

Cutaneous T-cell lymphoma – combination modalities in treatment

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Cutaneous T-cell lymphoma (CTCL)

- **Larger spectrum of diseases with two characteristic features:**
 - **1. Malignant expansion of T- cells clones stopped on the way from bone marrow precursor cells to helper cells**
 - **2. Forming and location of lymphoma in the skin**

CTCL¹: EORTC² Classification

- **Indolent**

- Mycosis fungoides (MF)

- Mycosis fungoides plus follicular mucinosis

- Pagetoid reticulosis

- Large-cell CTCL, CD30+

- Lymphomatoid papulosis

- **Aggressive**

- Sézary syndrome (SS)

- Large-cell CTCL, CD30-

- Immunoblastic T-cell lymphoma

- Pleomorphic T-cell lymphoma

- **Provisional**

- Granulomatous slack skin

- CTCL, pleomorphic small/medium-sized T-cell lymphoma

- Subcutaneous panniculitis-like T-cell lymphoma

¹ CTCL Cutaneous T-Cell Lymphoma, ² EORTC European Organisation for Research and Treatment of Cancer

Cutaneous T-cell lymphoma

- **Three stages of CTCL with epidermotrophism:**
 - **I. Eczematoid stage (premycotic, patch stage)**
 - **II. Infiltrative stage (plaque stage)**
 - **III. Tumor stage**
- **The disease usually proceeds from stage to stage, various alterations of more stages can be present simultaneously as well.**

CTCL: Stage and Prognosis

	<u>IA</u>	<u>IB</u>	<u>IIA</u>	<u>IIB</u>	<u>III</u>	<u>IVA</u>	<u>IVB</u>
5-year DSS (%) *	100	96	68	80	40	0	
10-year DSS (%)	98	83	68	42	20	0	
Median survival (yr)	>32	12.1	10.0	2.9	3.6-4.6	1.1	1.1
ODP (%) [†]	9	20	34				
5-year RFS** (%)	50	36	9				
10-year RFS (%)	31	3					

¹ DSS, disease-specific survival; ² ODP, overall disease progression; ³ RFS, relapse-free survival

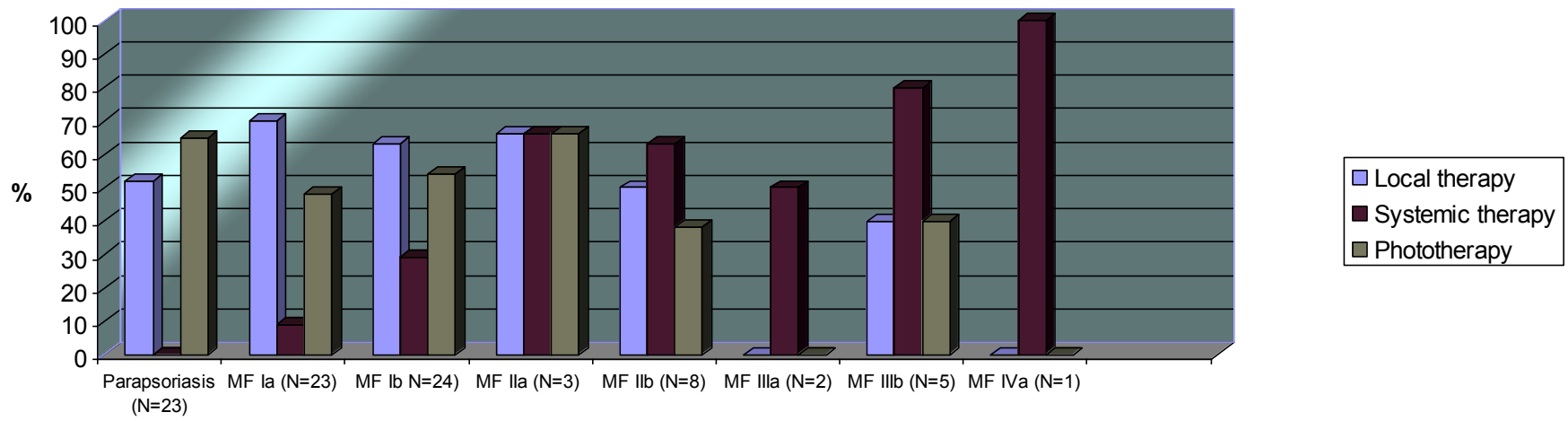
Methods used for CTCL treatment in the 1st Dept. of Derm. in Brno

- **Topically**: steroids
tar
- **Phototherapy**: UVB 311 nm
SUP
CUP
PUVA
- **Photodynamic therapy**
- **Systemic treatment**: acitretin
Interferon α 2a
Interferon α 2b
(steroids)
bexarotene
- **Radiotherapy** in co-operation with Dept. of Oncology

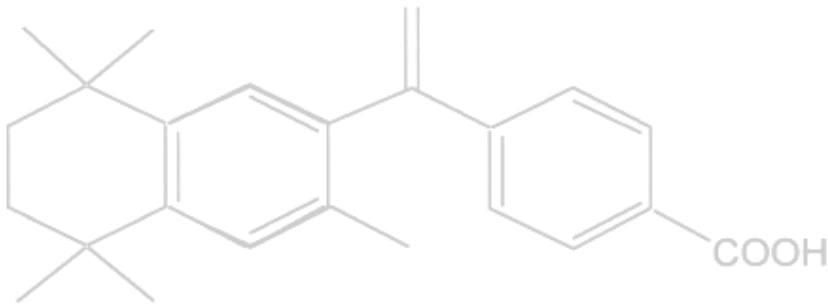
Our experience with combination of therapeutical modalities for advanced CTCL

- PUVA / UVB 311nm + retinoids
- PUVA + interferons
- PUVA + retinoids + interferons
- PUVA + retionoids + interferons +
radiotherapy
- PUVA + bexarotene
- Other combinations

