80%, T-cells
  - 20-25%, B-cells
- Some of them same names/morphology as systemic lymphoma
- Different diseases. Different treatment



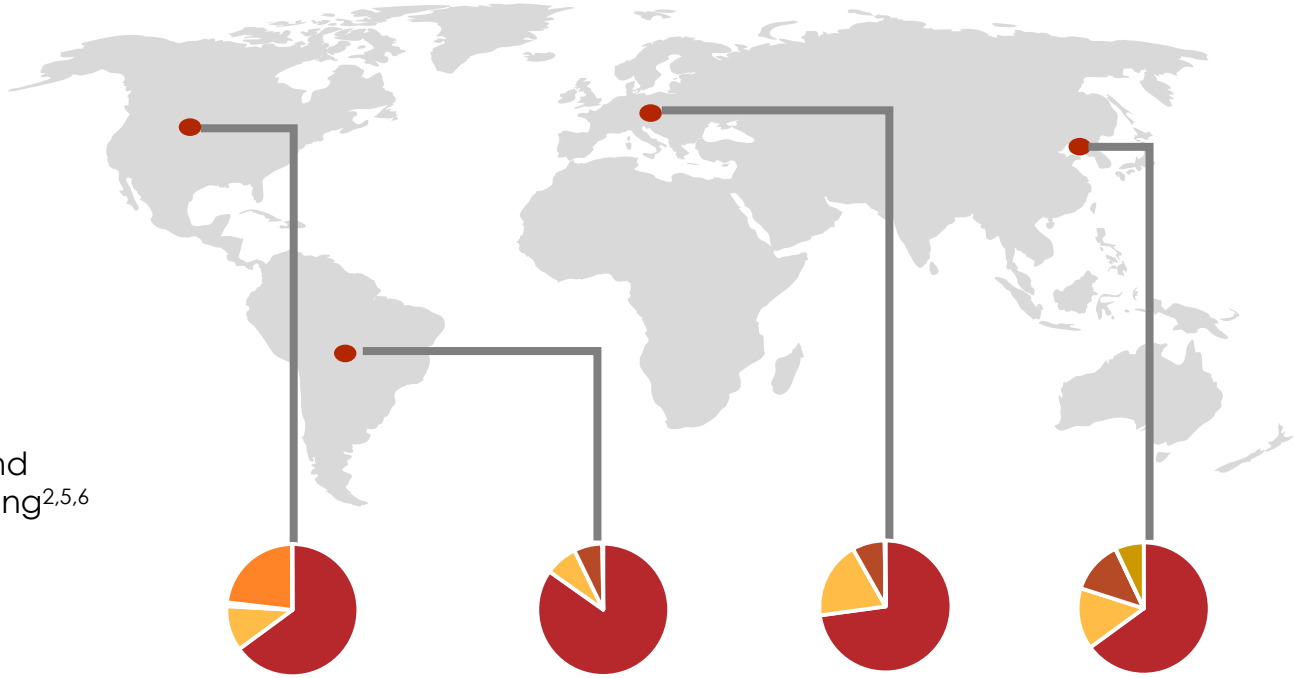
1. Swerdlow SH, et al. Blood 2016;127:2375–90; 2. Willemze R, et al. Blood. 2019 Sep 26;134(13):1703–1714; 3. Swerdlow SH IARC Press; 7 Sept 2017: ISBN-13 (Print Book); 4. R La Selva et al. Indian J Dermatol. 2017 Mar-Apr; 62(2): 146–157

Primary cutaneous T-cell lymphoma

Epidemiology

- MF/SS
- CD30+ LPD
- Rare CTCL
- Unclassified/NOS
- ATLL

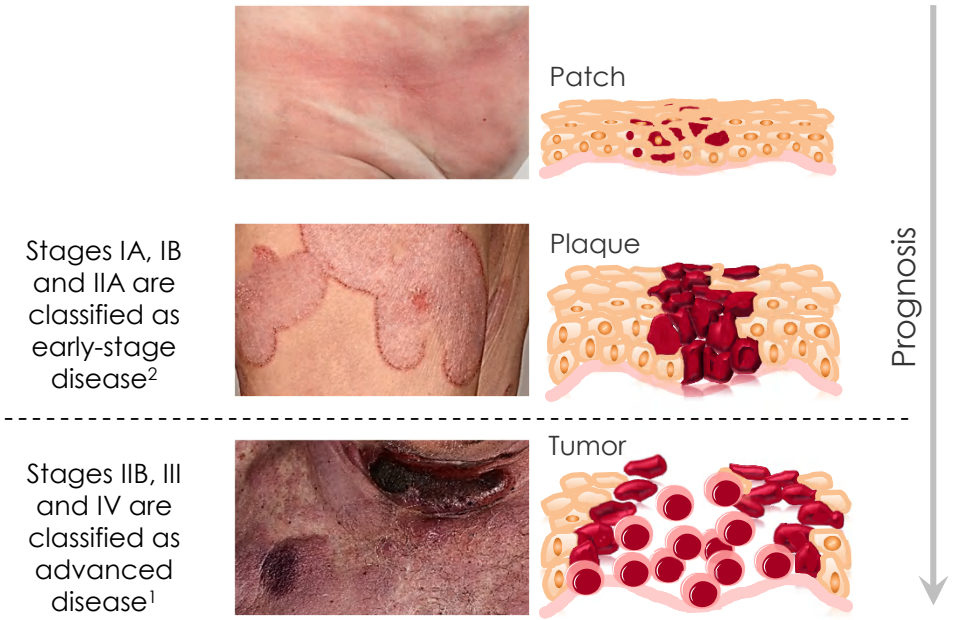
changing trends and geographic clustering[2,5,6]



1. Dobos, G., et a.. (2020). Cancers (Basel) *12*.; 2. Dobos, G., *et al.* (2020). Br J Dermatol. [online, ahead of print]; 3. Ottevanger, R., *et al.* (2021). Br J Dermatol; 4. Dores, G.M., et al. (2005). J Clin Oncol *23*, 7246-7248.; 5. Ghazawi, F.M., *et al.* (2017).. Cancer *123*, 3550-3567.; 6. Litvinov, I.V., *et al.* (2015). Cancer Med *4*, 1440-1447.

Mycosis fungoides

SLOWLY PROGRESSING DISEASE



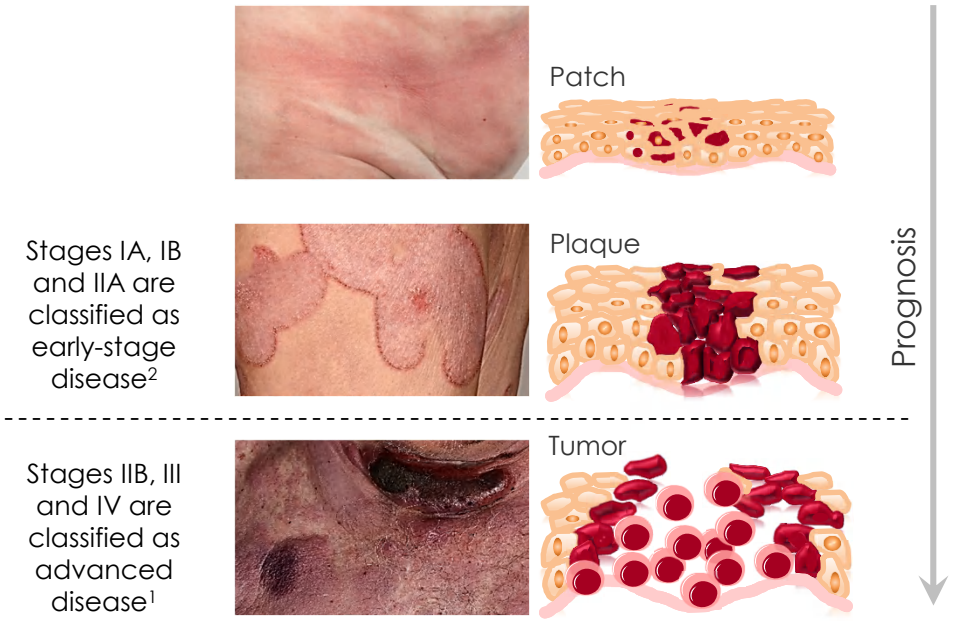
ISCL/EORTC revision to the staging of MF/SS[2]

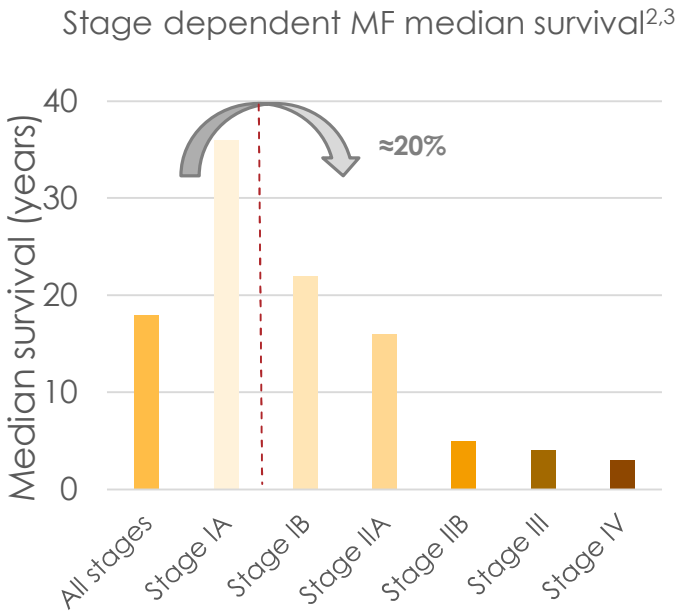
	T	N	M	B
IA	1	0	0	0–1
IB	2	0	0	0–1
IIA	1–2	1–2	0	0–1
IIB	3	0–2	0	0–1
IIIA	4	0–2	0	0
IIIB	4	0–2	0	1
IVA1	1–4	0–2	0	2
IVA2	1–4	3	0	0–2
IVB	1–4	0–3	1	0–2

1. https://www.nccn.org/patients/guidelines/nhl-mycosis/index.html#1/z; 2. Olsen, E., et al. (2007). Blood **110**(6): 1713-1722.

Mycosis fungoides

MOST PATIENTS REMAIN IN EARLY STAGE DISEASE





1. https://www.nccn.org/patients/guidelines/nhl-mycosis/index.html#1/z; 2. Agar NS et al. J Clin Oncol 2010;28:4730–9.; 3. Scarisbrick JJ et al., J Clin Oncol. 2015 Nov 10;33(32):3766-73

The challenge

EARLY AND ACCURATE DIAGNOSIS

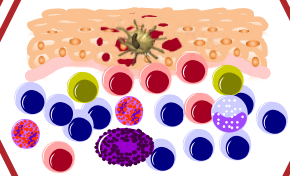
Mis-diagnoses are common [1]

Multiple doctors on the diagnostic journey [2]

70–80% of patients diagnosed with early-stage MF [3,4]

4–6 years from initial symptoms to diagnosis [1]

Inflammatory dermatosis main differential diagnosis [5-7]

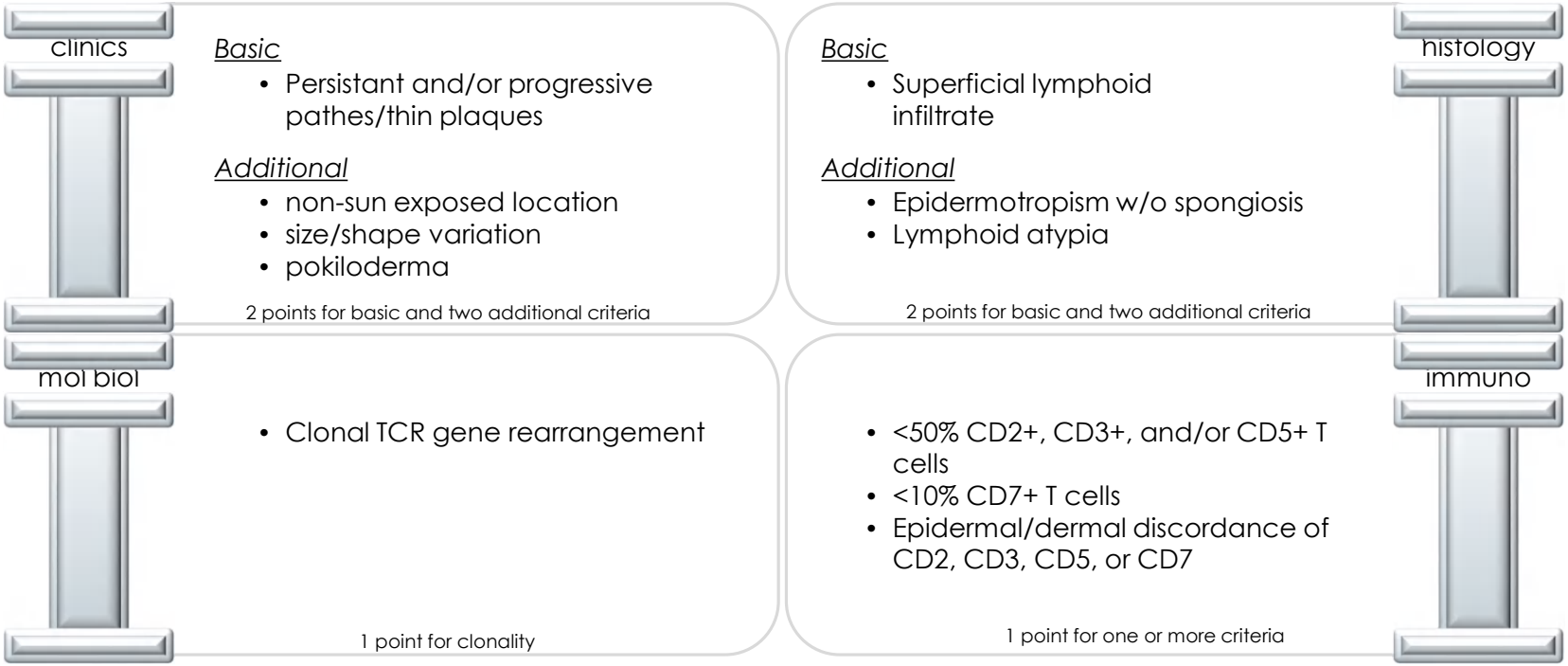


1. Scarisbrick JJ et al., Br J Dermatol. 2019 181(2):350-357.; 2. Girardi M et al. N Engl J Med 2004;350:1978–88.; 3. Agar NS et al. J Clin Oncol 2010;28:4730–9.; 4. Assaf C et al. JDDG 2007;5:662–9.; 5. Kelat A et al. Int J Womens Dermatol. 2017 Jan 30;3(2):100-106; 6. Saulite I et al. Biomed Res Int. 2016;2016:9717530; 7. DeSimone JA et al. Curr Opin Oncol. 2015 27(2):128-33

