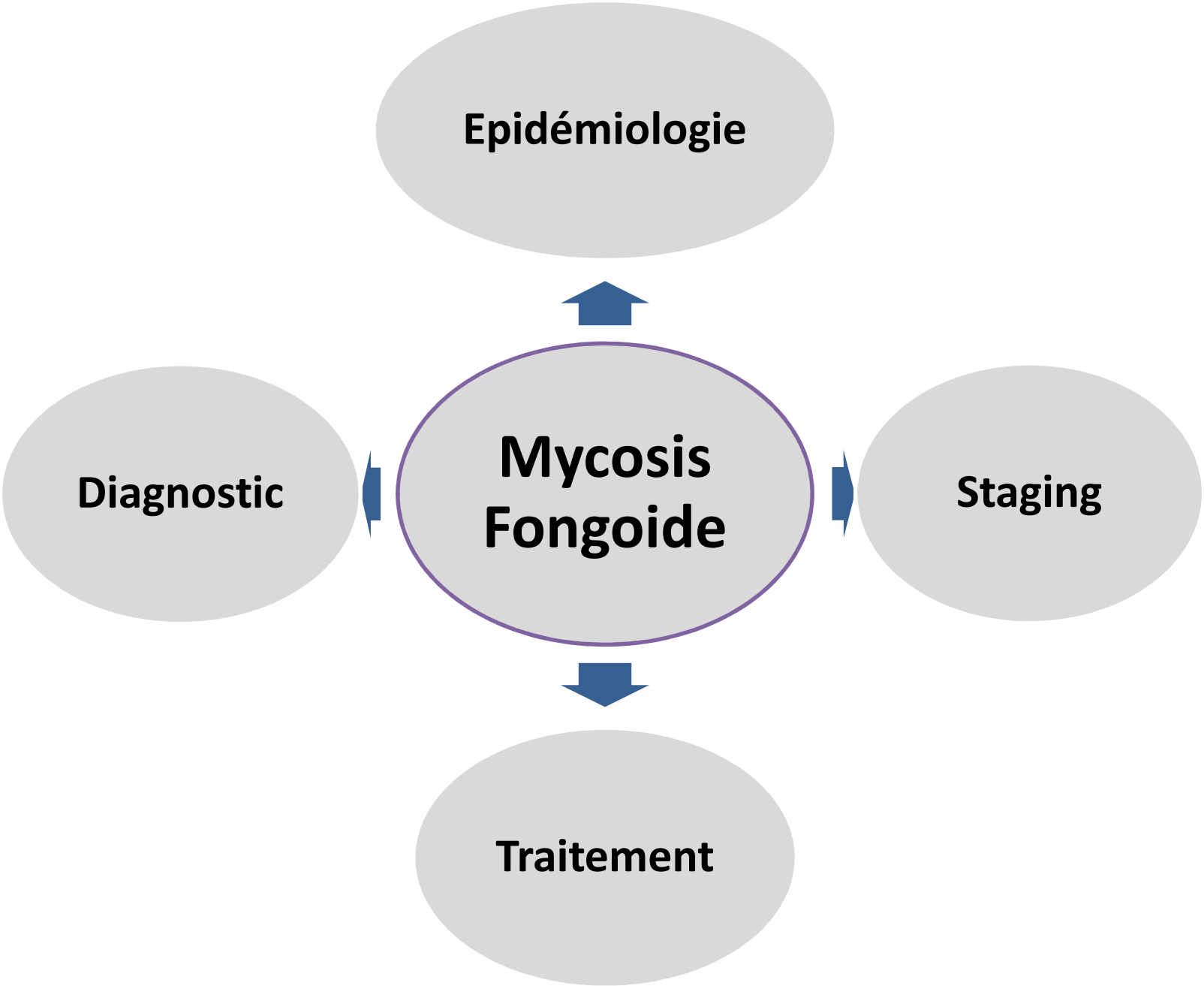
Mycosis fongoïde.
Problématique au quotidien

H. BENCHIKHI

Congrès Maghrébin d'Hématologie
23 & 24 Mai 2014 Agadir


Epidémiologie
Diagnostic
Mycosis Fongoide
Staging
Traitement

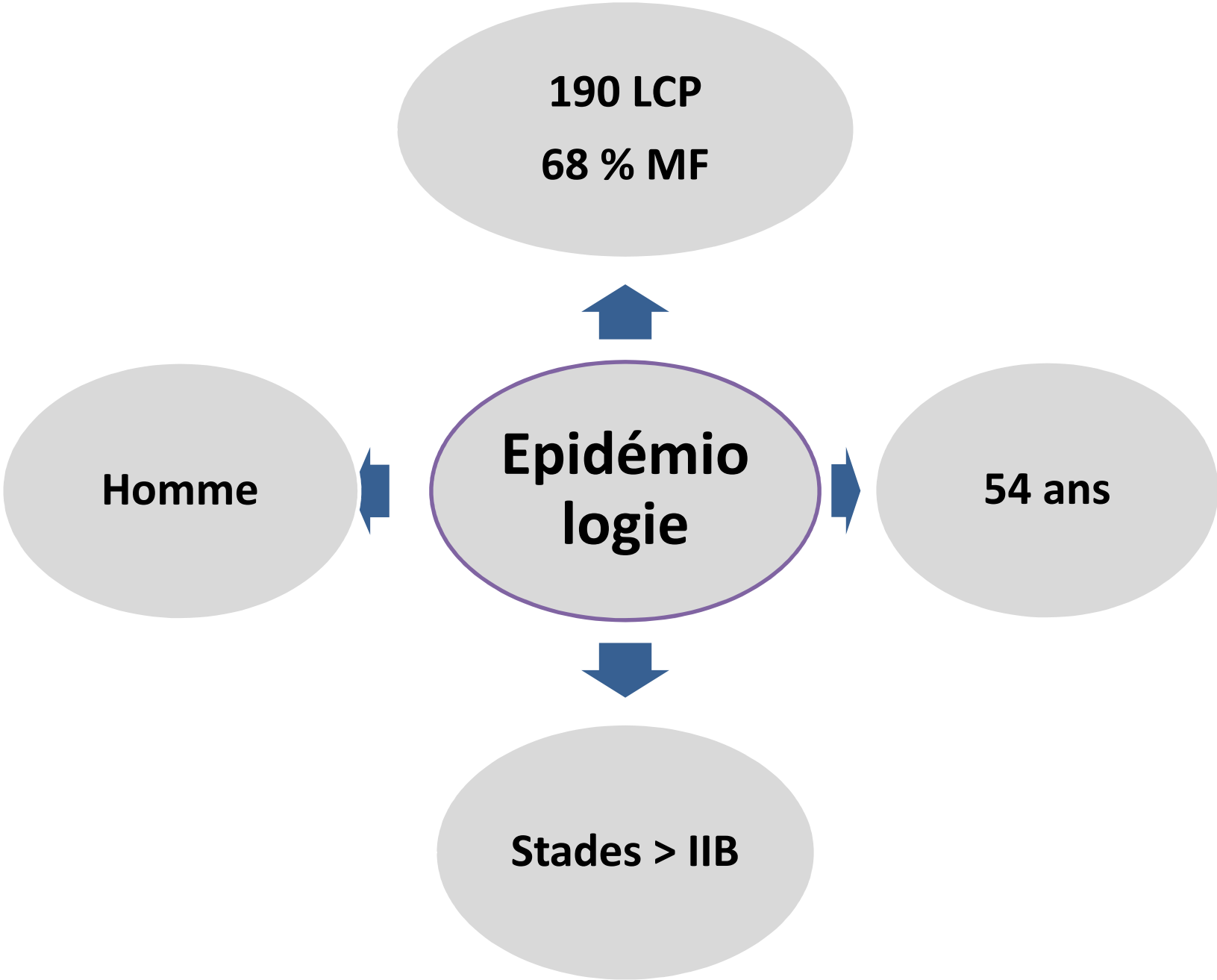
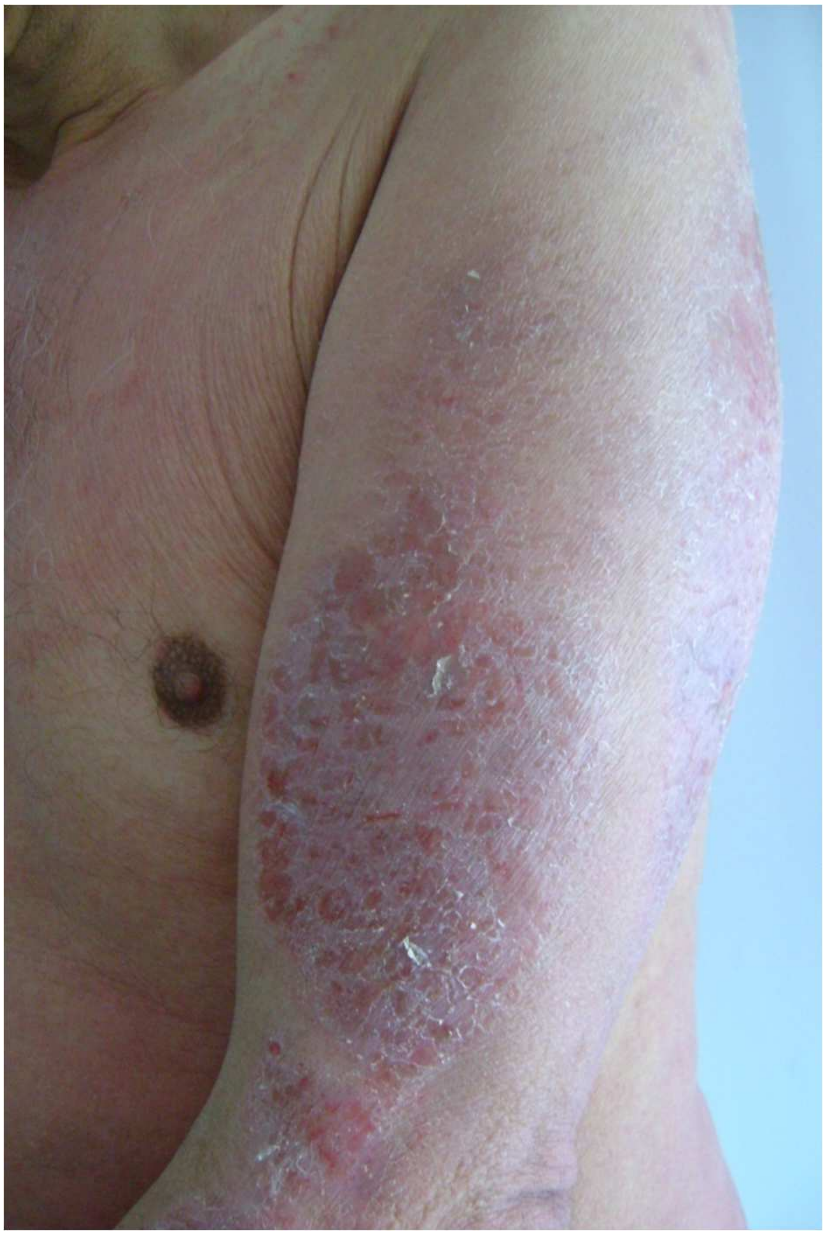
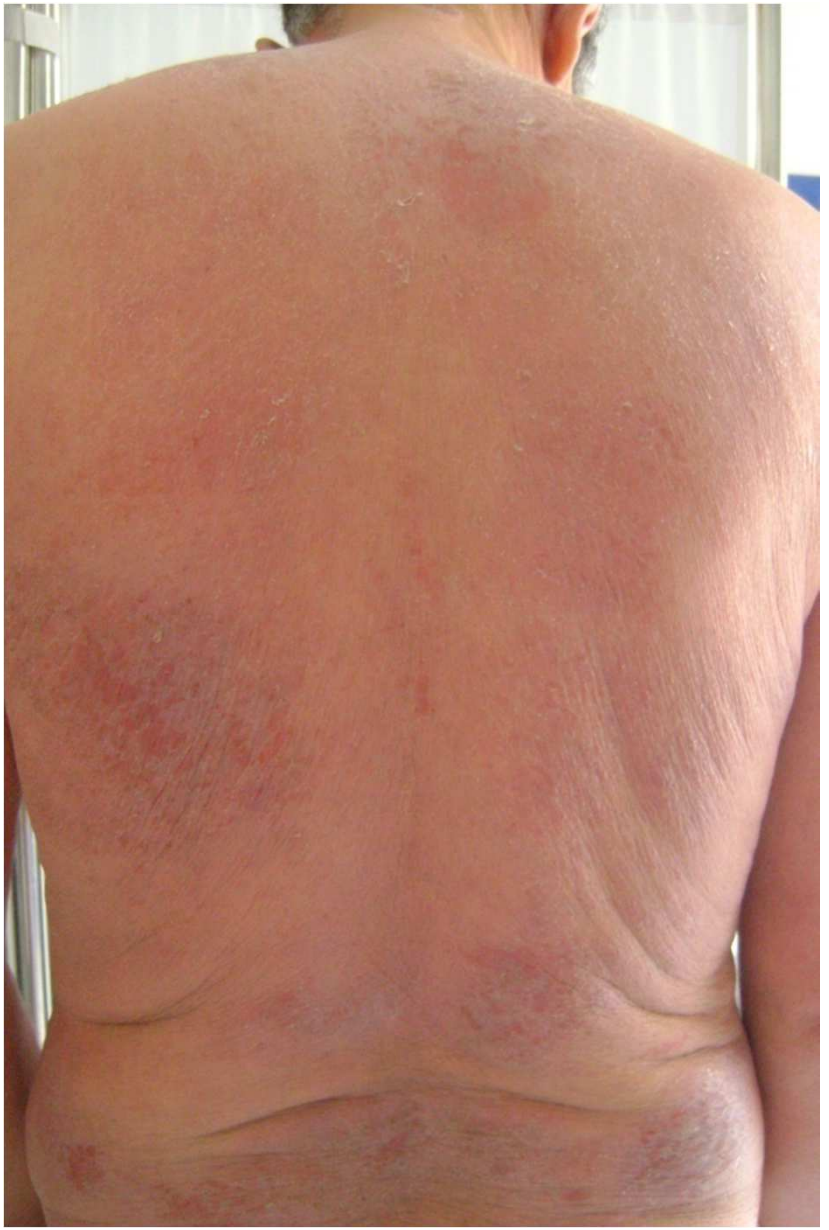

