Caso Clinico 2

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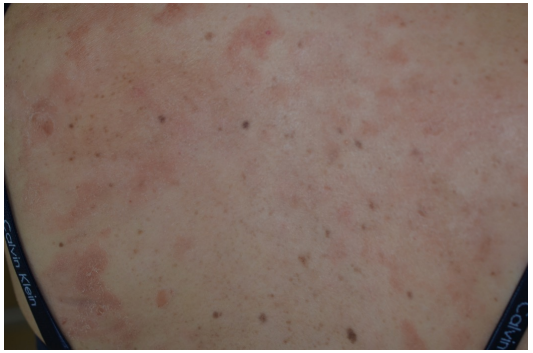
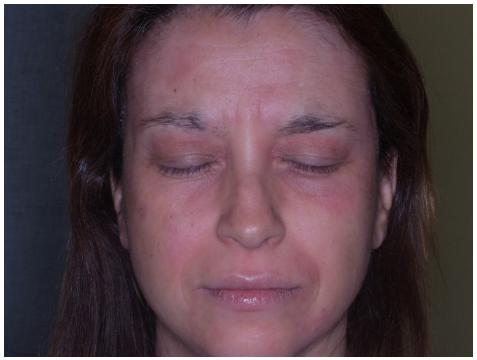
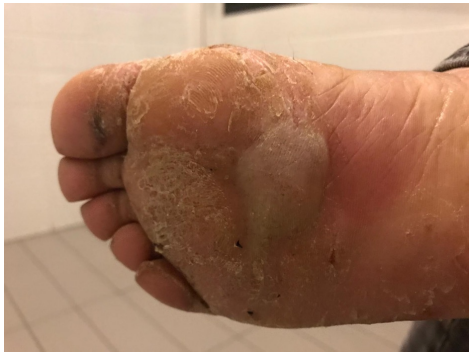
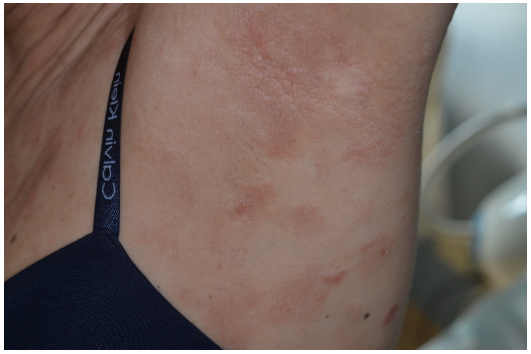
FONDAZIONE IRCCS CA' GRANDA
OSPEDALE MAGGIORE POLICLINICO

Donna di 38 aa, caucasica, di origine sarda
Prima visita dermatologica Marzo 2018

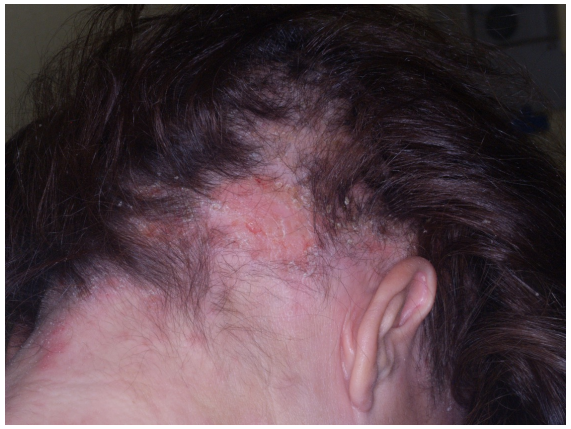
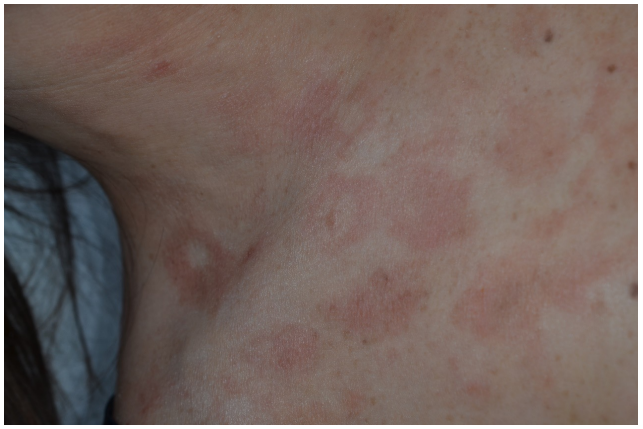
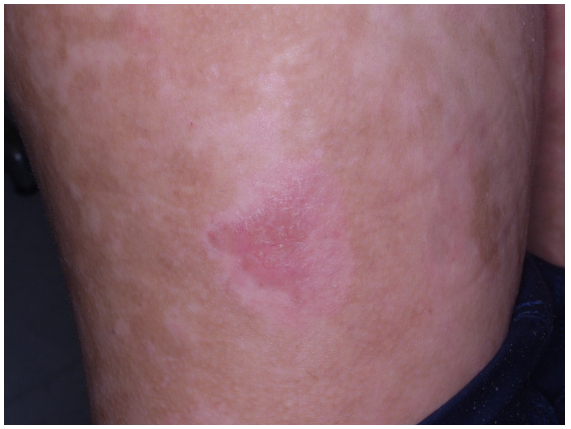
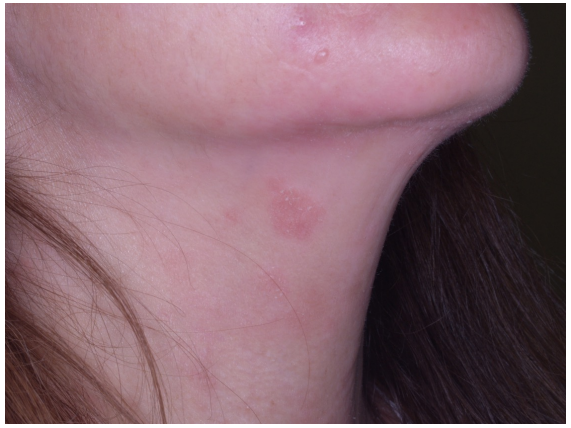
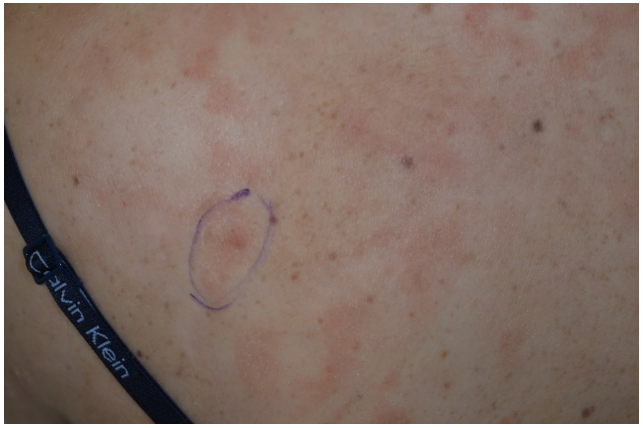
- Dal 1999 comparsa di **dermatite** alle ascelle e poi diffusa su tutto l'ambito cutaneo interpretata come **Dermatite atopica** con lesioni a tipo prurigo e nummulari escoriate: alle mani e ai piedi quadro xerotico ipercherastosico.
- In precedenza, eseguito ciclo con ciclosporina per os a 3 mg /kg a scalare per 2 mesi + terapia topica con scarso beneficio.

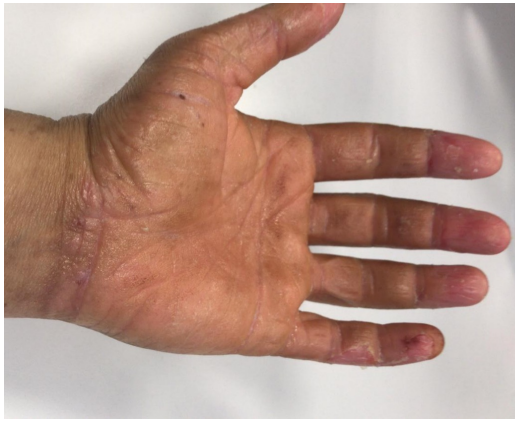





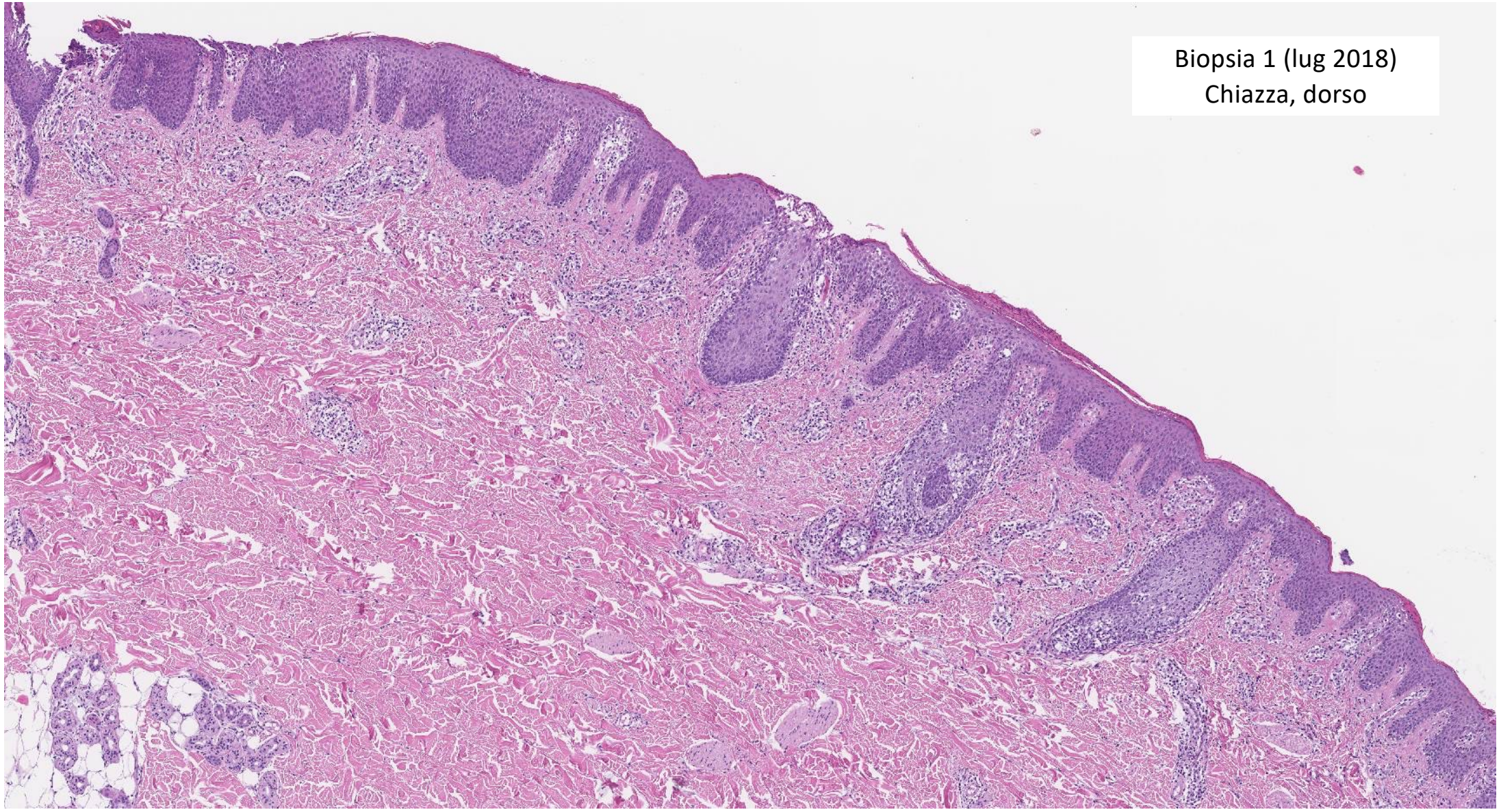
Prima visita dermatologica Marzo 2018

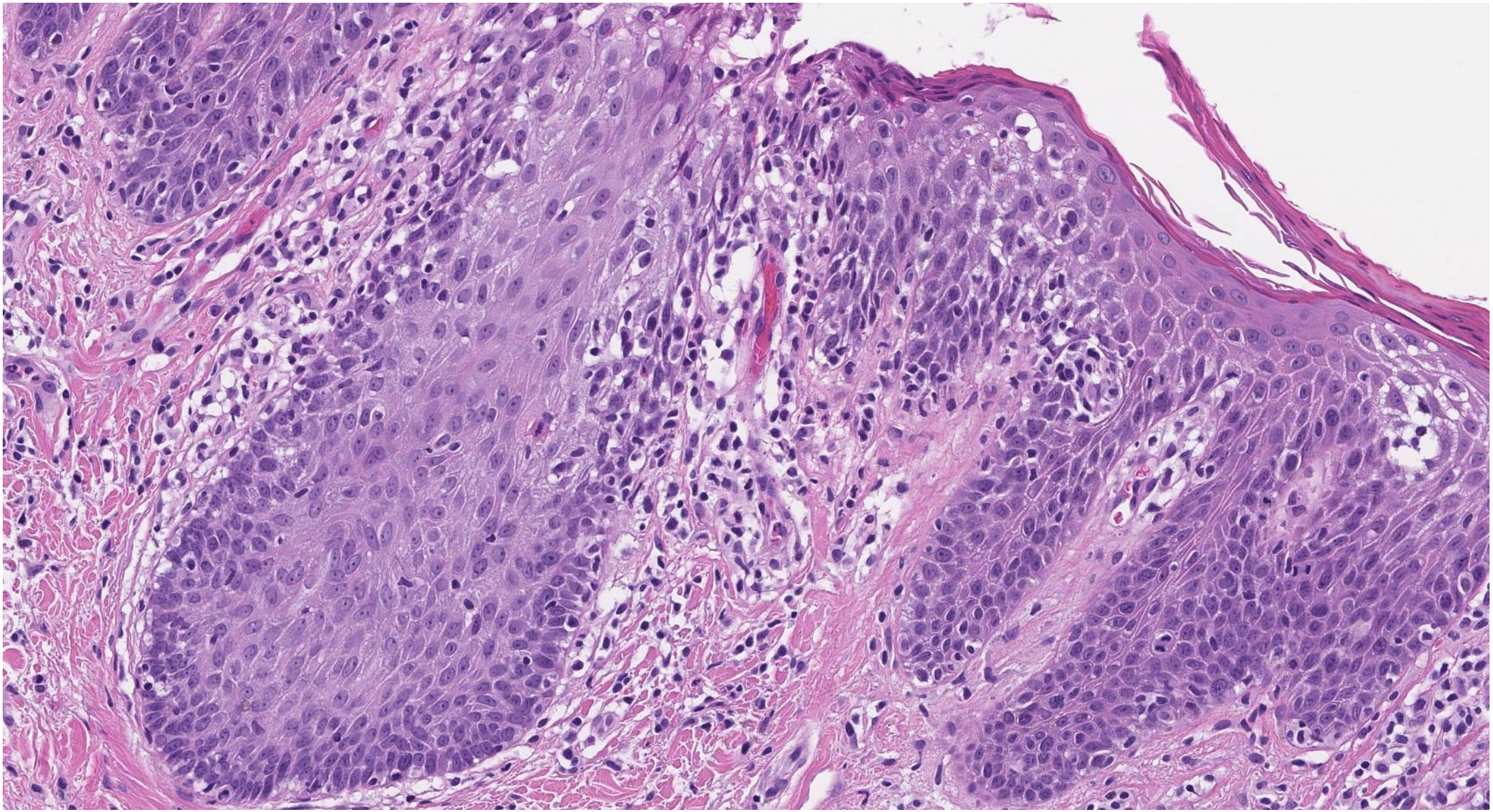
- Anamnesi patologica remota muta
- In terapia con estroprogestinico a scopo anticoncezionale
- Esami ematochimici nella norma salvo IgE totali di 250 UI con Rast per alimenti negativo.

