

Cutaneous T-cell lymphoma – combination modalities in treatment

Vašků V.

Ist Dept. of Dermatology and Venereology,
Medical Faculty Masaryk University and
St. Ann's Faculty Hospital, Brno,
Czech Republic

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

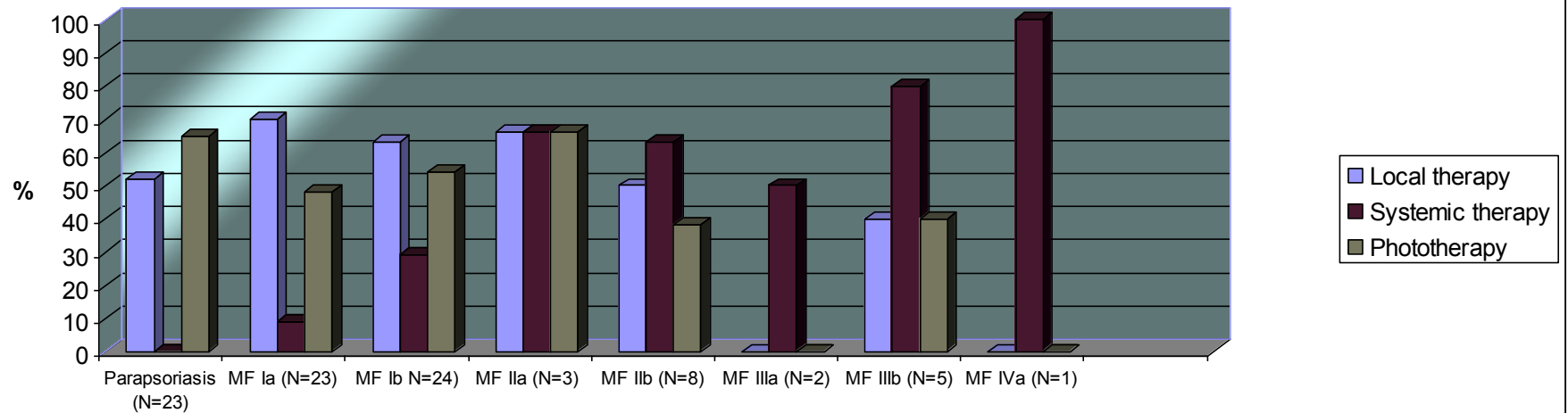
Methods used for CTCL treatment in the 1st Dept. of Derm. in Brno

- **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

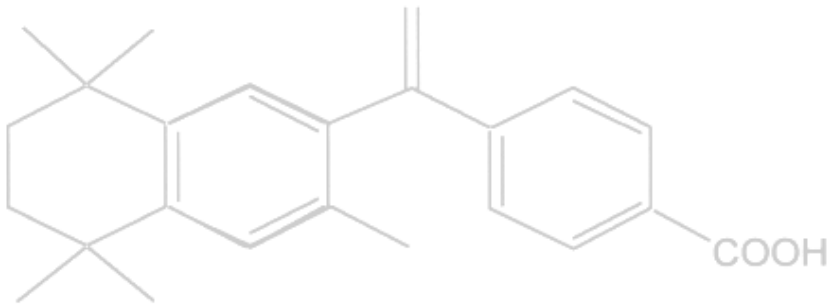
Our experience with combination of therapeutical modalities for advanced CTCL

- 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

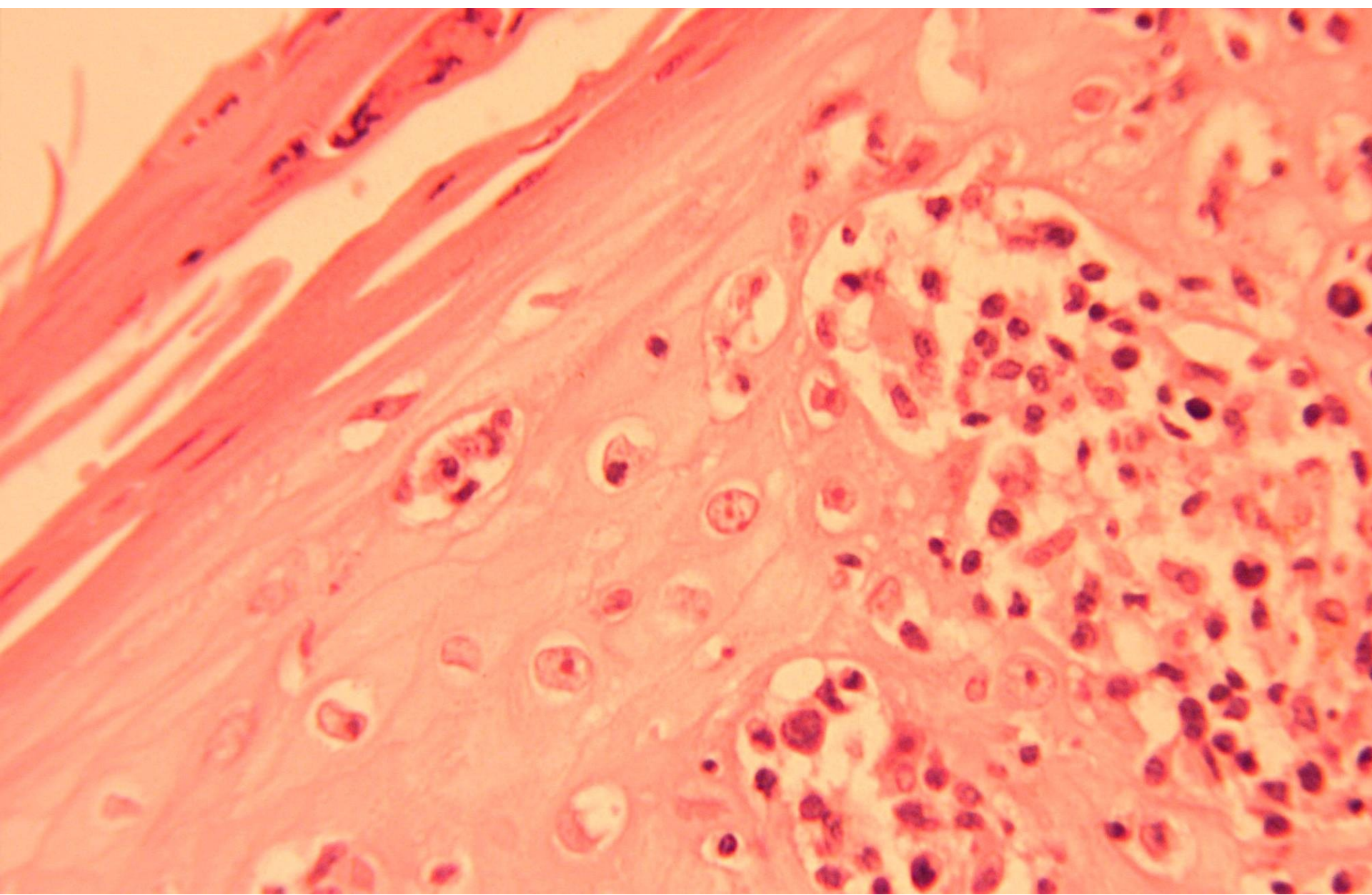


- Novel retinoid rexinoid
- Selective retinoid X receptor (RXR) antagonist
- Modulates expression of genes regulated by retinoid response elements
- Available as topical or systemic treatment
- Mono- or combination therapy