190 LCP
68 % MF
Homme
Epidémio logie
54 ans
Stades > IIB

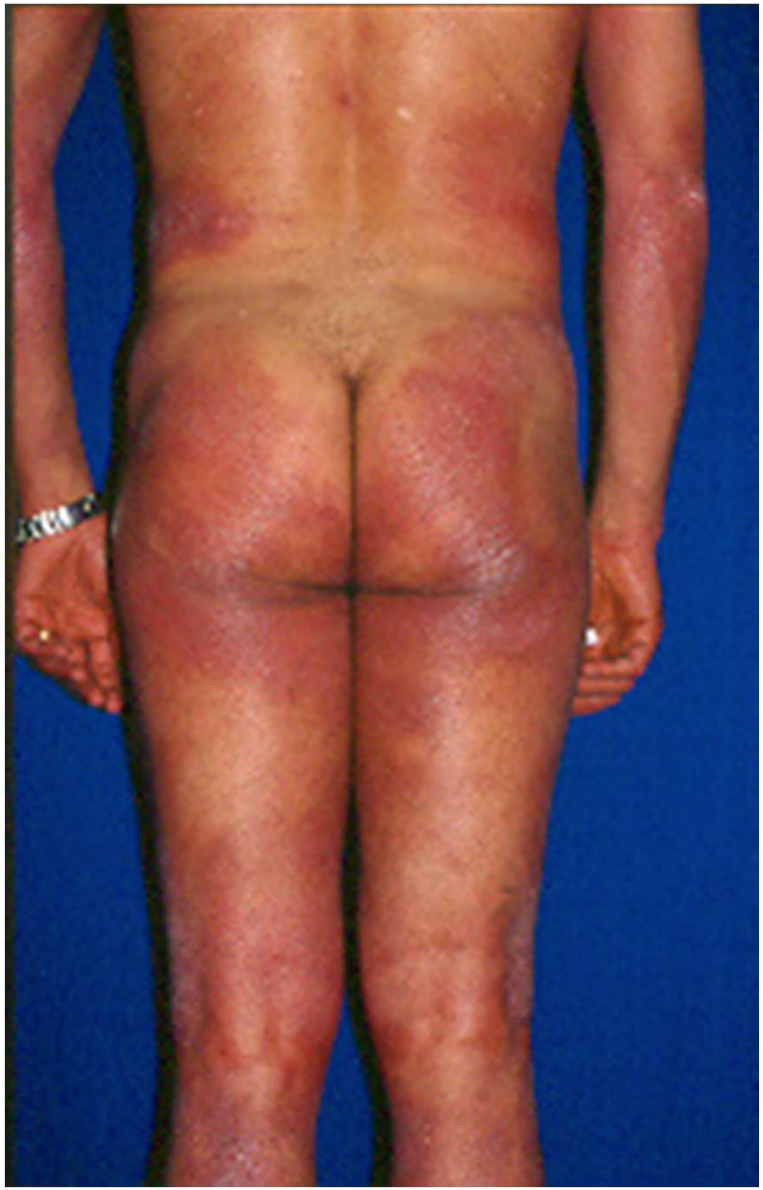
Tableau 1 Type histologique des cancers cutanés colligés durant 1971–1991 et 1992–2010 au service de dermatologie de Casablanca.

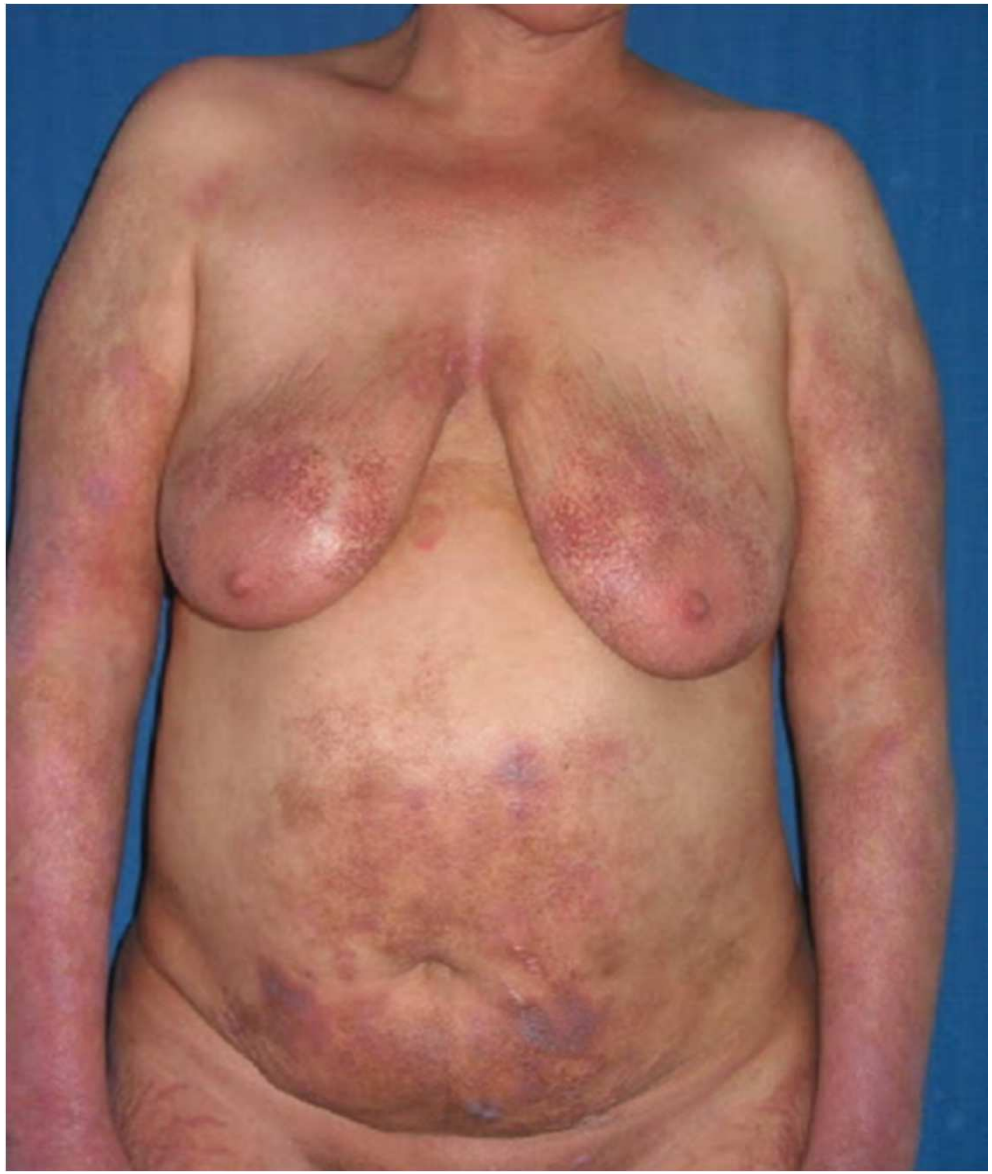
	Période 1992–2010 (19 ans)	Période 1971–1991 (21 ans)	*p*
Carcinome basocellulaire	253 (26,9%)	2373 (58%)	< 0,05
Carcinome spinocellulaire	223 (23,7%)	1512 (32%)	< 0,05
Lymphomes	175 (18,6%)	65 (1,5%)	< 0,05
Mycosis fongoïde	116 (12,3%)	43 (0,9%)	< 0,05
Autres lymphomes	59 (6,2%)	22 (0,05%)	< 0,05
Mélanome	98 (10,4%)	151 (3,5%)	< 0,05
Sarcomes	99 (10,5%)	172 (4%)	< 0,05
Sarcome de Kaposi	66 (7%)	38 (0,8%)	< 0,05
Autres sarcomes	33 (3,5%)	77 (1,7%)	< 0,05
Métastases	28 (2,9%)	43 (1%)	< 0,05
Tumeurs annexielles	10 (1%)	–	
Autres	53 (5%)	–	
Total	939	4316	

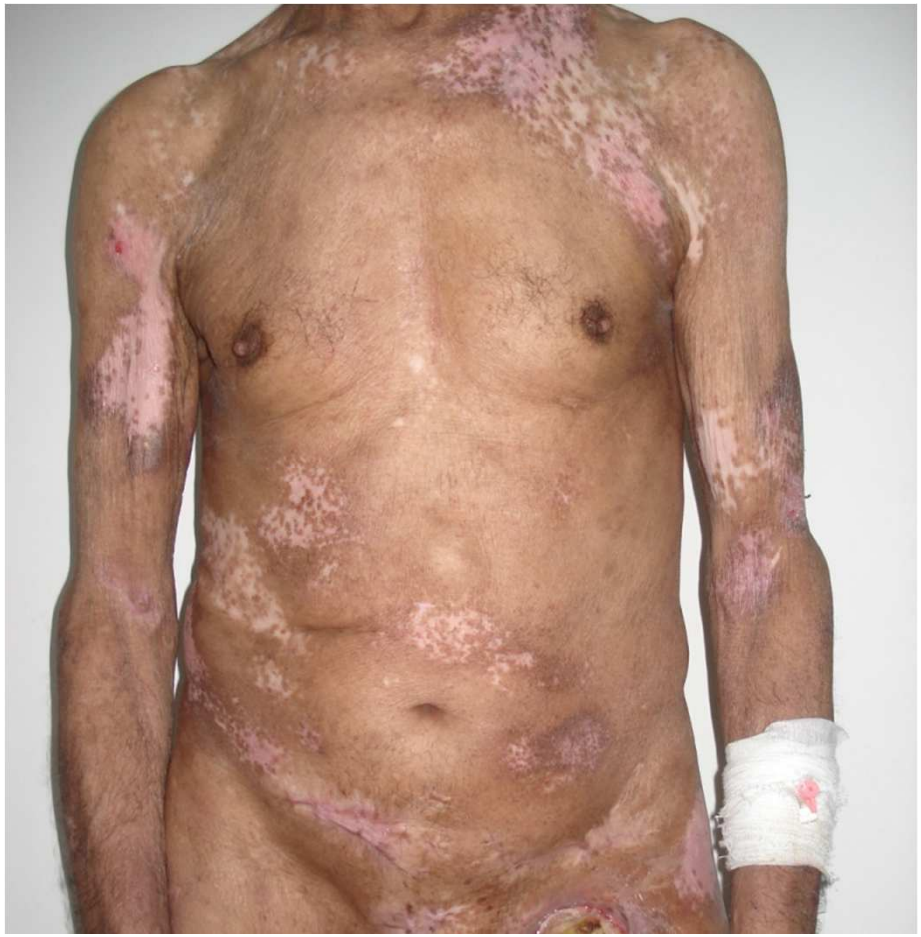
Benchikhi et coll, Ann Dermato Venereol Décembre 2012