MF: diagnostic criteria

THE BASIC CONCEPT

- MF if ≥ 4 points for diagnostic criteria[1]
- sensitivity 87.5% | specificity 60%[2]



1. Pimpinelli N et al. J Am Acad Dermatol 2005 53(6):1053-63.; 2. Vandergriff T et al. J Cutan Pathol. 2015 May;42(5):318-28.;

Staging evaluations

RECOMENDATIONS[1,2]

Complete clinical examination

- Skin (mSWAT, CAILS)
- lymph nodes

Laboratory studies

- Complete differential blood count & chemistry (incl LDH)
- Blood smear or FACS, CD4/CD8 ratio, measurement of CD4+CD7- cells and/or CD4+CD26- cells
- Clonality assessment (PCR, BIOMED-2 protocol)

Skin biopsy

- representative lesions
- mulitple biopsies
- clonality assessment (PCR, BIOMED-2 protocol)

Lymph node biopsy

- node ≥ 1.5 cm in diameter or suspicious
- Clonality assessment (PCR, BIOMED-2 protocol)

Imaging

- CT scans ± FDG-PET (optional in patients with early-stage MF)

Bone marrow biopsy

- not required unless indicated by other staging assessments

1. Dippel E et al., J Dtsch Dermatol Ges. 2017 Dec;15(12):1266-1273; 2, Willemze R et al, Ann Oncol. 2018 29(Suppl 4):iv30-iv40.

Sézary syndrome: diagnostic criteria

BLOOD STUDIES

International Society for Cutaneous Lymphomas (ISCL)[1]:

One or more of the following:

- Sezary count > 1000 cells/mm3 (FACS)
- Increased lymphocyte counts + immunophenotypical abnormalities : CD4/CD8 ratio > 10 and/or loss of one or more T-cell antigens (CD2, 3, 4, 5, 7, 26)
- Demonstration of T-cell clonality in the blood

WHO–EORTC classification for cutaneous lymphomas[2]:

- T-cell clonality (ideally blood + skin) + one of the above

Current EORTC proposal*[3]:

- B0<250/µL
- B1≥250/µL and <1000/µ
- B2≥1000/µL CD4+CD7- or CD4+CD26- cells per µL blood

*Historical: B0≤5%, B1>5% and <1000, B2 ≥ 1000 Sézary cells per µL blood

ISCL/EORTC revision to the staging of MF/SS[4]

	T	N	M	B
IA	1	0	0	0–1
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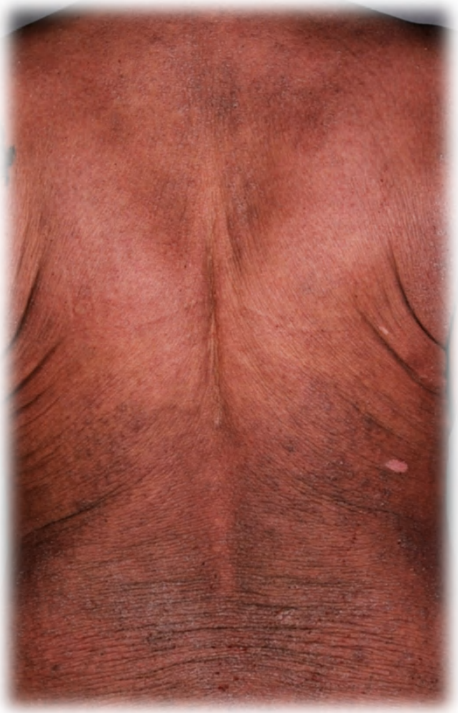
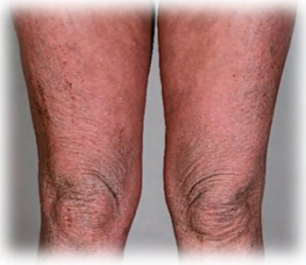
IVA1	**1–4**	**0–2**	**0**	**2**
IVA2	1–4	3	0	0–2
IVB	1–4	0–3	1	0–2

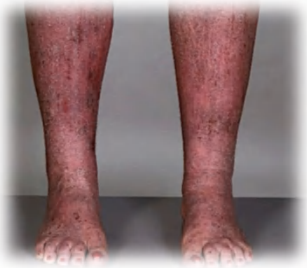
1. Vonderheid, E. C., et al. (2002). J Am Acad Dermatol **46**(1): 95-106.; 2. Willemze, R., et al. (2005). Blood **105**(10): 3768-3785.; 3. Scarisbrick, J. J., et al. (2018). Eur J Cancer **93**: 47-56; 4. 2. Olsen, E., et al. (2007). Blood **110**(6): 1713-1722

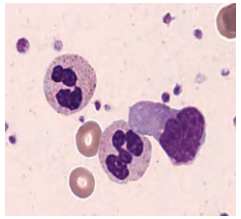
Sézary syndrome

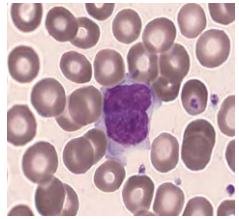
CLINICAL CASE











3/4 atypical lymphocytes
(= 3.7 G/l)

46 year old patient with skin rash and itch

Since >6 years itch, exematous plaques

Weight loss of 6kg in 12 Mt

= Pruritic erythroderma

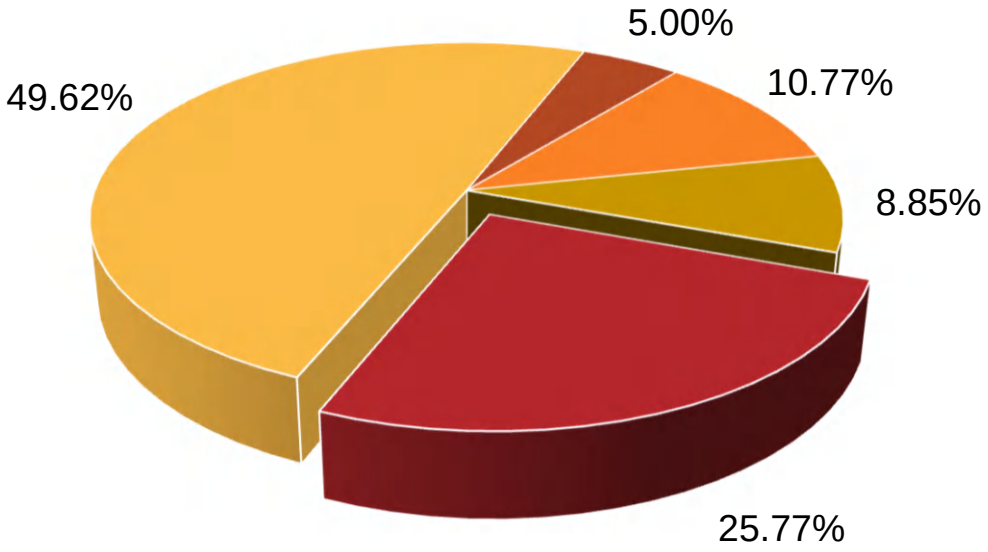
Clinic

Total Leukocytes	6117 [850-2500/µl]
CD4+CD7-CD26-	97 [<30/40%]
CD4/CD8	47.5 [1-5]
CD4+Vβ2+	96.83 [5.4-12.8%]

Sézary syndrome

CLINICAL IMAGE CAN BE LARGELY UNSPECIFIC

- Type 1: Typical erythroderma
- Type 2: Non-specific dermatitis
- Type 3: Atopic dermatitis-like
- Type 4: Mycosis fungoides-like
- Type 5: Leukaemic without initial erythroderma

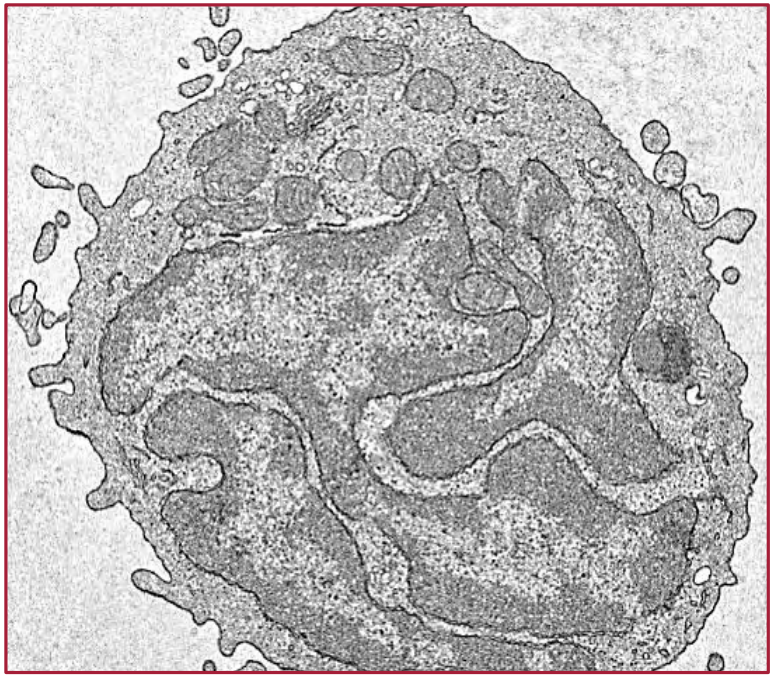


1. Kresbach H, Guenova E. Dermatologie Praxis 2017;1–11; 2. Mangold AR, et al. J Am Acad Dermatol 2017;77:719–27.

Prognostic factors for MF/SS

RESEARCH ONGOING

- Stage IV disease[3]
- Age >60[3]
- Large cell trasnformation[3]
- ↑ LDH[3]
- TCR frequency >25% for ≥stage IB disease[4]



Ultrastructural appearance of a Sézary cell

1. Alibert JL. Paris, Baillière, 1832.; 2. Karamanou M et al. J BUON. 2014 Apr-Jun;19(2):585-8.; 3. Scarisbrick JJ et al., J Clin Oncol. 2015 Nov 10;33(32):3766-73; 4. de Masson A et al. Sci Transl Med. 2018; 9;10(440).