Therapy of CTCL patients according to staging



Bexarotene Properties

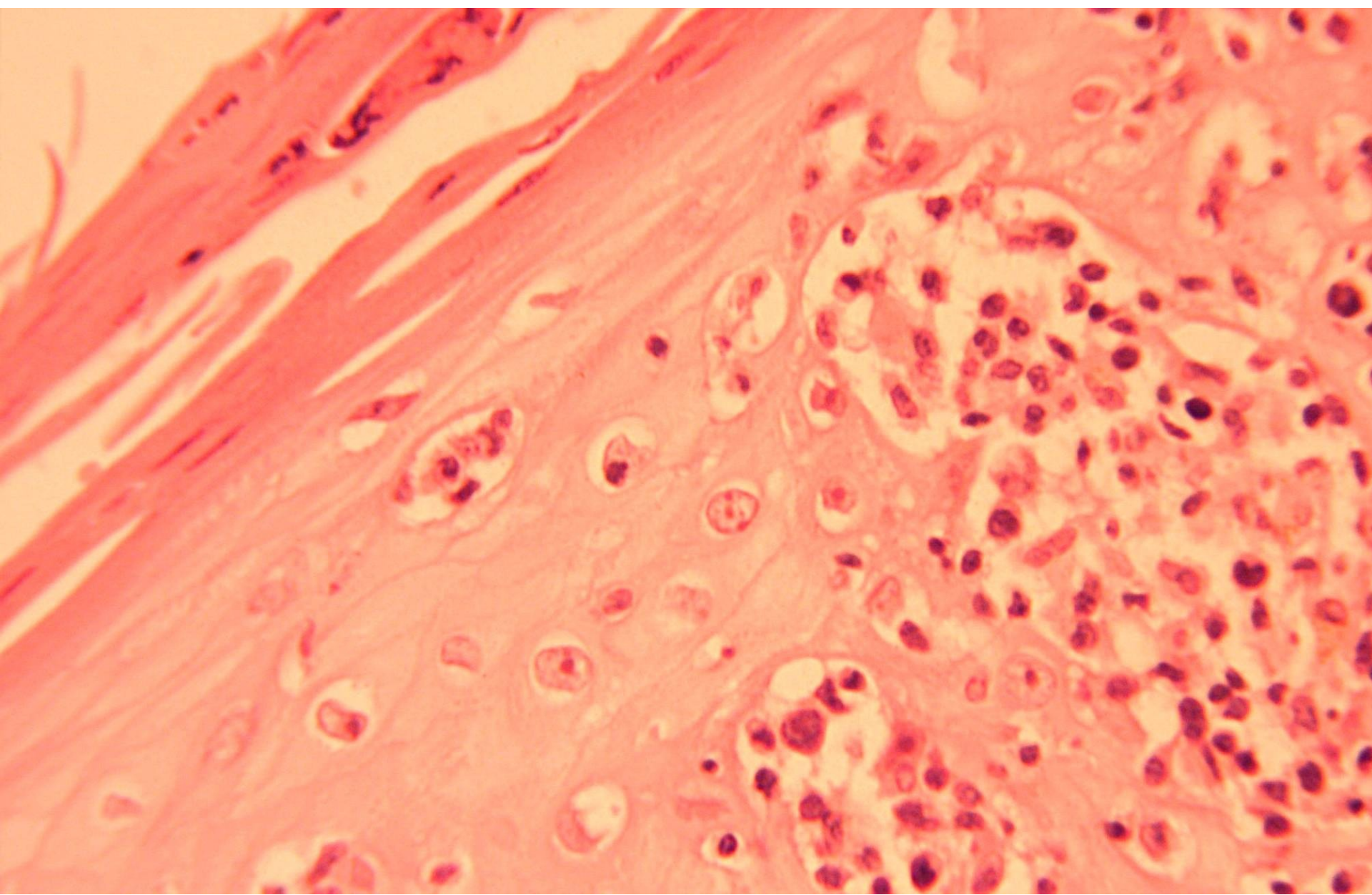


- Novel retinoid rexinoid
- Selective retinoid X receptor (RXR) antagonist
- Modulates expression of genes regulated by retinoid response elements
- Available as topical or systemic treatment
- Mono- or combination therapy

Bexarotene: Adverse Events

Adverse event	Incidence by initial dose (mg/m ² /day)	
	300 (n=84)	> 300 (n=53)
Hyperlipidaemia	79%	79%
Hypercholestaemia	32%	62%
Headache	30%	42%
Hypothyroidism	29%	53%
Pruritus	25%	15%
Asthenia	20%	45%
Leukopenia	17%	47%
Rash	17%	23%
Infection	13%	23%
Exfoliative dermatitis	10%	28%
Diarrhoea	7%	42%
Anaemia	6%	25%
Anorexia	2%	23%