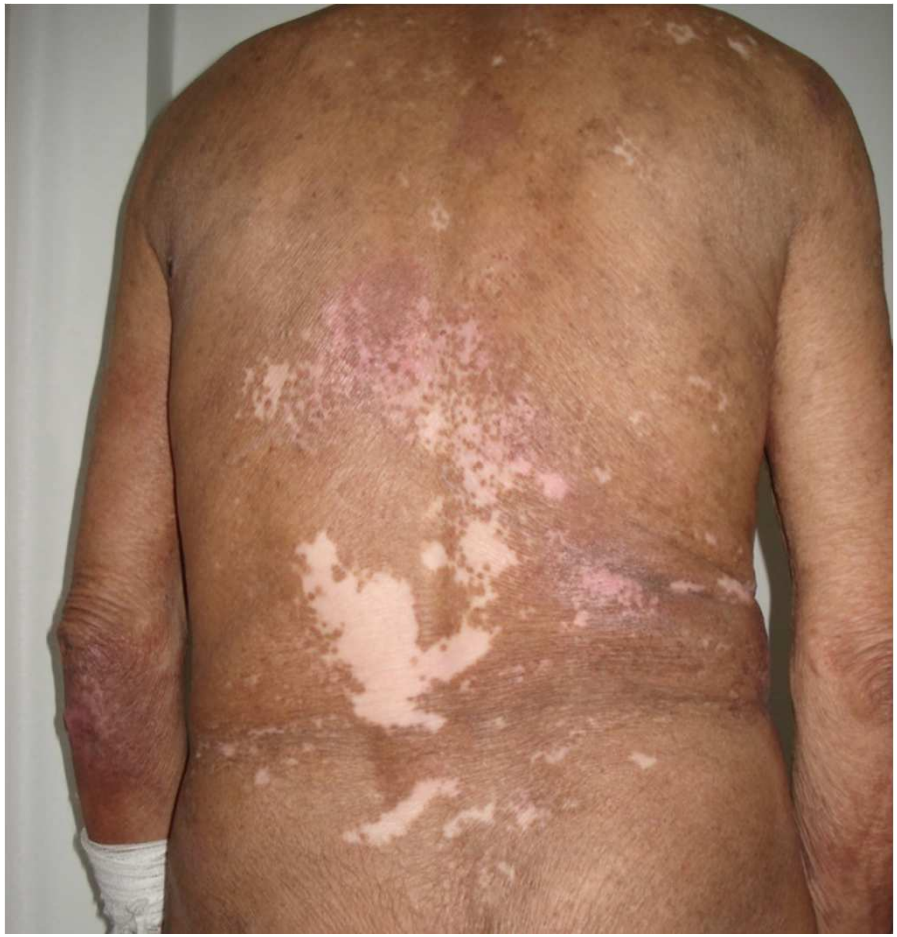


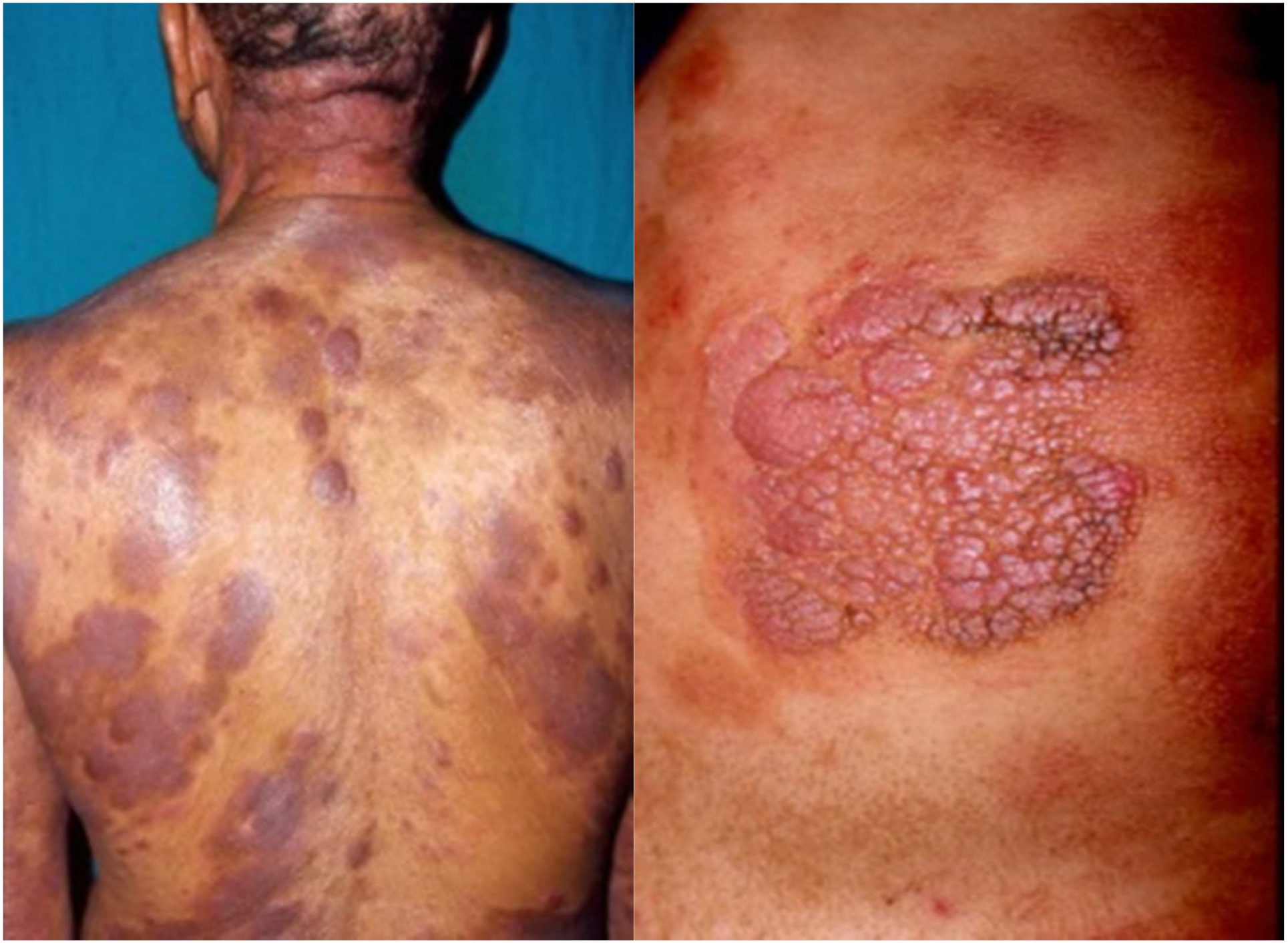


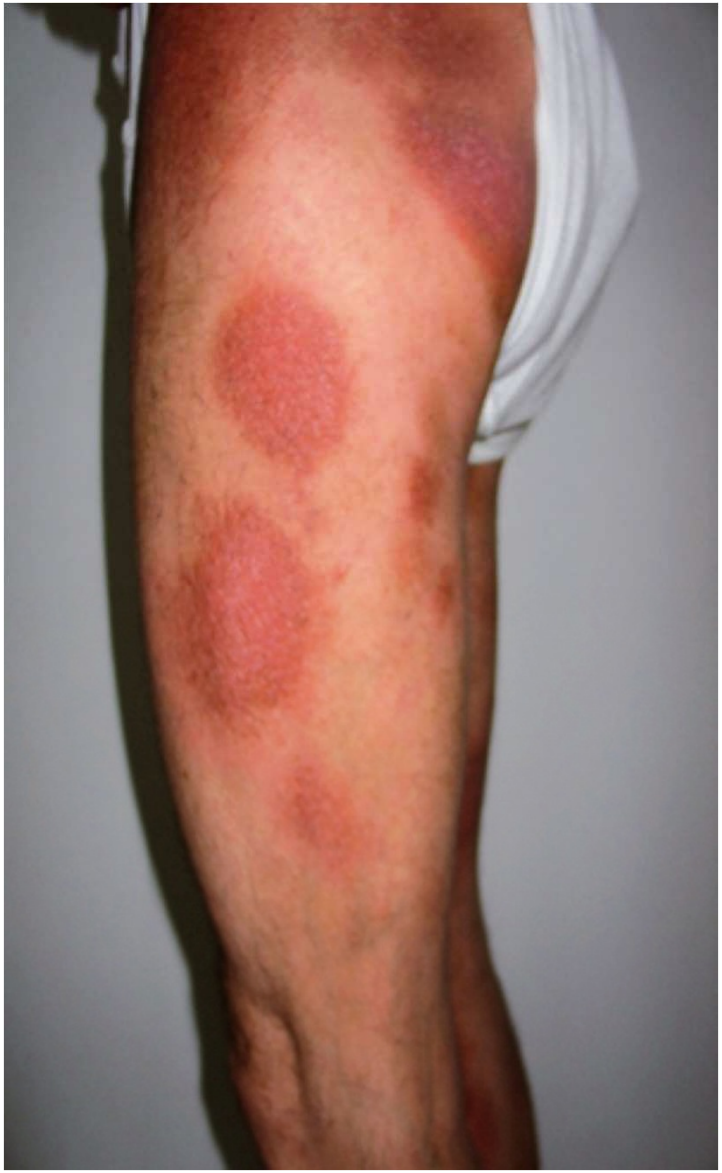


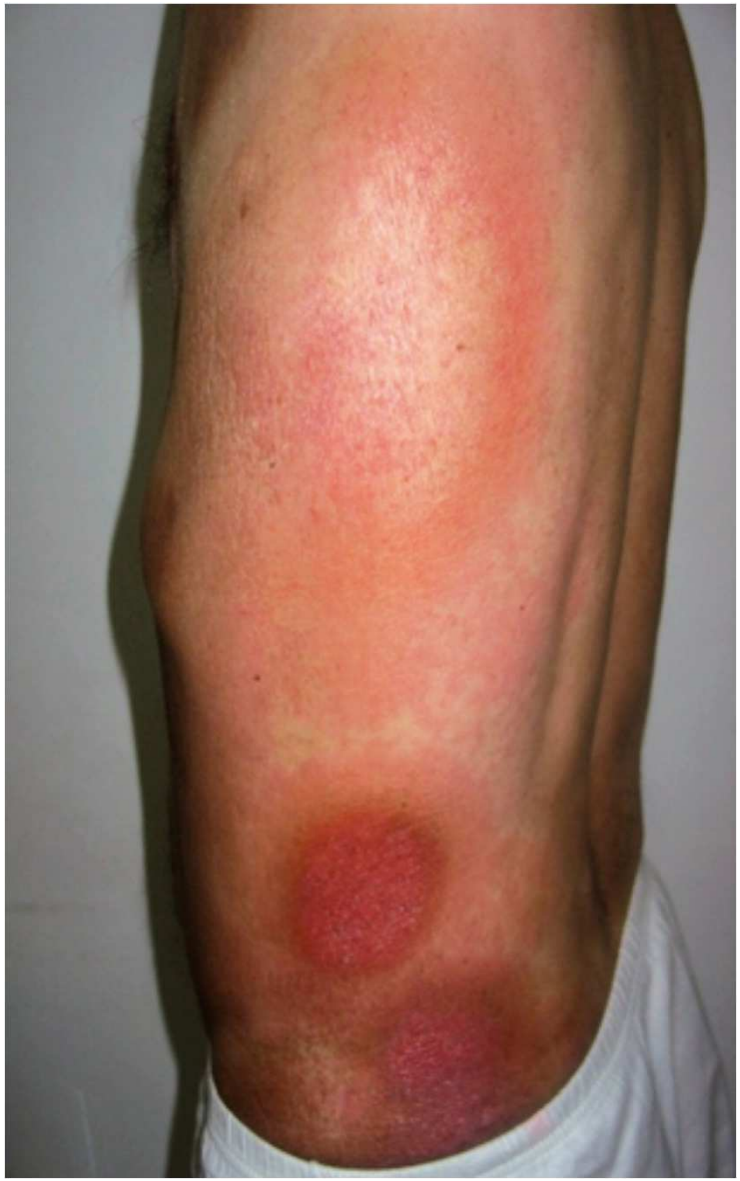


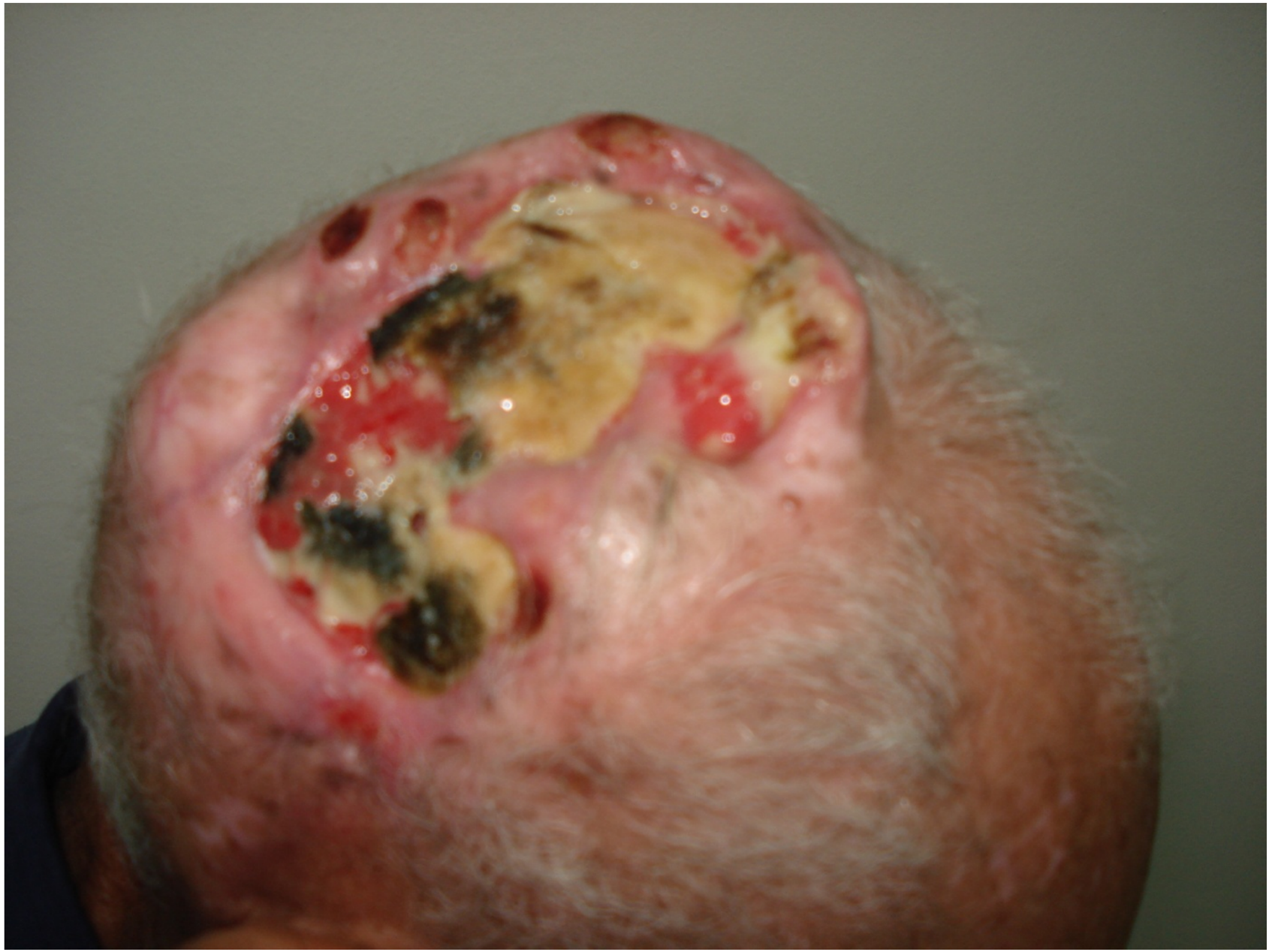


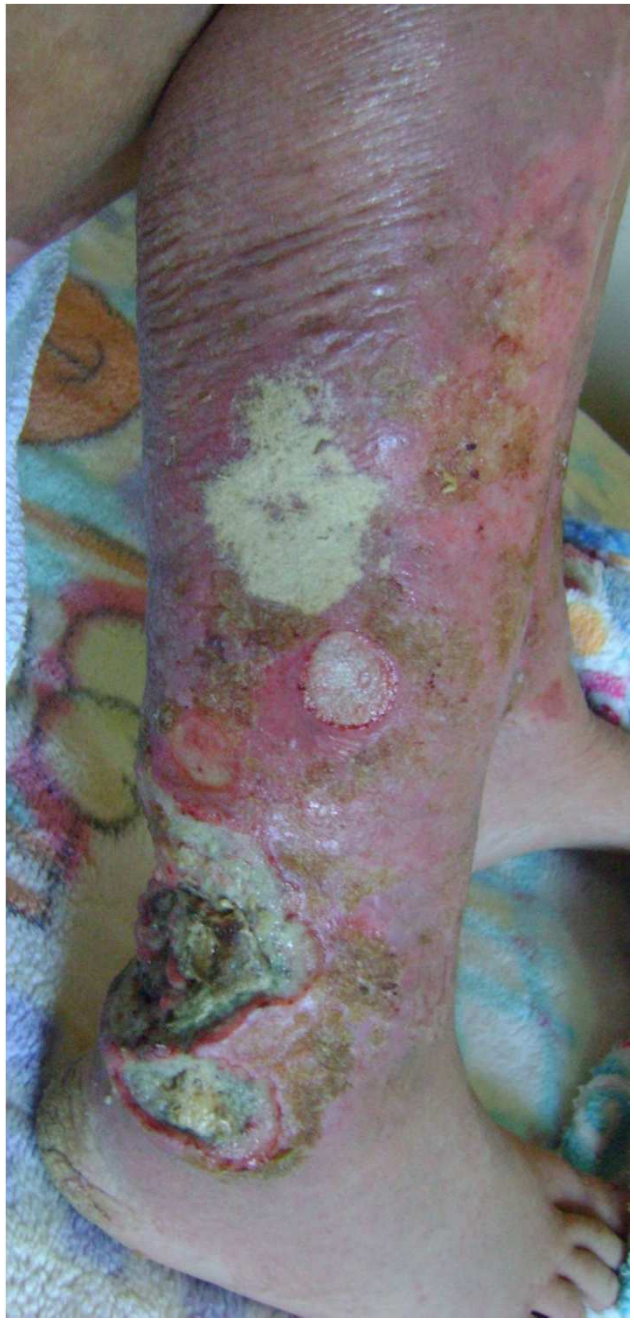


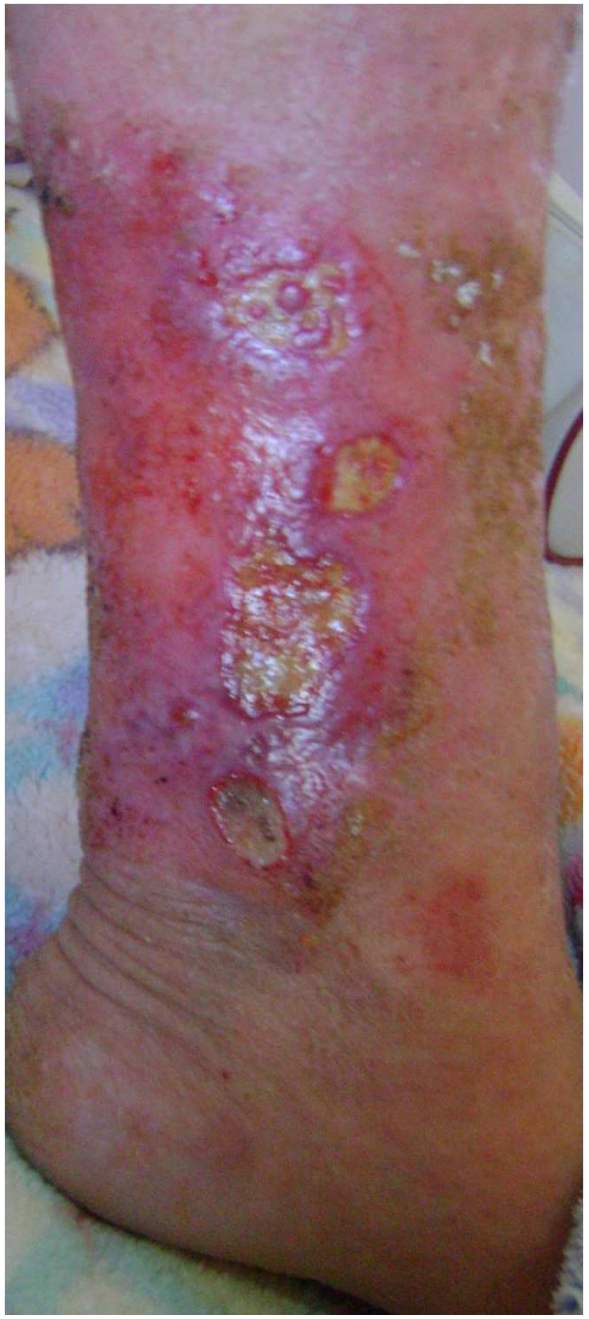


