AAD **ANNUAL** MEETING **2025**

AEDV 7 - 11 MARZO ORLANDO

highlights

DERMATOPATOLOGÍA

Sonsoles Berenguer Ruiz

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AEDV 7 - 11 MARZO ORLANDO

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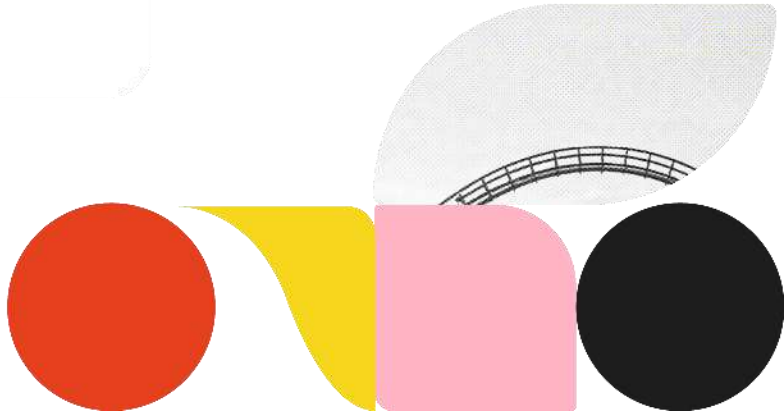
NO TENGO CONFLICTOS DE INTERÉS



TRBC1

TRBC1: anticuerpo monoclonal (mAb) contra la región constante C1 de la cadena TCR

Las poblaciones de células T neoplásicas expresan exclusivamente TRBC1 o TRBC2.

La expresión restringida de TRBC1 puede, por lo tanto, servir como un marcador de clonalidad.

RESEARCH LETTER · Volume 90, Issue 4, P839-841, April 2024 Download Full Issue

TRBC1 immunohistochemistry distinguishes cutaneous T-cell lymphoma from inflammatory dermatitis: A retrospective analysis of 39 cases

Sarah E. Nocco, MD [a] · Mark D. Ewalt, MD [b] · Andrea P. Moy, MD [b] · ... · Cecilia Lezcano, MD [b] · Klaus Busam, MD [b] · Melissa Pulitzer, MD [b] ... Show more

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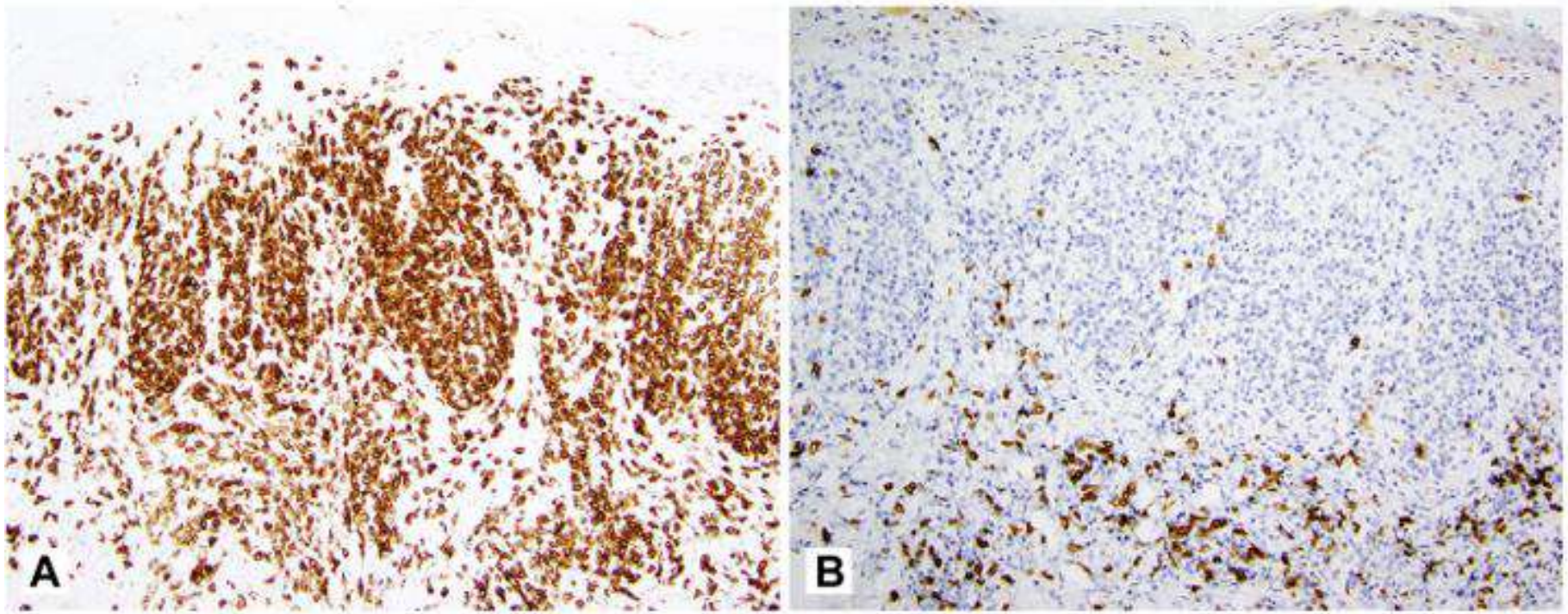

Fig 1. Skin biopsy specimen from a patient with mycosis fungoides showing an atypical lymphocytic infiltrate predominantly located in the epidermis. Atypical lymphocytes are diffusely positive for CD3 (**A**, original magnification: ×400) and negative for TRBC1 (**B**, original magnification: ×400), consistent with a monotypic-negative TRBC1 expression pattern. The underlying dermal reactive immune infiltrate shows a TRBC1 polytypic expression pattern.

Carcinoma Merkel: POU4F3

MODERN PATHOLOGY
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RESEARCH ARTICLE · Volume 38, Issue 1, 100627, January 2025 Download Full Issue

POU4F3 Is a Sensitive and Specific Marker of Merkel Cell Carcinoma

Pawel Karpinski [a] · Javier E. Mendez-Pena [b] · Cheng-Lin Wu [c] · ... · Kristine M. Cornejo [b] · Yin P. Hung [b] · Mai P. Hoang [b] ... Show more

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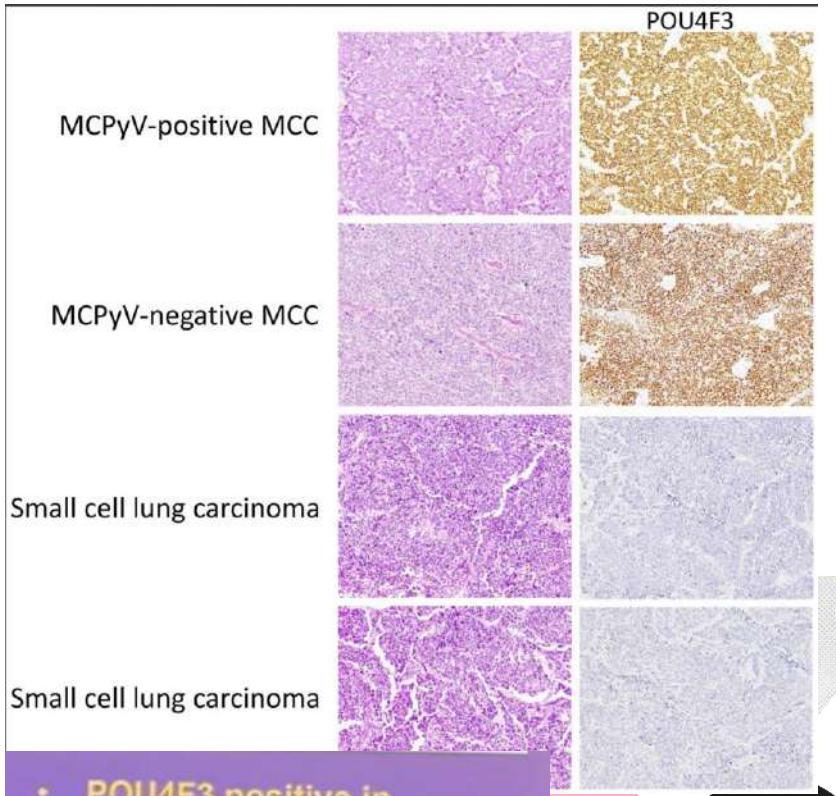
Table 1
Summary of POU4F3 expression in Merkel cell carcinomas and histologic mimics

Tumor type	N	POU4F3			
		Positive	3+	2+	Negative
Merkel cell carcinoma	153	151/153 (98.7%)	149	2	2
MCPyV-positive	82	82/82	81	1	0
MCPyV-negative	71	69/71	68	1	2
Keratin 20-negative	10	9/10	9	0	1
Keratin 20 focally positive	12	12/12	12	0	0
TTF1-positive	8	8/8	8	0	0
Non-Merkel cell carcinoma cases	180	3/180 (1.7%)			
Small cell carcinoma, total	95	3/95 (3.2%)	0	2	92
Small cell carcinoma of lung	55	2/55	0	2	53
Small cell carcinoma of cervix	12	0/12	0	0	12
Small cell carcinoma of vagina	3	1/3	1	0	2
Small cell carcinoma of endometrium	3	0/3	0	0	3
Small cell carcinoma of salivary gland/head and neck	6	0/6	0	0	6
Small cell carcinoma of bladder	11	0/5	0	0	11
Small cell carcinoma of prostate	3	0/1	0	0	3
Small cell carcinoma of pancreas	1	0/1	0	0	1
Small cell carcinoma of gallbladder	1	0/1	0	0	1
Ewing sarcoma	3	0/3	0	0	3
Rhabdomyosarcoma, alveolar	1	0/1	0	0	1
Synovial sarcoma, poorly differentiated	4	0/4	0	0	4
Lymphoblastic lymphoma	2	0/2	0	0	2
NUT carcinoma	3	0/3	0	0	3
Trichoblastoma	3	0/3	0[a]	0	3
Basal cell carcinoma	36	0/36	0	0	36
Metastatic melanoma	22	0/22	0	0	22
Malignant peripheral nerve sheath tumor	11	0/11	0	0	11

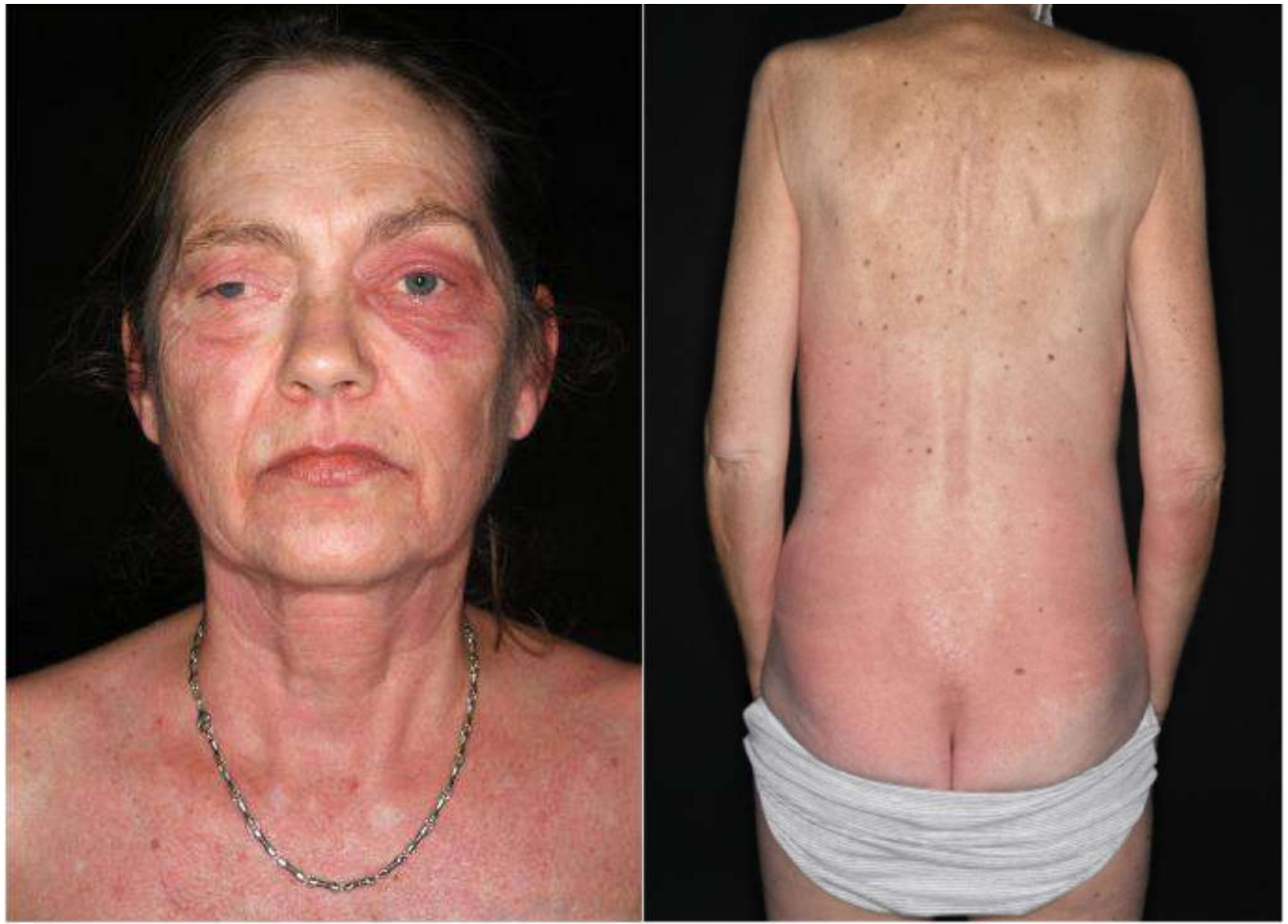
MCPyV, Merkel cell polyomavirus.
[a] Positive intratumoral Merkel cells in all 3 cases.



Tebentafusp

Clinical and pathological characterization of tebentafusp-associated skin toxicity: A cohort study with 33 patients

Dirk Tomsitz, MD,[a] Katrin Kerl, MD,[a,b] Lars Einar French, MD,[a,c] and Lucie Heinzerling, MD, MPH[a,d]



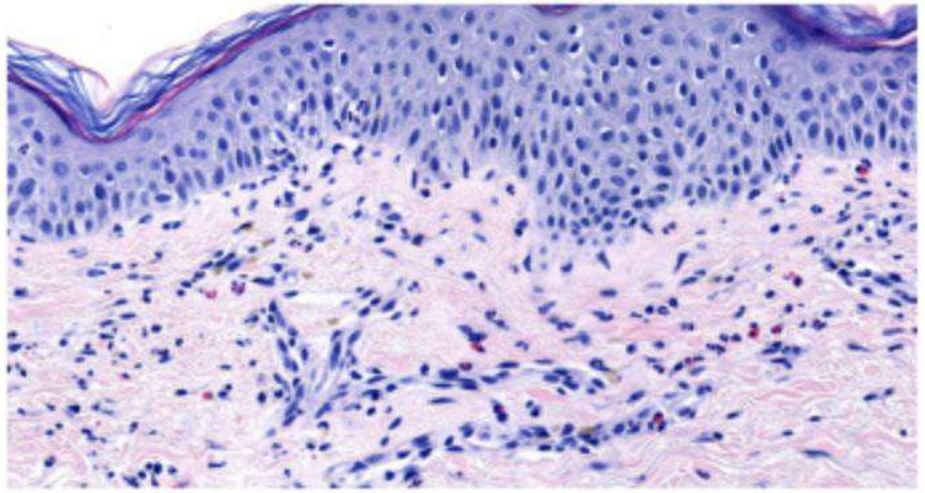
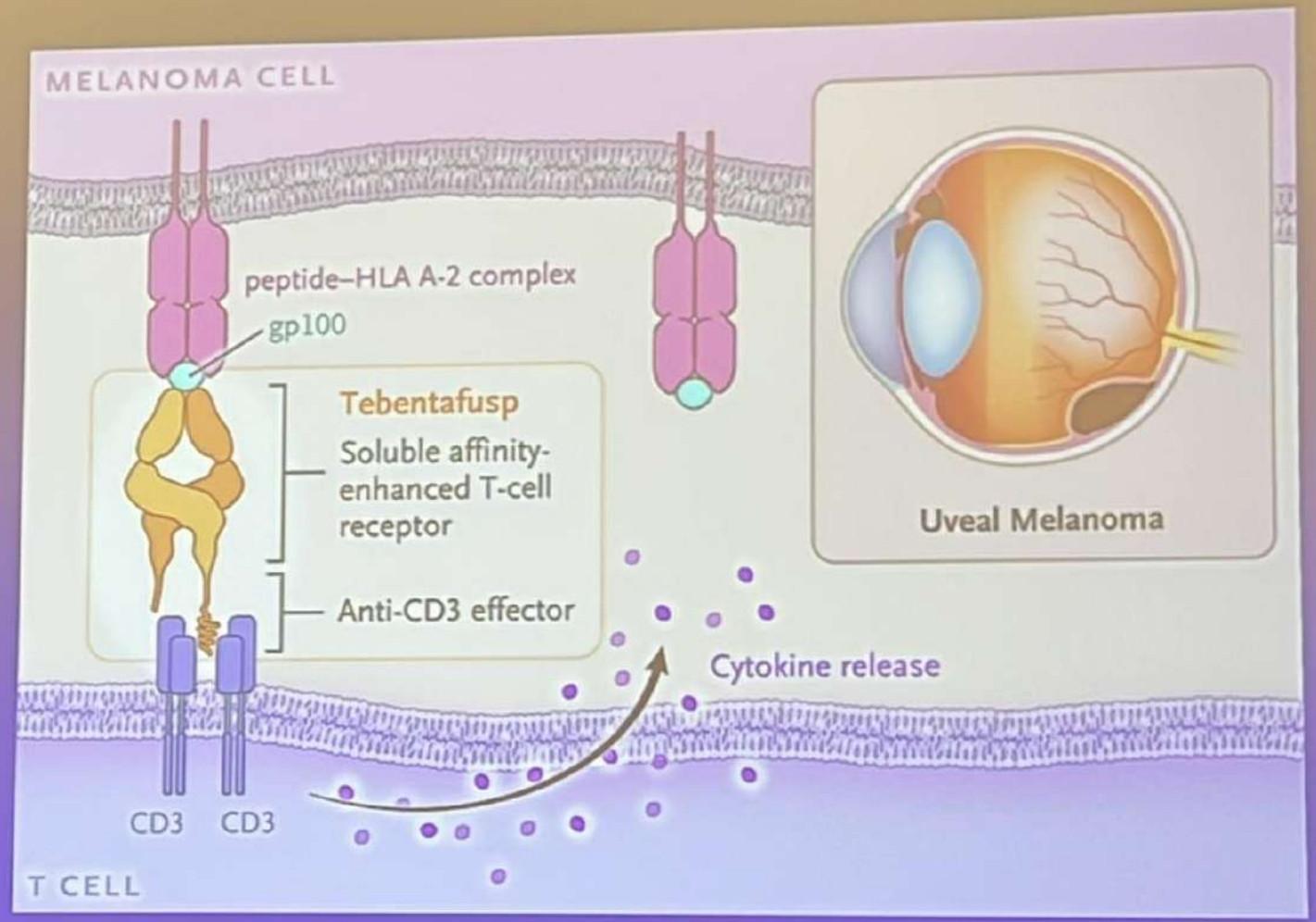


Fig 4. The main histologic reaction pattern showed perivascular lymphocytic infiltration and focal interface dermatitis (hematoxylin-eosin).

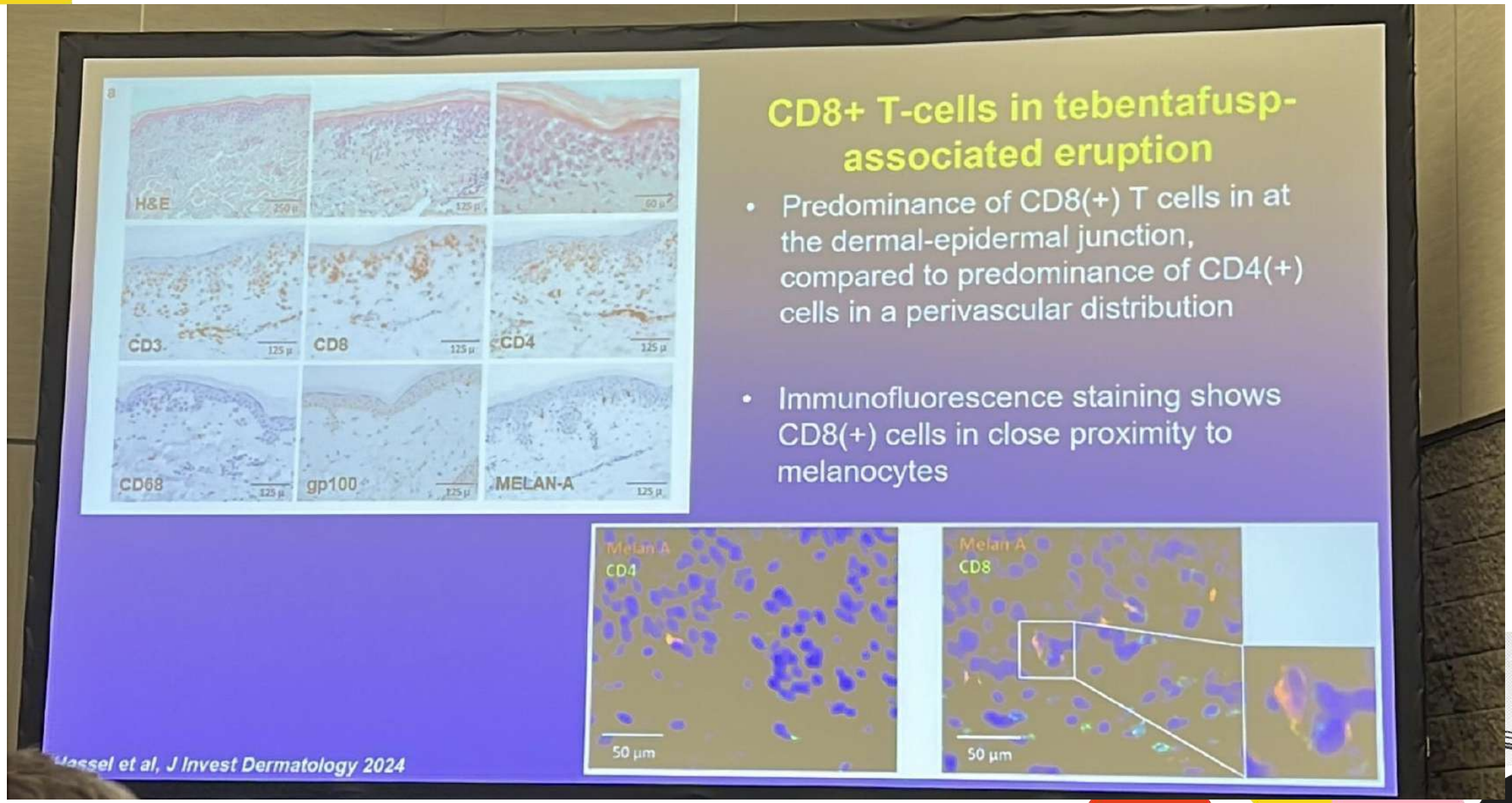
- 26/33 patients studied developed a skin reac (patients hospitalized for first 3 doses)
- 5 clinical patterns of skin toxicity noted
  - symmetrical erythematous patches (83.8%)
  - hemorrhagic macules (11.8%)
  - urticarial lesions (7.4%)
  - bullous lesions (1.5%)
  - skin (8.5%) and hair depigmentation (11.4%)
- 14 biopsies (11 from erythematous patches)
  - Focal interface changes, perivascular lympho inflammation
  - CD8(+) epidermal lymphocytes

Tebentafusp for uveal melanoma

- Bispecific gp100 peptide-HLA-directed CD3(+) T cell engager
  - Binds to both CD3 on activated T cells, gp100 on melanoma cells
- First in class immune-mobilizing monoclonal T-cell receptors against cancer (ImmTACs)
- FDA approved in 2022 in for **HLA-A*02:01-positive** adult patients with unresectable or metastatic uveal melanoma



Wespiser et al., Cancer Treatment Reviews 2023
https://medoncmd.com/emerging-clinical-trial-tebentafusp/


CD8+ T-cells in tebentafusp-associated eruption
• Predominance of CD8(+) T cells in at the dermal-epidermal junction, compared to predominance of CD4(+) cells in a perivascular distribution
• Immunofluorescence staining shows CD8(+) cells in close proximity to melanocytes
a
H&E
CD3
CD8
CD4
CD68
gp100
MELAN-A
Melan A
CD4
50 µm
Melan A
CD8
50 µm
Hassel et al, J Invest Dermatology 2024

Cutaneous reactions as on-target effects of tebentafusp?