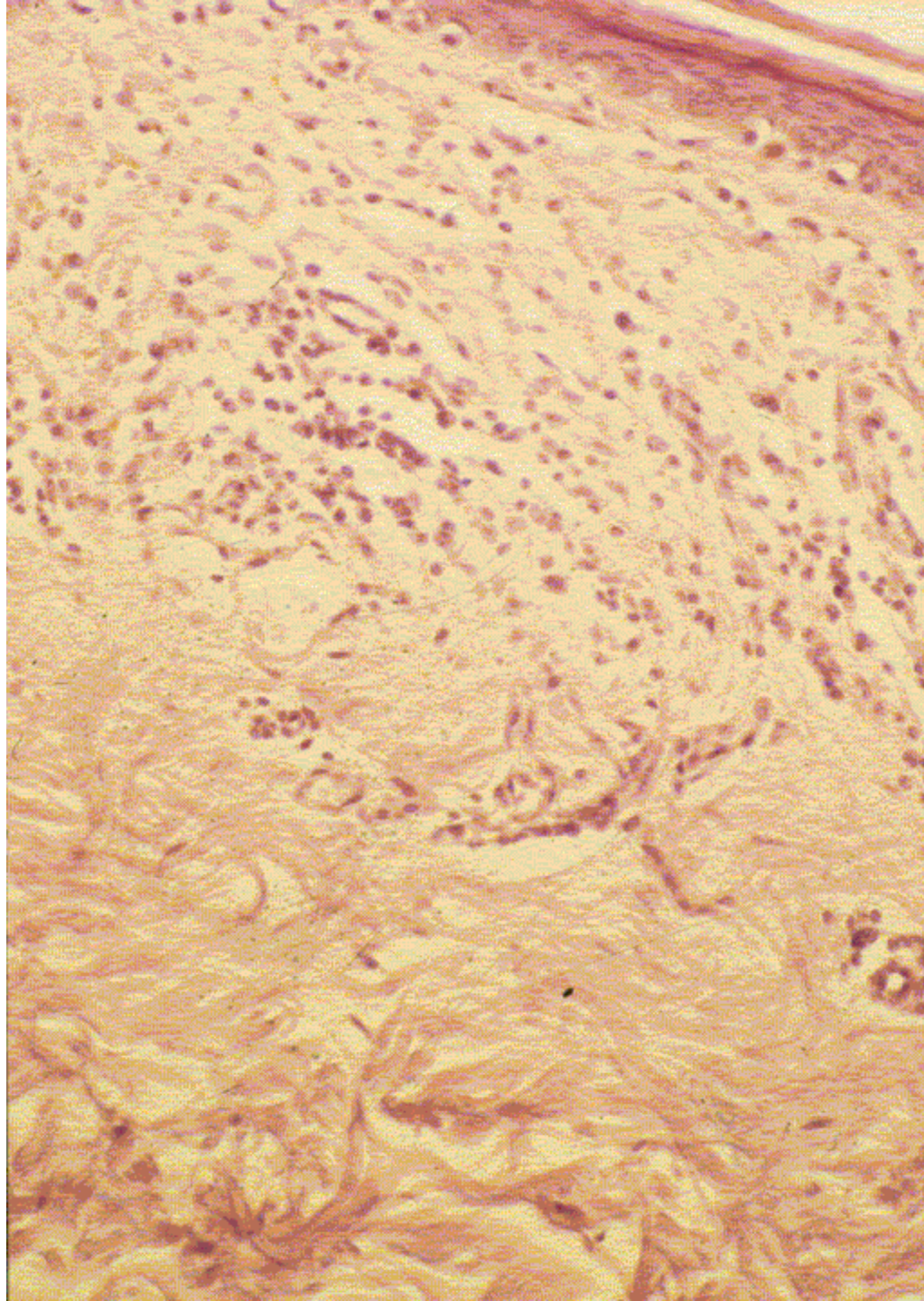




MF, after six month of
PUVA



MF, lichenoid form, 1999



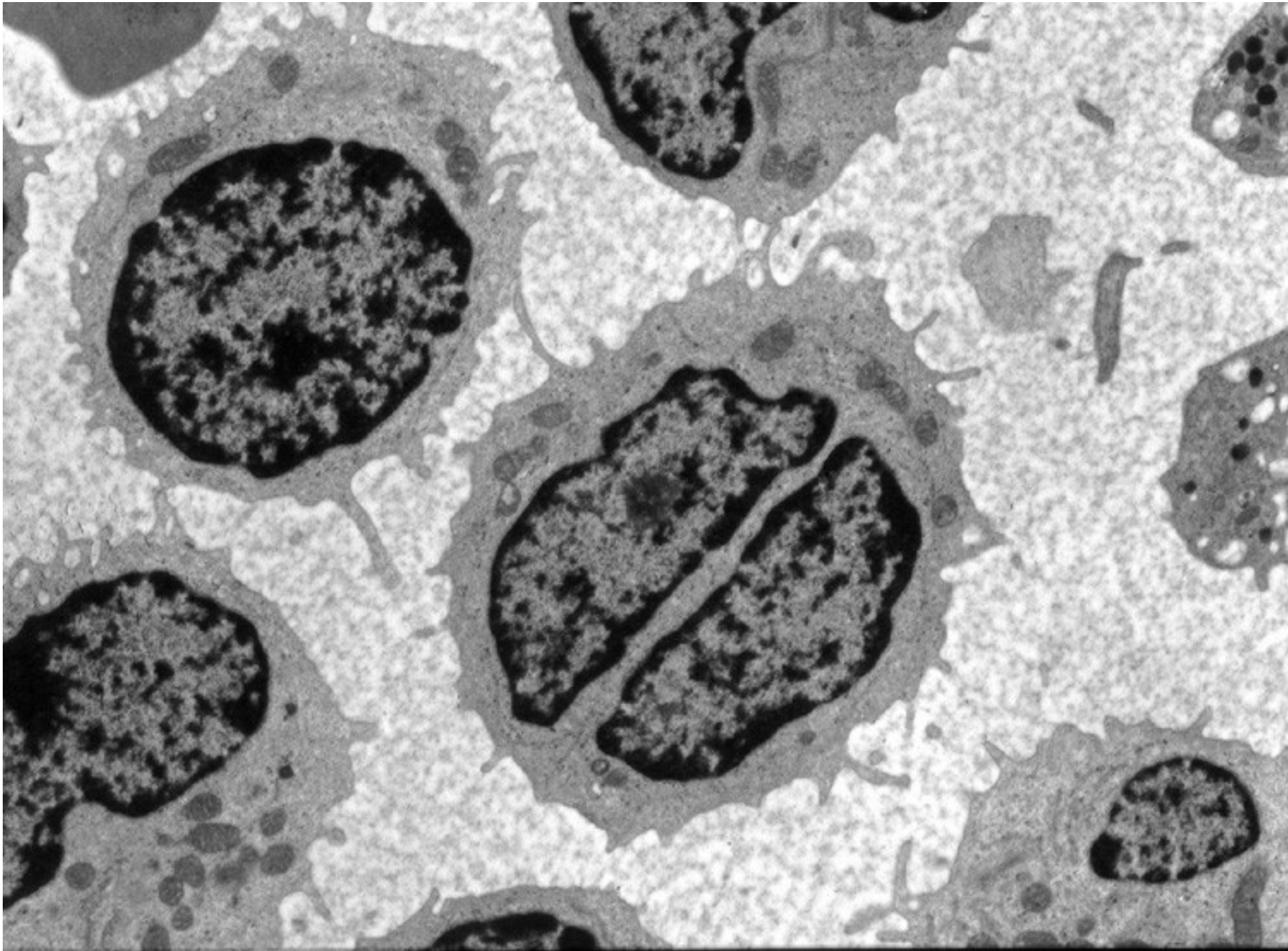


MF, lichenoid form, after eight month of PUVA,
cumulative dose 86 J/cm², remission until now

A close-up photograph of human skin affected by Sézary syndrome. The skin is covered with numerous small, red, scaly patches of varying sizes, which are characteristic of this type of cutaneous T-cell lymphoma. The patches are scattered across the visible area, with some appearing more prominent than others. The overall appearance is one of a widespread, erythematous, and scaly dermatitis.

