Webinars
Cutaneous Lymphoma

EuroBloodNet Topic on Focus

Patients' Organizations

Leids Universitair Medisch Centrum

Rare cancers

STICHTING HUID LYMFOOM

Speakers Prof. Maarten Vermeer, Mieke de Leeuw, Susan Thornton

Dutch Cutaneous Lymphoma Foundation (**Stichting Huidlymfoom**)

ERN-EuroBloodNet subnetwork
Country Netherlands
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LYMPHOMA COALITION

CUTANEOUS LYMPHOMA FOUNDATION

France Lymphome Espoir

EURORDIS RARE DISEASES EUROPE

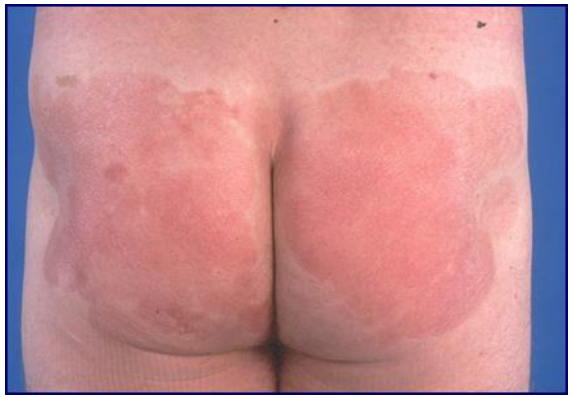
European Reference Network for rare or low prevalence complex diseases
Network Hematological Diseases (ERN EuroBloodNet)

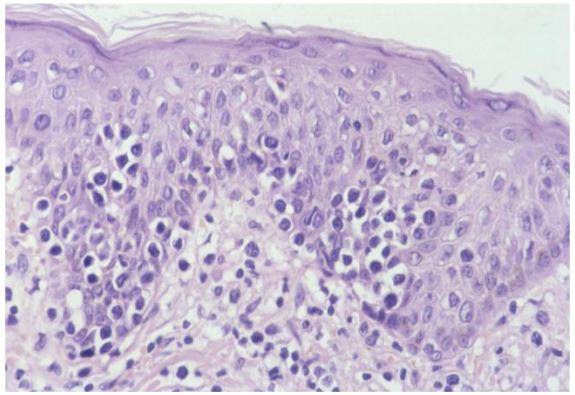
Cutaneous Lymphoma

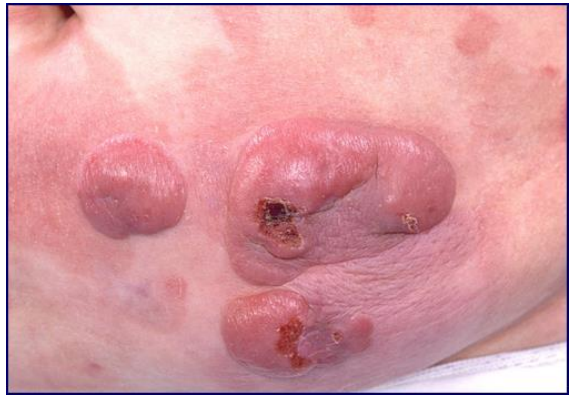
- A rare group of malignancies derived from lymphocytes that present in the skin.
- Different types of cutaneous lymphoma differ in prognosis and treatment approach.
- Diagnosis and treatment of cutaneous lymphomas needs specific expertise.
- Combining the clinical picture with skin histology is essential to make correct diagnosis.

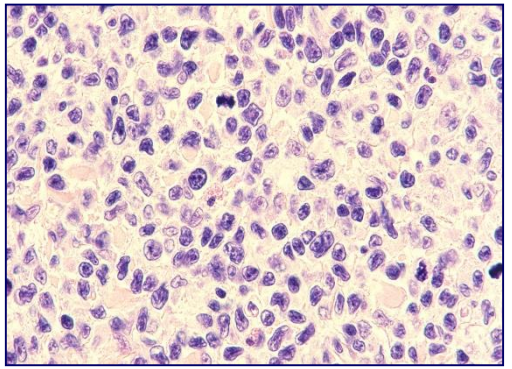
Mycosis Fungoides

- Most common type of CTCL (ca. 50%).
- Large majority of patients start with eczematous skin lesions (patches and plaques). In years to decades a slow progression is seen from patches to plaques to tumors.
- Development of nodal or visceral disease in a minority of patients.