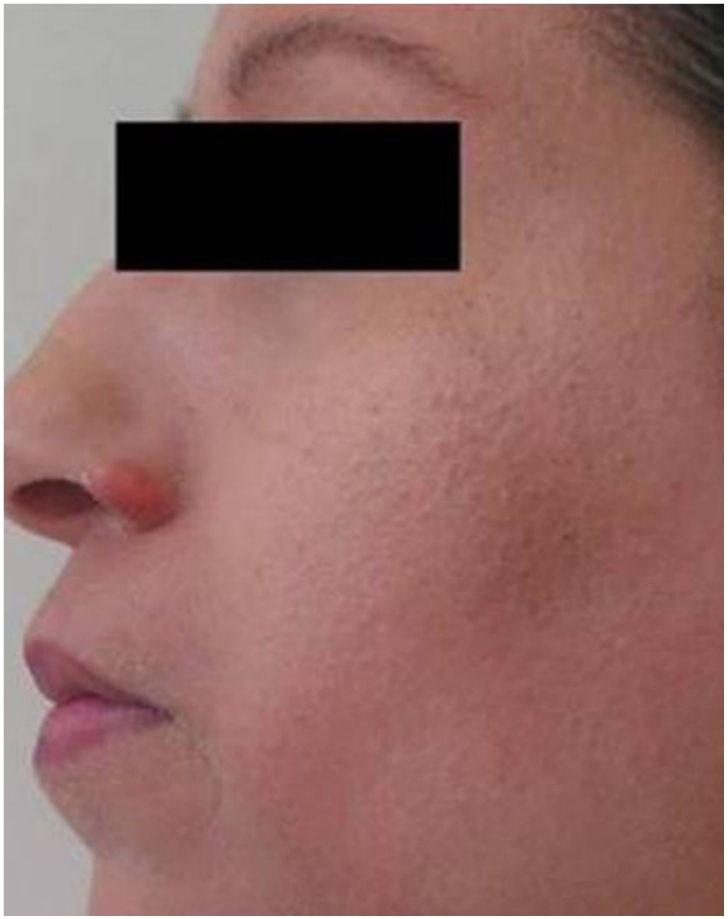


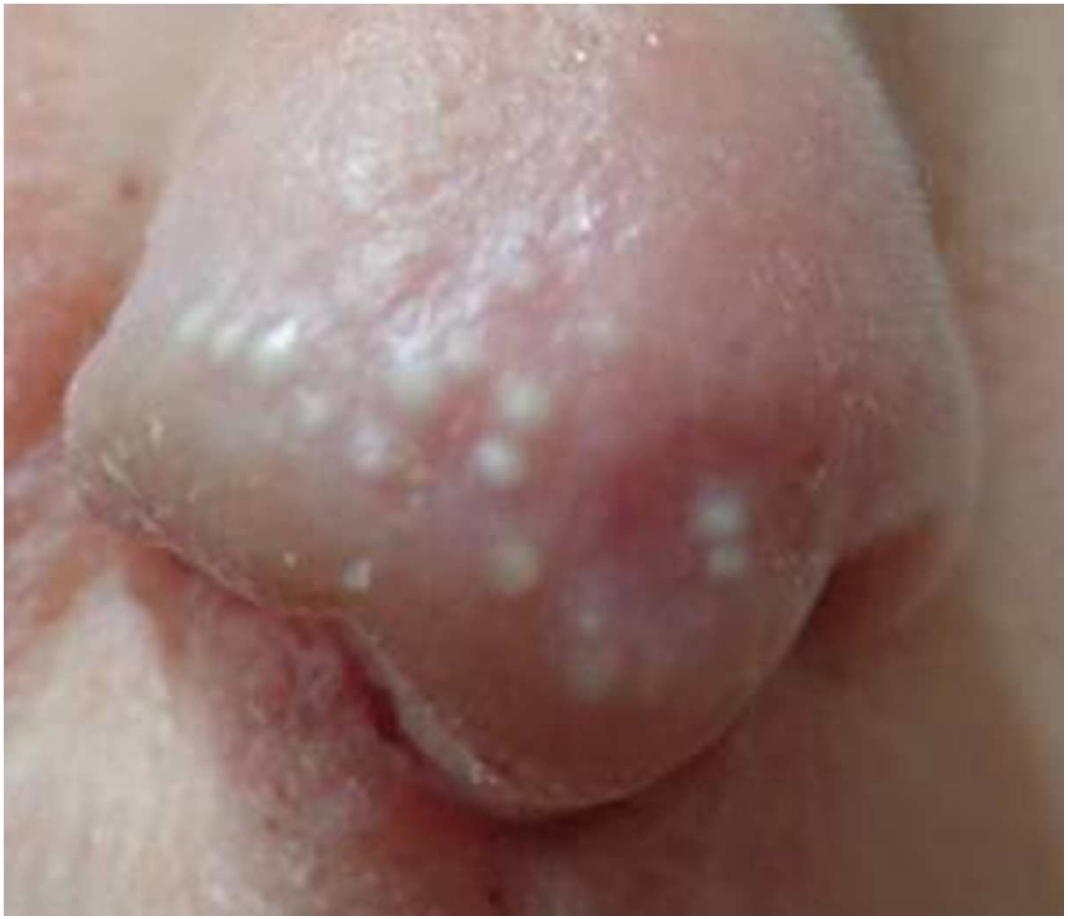


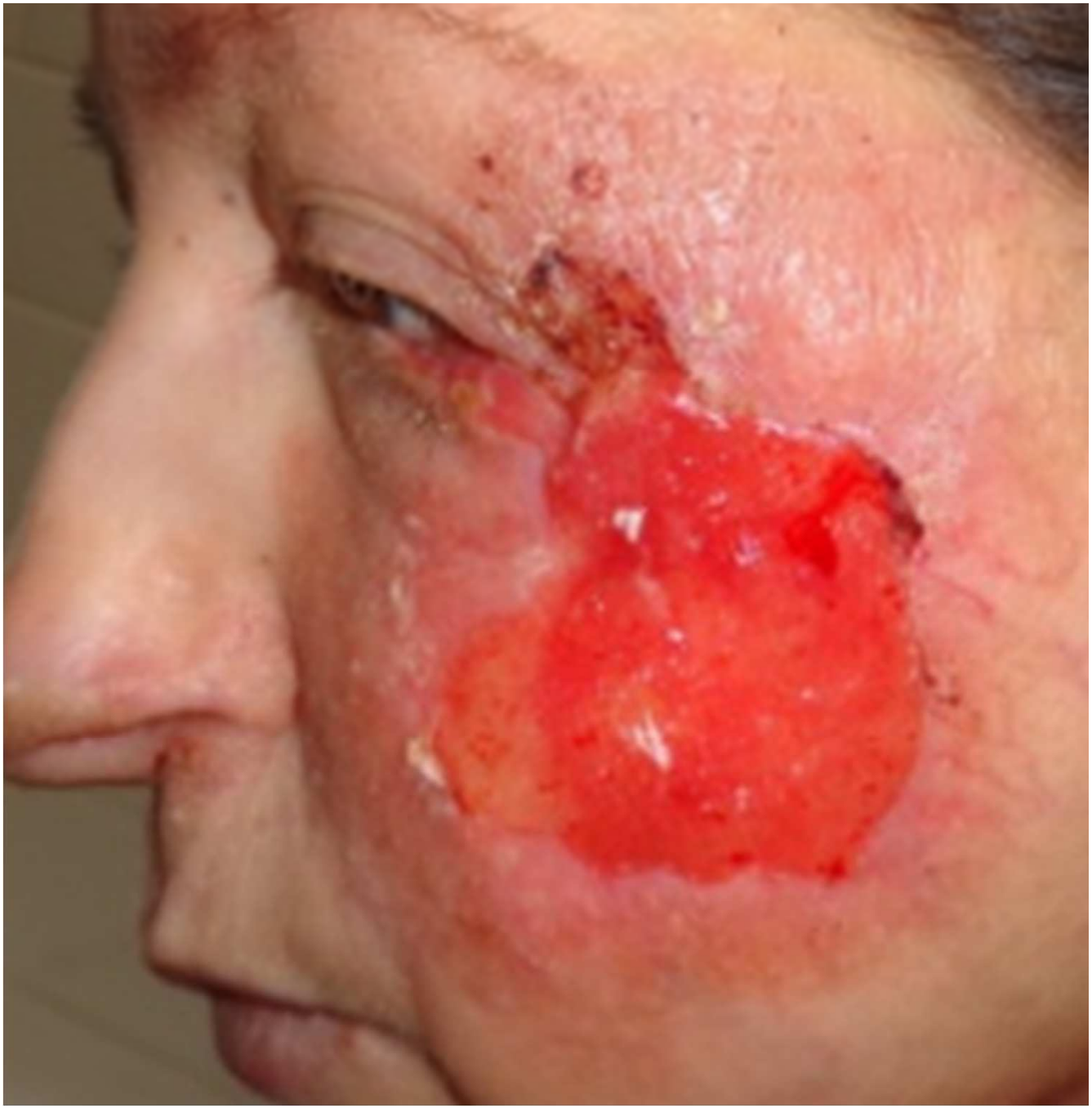




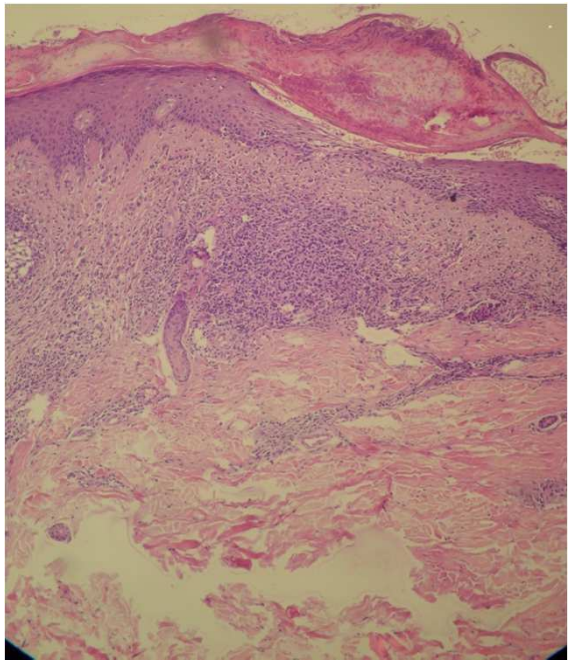


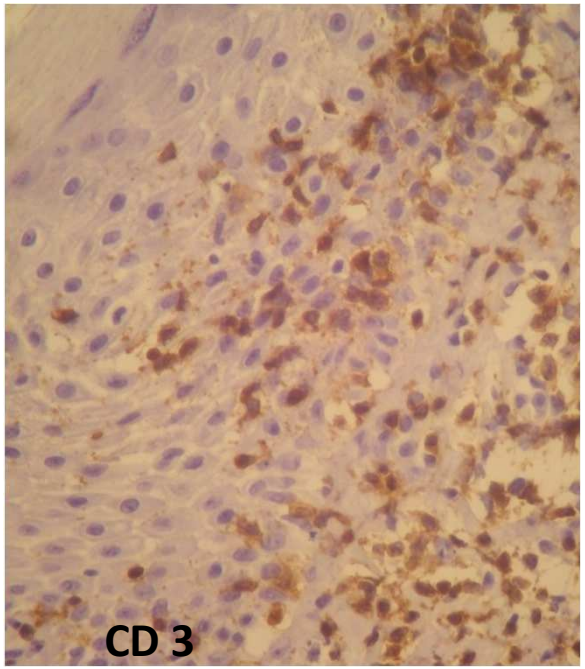


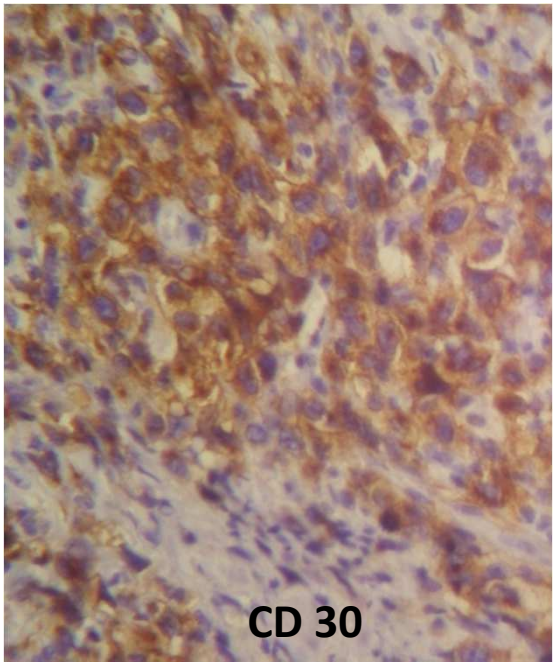




Histologie et immunohistochimie performantes!