Bexarotene: Adverse Events

Adverse event	Incidence by initial dose (mg/m ² /day)	
	300 (n=84)	> 300 (n=53)
Hyperlipidaemia	79%	79%
Hypercholesterolaemia	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%



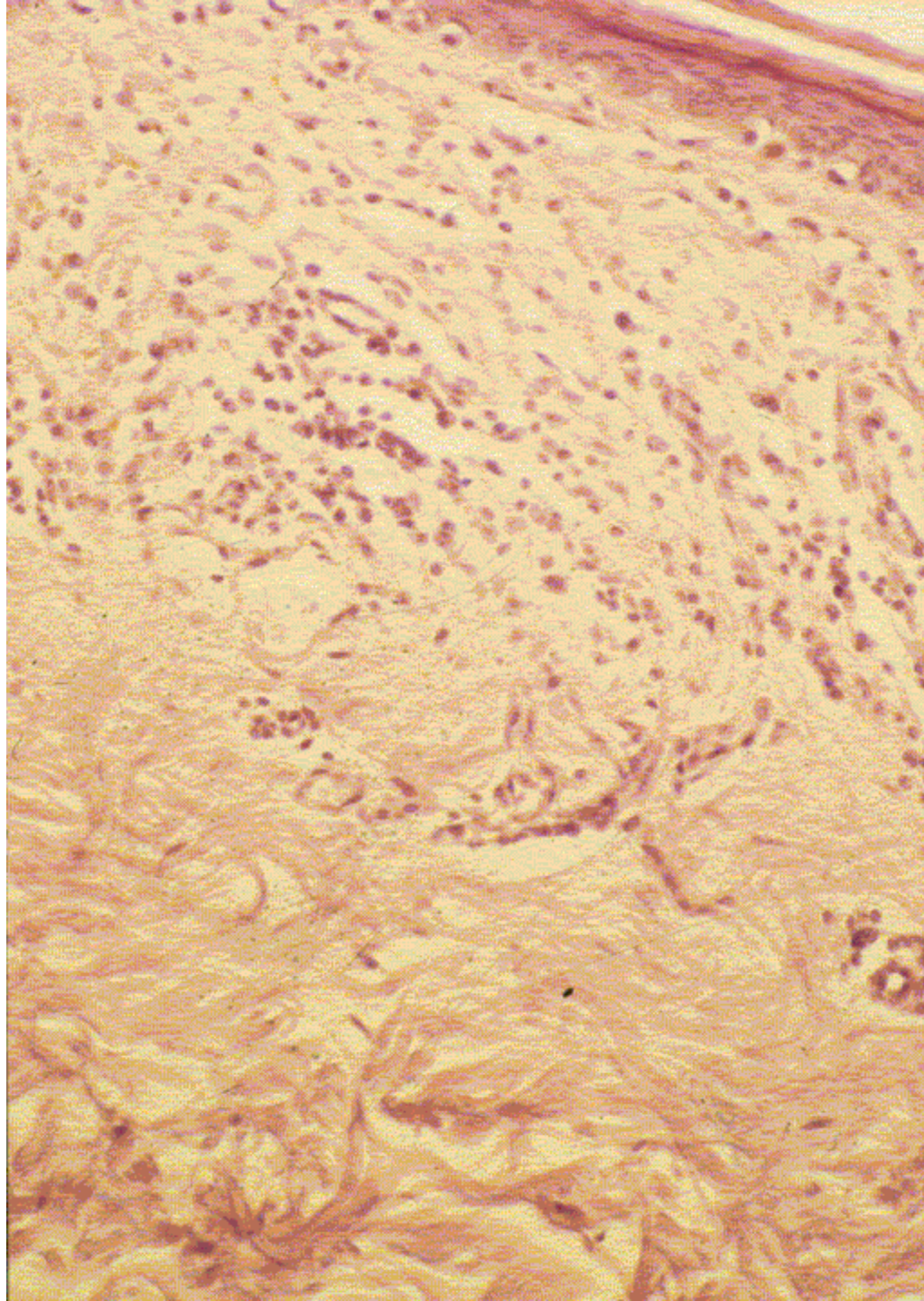


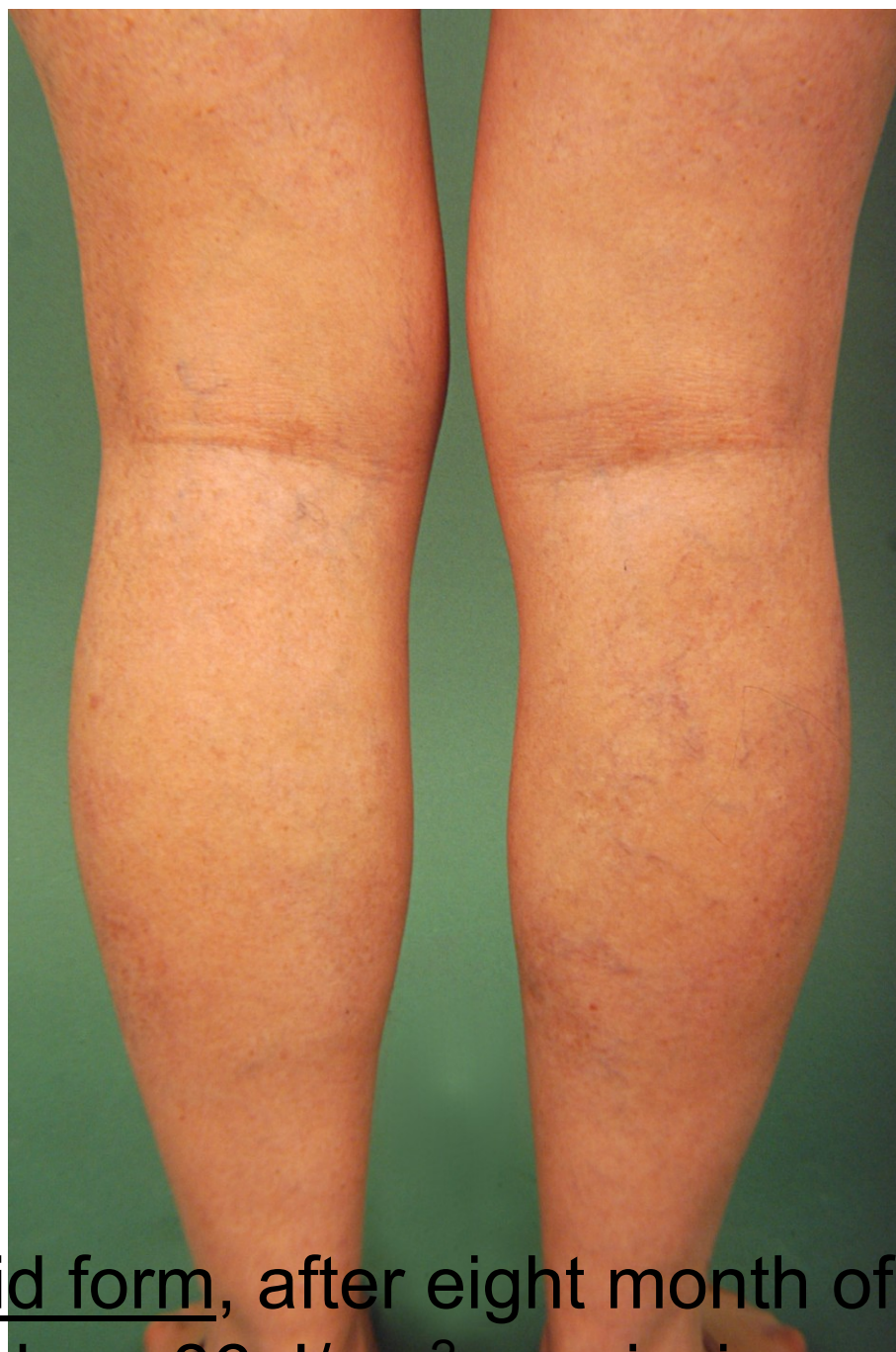


MF, after six month of
PUVA



MF, lichenoid form, 1999



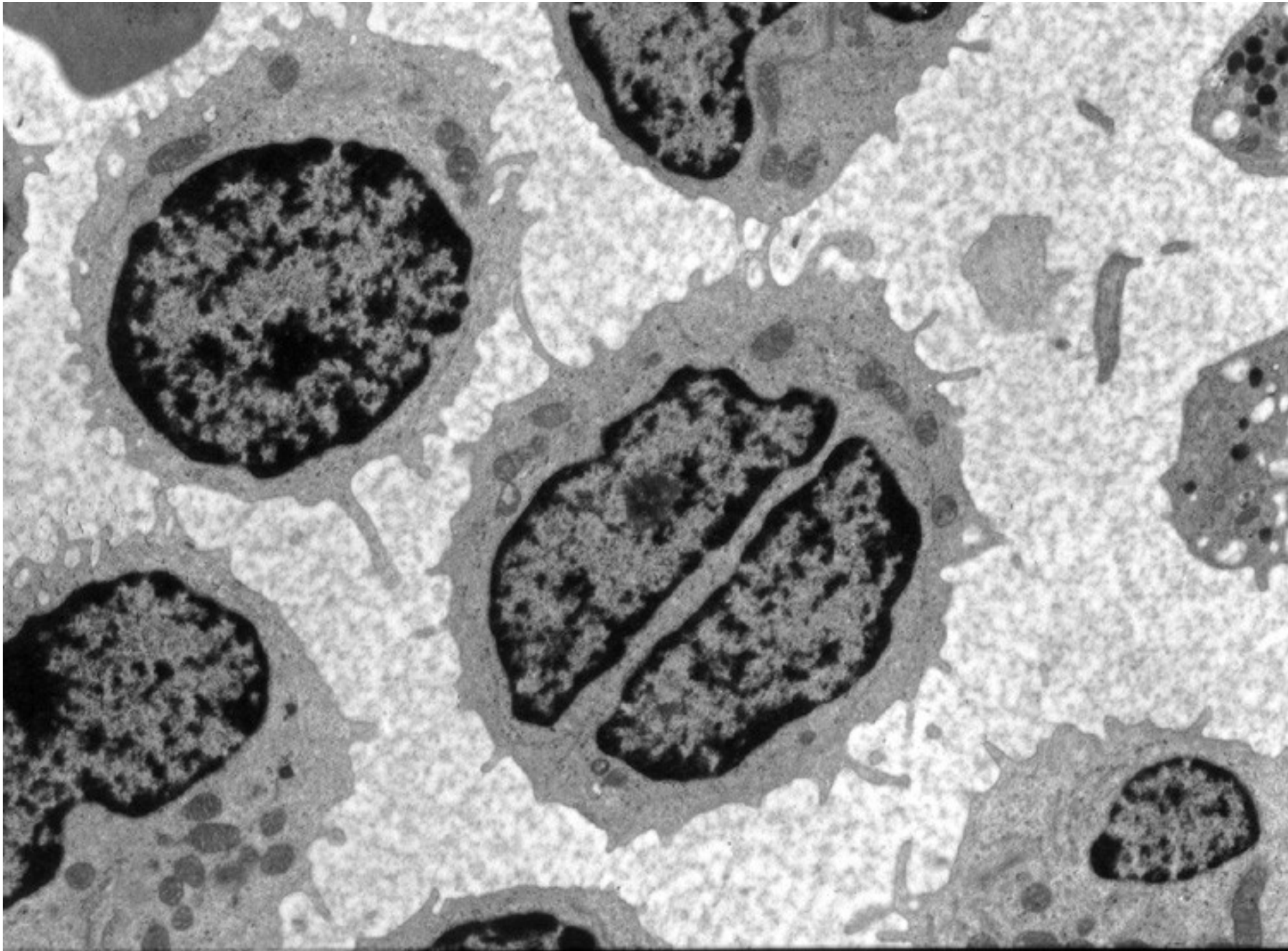


MF, lichenoid form, after eight month of PUVA,
cumulative dose 86 J/cm², remission until now

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 condition. The patches are distributed 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