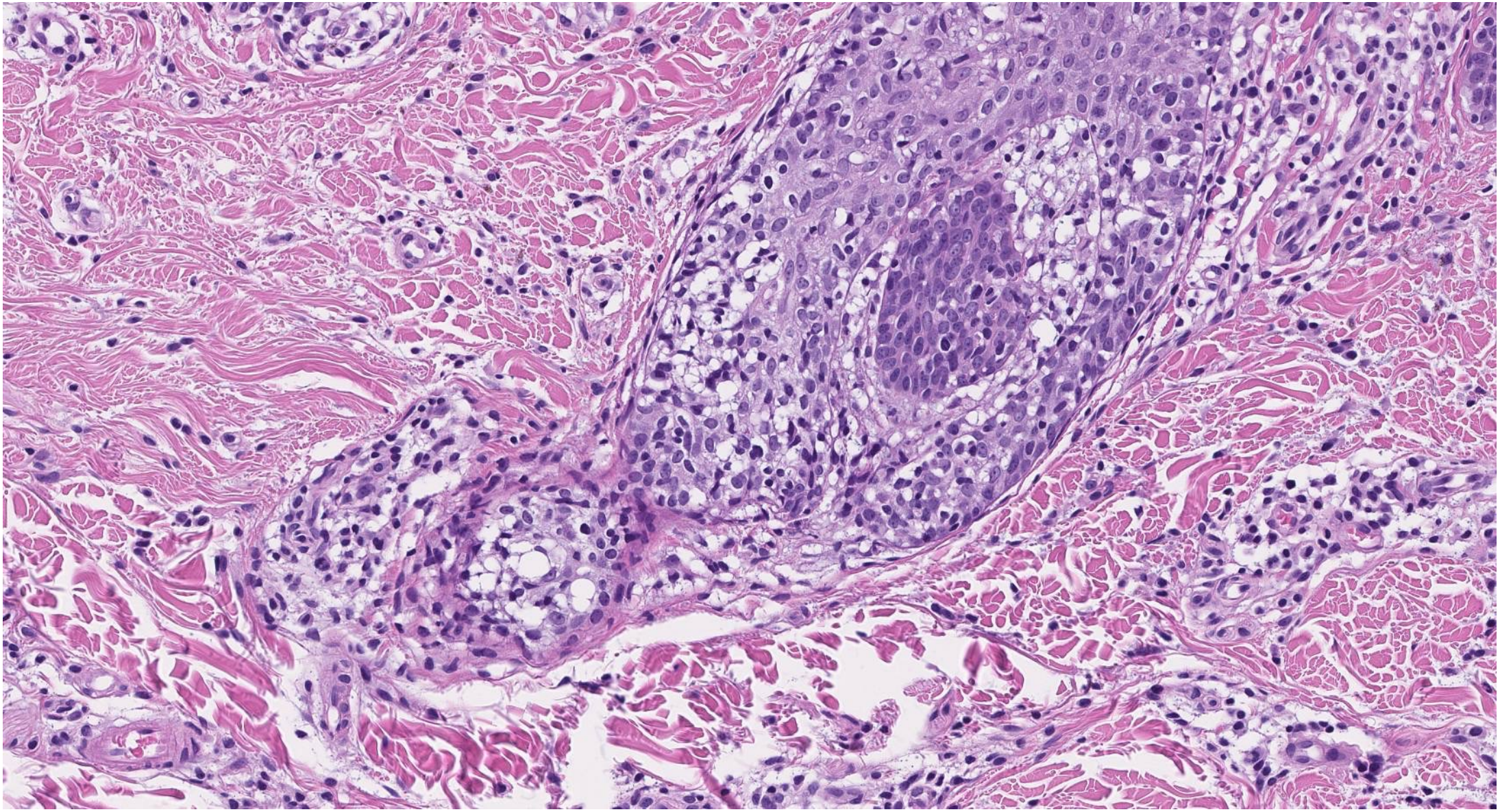
Prima visita dermatologica Marzo 2018

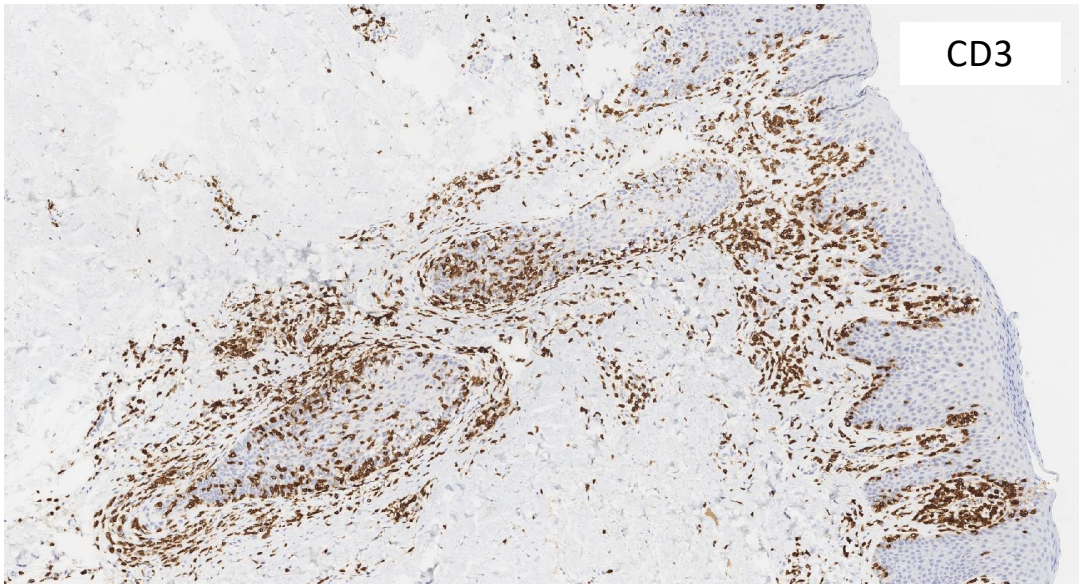






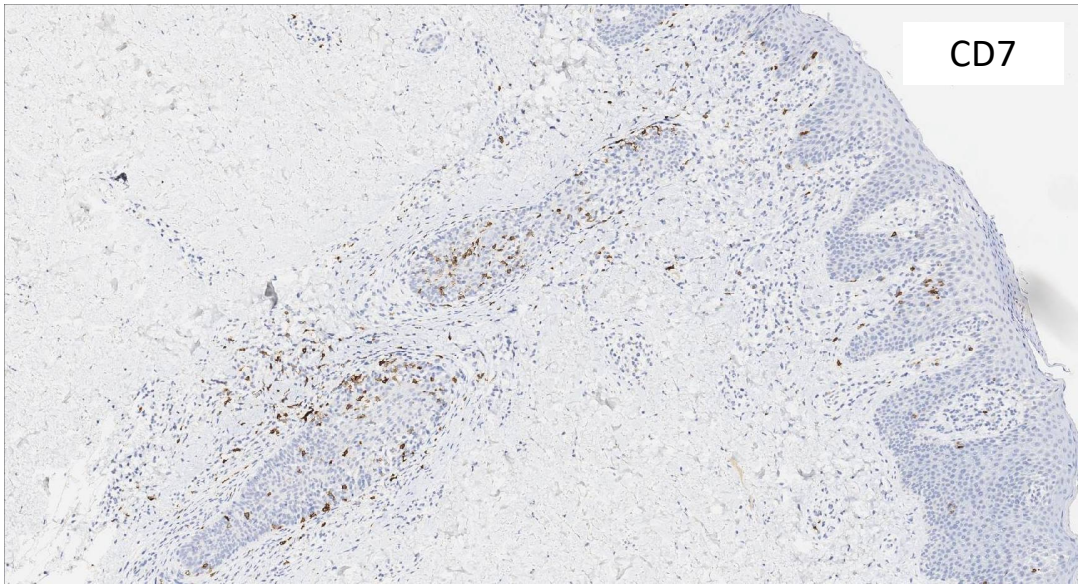



Biopsia 1 (lug 2018)
Chiazza, dorso






CD3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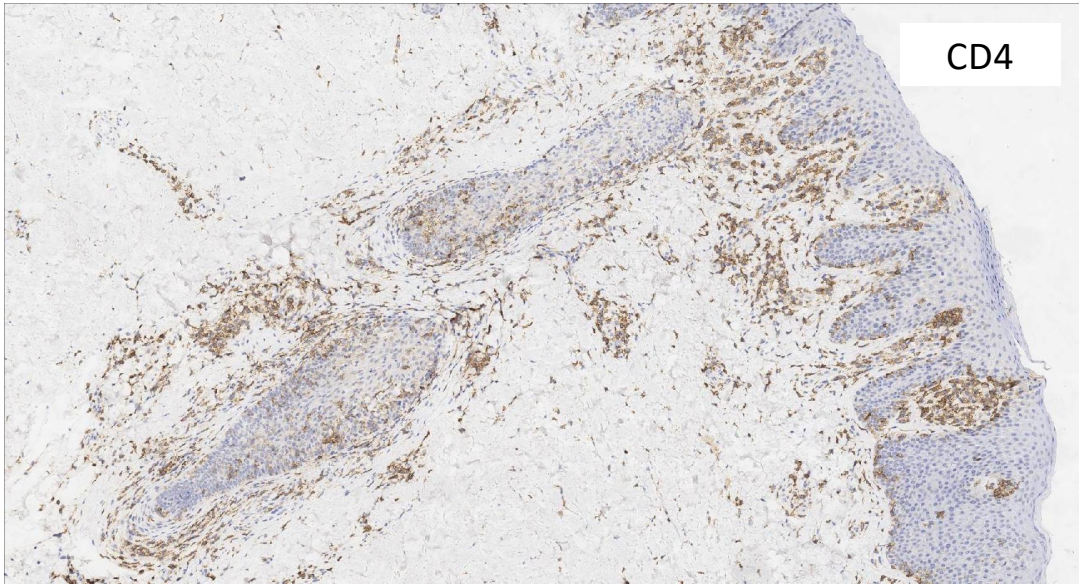
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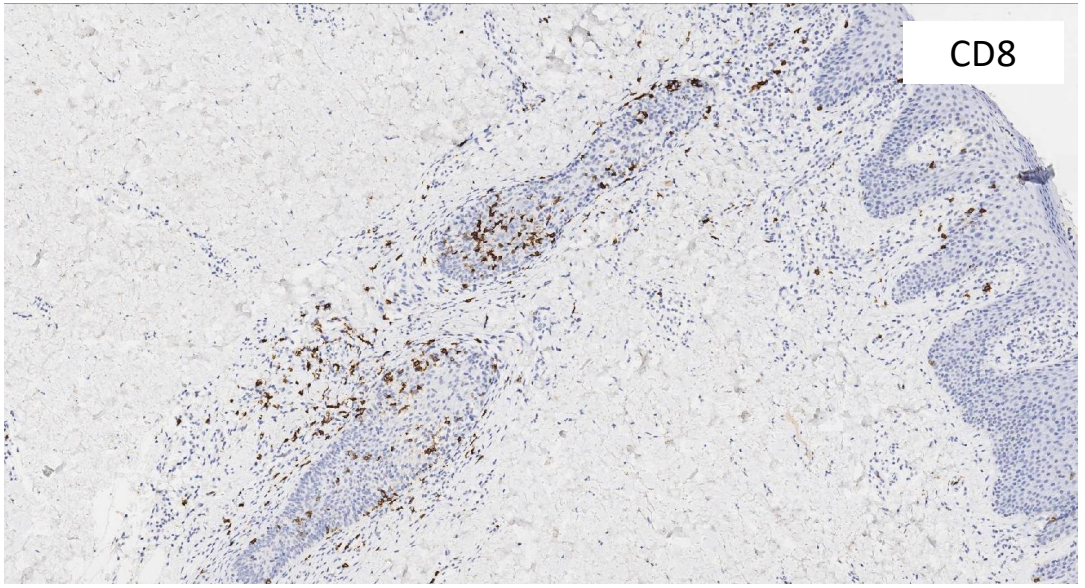
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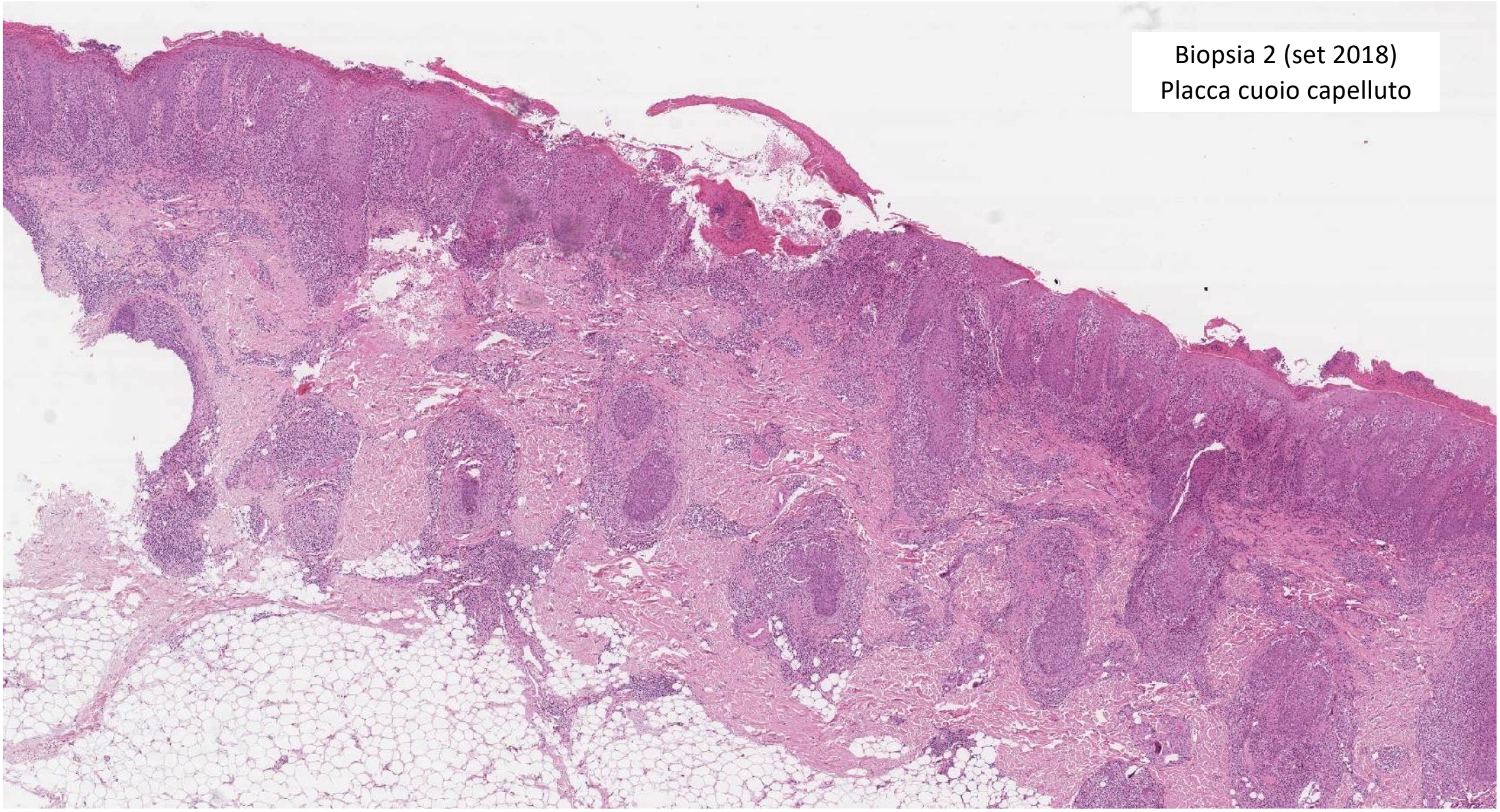
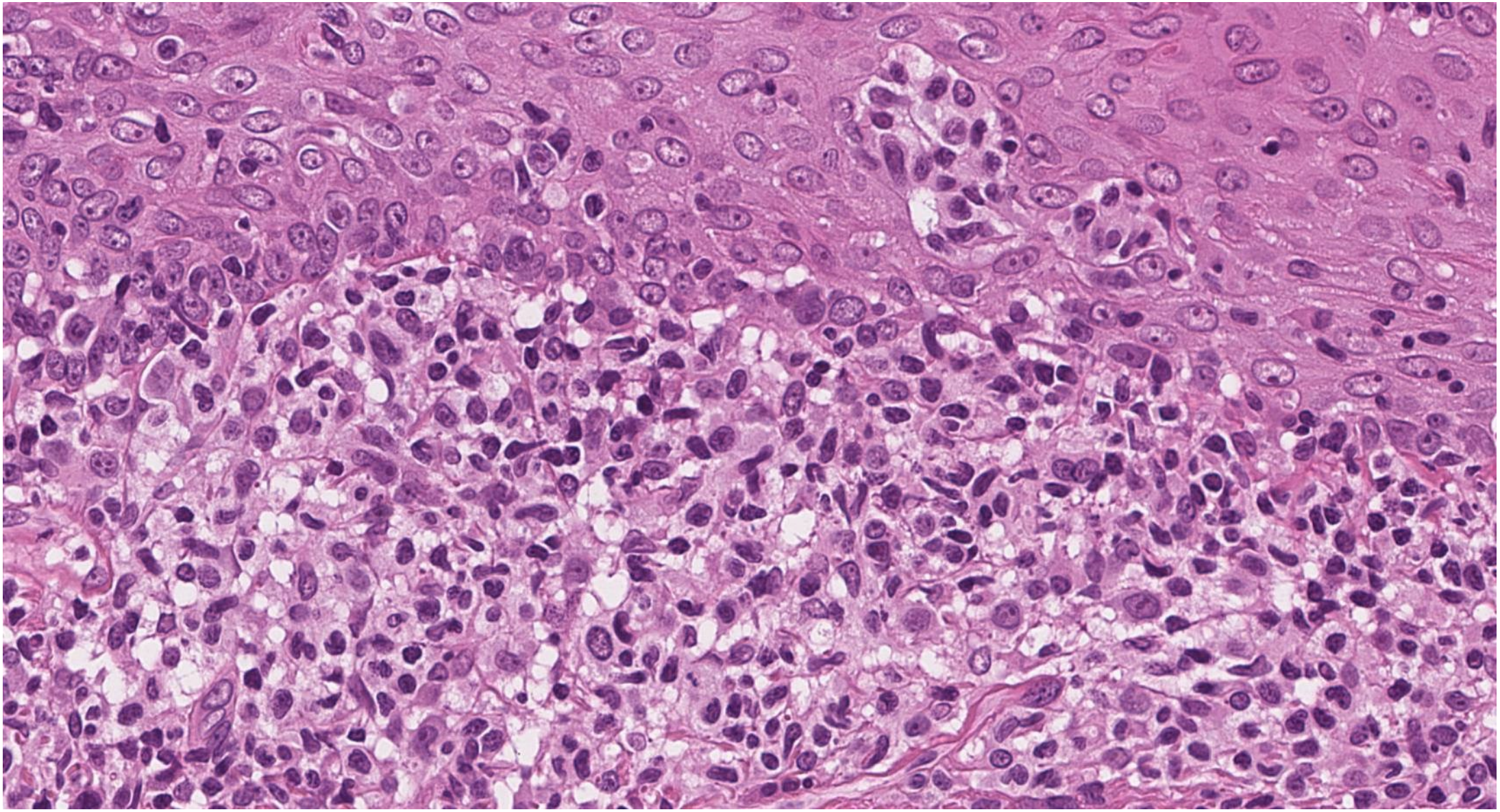
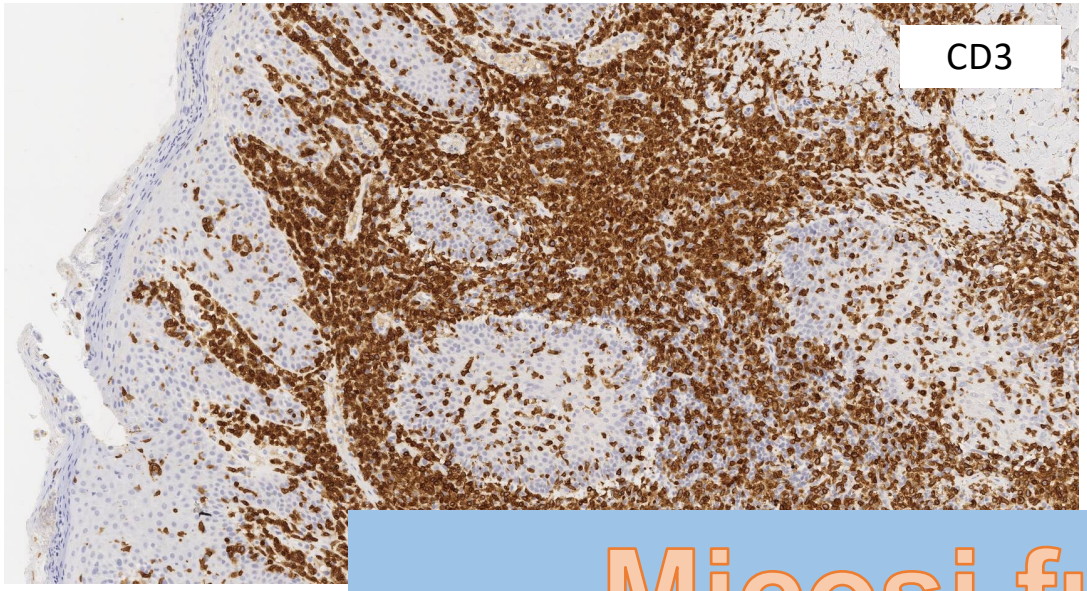
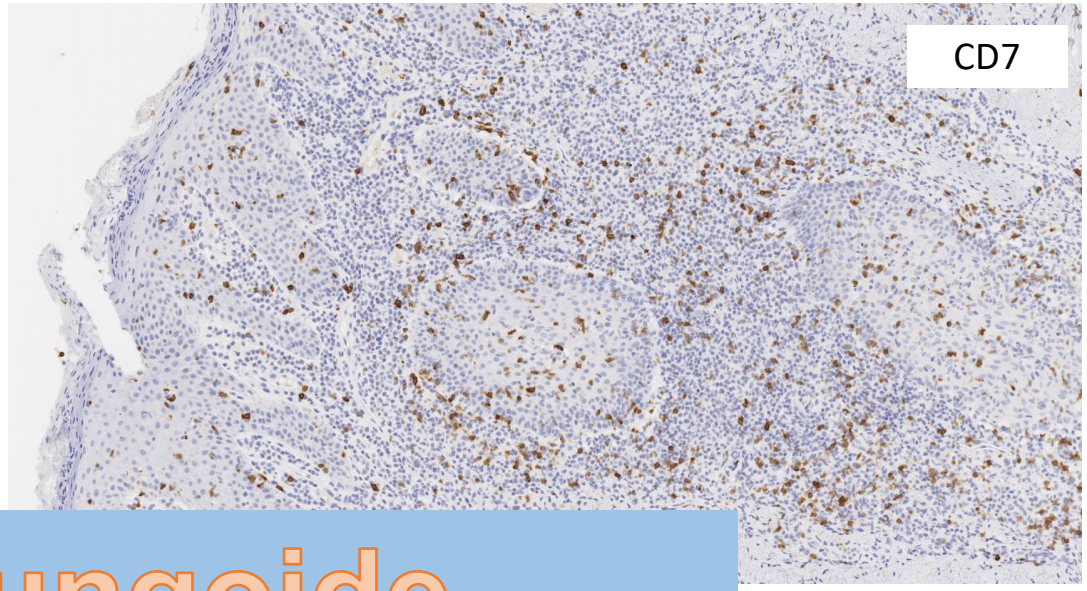
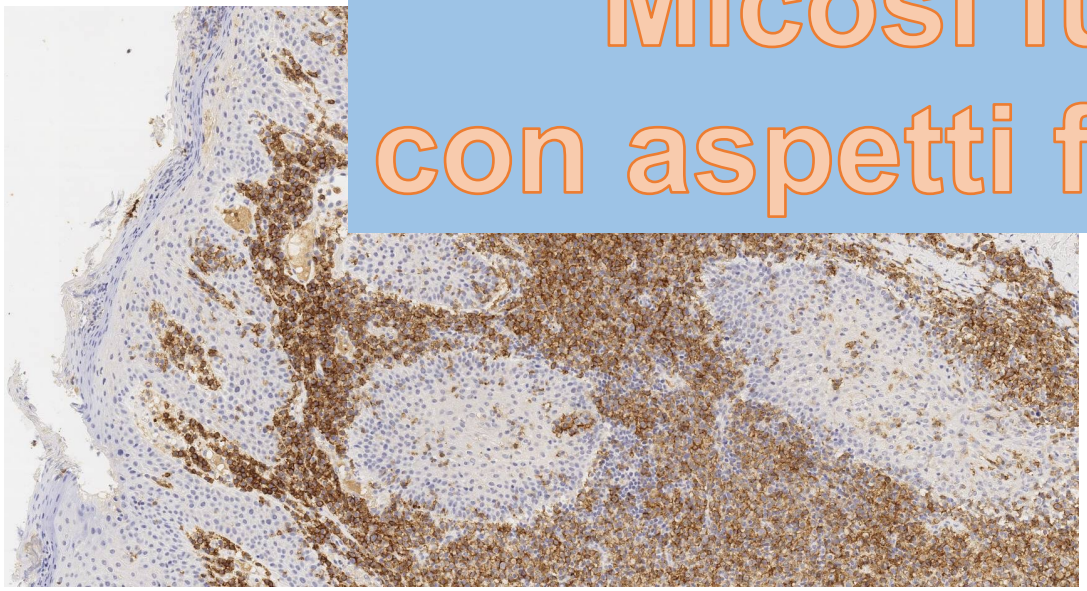
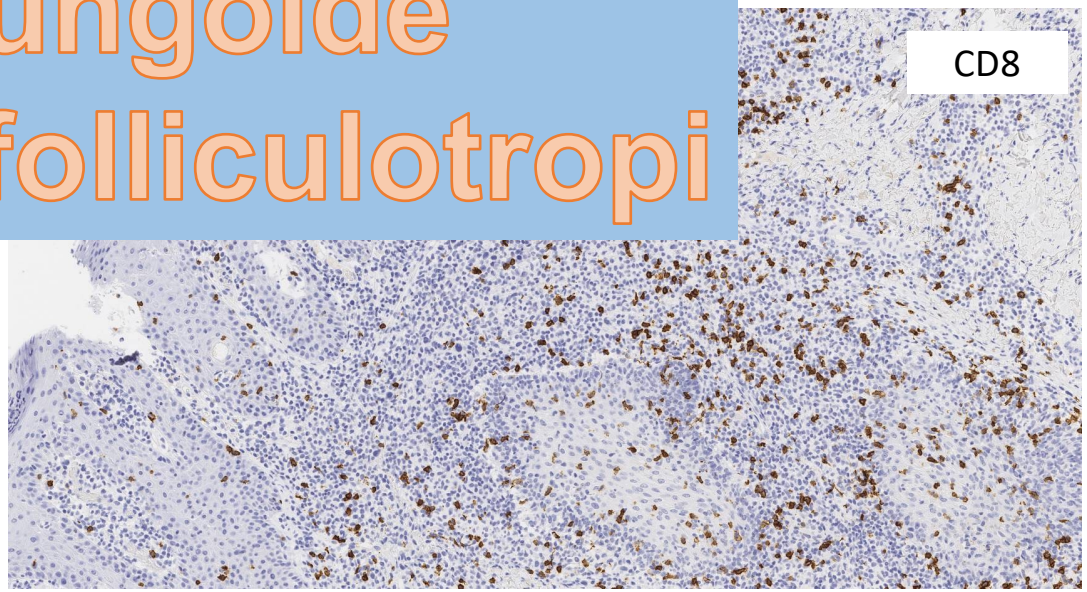

Biopsia 2 (set 2018)
Placca cuoio capelluto



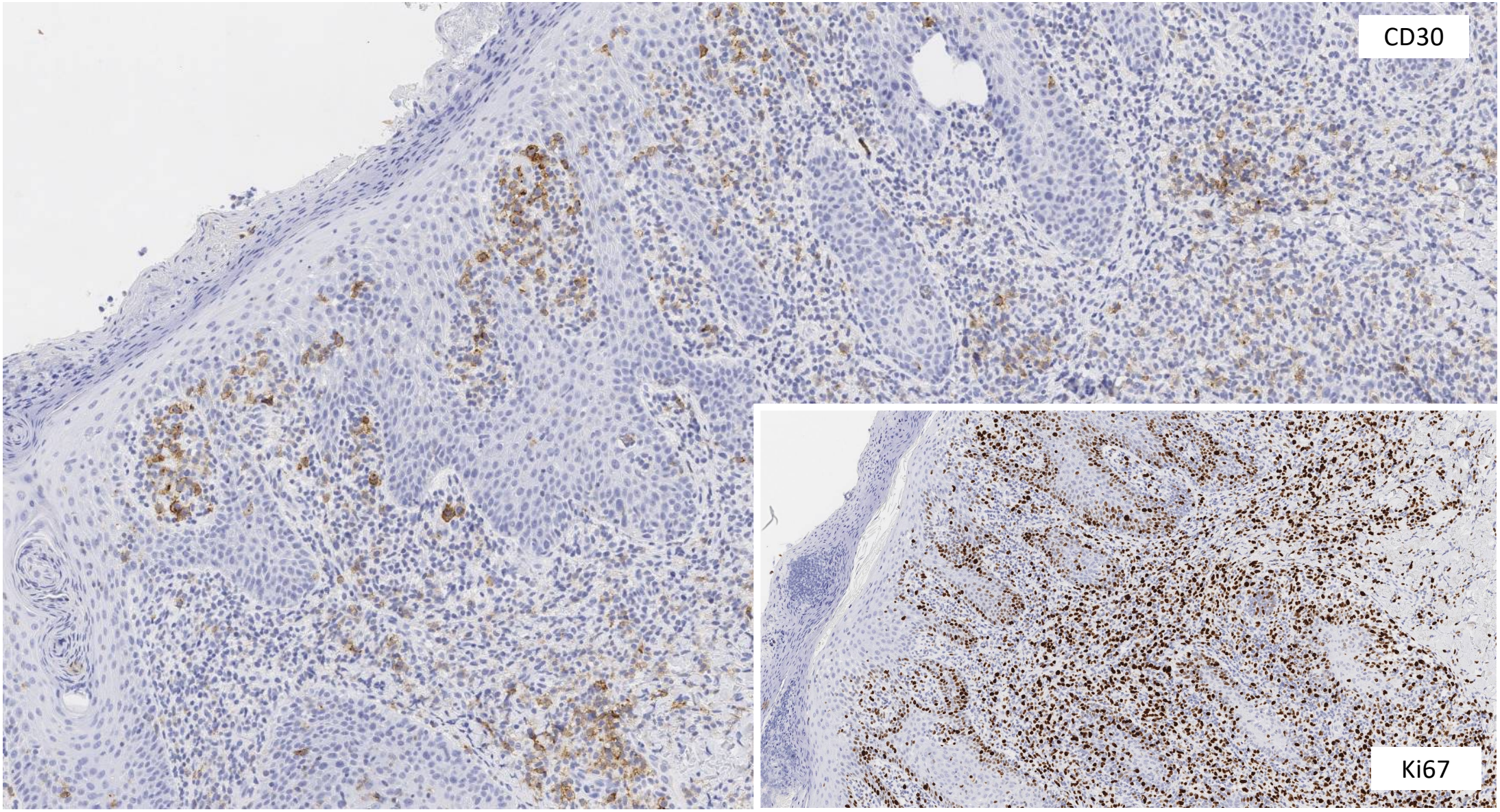








Micosi fungoide con aspetti folliculotropi


CD30
Ki67

Staging

- **Ecografia linfonodale**: non linfonodi di aspetto patologico, diffusi linfonodi con caratteristiche reattive con diametro massimo 13 mm
- **TC total body**: linfonodi centrimetrici di aspetto reattivo a livello del collo, ascellari (diametro massimo 18x15 mm), inguinali (massimo 15 mm). Nella loggia timica presenza di tessuto solido di 28X17 mm (residuo timico?)
- **Emocromo:** GB 10.160/mmc (Neutrofili 7070/mmc, Linfociti 1890/mmc, Eosinofili 570/mmc), Hb 12.8 g/dL, PLT 328.000/mmc
- **Citofluorimetria su sangue periferico:** CD3+CD4+ 60%, CD3+CD8+16%, CD7-18%, CD26-17%, CD4/CD8 3.7
- **Valutazione midollare con esame istologico e ricerca clonalità TCR su sangue midollare**: negativa
- **PET**: linfonodi di dimensioni aumentate con debole captazione aspecifica (SUV max 2.7)

Staging

Skin	
T_1	Limited patches,* papules, and/or plaques† covering < 10% of the skin surface. May further stratify into T_{1a} (patch only) vs T_{1b} (plaque ± patch).
T_2	Patches, papules or plaques covering ≥ 10% of the skin surface. May further stratify into T_{2a} (patch only) vs T_{2b} (plaque ± patch).
T_3	One or more tumors‡ (≥ 1-cm diameter)
T_4	Confluence of erythema covering ≥ 80% body surface area
Node	
N_0	No clinically abnormal peripheral lymph nodes§; biopsy not required
N_1	Clinically abnormal peripheral lymph nodes; histopathology Dutch grade 1 or NCI LN_{0-2}
N_{1a}	Clone negative#
N_{1b}	Clone positive#
N_2	Clinically abnormal peripheral lymph nodes; histopathology Dutch grade 2 or NCI LN_3
N_{2a}	Clone negative#
N_{2b}	Clone positive#
N_3	Clinically abnormal peripheral lymph nodes; histopathology Dutch grades 3-4 or NCI LN_4; clone positive or negative
N_x	Clinically abnormal peripheral lymph nodes; no histologic confirmation
Visceral	
M_0	No visceral organ involvement
M_1	Visceral involvement (must have pathology confirmation¶ and organ involved should be specified)
Blood	
B0	Absence of significant blood involvement: ≤ 5% of peripheral blood lymphocytes are atypical (Sézary) cells‖
B_{0a}	Clone negative#
B_{0b}	Clone positive#
B1	Low blood tumor burden: > 5% of peripheral blood lymphocytes are atypical (Sézary) cells but does not meet the criteria of B_2
B_{1a}	Clone negative#
B_{1b}	Clone positive#
B2	High blood tumor burden: ≥ 1000/μL Sézary cells‖ with positive clone#

Olsen E. et al. , Blood 2007

	T	N	M	B
IA	1	0	0	0,1
IB	2	0	0	0,1
II	1,2	1,2	0	0,1
IIB	3	0-2	0	0,1
III	4	0-2	0	0,1
IIIA	4	0-2	0	0
IIIB	4	0-2	0	1
IVA_1	1-4	0-2	0	2
IVA_2	1-4	3	0	0-2
IVB	1-4	0-3	1	0-2

T2NxM0B1

Stadio IIA

Terapia di I linea Ottobre 2018

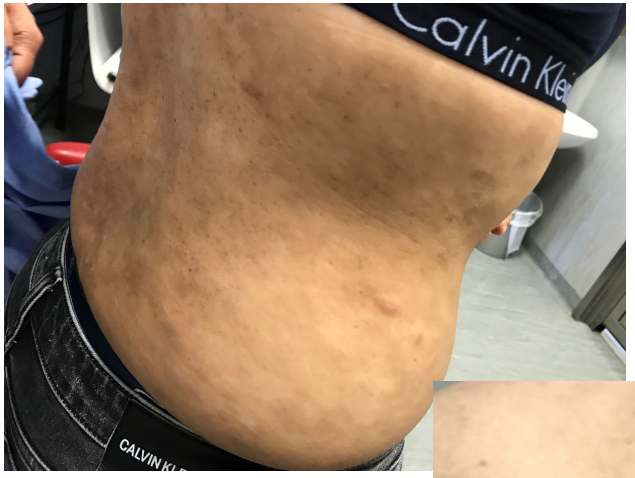
❖ Early Stage (II a)

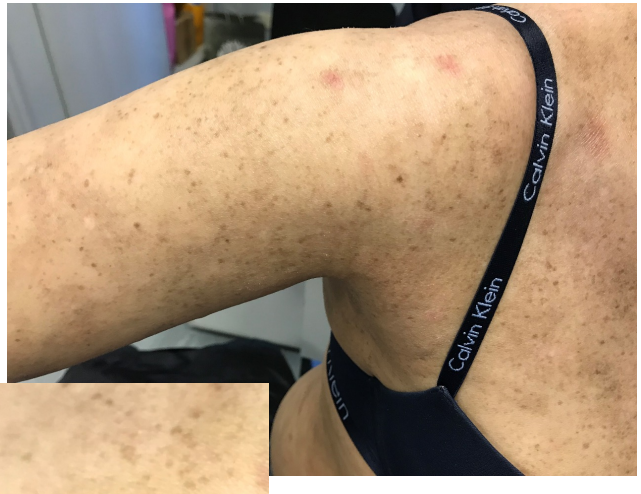
- ✓ Paziente giovane (38 aa)
- ✓ Possibilità di prospettiva trapiantologica
- ✓ Malattia estesa e lunga storia
- ✓ Caratteristiche istologiche di «aggressività»

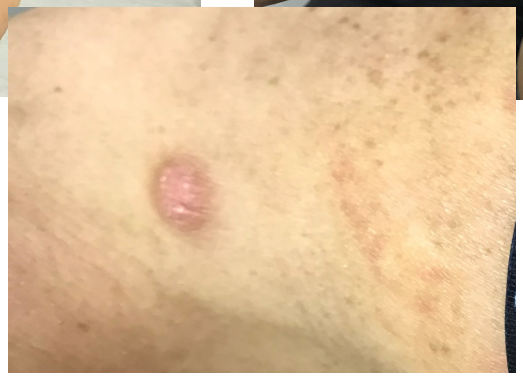
→ **Gemcitabina 1000 mg/mq (schedula G1-G8-G15 ogni 28) per 8 cicli**

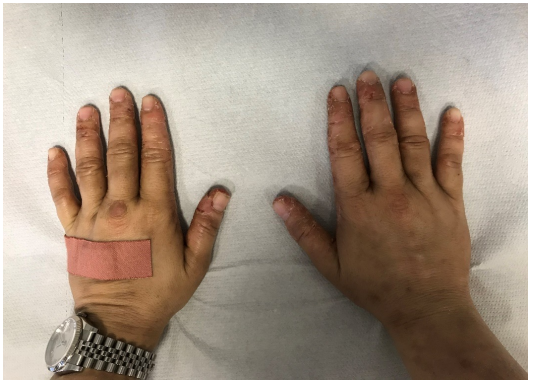
Complicata da ascesso perineale, associato febbre, e trattato chirurgicamente e con terapia antibiotica

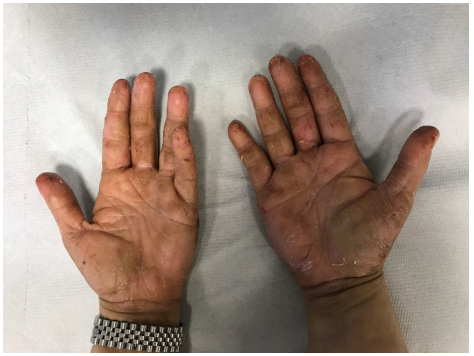
Rivalutazione post Gemcitabina Maggio 2019











Esiti discromici diffusi con un'unica placca di circa 1 cm a livello laterale del collo e desquamazione psoriasiforme ragadiforme palmo-plantare.