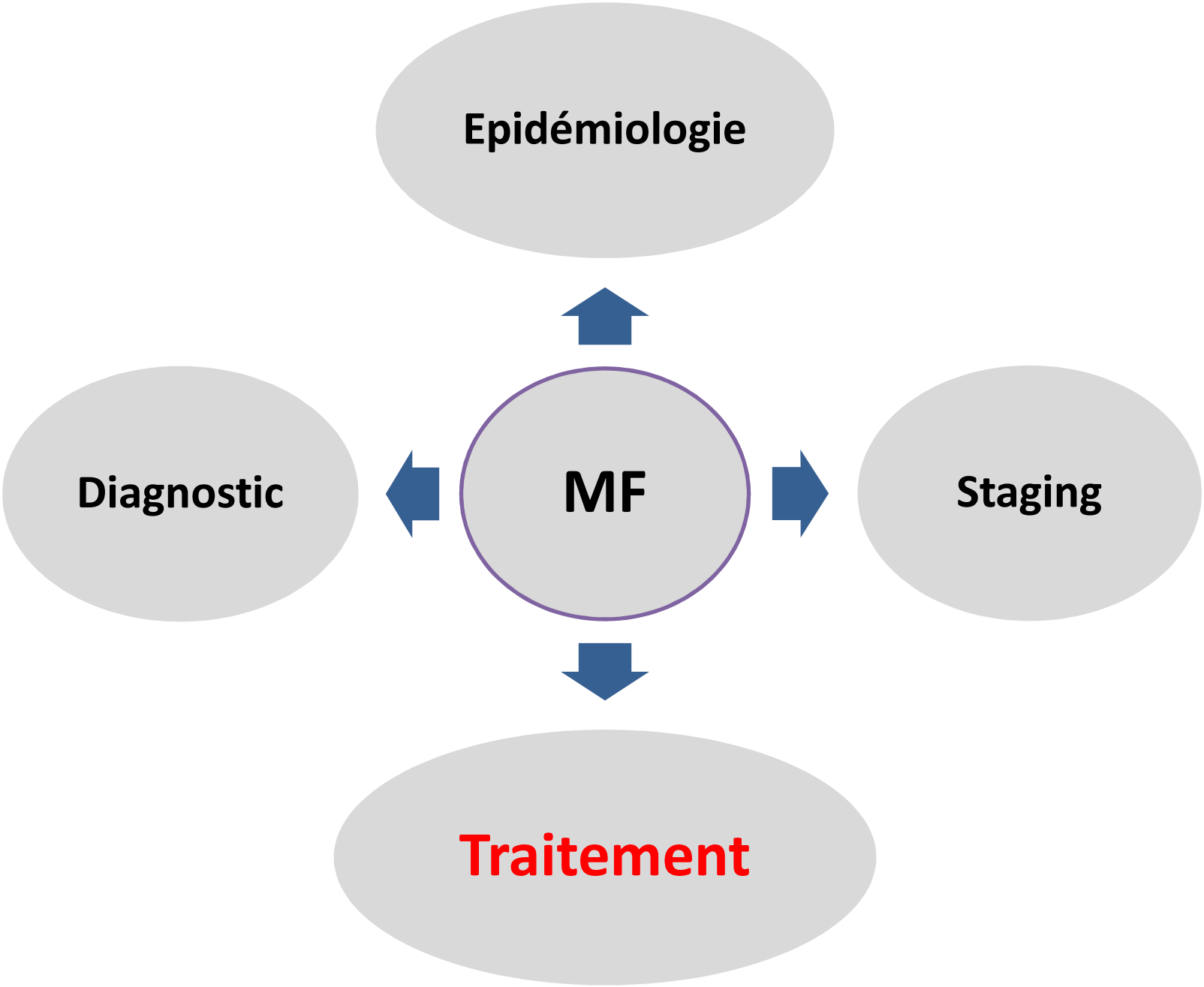
H.E x 10 : MF : Infiltrat lymphoïde dermique dense avec épidermotropisme.

Classification		
Cutaneous T-cell and NK-cell lymphomas	Mycosis fungoides	
	MF variants and subtypes	• Folliculotropic MF • Pagetoid reticulosis • Granulomatous slack skin
	Sézary syndrome	
	Adult T-cell leukemia/lymphoma	
	Primary cutaneous CD30+ 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+ T-cell lymphoma (provisional) • Cutaneous gamma/delta 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

Table 1. WHO-EORTC classification of cutaneous lymphoma with primary cutaneous manifestations[1]

Limited-stage Disease	
IA	T1, N0, M0, B0-1
IB	T2, N0, M0, B0-1
IIA	T1-2, N1-2, M0, B0-1
Advanced-stage Disease	
IIB	T3, N0-2, M0, B0-1
IIIA	T4, N0-2, M0, B0
IIIB	T4, N0-2, M0, B1
IVA_1	T1-4, N0-2, M0, B2
IVA_2	T1-4, N3, M0, B0-2
IVB	T1-4, N0-3, M1, B0-2

Table 5. Staging of MF/SS (ISCL/EORTC revision)[2,3]
T1-4: tumor stage; N0-3: nodal stage; M0-1: visceral organs; B1-2: peripheral blood


Epidémiologie
Diagnostic
MF
Staging
Traitement

Patch, plaques

Dermocorticoïdes

Caryolysine

Puvathérapie

Méthotrexate

Nodules,tumeurs

Interféron

Méthotrexate

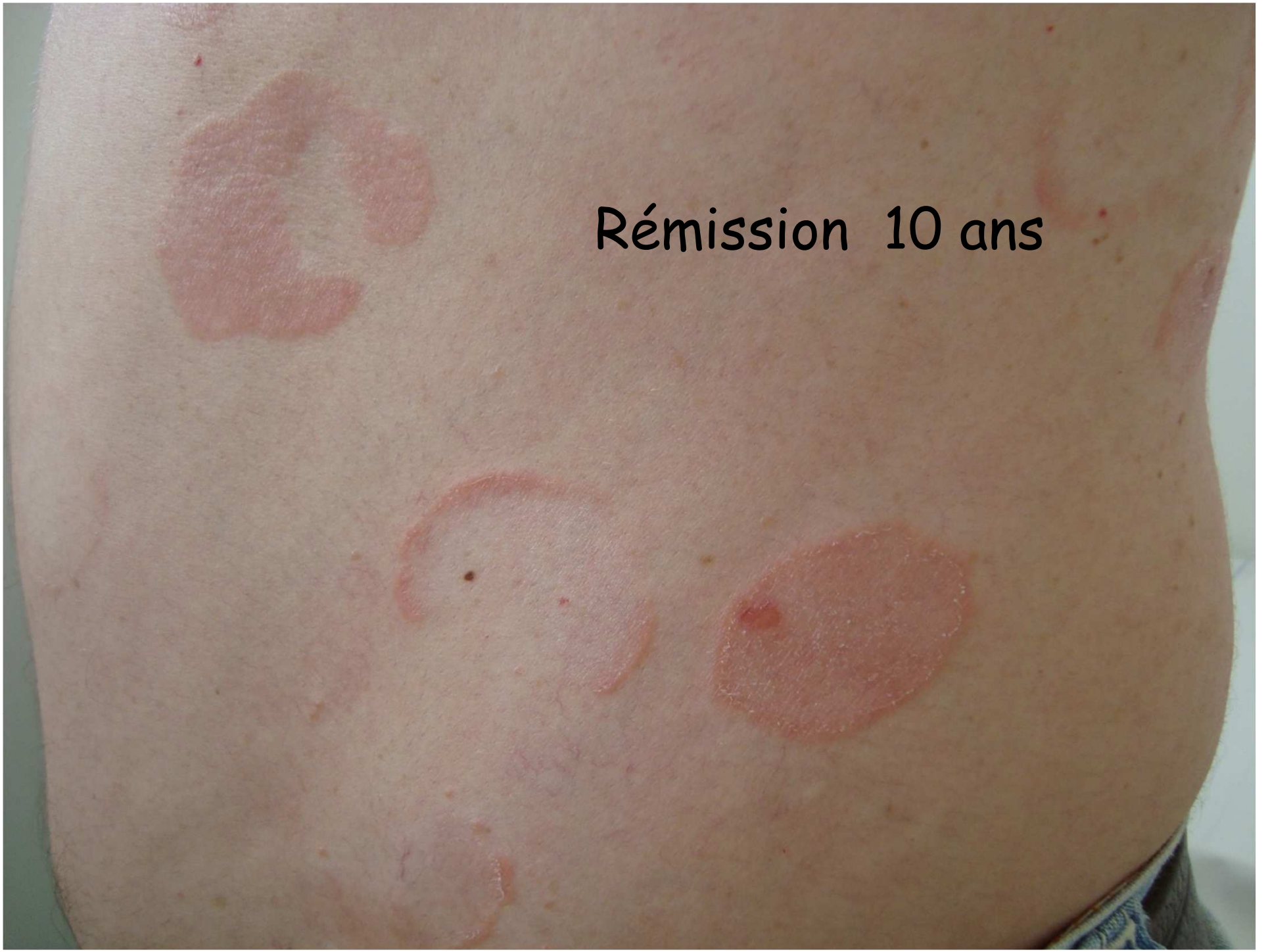
Chimiothérapie

Autres

Mycosis fongoïde et PUVA

- **96 patients:**
  - 84 % H , 16 % F
- **Moyenne d´âge:** 52 ans(31 -74 ans)
- **Les stades de mycosis fongoïde:**
  - stade IA : 1 %
  - stade IB : 50 %
  - stade IIA : 13%
  - stade IIB : 36 %

Evolution favorable à moyen terme


Rémission 10 ans

- Patch, plaques

Dermocorticoïdes

Caryolysine

Puvathérapie

Méthotrexate

Nodules,tumeurs

Interféron

Méthotrexate

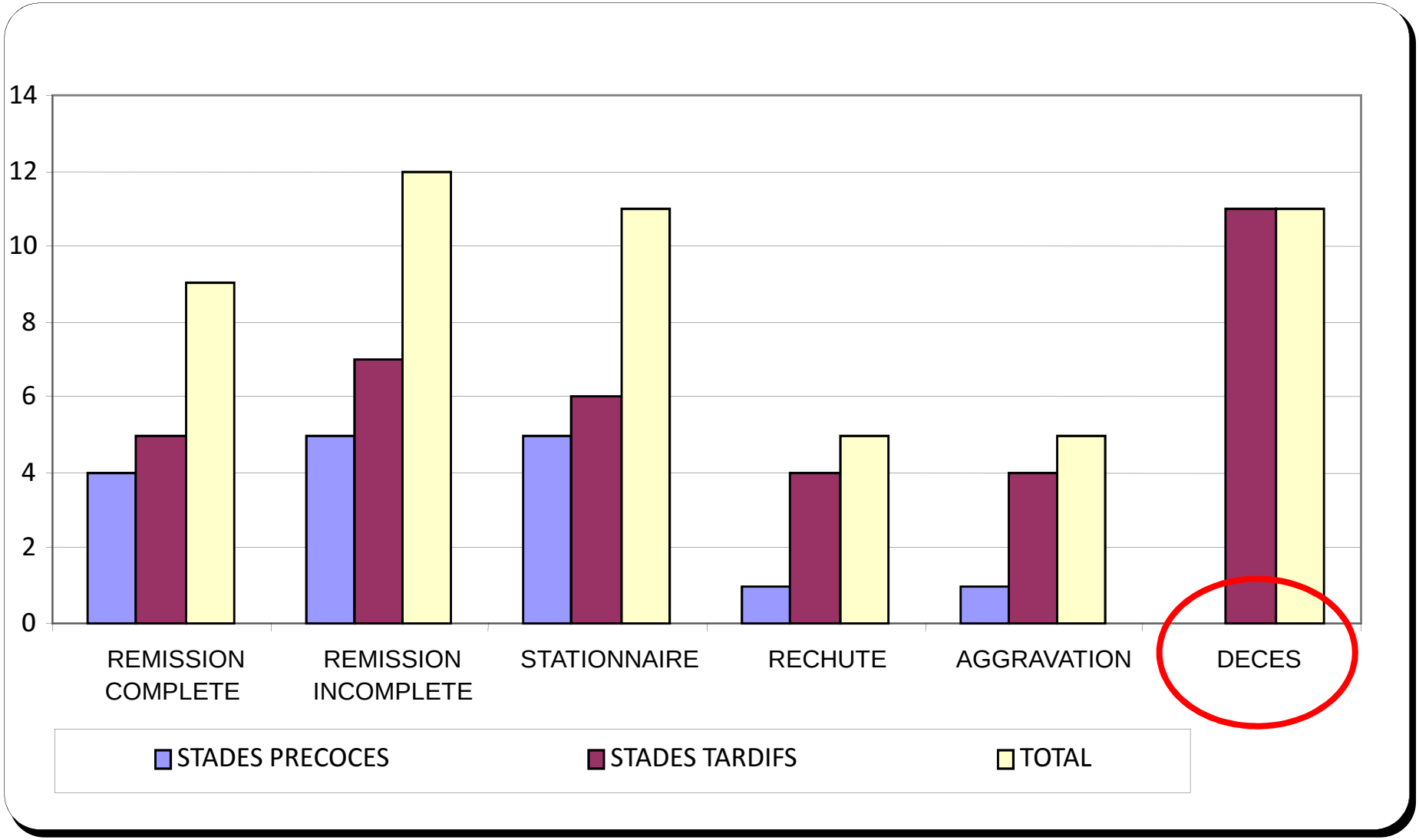
Chimiothérapie

Autres

Mycosis fongoïde. Traitement/stades. 63 cas

	STADES PRECOCES		STADES TARDIFS		TOTAL	
	Nbre cas	%	Nbre cas	%	Nbre cas	%
DERMOCORTICOIDES	17	25%	7	10%	24	35%
CARYOLYSINE	11	16%	12	18%	23	34%
PHOTOTHERAPIE	6	9%	8	12%	14	21%
CHIMIOTHERAPIE	3	4%	28	41%	31	46%
COP	2	3%	24	35%	26	38%
CHOP	0	0%	4	6%	4	6%
AUTRES	1	1%	10	15%	11	16%
DIVERS	2	3%	0	0%	2	3%

ASPECTS EVOLUTIFS DU MF. 63 cas.