Sézary syndrome 1998



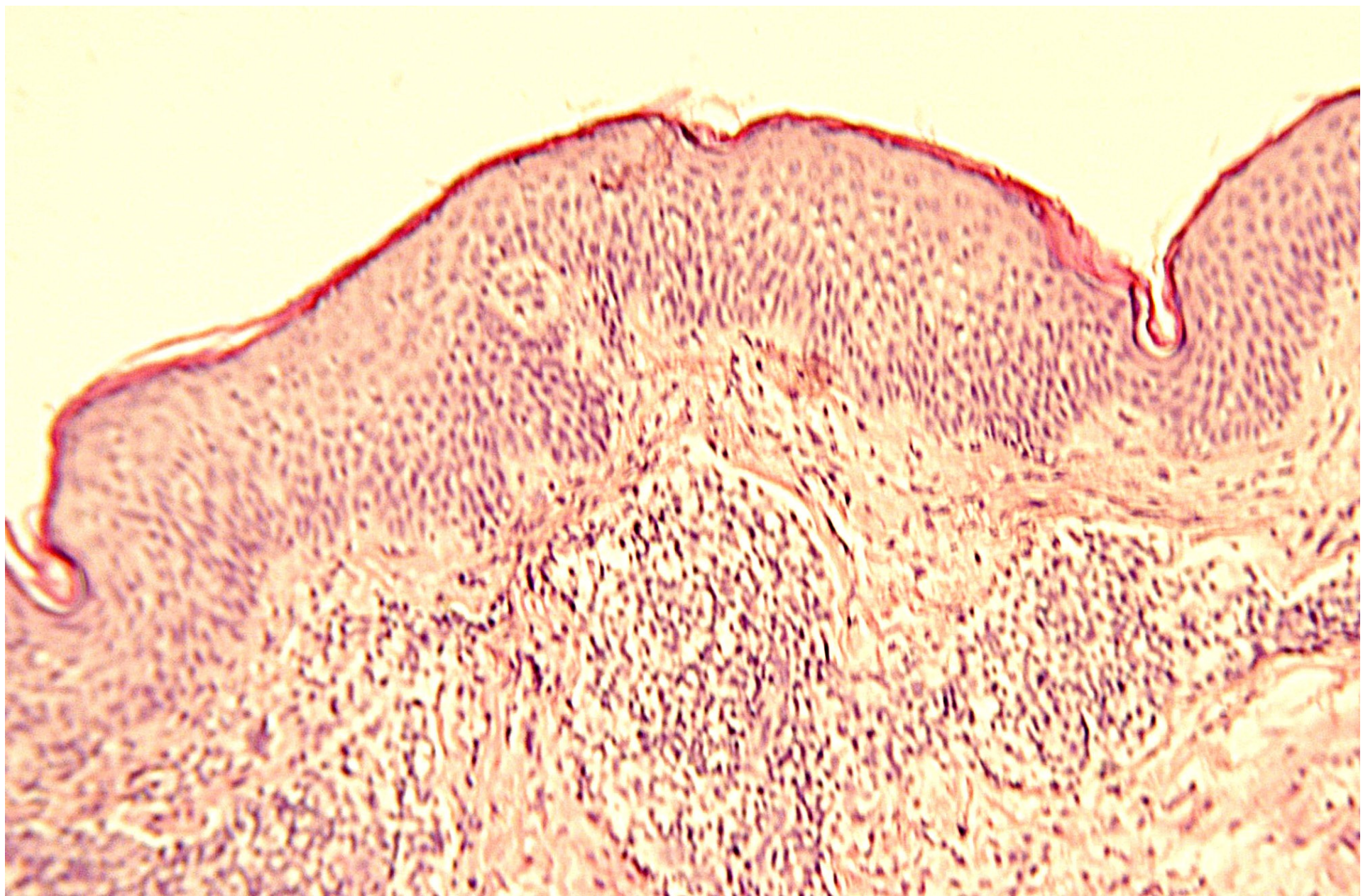


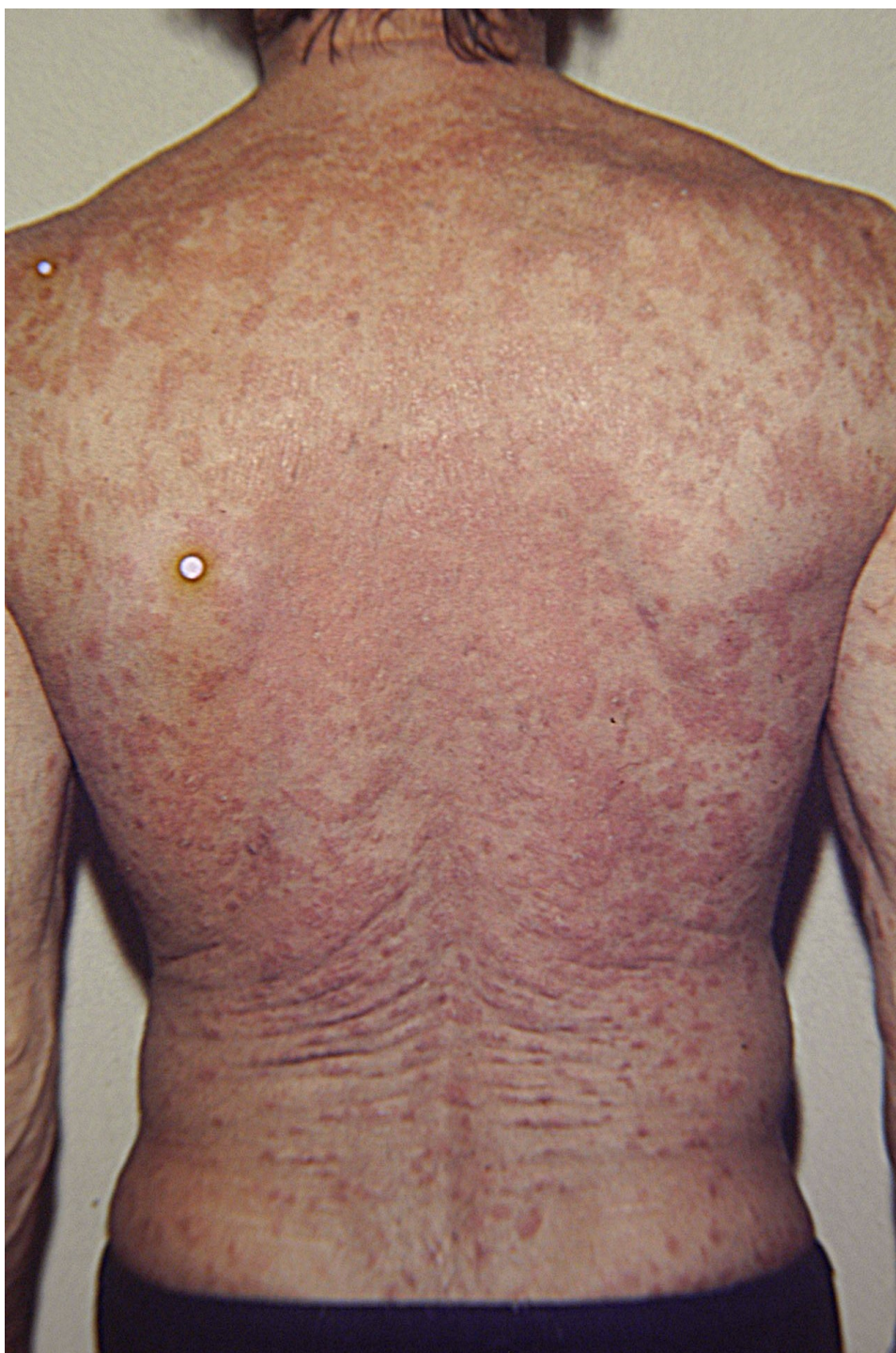


Sézary syndrome,
after rePUVA
1054 J/cm²



MF 1994





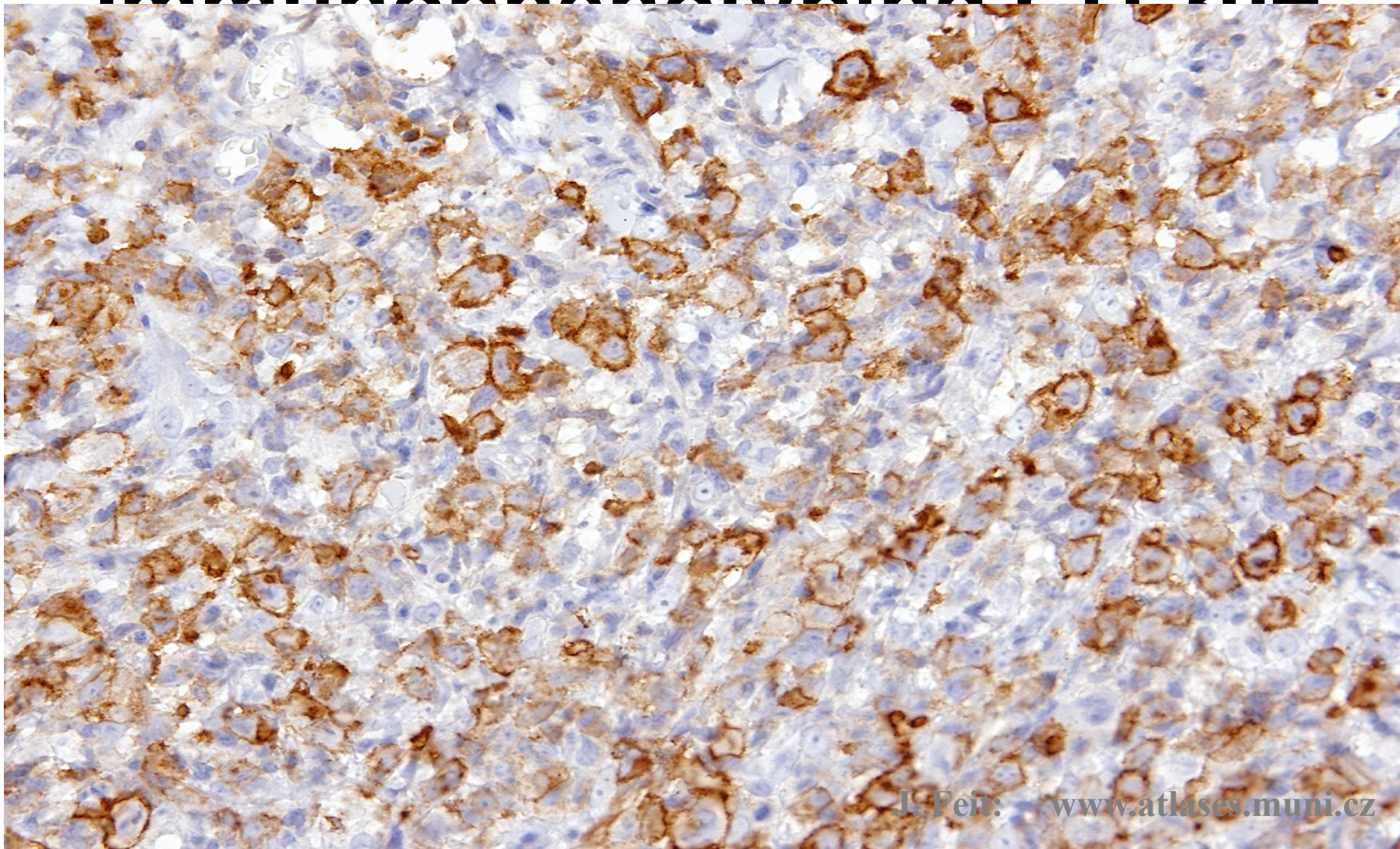


In remission after IFN α + acitretin until 2009



LyP