Terapia di consolidamento Giugno - Settembre 2019

→Methotrexate sottocute per lesioni residue

quadro cutaneo stabile in lieve miglioramento, sul tronco a sinistra piccole placche e lesione cuoio capelluto in regione temporale destra.

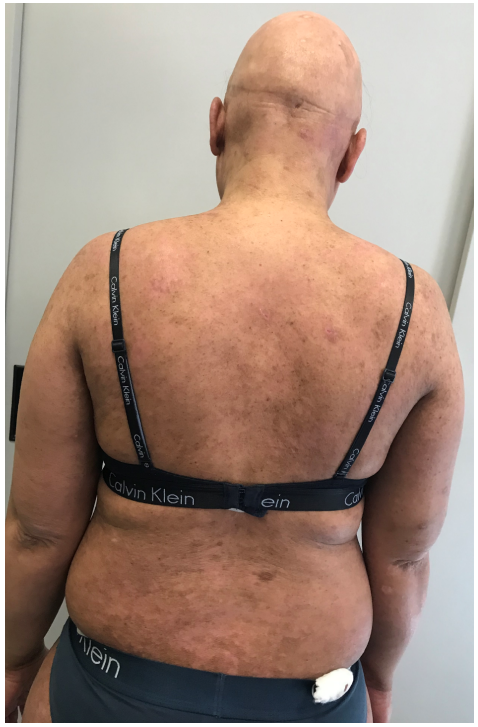
Per giovane età e malattia aggressiva → indicazione a trapianto,

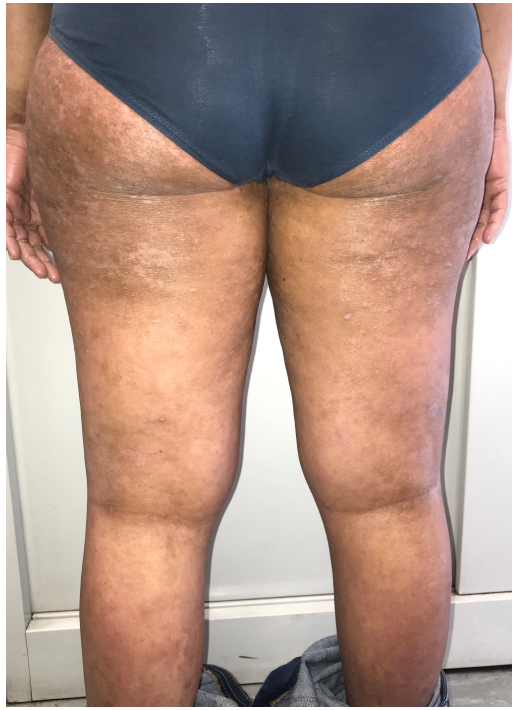
No fratria→ attivata ricerca MUD + tipizzati cugini → cugina aploidentica

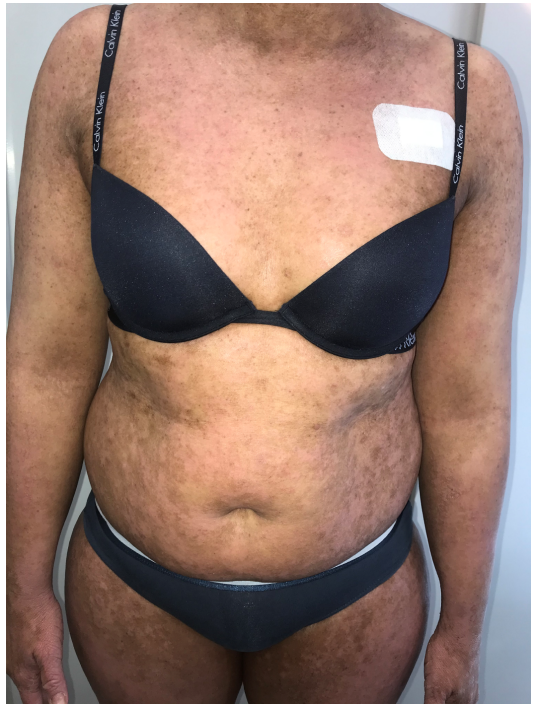
→Total Skin Electron Beam Irradiation (TSEB): bridge to transplant

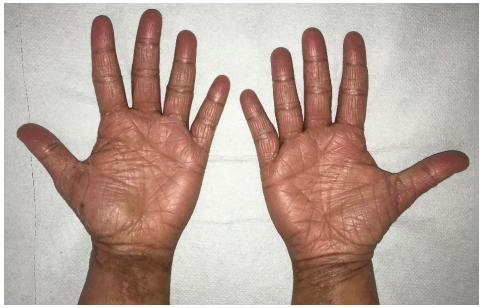
III sedute da 10.8 Gy (32.4 Gy totali)

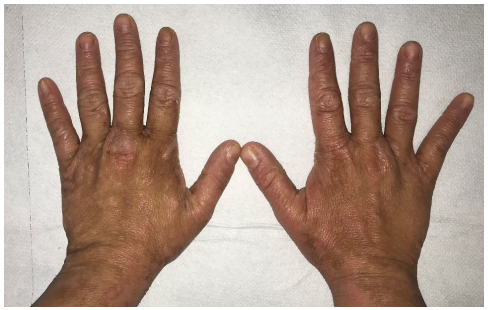
Rivalutazione post TSEB Settembre 2019







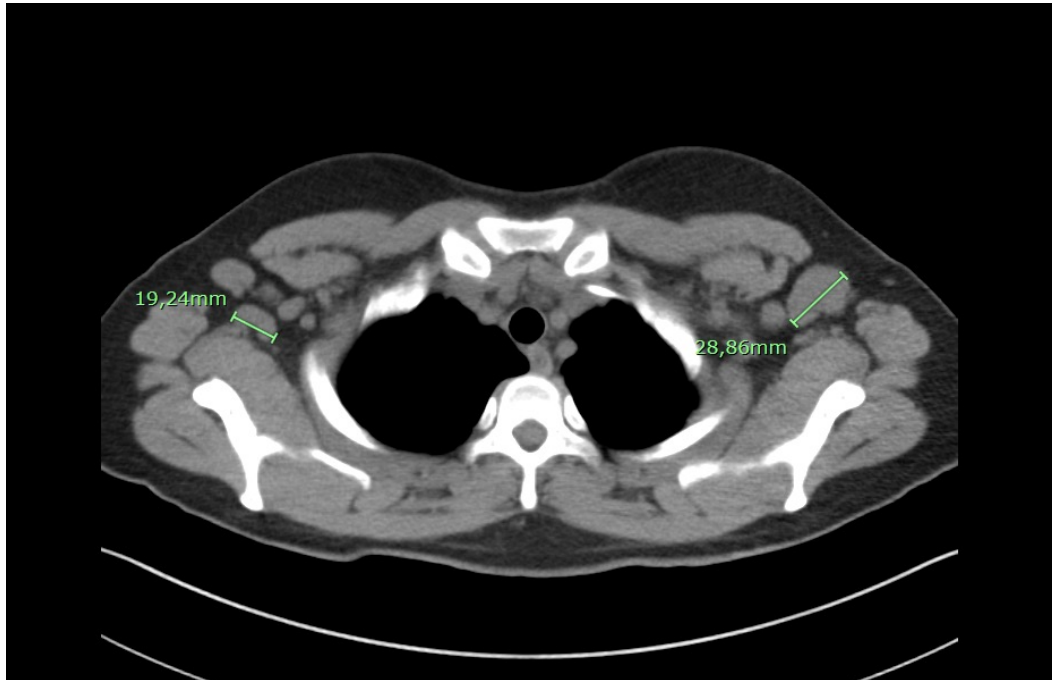




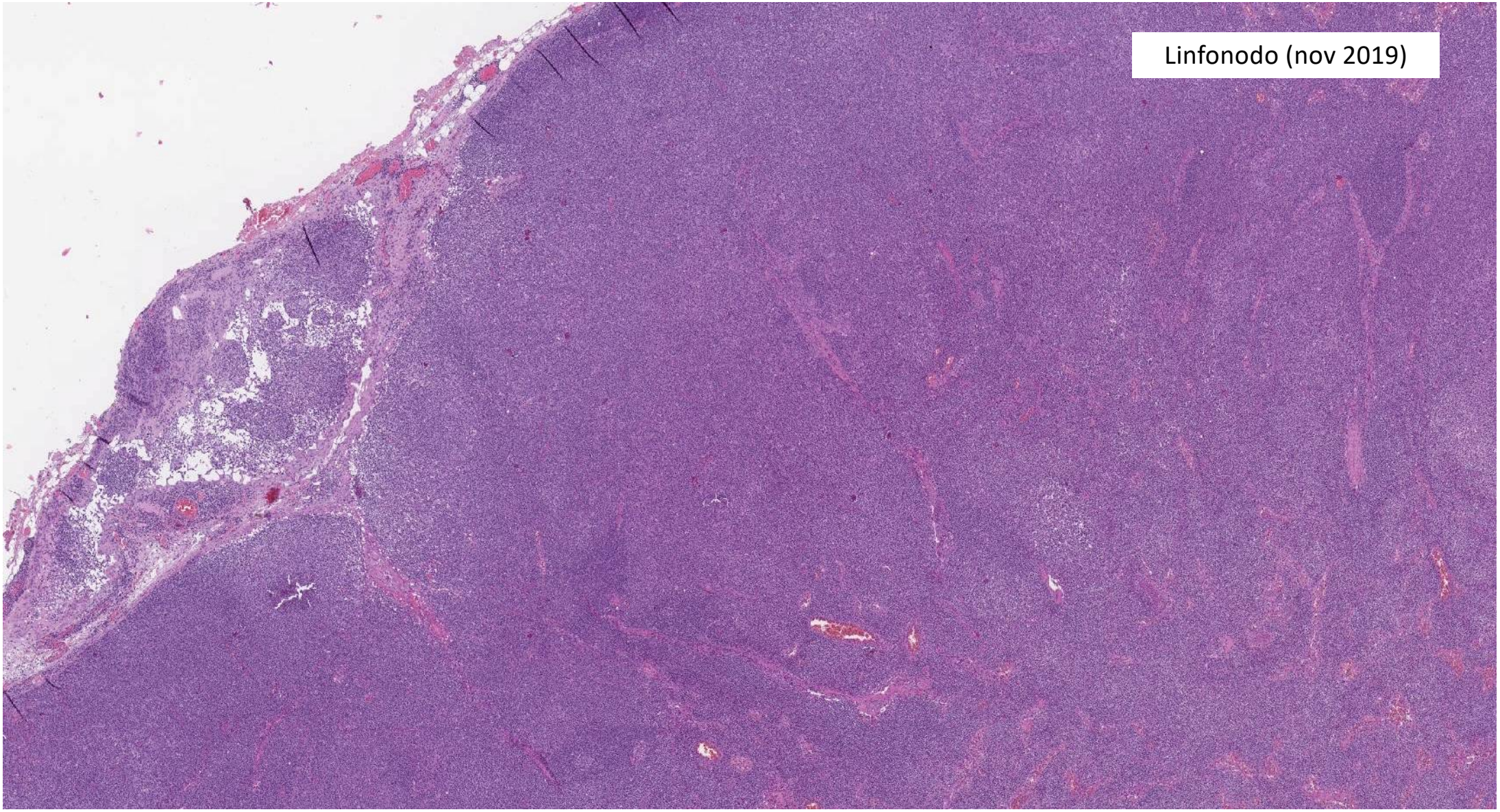
Remissione quasi completa del quadro linfoproliferativo della cute, con pigmentazione brunastra in assenza di erosioni, persiste ipercheratosi psoriasiformi palmoplantare

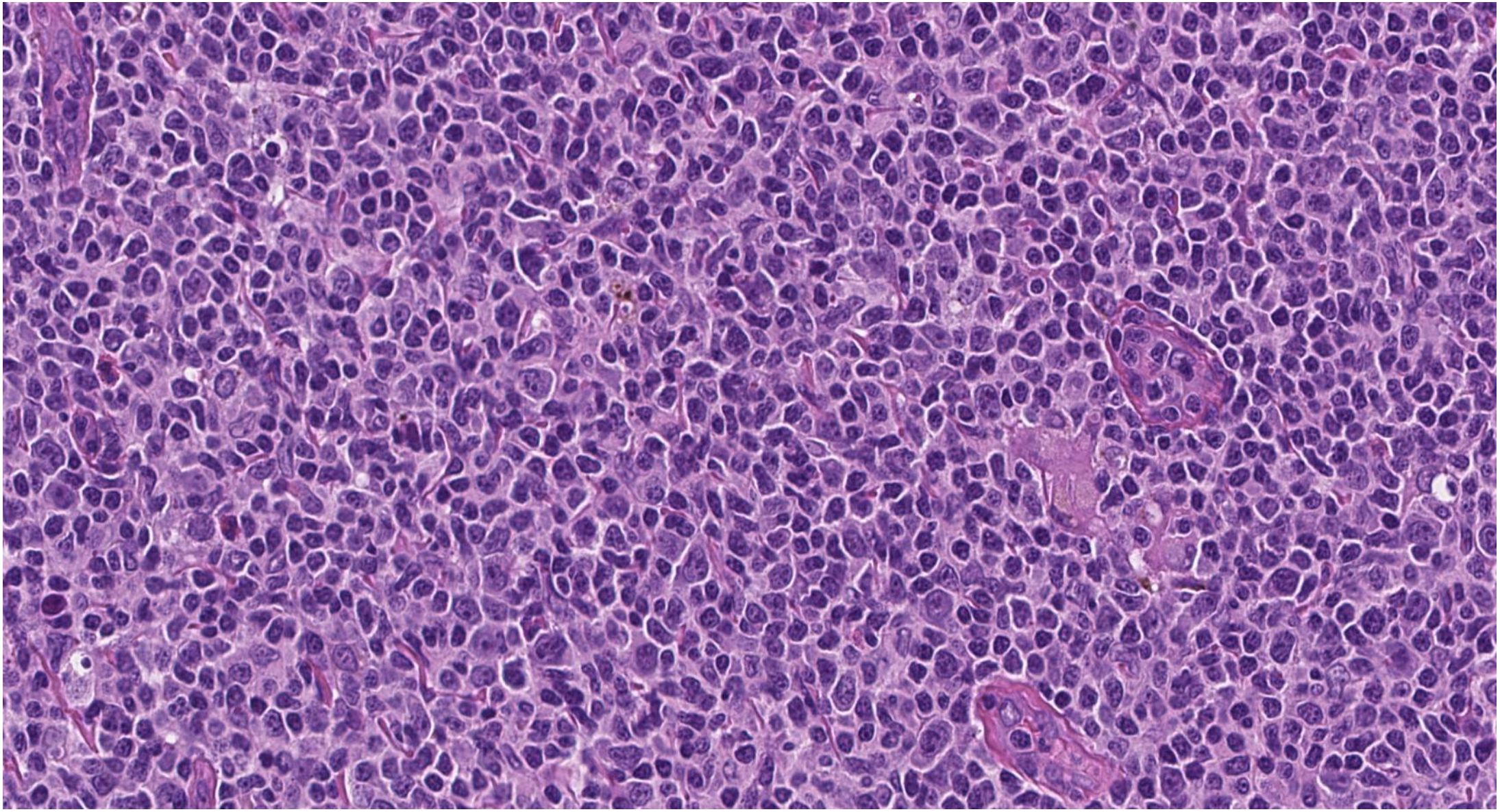
Valutazioni pre-trapianto Ottobre 2019

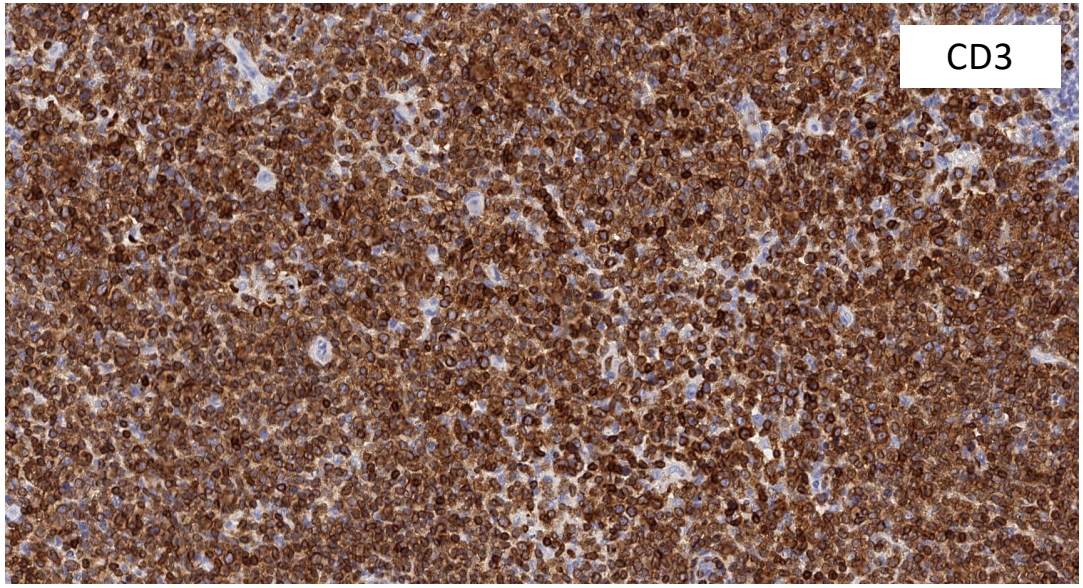
TC total body: Linfonodi ascellari di dimensioni aumentate: 2.9 cm sn, 1.9 cm a dx. Invariato tessuto solido in loggia timica. Non linfadenopatie in loggia mediastinica.

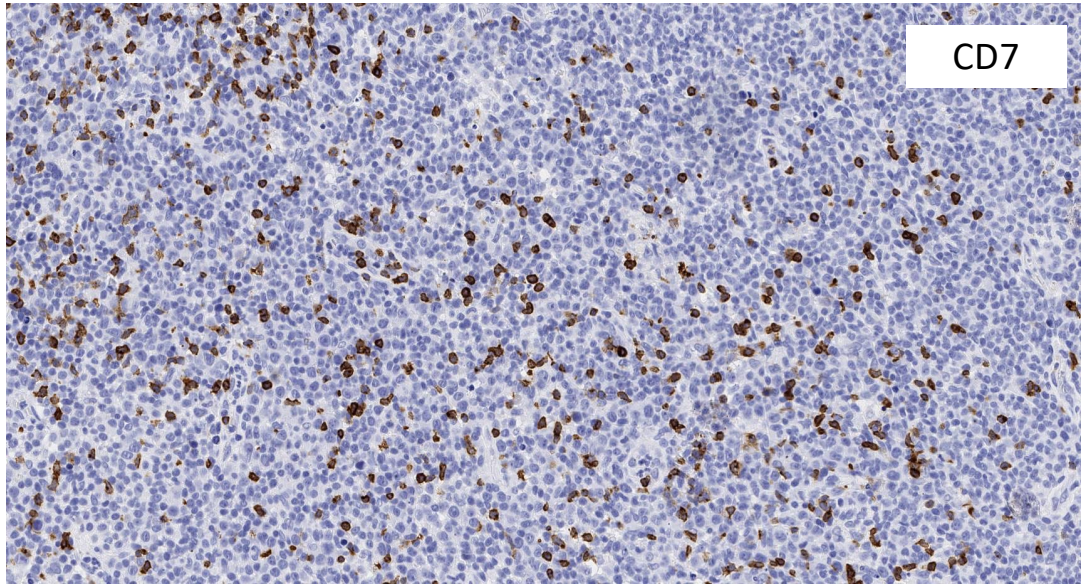


→ **Linfoadenectomia con esame istologico**


Linfonodo (nov 2019)




CD3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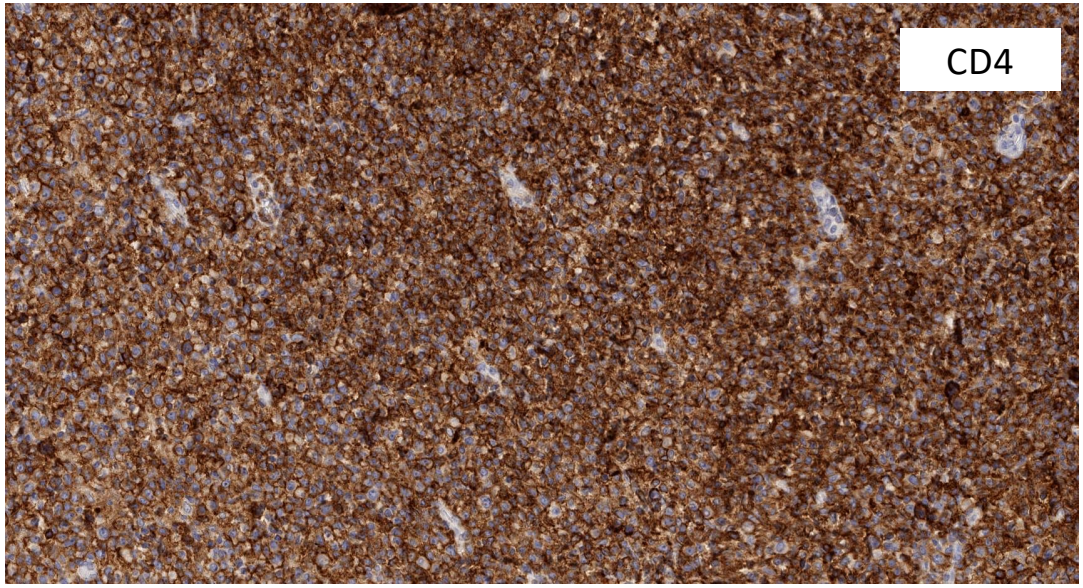
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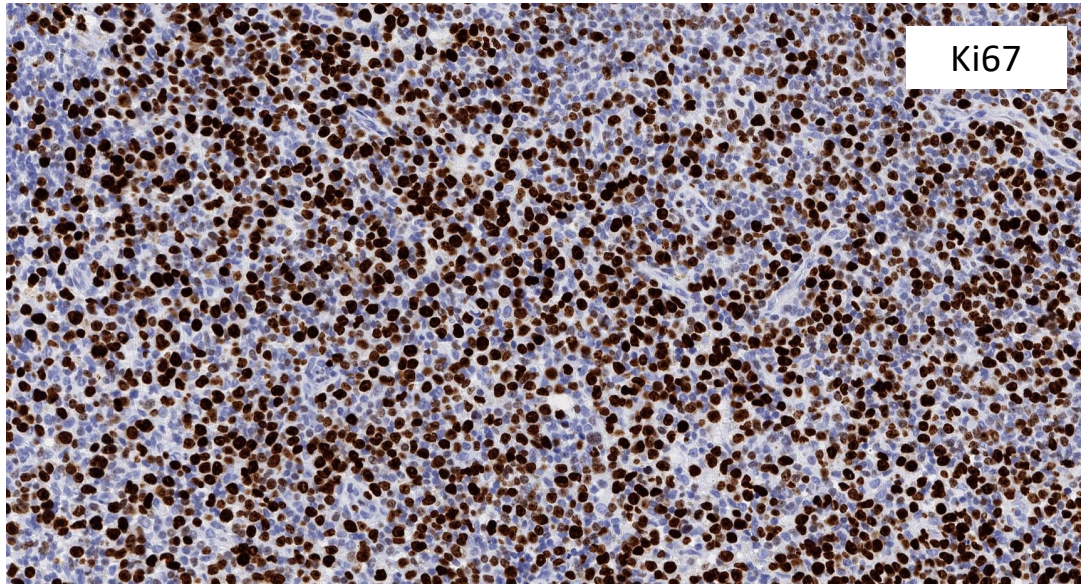
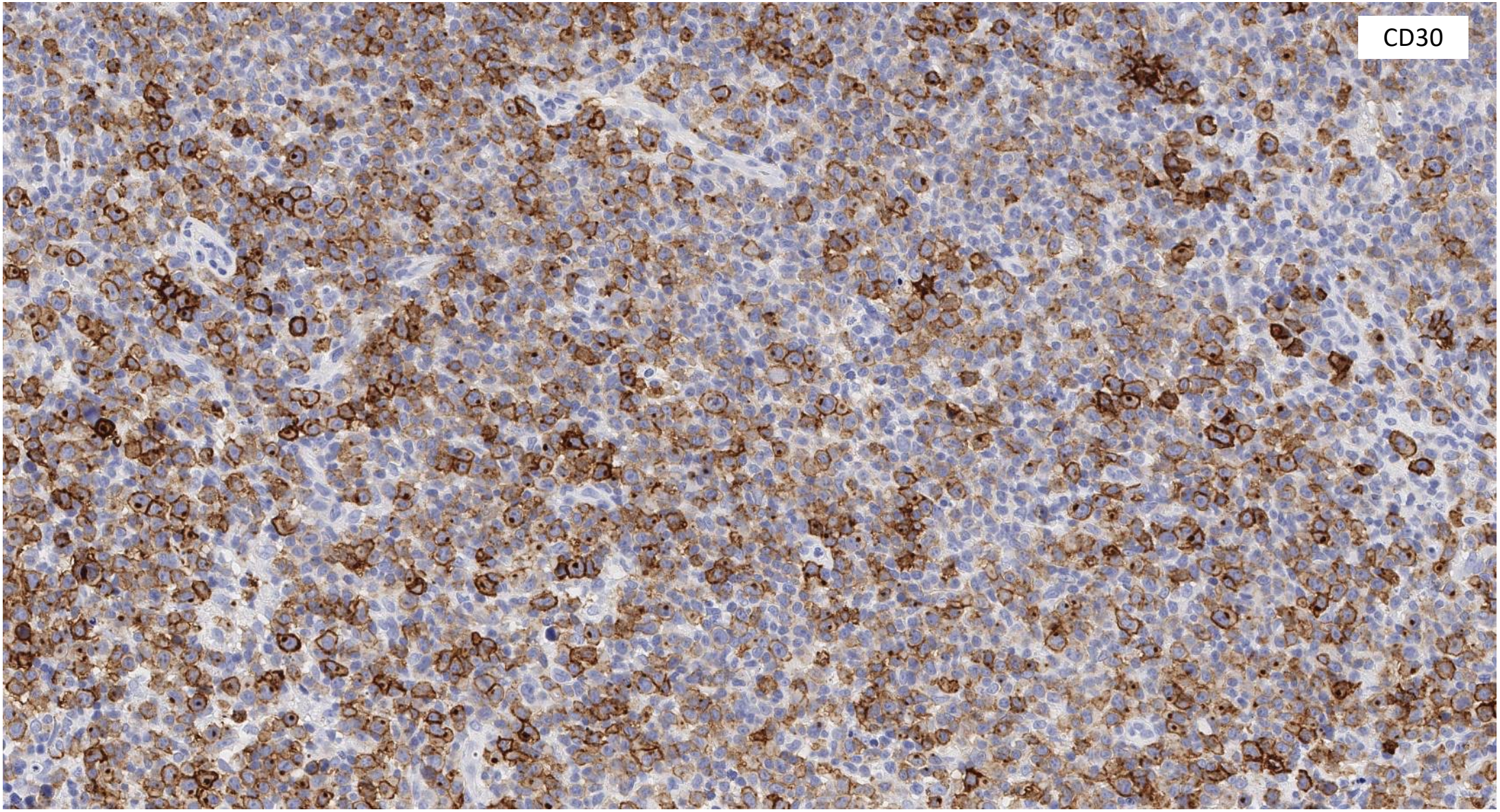