Am J Ther. 2014 Apr 11. [Epub ahead of print]

Polish Lymphoma Research Group Experience With Bexarotene in the Treatment of Cutaneous T-Cell Lymphoma.

Sokolowska-Wojdylo M[1], Florek A, Zaucha JM, Chmielowska E, Giza A, Knopinska-Posluszny W, Kulikowski W, Prejzner W, Romejko-Jarosinska J, Paszkiewicz-Kozik E, Osowiecki M, Walewski J, Rogowski W, Grzanka A, Placek W, Lugowska-Umer H, Kowalczyk A, Nowicki R, Jurczak W.

MF et bexarotène, 21 patients
300 mg/m, durée 14,5 mois
Réponse globale 81%
Mortalité 52,8%
Pas d'efficacité dans les stades avancés

Acta Derm Venereol. 2014 May 7. doi: 10.2340/00015555-1886. [Epub ahead of print]

Vorinostat for Refractory or Relapsing Epidermotropic T-cell Lymphoma: a Retrospective Cohort Study of 15 Patients.

Kogge A[1], Volteau C, Saint-Jean M, Peuvrel L, Brocard A, Knol AC, Renaut JJ, Dréno B, Quéreux G.

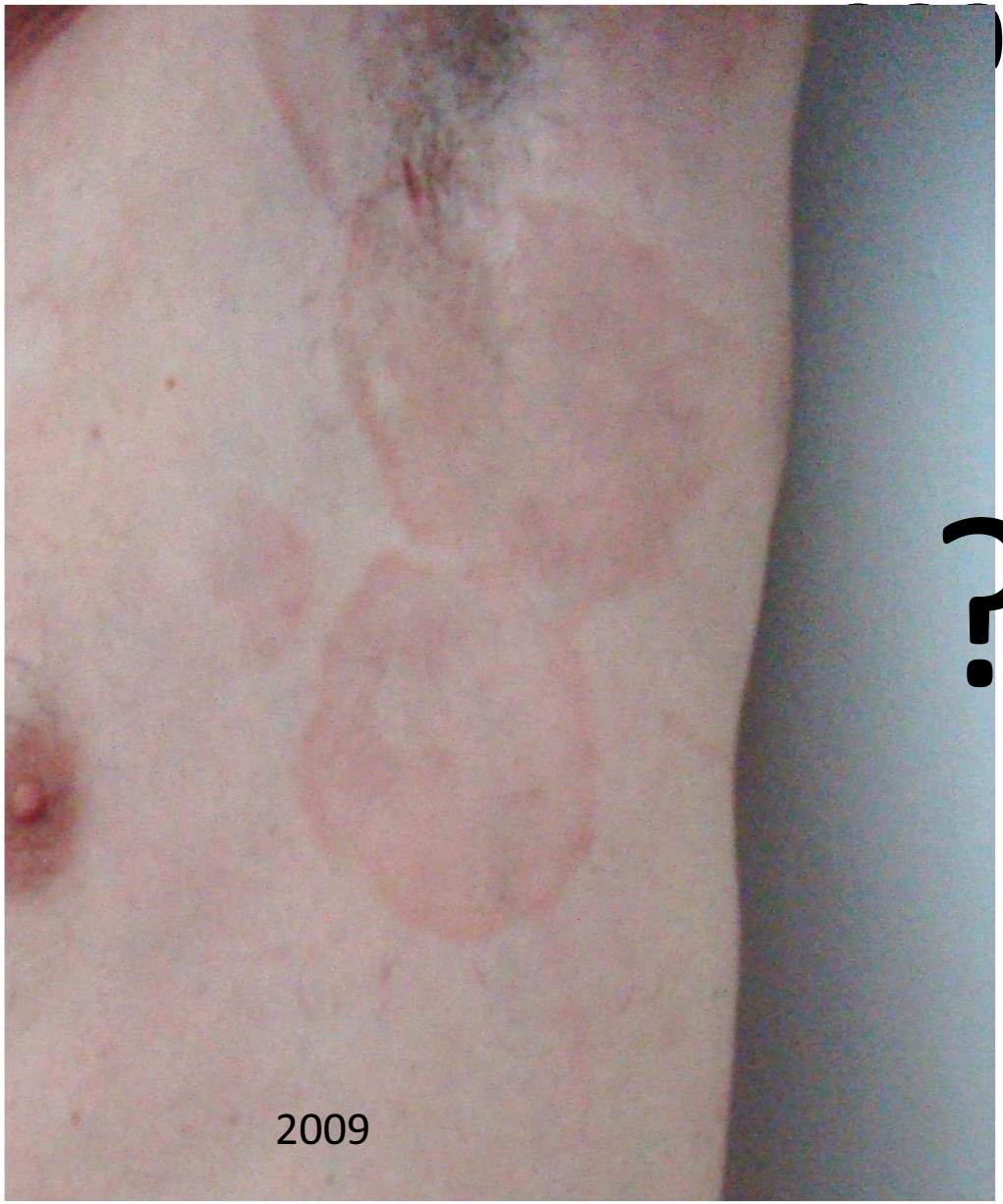
15 patients dont 6 MF, tous en échec, 1 à 7 tt,
5 Rémissions, 4 stabilisation, 6 aggravations
Durée réponse : 300 jours

Facteurs pronostiques du MF

	Characteristics	Better OS, DSS or decreased RDP	Worse OS, DSS or increased RDP
Univariate analysis	Advanced clinical stage; increased age; male sex; increased LDH; large-cell transformation		OS, DSS and RDP
	Hypopigmented MF; MF with lymphomatoid papulosis; poikilodermatous MF;	OS and RDP	
	Folliculotropic MF		RDP only
Multivariate analysis	Advanced skin (T) stage; blood stage B_{0b} (blood clone without Sézary cells); increased LDH; folliculotropic MF		OS, DSS and RDP
	Large-cell transformation		RDP only
	Advanced N, M and B stages; increased age; male sex		OS and DSS

Table 6. Prognostic characteristics in MF/SS defined from a cohort of 1,502 patients[2,14]
OS = overall survival; DSS = disease-specific survival; RDP = risk of disease progression

Risque de progression : Stades avancés ++++


2009

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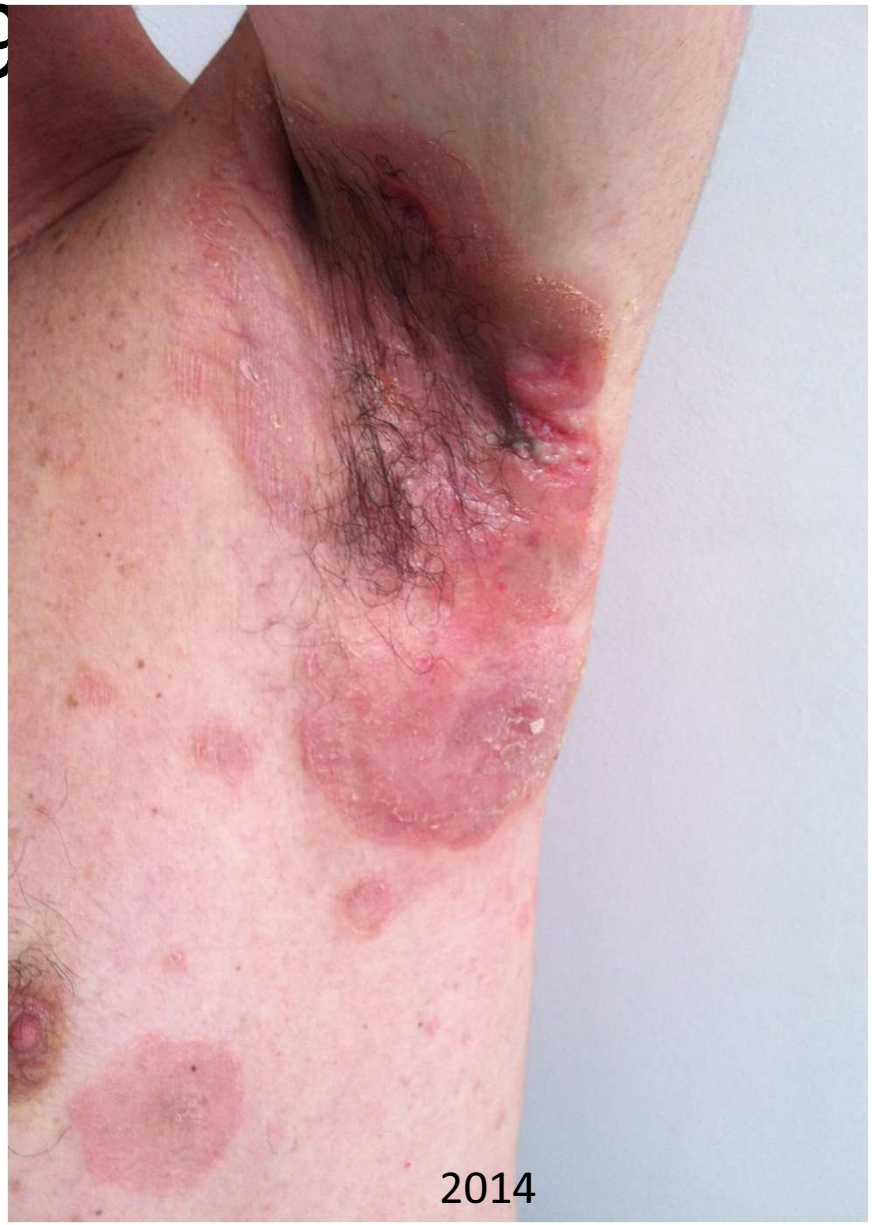
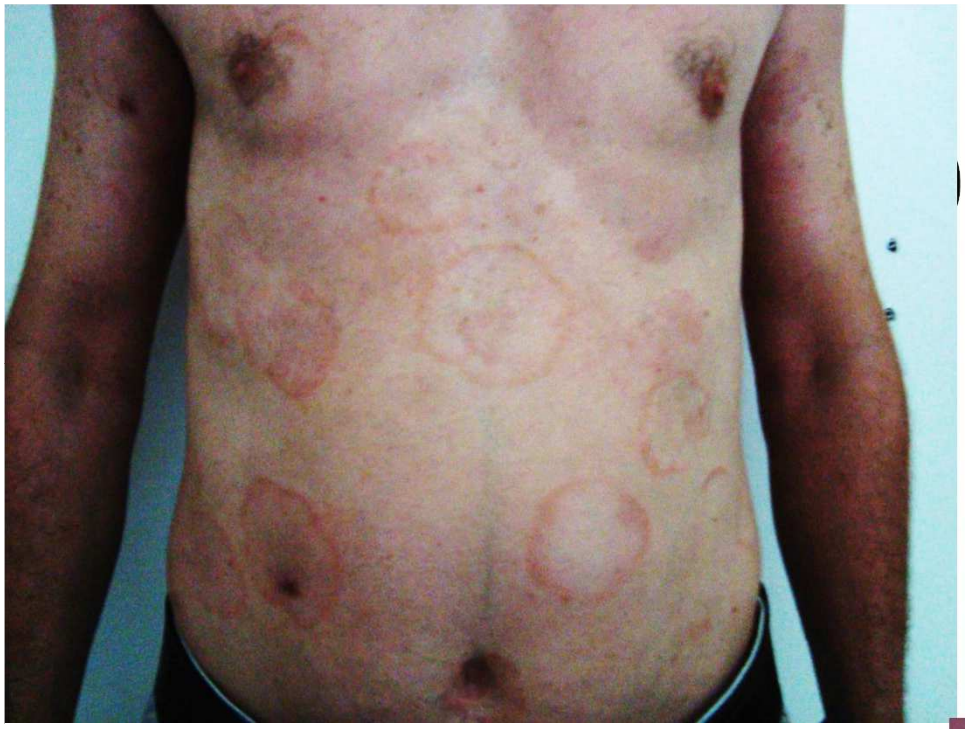