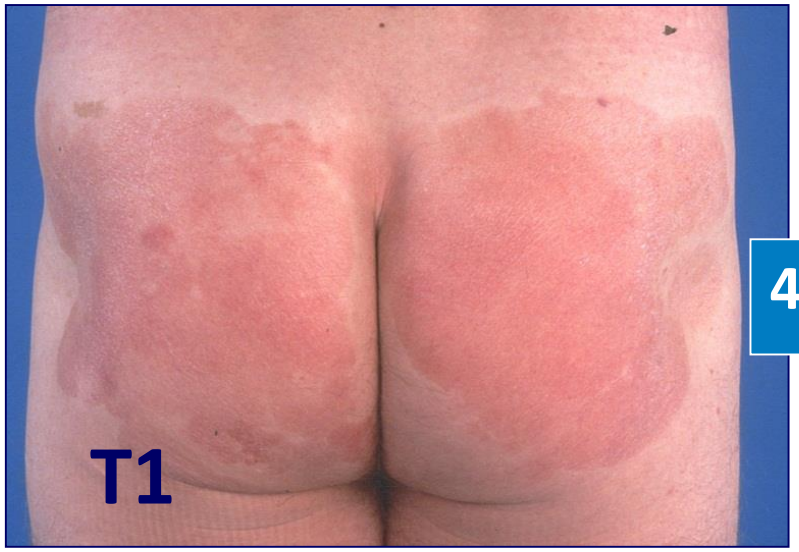








MF Clinical stage and Prognosis



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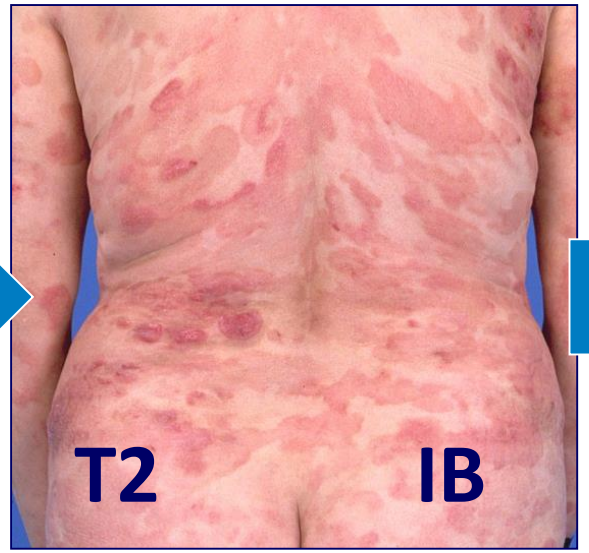

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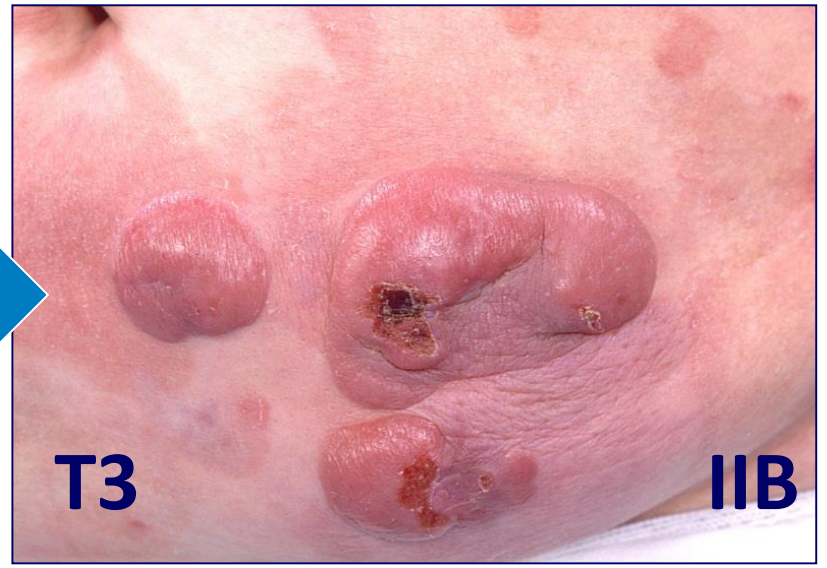