Ki67

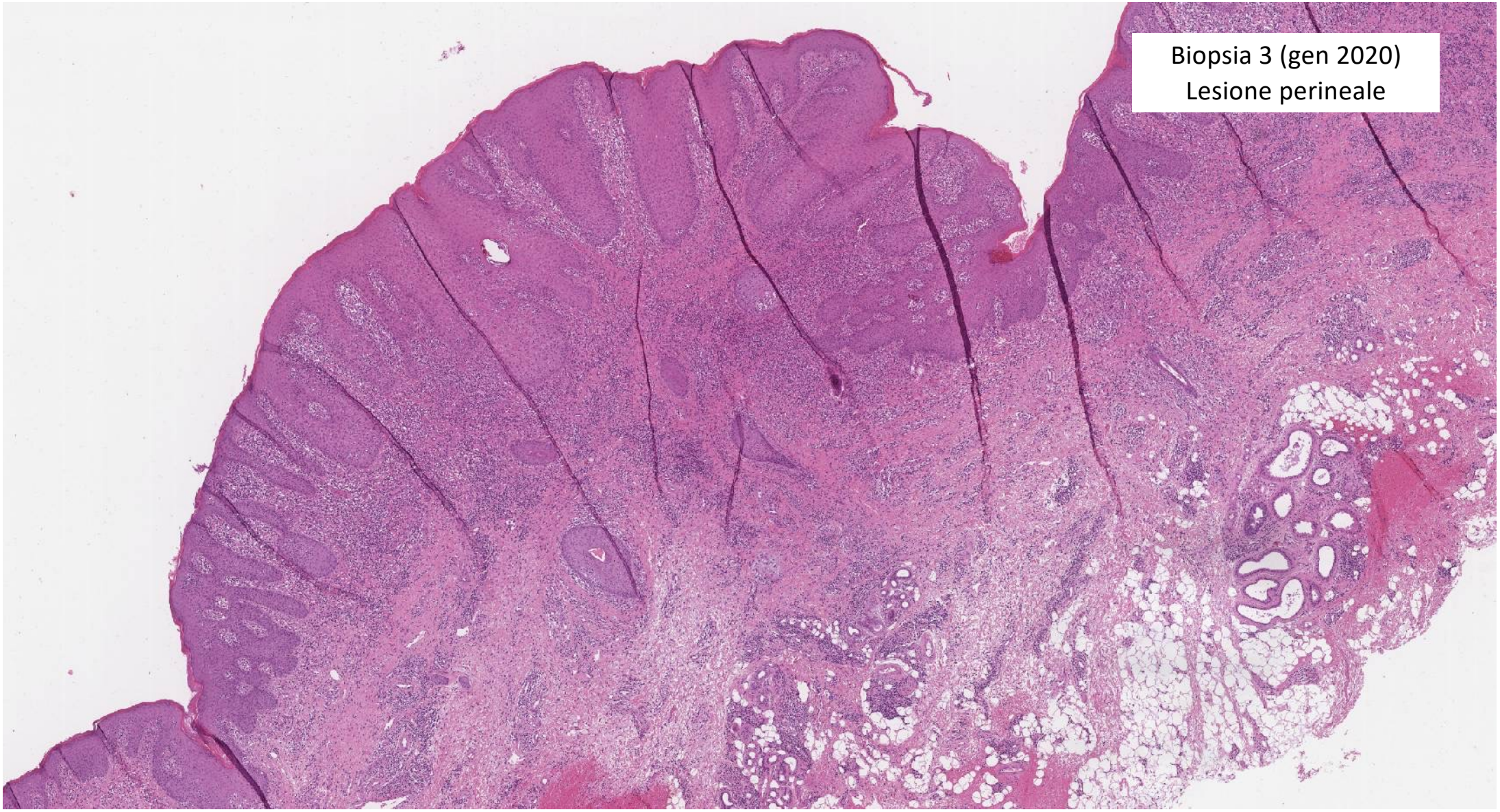

CD30

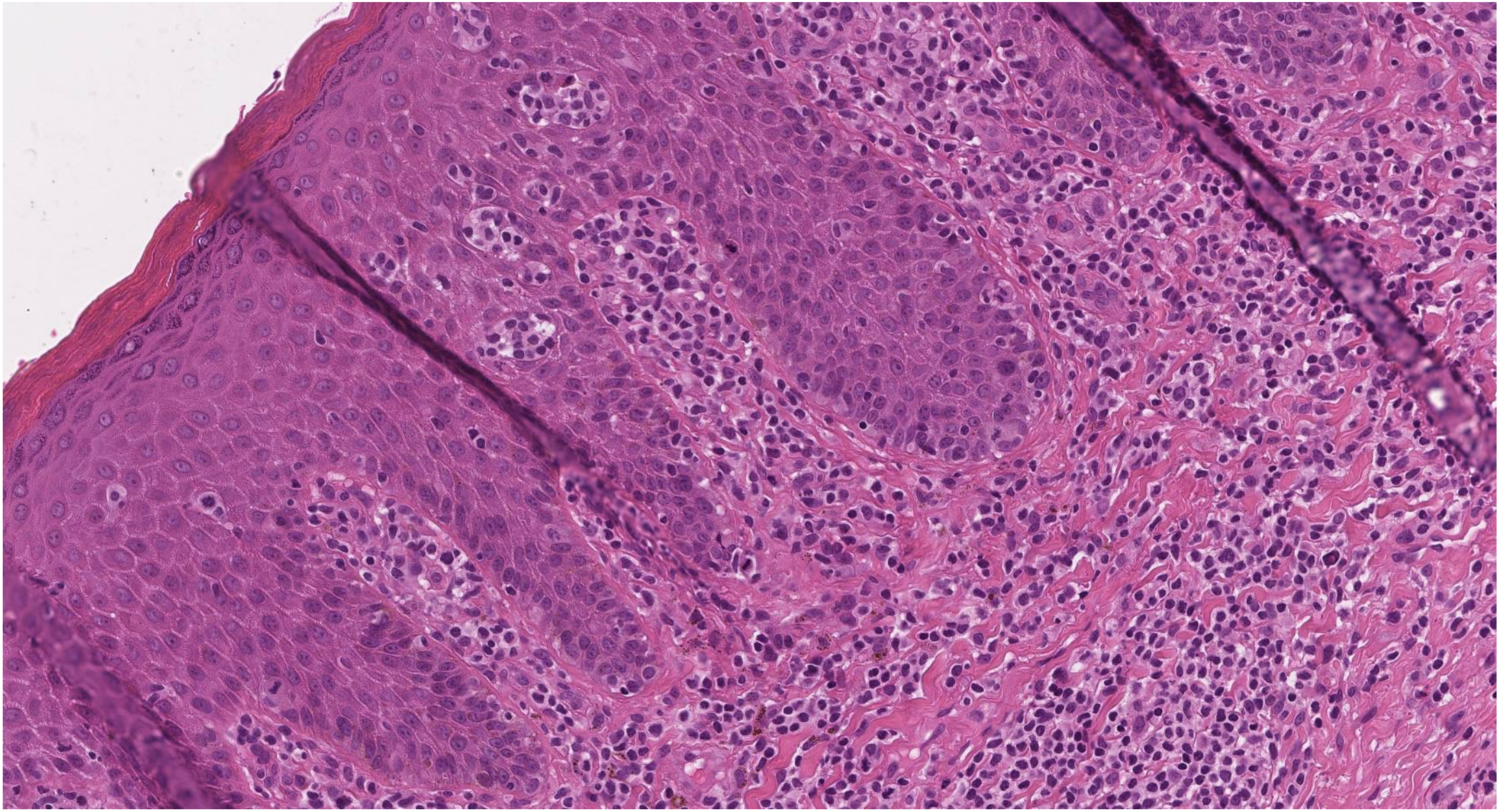
Terapia II linea Novembre 2019

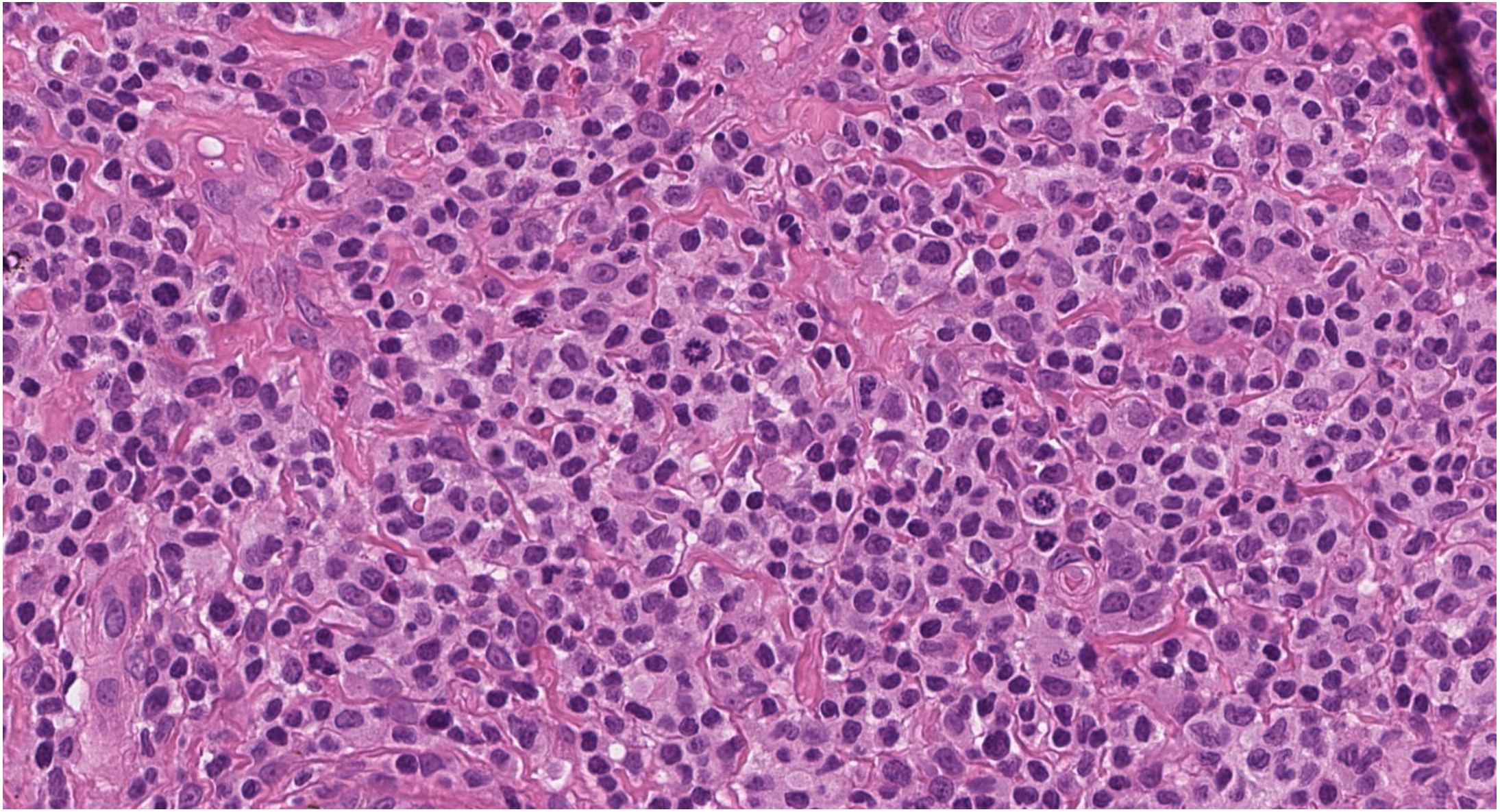
→ **Brentuximab Vedotin 1.8 mg/Kg ogni 21 giorni**
5 cicli

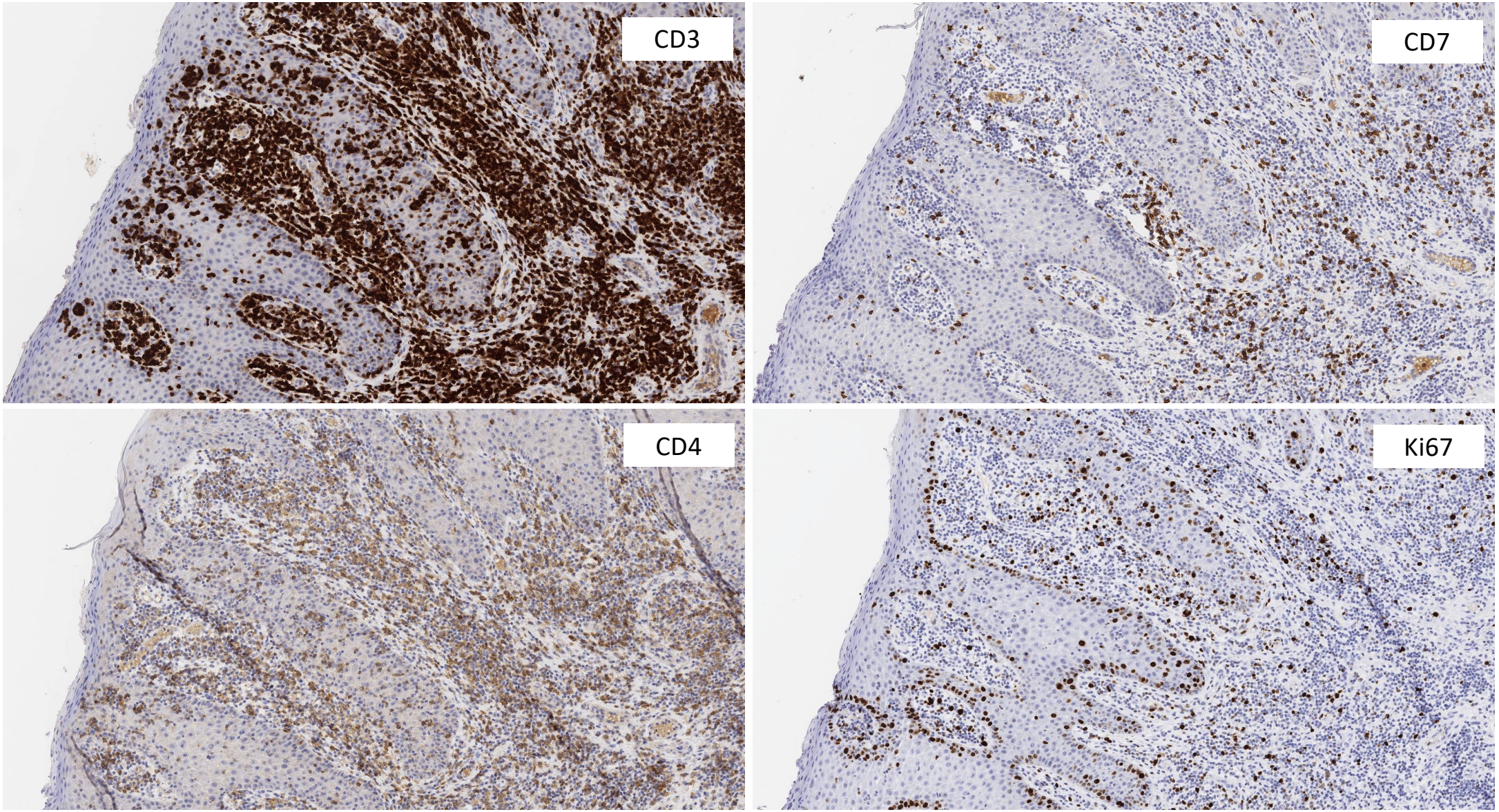
Iniziale miglioramento obiettivo delle linfoadenopatie, tuttavia comparsa di nuove lesioni papillomatose perianali (Micosi Fungoide o Condilomi HPV+?)

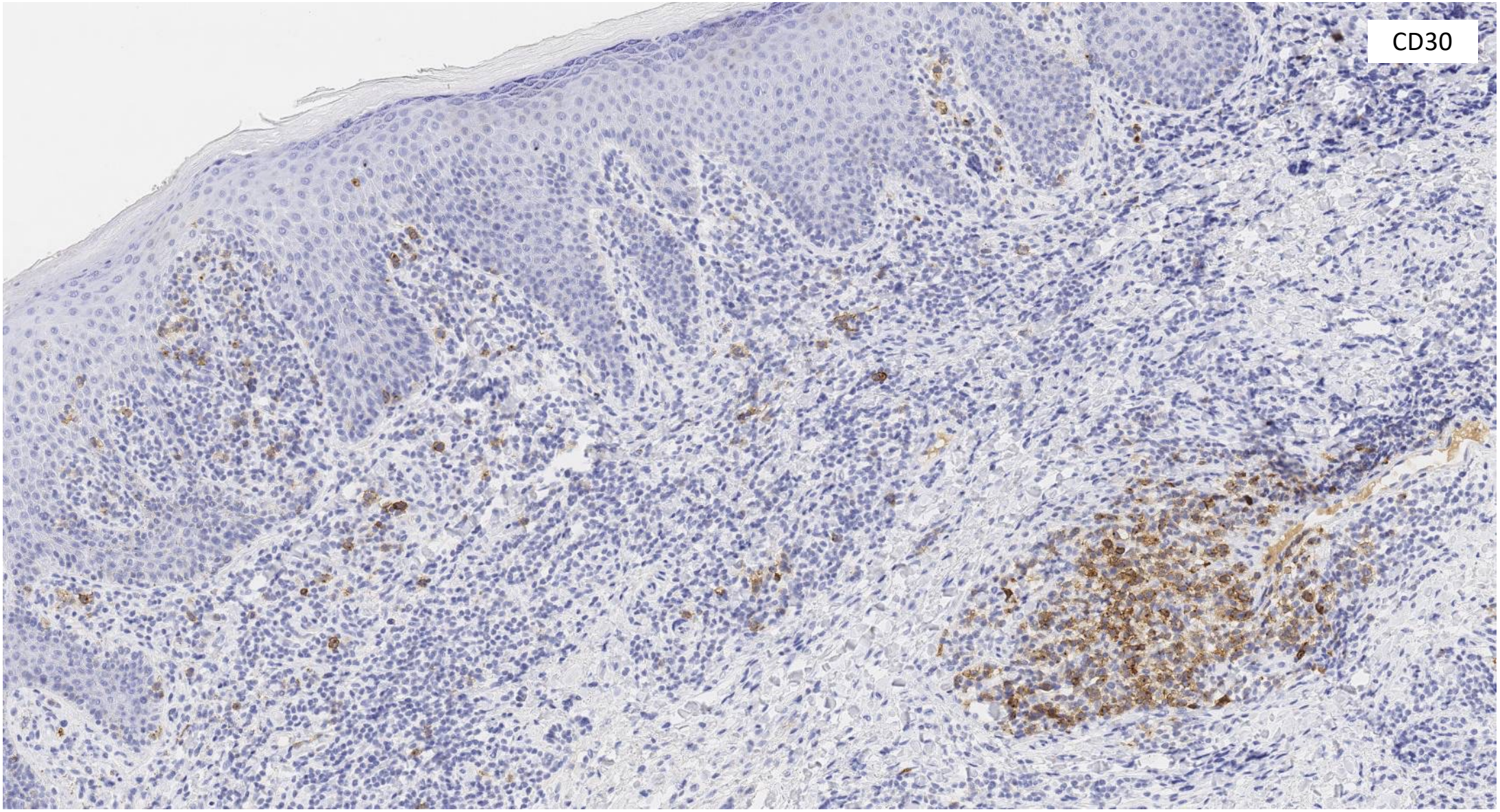
→ **Biopsia lesioni**


Biopsia 3 (gen 2020)
Lesione perineale



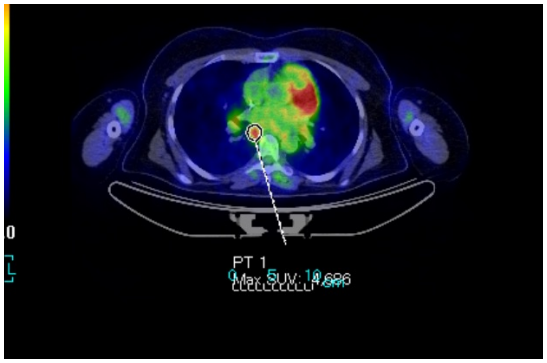



CD3
CD7
CD4
Ki67


CD30

Terapia III linea Marzo 2020

TC torace: Linfonodi ingranditi in sede paratracheale e sottocarenale.
PET total body: linfoadenomegalie modestamente captanti in sede mediastinica (SUV max 4.7)



→ **II CHOEP,** per comparsa nuove linfoadenopatie e lesioni nuove da malattia in corso di BV

Miglioramento clinico lesioni cutanee e linfonodi palpabili →VGPR

Trapianto aploidentico Aprile 2020

HCT-CI Sorror: 0 **DRI**: int **EBMT score:** 4
Familiare aploidentico, D/R: F/F, 0pos/Apos, CMV IgG neg/pos
Condizionamento: Thiotepa+Ciclofosfamide+Fludarabina+ TBI200
Profilassi GVHD: ATG 2,5 mg/Kg, CTX-PT, ciclosporina, micofenolato

Complicanze:

→ Enterite da Adenovirus (Cidofovir), evoluta in GVHD intestinale (PDN 2 mg/kg)

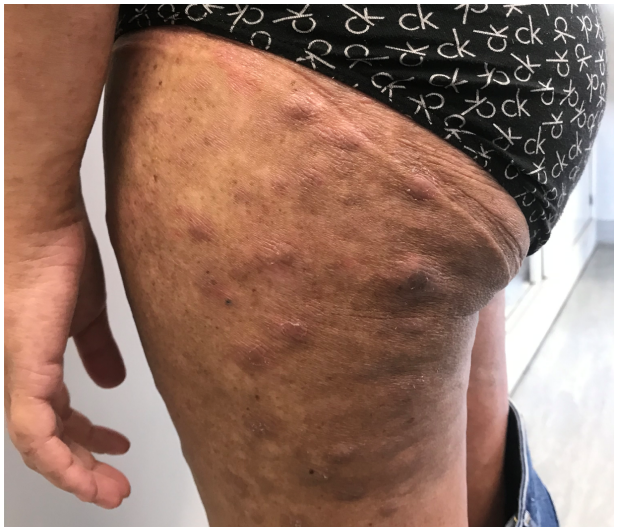
→ Difficoltà alla deambulazione post allettamento e ipostenia AAII

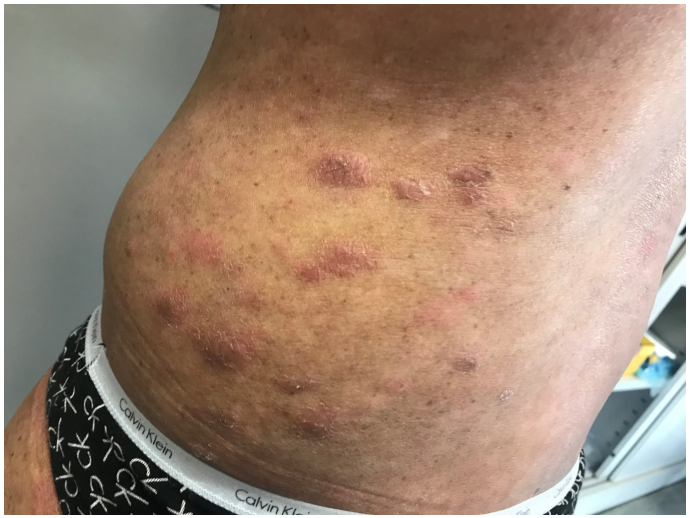
Rivalutazioni post trapianto

- **Valutazioni midollari +30, +60 e + 100:** chimerismo 100% donatore su cellule CD3+ periferiche e sangue midollare in toto
- **TC total body + 100:** Non linfoadenopatie di aspetto patologico; qualche linfonodo infracentimetrico in regione ascellare bilaterale

→ Settembre 2020 (+ 5 mesi): comparsa nuove lesioni

RECIDIVA



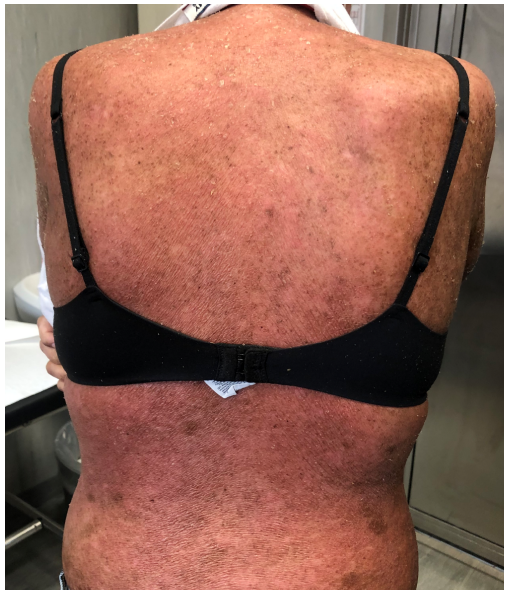


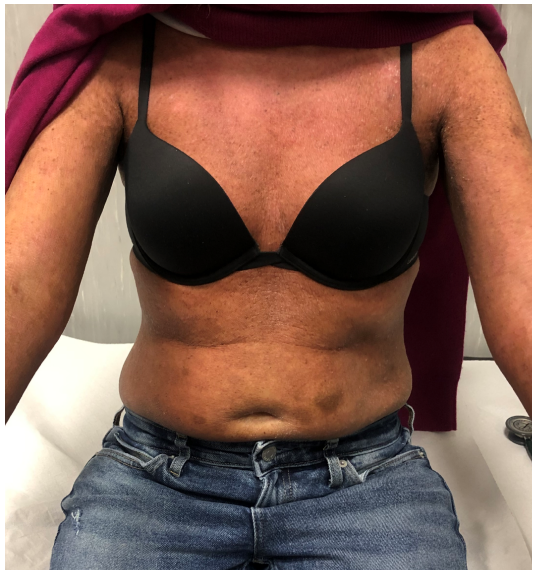
Terapia post trapianto Ottobre 2020

→ Ridotto steroide e ciclosporina rapidamente (+ 6 mesi)