2014



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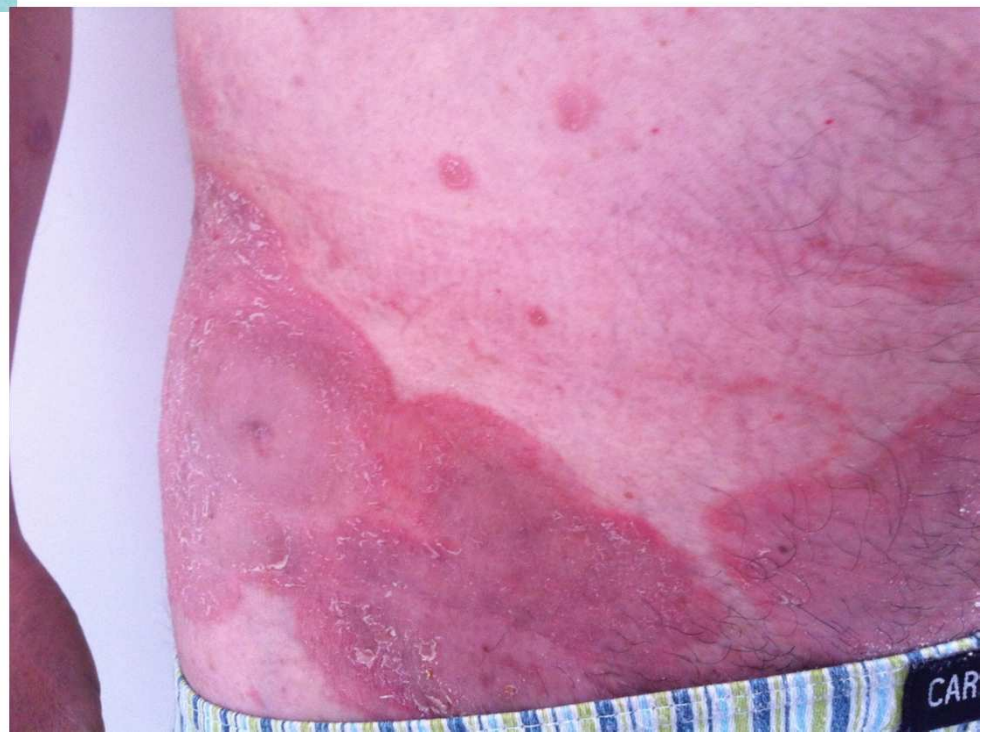
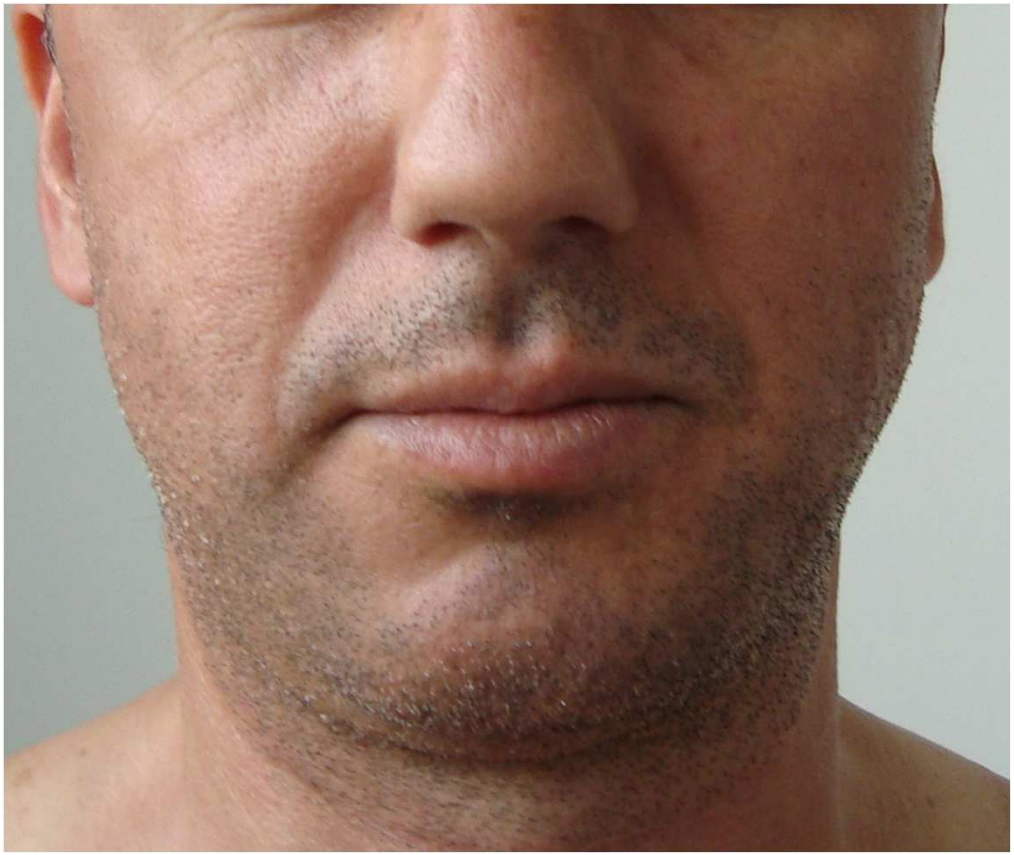
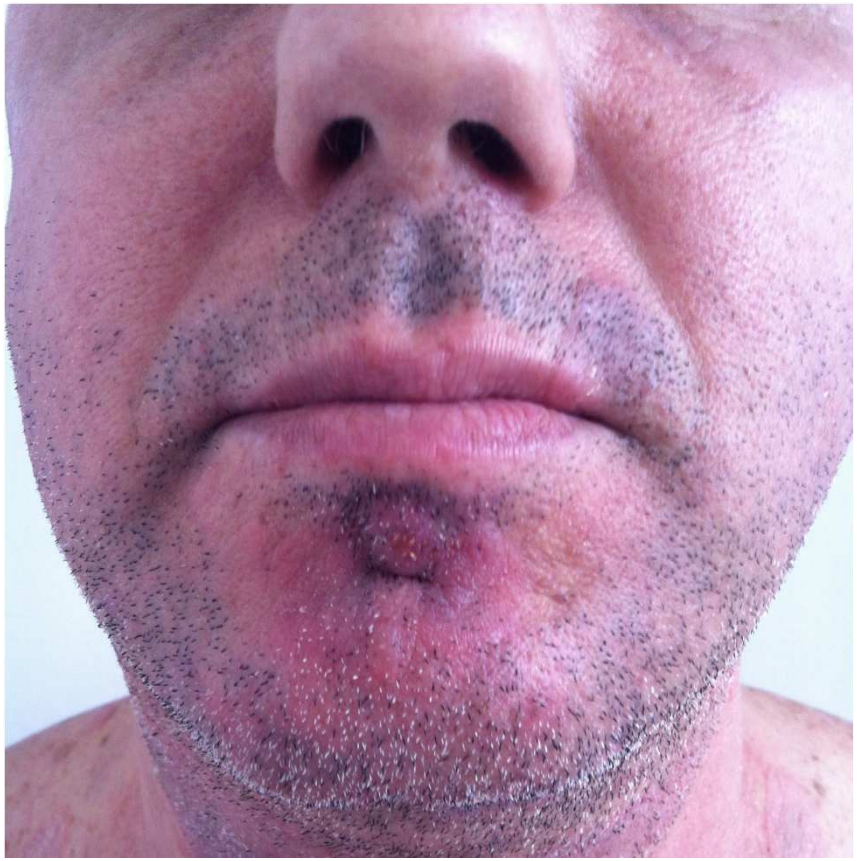






Br J Dermatol. 2013 Nov 1. doi: 10.1111/bjd.12717. [Epub ahead of print]

A specific DNA methylation profile correlates with a high risk of disease progression in stage I classical (Alibert-Bazin type) mycosis fungoides.

Ferrara G[1], Pancione M, Votino C, Quaglino P, Tomasini C, Santucci M, Pimpinelli N, Cusano F, Sabatino L, Colantuoni V; The Gruppo Italiano Linfomi Cutanei (GILC).

Author information

Abstract

BACKGROUND: Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma; it evolves slowly in its classical presentation, while can have an aggressive course in a subset of patients.

OBJECTIVES: To investigate the impact of epigenetic mechanisms on early stage MF progression.

METHODS: We analyzed DNA methylation at twelve different loci and long interspersed nucleotide elements-1 (LINE-1), as a surrogate marker of global methylation, on tissue samples from 41 stage I MF patients followed up for at least 12 years or until disease progression. The methylation profiles were also analyzed in two T-cell lymphoma cell lines and correlated with gene expression.

RESULTS: The selected loci were methylated in a tumour-specific manner; concomitant hypermethylation of at least 4 loci was more frequent in cases progressing within 1-3 and 3-6 years than in late-progressive or non-progressive cases. LINE-1 methylation was significantly lower in rapidly progressive MF at 3 years (61%, $p < 0.001$) than in those at 12 years (66.5%). PPARG, SOCS1 and NEUROG1 methylation showed remarkable differences among the prognostic groups, but only PPARG was a significant predictor of disease progression within 6 years after adjustment for patients' age or gender. Strikingly, a methylation profile similar to progressive cases was found in highly proliferative Sézary-derived HUT78 cells but not in MF-derived HUT102 cells. Exposure to a DNA demethylating agent restored sensitivity to apoptosis and cell cycle arrest.

CONCLUSIONS: Epigenetic silencing of specific biomarkers can predict the risk of disease progression in early stage MF, providing insights into its pathogenesis, prognosis and therapy.

Des biomarqueurs génétiques prédictifs de la progression?

Int J Dermatol. 2014 Apr 2. doi: 10.1111/ijd.12425. [Epub ahead of print]

Treatment of stage Ia and Ib mycosis fungoides with psoralen UVA monotherapy: an observational study in tertiary hospitals in the Canary Islands.

Hernández Z[1], Peñate Y, Hernández-Machín B, Pérez-Méndez L, Suárez-Hernández J, Hernández J, Fernández-de-Misa R.

Author information

MF et PUVA, 31 patients, Stade I,
Patchs 68%, Plaques 32%
Réponse complète 71 %
Intervalle libre sans récidive 57,5 mois
Récidive 58%
Maintien PUVA ne réduit rechute

J Am Acad Dermatol. 2014 Feb;70(2):223.e1-17; quiz 240-2. doi: 10.1016/j.jaad.2013.08.033.

Primary cutaneous T-cell lymphoma (mycosis fungoides and Sézary syndrome): part II. Prognosis, management, and future directions.

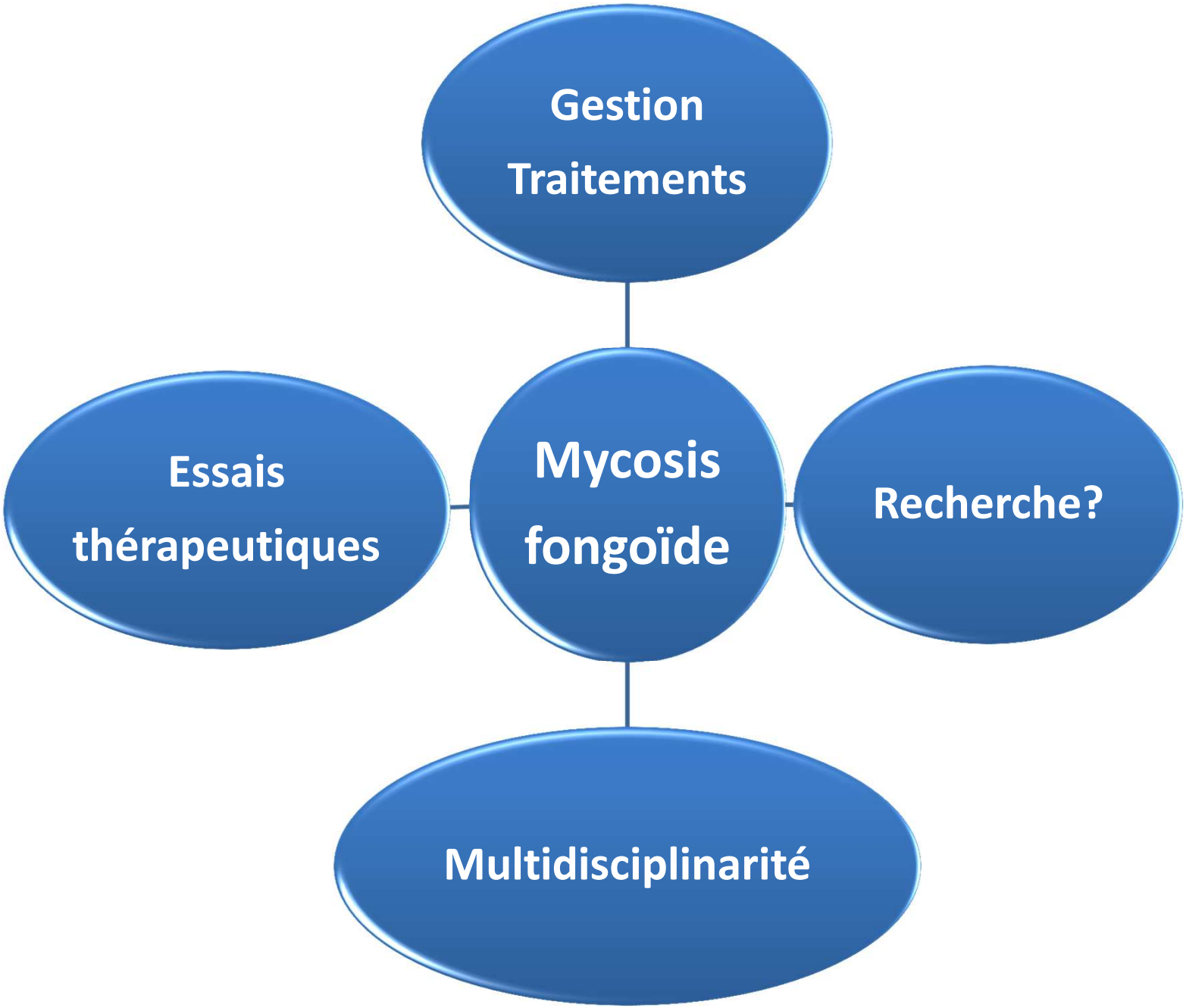
Jawed SI[1], Myskowski PL[1], Horwitz S[2], Moskowitz A[2], Querfeld C[3].