Ø Genetic predisposition/heredity

The Danish Twin Registry Study[1]

Study

30+-year period

42 twins with CTCL (case twins)

their 42 co-twins

13 monozygotic, 27 dizygotic,

2x 420 age- and sex-matched case controls

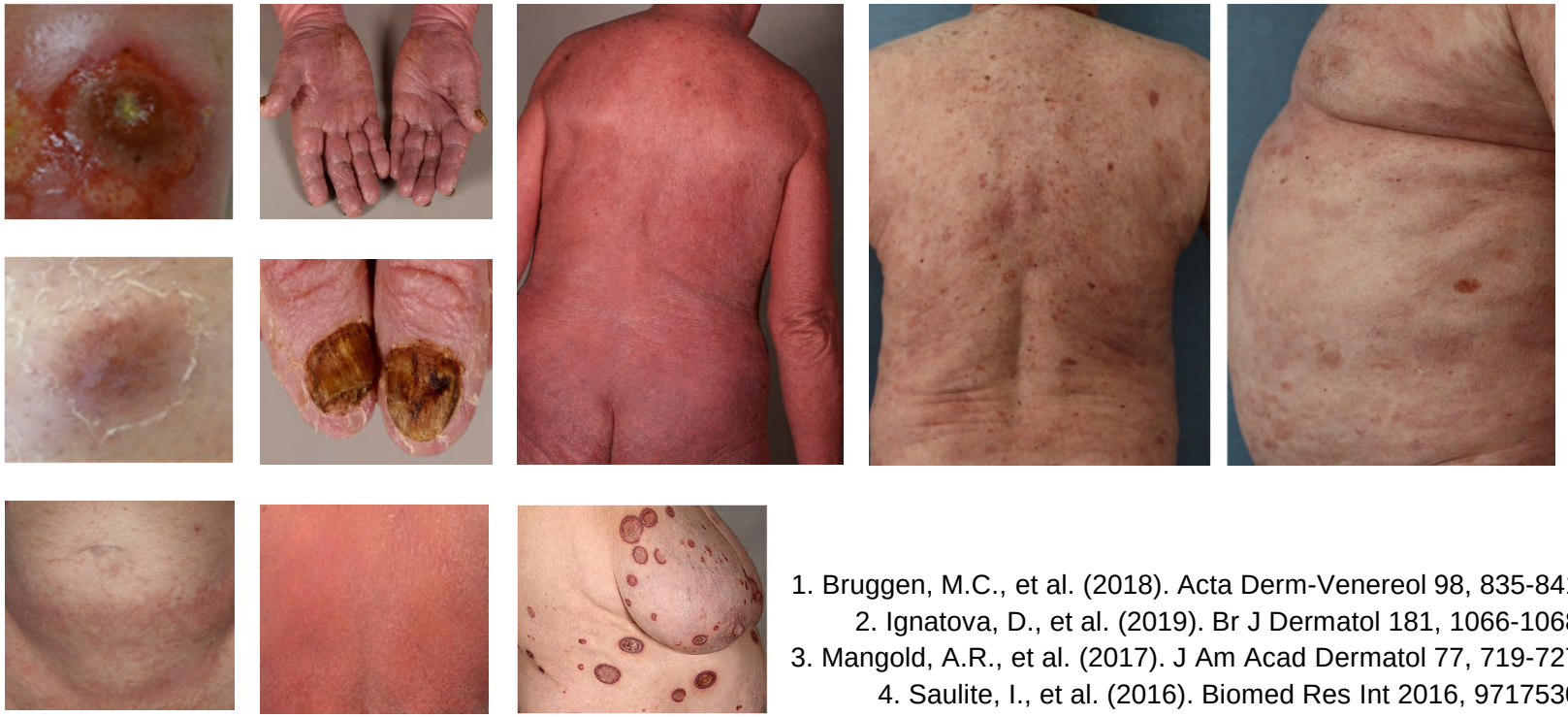
Results

None of the co-twins diagnosed with CTCL

1. Odum N et al. (2017). Blood Cancer J. 7(1):e517.

Cutaneous T cell lymphomas

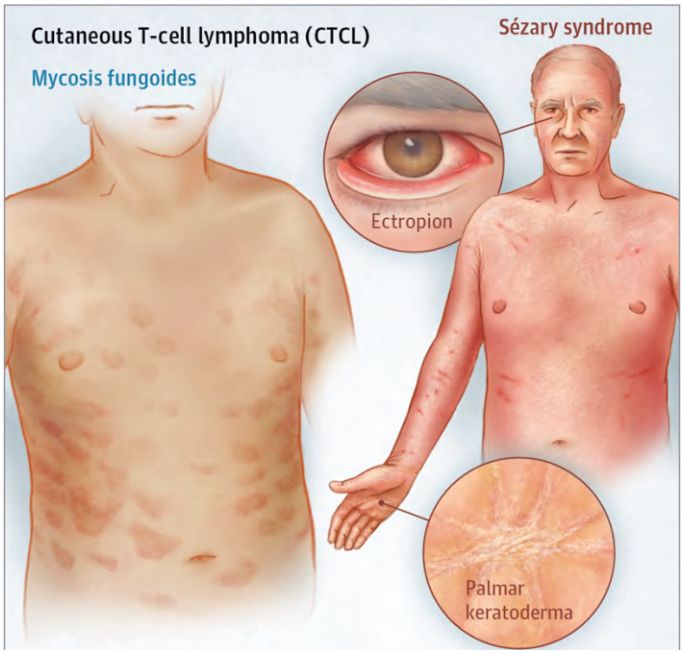
The great imitators

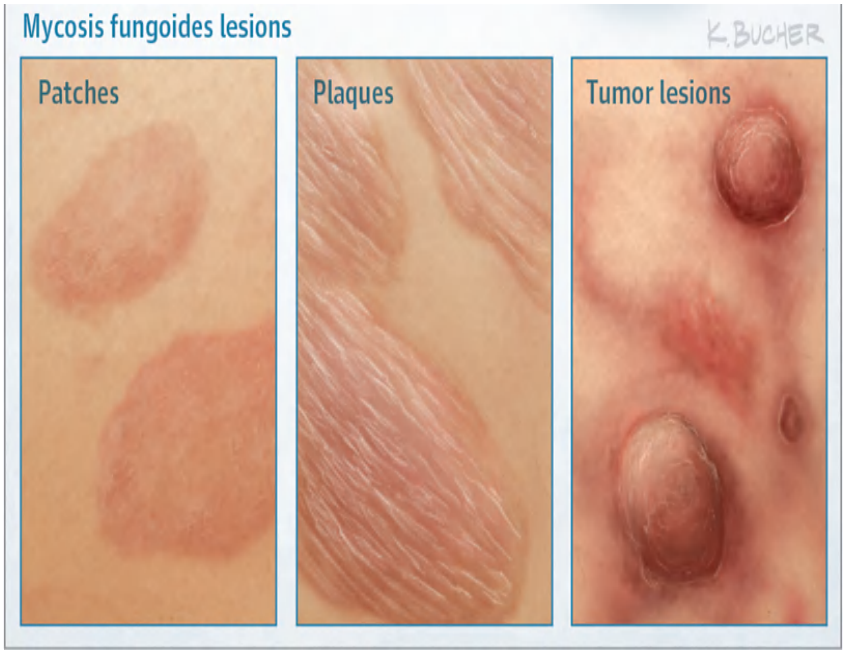


1. Bruggen, M.C., et al. (2018). Acta Derm-Venereol 98, 835-841.
2. Ignatova, D., et al. (2019). Br J Dermatol 181, 1066-1068.
3. Mangold, A.R., et al. (2017). J Am Acad Dermatol 77, 719-727.
4. Saulite, I., et al. (2016). Biomed Res Int 2016, 9717530.

MF & SS

KEY FEATURES OF THEIR CLINICAL PRESENTATION

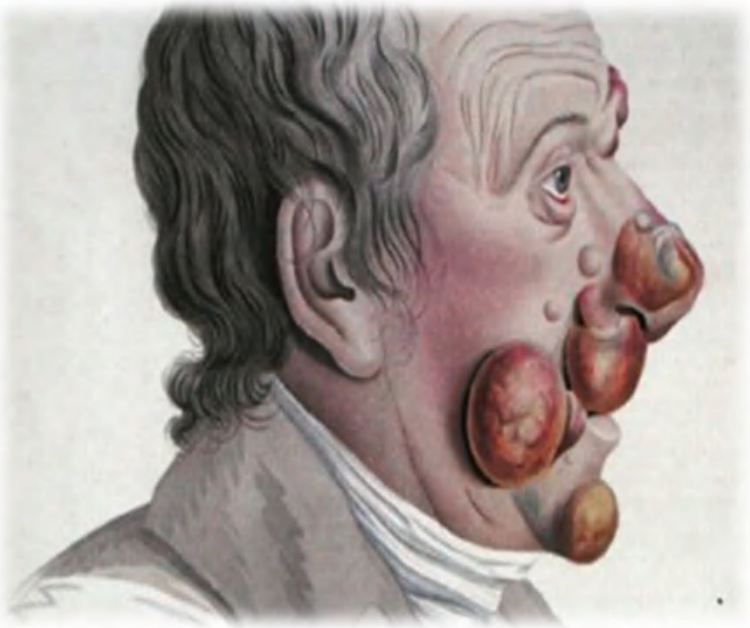




Dai J et al. *JAMA Dermatol.* 2017;153(6):620.

CUTANEOUS T-CELL LYMPHOMA

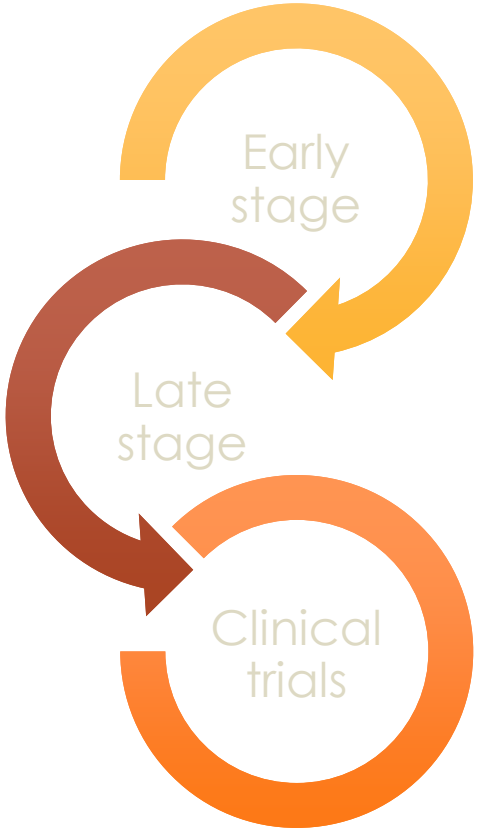
TREATMENT



Mr. Lucas; 1st MF patient described by Alibert[1,2]