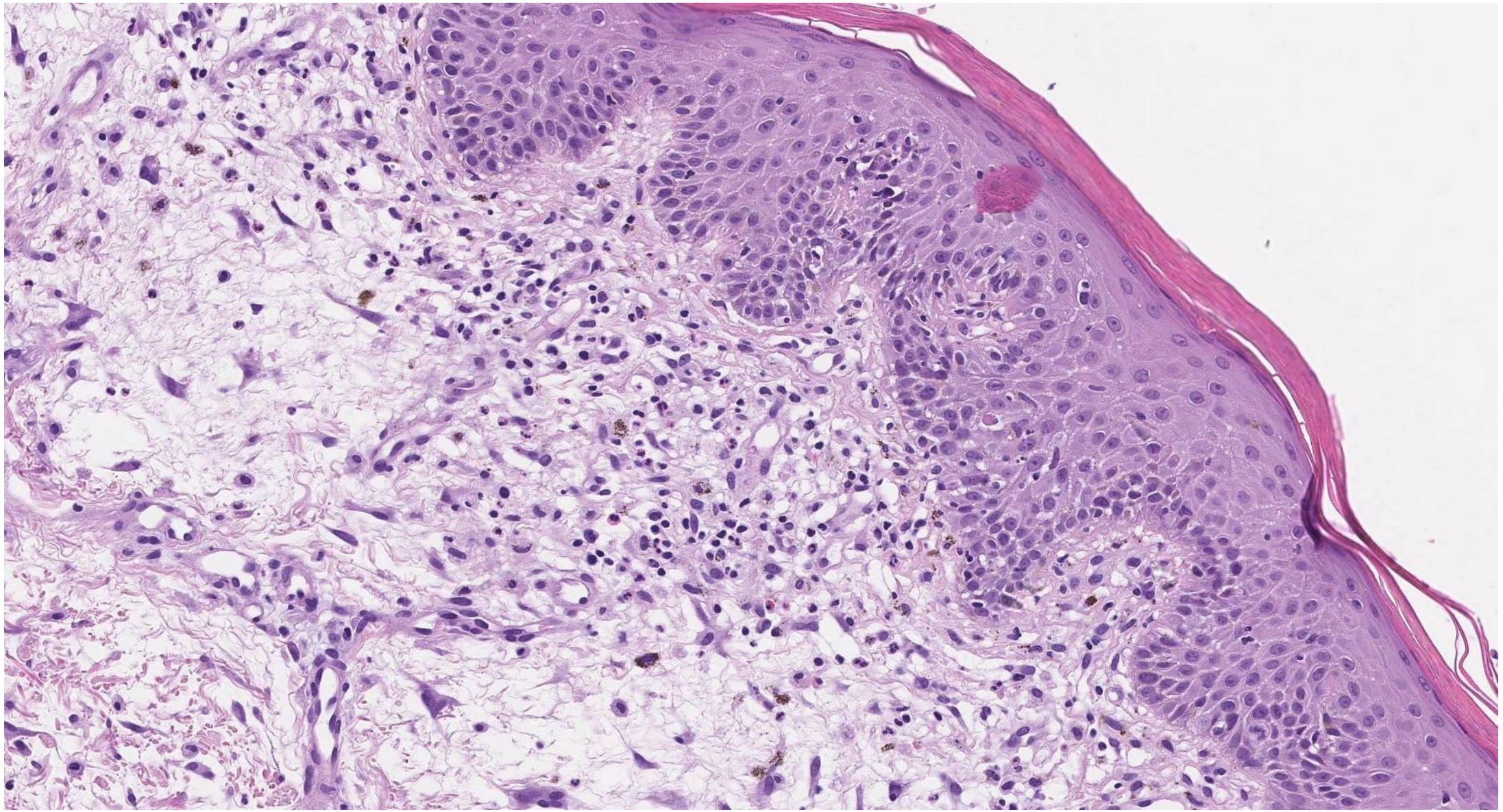
→ TSEB 12 sedute (12 Gy → 44.4 Gy totali)

→Novembre 2020 (+ 7 mesi): eritema e desquamazione diffusa





→**biopsia cute (RT? malattia? GVHD?)**



Follow up post trapianto Novembre 20 – Marzo 21

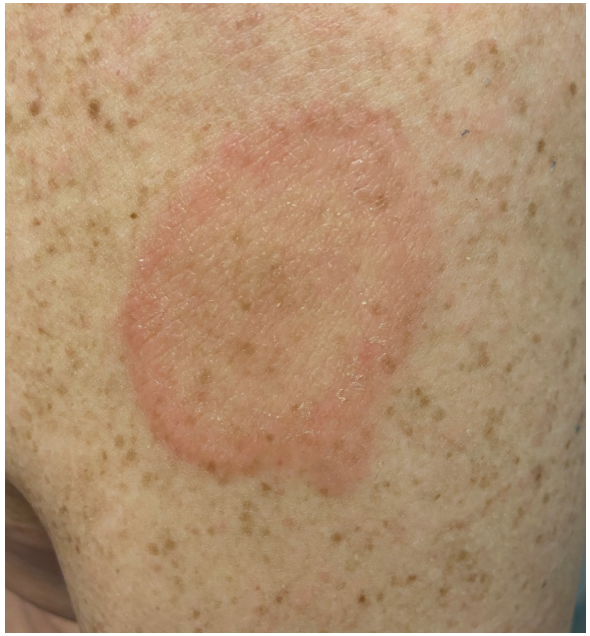
→Steroide PDN 1 mg/Kg

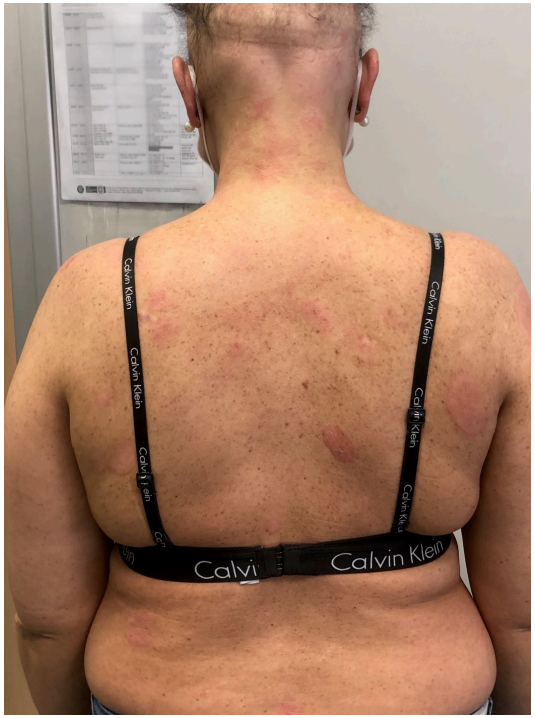
→Ruxolitinib 5 mg BID, incrementato a 10 mg BID

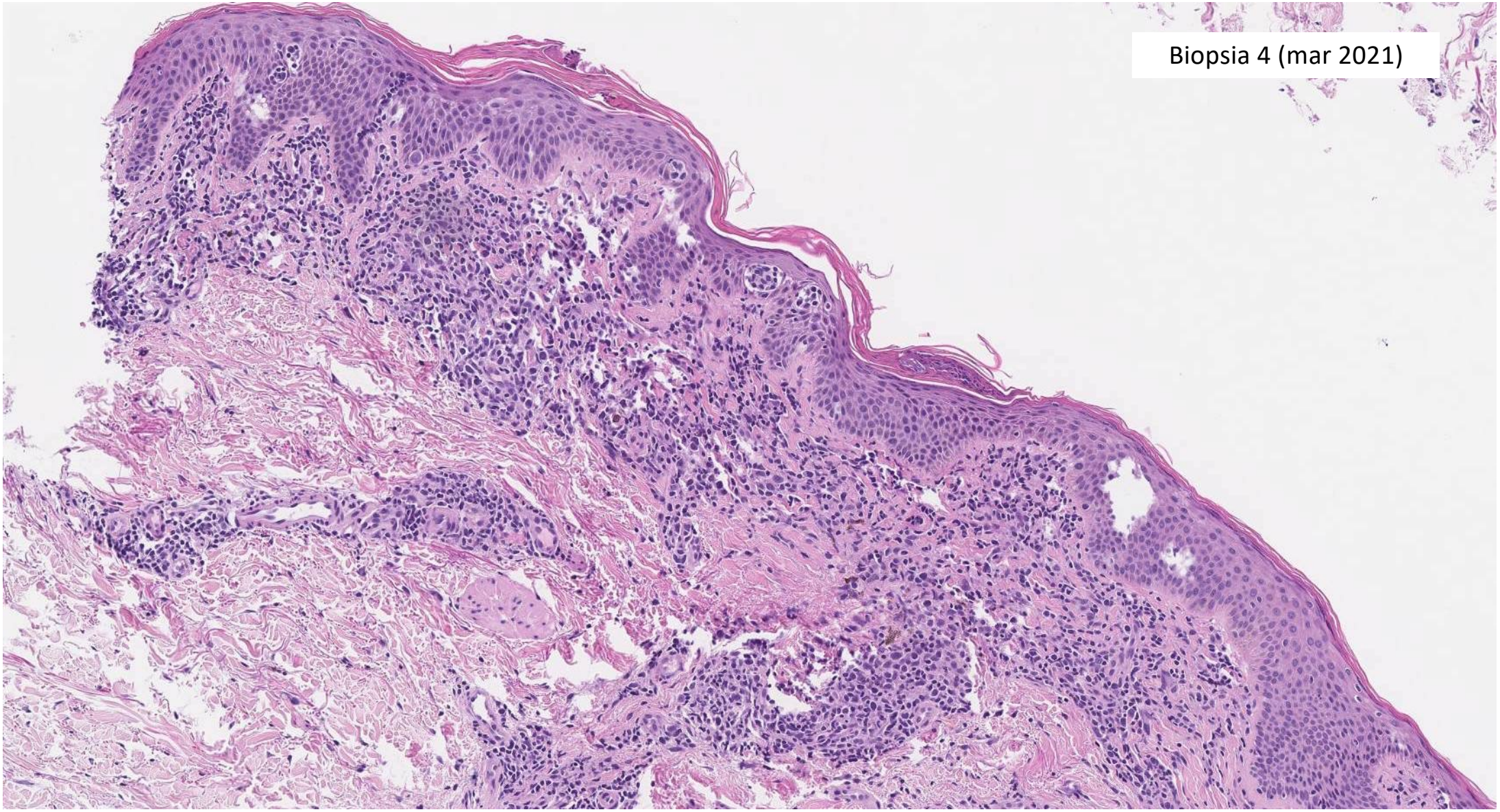
→Marzo 2021 (+ 11 mesi): nuove lesioni

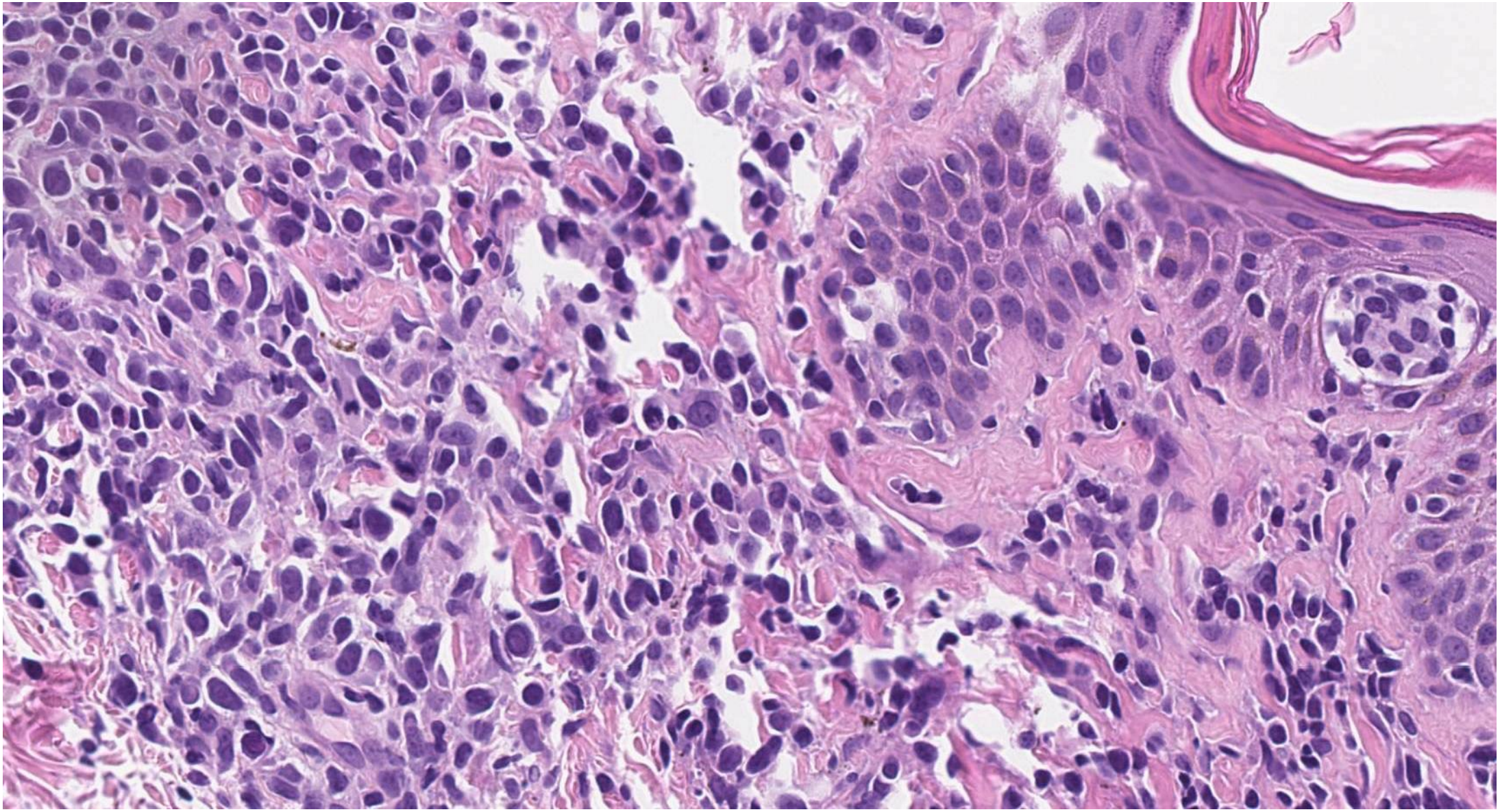
→Perdita del chimerismo (78% donor su CD3+ periferiche)

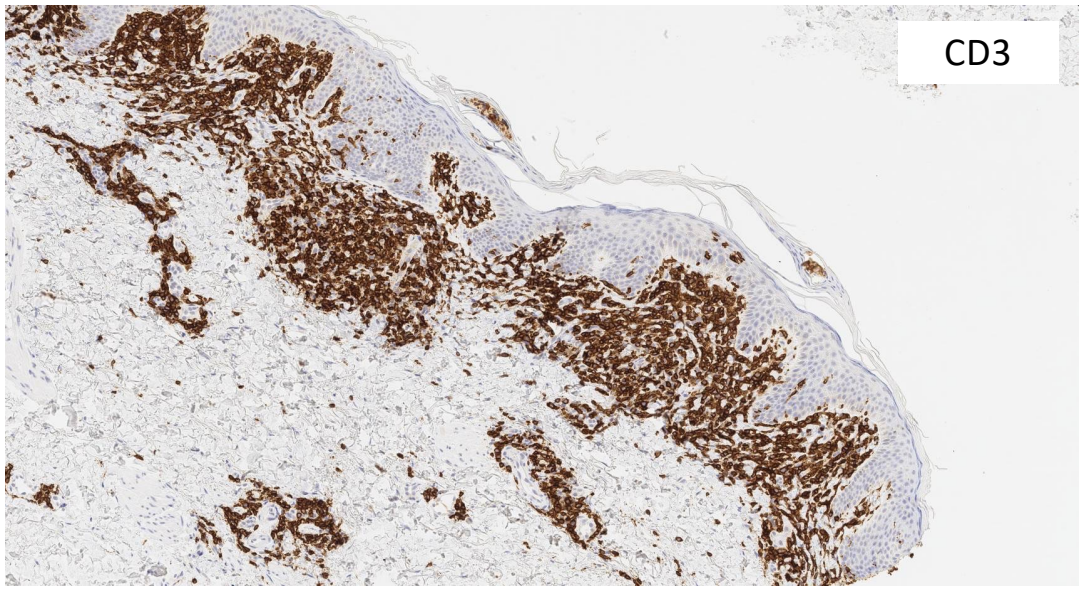
→**biopsia cute (malattia? GVHD?)**

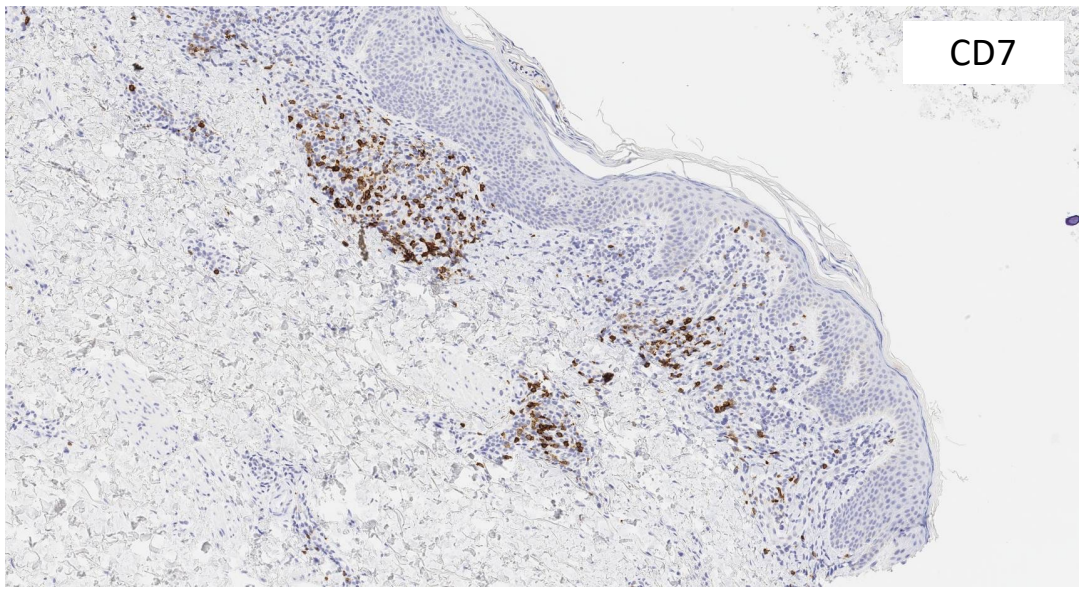


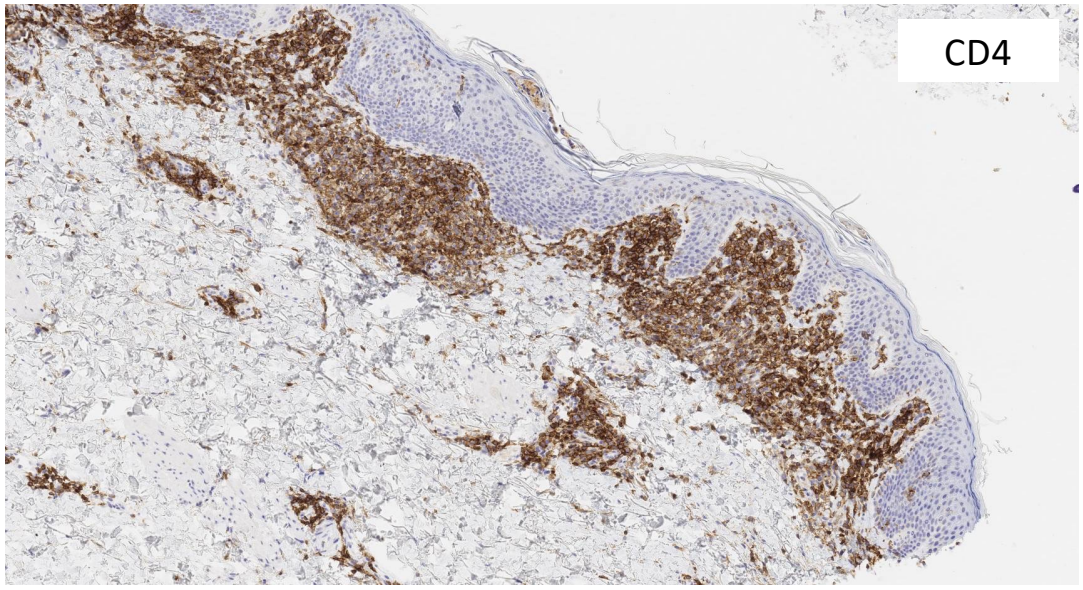


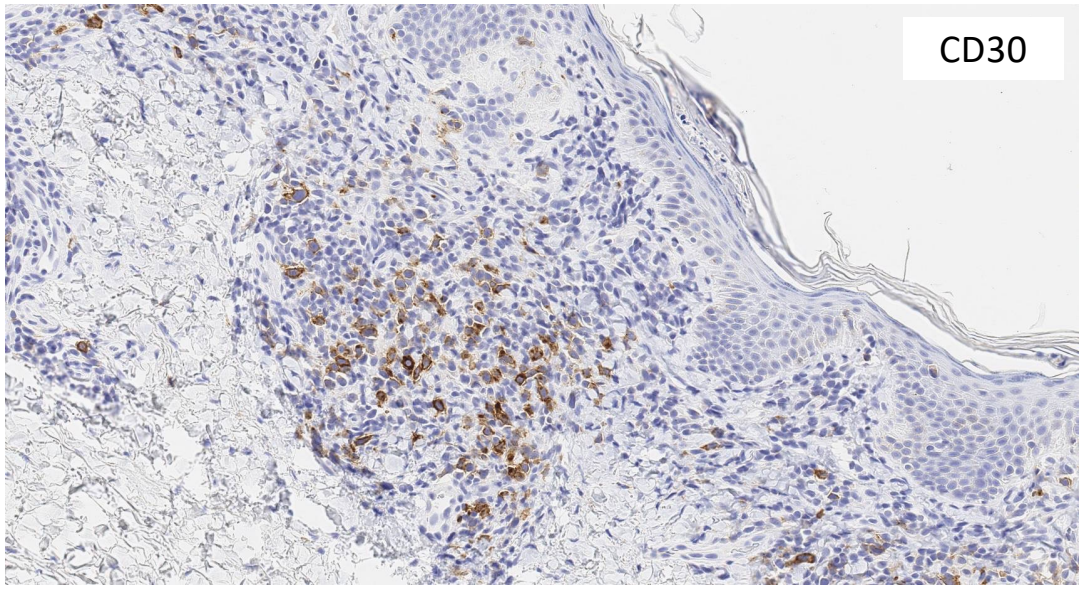

Biopsia 4 (mar 2021)




CD3


CD7

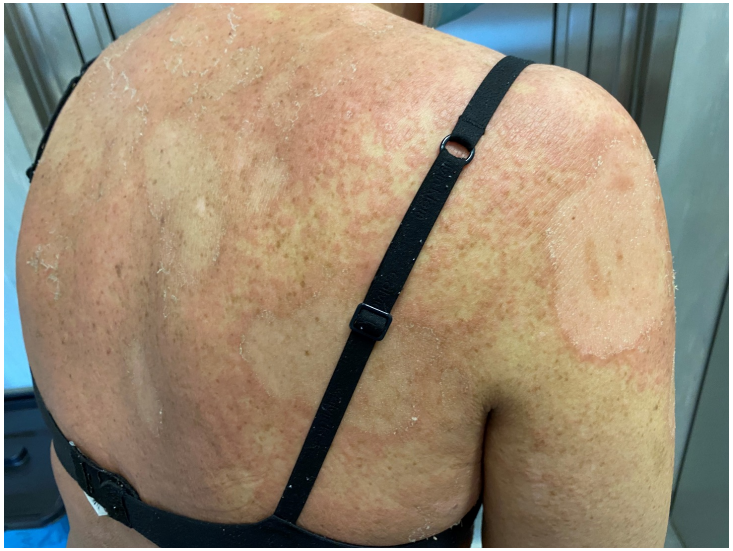

CD4


CD30

Terapia post trapianto Maggio 2021

→ Sospende steroide e Ruxolitinib
→Riprende Brentuximab Vedotin 1,8 mg/Kg ogni 21 giorni, previo TC total body (linfoadenopatie infracentimetriche di aspetto reattivo)
(5 cicli→ 10 cicli tot)

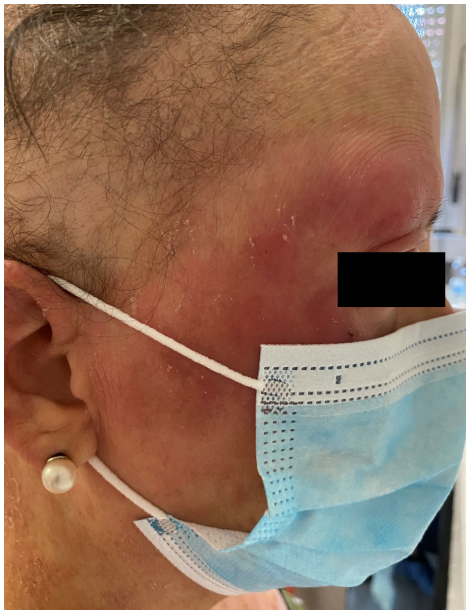
In corso di trattamento, comparsa di rash eritematoso agli arti e al tronco
→visita dermatologica: rash pomfoide verosimilmente da farmaco, risolto con cetirizina 1 cp la sera per 10 gg.

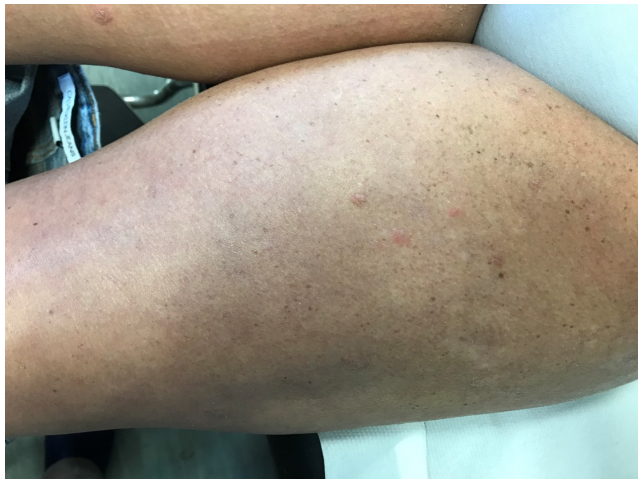


Terapia post trapianto Agosto 2021

→ **Inizia Peginterferone alfa-2a** per PR, ma ripresa chimerismo donatore (95% donor su CD3+ periferiche)

→Ultimo controllo: quadro di VGPR sul corpo con persistenza di unica lesione a livello periorbitario e rare sporadiche lesioni agli arti





Conclusione 1

Importanza interazione tra clinico e anatomopatologo nella fase diagnostica

GENERAL DERMATOLOGY

BJD
British Journal of Dermatology

British Journal of Dermatology (2019) **181**, pp350–357

The PROCLIPI international registry of early-stage mycosis fungoides identifies substantial diagnostic delay in most patients

Table 1 Clinical data of 348 patients with early-stage mycosis fungoides (MF)

	Stage IA	Stage IB	Stage IIA	All
Patients (n)	172	149	27	348
Median (IQR) age (years)	54 (44–66)	57 (45–67)	61 (44–73)	57 (44–67)
Female	64 (37·2)	58 (38·9)	7 (25·9)	129 (37·1)
Male	108 (62·8)	91 (61·1)	20 (74·1)	219 (62·9)
Classical MF	140 (81·4)	112 (75·2)	22 (81·5)	274 (78·7)
Folliculotropic MF	28 (16·3)	37 (24·8)	5 (18·5)	70 (20·1)
Clinical alopecia	13 (7·6)	27 (18·1)	9 (33·3)	49 (14·1)
Follicular skin lesions	30 (17·4)	48 (32·2)	7 (25·9)	85 (24·4)
Poikiloderma	22 (12·8)	26 (17·4)	5 (18·5)	53 (15·2)
Hypopigmentation	10 (5·8)	15 (10·1)	3 (11·1)	28 (8·0)
Confluent erythema	4 (2·3)	17 (11·4)	6 (22·2)	27 (7·8)
Median (IQR) mSWAT patch	3 (1–5)	15 (10–25)	10 (3–39·8)	6 (2–15)
Median (IQR) mSWAT plaque	0 (0–2)	2 (0–11)	6 (1–12)	0·9 (0–5)
Median (IQR) mSWAT tumour	0	0	0	0
Median (IQR) mSWAT score	5 (2–8)	26 (17–45)	32·2 (11–70)	11 (5–28)
Duration of MF-like lesions (months)	36 (12–72)	48 (24–100)	33 (15–87)	36 (12–90)

Data are n (%) unless otherwise indicated. IQR, interquartile range; mSWAT, modified severity-weighted assessment tool.