Immunophenotyping CD 20+

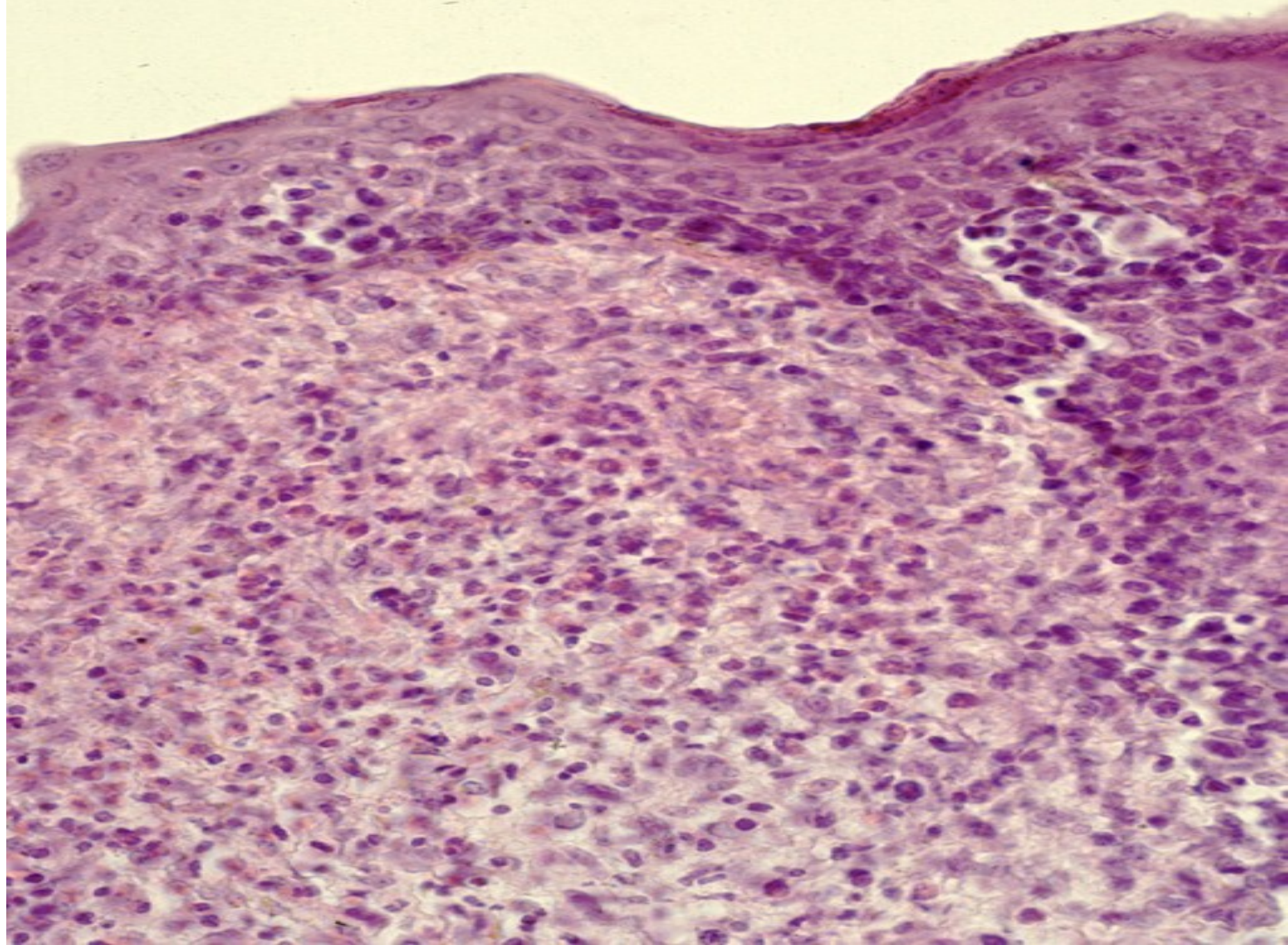




Remission after rePUVA treatment



MF 1998

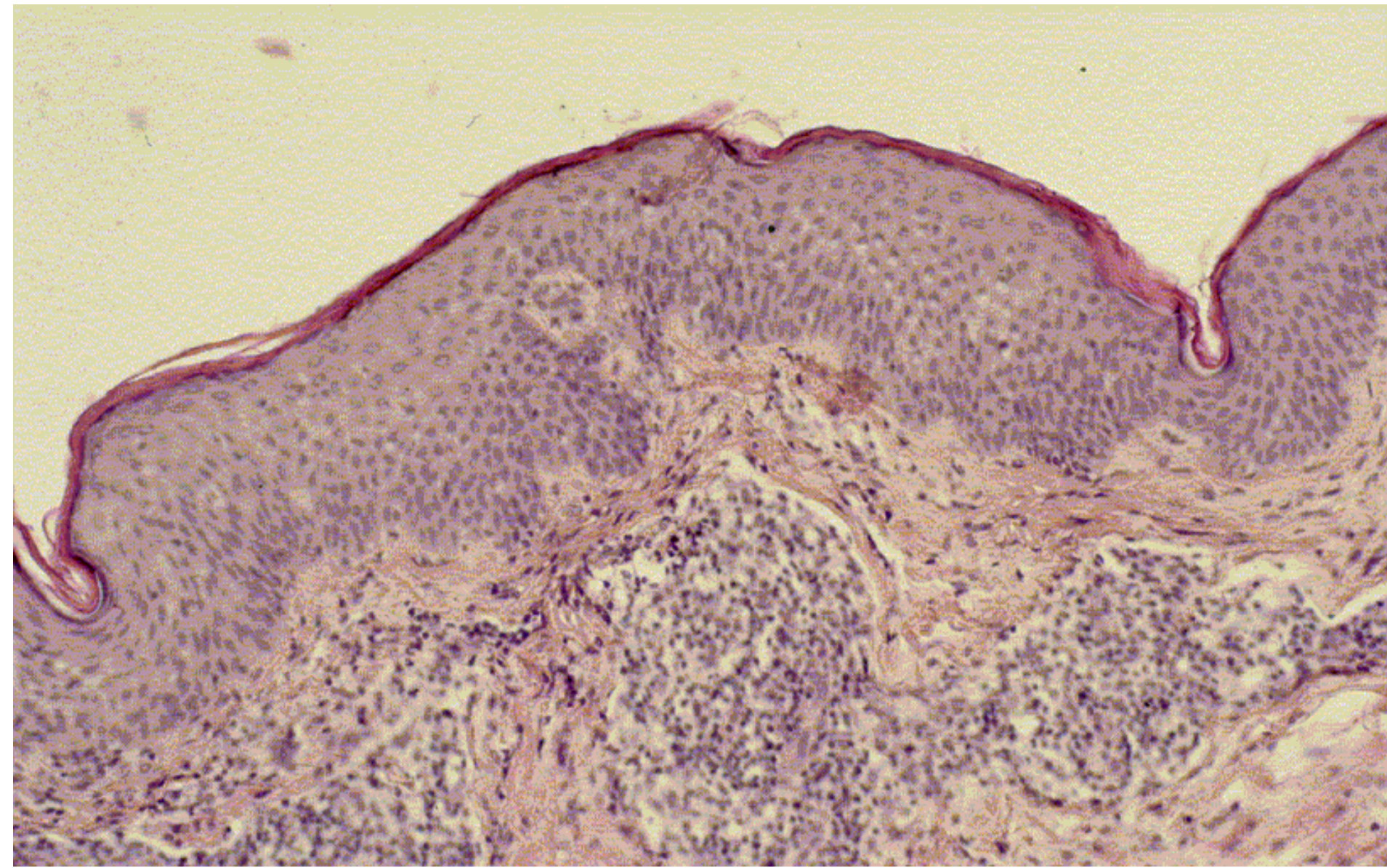




MF after 12 month of PUVA and Intron-A cumulative dose 210 J/cm², in remission with low dose of acitretin until now