Patches

Plaques

Tumors

10-yr DSS: 97%

10-yr DSS: 83%

10-yr DSS: 42%

Therapy Mycosis Fungoides

Diagnosis

- Inspection of skin
- Skin histology

Staging

- Only if indicated by additional symptoms

Treatment

- MF limited to the skin:
  - Skin-directed therapies (SDT).
  - Type of SDT adjusted to the type and extent of skin lesions (patch plaque tumor)
- Nodal or visceral involvement:
  - Systemic therapy, combined with or followed by SDT.

Of note:

- Early agressive treatment with CHOP-chemotherapy does not improve prognosis (Kaye: NEJM 1989;321:1784-90).

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

EORTC
The future of cancer therapy

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

European Journal of Cancer 77 (2017) 57–74

NCCN National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Primary Cutaneous Lymphomas

Version 2.2020 — April 10, 2020

NCCN.org

GUIDELINES

BJD British Journal of Dermatology

British Association of Dermatologists and U.K. Cutaneous Lymphoma Group guidelines for the management of primary cutaneous lymphomas 2018

D. Gilson,[1] S.J. Whittaker,[2] F.J. Child,[2] J.J. Scarisbrick,[3] T.M. Illidge,[4] E.J. Parry,[5] M.F. Mohd Mustapa,[6] L.S.Exton,[6] E. Kanfer,[7] K. Rezvani,[8] C.E. Dearden[9] and S.L. Morris[10]

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[10]Guy's and St Thomas' NHS Foundation Trust, Guy's Hospital, London SE1 9RT, U.K.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Annals of Oncology 29 (Supplement 4): iv30–iv40, 2018
doi:10.1093/annonc/mdy133

CLINICAL PRACTICE GUIDELINES

Primary cutaneous lymphomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

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European Reference Network
for rare or low prevalence complex diseases
Network Hematological Diseases (ERN EuroBloodNet)