Tebentafusp Induces a T-Cell–Driven Rash in Melanocyte-Bearing Skin as an Adverse Event Consistent with the Mechanism of Action

Jessica C. Hassel[1], Sarah Stanhope[2], Alexander Greenshields-Watson[2], Devayani Machiraju[1], Alexander Enk[1], Christopher Holland[2], Shaad E. Abdullah[2], Adel Benlahrech[2], Marlana Orloff[3], Paul Nathan[4], Sophie Piperno-Neumann[5], Ramon Staeger[6,7], Reinhard Dummer[6,7] and Barbara Meier-Schiesser[6,7]

Tebentafusp is a gp100xCD3-bispecific ImmTAC designed to redirect polyclonal T cells against cells presenting the melanocyte lineage–specific antigen gp100 on HLA-A*02:01. Skin-related adverse events, predominantly rash, are frequent and occur within a few hours after initial infusions; yet, the mechanisms are unknown. In this study, we analyzed clinical data from the randomized phase 3 trial (NCT03070392) of tebentafusp ($n = 252$) versus investigator's choice ($n = 126$). Translational analyses were performed on paired on-treatment skin samples from 19 patients collected in the phase 1 trial (NCT01211262). Our analyses showed that rash is a clinical manifestation of tebentafusp-induced recruitment of T cells to cutaneous melanocytes. Development of rash depended on baseline expression levels of gp100 and other melanin pathway genes in the skin. On treatment, melanocyte number was reduced, and expression of melanocytic genes decreased, whereas gene expression related to immunity and cytokine signaling increased. When adjusted for baseline prognostic features, patients with rash within the first week of tebentafusp treatment had the same overall survival as patients without a rash in the phase 3 randomized trial IMCgp100-202 (hazard ratio = 0.84, 95% confidence interval = 0.53–1.32). In summary, skin rash is an off-tumor, on-target effect of tebentafusp against gp100+ melanocytes, in line with the mechanism of action.

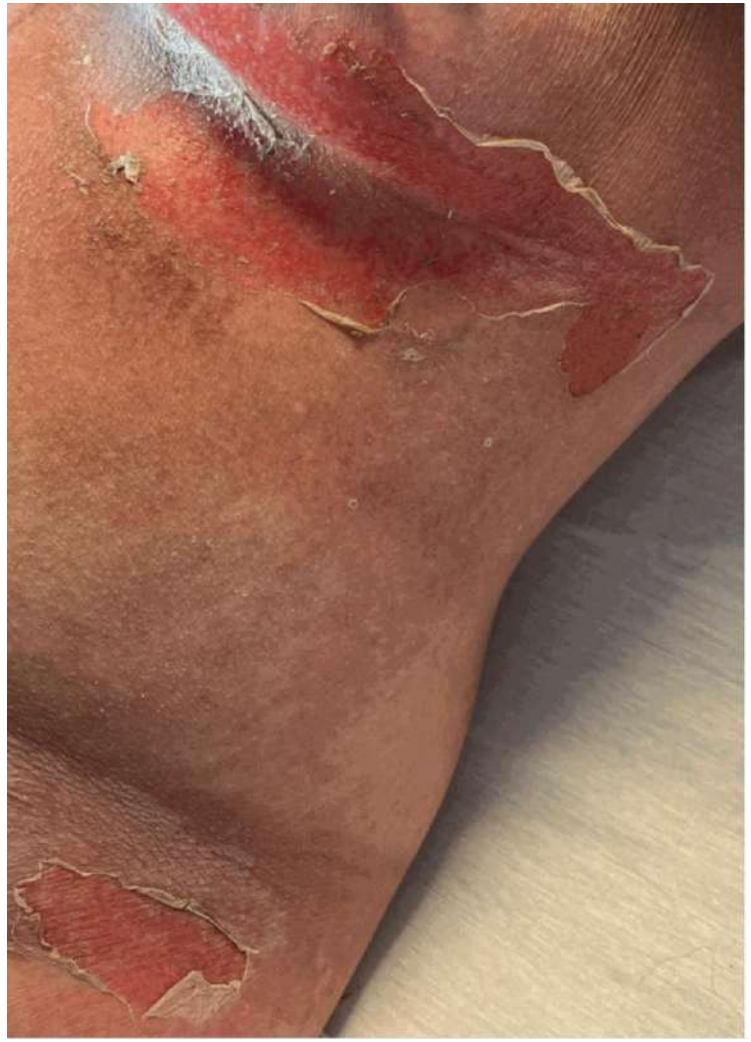
Keywords: Bispecific T-cell engager, gp100, Rash, Tebentafusp

Journal of Investigative Dermatology (2024) ■, ■–■; doi:10.1016/j.jid.2024.03.048

- Hypothesis: rapid onset of skin rash in patients treated with tebentafusp is a direct consequence of tebentafusp redirecting T cells to gp100(+) skin melanocytes

ssel et al., Eur J Cancer 2023
ssel et al, J Invest Dermatology 2024

Enfortumab vedotin



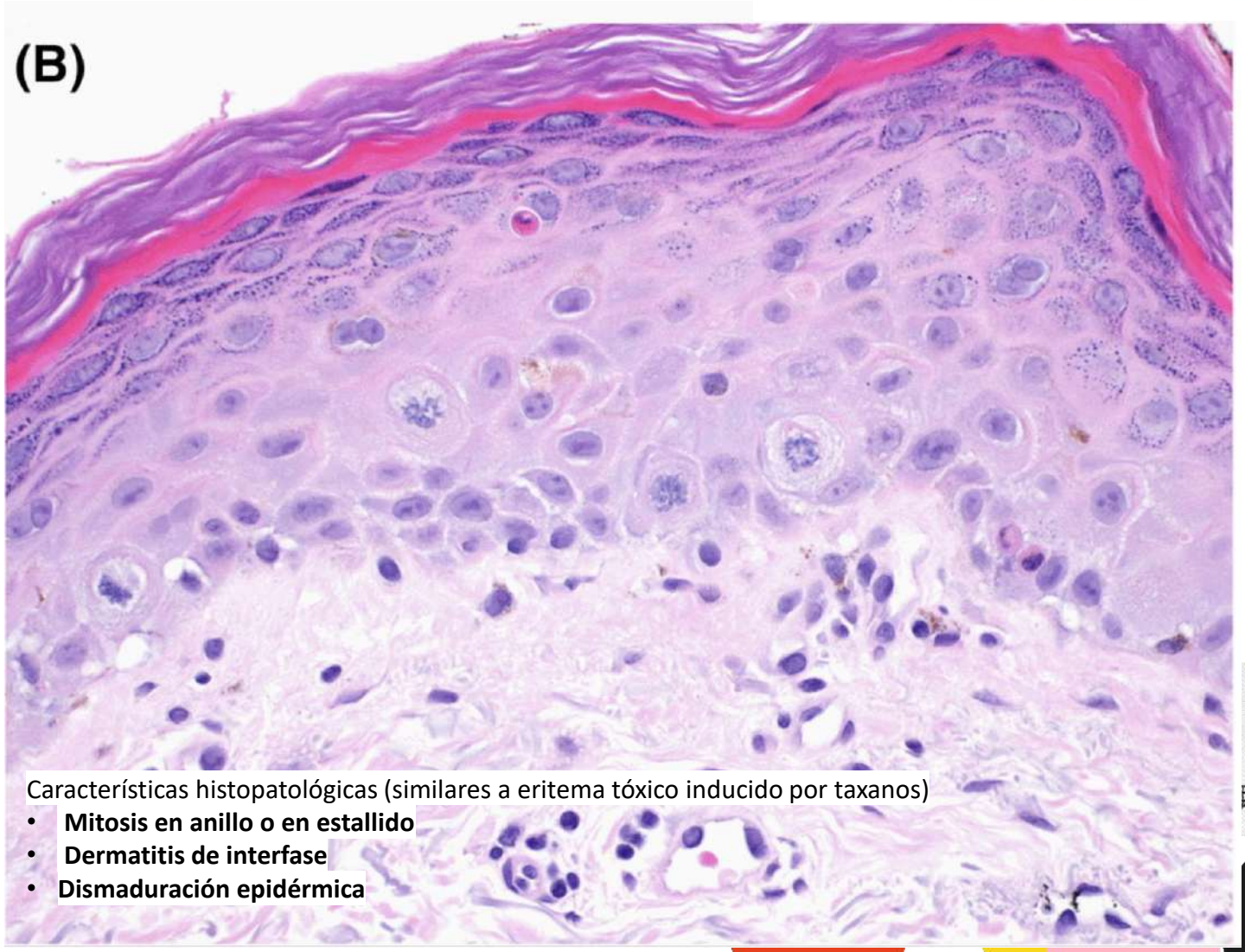
JOURNAL OF CUTANEOUS PATHOLOGY

CASE STUDY | Open Access

Enfortumab vedotin-induced cutaneous eruption: Ring mitotic figures as a distinctive histopathologic feature

Catherine Sport, Rebecca C. Clawson, Lauren E. Tisdale, John W. Melson, Mark C. Mochel

First published: 15 July 2024 | https://doi.org/10.1111/cup.14689 | Citations: 1



Características histopatológicas (similares a eritema tóxico inducido por taxanos)

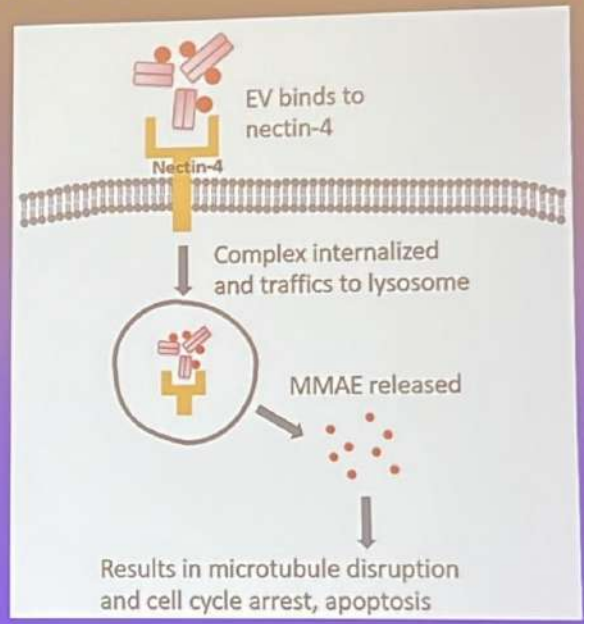
- **Mitosis en anillo o en estallido**
- **Dermatitis de interfase**
- **Dismaduración epidérmica**

Sport C, Clawson RC, Tisdale LE, Melson JW, Mochel MC. Enfortumab vedotin-induced cutaneous eruption: Ring mitotic figures as a distinctive histopathologic feature. *J Cutan Pathol*. 2024;51(11):847-851. doi:10.1111/cup.14689

Enforntumab vedotin

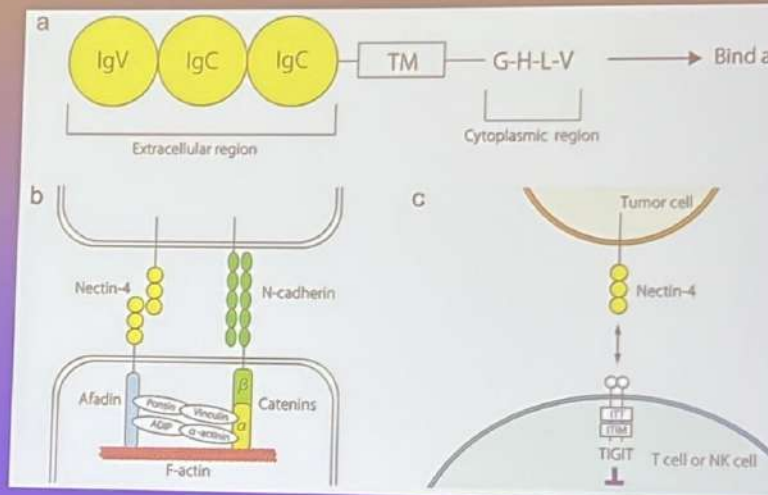
Enfortumab vedotin

- Anti-Nectin-4 antibody conjugated to monomethyl auristatin E, a microtubule-disrupting agent
- FDA approved for use in treatment of advanced urothelial carcinoma, following progression on platinum-based chemotherapy and PD-1 or PD-L1 inhibitor



Nectin-4 as a target in cancer

- Tumor-associated antigen, overexpressed in lung, breast, gastric, urothelial cancer cells
- Calcium-dependent transmembrane adhesion molecule, normally expressed in the skin and upper aerodigestive tract



Hashimoto et al., Curr Treat Options Onco

Enfortumab vedotin vs otros fármacos

ORIGINAL STUDY

Histopathologic Comparison Among Drug Eruptions Induced by Enfortumab Vedotin, Brentuximab Vedotin, and Taxanes

Iwahashi, Yoshifumi MD[*,†]; Goto, Keisuke MD[*,‡,§,¶,‖]; Ohe, Shuichi MD, PhD[§§]; Bun, Shota MD[§§]; Kido, Kansuke MD, PhD[¶¶]; Matsui, Takahiro MD, PhD[¶¶]; Morii, Eiichi MD, PhD[¶¶]; Honma, Keiichiro MD, PhD[*]

Author Information

atopathology 47(3):p 191-196, March 2025. | **DOI:** 10.1097/DAD.0000000000002911

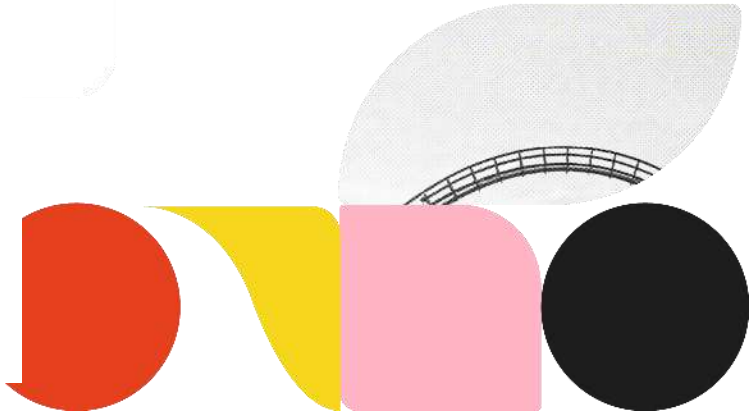
TABLE 2. Histopathologic Summary in all 22 Cases of This Study

Histopathologic Findings	Enfortumab Vedotin-Induced Eruption	Brentuximab Vedotin-Induced Eruption	Docetaxel-Induced Eruption	Paclitaxel-Induced Eruption
Ring mitotic figures in the epidermis (*n*)	5/5, 100% (range 1–5.5; median 1.5)	2/5, 40% (range 0–3; median 0)	1/5, 20% (0–1.5, median 0)	0/7, 0% (0–0, median 0)
Mitotic arrest figures, including ring mitosis in the epidermis (*n*)	5/5, 100% (range 1.5–55.5; median 16)	2/5, 40% (range 0–22; median 0)	2/5, 40% (0–3.75, median 0)	3/7, 43% (0–22, median 0)
Ring mitotic figures in the sweat ductoglandular unit (*n*)	2/5, 40% (range 0–1; median 0)	0/5, 0% (range 0–0; median 0)	0/5, 0% (range 0–0; median 0)	0/7, 0% (range 0–0; median 0)
Mitotic arrest figures, including ring mitosis in the sweat ductoglandular unit (*n*)	3/5, 60% (range 0–10.5; median 3)	1/5, 20% (range 0–3; median 0)	0/5, 0% (range 0–0; median 0)	0/7, 0% (range 0–0; median 0)
Ring mitotic figures in the follicular epithelium (*n*)	0/5, 0% (range 0–0; median 0)	0/5, 0% (range 0–0; median 0)	0/5, 0% (range 0–0; median 0)	0/7, 0% (range 0–0; median 0)
Mitotic arrest figures, including ring mitosis in the follicular epithelium (*n*)	0/5, 0% (range 0–0; median 0)	0/5, 0% (range 0–0; median 0)	0/5, 0% (range 0–0; median 0)	0/7, 0% (range 0–0; median 0)
Multinucleated keratinocytes (*n*)	4/5, 80% (range 0–13; median 6)	3/5, 60% (range 0–2; median 0.5)	2/5, 40% (range 0–37.5; median 0)	4/7, 57% (range 0–3; median 0.5)
Apoptotic keratinocytes distributed predominantly in the upper part of the epidermis	4/5, 80%	3/5, 60%	2/5, 40%	0/7, 0%
Parakeratotic cornified layer	3/5, 60%	4/5, 80%	2/5, 40%	1/7, 14%
Spongiotic change	Mild: 2/5, 40% Moderate: 3/5, 60%	No: 1/5, 20% Moderate: 4/5, 80%	No: 1/5, 20% Mild: 3/5, 60% Moderate: 1/5, 20%	No: 2/7, 29% Mild: 1/7, 14% Moderate: 4/7, 57%
Interface vacuolar change	No: 1/5, 20% Mild: 3/5, 60% Severe: 1/5, 20%	No: 1/5, 20% Mild: 4/5, 80%	No: 2/5, 40% Mild: 3/5, 60%	No: 3/7, 43% Mild: 3/7, 43% Moderate: 1/7, 14%
Dermal eosinophilic infiltrate	No: 3/5, 60% Mild: 1/5, 20% Moderate: 1/5, 20%	No: 4/5, 80% Moderate: 1/5, 20%	No: 5/5, 100%	No: 5/7, 71% Moderate: 2/7, 29%

n: number observed in 1 skin tissue section of 3 mm-sized punch biopsy.

Ring mitosis:

+ frecuentes en enfrontumab-vedotina>brentuximab-vedotina>docetaxel/paclitaxel



Enfortumab vedotin

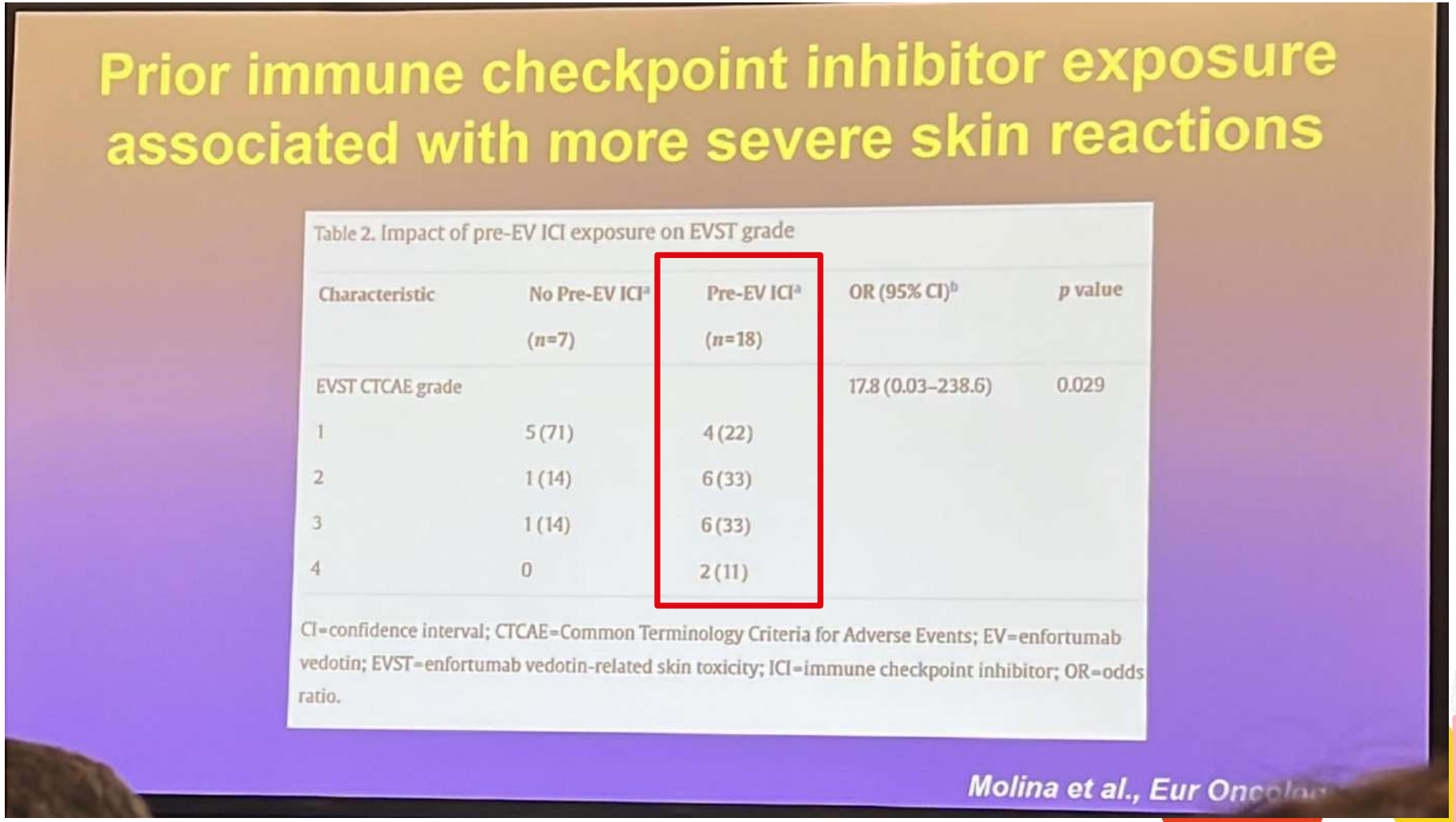


Table 2. Impact of pre-EV ICI exposure on EVST grade

Characteristic	No Pre-EV ICI[a] (*n*=7)	Pre-EV ICI[a] (*n*=18)	OR (95% CI)[b]	*p* value
EVST CTCAE grade			17.8 (0.03–238.6)	0.029
1	5 (71)	4 (22)		
2	1 (14)	6 (33)		
3	1 (14)	6 (33)		
4	0	2 (11)		

CI=confidence interval; CTCAE=Common Terminology Criteria for Adverse Events; EV=enfortumab vedotin; EVST=enfortumab vedotin-related skin toxicity; ICI=immune checkpoint inhibitor; OR=odds ratio.