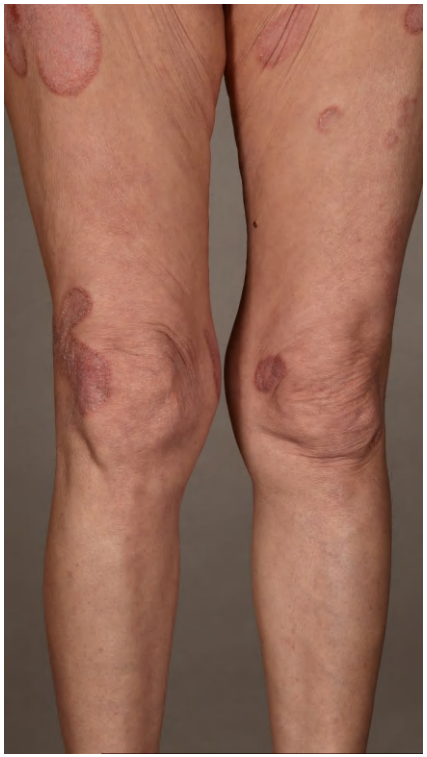
EMMANUELLA GUENOVA, MD, PhD

Treatment for MF/SS is based on patient's disease stage

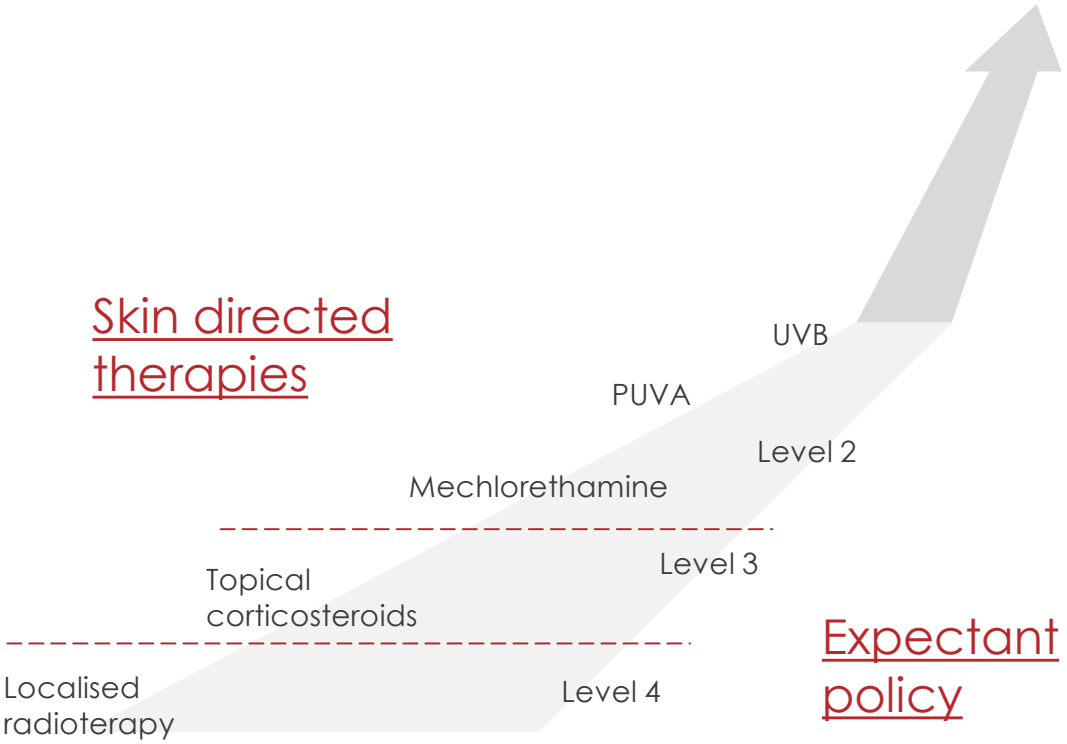


Early stage

FIRST LINE TREATMENT



$T_1N_0M_0B_0$, MF stage IA

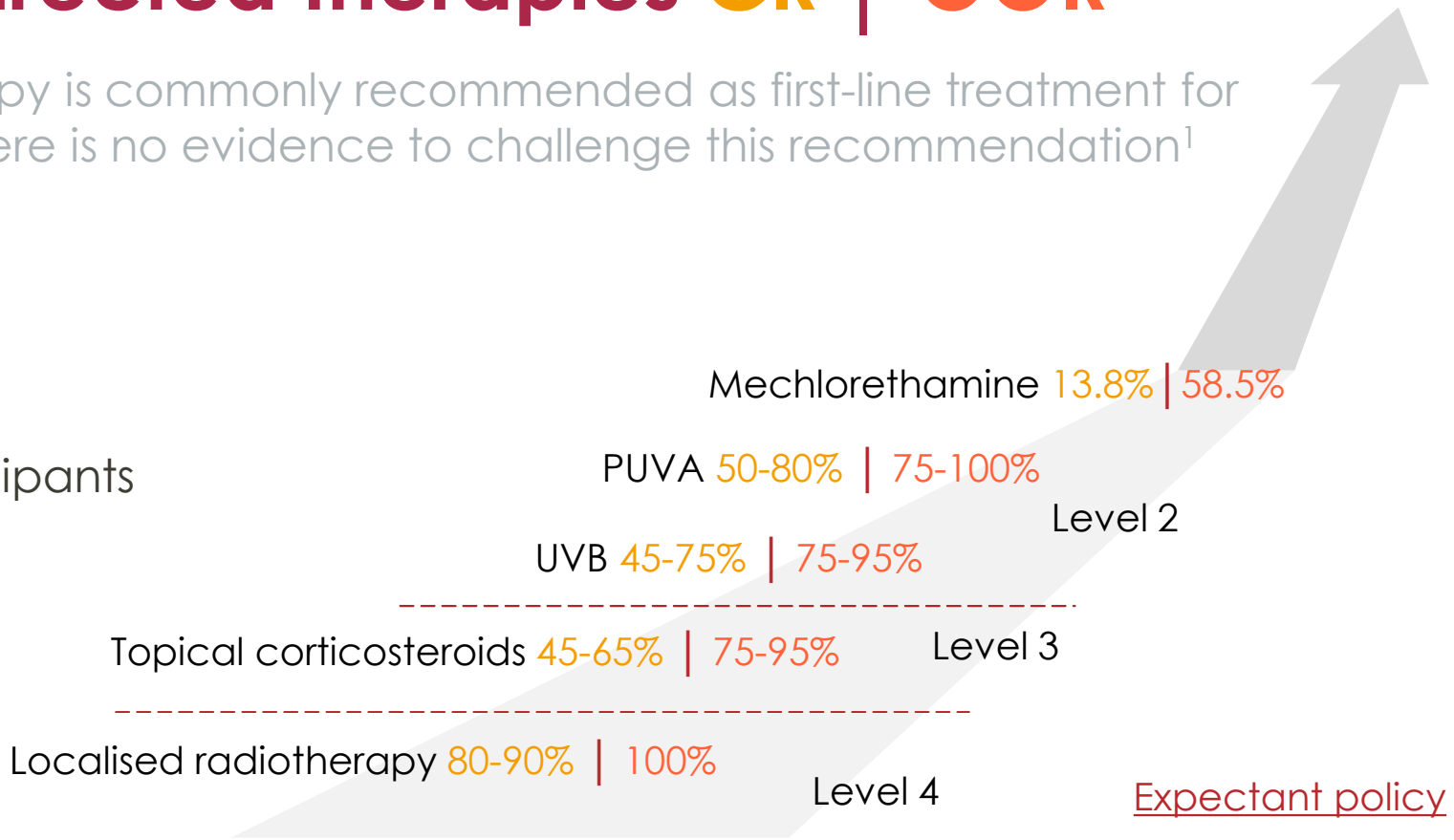


1. Trautinger, F., et al. Eur J Cancer 2017 **77**: 57-74.; 2. Zackheim, H. S. (2003). "Treatment of patch-stage mycosis fungoides with topical corticosteroids." Dermatol Ther **16**(4): 283-287.; 3. Zackheim, H. S., M. Kashani-Sabet and S. Amin (1998). "Topical corticosteroids for mycosis fungoides. Experience in 79 patients." Arch Dermatol **134**(8): 949-954.; 4. 2. Mehta-Shah, N., et al. J Natl Compr Canc Netw 2020 **18**(5): 522-536.

Skin directed therapies CR | OOR

Phototherapy is commonly recommended as first-line treatment for MF, and there is no evidence to challenge this recommendation[1]

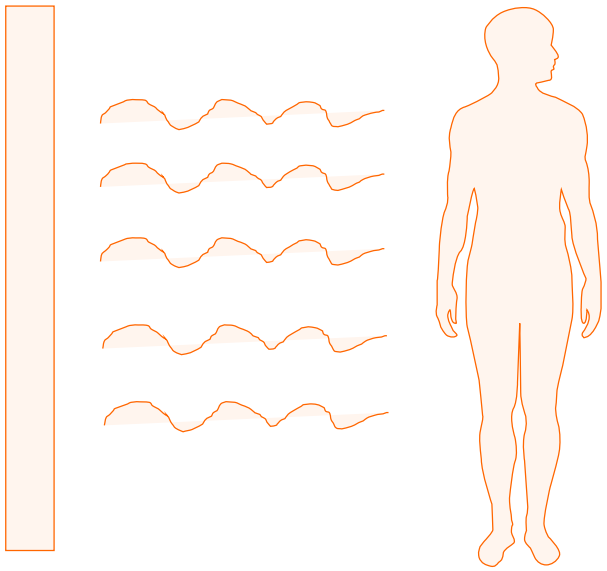
20 RCT
1369 participants



1. Valipour, A., M. Jager, P. Wu, J. Schmitt, C. Bunch and T. Weberschock (2020). "Interventions for mycosis fungoides." Cochrane Database Syst Rev **7**: CD008946.; 2. Agar NS et al. J Clin Oncol 2010;28:4730–9; 3. Lessin SR et al. JAMA Dermatol. 2013;149:25–32

UVB vs. PUVA

FOR EARLY STAGE MF



Systematic Review and Meta-analysis[4]:

- CR to PUVA (73%) > UVB (62%)
- Comparable side-effects

PUVA for MF

- First introduced in 1976
- ↑QoL[1] (prospective, randomized, single-center trial)

nbUVB for early MF

§ First demonstrated in 1999

§ Lack of evidence for inferiority[2] (comparative study)

§ Lack of prospective studes

Current consensus:

§ nbUVB for T1a and T2a (patches only)[3]

§ PUVA for T1b and T2b (plaques)[3]

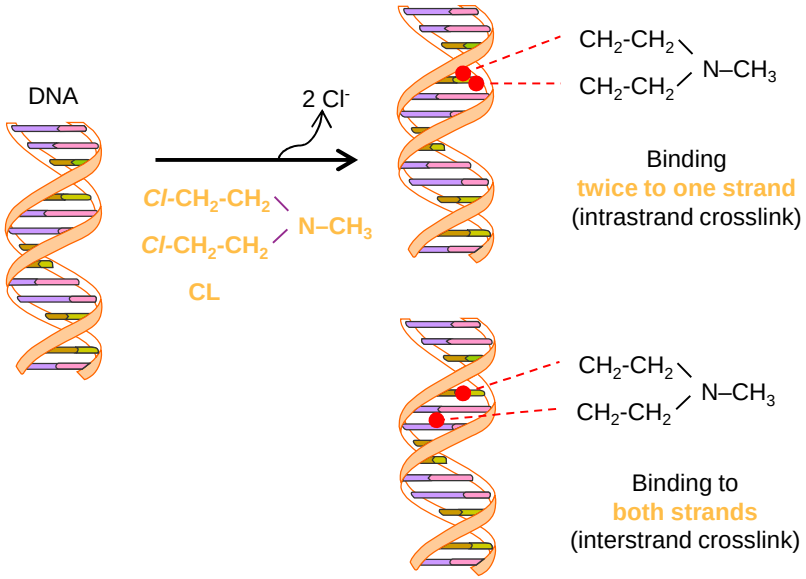
1. Graier T et al. Front Med. 2020 7:330; 2.P. Ponte, et al., J Eur Acad Dermatol Venereol 24, 716-721 (2010).; 3. Trautinger, F., et al. Eur J Cancer 2017 77: 57-74; 4. Phan K et al. JAMA Dermatol. 2019 155(3):335-341.

Topical Chlormethine

ALKYLATING AGENT (CHEMOTHERAPY)

- CHM gel is the most recently developed, stable and approved formulation[1]
- Topical agent for all MF stages[2]
- Can be applied to large areas[3,4]
- No systemic absorption[5]

- CAVEAT!
- Local irritative/allergic skin reactions-> assessment of response difficult



Bifunctional alkylating agent

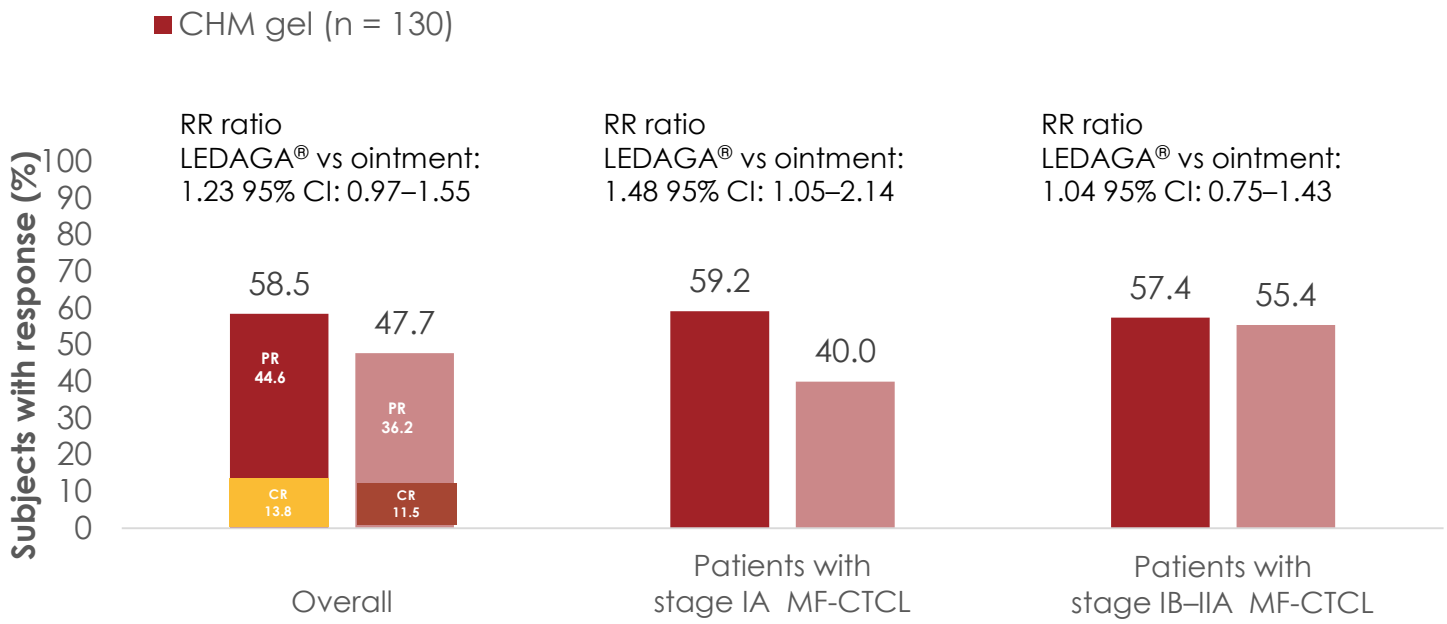
- Two reactive sites; connects via alkyl groups to DNA, RNA, and other proteins
- DNA replication blocked
- Apoptosis

1.Benjamin CA et al. Clin J Oncol Nurs 2015;19:E131−9; 2. LEDAGA® Assessment report. EMA 2016; Kim YH et al. Arch Dermatol 2003;139:165–73;; 4. Querfeld C et al, Deramtology 2021 4;1-11.; 5. Querfeld C et al. J Invest Dermatol. 2021 141(6):1601-1604.e2

Topical Chlormethine

CAILS RESPONSE[1]

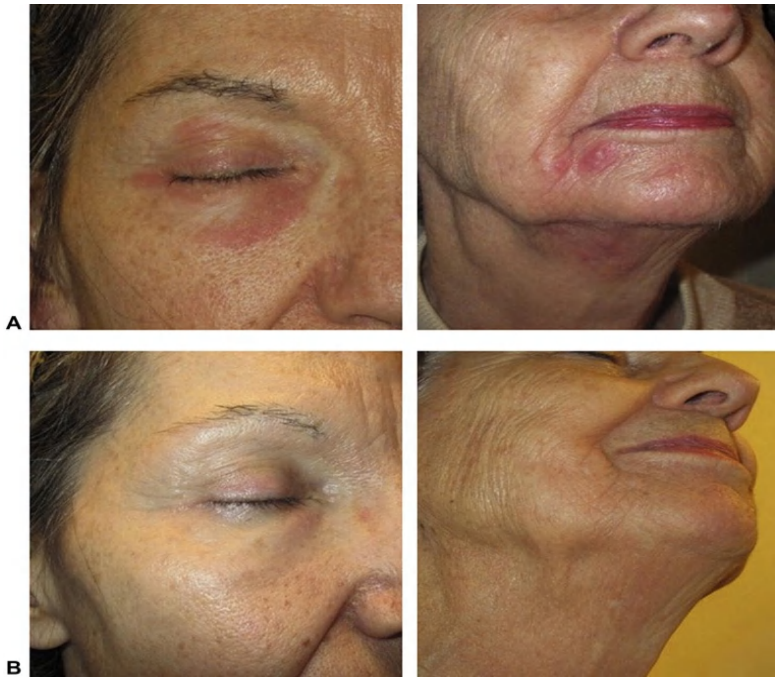
- CAILS: composite assessment of index lesion severity