Webinars
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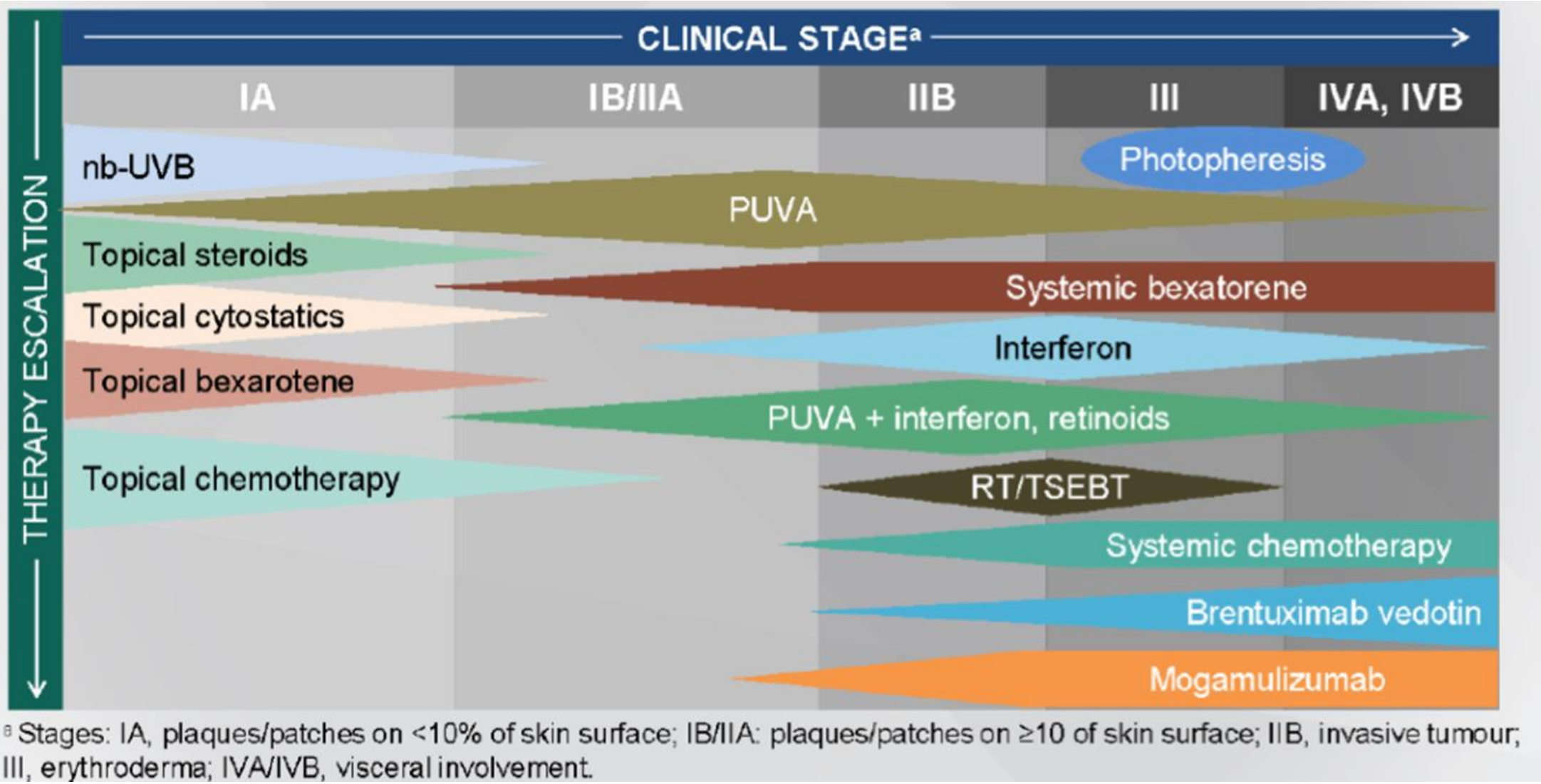
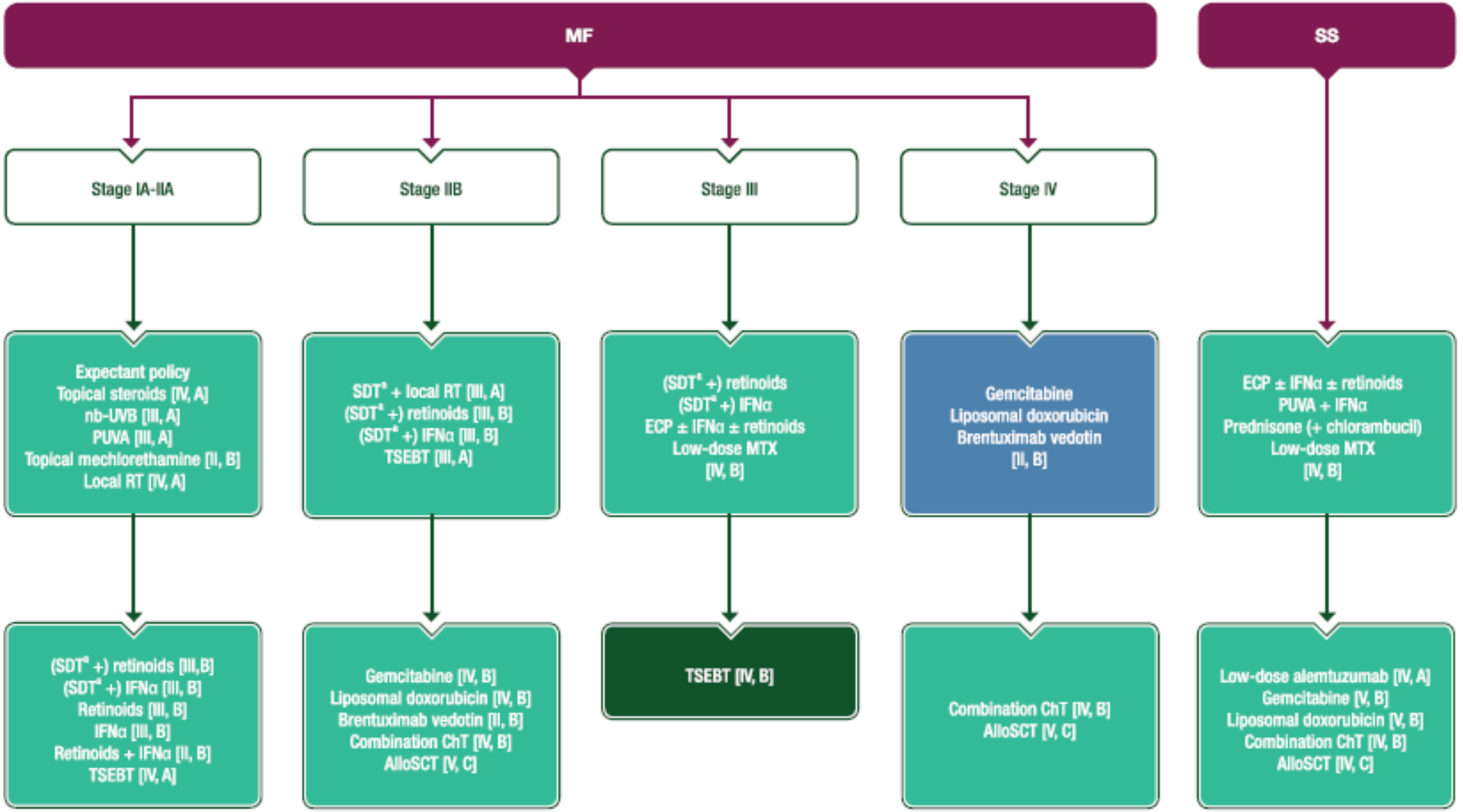
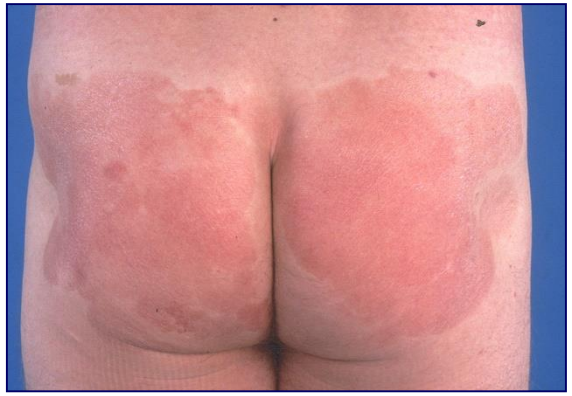