What's already known about this topic?

- Mycosis fungoides (MF) is a rare skin cancer that may closely mimic common inflammatory dermatoses in early-stage disease.
- There is no singular diagnostic test for MF.
- Diagnosis of early-stage MF requires close clinical, pathological and genotypic correlation.

What does this study add?

- This study reports on the clinical characteristics of a large international cohort of patients with early-stage MF whose diagnosis has been confirmed following clinicopathological review.
- The median age of presentation is 57 years, which is significantly younger than those presenting with advanced-stage MF (66 years).
- This study confirmed a worldwide male predominance in early-stage MF (1·7 males : 1 female).
- A diagnostic delay is frequent (median 3 years).

J Cutan Pathol. 2021;1–9.

Spiky/keratosis-pilaris-like early follicular mycosis fungoides: A clinicopathologic study of 20 cases with extended follow-up

Carlo Tomasini MD[1,2] | Andrea Michelerio MD[1,2] | Pietro Quaglino MD[3]

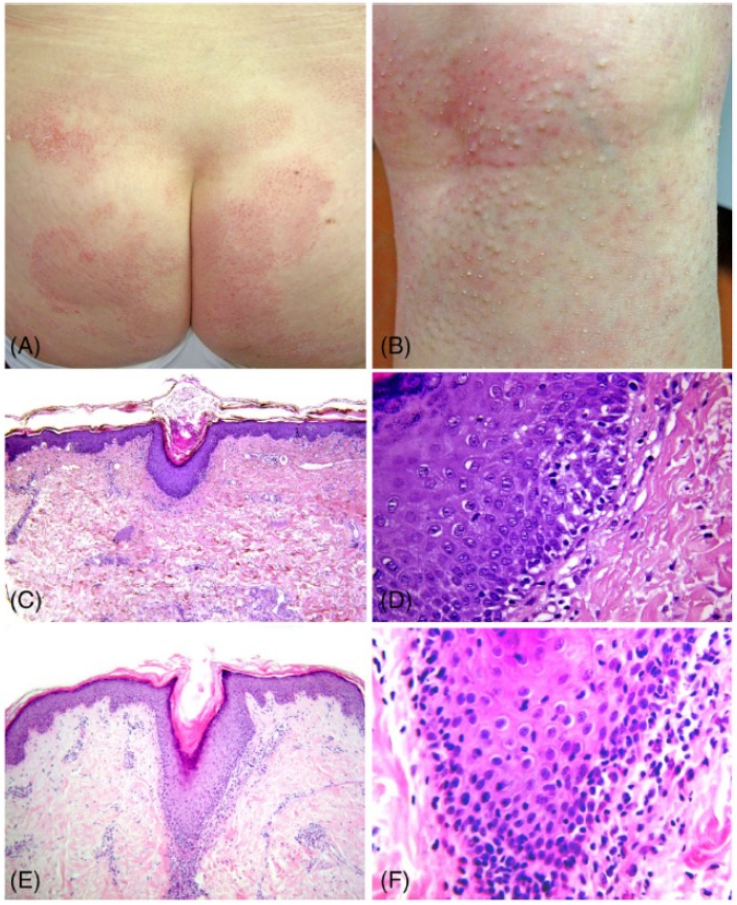


TABLE 1 Clinical data of 20 patients with spiky/keratosis-pilaris-like mycosis fungoides

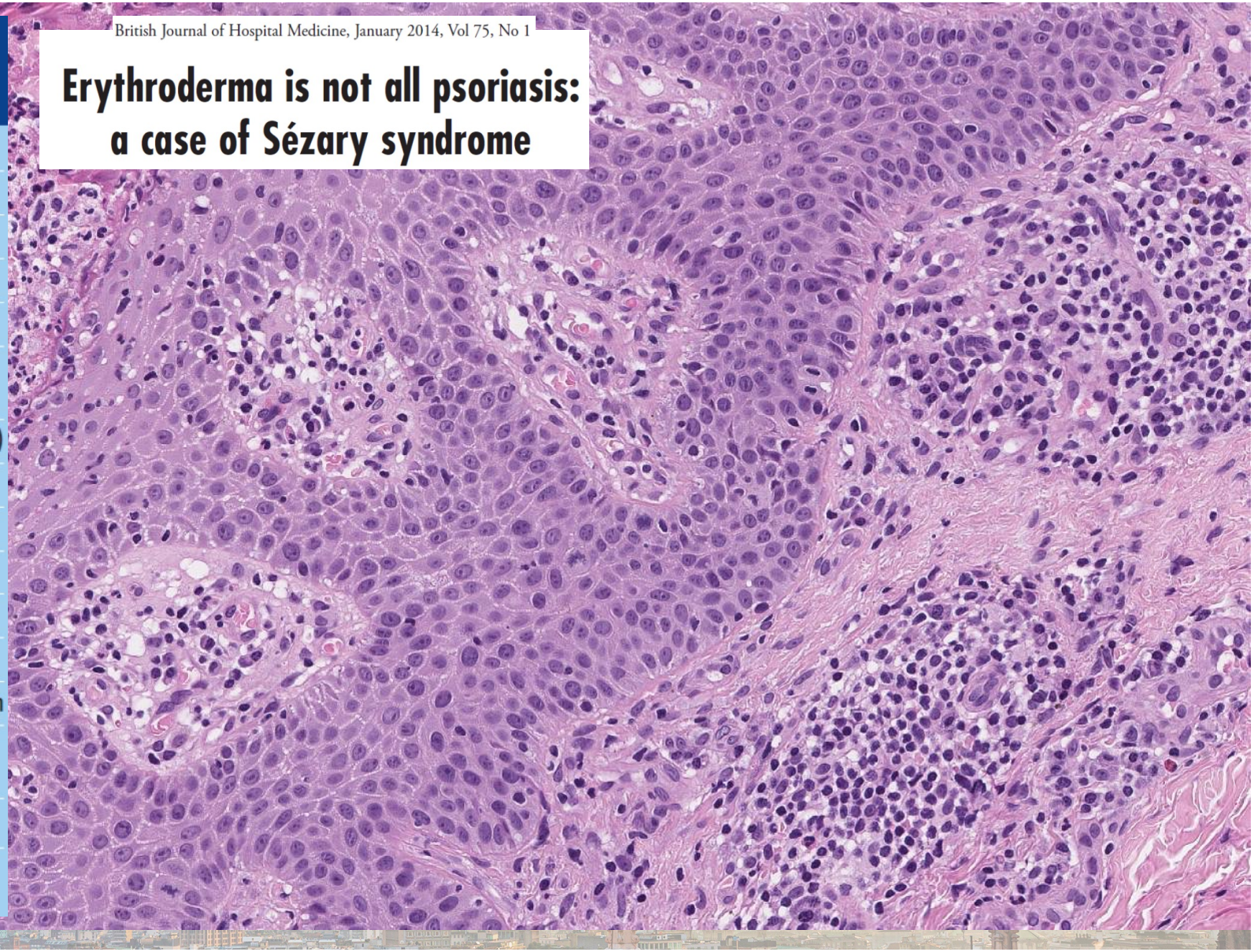
Patient/ Gender	Age at diagnosis (y)	Time from onset to diagnosis (mo)	Site of involvement	Clinical diagnosis	Stage at diagnosis	Follow-up (mo)	Disease evolution
1/M[a]	71	6	Trunk	MF, follicular lichen	IB	134	AWD
2/M[a]	48	6	Trunk, neck, buttocks	Folliculotropic MF, tinea incognita, mucinosis, lupus erythematosus, seborrheic dermatitis	IB	134	AD
3/M[a]	46	8	Trunk, lower extremities	Mucinosis	IB	98	AD
4/M[a]	47	9	Trunk, upper extremities	Lichen spinulosus	IB	82	AD
5/F[a]	61	36	Trunk, pubis, thighs	Lichen nitidus	IB	77	AWD
6/F[a]	47	60	Trunk, buttocks, upper and lower extremities	Mucinosis, MF, lichen spinulosus	IB	86	AD
7/F[a]	74	10	Trunk	Follicular keratosis	IB	180	AD
8/M[a]	49	2	Trunk, upper and lower extremities	Pityriasis rubra pilaris, psoriasis, secondary syphilis	IB	12[b]	AD
9/F	42	53	Chin	Parapsoriasis	IA	52	AD
10/M	86	3	Trunk, buttocks	Papular mycosis fungoides	IB	20[c]	AD
11/M	68	18	Upper and lower extremities	Follicular MF, mucinosis, keratosis pilaris, lichen spinulosus	IB	55	AWD
12/F	62	120	Lower extremities and plantar surfaces	Papular mycosis fungoides	IB	45	AD
13/M	77	77	Buttocks, thighs, scalp	Folliculotropic MF, lichen spinulosus	IB	58	AWD
14/F	52	168	Lower and upper extremities, buttocks, trunk	Folliculotropic MF	IB	45	AD
15/M	73	62	Lower and upper extremities, buttocks, trunk	Dermatitis with lichenification, MF	IB	72[c]	DP
16/F	50	64	Trunk	Pityriasis rubra pilaris, mucinosis, follicular eczema	IB	97	AD
17/F	58	12	Trunk, upper and lower extremities, buttocks	Pityriasis rubra pilaris, mucinosis,	IB	146	AWD
18/M	66	80	Buttocks, thighs	Keratosis pilaris	IA	144	AD
19/M	55	42	Buttocks	Mucinosis	IB	96	AD
20/M	44	12	Trunk, upper and lower extremities	Folliculitis, folliculotropic MF	IB	49	AD

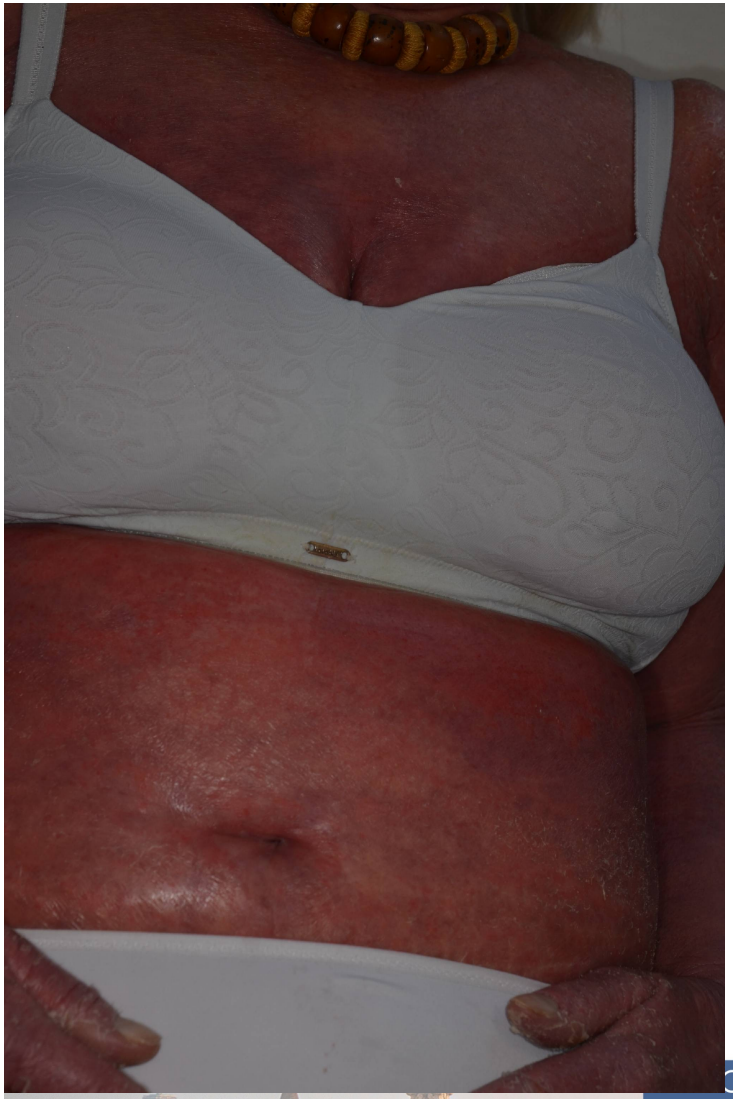
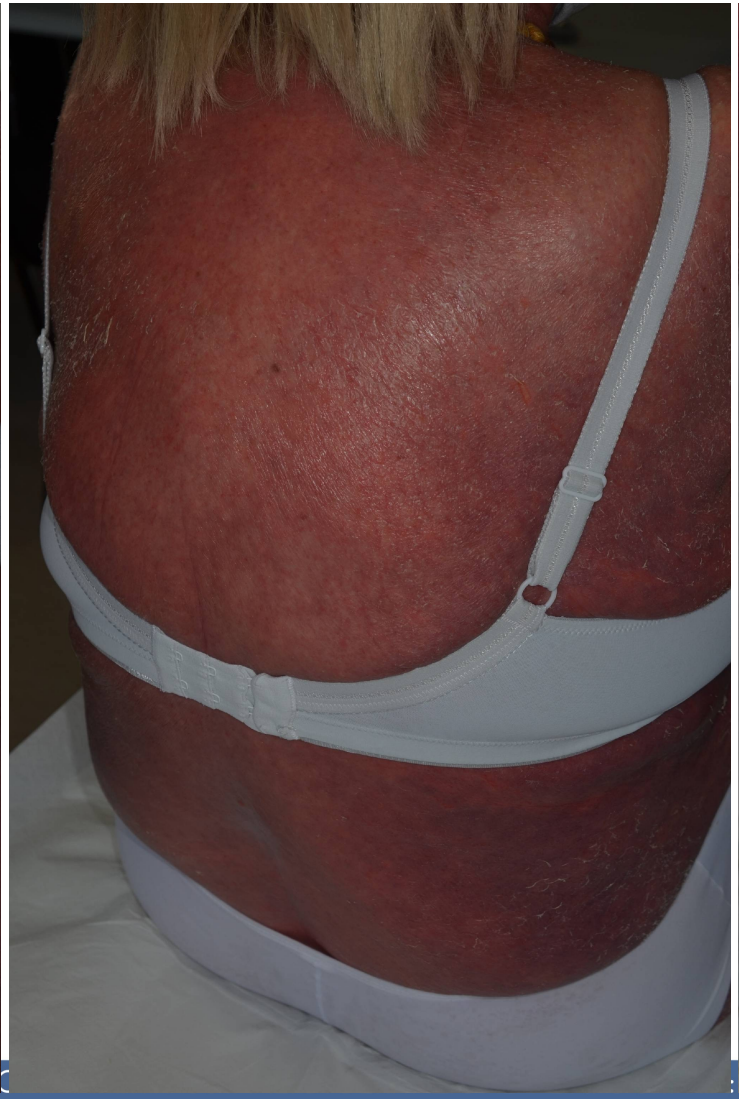
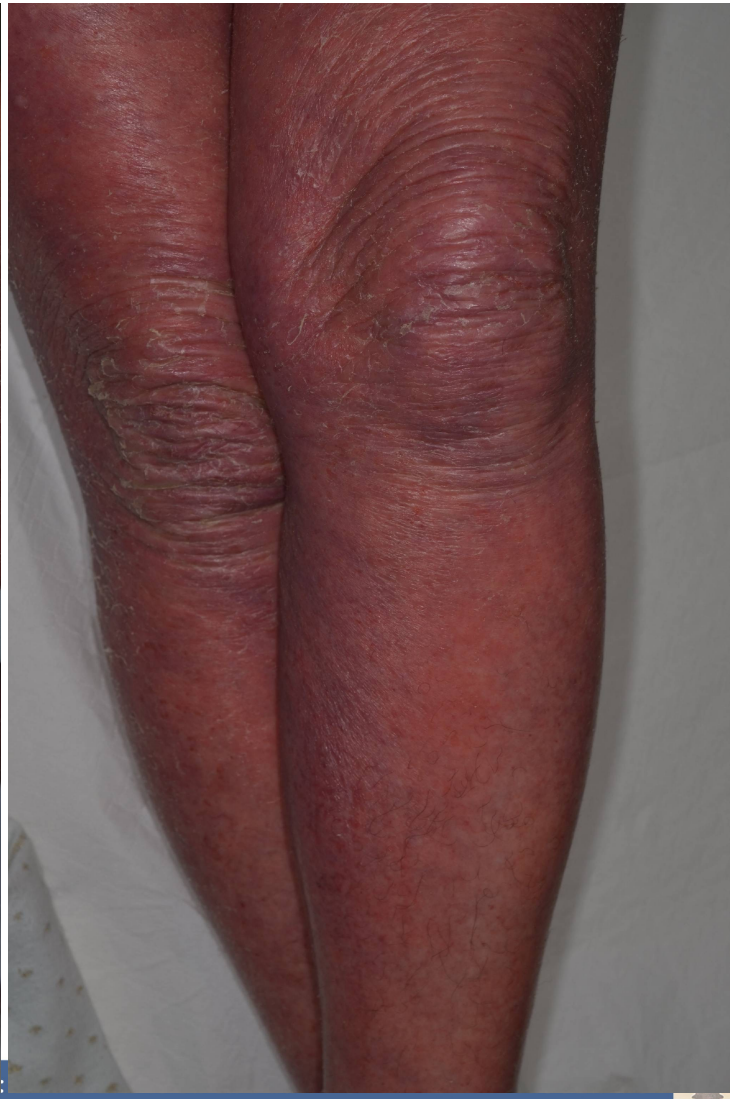
British Journal of Hospital Medicine, January 2014, Vol 75, No 1

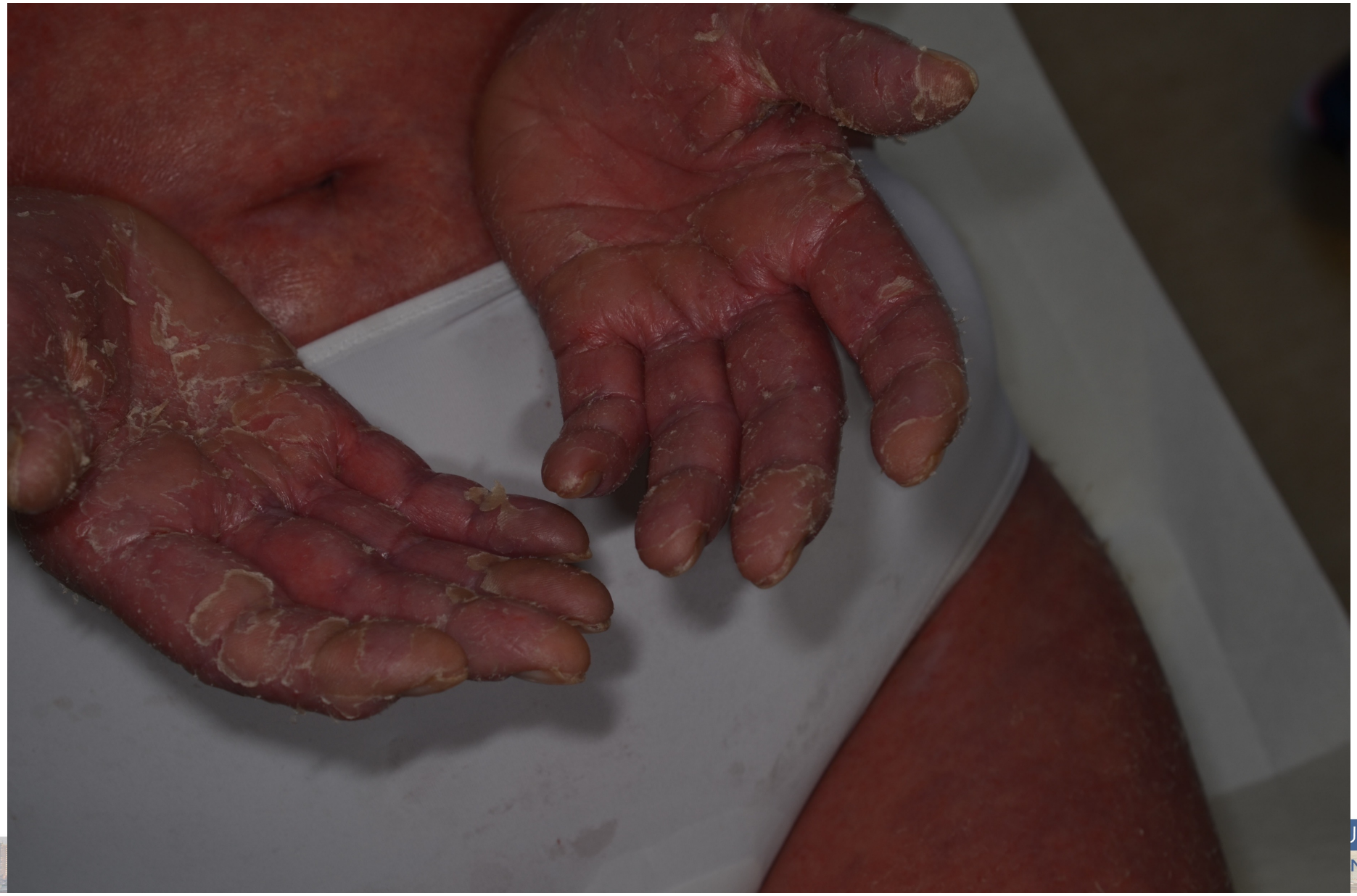
Erythroderma is not all psoriasis: a case of Sézary syndrome

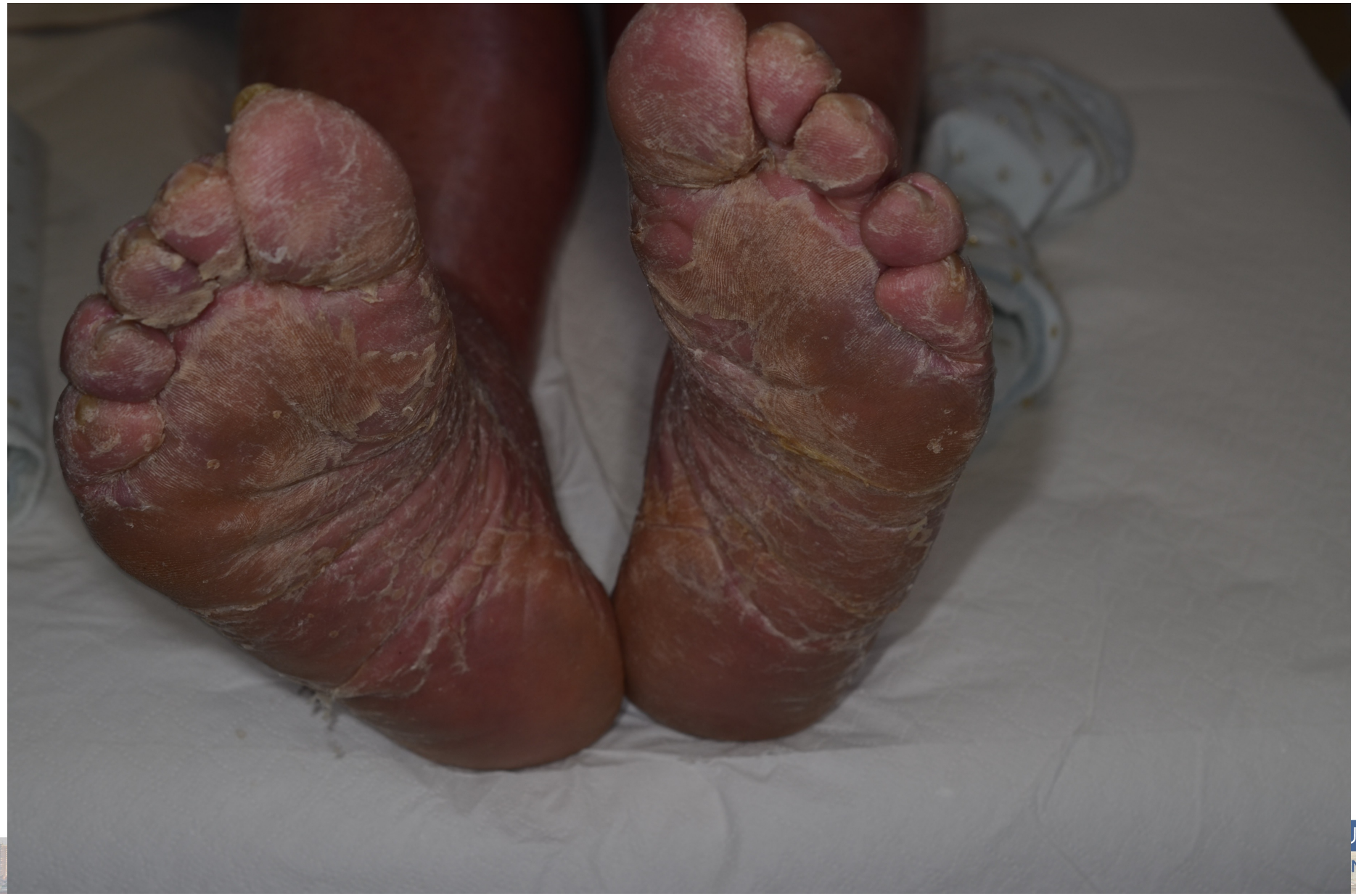
Table 1. Differential diagnoses of erythroderma

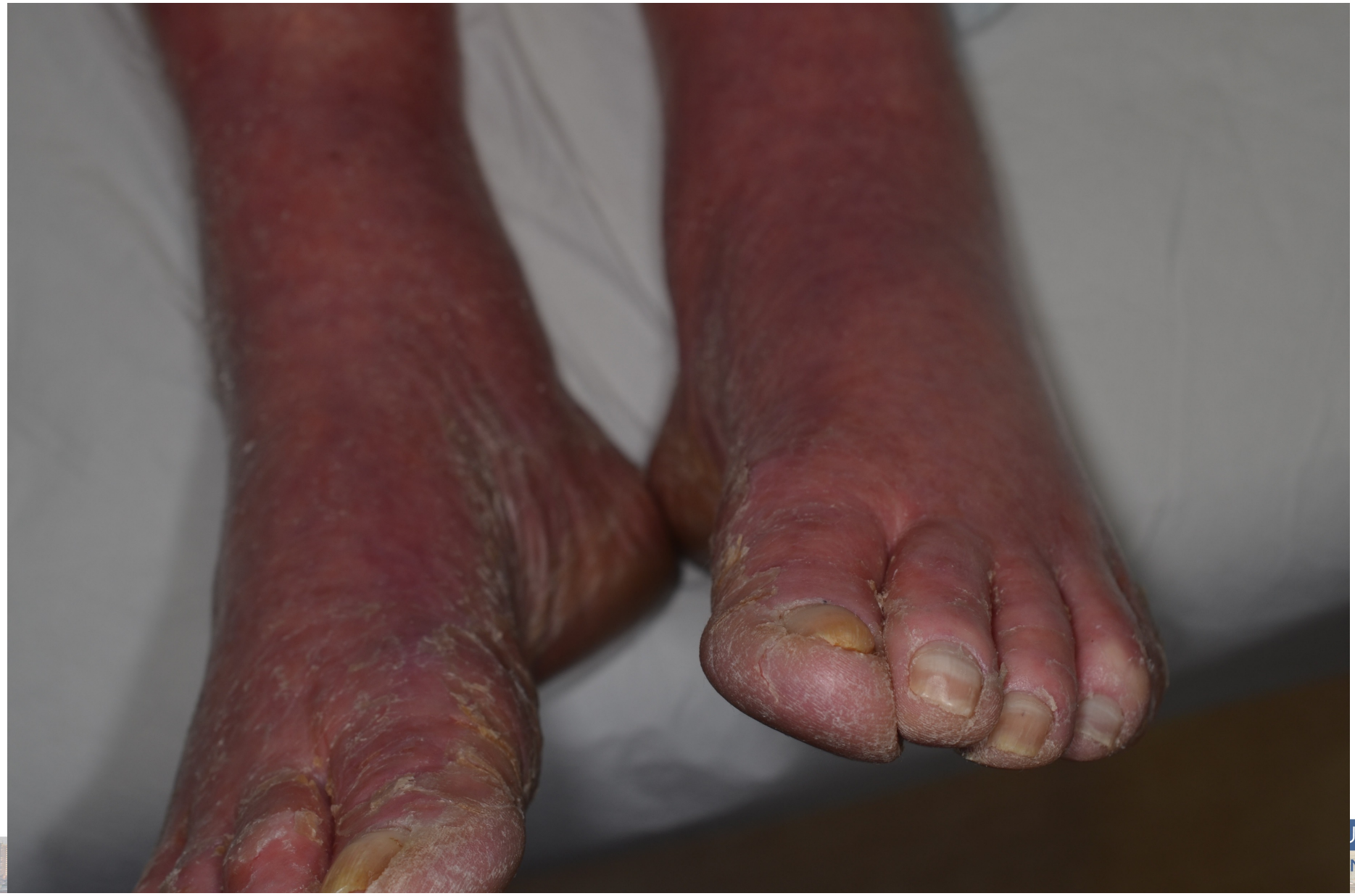
Eczema
Psoriasis
Seborrheic dermatitis
Pityriasis rubra pilaris
Lichen planus
Drug induced (e.g. lithium, carbamazepine, antimalarials, gold, phenytoin, allopurinol)
Contact dermatitis (i.e. rubber, solvents, detergents)
Stasis dermatitis (gravitational eczema)
Bullous diseases (e.g. pemphigous, pemphigoid)
Human immunodeficiency virus (HIV) infection
Graft *vs* host disease
Connective tissue disease
Internal malignancy as a non-metastatic manifestation
Haematological malignancies (lymphoma, Hodgkin's disease, leukaemia)
Cutaneous T-cell lymphoma (Sézary syndrome)
Idiopathic (may account for as many as 30% of cases)