1. Lessin SR et al. JAMA Dermatol. 2013;149:25–32; 2. Actelion 2017 Data on file

Radiotherapy for CTCL lesions

SECOND LINE TREATMENT



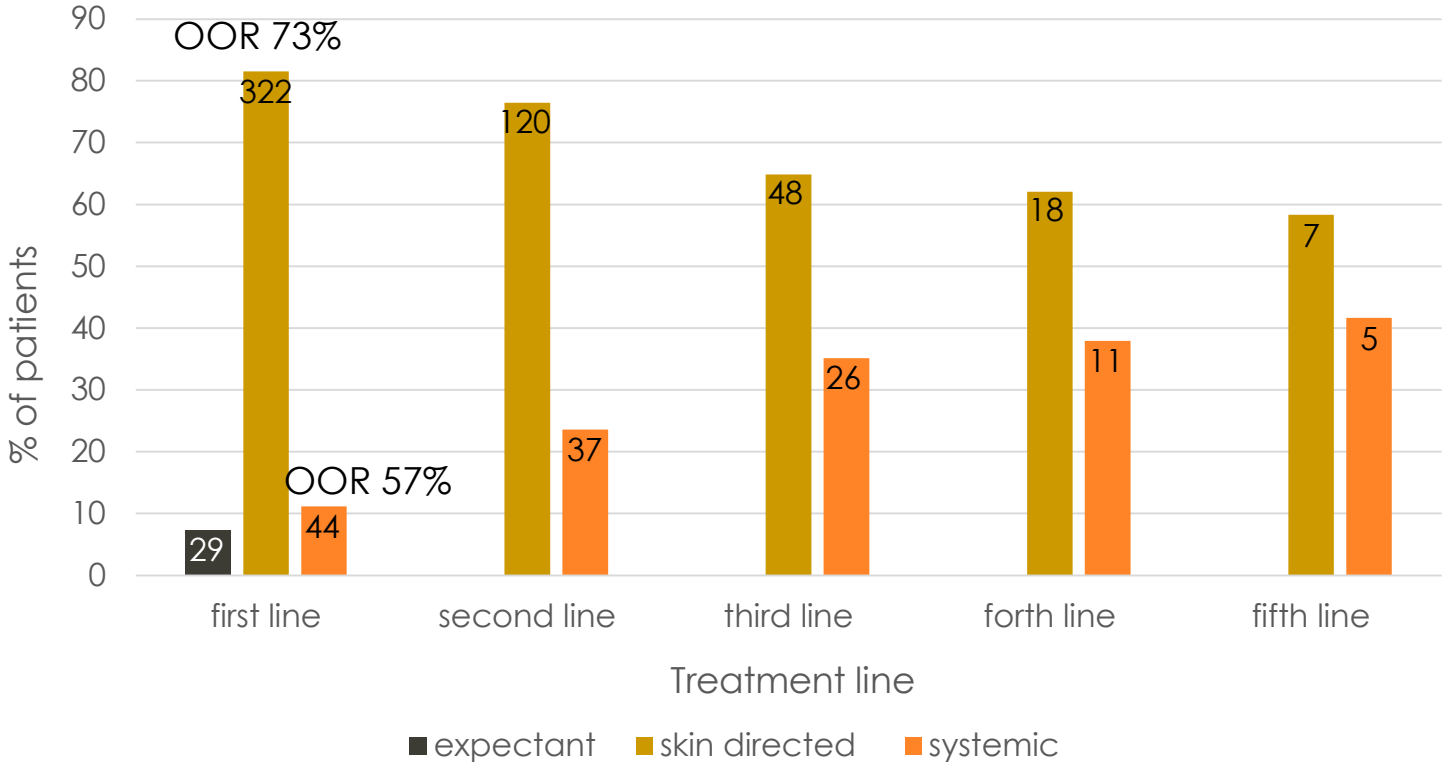
Low-dose brachytherapy for facial CTCL lesions.
Desimone JA et al, J Am Acad Dermatol. 2013 69(1):61-5

- **Palliative treatment**
- **May induce long term remission for unilesional disease[2]**
- **Improved survival**
  - Suggested in one smalls retrospective study in high-risk early-stage patients[3]
- **Dosage[1,2]**
  - Often up to 20-24gy
  - Better 2x4 Gy
- **FLASH-radiotherapy**
  - First in human application, MF patient[4]

1. L. Specht et al., Int J Radiat Oncol Biol Phys 92, 32-39 (2015); 2. J. A. DeSimone et al.,. Journal of the American Academy of Dermatology 69, 61-65 (2013): 3. J . T. O'Malley et al., Clin. Cancer Res. 26, 408-418 (2020).; J. Bourhis et al., Radiother Oncol 139, 18-22 (2019).

Physician treatment choice

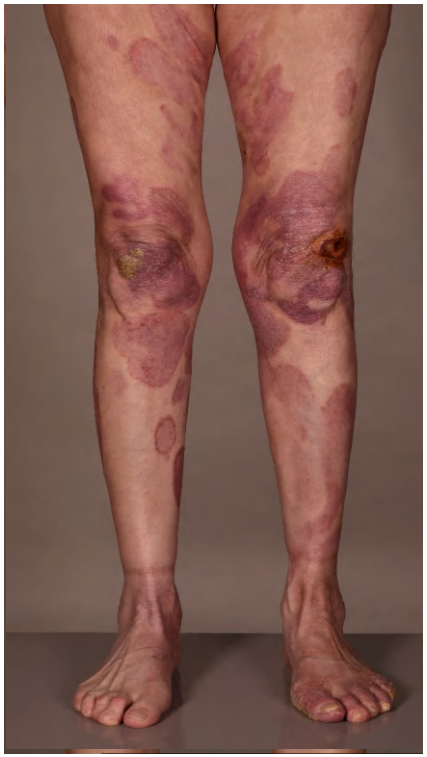
395 newly diagnosed patients with early-stage MF (IA-IIA)



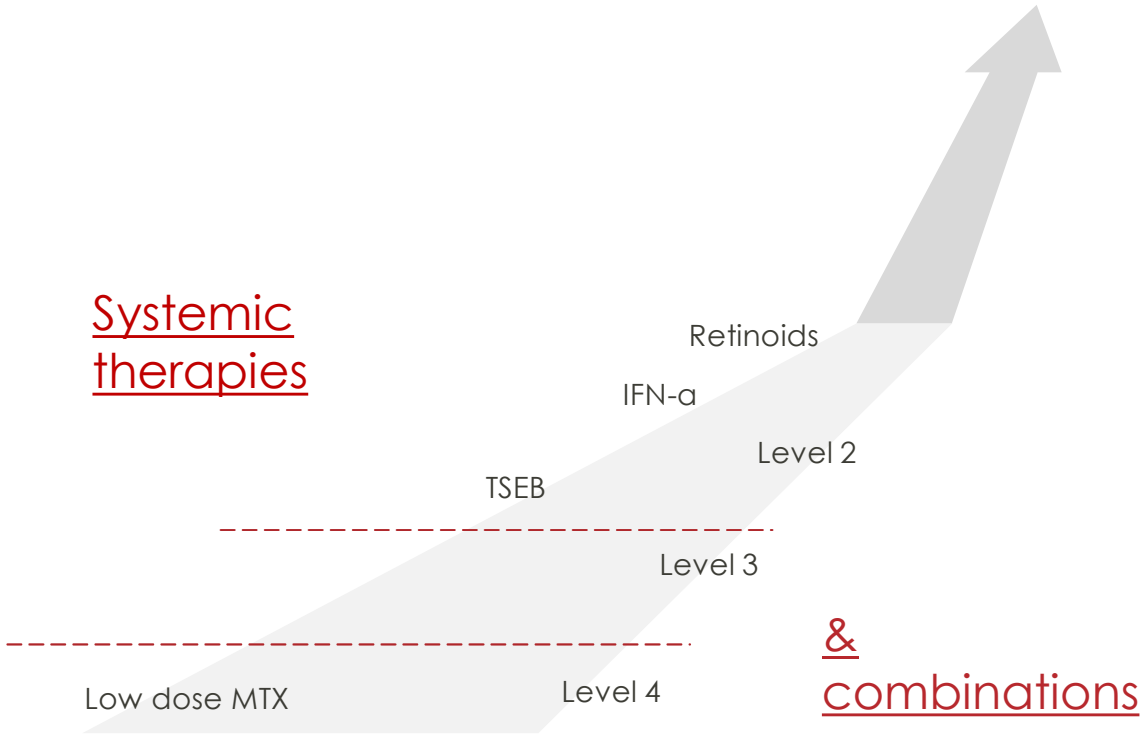
1. Quaglino, P., et al. "Treatment of early-stage mycosis fungoides: results from the PROspective Cutaneous Lymphoma International Study (PROCLIPI study)." Br J Dermatol. 2020 [epub, ahead of print]

Early stage

SECOND LINE TREATMENT



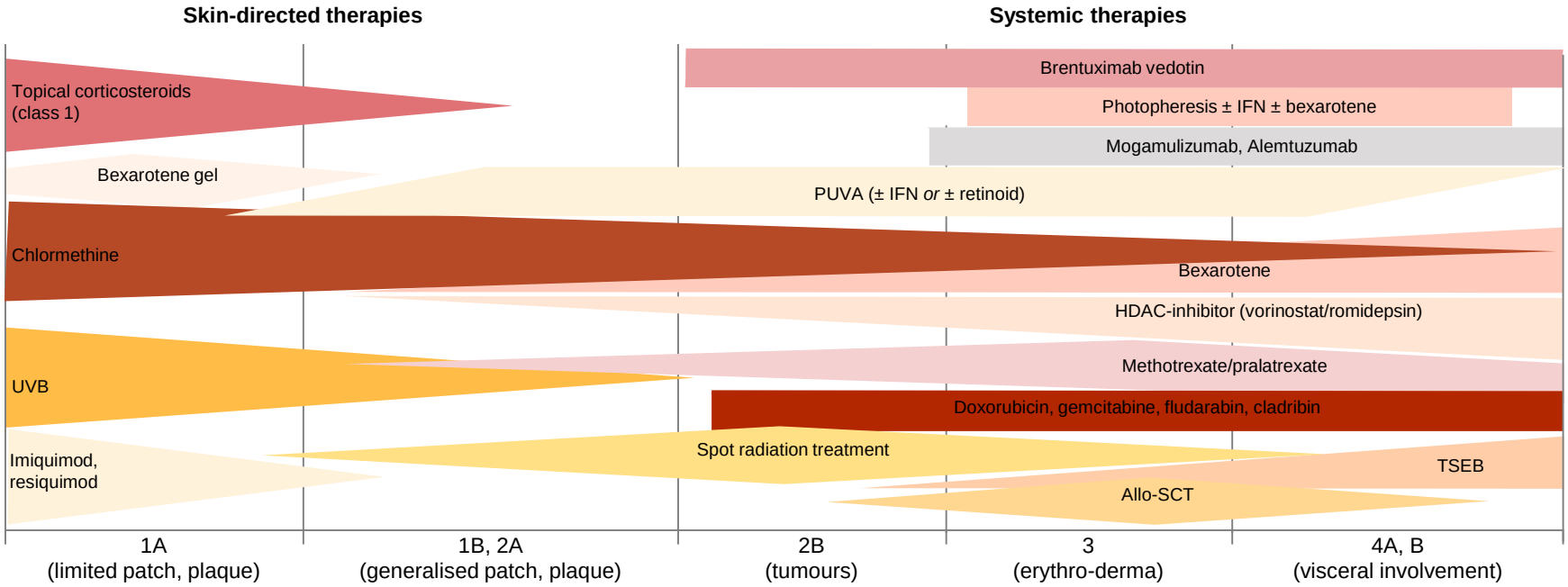
$T_2N_0M_0B_0$, MF stage IB



1. Trautinger, F., et al. Eur J Cancer 2017 **77**: 57-74.; 2. Zackheim, H. S. (2003). "Treatment of patch-stage mycosis fungoides with topical corticosteroids." Dermatol Ther **16**(4): 283-287.; 3. Zackheim, H. S., M. Kashani-Sabet and S. Amin (1998). "Topical corticosteroids for mycosis fungoides. Experience in 79 patients." Arch Dermatol **134**(8): 949-954.; 4. 2. Mehta-Shah, N., et al. J Natl Compr Canc Netw 2020 **18**(5): 522-536.