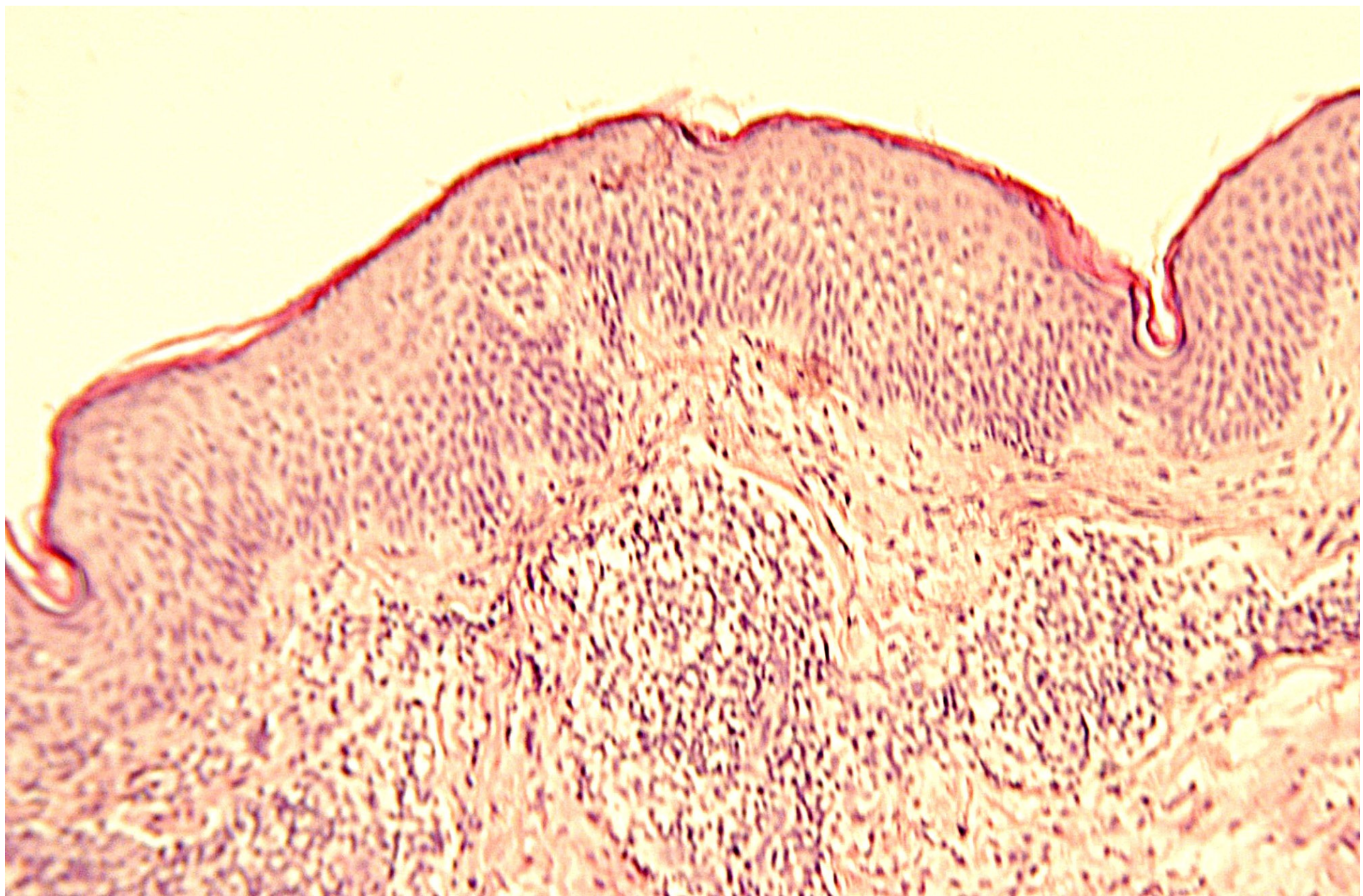


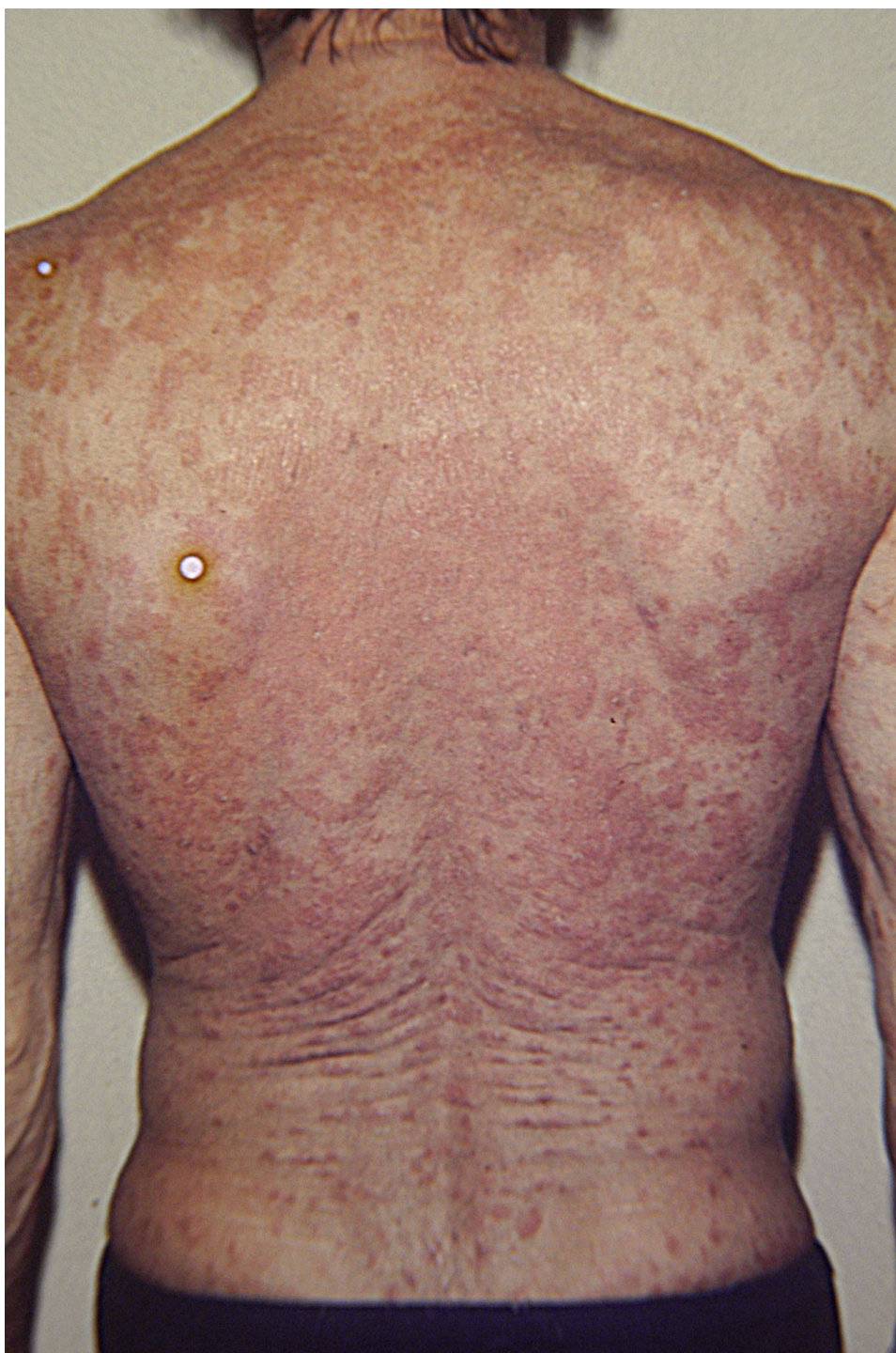


Sézary syndrome,
after rePUVA
1054 J/cm²



MF 1994





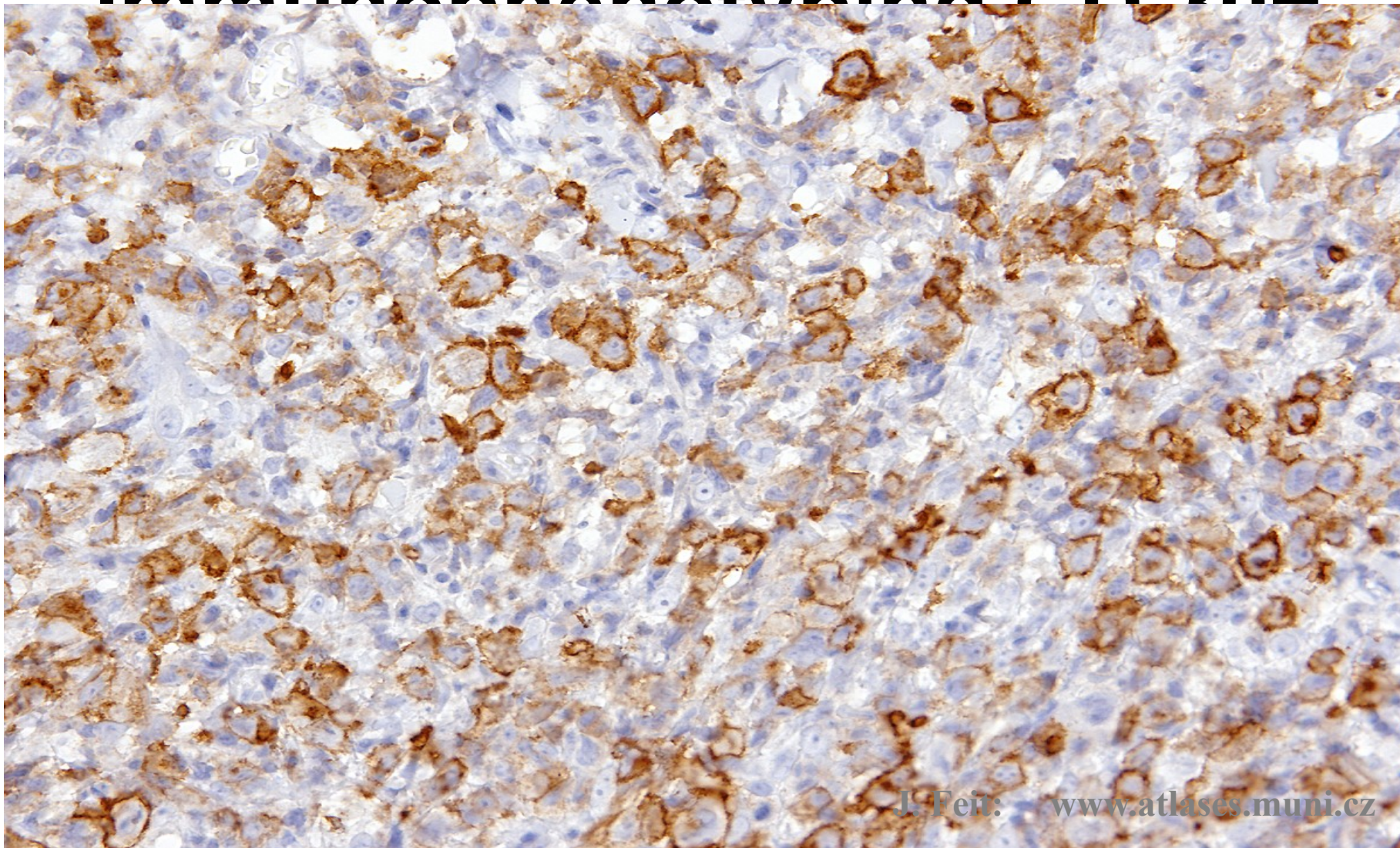