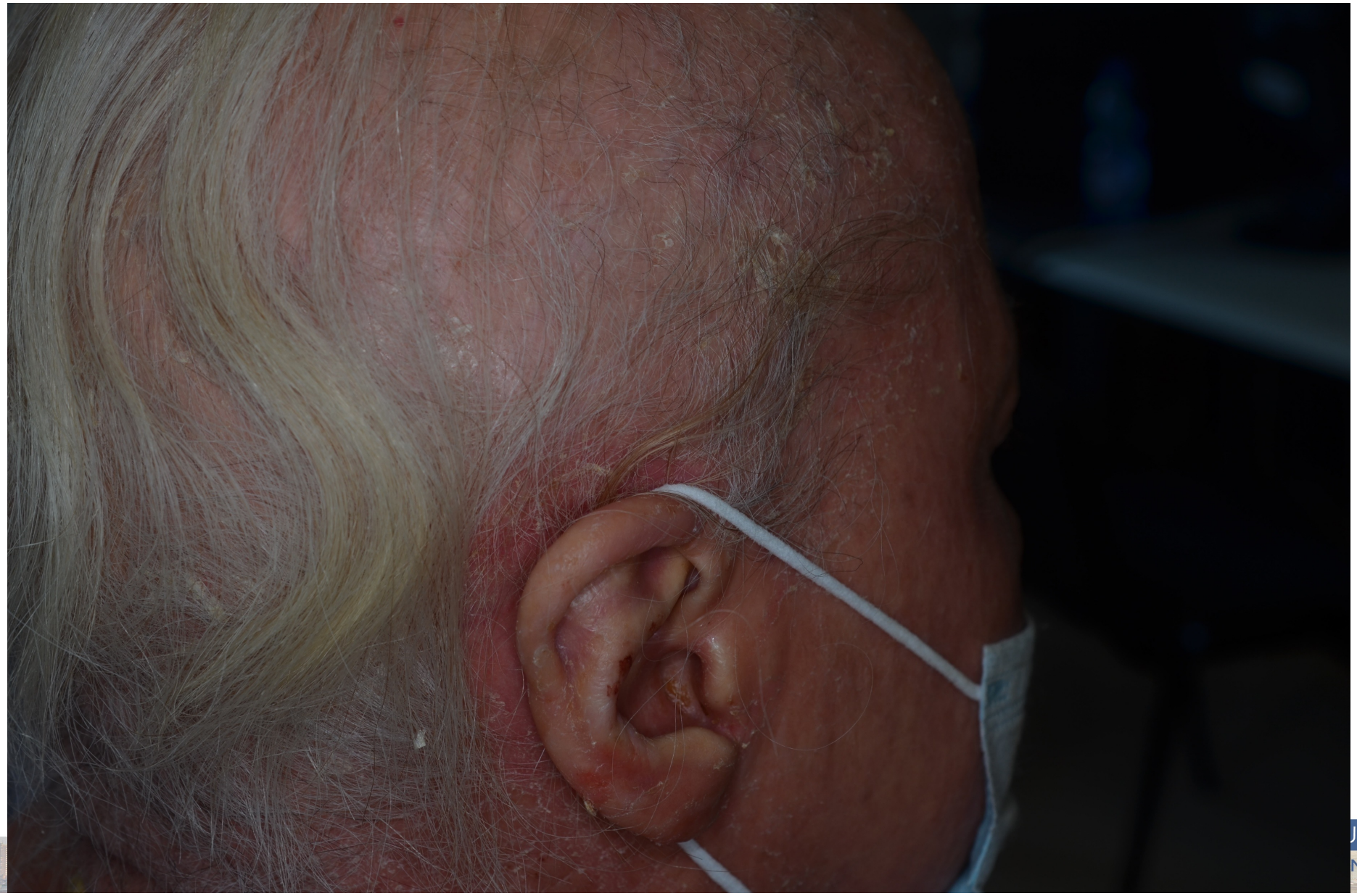




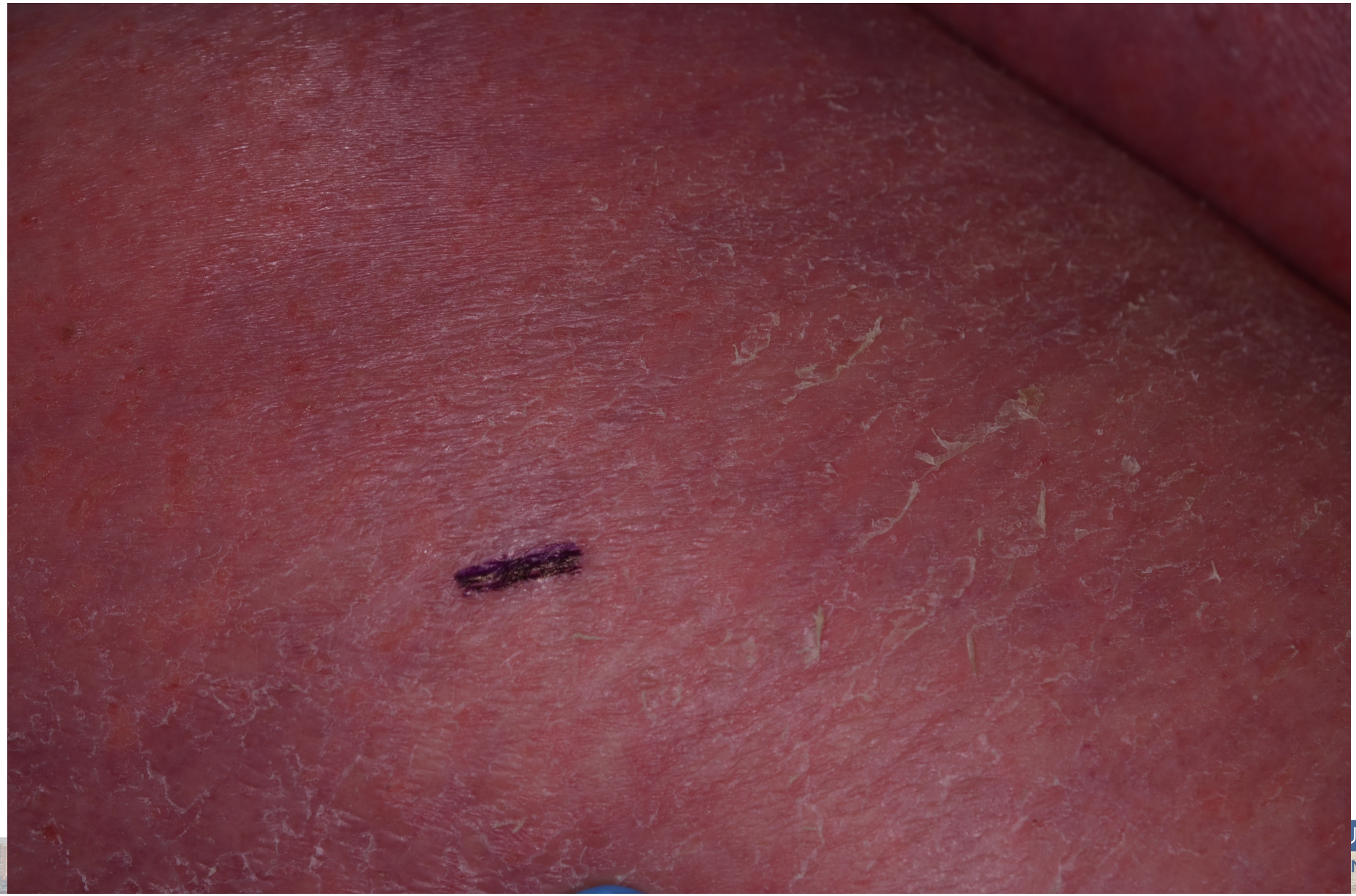


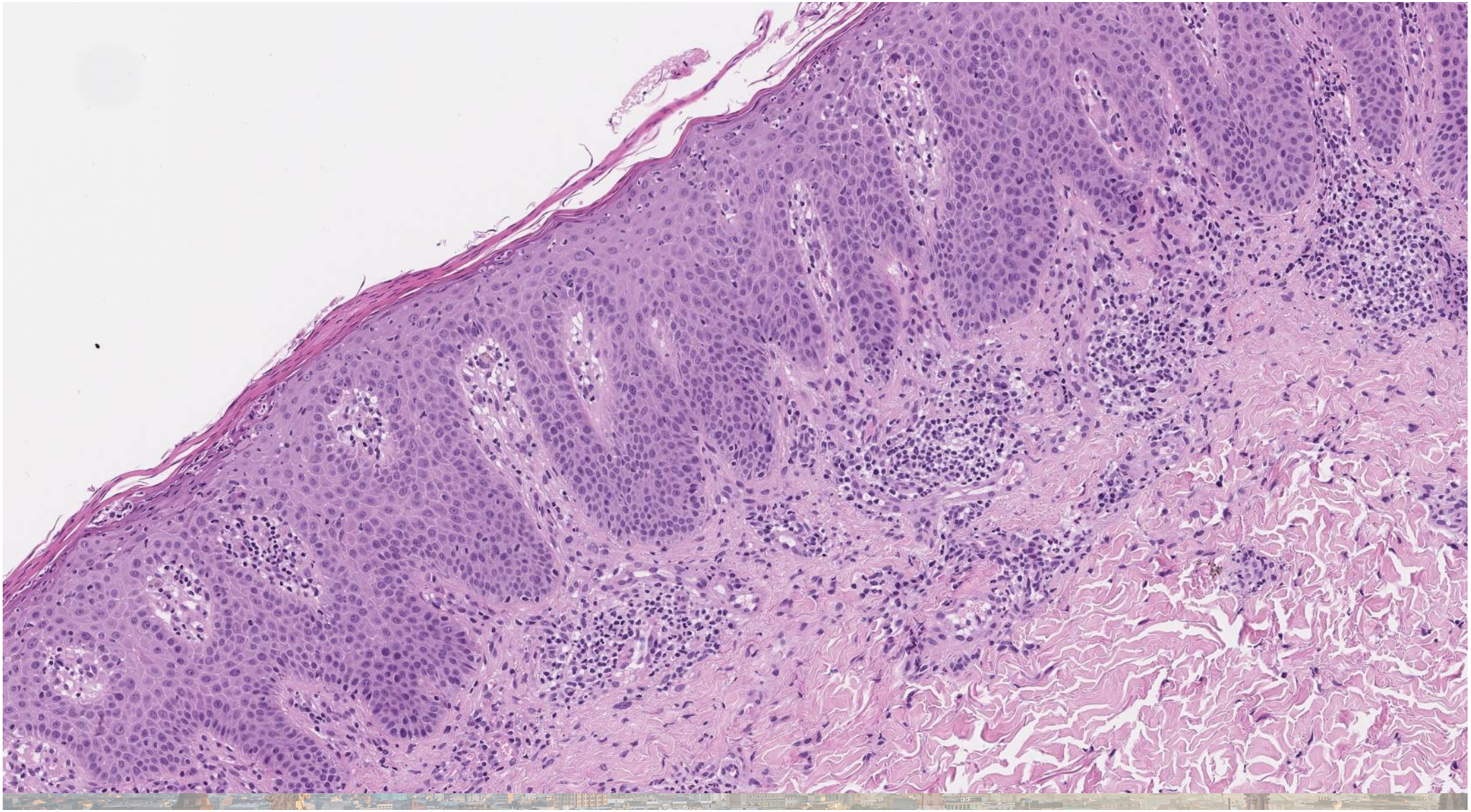


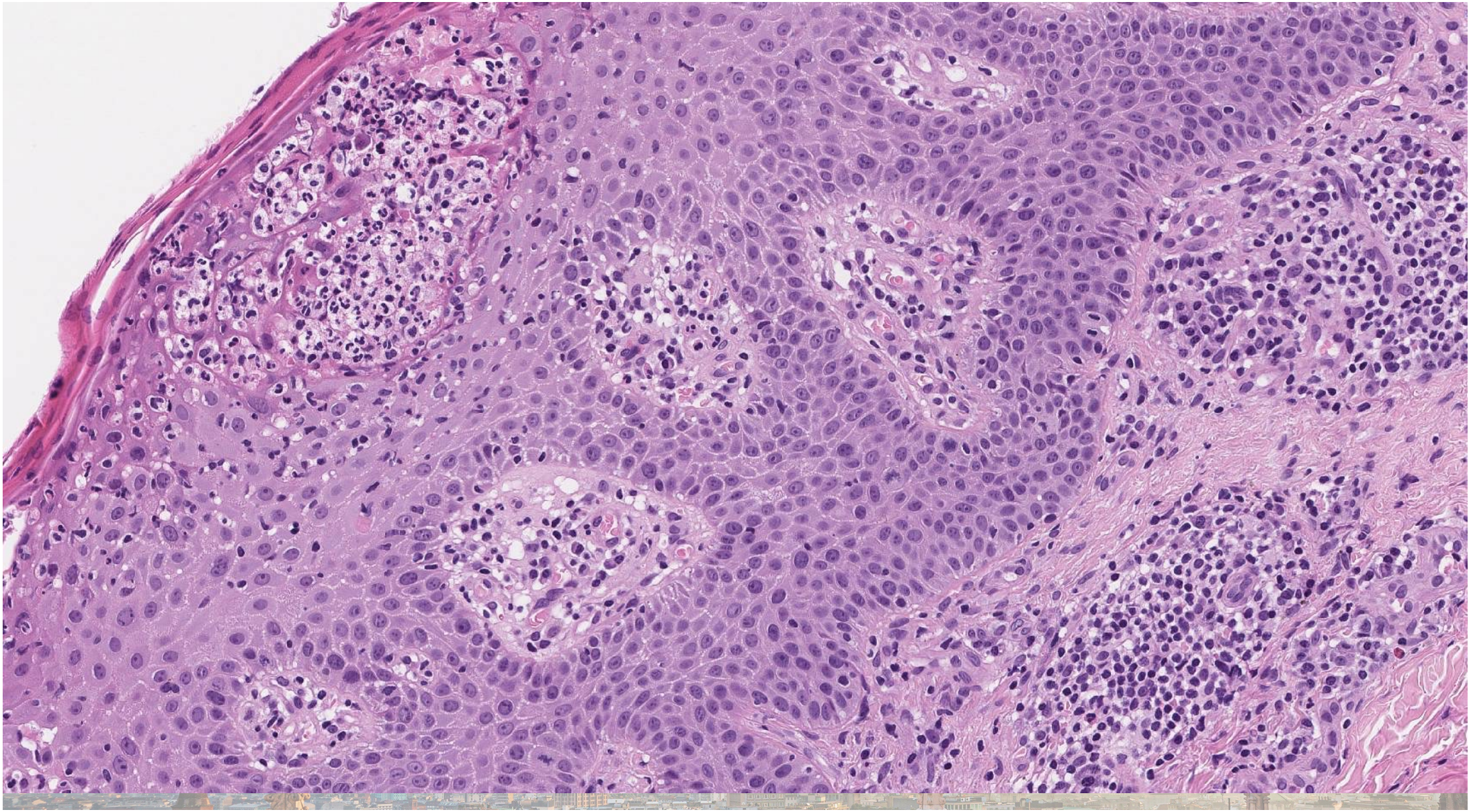

ULTATO
MILANO

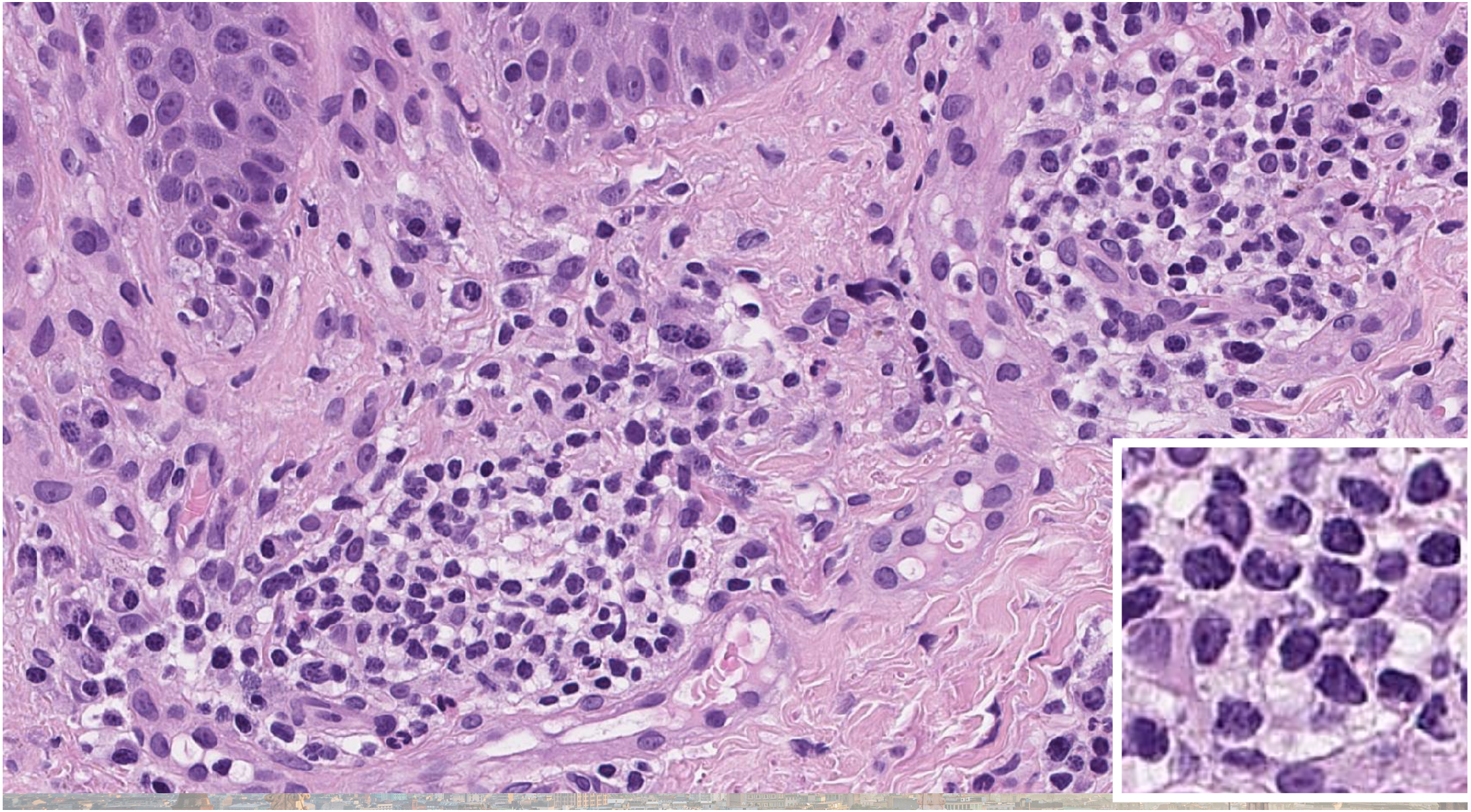
Caso clinico

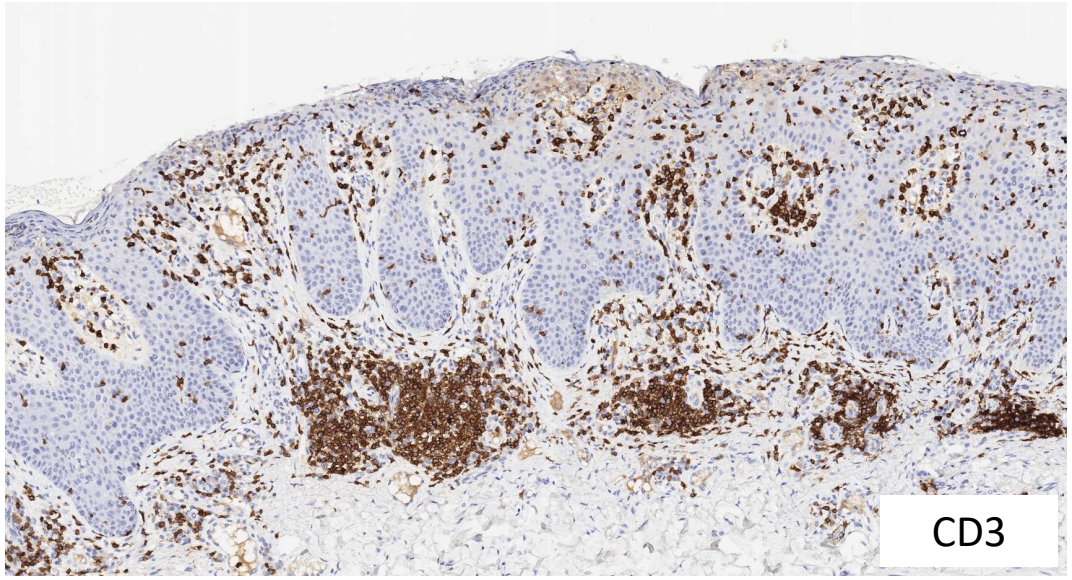
- F, 74 anni;
- in anamnesi: angioplastica coronarica nel 2019 in elezione; appendicectomia
- paziente con diagnosi clinica di psoriasi eritrodermica
- in trattamento con Infliximab, con buona risposta dopo i primi due mesi
- da maggio 2021: ripresa della manifestazione eritrodermica; picchi di iperpiressia fino a 39-40 °C che risolvono con assunzione di tachipirina; disponibili foto cliniche, effettuata biopsia cutanea
- assenza di sintomatologia sistemica

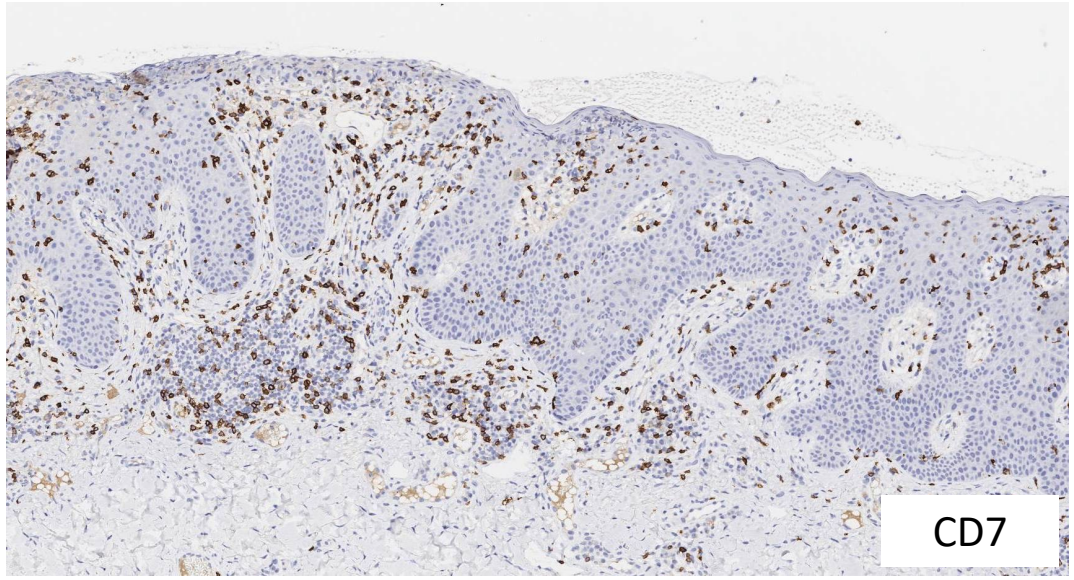


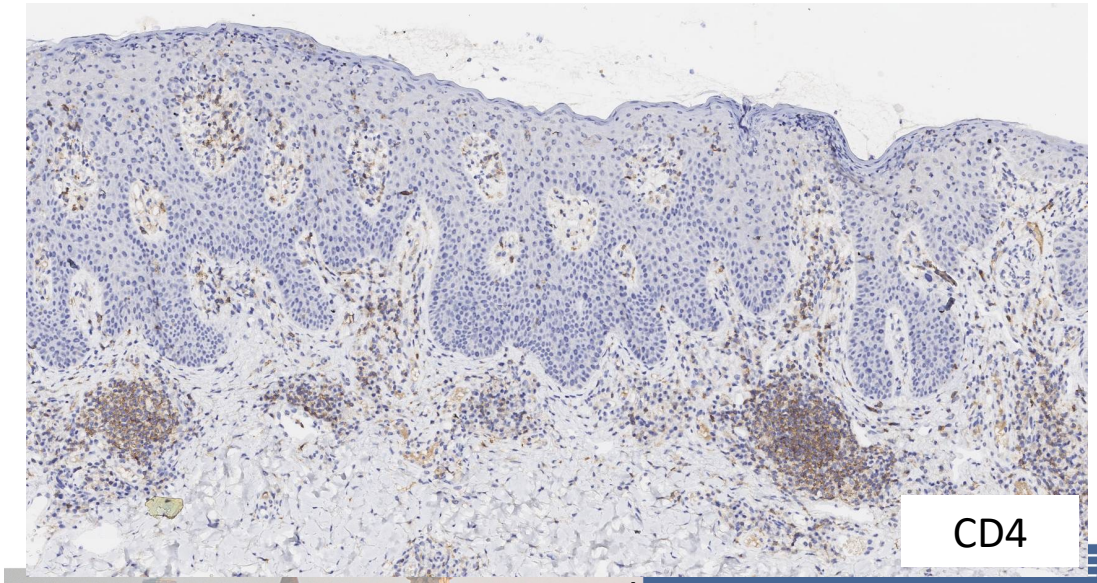


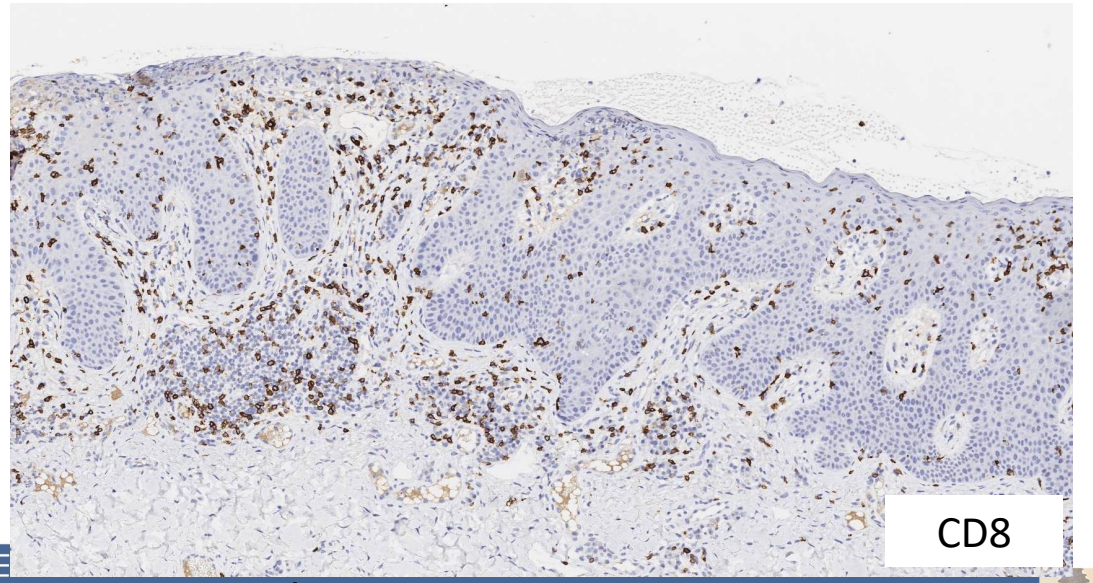












Restante fenotipo: CD2+/-, CD5+, CD30- (<1%), PD-1-. Ki67/Mib1: 10% circa

Determinazione riarrangiamento TCR-gamma

- Riarrangiamento monoclonale, con analogo clone nel sangue periferico

Valutazione sangue periferico

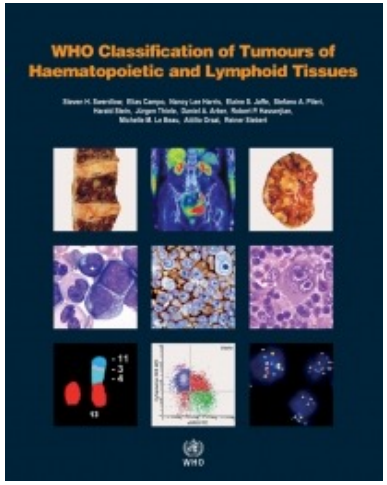
- Emocromo: Hb 10.9, PLT 567.000, GB 17.170 (N 12.220, Ly 2.890, Mo 1030, E 690,
- Immunofenotipo: CD3+CD4+CD7-CD26-CD30- 43%

Stadiazione

- Piccole adenopatie palpabili
- In corso TC e BOM

Diagnosi

Neoplasia dei linfociti T maturi, compatibile con sindrome di Sezary



Definition

Sézary syndrome (SS) is defined by the triad of erythroderma, generalized lymphadenopathy, and the presence of clonally related neoplastic T cells with cerebriform nuclei (Sézary cells) in skin, lymph nodes, and peripheral blood. In addition, one or more of the following criteria are required: an absolute Sézary cell count ≥ 1000/μL, an expanded CD4+ T-cell population resulting in a CD4:CD8 ratio of ≥10, and loss of one or more T−cell antigens. SS and mycosis fungoides are closely related neoplasms, but are considered separate entities on the basis of differences in clinical behaviour and cell of origin {4211}.