Late stage

TREATMENT OPTIONS

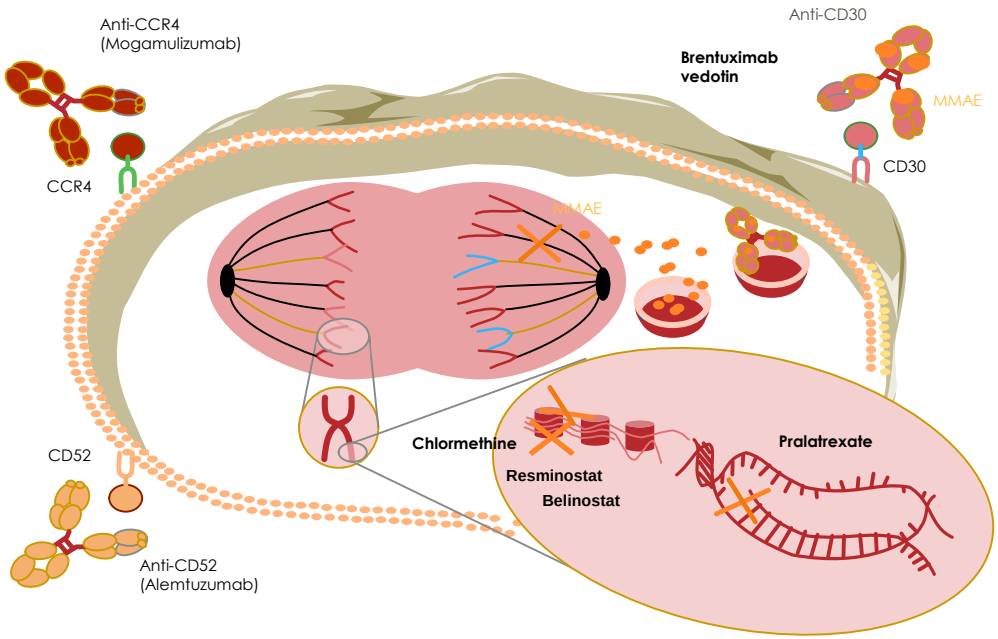


Allo-SCT, allogenic haematopoietic stem cell transplantation; IFN, interferon; HDAC; histone deacetylase; PUVA, psoralen and ultraviolet A; SS, Sézary syndrome; TSEB, total skin electron beam; UVB, ultraviolet B.

1. Bloom T, et al. Curr Treat Options Oncol 2012;1:102–21; 2. Trautinger F, et al. Eur J Cancer 2017;77:57–74; 3. Rook AH, et al. Blood 2015;126:1452–61; 4. Martínez-González MC, et al. Eur J Dermatol 2008;18:148–52; 5. Willemze R, et al. Ann Oncol 2018;29:iv30–40; Quaglino P, et al. Br J Dermatol. 2020 [ahead of print].

Specific drug development

FOR CUTANEOUS T CELL LYMPHOMA

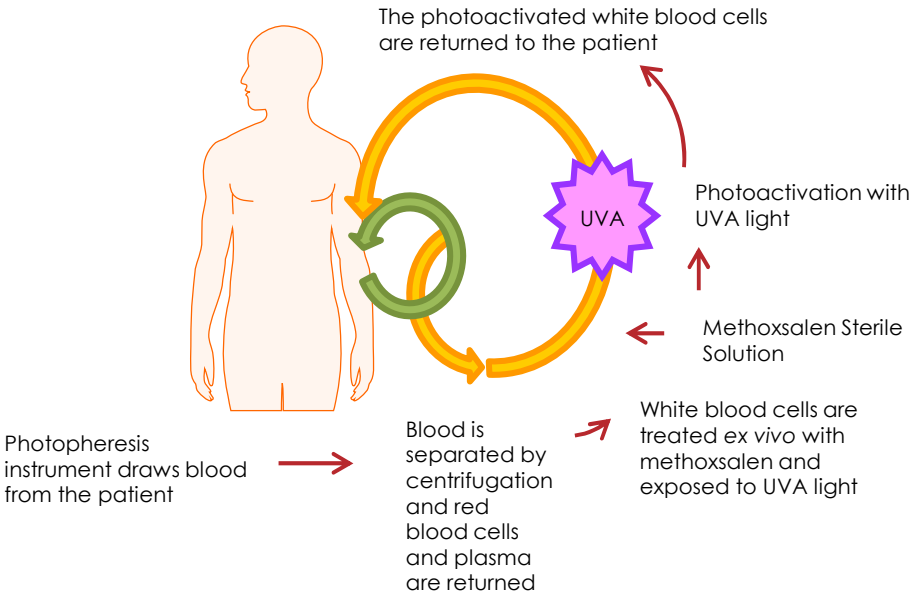


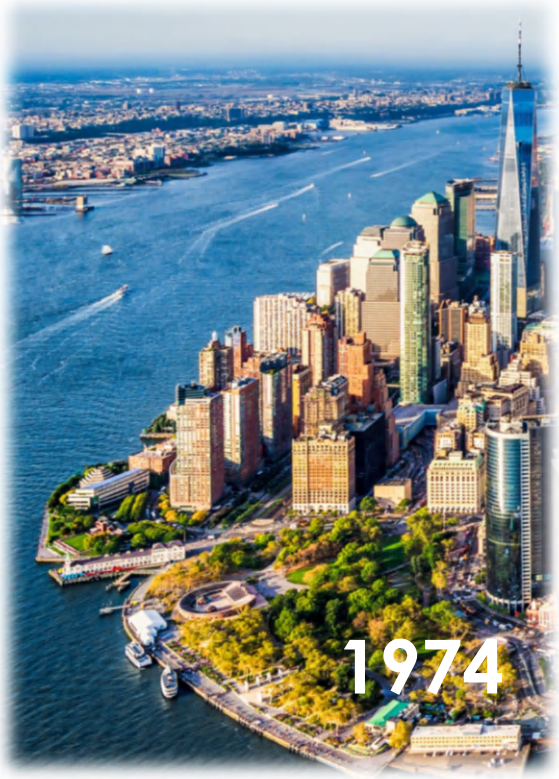
Drugs	Class	Indications	Status CH
Photopheresis	Medical device	US and Europe: L-CTCL (1988)	L-CTCL (2020)
Bexaroten	retinoid X receptors agonist	US (1999) and Europe (2001): CTCL	Not yet approved
Pralatrexate	Antifolate	US FDA: PTCL (2009)	PTCL
Romidepsin	HDAC inhibitor	US FDA: CTCL (2009) and PTCL (2011)	
Brentuximab vedotin	Anti-CD30 ADC	US FDA and Europe: ALCL (2011) and CTCL (2017)	sALCL CTCL
Belinostat	HDAC inhibitor	US FDA: PTCL (2014)	
Mogamulizumab	Anti-CCR4 mAb	Japan: ATLL (2012) PTCL and CTCL (both 2014) US FDA and Europe EMA (2018)	Not yet approved
CL gel	Topical alkylating agent	US FDA: MF-CTCL (2013) Israel (2016) Europe EMA (2017)	Not yet approved
Forodesine	PNP inhibitor	Japan: PTCL (2017)	

ADC, antibody drug conjugate; ALCL, anaplastic large-cell lymphoma; ATLL, adult T-cell leukaemia lymphoma; CCR, C–C chemokine receptor; CD, cluster of differentiation; CH, Switzerland; CL, chlormethine; EMA, European Medicines Agency; FDA, Food and Drug Administration; mAb, monoclonal antibody; MMAE, monomethyl auristatin E; PNP, purine nucleoside phosphorylase; PTCL, peripheral T-cell lymphoma; sALCL, systemic anaplastic large-cell lymphoma; US, United States.

Extracorporeal photopheresis

LEUKAPHERESIS + PHOTOCHEMOTHERAPY1,2





1. . R. Edelson et al. Successful management of the Sézary syndrome. Mobilization and removal of extravascular neoplastic T cells by leukapheresis. NEJM 1974; 291: 293–4.
2. R. Edelson et al. Treatment of Cutaneous T-Cell Lymphoma by Extracorporeal Photochemotherapy. N Engl J Med 1987 316:297-303

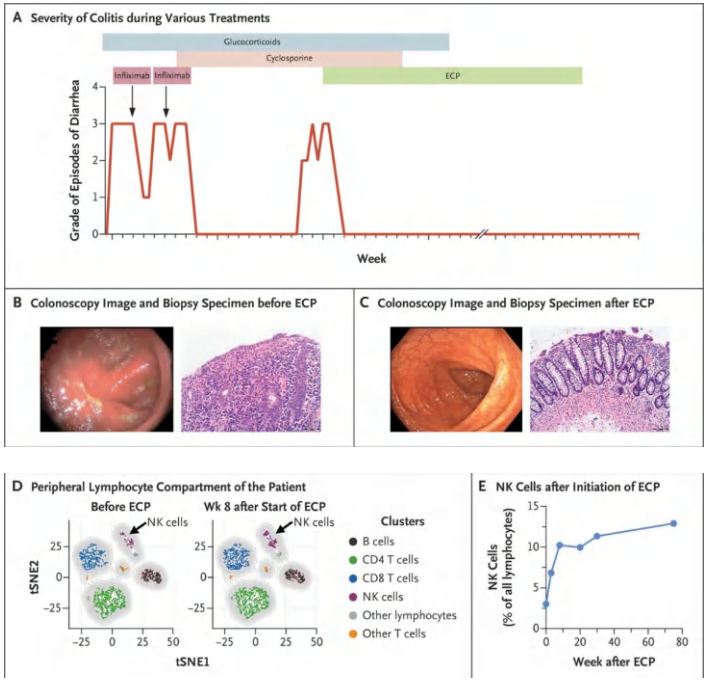
Extracorporeal photopheresis

OBSERVATIONS REGARDING MODE OF ACTION

- Damaged DC à T_{REG} ; apoptosis
- IL-1 and integrin signaling pathways ↑
- CD14+ monocytes à T cell proliferation
- CD71 as surrogate for T cell proliferation ↓
- Neutrophils dampen APC activation
- Plus IL-2 for GvHD
- Antigen-specific T- & B-cell responses ≈
- NK cells numbers and function ↑

ECP for Colitis Induced by Checkpoint-Inhibitor Therapy[8]

29-year-old man[8]



1. Ying Z, et al. Oncotarget. 2019;10(34):3183-97; 2.Wiese F, et al. Clin Exp Immunol. 2019;195(3):369-80.; 3. Schwab L, et al. Vox Sang. 2019.; 4.Ni M, et al. Front Immunol. 2019;10:547.; 5. Franklin C, et al. J Leukoc Biol. 2019;106(2):481-93.; 6. Belizaire Ret al. Blood Adv. 2019;3(7):969-79.; 7. Wang L, et al. Front Immunol. 2018;9:2207.; 8. Apostolova P. et al. (2020) New Engl J Med. 382(3):294-296.. 9. Iselin C. et al. (2021) Oncoimmunology. 10(1):1873530.

Extracorporeal photopheresis

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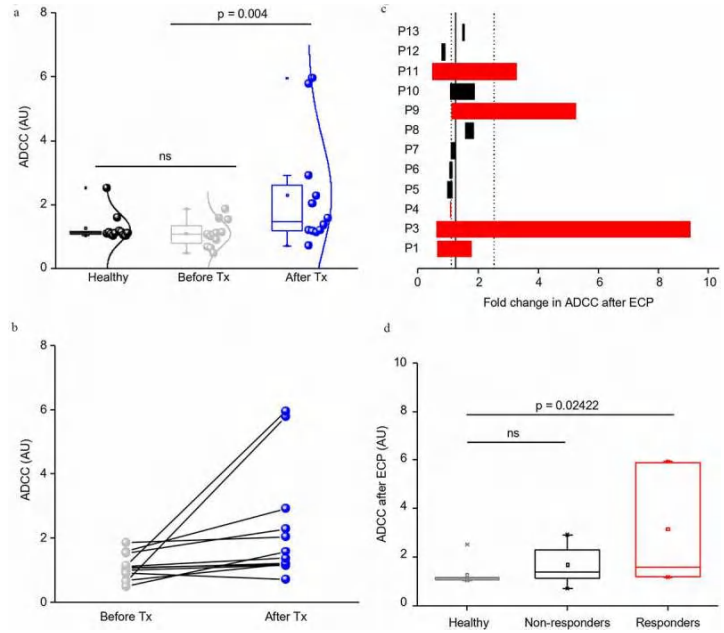
↑ ADCC is associated with treatment response[9]

Cohort study[9]

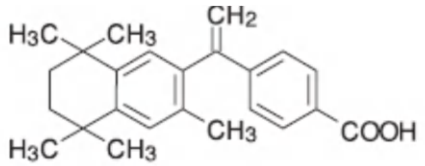


1. Ying Z, et al. Oncotarget. 2019;10(34):3183-97; 2.Wiese F, et al. Clin Exp Immunol. 2019;195(3):369-80.; 3. Schwab L, et al. Vox Sang. 2019.; 4.Ni M, et al. Front Immunol. 2019;10:547.; 5. Franklin C, et al. J Leukoc Biol. 2019;106(2):481-93.; 6. Belizaire Ret al. Blood Adv. 2019;3(7):969-79.; 7. Wang L, et al. Front Immunol. 2018;9:2207.; 8. Apostolova P. et al. (2020) New Engl J Med. 382(3):294-296.. 9. Iselin C. et al. (2021) Oncoimmunology. 10(1):1873530.