In remission after IFN α + acitretin until 2009



LyP

Immunophenotyping CD 20+

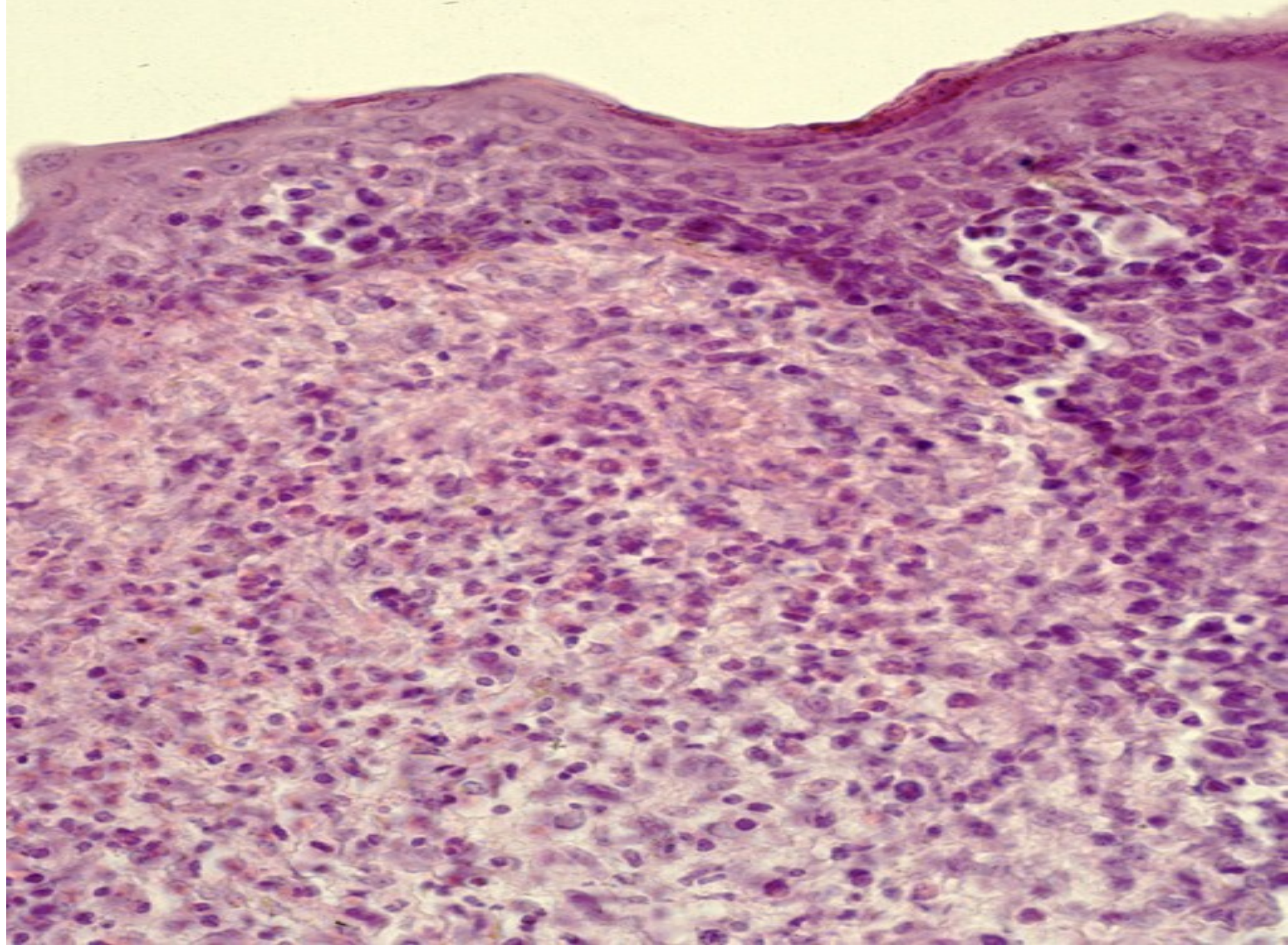




Remission after rePUVA treatment