NECTIN-4 y otros tumores

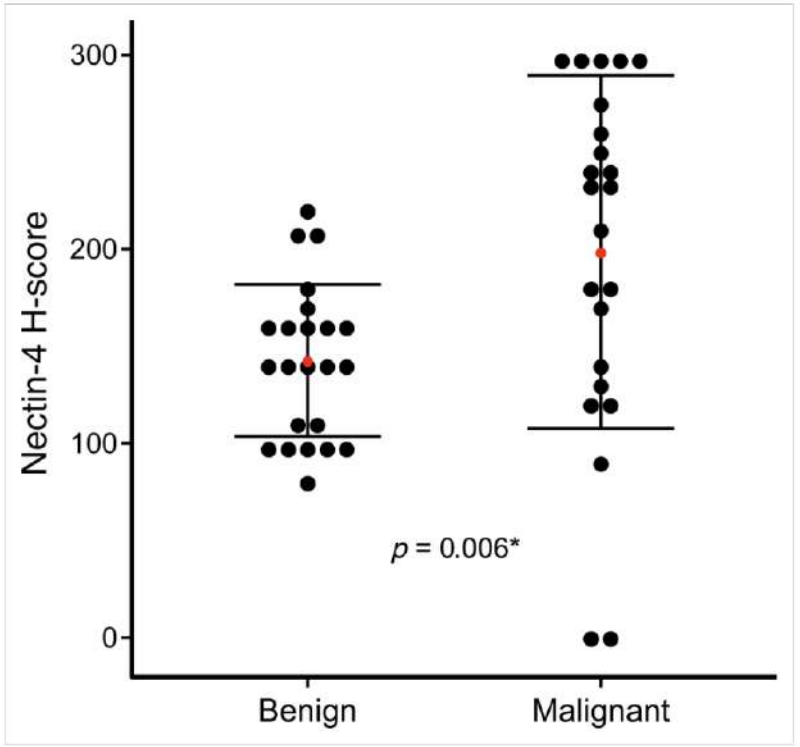


FIGURE 2 Open in figure viewer | PowerPoint

Nectin-4 H-score distribution and mean (±SD) H-scores (red dots) for the 23 benign (7 sebaceous adenomas, 8 poromas, and 8 trichilemmomas) and 23 malignant (8 digital papillary adenocarcinoma, 7 squamoid eccrine ductal carcinomas, and 8 sebaceous carcinomas) adnexal neoplasms. The adnexal carcinomas had a significantly higher mean H-score than did the benign adnexal neoplasms (*$p = 0.006$).

JOURNAL OF CUTANEOUS PATHOLOGY

ORIGINAL ARTICLE | Full Access

Nectin-4 expression in a subset of cutaneous adnexal carcinomas: A potential target for therapy with enfortumab vedotin

Woo Cheal Cho MD, Rayan Saade MD, Priyadharsini Nagarajan MD, PhD, Phyu P. Aung MD, PhD, Denái R. Milton MS, Mario L. Marques-Piubelli MD, Courtney Hudgens MS ... See all authors

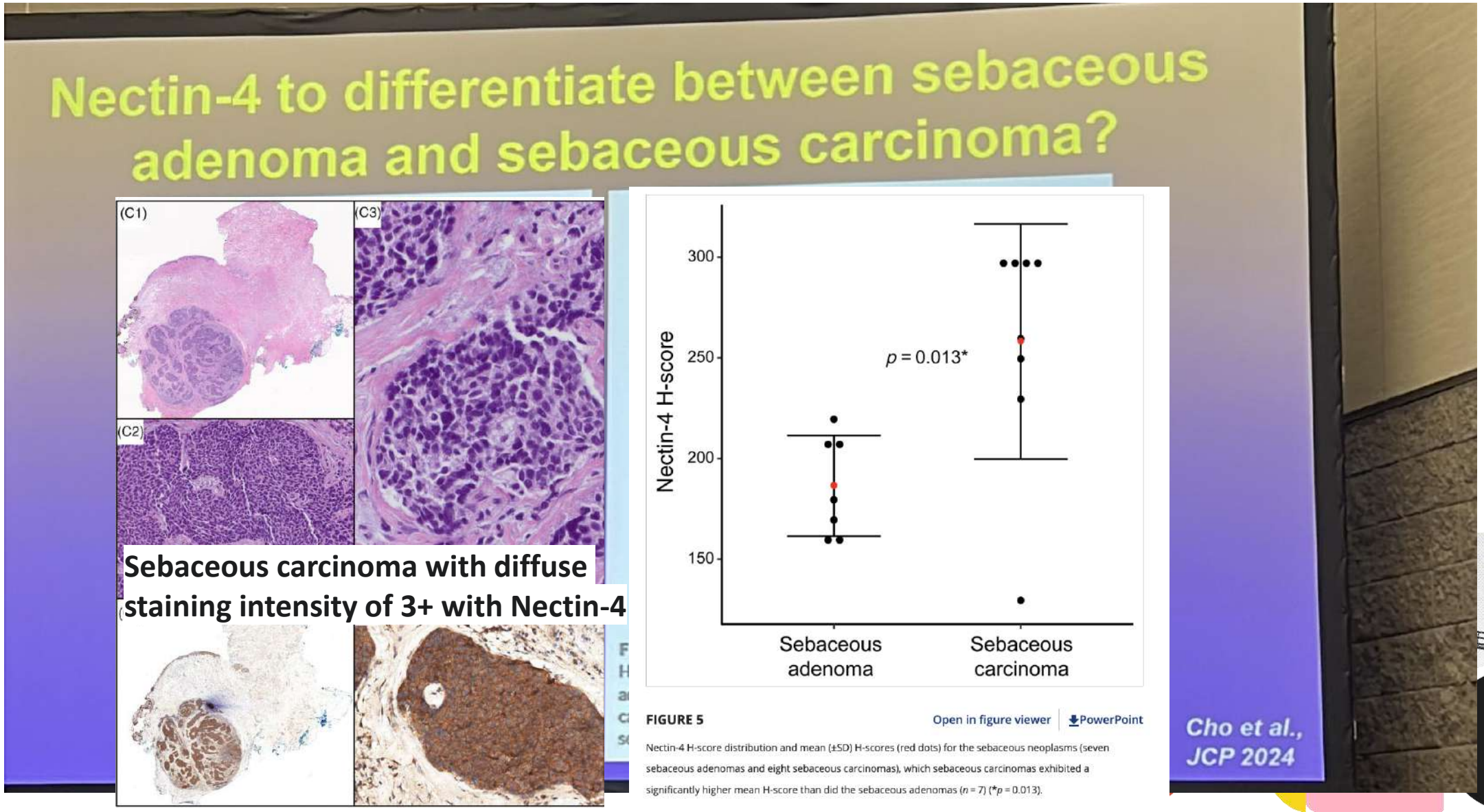
First published: 10 January 2024 | https://doi.org/10.1111/cup.14579

TABLE 1 Summary of demographic and clinical data with respective Nectin-4 H-score distribution and mean (±SD) in each adnexal tumor group.

Type of adnexal neoplasms	Cases, n	Age in years (range)	M:F	Site, n (%)	Nectin-4 expression, n (%)				Mean H-score ± SD
					Negative	Low	Medium	High	
Poroma	8	53 (36–87)	1:1	LE, 3 (38) UE, 2 (25) Flank, 2 (25) Back, 1 (12)		2 (25)	6 (75)		123.1 ± 30.8
Sebaceous adenoma	7	65 (63–76)	5:2	H&N, 5 (72) Shoulder, 1 (14) Back, 1 (14)			4 (57)	3 (43)	186.4 ± 25.0
Trichilemmoma	8	83 (38–86)	8:0	H&N, 7 (88) Chest, 1 (12)		8 (100)			123.8 ± 23.9
Digital papillary adenocarcinoma	8	49 (32–71)	1:3	Foot, 4 (50) Hand, 3 (38) LN, 1 (12)			4 (50)	4 (50)	197.5 ± 52.5
Squamoid eccrine ductal carcinoma	7	69 (53–79)	6:1	H&N, 4 (57) UE, 1 (14) LE, 1 (14) Back, 1 (14)	2 (29)	1 (14)	2 (29)	2 (29)	131.4 ± 114.1
Sebaceous carcinoma	8	73 (57–88)	1:1*	Eyelid, 4 (50) Orbit, 3 (38) LN, 1 (12)			1 (12)	7 (88)	258.1 ± 58.4

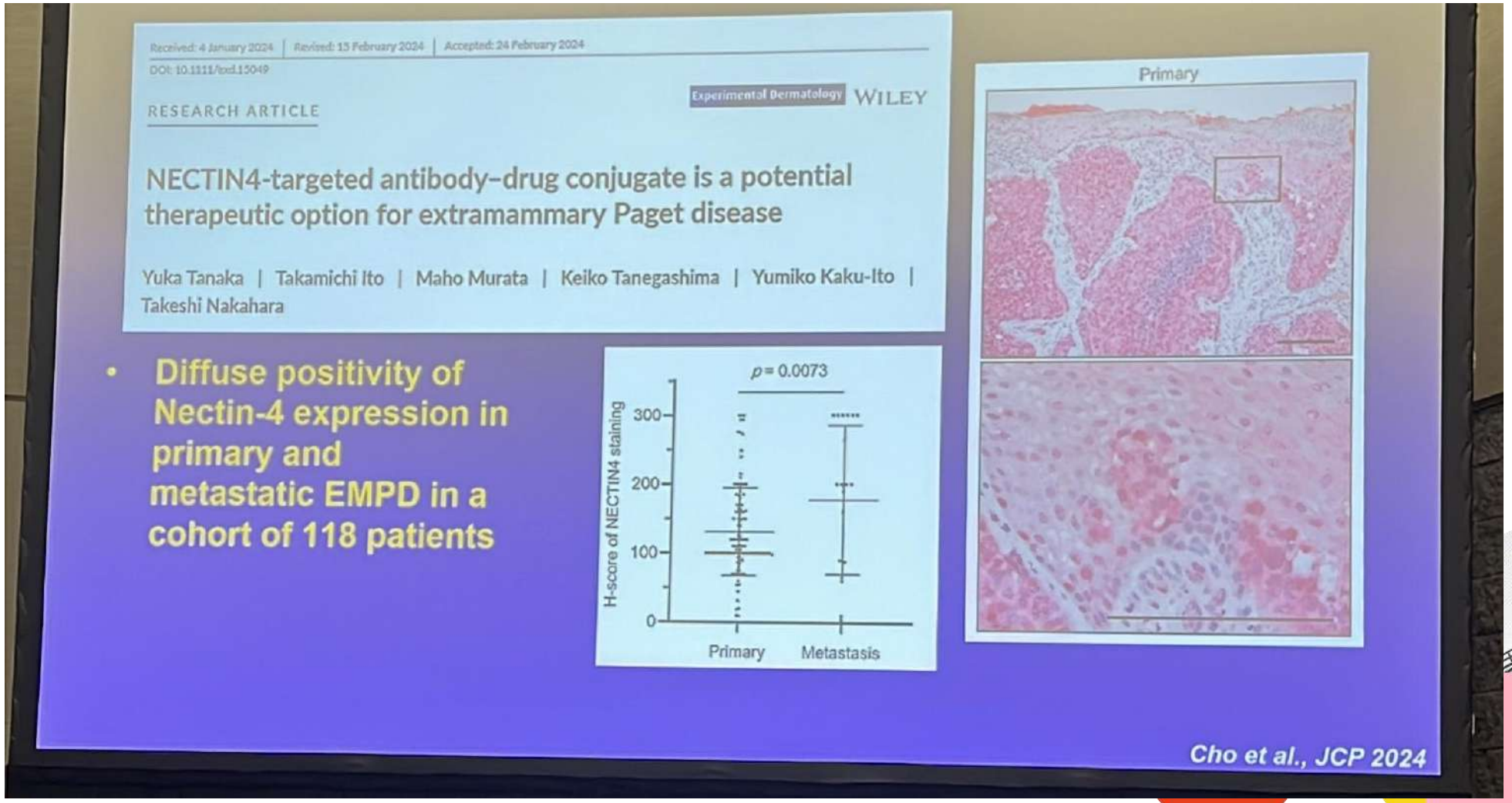
Abbreviations: F, female; H&N, head and neck; LE, lower extremity; LN, lymph node; M, male; n, number; SD, standard deviation; UE, upper extremity.
*Includes a lesion of lymph node metastasis for one patient.

NECTIN-4


Nectin-4 to differentiate between sebaceous adenoma and sebaceous carcinoma?
(C1)
(C3)
(C2)
Sebaceous carcinoma with diffuse staining intensity of 3+ with Nectin-4
Nectin-4 H-score
300
250
200
150
p = 0.013*
Sebaceous adenoma
Sebaceous carcinoma
FIGURE 5
Open in figure viewer
PowerPoint
Nectin-4 H-score distribution and mean (±SD) H-scores (red dots) for the sebaceous neoplasms (seven sebaceous adenomas and eight sebaceous carcinomas), which sebaceous carcinomas exhibited a significantly higher mean H-score than did the sebaceous adenomas (n = 7) (*p = 0.013).
Cho et al., JCP 2024

NECTIN-4 y otros tumores

Potential gap: Identification of potentially actionable biomarkers (for diagnosis and treatment) in cutaneous tumors



Variantes infrecuentes de micosis fungoide

Received: 2 November 2023 | Revised: 14 April 2024 | Accepted: 29 April 2024
DOI: 10.1111/cup.14642

CASE STUDY

JCP WILEY

Urticarial mycosis fungoides: A distinctive presentation with blood involvement and a peculiar immunophenotype

Juan Torre-Castro[1] | Concepción Postigo[2] | Salma Machan[1] | Margarita Estela Jo-Velasco[3] | Javier Díaz de la Pinta[3] | Jose Luis Rodríguez-Peralto[4] | Raúl Córdoba[5] | Luis Requena[1] | Socorro María Rodríguez-Pinilla[3]

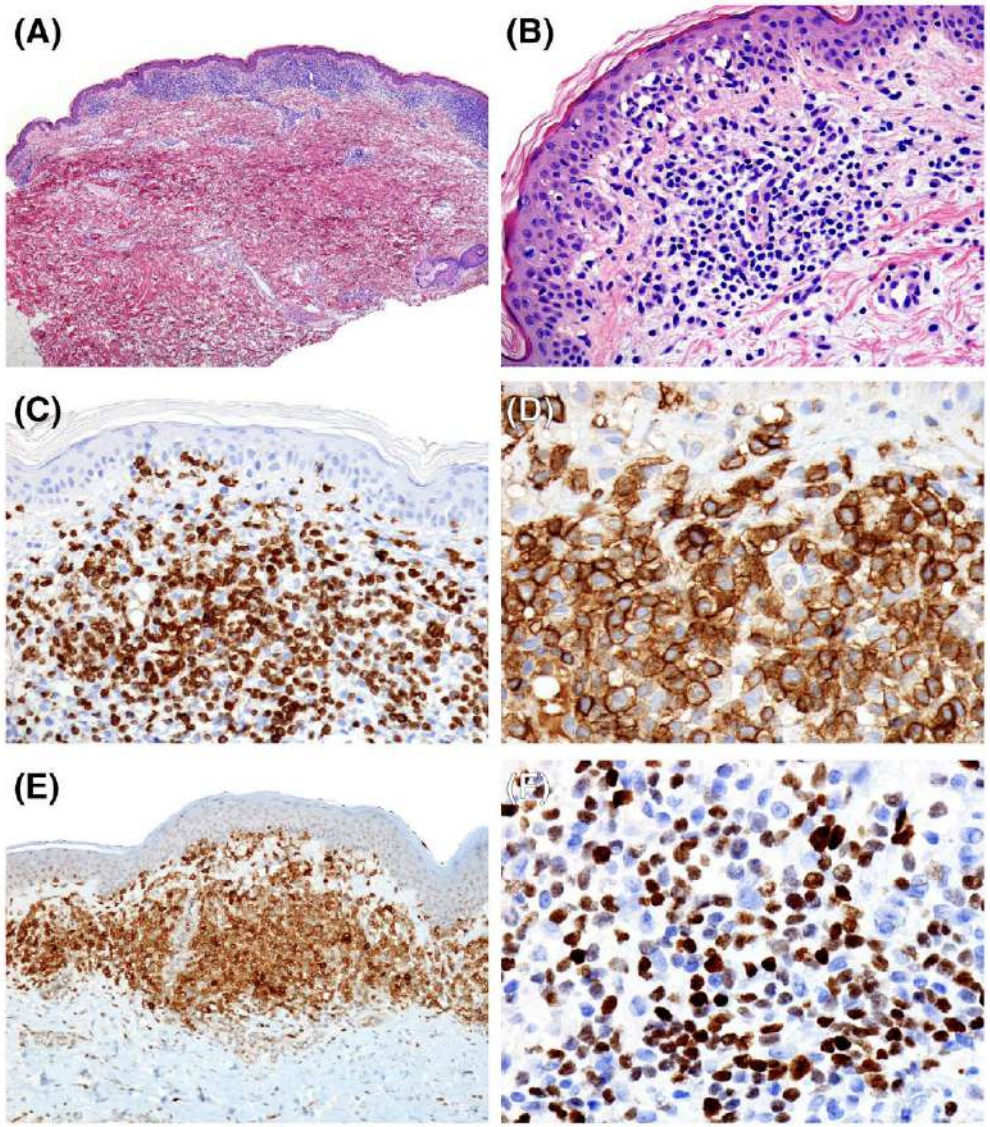
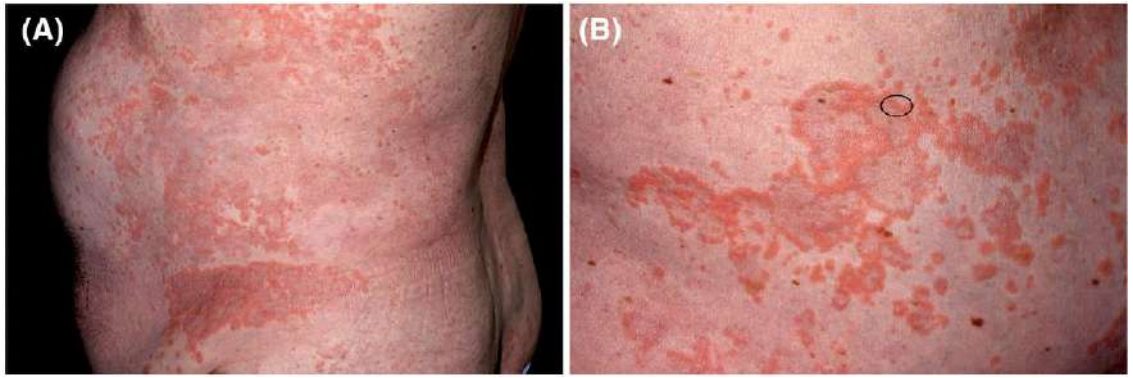


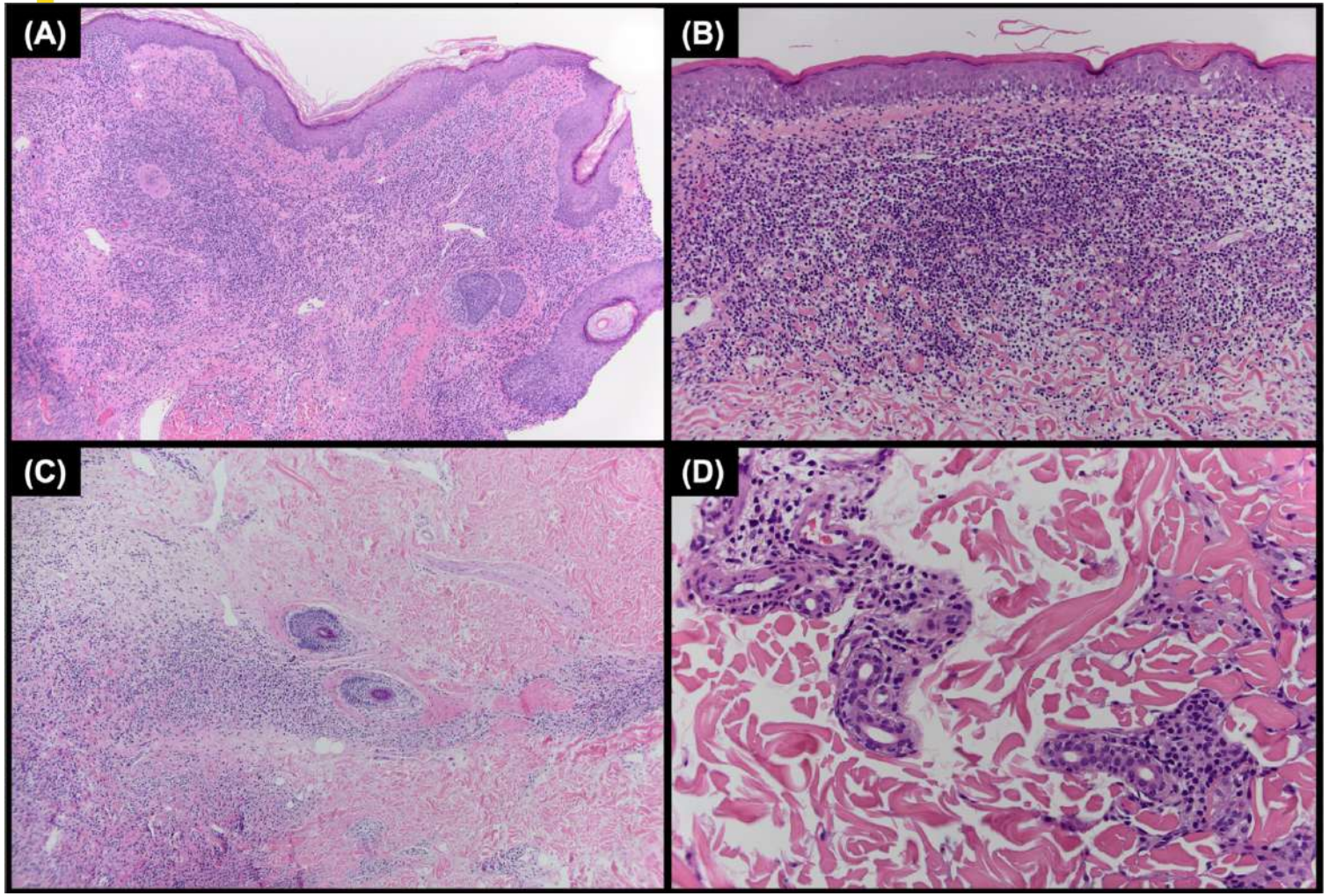
FIGURE 2 Histopathological appearance of the skin lesions. (A) Dense lymphocytic infiltrate in the papillary dermis. Hematoxylin–eosin (H-E), ×20. (B) Detail of the atypical lymphocytes. Note the epidermotropism and the lining up at the dermal–epidermal junction. H-E, ×100. (C) Immunohistochemical positivity with CD3, ×100. (D) Immunohistochemical positivity with PD1, ×200. (E) Immunohistochemical positivity with CD25, ×100. (F) Immunohistochemical positivity with FOXP3, ×200.