[a] Stages: IA, plaques/patches on <10% of skin surface; IB/IIA: plaques/patches on ≥10 of skin surface; IIB, invasive tumour; III, erythroderma; IVA/IVB, visceral involvement.

Example from ESMO Guideline



Therapy MF patch/plaque



- Local steroids.
  - Clobetasol propionate, 1dd, 4-7x a week

- Phototherapy (PUVA) 2 to 3x a week.
  - Normal schedule as in psoriasis en eczema.
  - In exceptional cases maintenance-PUVA 1x/ week-2 weeks.
  - Can be combined with: IFNα 3x a week $3x10^6$ IU or retinoids

- Local chemotherapy (chlormethine).
  - Chlormethine gel 1dd 4-7x a week

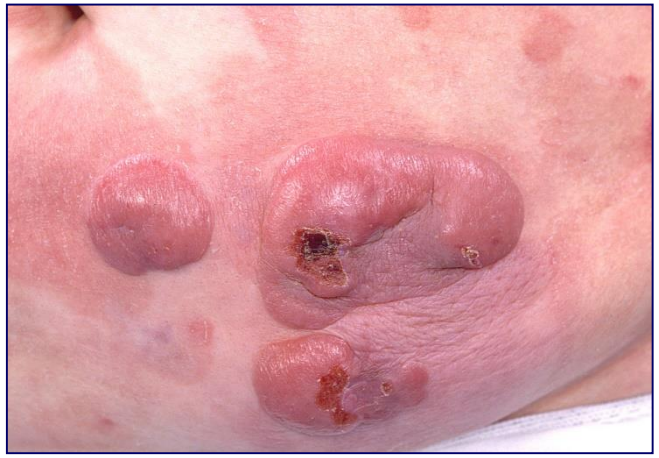
- Phototherapy (UVB; TL-01), only in minimaly infiltrated lesions.