Erythroderma: a prospective study of 309 patients followed for 12 years in a tertiary center

Denis Miyashiro ✉ & José Antonio Sanches

SCIENTIFIC REPORTS | (2020) 10:9774 | https://doi.org/10.1038/s41598-020-66040-7

	Psoriasis	Eczema	AD	Drug reaction	SS	MF	Miscellaneous	Idiopathic	Total
Alopecia (%)	4 (22.2)	6 (22.2)	3 (23.1)	5 (55.6)	10 (52.6)	4 (66.7)	5 (41.7)	9 (36.0)	46 (35.7)
PPK* (%)	16 (88.9)	14 (51.8)	5 (38.5)	7 (77.8)	16 (84.2)	3 (60.0)	7 (58.3)	22 (88.0)	90 (70.3)
Fissures (%)	7 (38.9)	7 (25.9)	3 (23.1)	3 (33.3)	11 (57.9)	1 (16.7)	5 (41.7)	11 (44.0)	48 (37.2)
Ungueal alterations** (%)	15 (83.3)	9 (33.3)	2 (15.4)	3 (33.3)	15 (78.9)	3 (50.0)	5 (41.7)	16 (64.0)	68 (52.7)
Weight loss (%)	9 (50.0)	8 (29.6)	5 (38.5)	7 (77.8)	10 (52.6)	4 (66.7)	7 (58.3)	14 (56.0)	64 (49.6)
Pruritus (%)	18 (100)	27 (100)	13 (100)	8 (88.9)	19 (100)	6 (100)	11 (91.7)	25 (100)	127 (98.4)
Lower limb edema (%)	14 (77.8)	20 (74.1)	4 (30.8)	6 (66,67)	11 (57.9)	3 (50.0)	8 (66.7)	14 (56.0)	80 (62.0)
Ectropion (%)	5 (27.8)	4 (14.8)	2 (15.4)	3 (33,33)	6 (31.6)	1 (16.7)	5 (41.7)	11 (44.0)	37 (28.7)
Mucosal lesions (%)	2 (11.1)	0	0	1 (11.1)	0	0	1 (8.3)	3 (12.0)	7 (5.4)
Vitiligoid lesions (%)	3 (16.7)	5 (18.5)	2 (15.4)	4 (44.4)	3 (15.8)	0	0	6 (24.0)	23 (17.8)
Areas of normal skin† (%)	7 (41.2)	19 (70.4)	9 (69.2)	2 (22.2)	6 (31.6)	1 (16.7)	5 (41.7)	12 (48.0)	61 (47.7)
Lymph node enlargement (%)	6 (33.3)	14 (51.8)	9 (69.2)	4 (44.4)	12 (63.2)	4 (66.7)	4 (33.3)	16 (64.0)	69 (53.5)
Hepatosplenomegaly (%)	0	0	0	0	1 (5.26)	0	1 (8.3)	1 (4.0)	3 (2.3)
Fever (%)	4 (22.2)	1 (3.7)	0	2 (22.2)	0	0	2 (16.7)	0	9 (6.7)
Tachycardia (%)	5 (27.8)	2 (7.4)	2 (15.4)	1 (11.1)	1 (5.26)	0	4 (33.3)	0	15 (11.6)
Hypotension (%)	1 (5.6)	0	0	0	0	0	1 (8.3)	0	2 (1.5)
Taquipnea (%)	1 (5.6)	0	1 (7.7)	0	1 (5.26)	0	4 (33.3)	3 (12.0)	10 (7.7)

Table 4. Clinical findings. *$P = 0.005$; **$P = 0.0001$; †$P = 0.035$.

Histopathologic Diagnosis of Lymphomatous Versus Inflammatory Erythroderma: A Morphologic and Phenotypic Study on 47 Skin Biopsies

Caroline Ram-Wolff, PhD, Nadine Martin-Garcia,*† Armand Bensussan, PhD,‡ Martine Bagot, PhD,‡§ and Nicolas Ortonne, PhD*†*

Am J Dermatopathol • Volume 32, Number 8, December 2010

TABLE 1. Histologic Features of Erythroderma Observed in 47 Skin Biopsies

Feature	CTCL (n = 18)	Drug (n = 5)	Psoriasis (n = 9)	Eczema (n = 5)	Other (n = 10)	EID (n = 29)	Total (n = 47)	*P* (Chi-2), CTCL versus EID
Dermoepidermal junction								
Focal interface dermatitis	6 (33%)	1 (20%)	2 (22%)	3 (60%)	2 (20%)	8 (28%)	14 (30%)	>0.9
Widespread interface dermatitis	1 (6%)	0	0	0	2 (20%)	2 (7%)	3 (6%)	>0.9
Melanophages	3 (17%)	0	0	0	2 (20%)	2 (7%)	5 (11%)	0.562
Presence of exocytosis	14 (78%)	4 (80%)	6 (67%)	4 (80%)	4 (40%)	18 (62%)	32 (68%)	0.419
Single lymphocytes epidermotropism	5 (28%)	4 (80%)	6 (67%)	2 (40%)	4 (40%)	16 (55%)	21 (45%)	**0.006**
Basilar lymphocytes	1 (6%)	0	0	0	0	0	1 (2%)	—
Pagetoid epidermotropism	0	0	0	2 (40%)	0	2 (7%)	2 (4%)	0.581
Pautrier microabcess	8 (44%)	0	0	0	0	0	8 (17%)	**0.004**
Exocytosis of eosinophils	0	0	0	0	0	0	0	—
Exocytosis of isolated neutrophils	1 (6%)	0	1 (11%)	1 (20%)	0	2 (7%)	3 (6%)	0.680
Corneal/subcorneal pustules	2 (11%)	1 (20%)	6 (67%)	1 (20%)	1 (10%)	9 (31%)	11 (23%)	0.222
Atypical lymphocytes	12 (66%)	1 (20%)	0	0	0	1 (3%)	13 (28%)	**0.014**
Circonvoluted nuclei	4 (22%)	0	0	0	0	0	4 (9%)	—
Dermal infiltrate								
Superficial infiltrate	18 (100%)	5 (100%)	9 (100%)	5 (100%)	10 (100%)	28 (100%)	47 (100%)	—
Superficial and deep infiltrate	0	0	0	0	0	0	0	—
Deep infiltrate	0	0	0	0	0	0	0	—
Hypodermic infiltrate	0	0	0	0	0	0	0	—
Band-like infiltrate	13 (72%)	1 (20%)	5 (56%)	1 (20%)	5 (50%)	12 (41%)	25 (53%)	0.164
Perivascular infiltrate	5 (28%)	4 (80%)	4 (44%)	4 (80%)	5 (50%)	17 (59%)	22 (47%)	0.077
Diffuse infiltrate	0	0	0	0	0	0	0	—
Slight density	1 (6%)	4 (80%)	7 (78%)	2 (40%)	7 (70%)	20 (69%)	21 (44%)	**<0.001**
Moderate density	12 (67%)	1 (20%)	2 (22%)	3 (60%)	3 (30%)	9 (31%)	21 (45%)	**0.036**
High density	5 (28%)	0	0	0	0	0	5 (11%)	**0.011**
Eosinophils	0	0	0	0	0	0	0	—
Neutrophils	1 (6%)	1 (20%)	3 (33%)	2 (40%)	3 (30%)	9 (31%)	10 (2%)	0.086

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Progression of undiagnosed cutaneous lymphoma after anti–tumor necrosis factor-alpha therapy

opment of CTCL.[28,32] Controversy surrounds the true prevalence of CL in patients with atopic dermatitis and psoriasis. One group reported a significantly increased risk for development of CTCL in patients with moderate-to-severe psoriasis independent of the systemic therapy received (adjusted hazard ratio, 9.25; 95% confidence interval, 95%). Another group cites misdiagnosis of CTCL as eczema as a major confounding factor in reporting the true prevalence of CTCL in patients with atopic dermatitis.[33-35] We acknowledge the

CAPSULE SUMMARY

- Cutaneous lymphoma (CL) diagnosed after anti–tumor necrosis factor-α (anti–TNF-α) therapy is most commonly associated with a misdiagnosis of psoriasis.
- Anti–TNF-α therapy can accelerate the course of CL.
- Before initiation of anti–TNF-α therapy, skin biopsy and peripheral blood analysis should be considered in patients with atypical presentation of psoriasis to exclude CL.

J Am Acad Dermatol July 2020

Progression of cutaneous T-cell lymphoma after dupilumab: Case review of 7 patients

4 months [range 3-27 months]) (Table I). Six of 7 patients experienced initial improvement (median duration 2 months [range 1-8 months]), followed by worsening body surface area (n = 7), pruritus (n = 5), lymphadenopathy (n = 3), and systemic symptoms (n = 3). The 4 patients with clinically presumed atopic dermatitis eventually received a diagnosis of cutaneous T-cell lymphoma after dupilumab. The 3 patients with cutaneous T-cell lymphoma before dupilumab use developed worsened blood involvement on flow cytometry and received a diagnosis of Sézary syndrome while receiving treatment. Two of the 3 patients died of disease progression (Supplement 1, available

VOLUME 33 · NUMBER 32 · NOVEMBER 10 2015

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Cutaneous Lymphoma International Consortium Study of Outcome in Advanced Stages of Mycosis Fungoides and Sézary Syndrome: Effect of Specific Prognostic Markers on Survival and Development of a Prognostic Model

Table 2. Number of Patients, Survival Ranges, and Probability of Survival With Univariable Analysis for the 10 Parameters Tested

Variable	No. of Patients With Complete Data (%)	No. of Patients	OS (months)			RM Survival (months)	Probability of Survival (%)			*P*
			Median	95% CI	IQR		1 Year	2 Years	5 Years	
Sex	1,262 (99.0)									.937
Male		789	63.0	52.7 to 73.7	25.0-NR	56.2	87.3	76.0	52.1	
Female		473	60.3	49.8 to 70.5	26.1-NR	55.8	89.3	77.3	50.4	
Age, years	1,265 (99.2)									< .001
≤ 60		452	NR	NA	34.2-NR	63.6	92.8	84.7	62.5	
> 60		813	51.0	45.2 to 61.0	21.7-NR	51.7	85.4	71.9	45.6	
FT	1,062 (83.3)									< .001
Absent		879	57.5	47.7 to 65.4	24.4-NR	54.6	87.9	75.2	49.3	
Present		183	NR	NA	44.8-NR	65.9	91.4	86.6	66.5	
WBC count	716 (56.2)									.006
Elevated		252	37.7	30.2 to 50.0	17.8-78.8	44.3	85.8	67.5	35.3	
Not elevated		436	54.4	44.4 to 65.4	24.8-NR	53.8	87.9	75.8	46.1	
Low		28	57.5	34.4 to NR	34.4-NR	60.0	95.5	84.9	48.8	
Absolute lymphocyte count	847 (66.4)									.358
Elevated		248	52.7	42.7 to 78.8	24.5-NR	53.5	88.8	76.8	49.5	
Not elevated		485	57.3	46.4 to 67.9	23.4-NR	54.7	87.8	74.1	48.4	
Low		114	42.2	34.4 to 65.4	18.6-NR	47.4	82.0	72.0	37.8	
LDH	894 (70.1)									< .001
Elevated		457	44.7	37.5 to 50.5	19.2-NR	48.6	84.6	68.6	39.0	
Not elevated		437	78.8	61.2 to NR	33.2-NR	60.5	90.9	81.9	58.4	
TCR clone	727 (57.0)									.086
Identical clone in blood and skin		357	49.8	44.7 to 69	24.4-NR	53.8	88.4	76.2	45.6	
No identical clone in blood and skin		370	73.4	61.0 to NR	30.2-NR	59.3	87.1	78.5	58.7	
LCT	1,098 (86.1)									.003
Yes		215	49.8	40.3 to 57.3	20.1-NR	48.9	84.8	68.6	38.5	
No		883	66.2	61.0 to NR	27.7-NR	57.8	89.3	78.4	54.9	
CD30	639 (50.1)									.331
Positive > 10%		149	55.7	45.4 to NR	22.3-NR	54.9	88.6	74.6	44.9	
Positive ≤ 10%		490	68.7	60.3 to NR	28.0-NR	58.7	87.8	78.2	56.7	
Ki-67	471 (36.9)									.552
Positive > 20%		182	50.1	44.8 to NR	25.2-NR	55.9	89.3	76.9	46.8	
Positive ≤ 20%		289	NR	47.2 to NR	30.8-NR	58.7	86.7	78.6	55.6	

Abbreviations: FT, folliculotropism; IQR, interquartile range; LCT, large-cell transformation; LDH, lactate dehydrogenase; NR, not reached; OS, overall survival; RM, restricted mean; TCR, T-cell receptor.

Valutazione predittiva del CD30

J Clin Oncol 33:3750-3758.

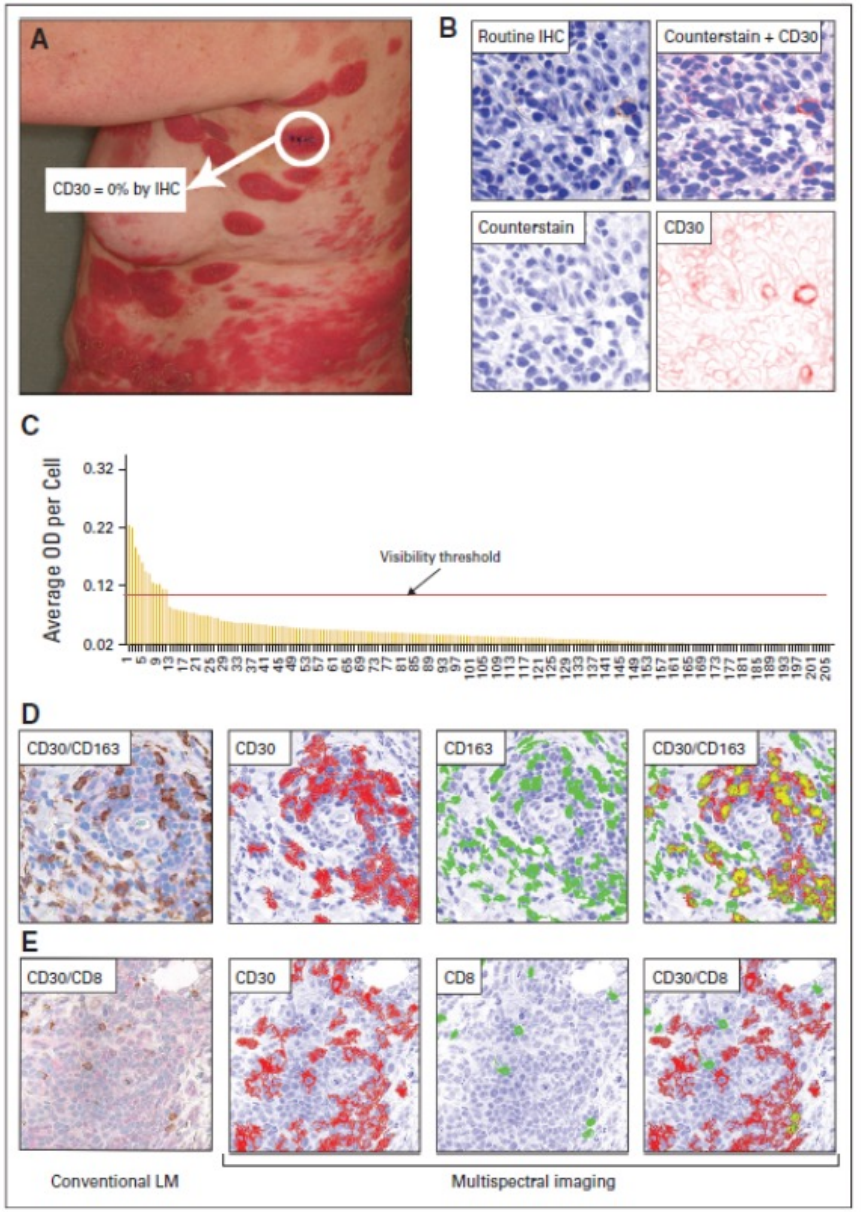
Phase II Investigator-Initiated Study of Brentuximab Vedotin in Mycosis Fungoides and Sézary Syndrome With Variable CD30 Expression Level: A Multi-Institution Collaborative Project

Youn H. Kim, Mahkam Tavallaee, Uma Sundram, Katrin A. Salva, Gary S. Wood, Shufeng Li, Sima Rozati, Seema Nagpal, Michael Krathen, Sunil Reddy, Richard T. Hoppe, Annie Nguyen-Lin, Wen-Kai Weng, Randall Armstrong, Melissa Pulitzer, Ranjana H. Advani, and Steven M. Horwitz

Table 1. Patient Baseline Demographics, Clinical Characteristics, and Clinical Response

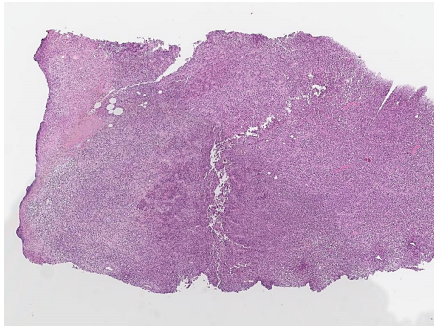
Characteristics	All Patients, N = 32, n (%)	Evaluable for Response, n = 30					
		CR	PR	SD	PD	NE	ORR,* n (%)
Sex							
Male	19 (59)	0	13	1	4	1	13 of 18 (72)
Female	13 (41)	1	7	3	1	1	8 of 12 (67)
Age, years, median (range)	62 (20-87)	78	60 (38-87)	60 (20-82)	64 (57-77)	60 (50-70)	
Clinical stage							
All	32 (100)	1	20	4	5	2	21 of 30 (70)
IB	4 (13)	0	3	1	0	0	3 of 4 (75)
IIB	18 (56)	0	14	2	2	0	14 of 18 (78)
IV/SS†	10 (31)	1	3	1	3	2	4 of 8 (50)
Adverse prognostic factors							
LCT or FMF	29 (90)	1	19	3	5	1	20 of 28 (71)
LCT	16 (50)	1	9	2	3	1	10 of 15 (67)
FMF	8 (25)	0	7	1	0	0	7 of 8 (88)
LCT + FMF	5 (16)	0	3	0	2	0	3 of 5 (60)
No. of prior systemic therapies							
< 3	15 (47)	0	8	2	4	1	8 of 14 (57)
≥ 3	17 (53)	1	12	2	1	1	13 of 16 (81)
CD30 grouping at screening							
A (< 10%)	14 (44)	0	7	4	2	1	7 of 13 (54)
B (10% to 50%)	14 (44)	0	11	0	3	0	11 of 14 (79)
C (> 50%)	4 (13)	1	2	0	0	1	3 of 3 (100)

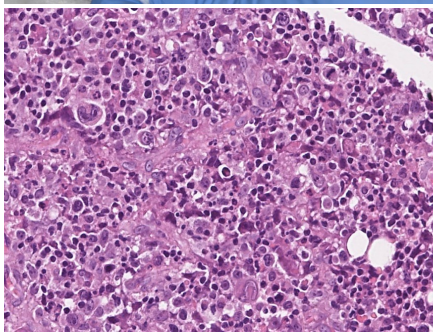
Abbreviations: CR, complete response; FMF, folliculotropic mycosis fungoides; LCT, large-cell transformation; NE, not evaluable; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease; SS, Sézary syndrome.
*Objective clinical response was observed in 21 (70%) of the 30 efficacy-evaluable patients
†Of 10 stage IV patients, three patients had SS with one CR, one PR, and one PD; one patient was stage IVB who had PR.

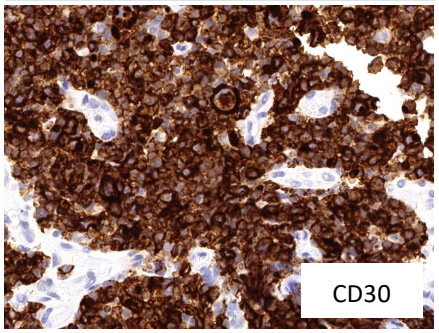


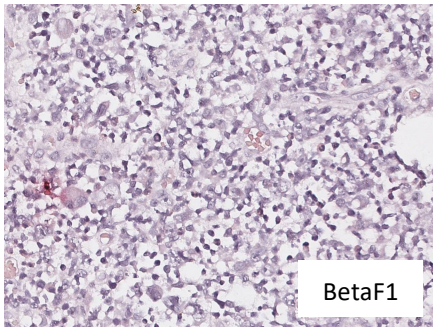
Valutazione diagnostica del CD30: clinica + fenotipo

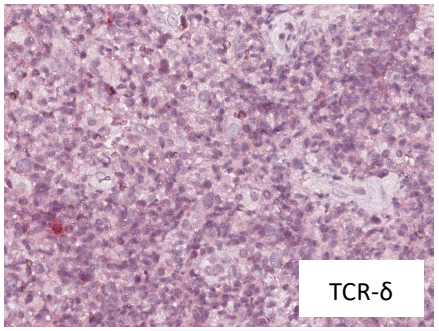
Lesioni papulo-nodulari recidivanti in pz affetta da MF











Haematologica 2010;95(10):1697-1704.

Disturbed expression of the T-cell receptor/CD3 complex and associated signaling molecules in CD30⁺ T-cell lymphoproliferations

Eva Geissinger,[1] Petra Sadler,[1] Sabine Roth,[1] Tina Grieb,[1] Bernhard Puppe,[1] Nora Müller,[1] Peter Reimer,[2] Claudia S. Vetter-Kauczok,[3] Jörg Wenzel,[4] Irina Bonzheim,[5] Thomas Rüdiger,[6] Hans Konrad Müller-Hermelink,[1] and Andreas Rosenwald[1]

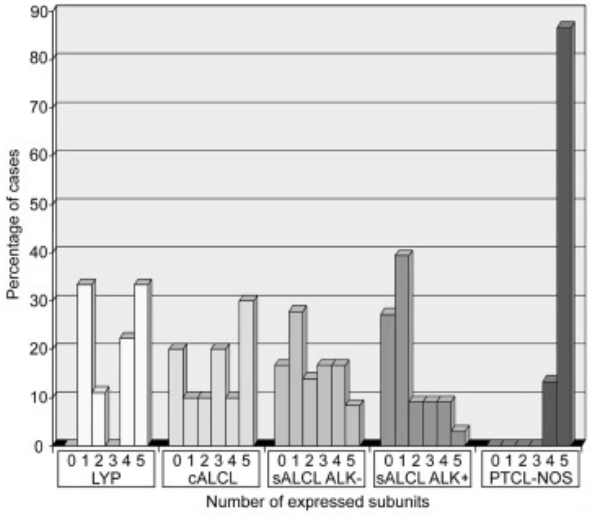


Figure 2. Bar chart of the TCR/CD3 complex expression data. For each entity, the percentage of cases that express a certain number of subunits (TCRβ, CD3δ, ε, γ, ζ) is plotted. Only cases for which expression data for all five TCR/CD3 subunits could be obtained are included [9 cases of lymphomatoid papulosis (LYP), 10 of cutaneous ALCL (cALCL), 36 ALK- systemic ALCL (sALCL), 33 ALK⁺ systemic ALCL (sALCL), 15 PTCL-NOS].

Conclusions

Severely altered expression of the T-cell receptor/CD3 complex, T-cell receptor-associated transcription factors and signal transduction molecules is a common characteristic of systemic and cutaneous CD30⁺ lymphoproliferations, although the clinical behavior of these entities is very different. Since peripheral T-cell lymphomas, not otherwise specified retain the full expression program required for functioning T-cell receptor signaling, the differential expression of a subset of these markers might be of diagnostic utility in distinguishing peripheral T-cell lymphomas, not otherwise specified from the entire group of CD30⁺ lymphoproliferations.

Conclusione 2

Multidisciplinarietà nelle scelte terapeutiche e di gestione di casi complessi