- 2 pts with urticarial non-scaly lesions and peripheral blood involvement
- (+)CD3, CD4, CD7,PD1, FOXP3 (ddx Sezary syn, HTLV1, T-cell prolymphocytic leukemia (T-PLL))

Ambos casos tenían características histológicas clásicas de MF y compartían un inmunofenotipo peculiar con positividad para CD25 y FOXP3.

Variantes infrecuentes de micosis fungoide



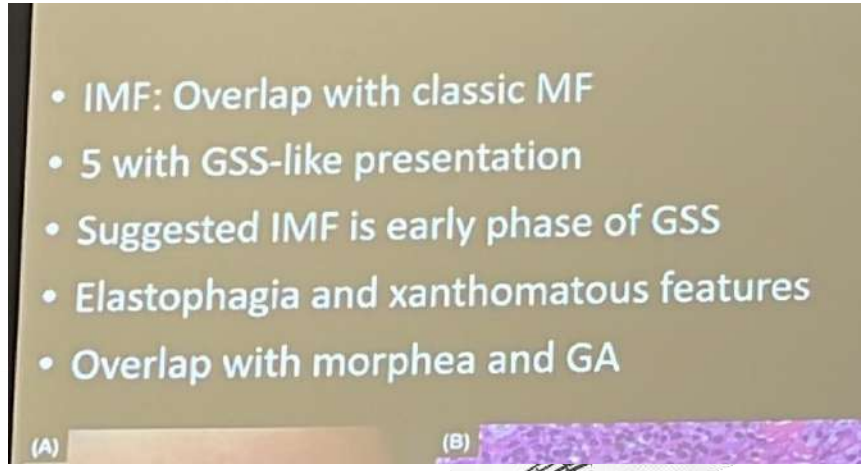
JOURNAL OF CUTANEOUS PATHOLOGY

ORIGINAL ARTICLE | Full Access

Interstitial mycosis fungoides: A rare presentation of mycosis fungoides with overlapping granulomatous and folliculotropic features

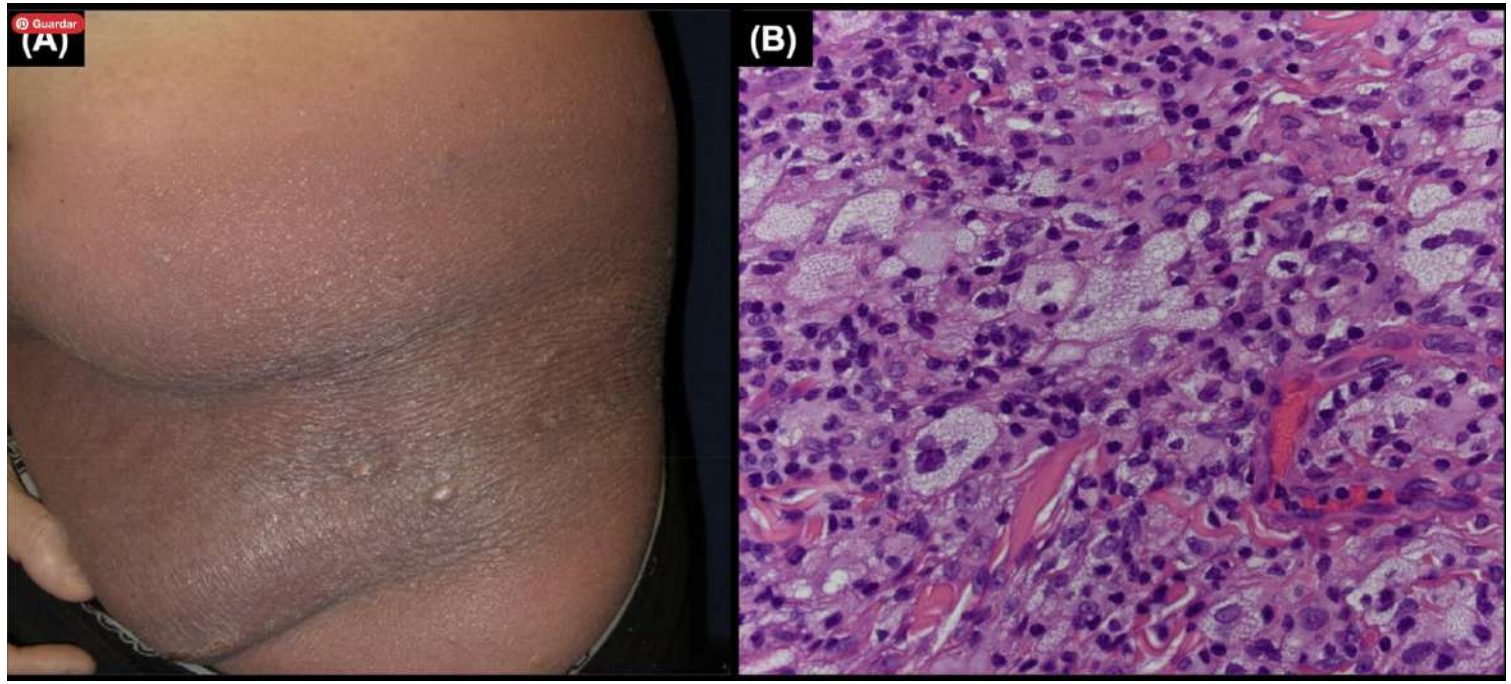
Christopher Chung MD, Bicong Wu MD, Tessa LeWitt MD, Teresa Griffin BS, Madeline Hooper BA, Xiaolong (Alan) Zhou MD, Jaehyuk Choi MD, PhD, Joan Guitart MD

First published: 05 March 2024 | https://doi.org/10.1111/cup.14599



Interstitial mycosis fungoides is characterized by atypical small–medium lymphocytes typically involving the upper and mid-dermis with limited but sometimes moderate epidermotropism as demonstrated The atypical lymphocytic infiltrate can sometimes be neurotropic, adnexotropic or syringotropic

Variantes infrecuentes de micosis fungoide



Interstitial mycosis fungoides with clinical features of granulomatous slack skin syndrome involving the lower abdomen and flank with large, indurated, pedunculated peu d'orange appearing erythematous plaque and in rare cases with associated yellow papules (A). Such yellow papules correlate with xanthogranulomatous changes seen on histopathology (B; 600×, H&E).

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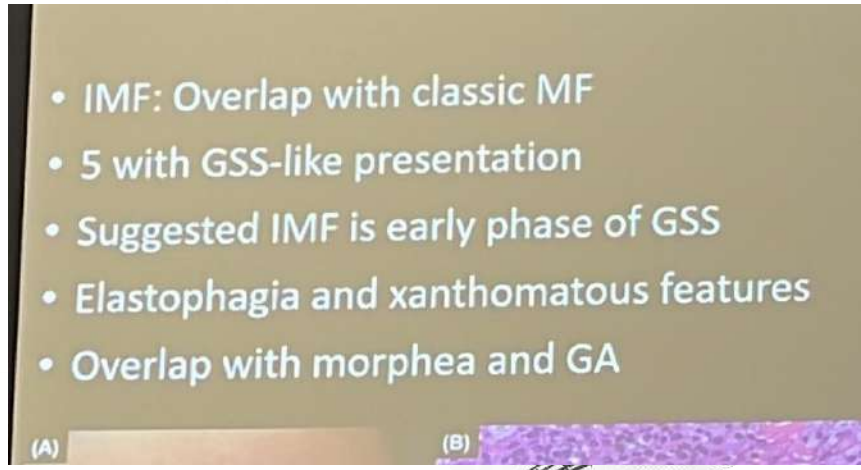
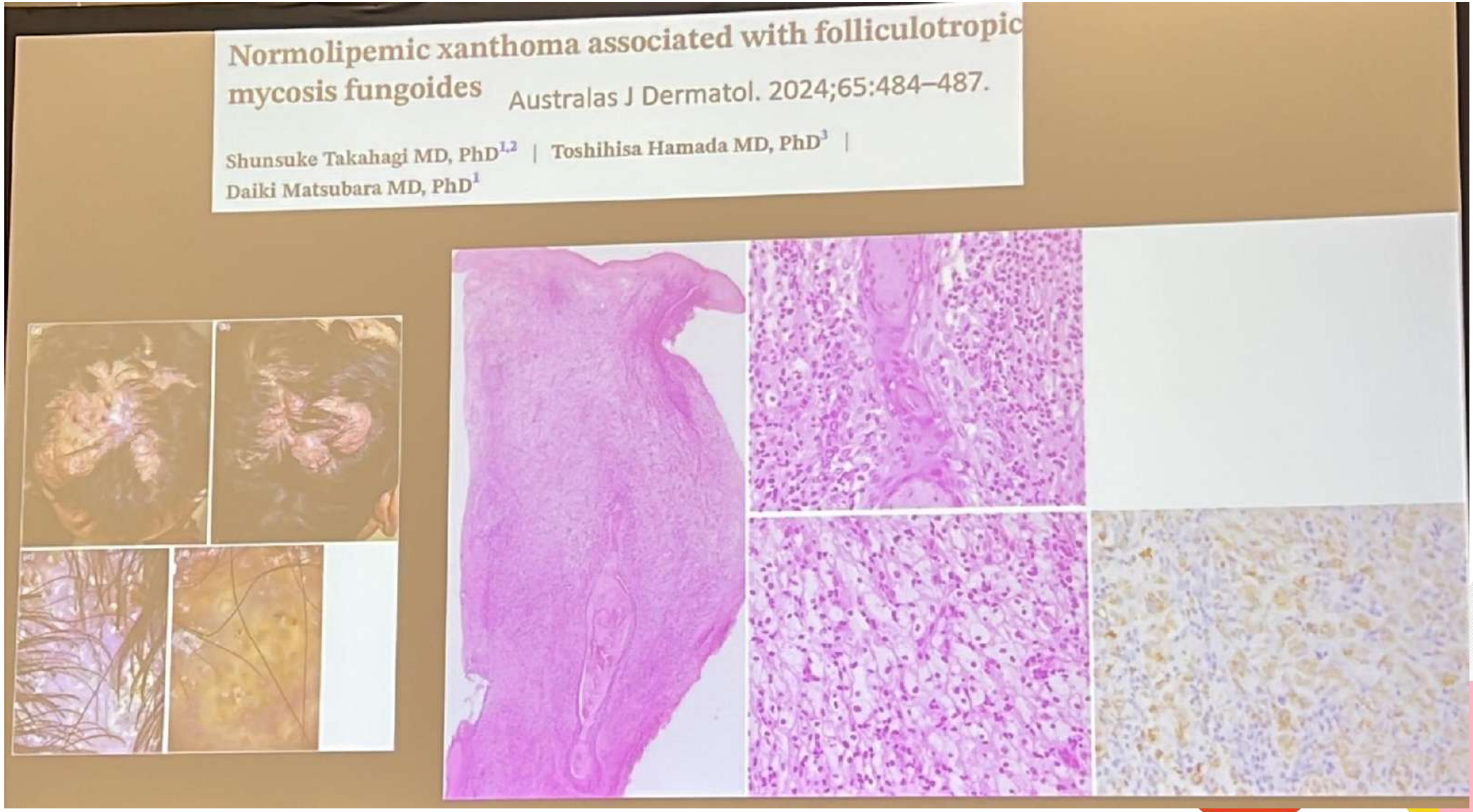


Variantes infrecuentes de micosis fungoide



AAD **ANNUAL** MEETING **2025**

AEDV 7 - 11 MARZO ORLANDO

highlights

What's new in dermatopatology?

Sábado 8 Marzo

Una iniciativa de:

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

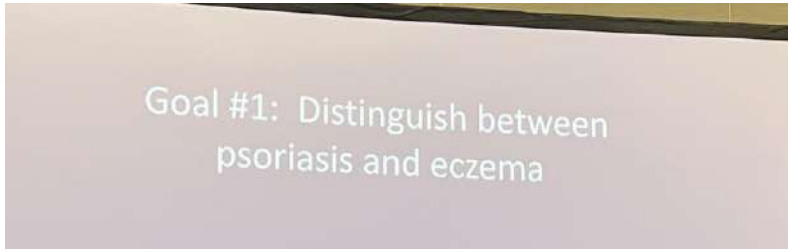
FUNDACIÓN AEDV PIEL SANA

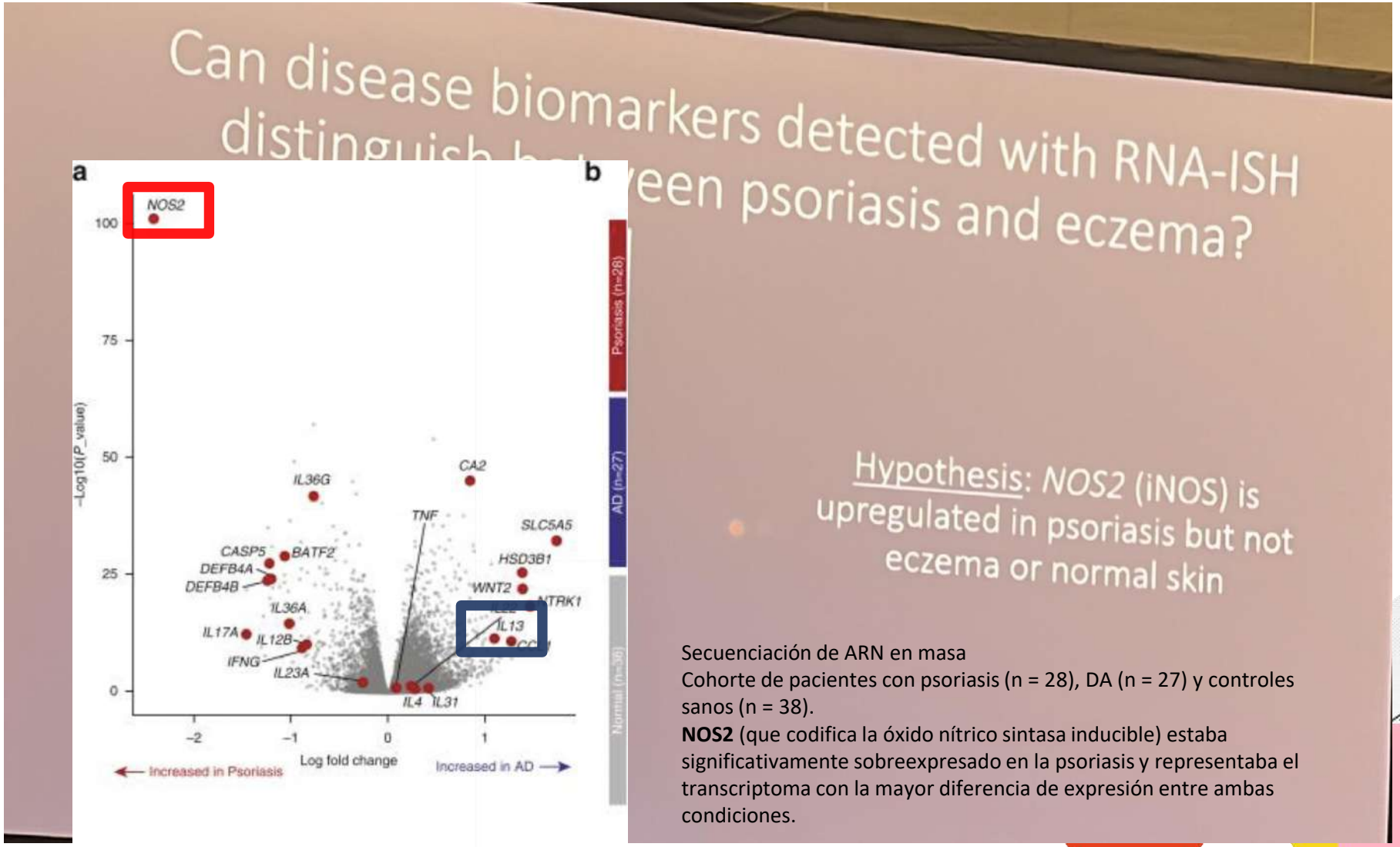
ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

Con el patrocinio de:

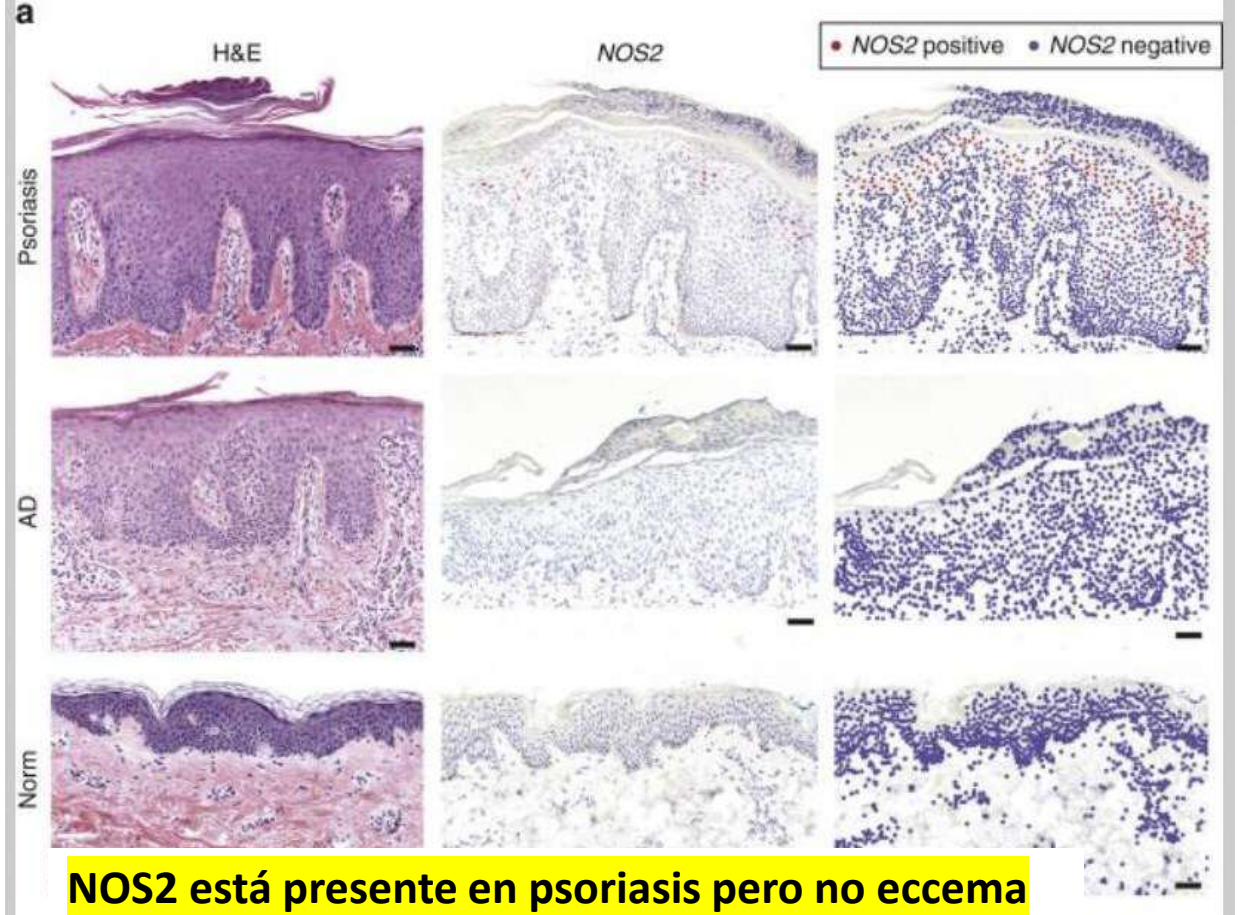
ucb

Psoriasis vs eccema

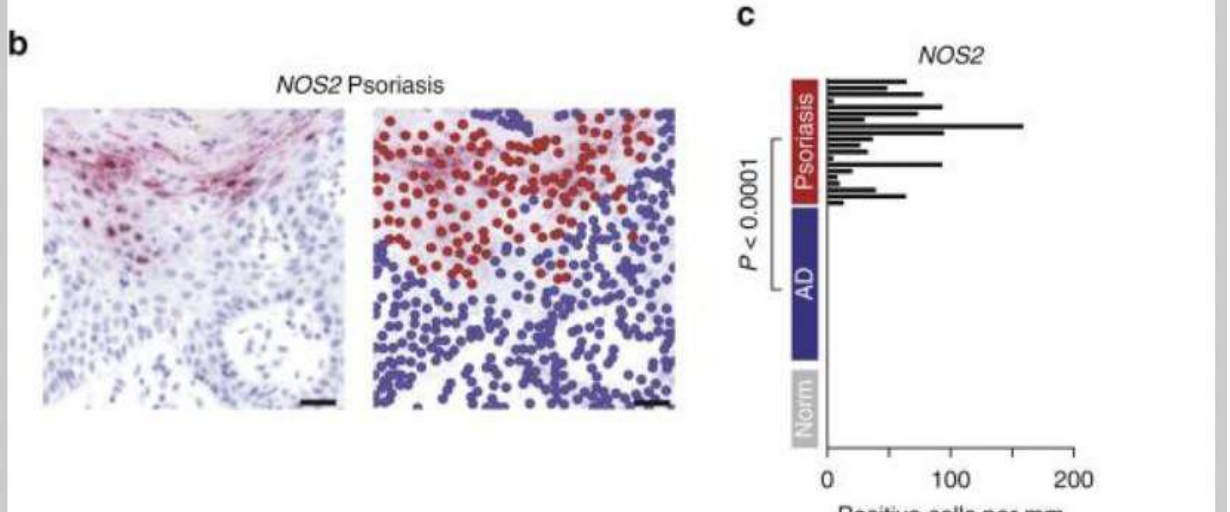


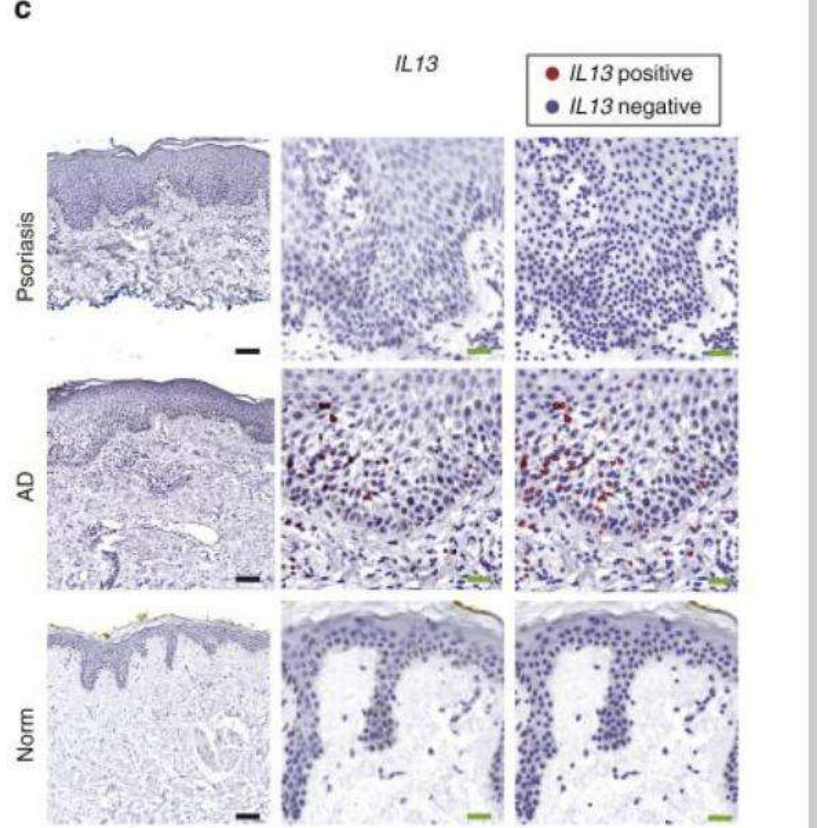


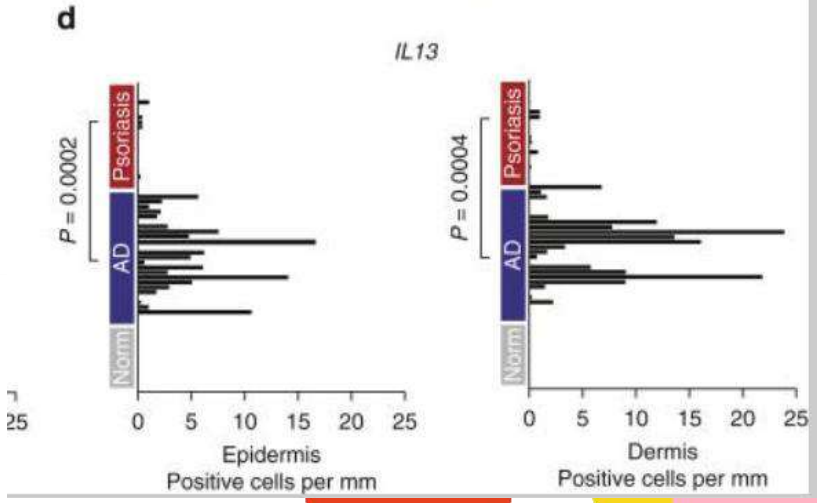
Secuenciación de ARN en masa
Cohorte de pacientes con psoriasis (n = 28), DA (n = 27) y controles sanos (n = 38).
NOS2 (que codifica la óxido nítrico sintasa inducible) estaba significativamente sobreexpresado en la psoriasis y representaba el transcriptoma con la mayor diferencia de expresión entre ambas condiciones.



NOS2 está presente en psoriasis pero no eccema

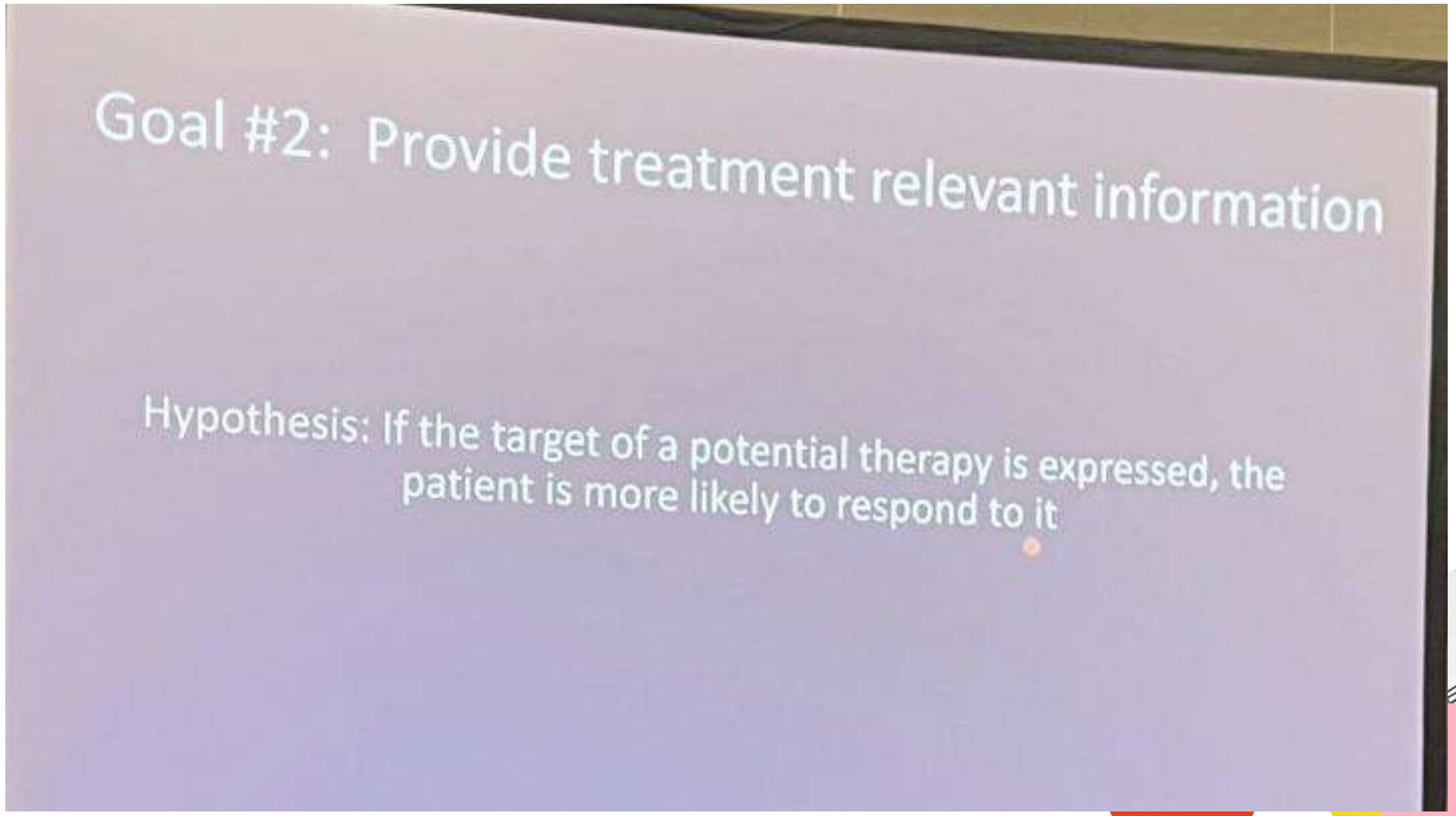






Wang A, Fogel AL, Murphy MJ, et al. Cytokine RNA In Situ Hybridization Permits Individualized Molecular Phenotyping in Biopsies of Psoriasis and Atopic Dermatitis. *JID Innov*. 2021;1(2):100021

Utilidad clínica



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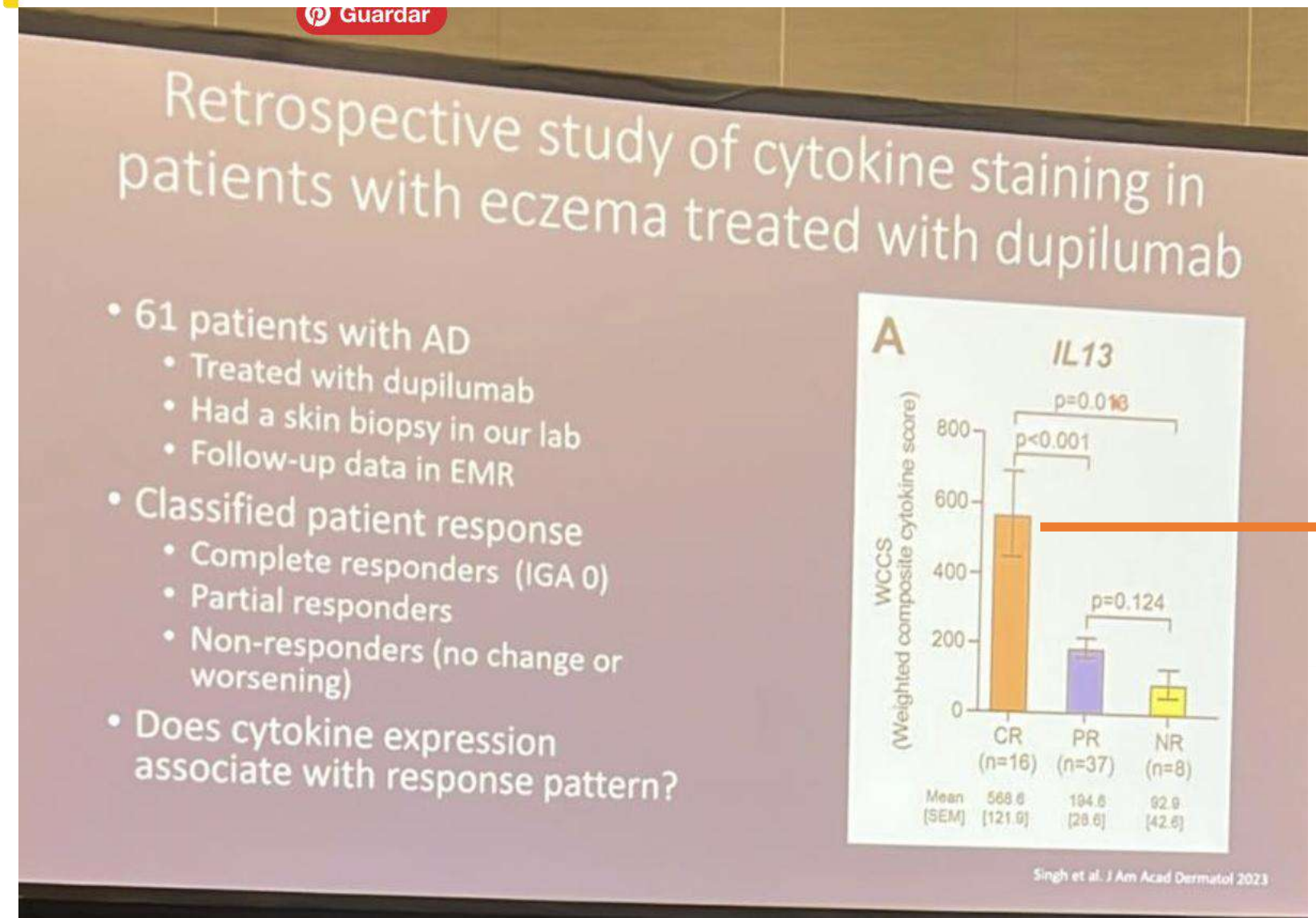
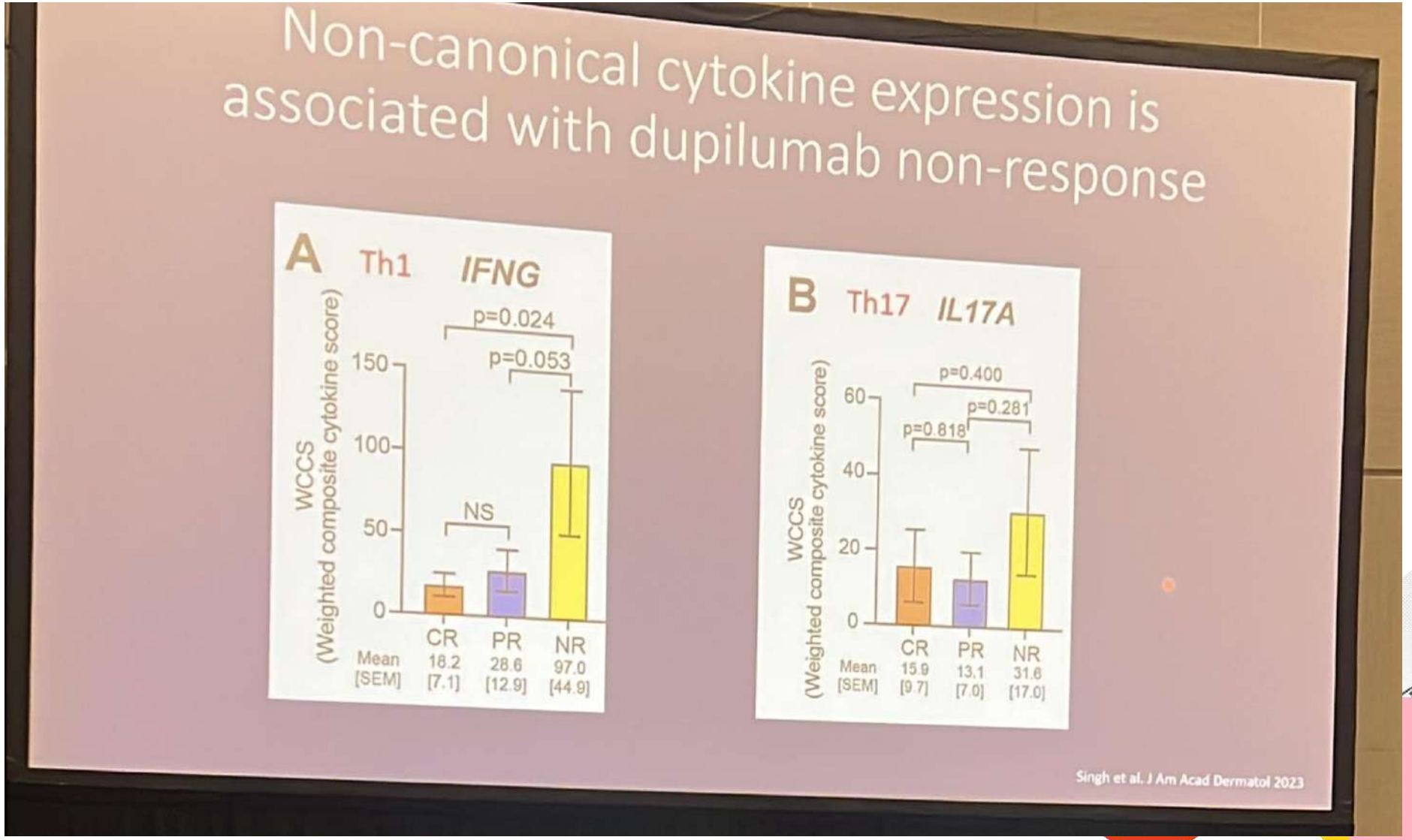
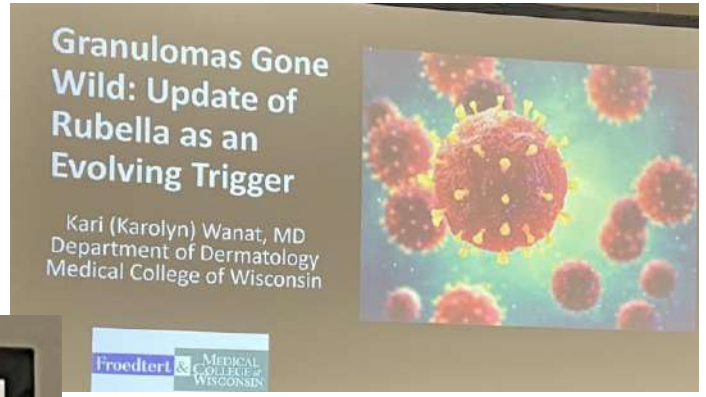


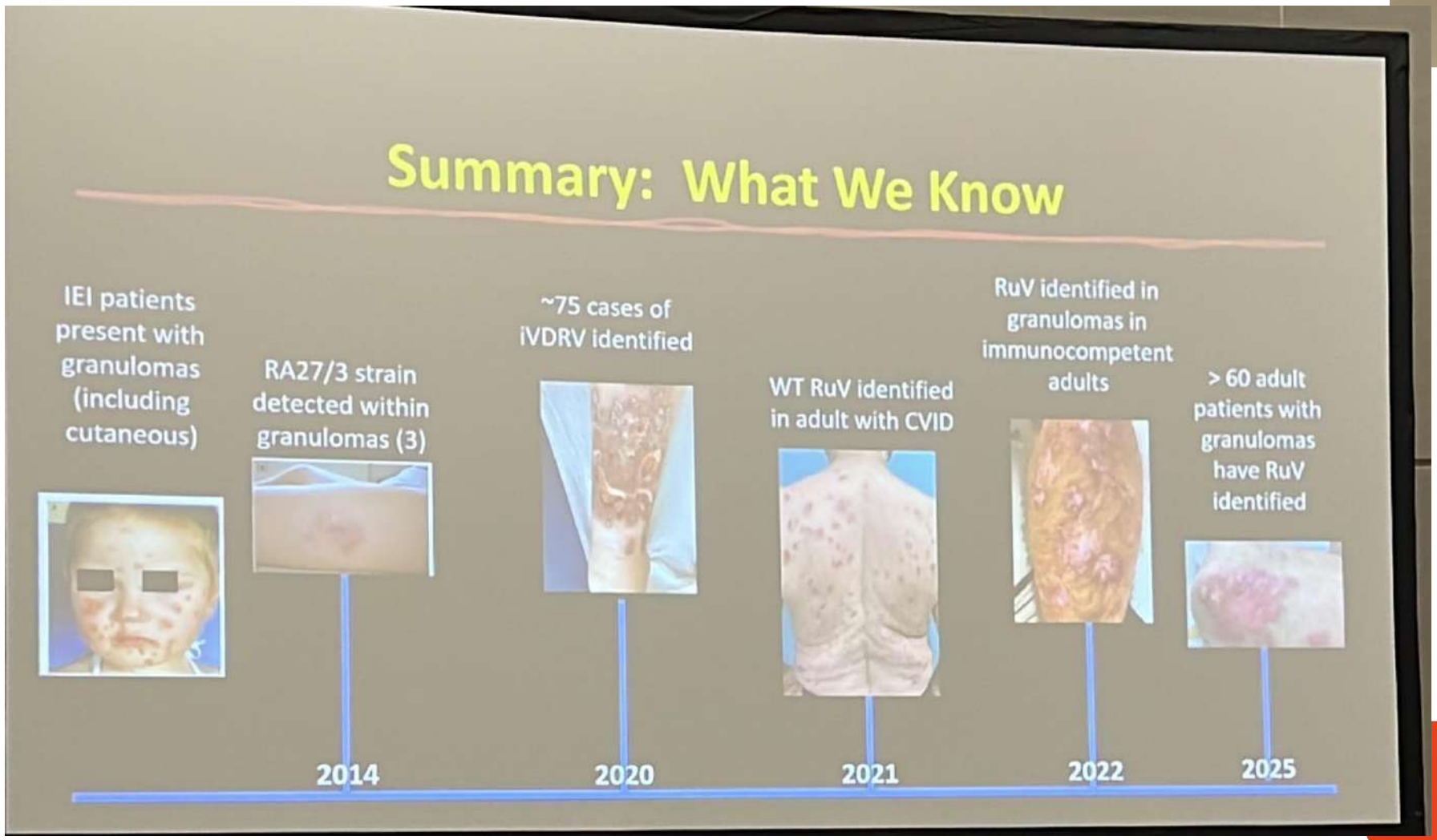
Mayor número de pacientes con respuesta completa (IGA 0)