Therapy MF tumors

- Generalised plaques/tumors
  - PUVA + Neotigason 0,5 mg/kg
  - PUVA + Interferon-α 3x a week $3x10^6$ IU

- One or several tumors:
  - Local radiotherapy, **8Gy** - 20Gy

- Generalised tumors:
  - Total skin electron beam



MF treatment ≥ stage IIB

- A small proportion of MF patients (15%) develop nodal or visceral disease or widespread tumors not responsive to skin-targeted therapies.

- Traditionally treated with CHOP.
- Increasing reluctance to use CHOP because of therapy-induced immunosuppression.

- Increasing number of new treatment modalities, but exact place in treatment MF has still to be defined.

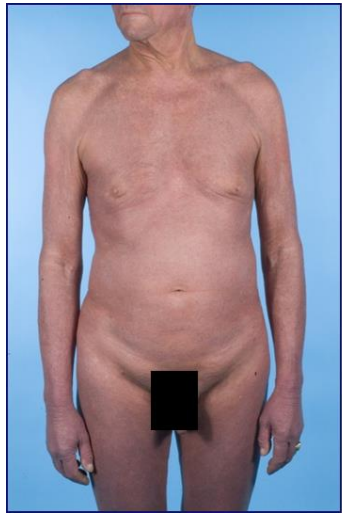
Therapies in Clinic for MF ≥ stage IIB

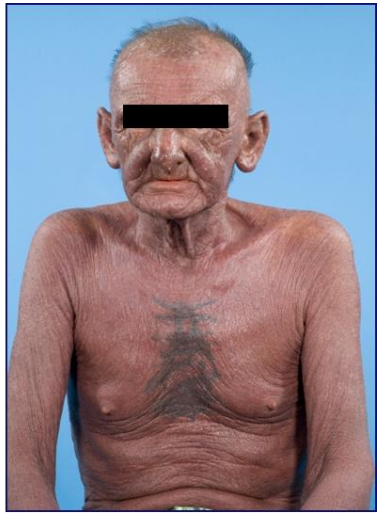
- Cytotoxic drugs
  - Pralatrexate, Gemcitibine, Pentostatin, Forodesine
- HDACi
  - Vorinostat, Romidepsin, Panobinostat
- Antibodies
  - αCD52, αCD30, αCCR4
- Allogeneic Stemcel transplantation

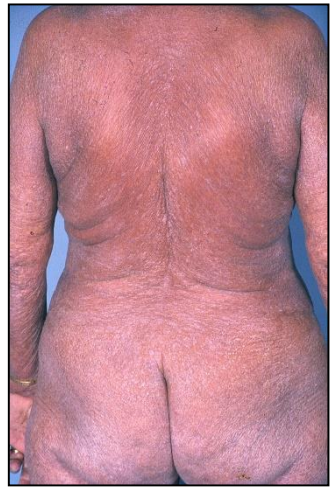
Sézary syndrome

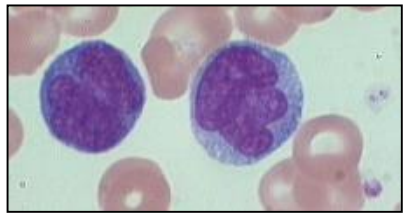
- Rare type of lymphoma derived from CD4+, skin-homing, memory T cells

- Clinical presentation:
  - Erythroderma
  - Lymphadenopathy
  - Atypical cells in skin, lymph nodes and blood
- Staging:
  - Skin histology
  - Blood
  - CT-scan
- Criteria:
  - T-cell clone in skin and blood
  - >1000 Sézary cells/mm^3
  - CD4:CD8 ratio >10.
  - Loss of CD2, CD3, CD4 en/of CD5









Therapy

- Skin directed therapies
  - PUVA, local steroids, Mustine
- Immuunmodulating
  - Interferon, Bexarotene, Extracorporeal photopheresis
- Chemotherapy
  - MTX, Leukeran, Forodesine
  - CHOP
- Immunotherapy
  - Antibodies: CD52, CCR4, CD30,
  - Cellular: allogenic Stemcell Transplantatie, CarT cells (future)

Discussion