MF 1998

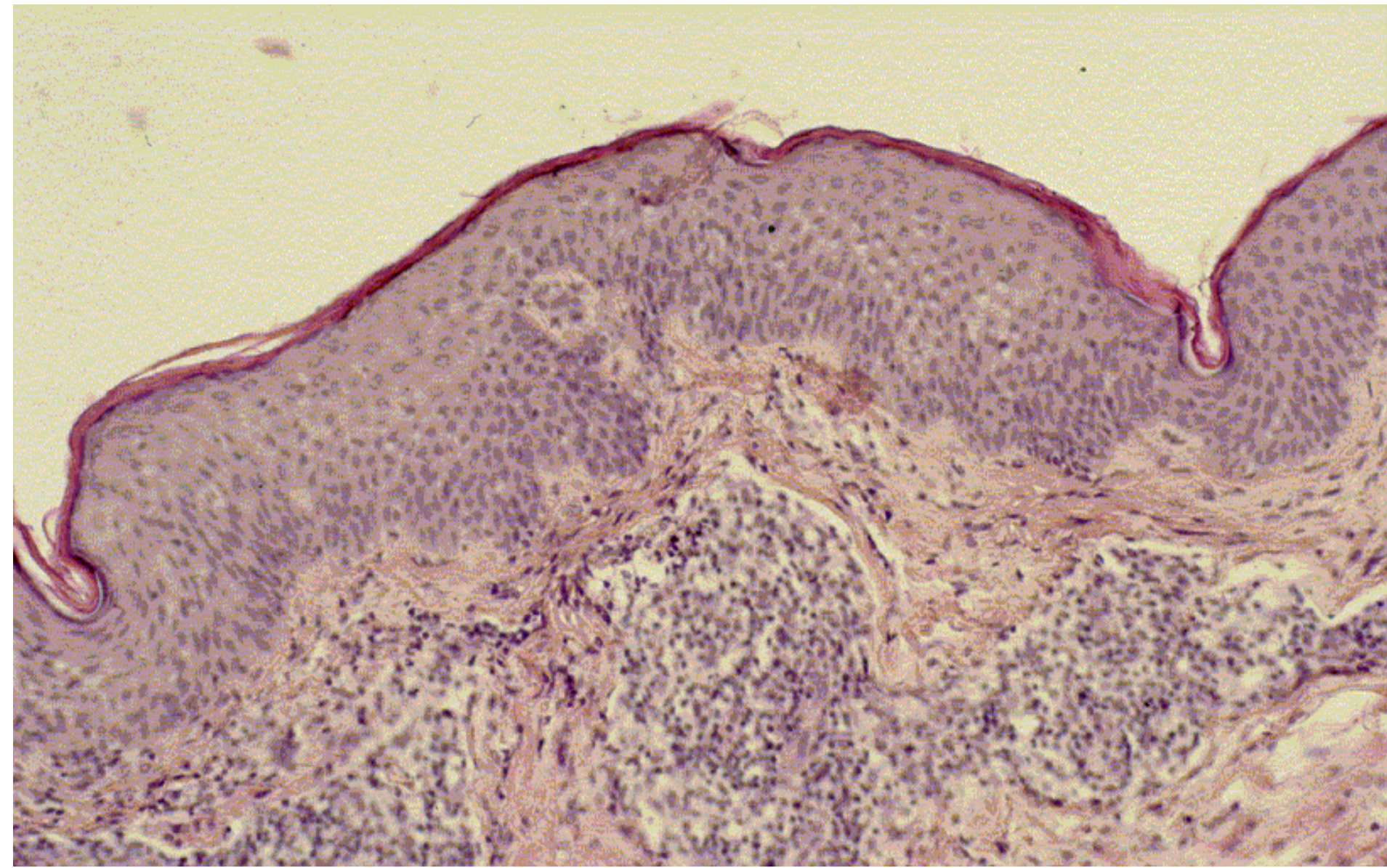




MF after 12 month of PUVA and Intron-A cumulative dose 210 J/cm², in remission with low dose of acitretin until now