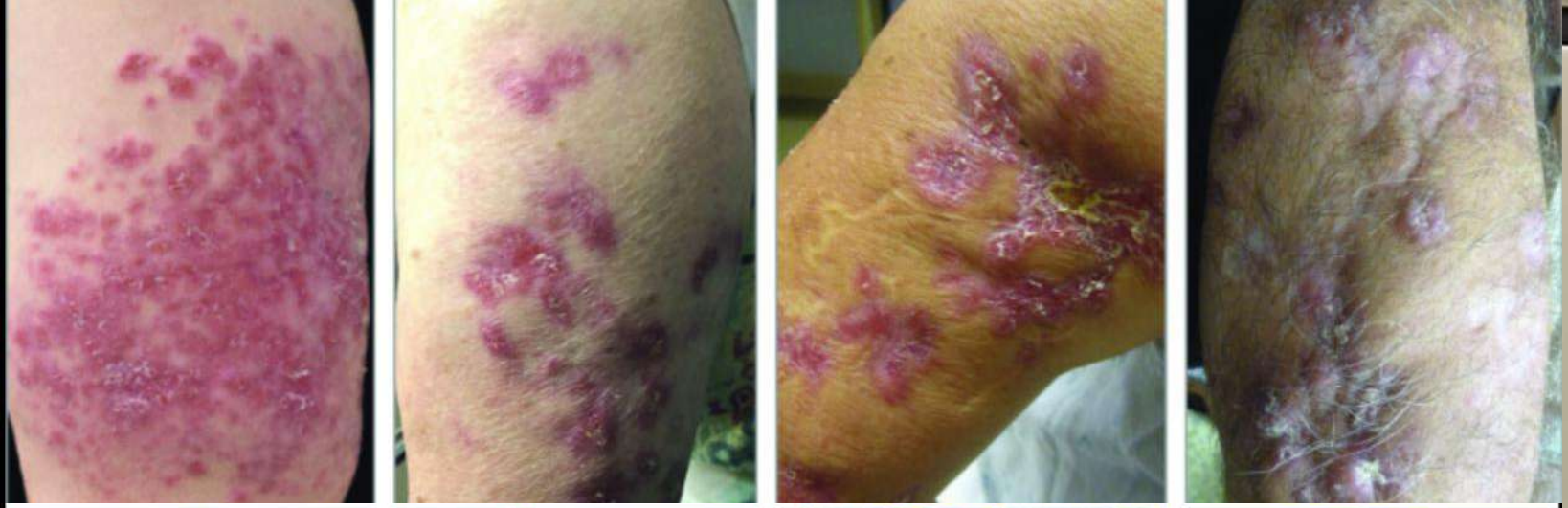
Utilidad clínica

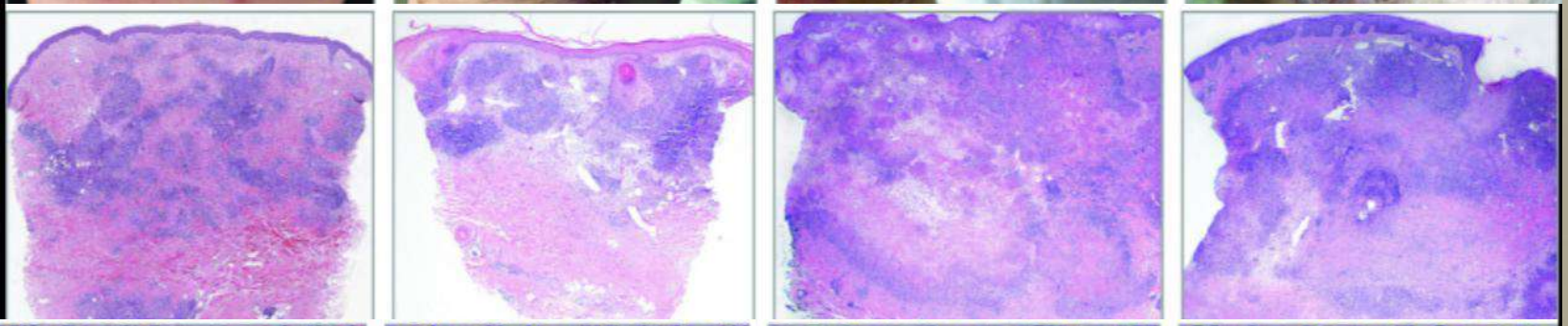


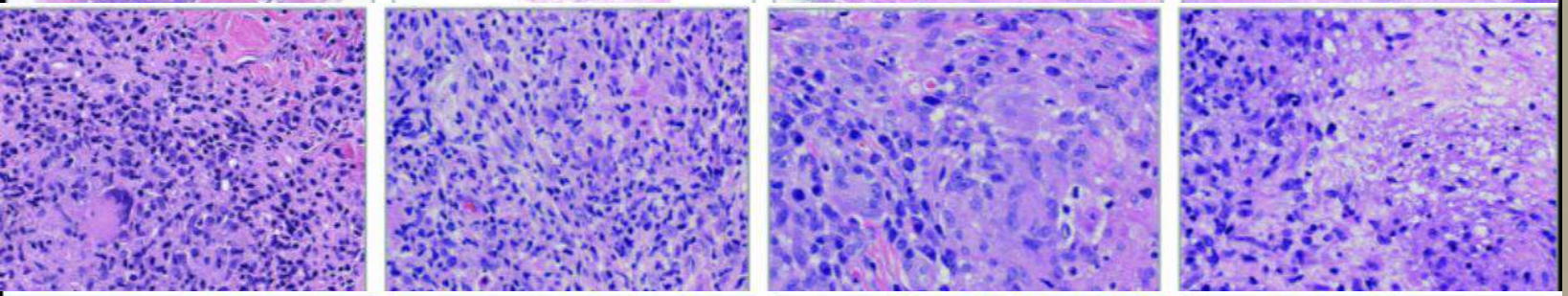
Rubéola y granulomas

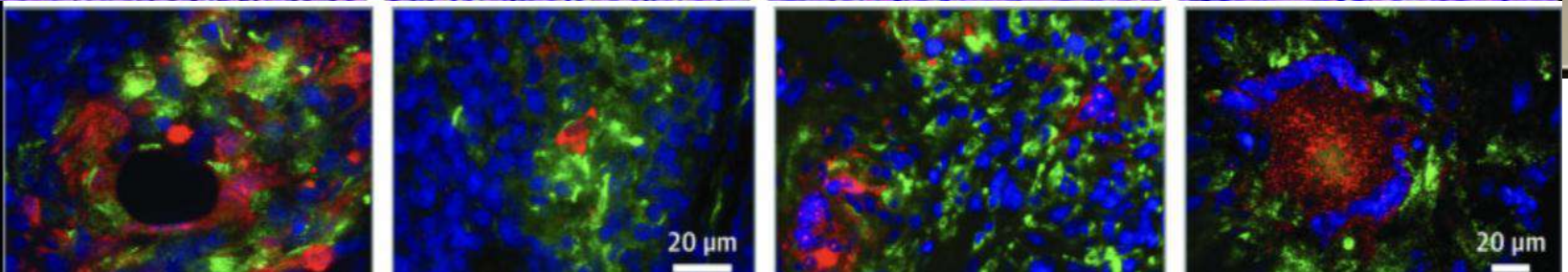








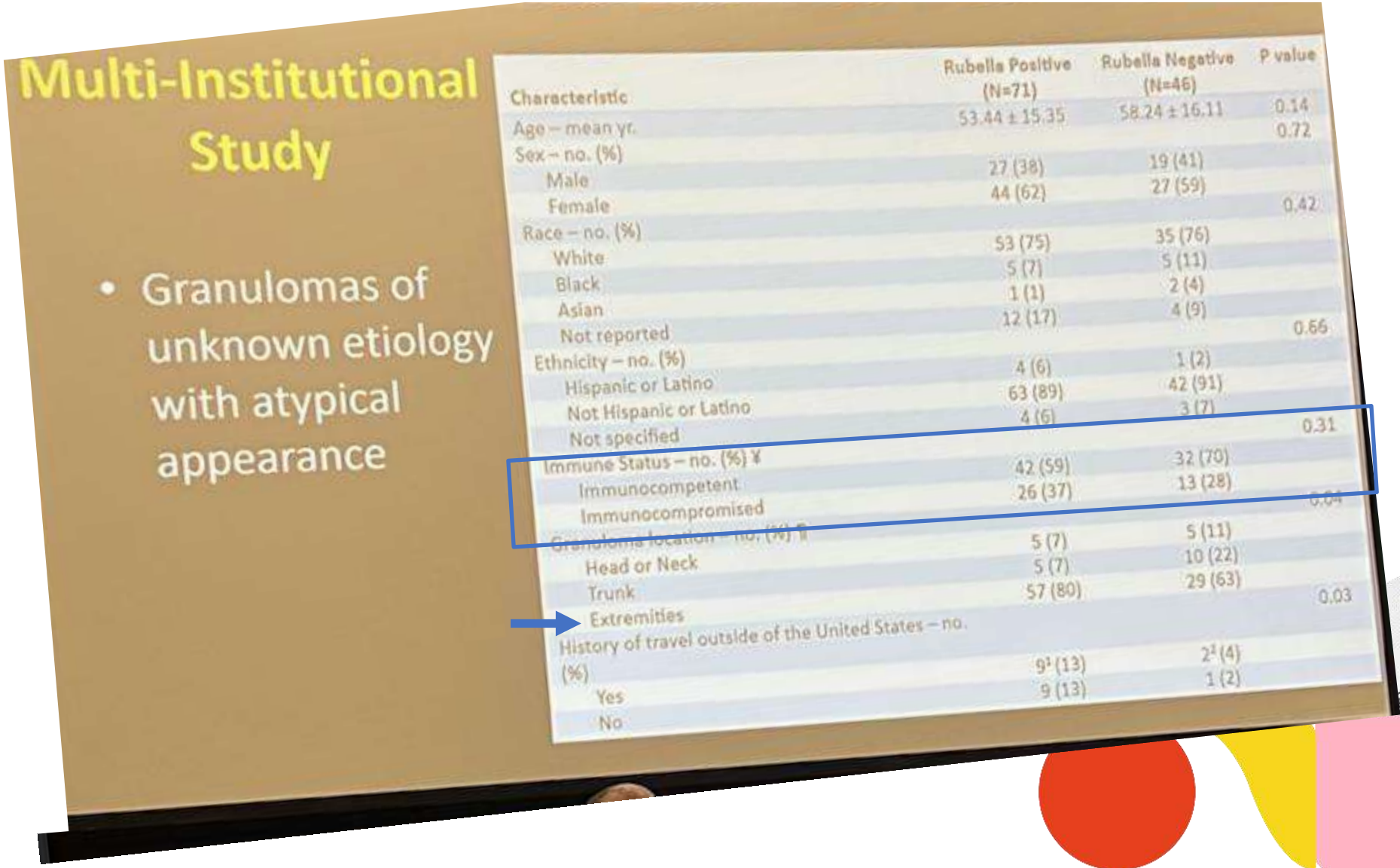




- Clinical appearance:
  - All on arm
  - Papule, nodules, indurated plaques, some pustules and draining with scarring
- Histopathology
  - Granulomatous inflammation with necrosis
- Immunohistochemistry
  - RuV within macrophages!

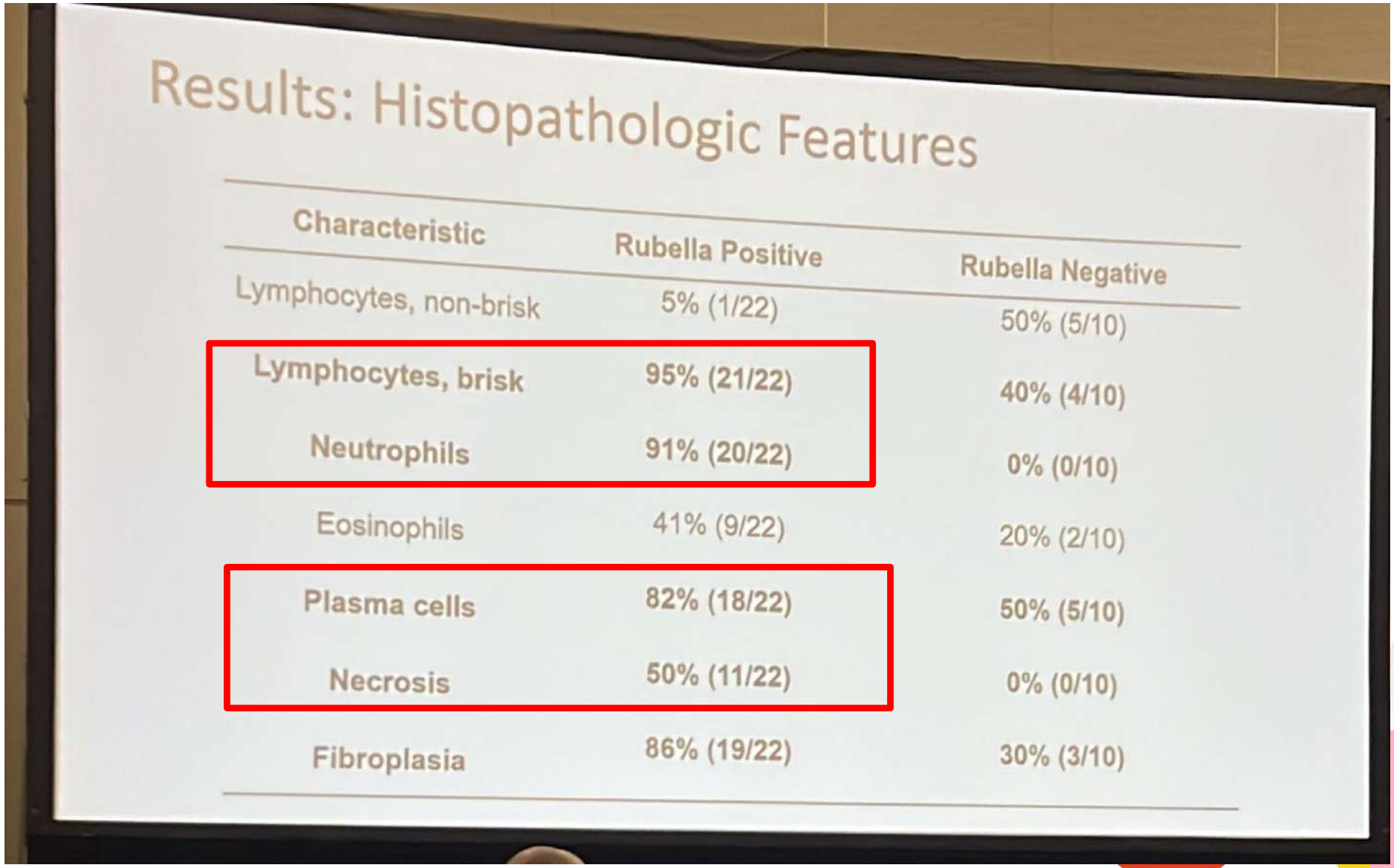
JAMA Dermatol. 2022;158(6):626-633.
Front Immunol. 2021 Dec 20;12:796065.
Curr Opin Allergy Clin Immunol. 2020 Dec;20(6):574-581.

Rubéola y granulomas



Characteristic	Rubella Positive (N=71)	Rubella Negative (N=46)	P value
Age – mean yr.	53.44 ± 15.35	58.24 ± 16.11	0.14
Sex – no. (%)			0.72
Male	27 (38)	19 (41)	
Female	44 (62)	27 (59)	
Race – no. (%)			0.42
White	53 (75)	35 (76)	
Black	5 (7)	5 (11)	
Asian	1 (1)	2 (4)	
Not reported	12 (17)	4 (9)	
Ethnicity – no. (%)			0.66
Hispanic or Latino	4 (6)	1 (2)	
Not Hispanic or Latino	63 (89)	42 (91)	
Not specified	4 (6)	3 (7)	
Immune Status – no. (%) ¥			0.31
Immunocompetent	42 (59)	32 (70)	
Immunocompromised	26 (37)	13 (28)	
Granuloma location – no. (%) ¥			0.04
Head or Neck	5 (7)	5 (11)	
Trunk	5 (7)	10 (22)	
Extremities	57 (80)	29 (63)	
History of travel outside of the United States – no. (%)			0.03
Yes	9[1] (13)	2[1] (4)	
No	9 (13)	1 (2)	

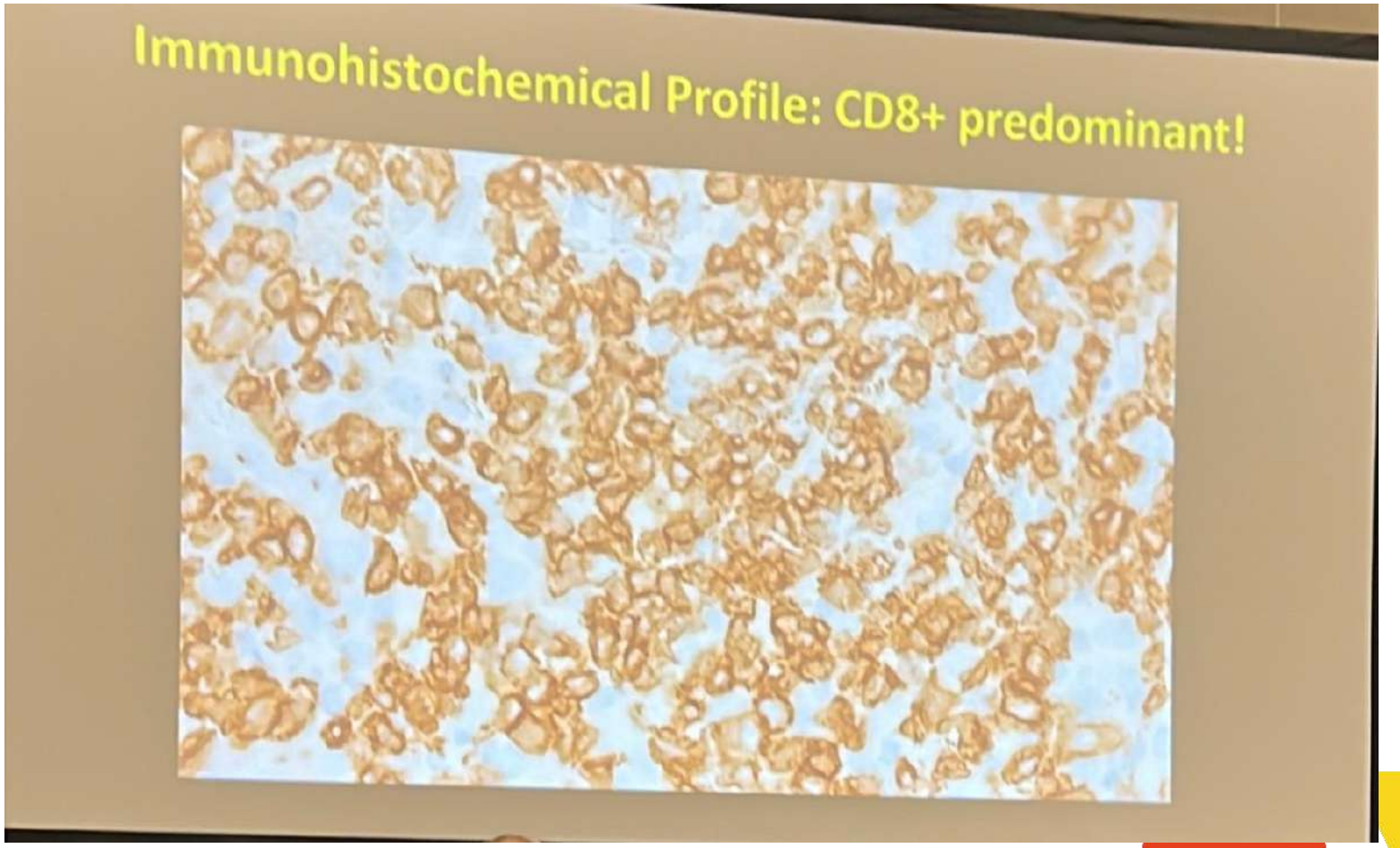
Rubéola y granulomas

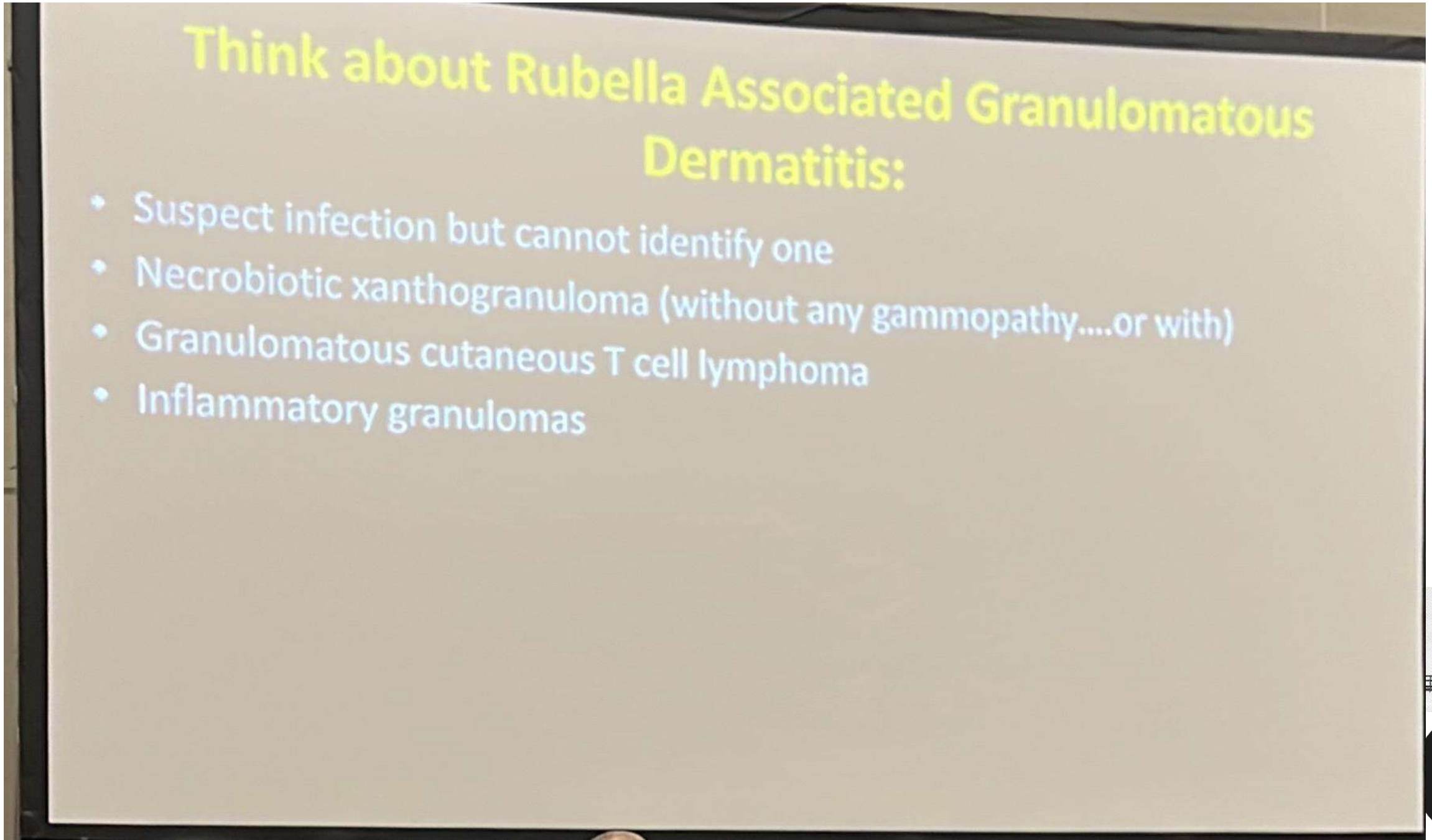


Results: Histopathologic Features

Characteristic	Rubella Positive	Rubella Negative
Lymphocytes, non-brisk	5% (1/22)	50% (5/10)
Lymphocytes, brisk	**95% (21/22)**	**40% (4/10)**
Neutrophils	**91% (20/22)**	**0% (0/10)**
Eosinophils	41% (9/22)	20% (2/10)
Plasma cells	**82% (18/22)**	**50% (5/10)**
Necrosis	**50% (11/22)**	**0% (0/10)**
Fibroplasia	86% (19/22)	30% (3/10)