MF 1995





MF 1998,_after rePUVA, cumulative dose 500 J/cm²



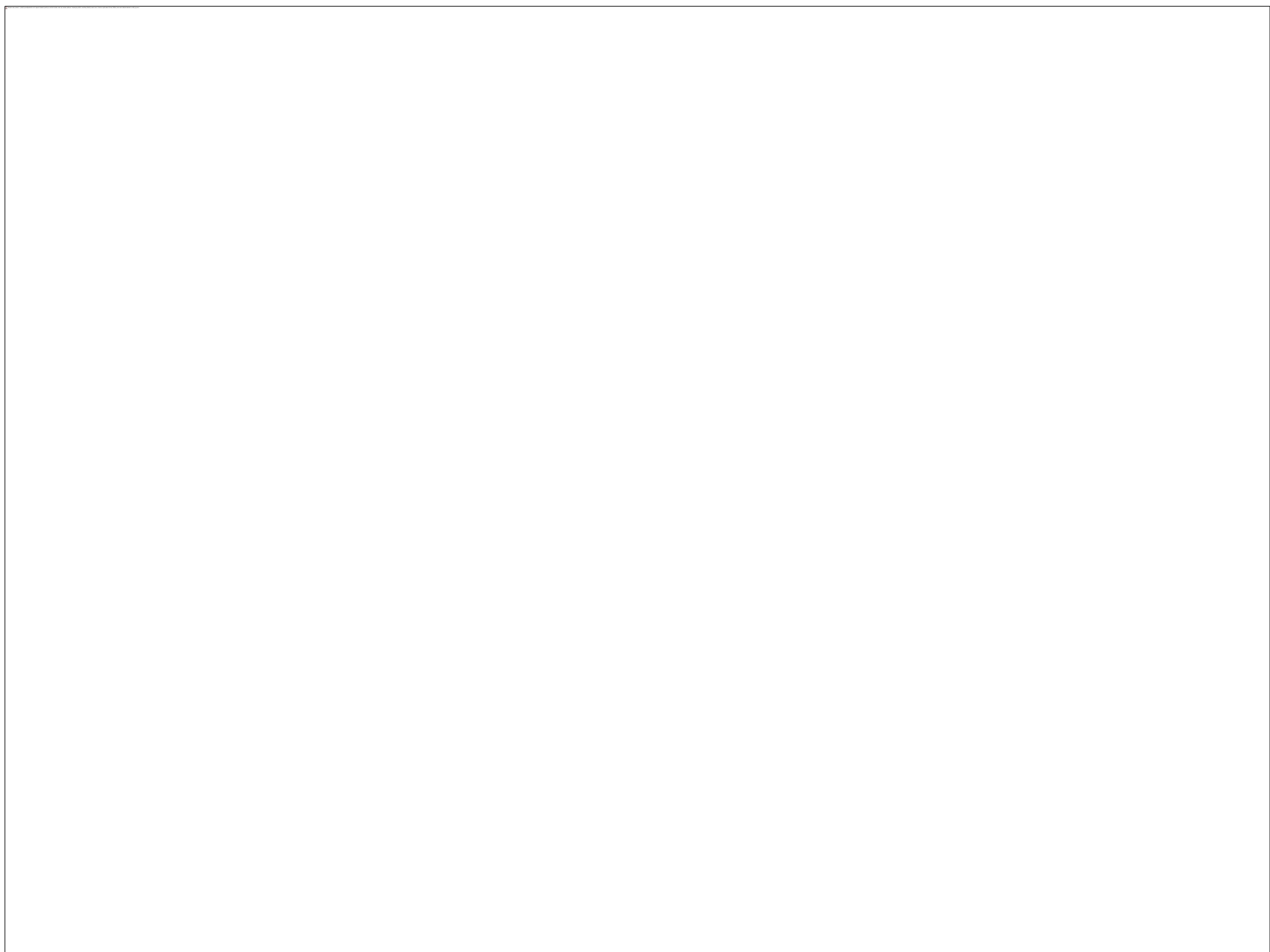


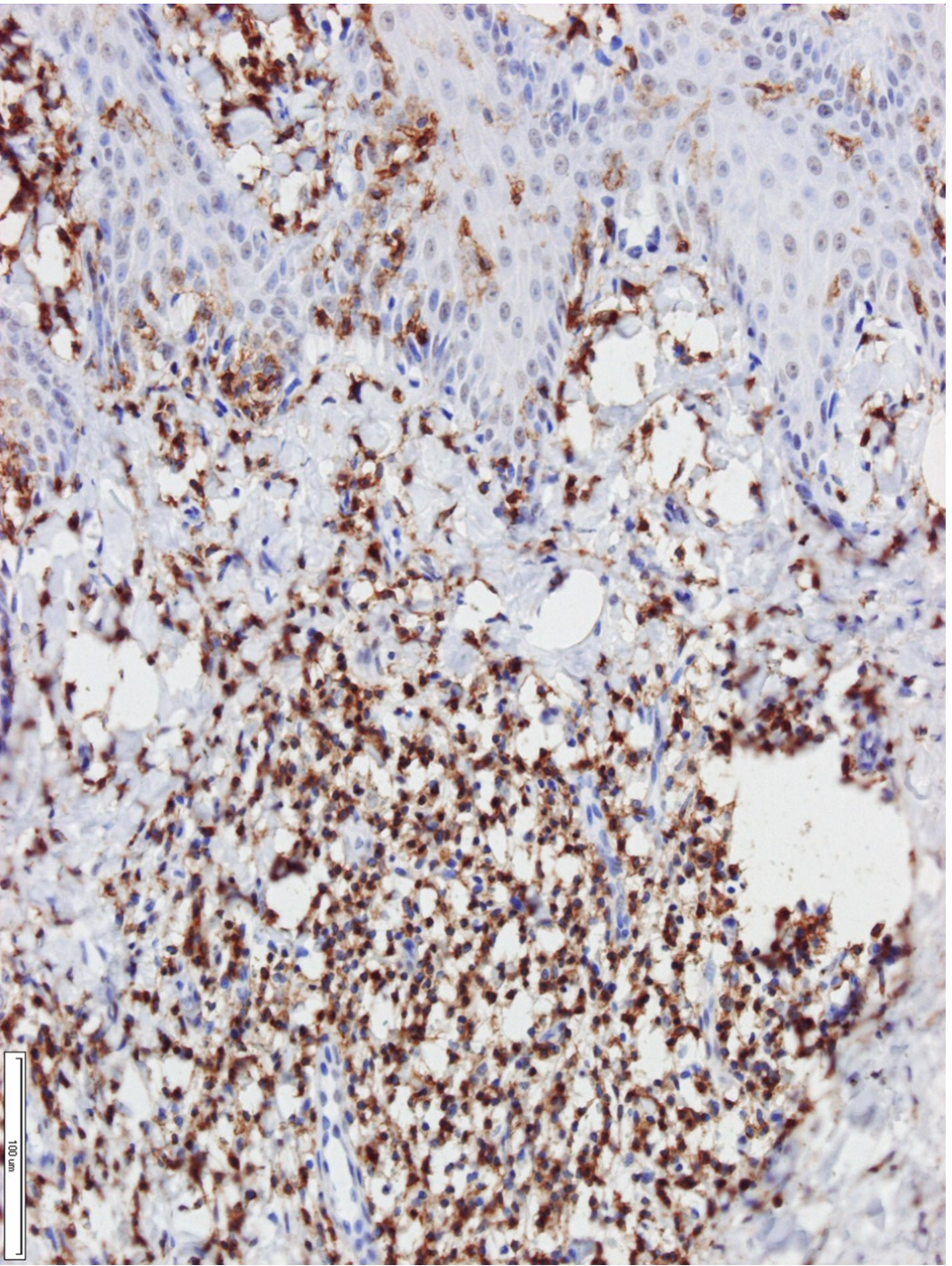


MF - before
therapy









100 μ m



Remission after IFN α + acitretin



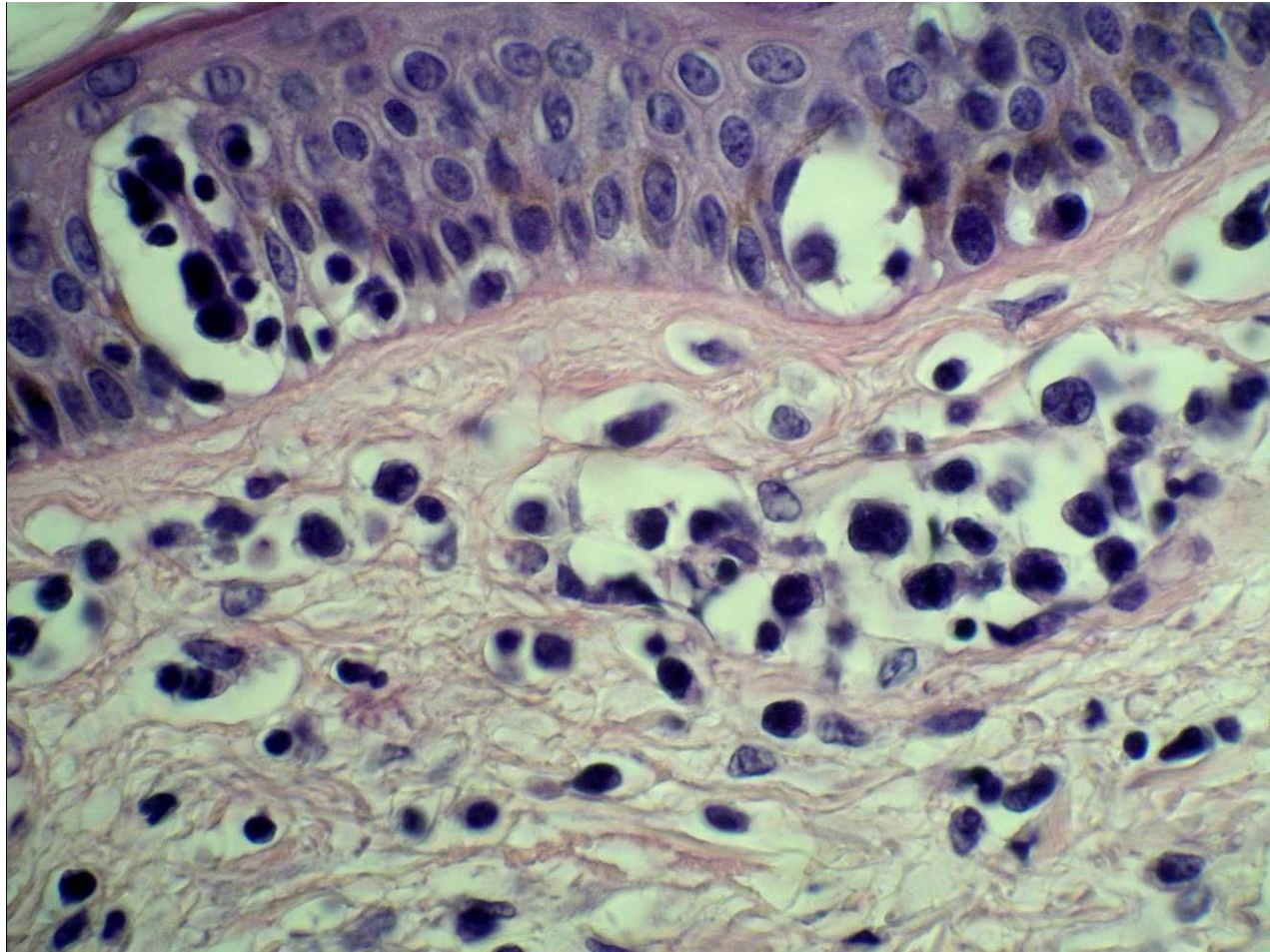


MF - before therapy, 2007











**Complete remission after
rePUVA + IFN α until now**





MF – before therapy, 2007