MF 1995





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





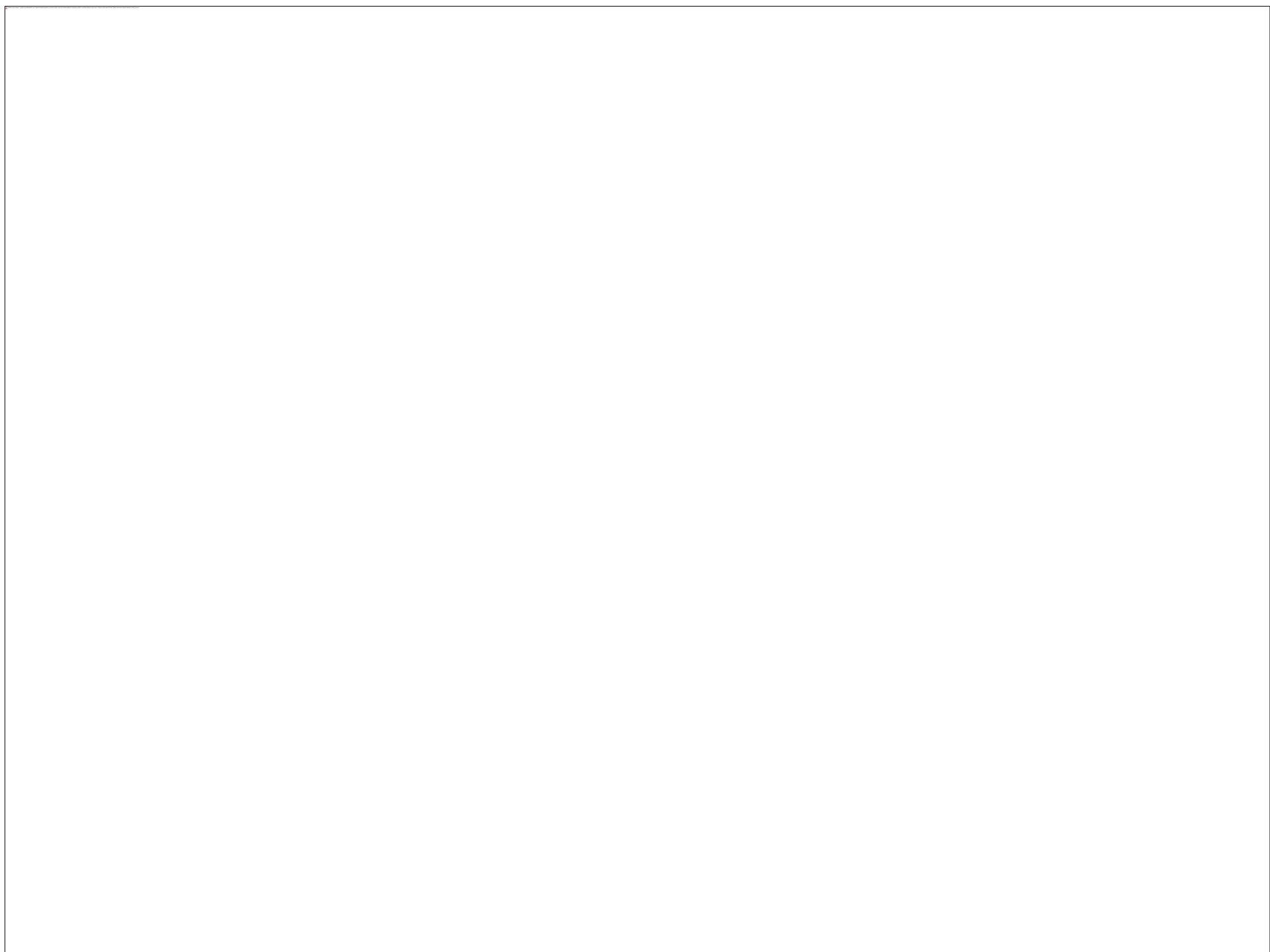
1/4x

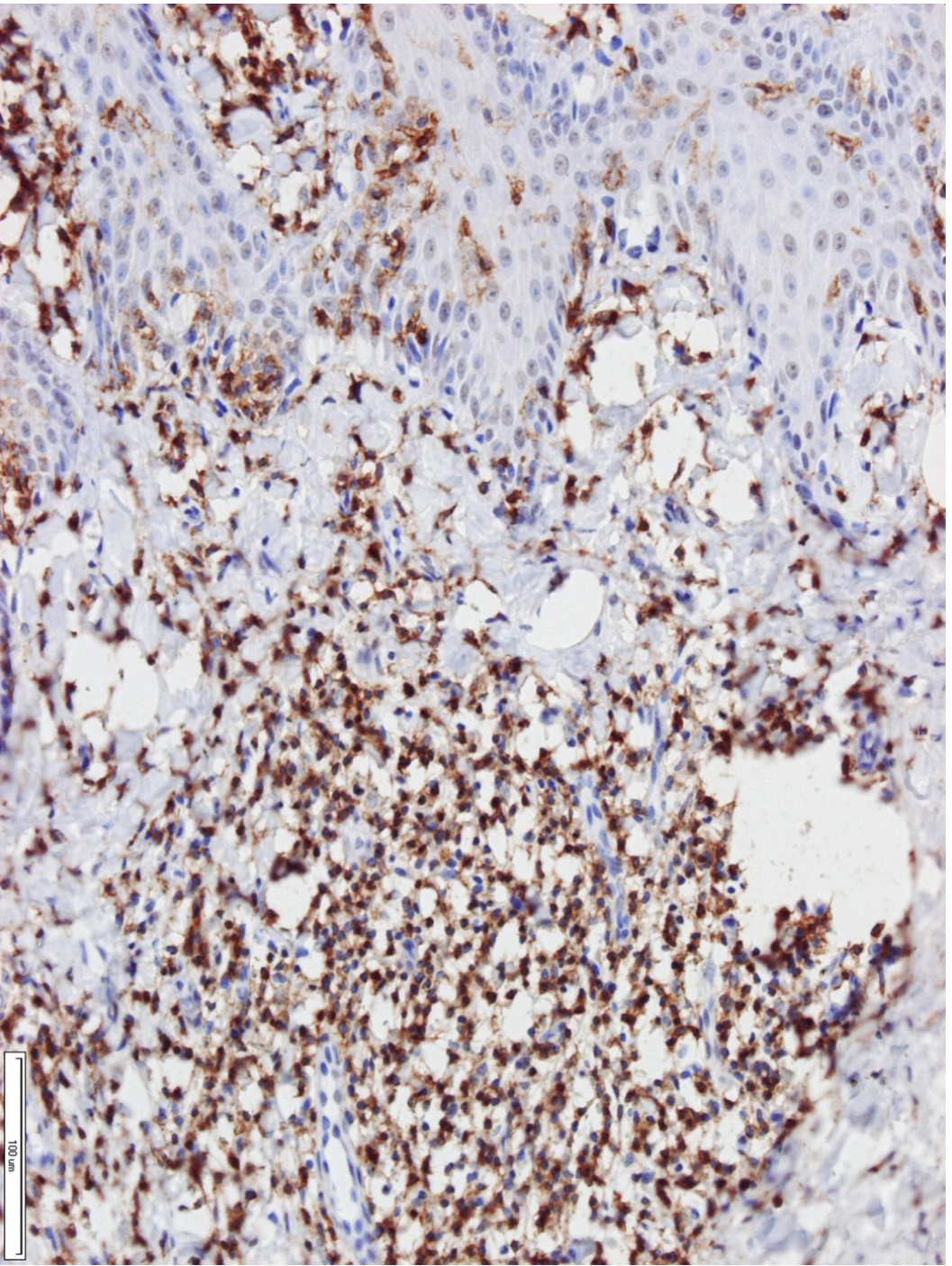


MF - before
therapy









100 μm



Remission after IFN α + acitretin