Rubéola y granulomas




Think about Rubella Associated Granulomatous Dermatitis:
• Suspect infection but cannot identify one
• Necrobiotic xanthogranuloma (without any gammopathy....or with)
• Granulomatous cutaneous T cell lymphoma
• Inflammatory granulomas

AAD **ANNUAL** MEETING **2025**

AEDV 7 - 11 MARZO ORLANDO

highlights

Casos clínicos

Viernes 7 Marzo

Una iniciativa de:

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

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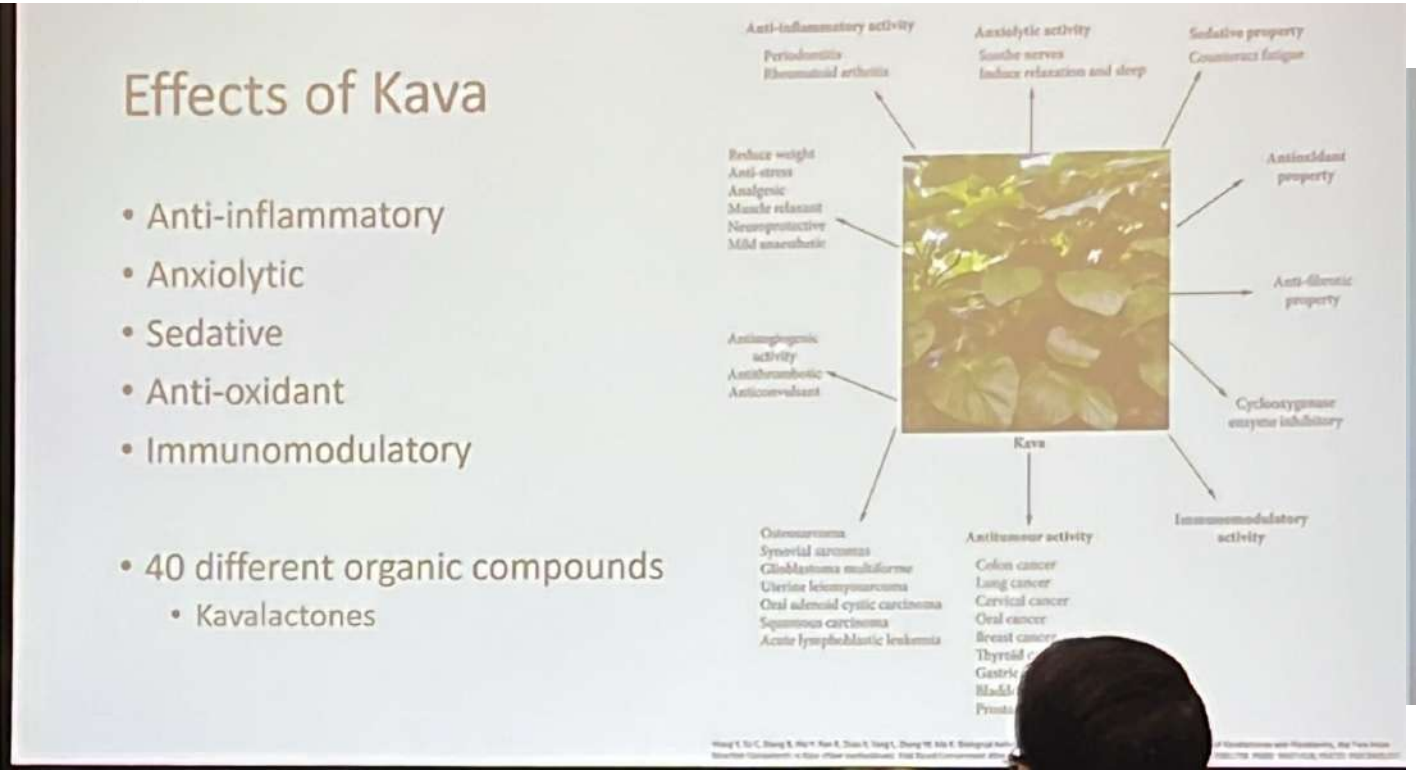
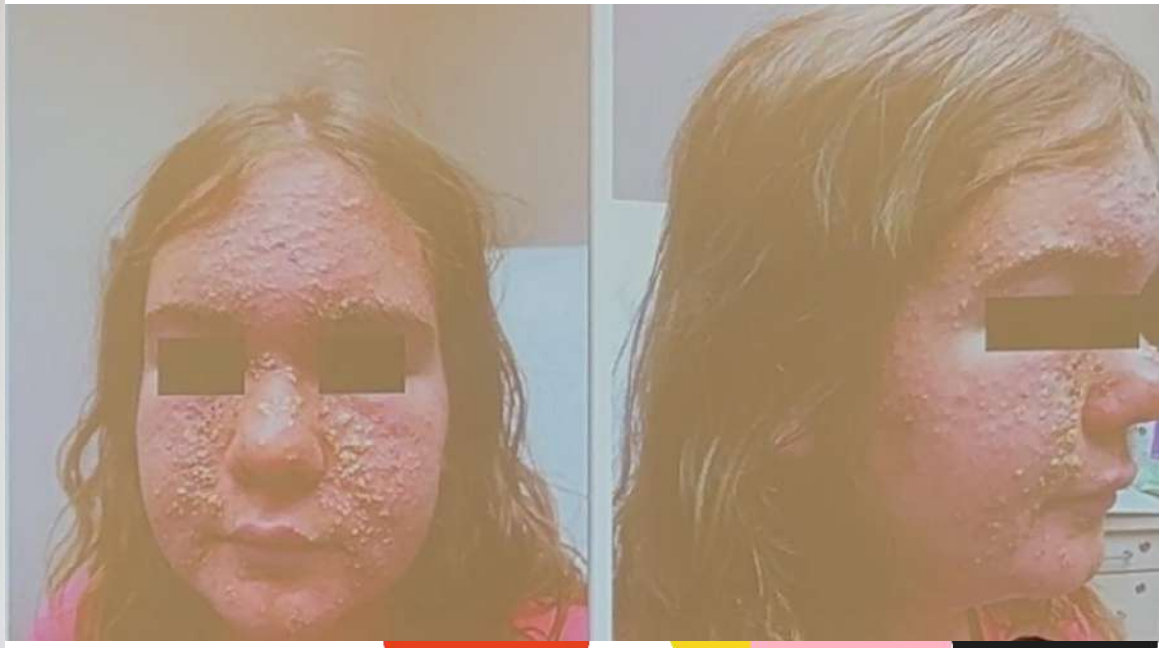
Con el patrocinio de:

ucb

Erupciones cutáneas por Kava

- Kava es un suplemento derivado de una planta originaria de las islas occidentales del Pacífico (Piper methysticum), que se consume normalmente como bebida para proporcionar efectos relajantes, analgésicos y ansiolíticos





Erupciones cutáneas por Kava

Kava Eruptions: Clinical features

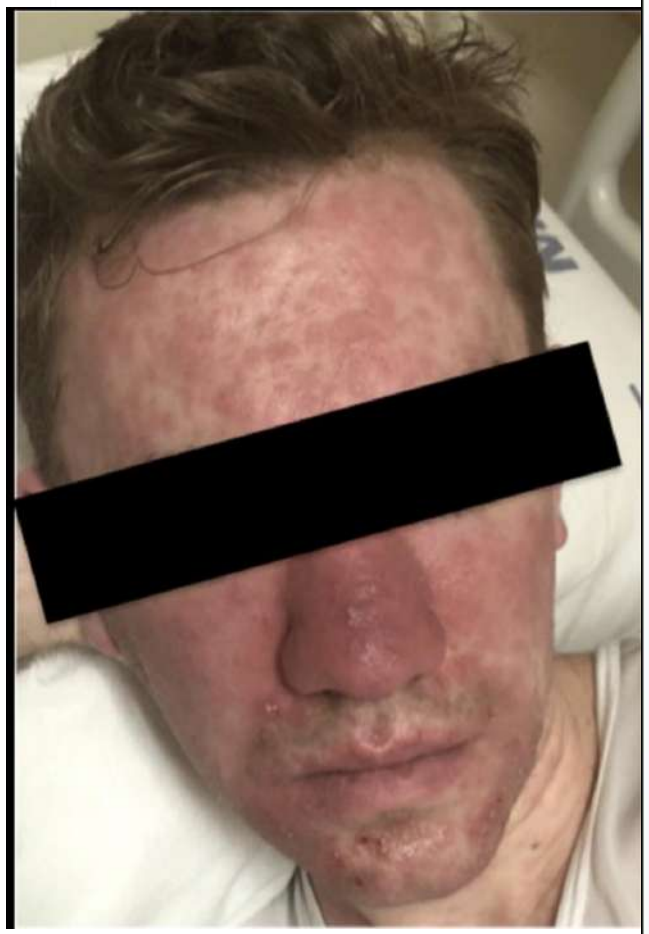
- Chronic ichthyosiform eruption
  - Reversible ichthyosiform pellagroid dermop
  - More common in Pacific Islands
- Sebotropic
  - Rapid onset ~2 weeks
- Dermatomyositis-like eruption
- Urticaria
- SJS

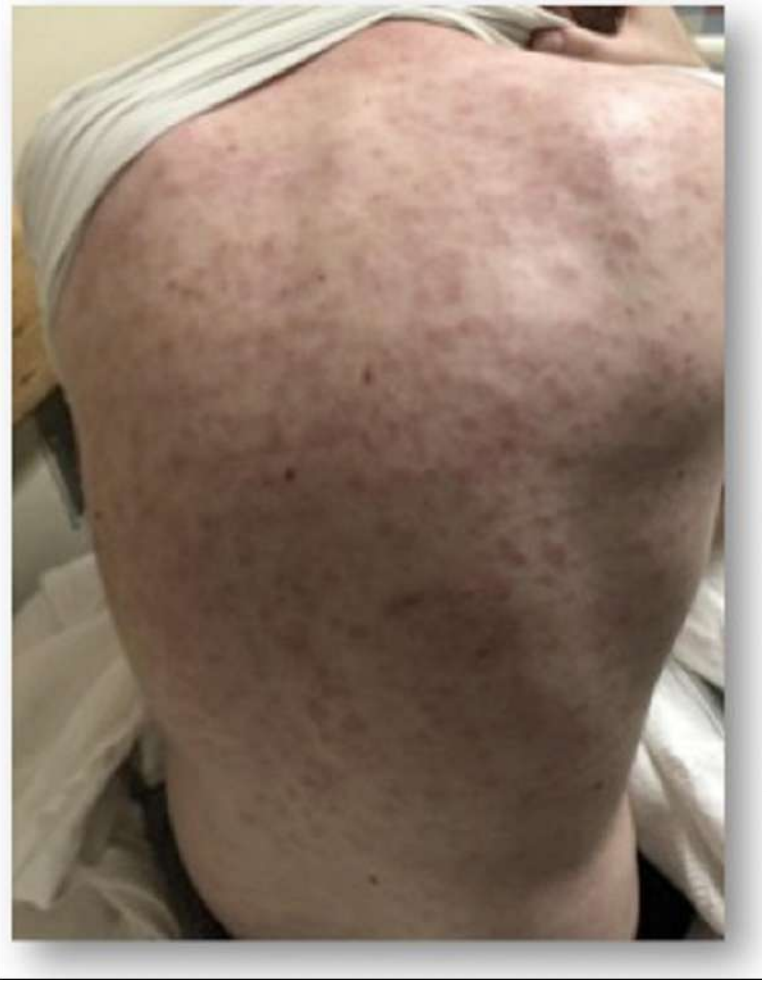
Toxic alkaloids in leaves

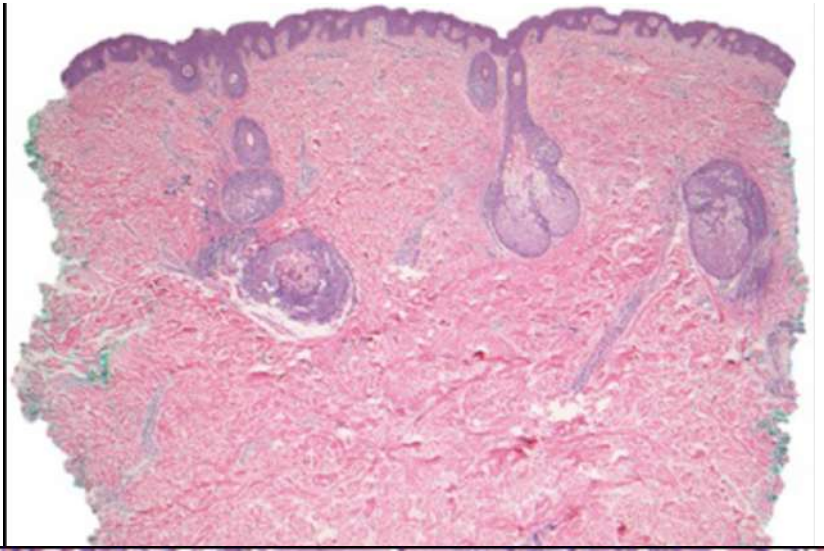
Synthetic kavain and mycotoxins present in the kava root when not consumed fresh

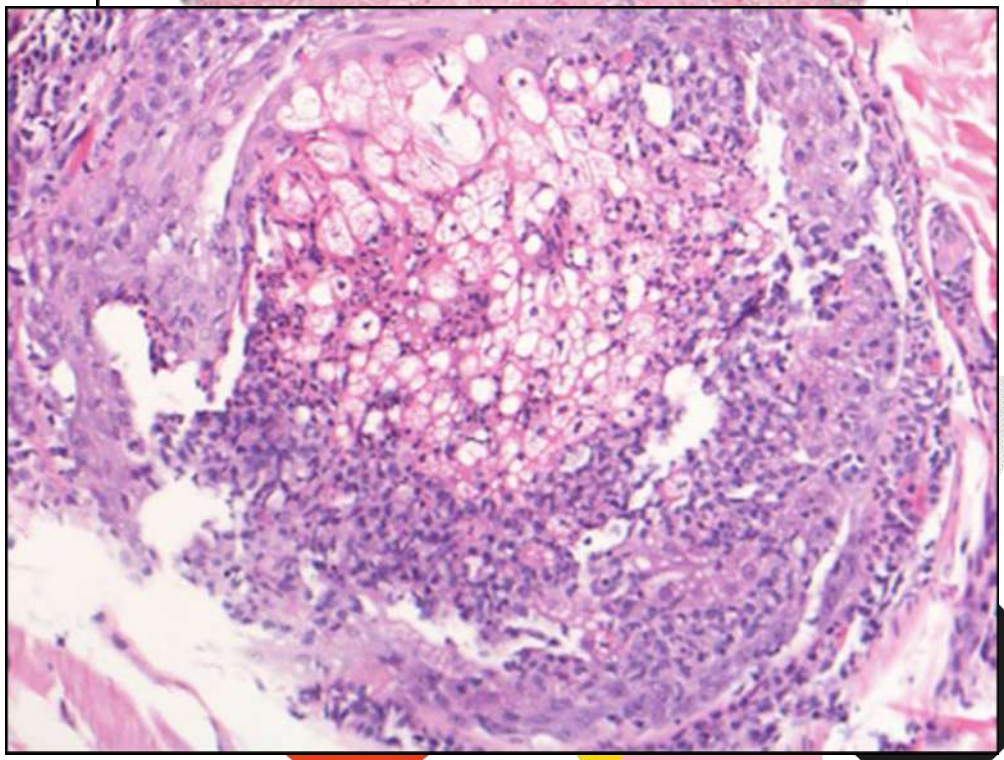
Erupciones cutáneas por Kava

Sebotrópica:









Rzepecki AK, Wald J, Amin B, Leung E, Choi E, Balagula Y. Kava-induced acute cutaneous toxicity: An increasingly recognized characteristic clinicohistologic pattern. *JAAD Case Rep*. 2018;4(10):1037-1038.

Erupciones cutáneas por Kava

Sebotrópica:

- Infiltrado inflamatorio folicular y perifolicular que afecta toda la unidad pilosebácea
- Predominio de neutrófilos con algunas células mononucleares y eosinófilos también presentes

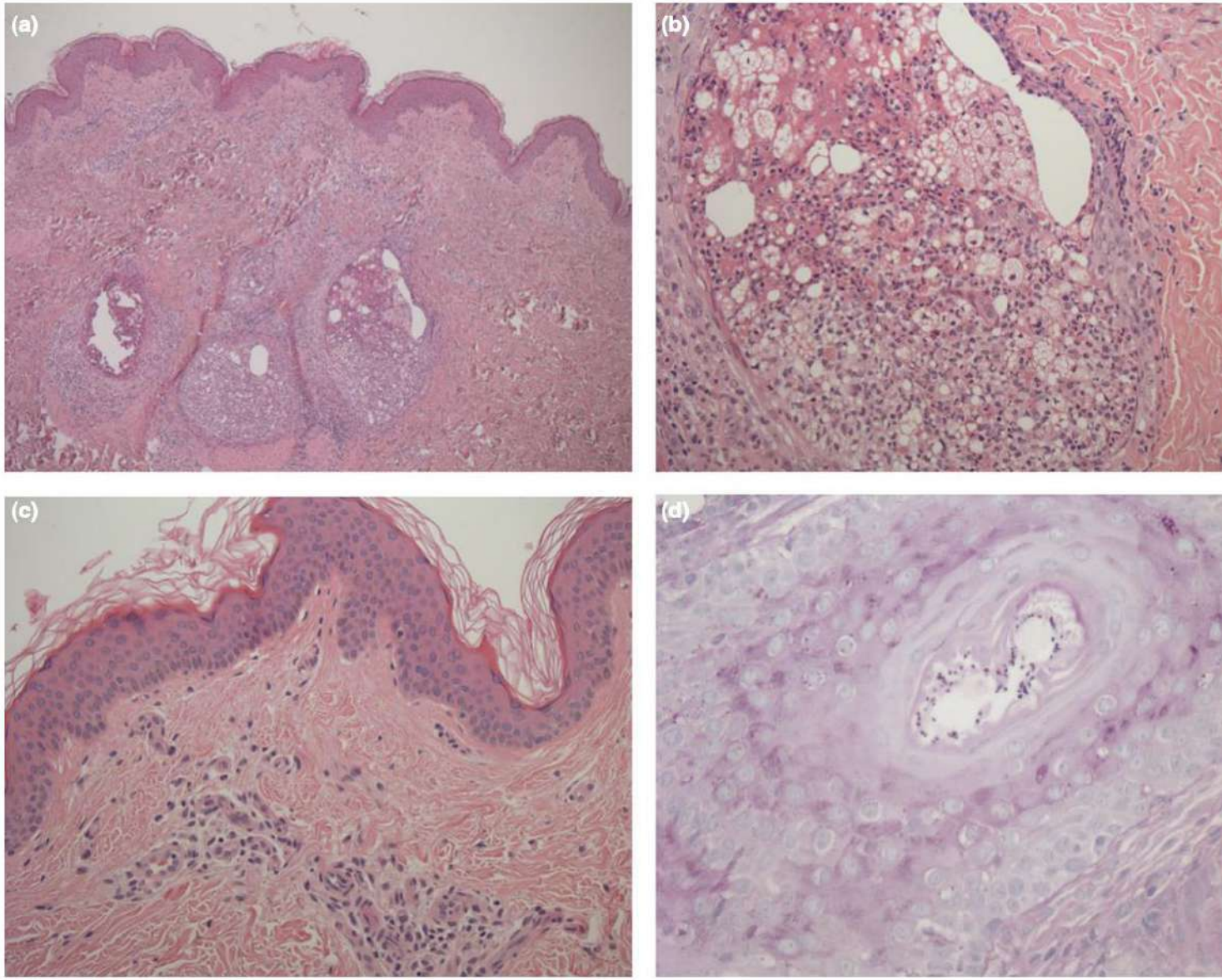


Figure 2 (a) Mixed follicular and perifollicular inflammatory infiltrate affecting the whole pilosebaceous unit, rich in neutrophils, some mononuclear cells and eosinophils also present. (b) Folliculocentric inflammation. (c) Mild perivascular lymphocytic infiltrat present in the dermis with an unremarkable epidermis. Haematoxylin and eosin, original magnification (a) × 2.5; (b) × 10; (c) (d) Fungal spores were visible, although these may have been commensal (periodic acid–Schiff × 20).

Rzepecki AK, Wald J, Amin B, Leung E, Choi E, Balagula Y. Kava-induced acute cutaneous toxicity: An increasingly recognized characteristic clinicohistologic pattern. *JAAD Case Rep*. 2018;4(10):1037-1038. Published 2018 Nov 10. doi:10.1016/j.jdcr.2018.08.011

Erupciones cutáneas por Kava

Calcinosis cutis y necrólisis epidérmica

Healing retardation of epidermal necrolysis due to calcinosis cutis

Calcinosis cutis probably related to caspofungin intake

Between 2015 and 2021:

- 4 patients who presented with TEN and atypical healing retardation due to calcinosis cutis
- 3 M/1 F, aged from 40 to 59 YO (idiopathic, ibuprofen, pantoprazole, allopurinol)
- 3 to 22 days after the beginning of cutaneous healing: secondary cutaneous detachment with atone plaques
- 1 patient died without healing, complete healing was slowly obtained within 5.5 and 11 months for the other patients

The 4 patients were treated with caspofungin for invasive fungal infection to *Candida parapsilosis, Candida lusitaniae, Candida albicans* or non-documented septic shock 1-8 days before the secondary epidermal detachment

JEADV JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

Letter to the Editor | Full Access

Calcinosis cutis in epidermal necrolysis: role of caspofungin?