After 2 years of
bexarotene therapy



MF – before therapy



MF – after 2 months bexarotene therapy



Erythrodermic MF – before therapy 2003



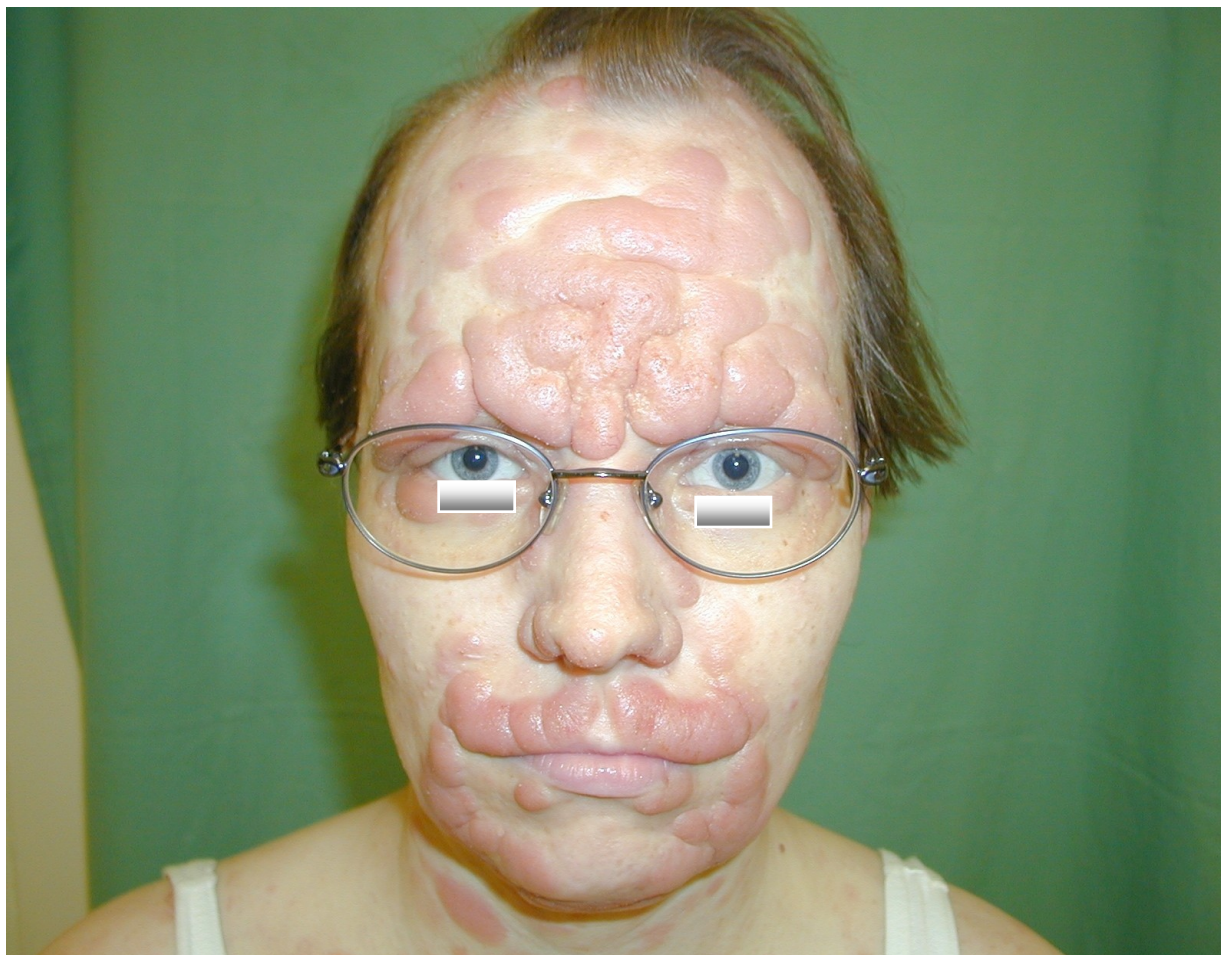


2006 – after IFN α + acitretin + TSEB



2009 – bexarotene therapy

MF – before therapy



MF – before therapy

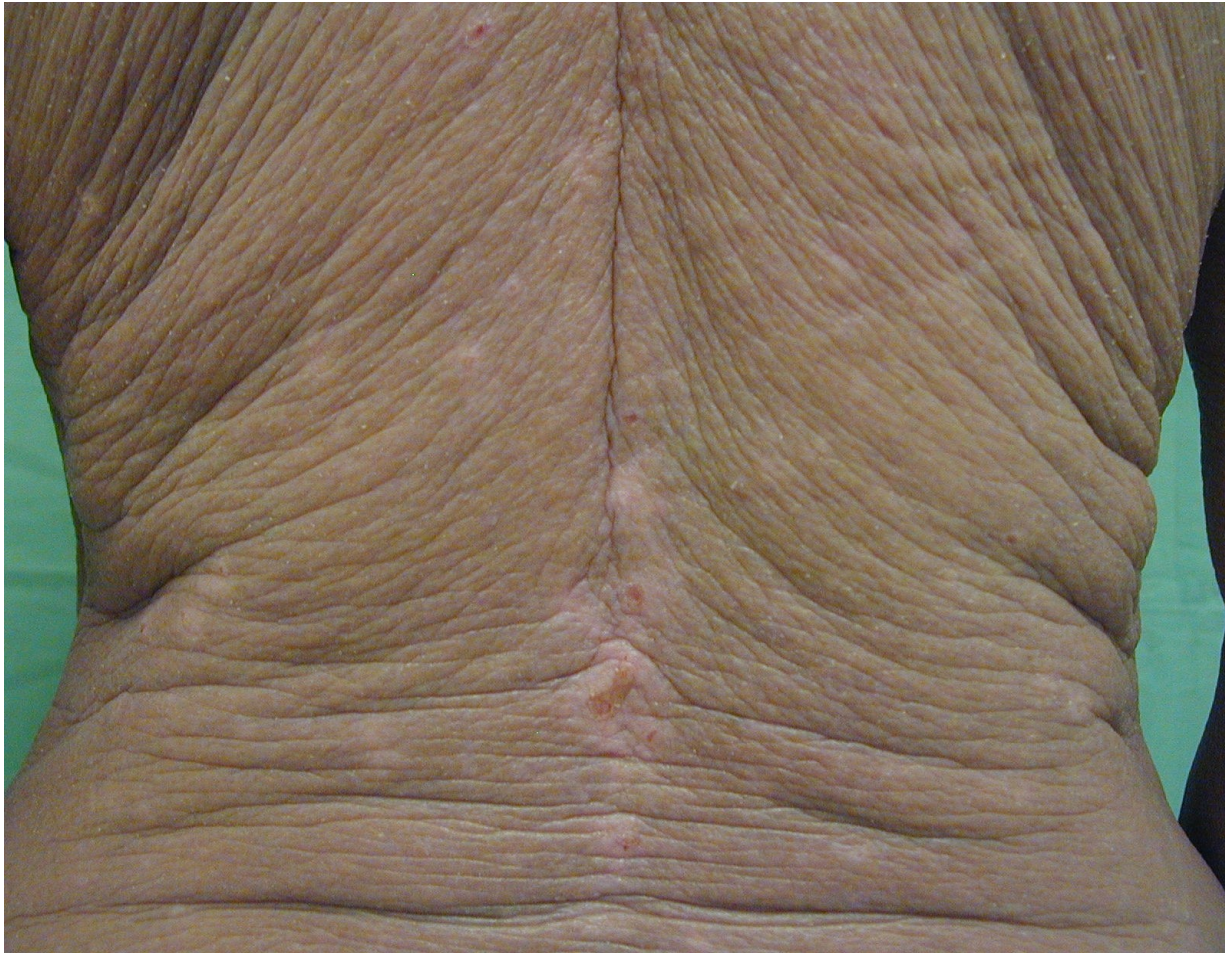


3 months bexarotene therapy + PUVA





Sézary syndrome



Sézary syndrome – 3 months bexarotene + PUVA therapy





MF before PDT



After PDT

Conclusion

- In dermatology we have possibilities to treat CTCL by many methods according to diagnose and staging.
- In initial stage of mycosis fungoides we are able to stop or to control it's development
- In Sézary syndrome recent immunotherapy can attribute to longer remission