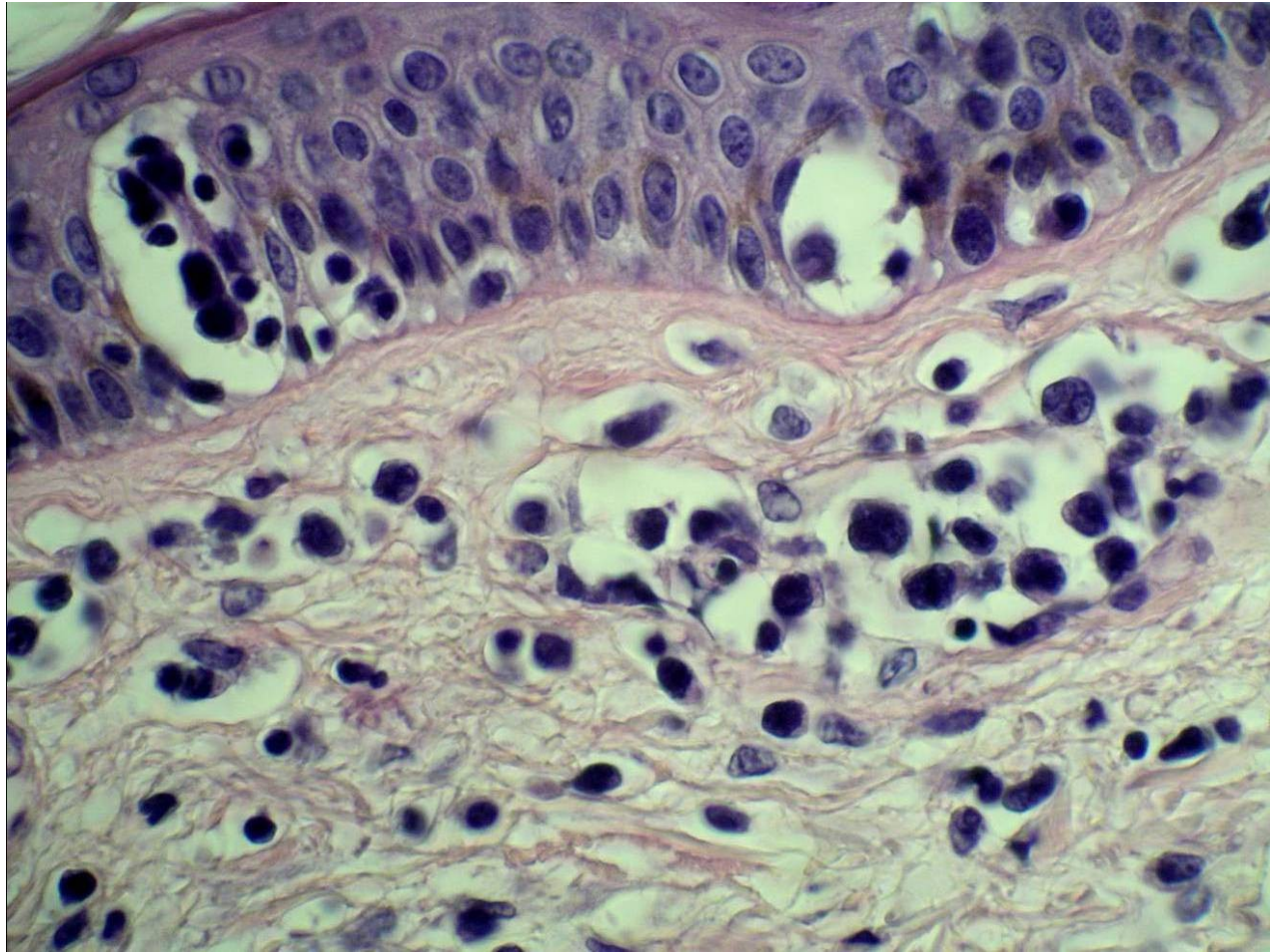


MF - before therapy, 2007











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



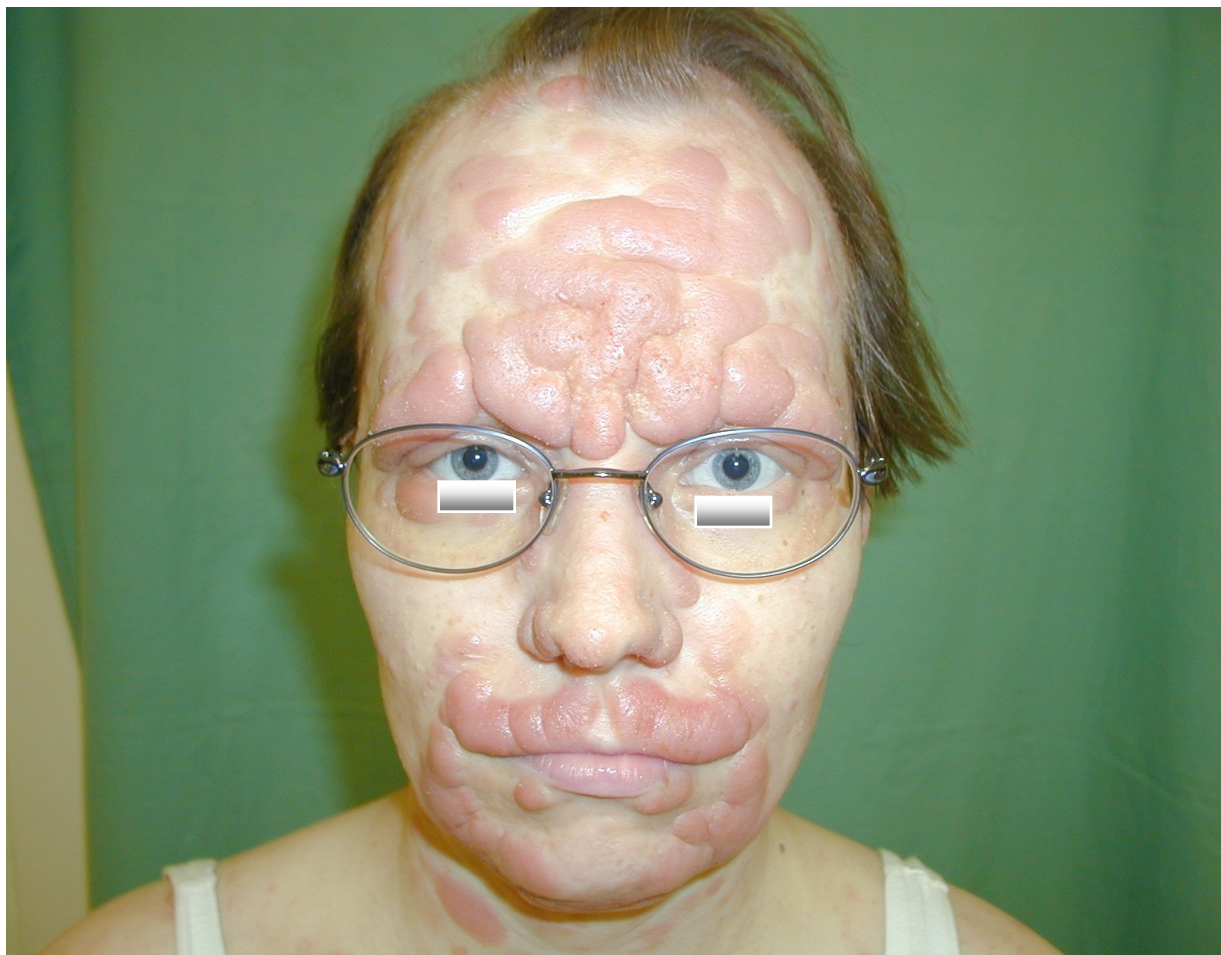


2006 – after IFN α + acitretin + TSEB