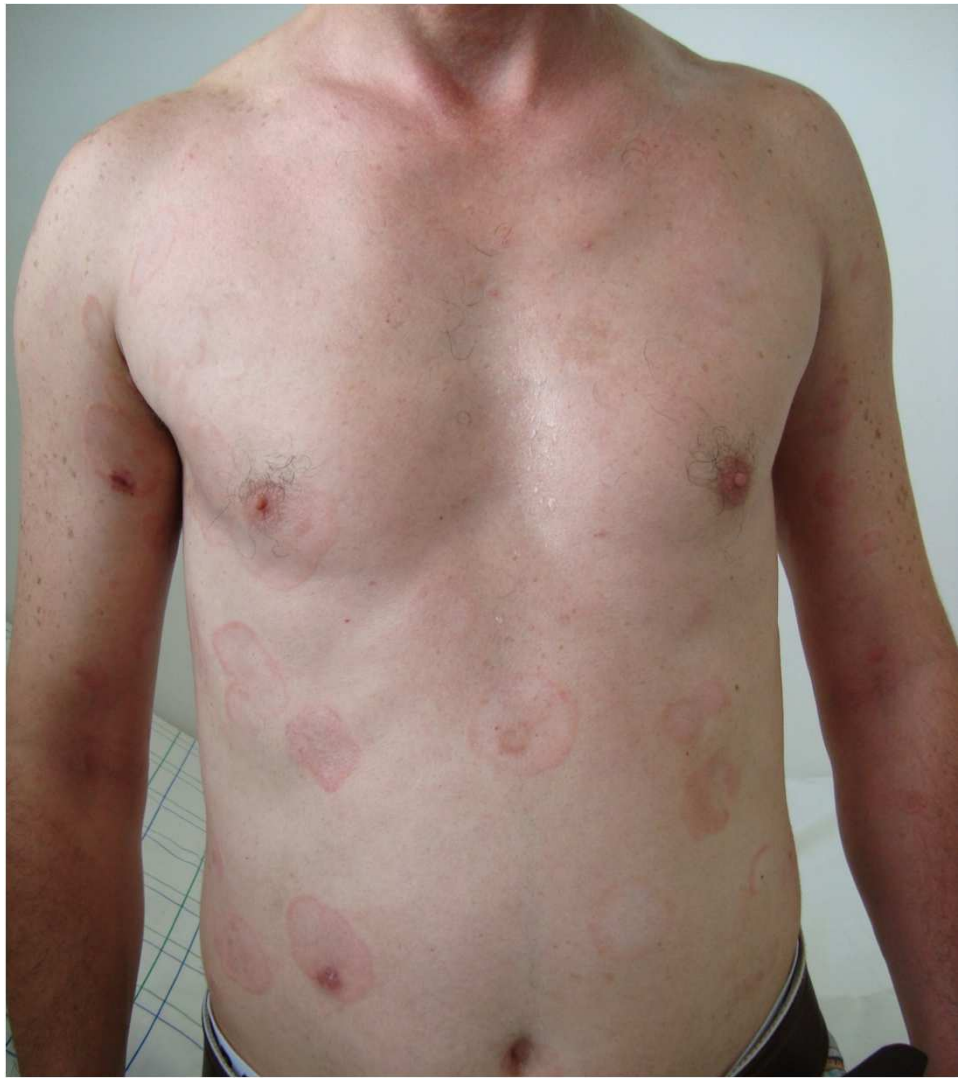
Author information

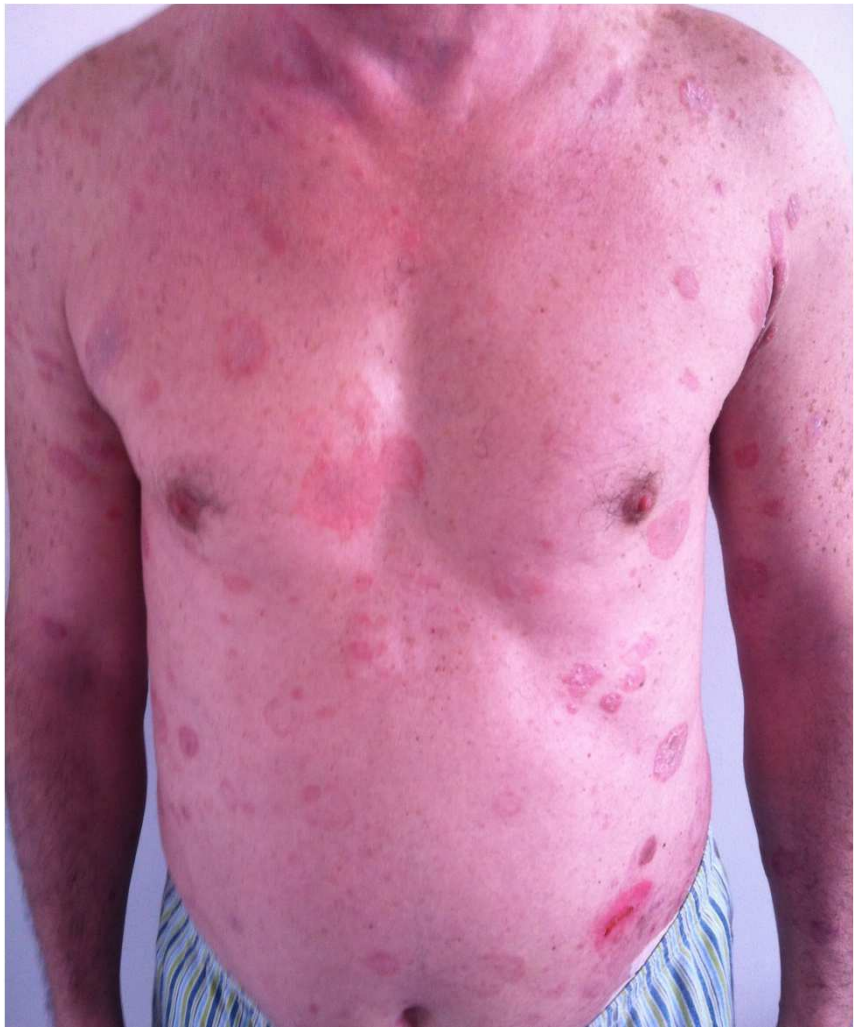
Abstract

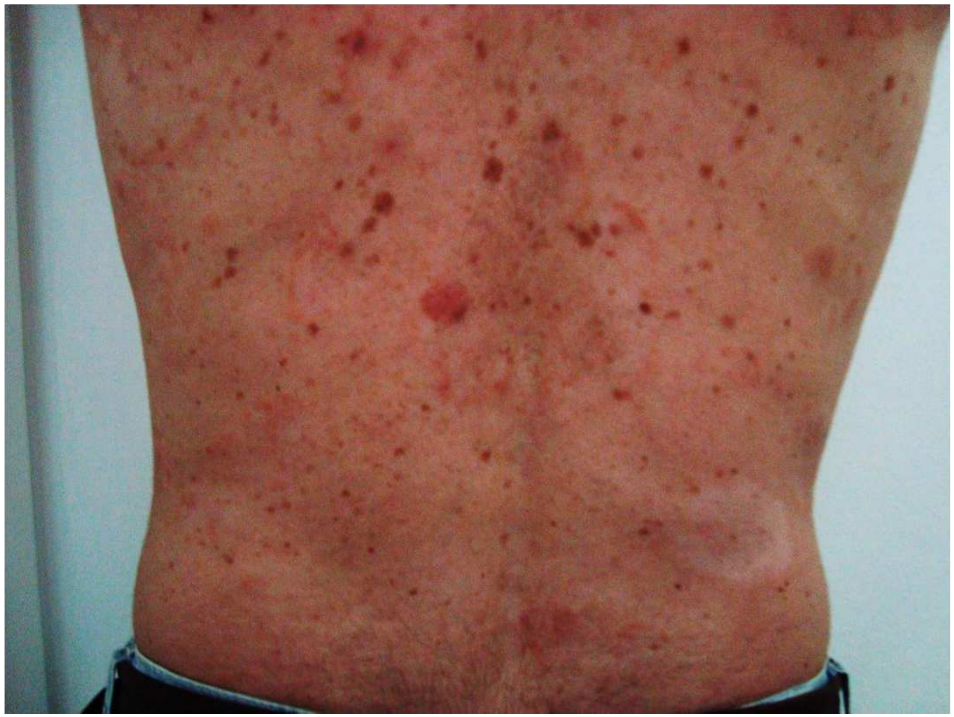
Both mycosis fungoides (MF) and Sézary syndrome (SS) have a chronic, relapsing course, with patients frequently undergoing multiple, consecutive therapies. Treatment is aimed at the clearance of skin disease, the minimization of recurrence, the prevention of disease progressi and the preservation of quality of life. Other important considerations are symptom severity, including pruritus and patient age/comorbidities. In general, for limited patch and plaque disease, patients have excellent prognosis on ≥1 topical formulations, including topical corticosteroids and nitrogen mustard, with widespread patch/plaque disease often requiring phototherapy. In refractory early stage MF, transformed MF, and folliculotropic MF, a combination of skin-directed therapy plus low-dose immunomodulators (eg, interferon or bexarotene) may be effective. Patients with advanced and erythrodermic MF/SS can have profound immunosuppression, with treatments targeting tumor cells aimed for immune reconstitution. Biologic agents or targeted therapies either alone or in combination--including immunomodulators and histone-deacetyla inhibitors--are tried first, with more immunosuppressive therapies, such as alemtuzumab or chemotherapy, being generally reserved for refracto or rapidly progressive disease or extensive lymph node and metastatic involvement. Recently, an increased understanding of the pathogenesis MF and SS with identification of important molecular markers has led to the development of new targeted therapies that are currently being explored in clinical trials in advanced MF and SS.

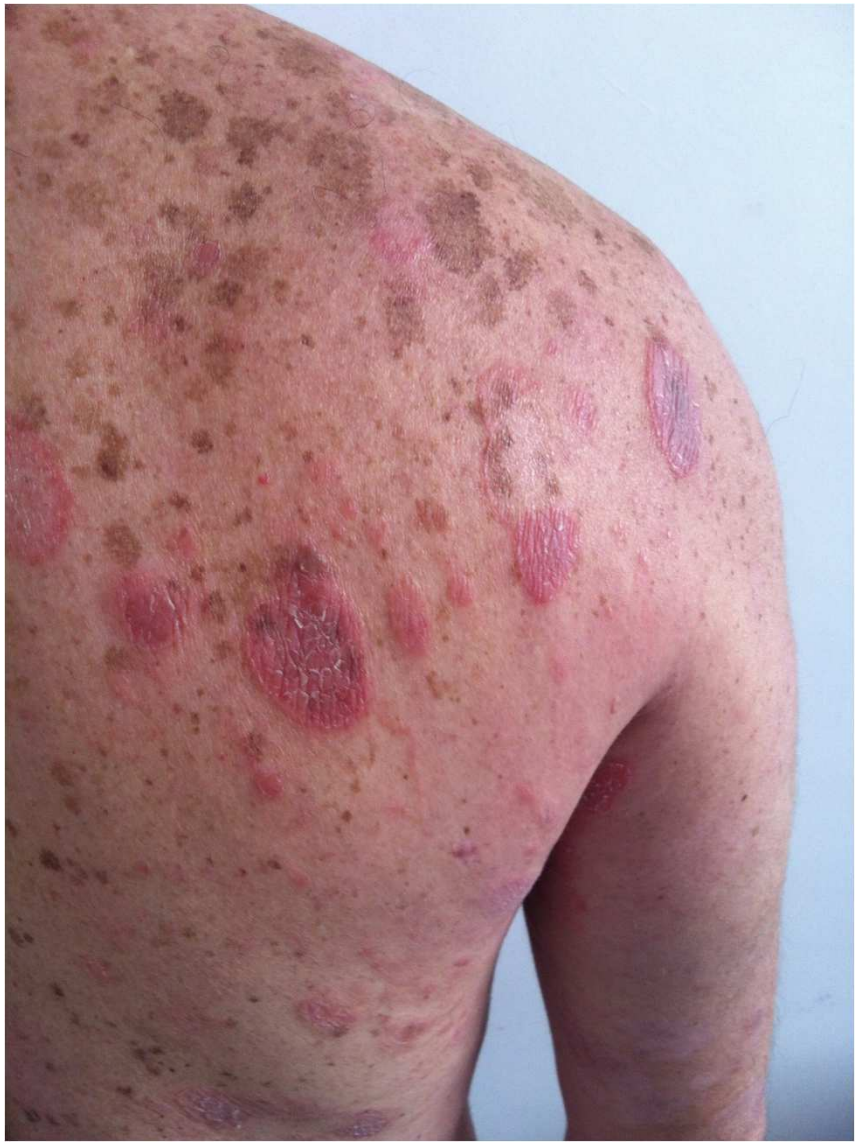
Agents biologiques, thérapies ciblées : immunomodulateurs, histone-deacétylase inhibiteurs,
Avec immunosuppressives : alemtuzumab ou chimiothérapies


Gestion
Traitements
Essais
thérapeutiques
Mycosis
fongoïde
Recherche?
Multidisciplinarité









Clin Lymphoma Myeloma Leuk. 2014 Feb 4. pii: S2152-2650(14)00026-3. doi: 10.1016/j.clml.2014.01.010. [Epub ahead of print]

Pralatrexate Alone or in Combination With Bexarotene: Long-Term Tolerability in Relapsed/Refractory Mycosis Fungoides.

Talpur R[1], Thompson A[1], Gangar P[1], Duvic M[2].

Author information

Abstract

BACKGROUND: This study aimed to assess the long-term tolerability of pralatrexate alone or in combination with oral bexarotene for relapsed or refractory mycosis fungoides (MF).

PATIENTS AND METHODS: Patients with MF in this report were participants in 1 of 2 multicenter trials. During the dose-ranging phase I/II study, participants were treated with pralatrexate alone for 3 of 4 weeks. During a second phase I/II dose-ranging combination trial, participants were treated with pralatrexate at 15 mg/m^2/wk for 3 of 4 weeks combined with 150 to 300 mg/m^2 of daily oral bexarotene.

RESULTS: Twenty-six patients were enrolled at our center, including 12 receiving pralatrexate and 14 receiving pralatrexate plus bexarotene. Four of 12 patients (33%) treated with pralatrexate alone responded. Of 14 patients treated with bexarotene plus pralatrexate, 7 (50%) responded. Ten participants, with a median age of 71 years (range, 41-82 years), received more than 9 cycles of pralatrexate, including 3 receiving pralatrexate and 7 receiving combination therapy. Median time to response was 15.75 weeks (range, 4-24 weeks), and the median duration of response was 26.75 weeks (range, 8.5-49.5 weeks). The most common adverse event (AE) was mucositis in 8 (80%) patients. Other AEs of any grade included arthralgias (n = 1), headache (n = 1), neutropenia (n = 5), and skin necrosis (n = 2). Two patients initially had lower leg tumors that responded to therapy, leaving residual chronic leg ulcers.

CONCLUSION: Pralatrexate alone or in combination with low-dose oral bexarotene is well tolerated and capable of providing long-term responses in patients of advanced age with advanced-stage MF.