Bexarotene

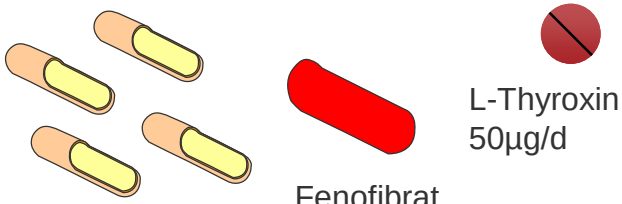
SELECTIVE RETINOID X RECEPTOR AGONIST[1,2,3]

- approved by the FDA and EMA since 1999 for the treatment of advanced CTCL
- exact mechanism of action in CTCL unknown
- dosage:300mg/m2/day
- overall response: 30-50%



http://targretin.com

- CAVEAT!
- hypertriglyceridemia (associated rarely with pancreatitis) and hypothyroidism

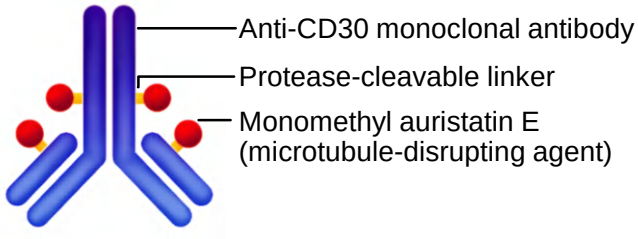


1. Gniadecki R et al. Br J Dermatol. 2007 157(3):433-40; 2. Amitay-Laish I et al. J Dermatolog Treat. 2019 30(3):258-263.: 3. Hamada T et al. J Dermatol. 2019 46(7):557-563.

Brentuximab vedotin

ANTIBODY-DRUG CONJUGATE[1]

- Anti-CD30 monoclonal antibody
- Monomethyl auristatin E (microtubule-disrupting agent)
- Protease-cleavable linker



- CAVEAT!
- Peripheral neuropathy

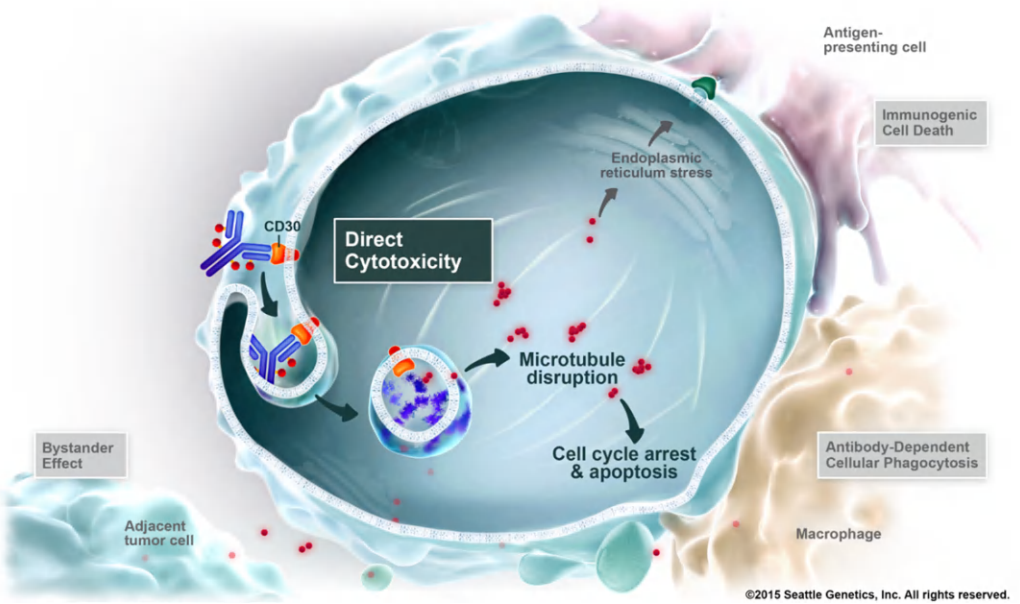
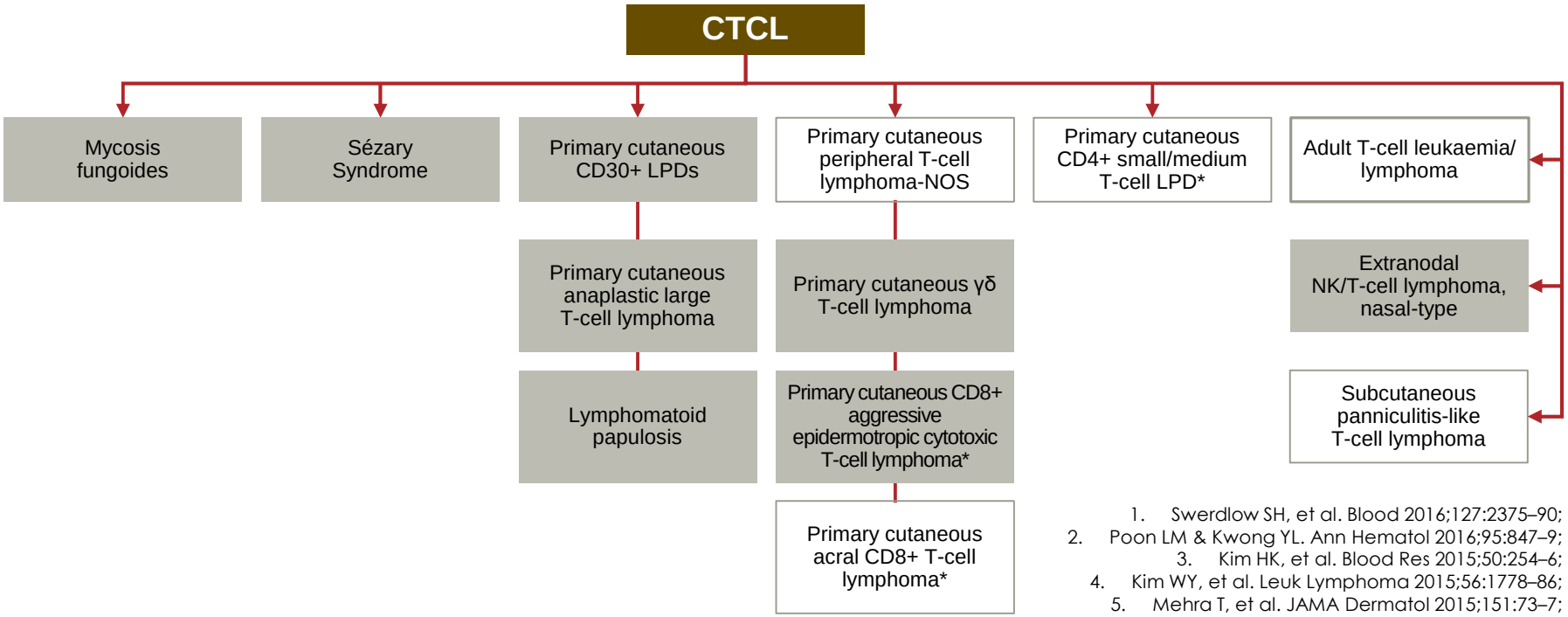


Figure used with permission from Seattle Genetics, Inc.

1. Katz J, et al. Clin Cancer Res 2011;17:6428–36.

Subtypes of primary cutaneous lymphoma

REPORTED CD30 EXPRESSION



1. Swerdlow SH, et al. Blood 2016;127:2375–90;
2. Poon LM & Kwong YL. Ann Hematol 2016;95:847–9;
3. Kim HK, et al. Blood Res 2015;50:254–6;
4. Kim WY, et al. Leuk Lymphoma 2015;56:1778–86;
5. Mehra T, et al. JAMA Dermatol 2015;151:73–7;
6. Cyrenne BM, et al. Int J Dermatol 2017;56:1448–50;
7. Rubio-Gonzalez B, et al. JAMA Dematol 2016;152:1388–90:
8. Wehkamp U et al. Br J Dermatol. 2021 [Online ahead of print].

Subtypes of primary cutaneous lymphoma

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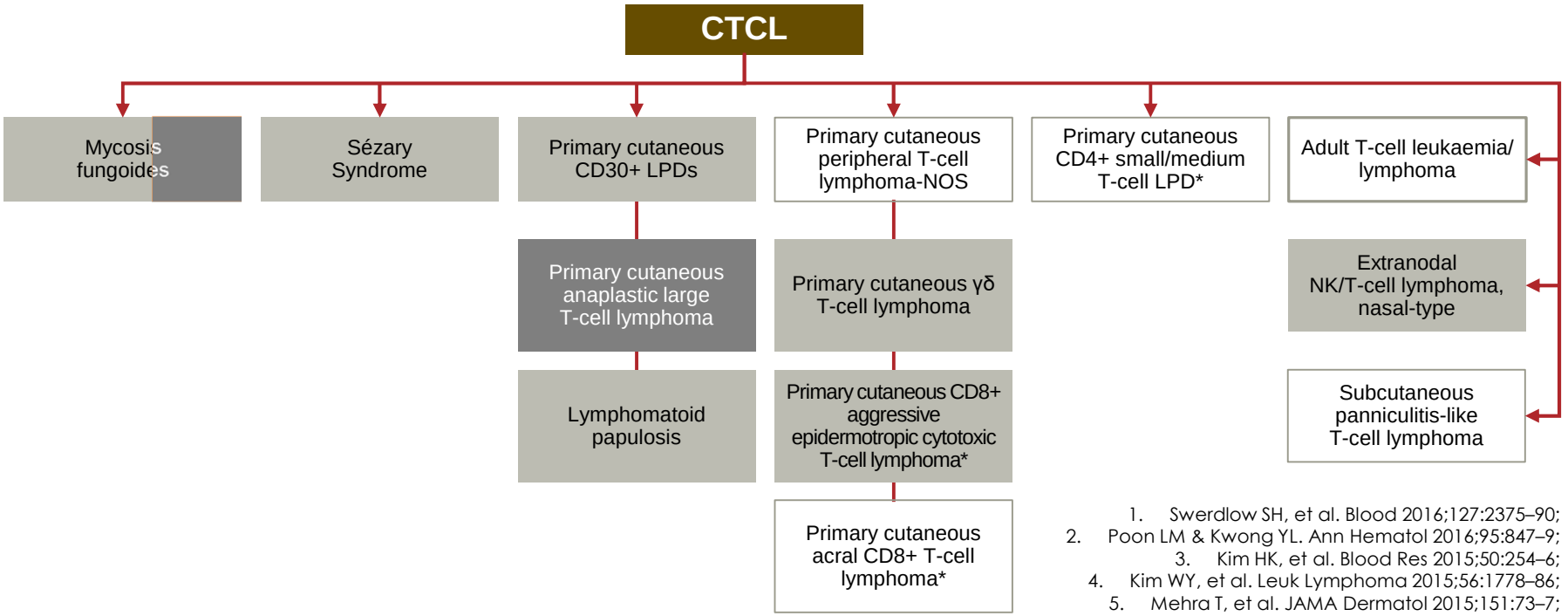

1. Swerdlow SH, et al. Blood 2016;127:2375–90;
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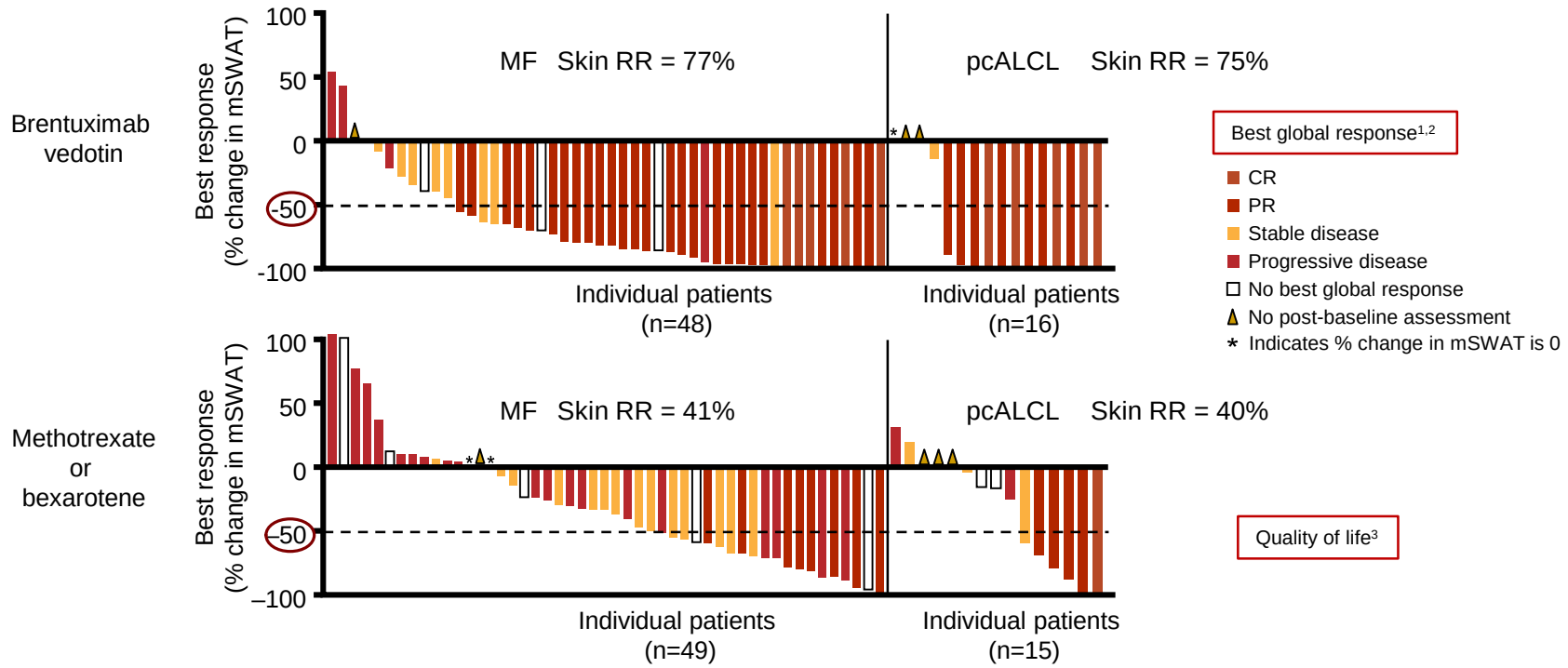
6. Cyrenne BM, et al. Int J Dermatol 2017;56:1448–50;
7. Rubio-Gonzalez B, et al. JAMA Dematol 2016;152:1388–90:
8. Wehkamp U et al. Br J Dermatol. 2021 [Online ahead of print].