2009 – bexarotene therapy

MF – before therapy



MF – before therapy

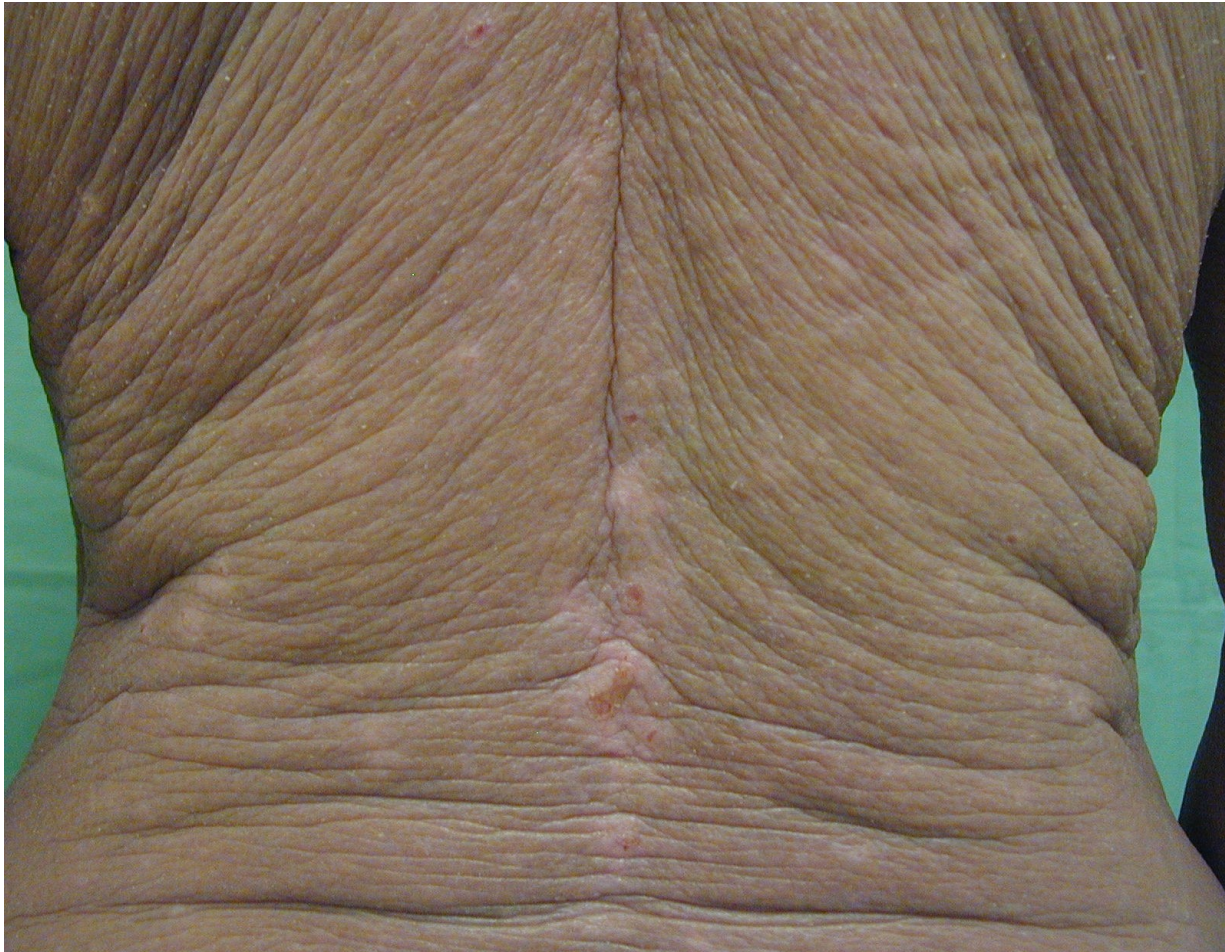


3 months bexarotene therapy + PUVA





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