Brentixumab

MAXIMUM PERCENTAGE CHANGE IN SKIN mSWAT SCORE



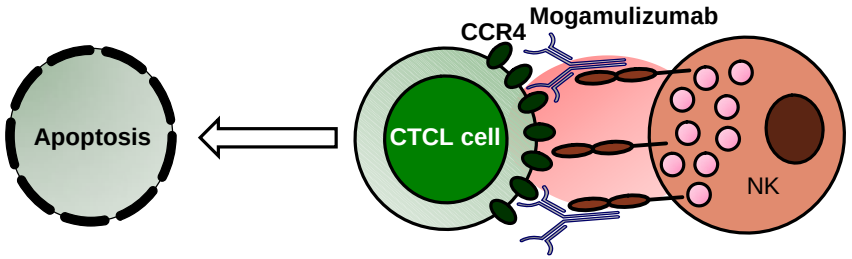
mSWAT: modified severity weighted assessment tool

1. Prince HM, et al. Lancet 2017;390:555–66;
2. Kim YH, et al. Oral presentation at SID 2017 (abst 262).
3. Dummer R, et al. Eur J Cancer. 2020 33:120-130.

Mogamulizumab

HUMANISED ANTI-CCR4 ANTIBODY

- Targets CCR4+ skin homing T cells
- CCR4 is expressed throughout all stages of CTCL[1-4]
- Induces antibody mediated ADCC[5]
- Phase III study of mogamulizumab versus vorinostat[6]



Higher ADCC due to a defucosylated Fc region

- CAVEAT!
- Skin rash -> assessment of response difficult[7]
- Infections (pneumonia)[7]

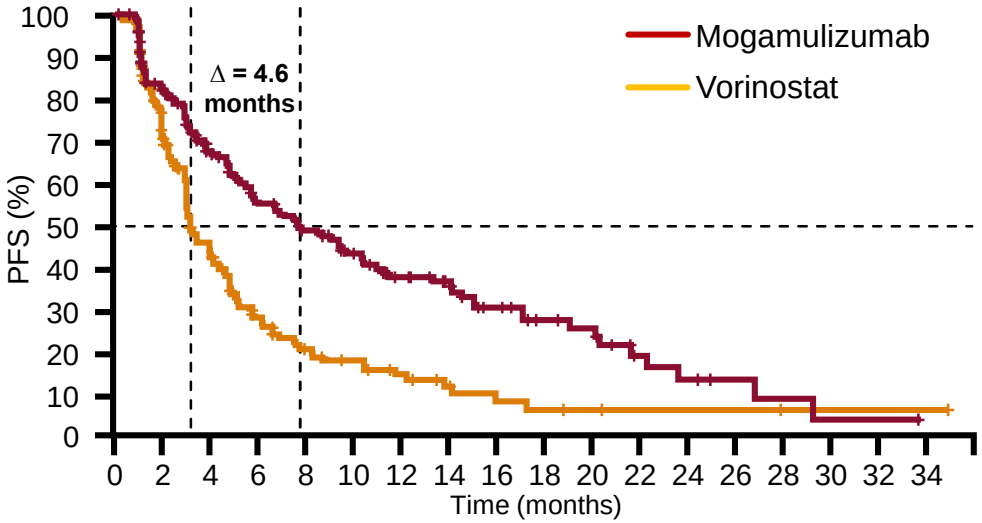
ADCC: antibody-dependent cellular cytotoxicity
CCR4: CC chemokine receptor 4

1.Ferenczi K, et al. *J Invest Dermatol*. 2002;119:1405-1410. 2.Kallinich T, et al. *J Invest Dermatol*. 2003;121:1045-1052. 3.Krejsgaard T, et al. *Semin Immunopathol*. 2017;39:269-282. 4.Saeki H, Tamaki K. *J Dermatol Sci.* 2006;43(2):75-84. 5. Subramaniam JM et al. Drugs 2012;72:1293–8; 6. Kim YH et al, Lancet Oncol. 2018 Sep;19(9):1192-1204; 7.https://www.ema.europa.eu/en/medicines/human/EPAR/poteligeo

Mogamulizumab

CLINICAL RESPONSE

Progression-free survival by investigator assessment[1]

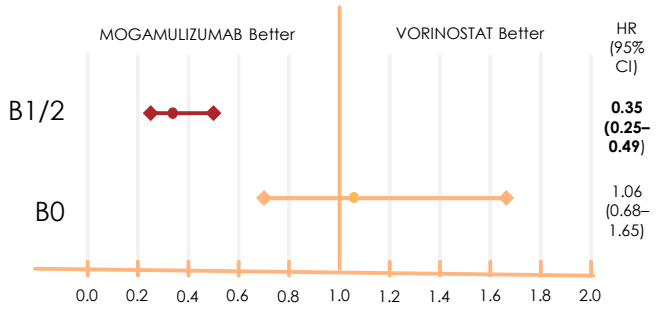


	Mogamulizumab	Vorinostat
Median PFS, months	7.7	3.1

Response rate[2]

	Mogamulizumab	Vorinostat
ORR, n/N	52/186 (28%)	9/186 (5%)
MF	22/105 (21%)	7/99 (7%)
SS	30/81 (37%)	2/87 (2%)

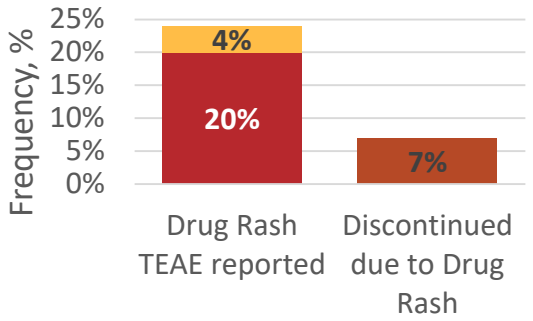
Progression-free survival stratified by B-class[3]

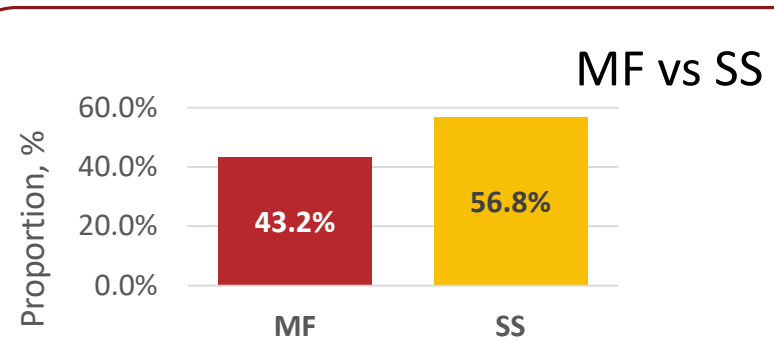


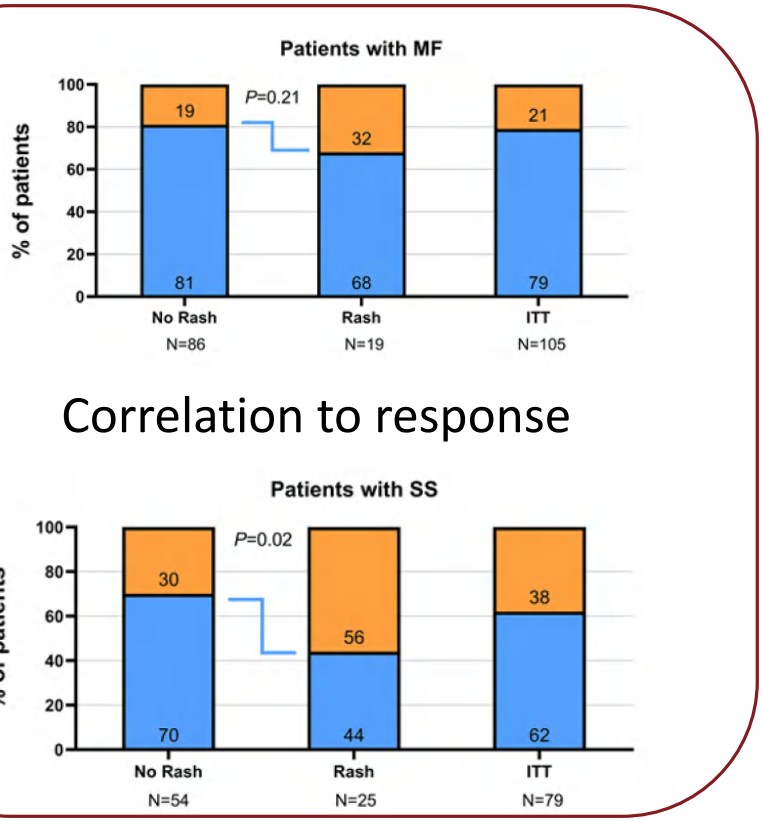
1. Kim, YH et al. Blood 2017;130:817.; 2. Kim YH et al, Lancet Oncol. 2018 Sep;19(9):1192-1204; 3.https://www.ema.europa.eu/en/medicines/human/EPAR/poteligeo

Mogamulizumab

DRUG RASH in the MAVORIC trial (n=184)



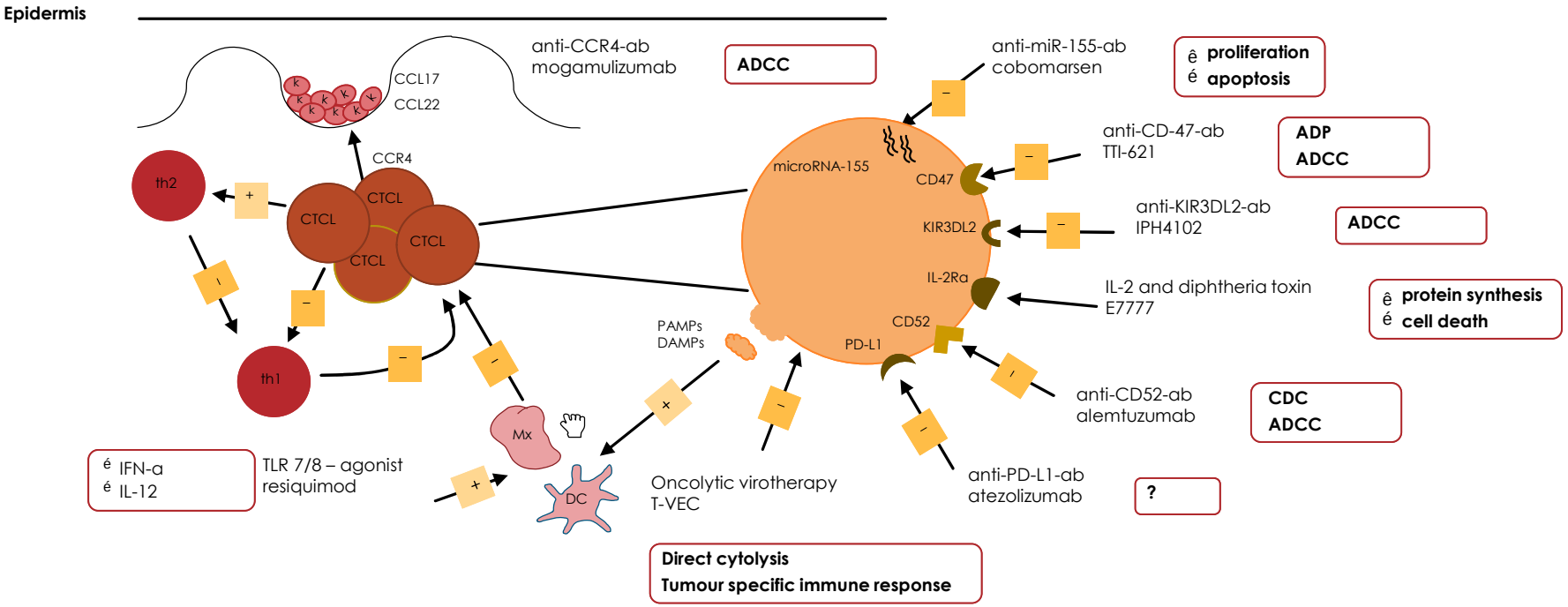




1. *Musiek Am et al. Blood*. 2020;136(Supplement 1): 23–24.

OUTLOOK

PRODUCTS UNDER INVESTIGATION[1]



ADCC, antibody-dependent cell-mediated cytocoxicity; ADP, antibody-dependent phagocytosis; CDC, complement-dependent cytotoxicity; DC, dendritic cell; IL, interleukin; TLR, Toll-like receptor.

1. Ramelyte E, Dummer R, Guenova E. Investigative drugs for the treatment of cutaneous T-cell lymphomas (CTCL): an update. 2019 (9):799-809.

CUTANEOUS T CELL LYMPHOMA

CONCLUSION

EMMANUELLA GUENOVA, MD, PhD

virtuel | 18.09.2021

THANK YOU!

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