H. Colboc, T. Bettuzzi, M. Badrignans, D. Bazin, A. Boury, E. Letavernier, V. Frochot, E. Tang, P. Moguelet, N. Ortonne, N. de Prost, S. Ingen-Housz-Oro

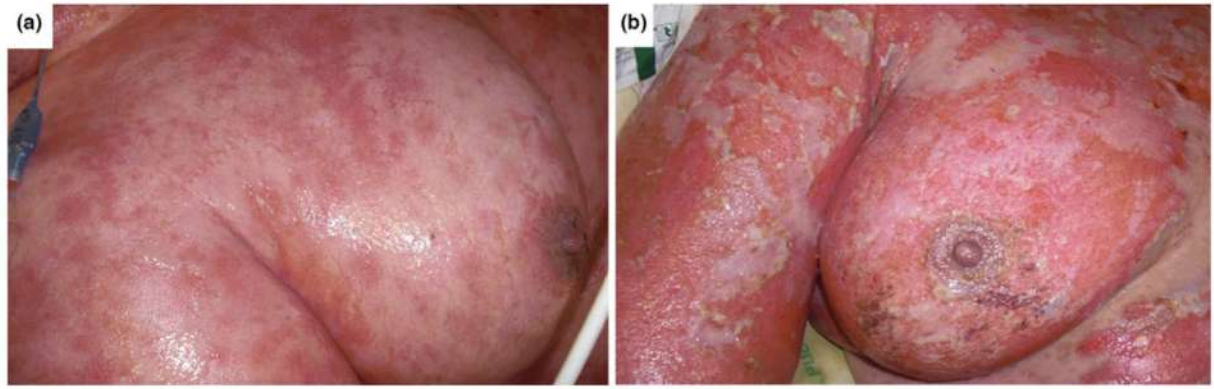


Figure 1 Clinical presentation of one patient. (a) Dermatological examination on day 12, revealing almost complete mucocutaneous healing. (b) Dermatological examination on day 29, 11 days after the introduction of caspofungin, revealing diffuse epidermal detachment associated with the presence of fibrinous plaques.

Calcinosis cutis y necrólisis epidérmica

- Deposito de calcio en epidermis y dermis superficial

Physiopathology :

Caspofungin = **agonist of ryanodine receptor (RyR),** strongly expressed in keratinocytes

→ modification of keratinocytes'calcium intracellular concentration,

→ alteration of the new keratinocytes at the very initial stage of cutaneous healing,

→ explaining the presence of upper dermis and epidermal calcifications

→ and *the relapse of epidermal detachment followed by a major healing retardation*

Calcinosis cutis in epidermal necrolysis: role of caspofungin?

Take-home message

Liposomal amphotericin B or fluconazole might, therefore, be preferred for patients with TEN in case of invasive fungal infection

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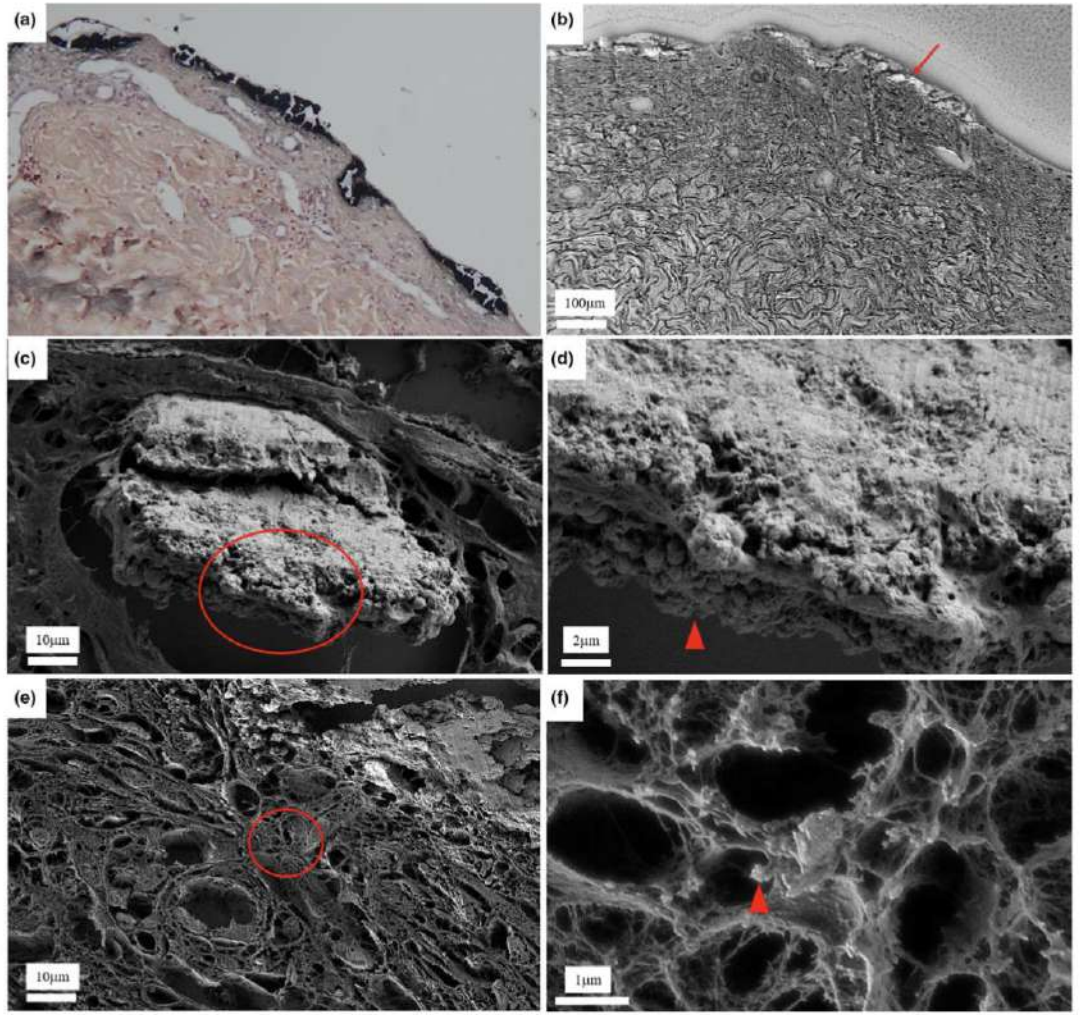
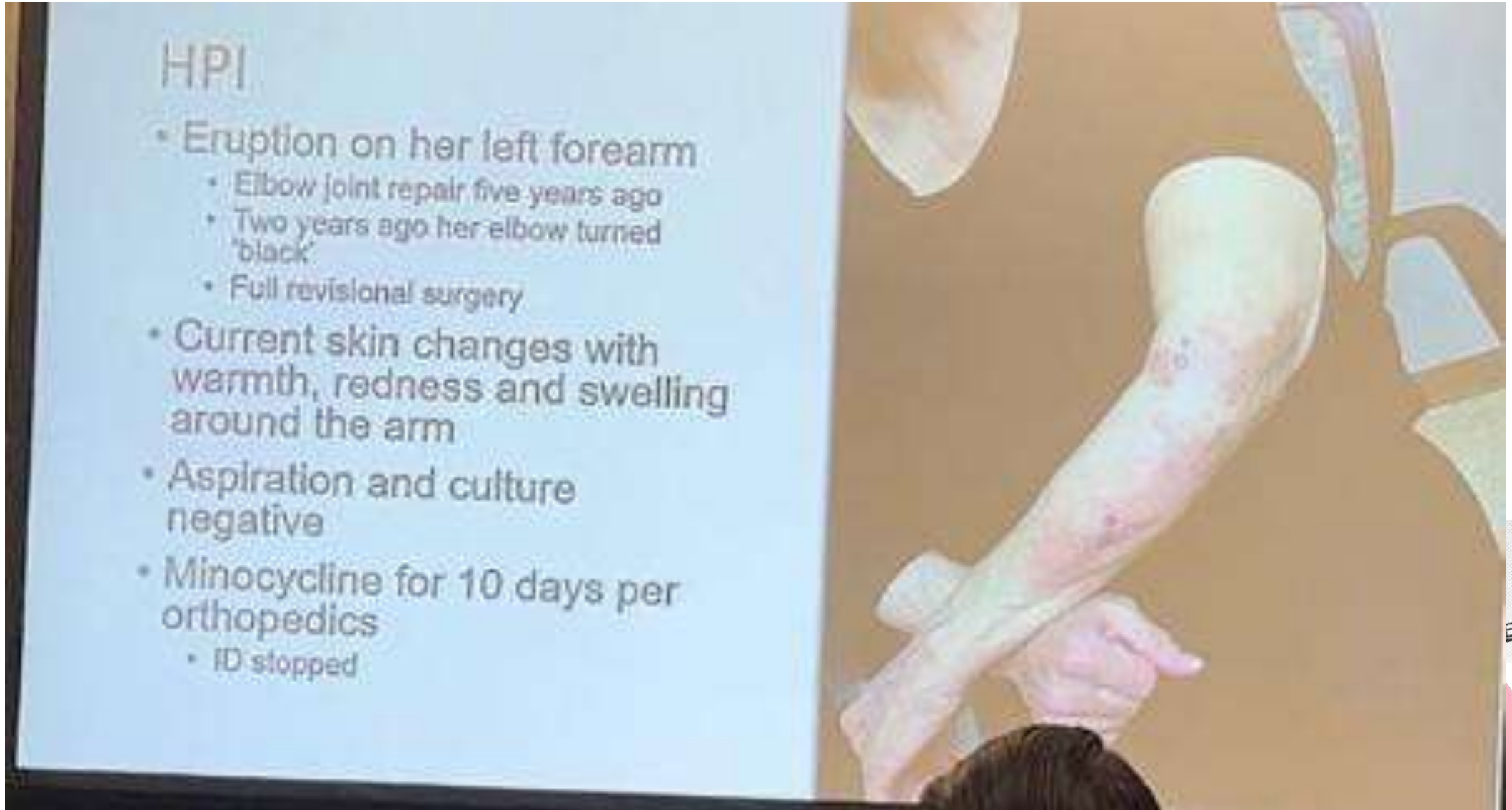


Figure 2 Skin biopsy sections. Diffuse necrosis of the corneal layer associated with calcium deposition in the superficial dermis. (a) Von Kossa staining (×100). (b) Field emission scanning electron microscopy. Arrow indicates the voluminous calcifications. (c–f) Field emission scanning electron microscopy. (c) The lower part of the voluminous calcification (circle) consists of many small aggregated spherical entities. (d) High magnification of panel (c) circled area. (e) Papillary dermis below voluminous calcification. (f) High magnification of panel (e) circled area, showing many spherical calcifications within the papillary dermis.

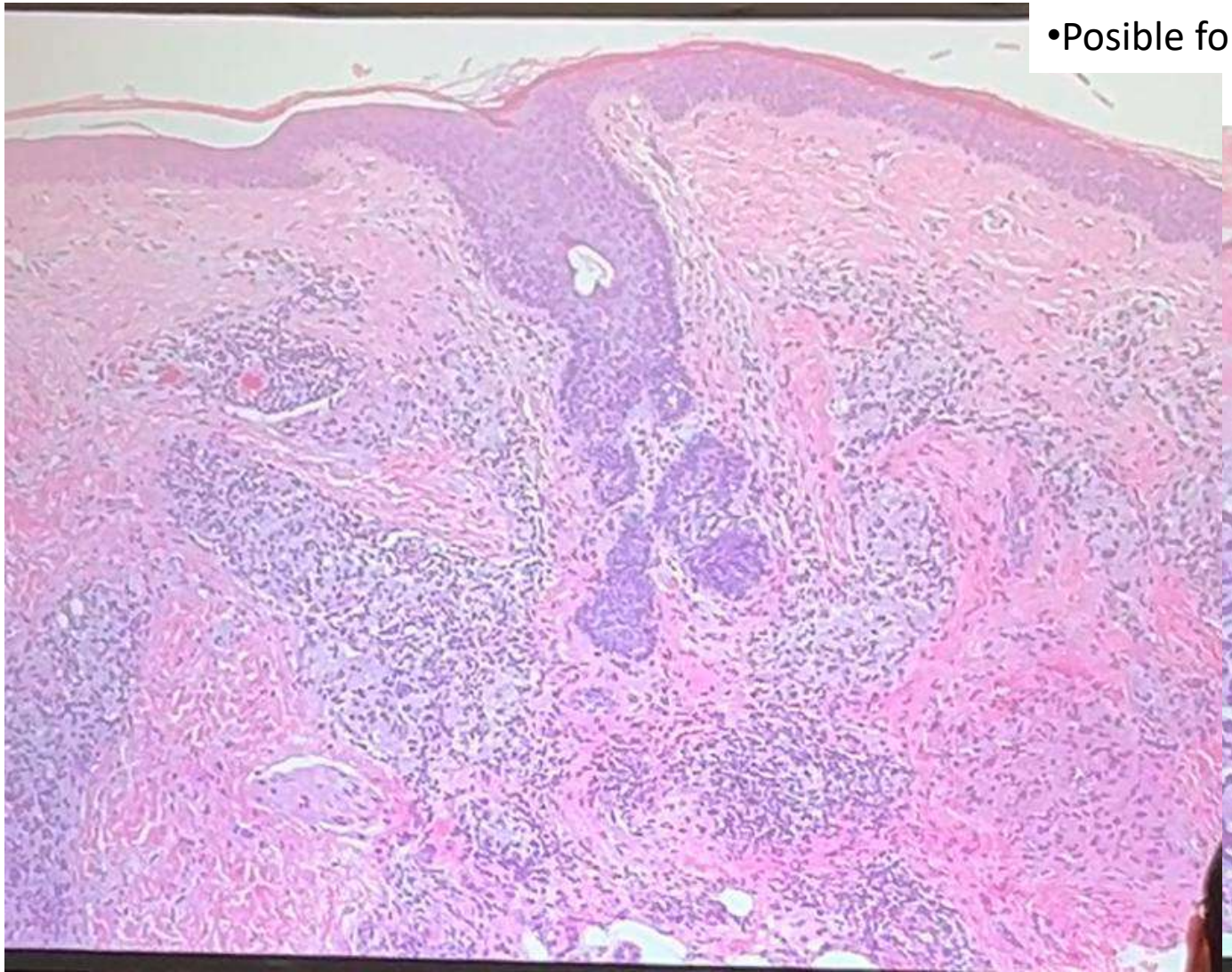
Metalosis cutánea

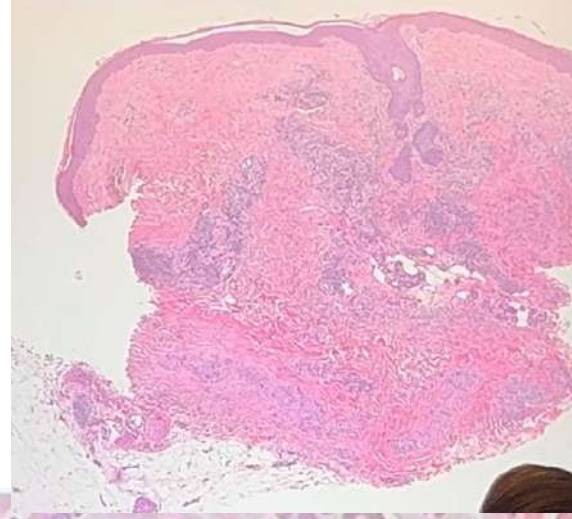


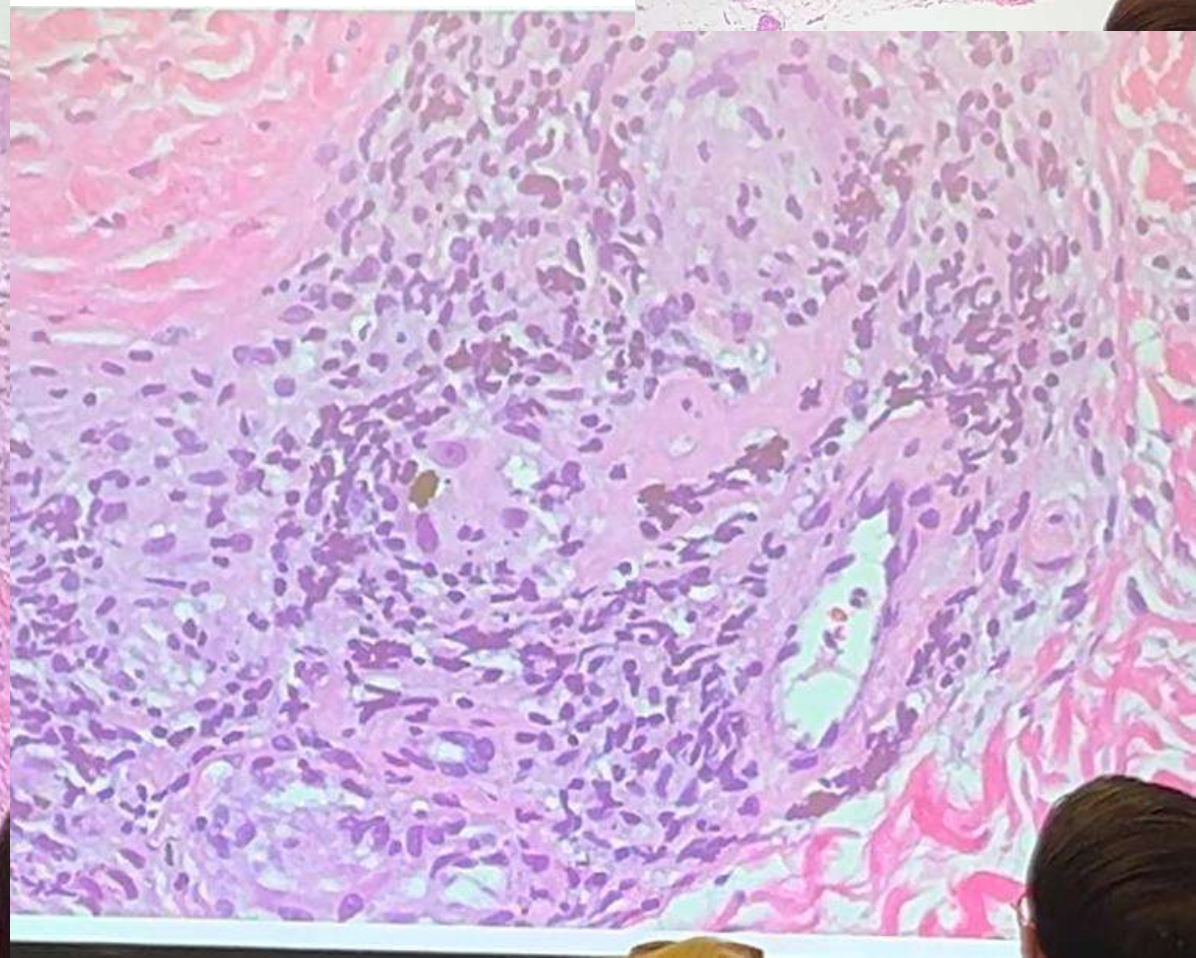
Metalosis cutánea

Metalosis Cutánea: Características Histopatológicas

- Gránulos de pigmento exógeno negro
- Intra y extracelular
- Infiltrado linfohistiocítico
- Posible formación de granulomas







Metalosis cutánea

- Rare manifestation of metallosis complicating joint arthroplasty
- 13 case reports of skin involvement
- Fracture of ceramic liner
- Deposits of titanium alloy or cobalt-chromium alloy

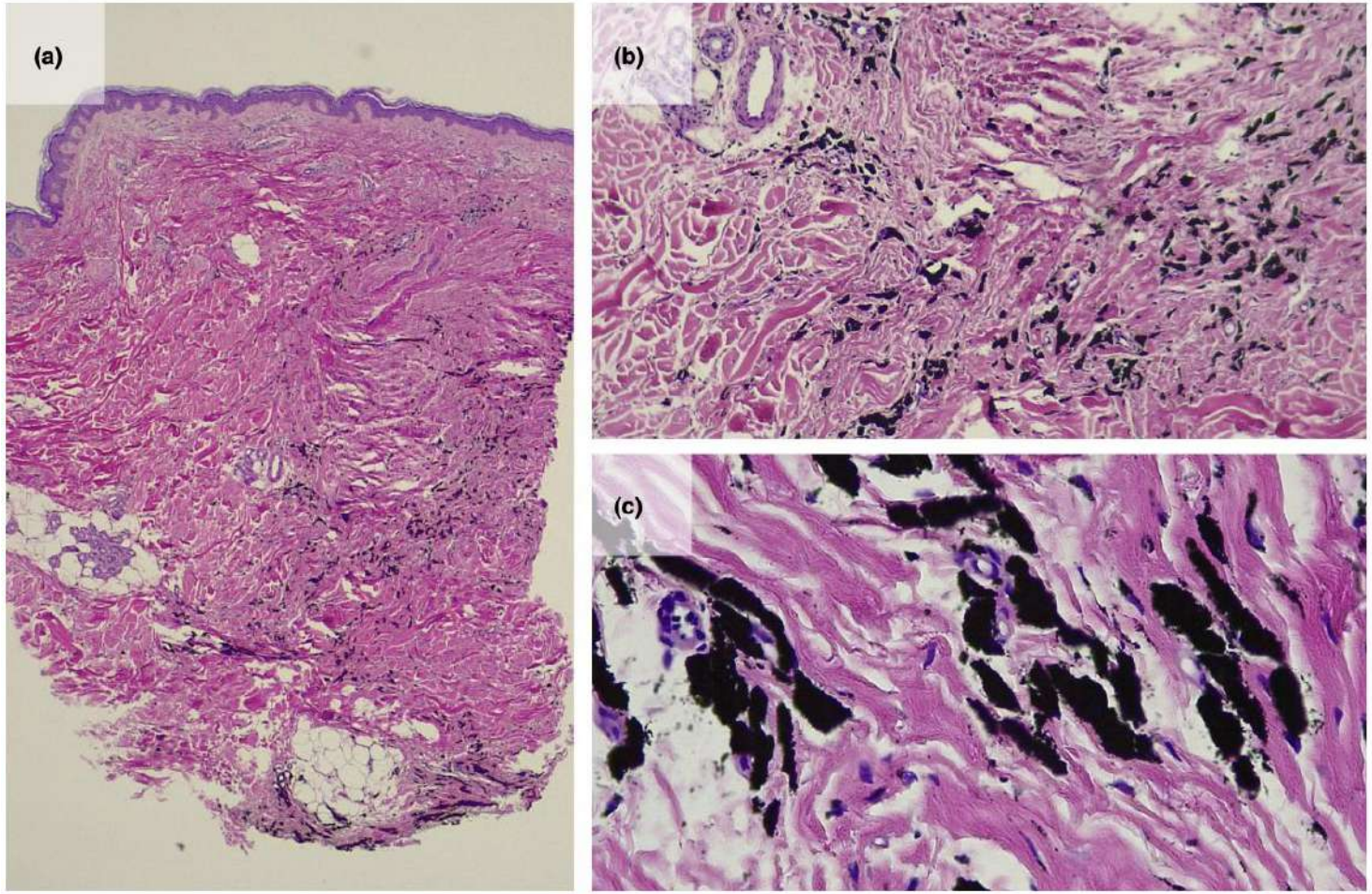


Figure 2 (a–c) Punch biopsy sample from the blue–grey skin over the the replaced joint, showing (a) black pigment in reticular dermis and subcutaneous tissues, and (b,c) interstitial black pigment with minimal inflammatory infiltrate. Haematoxylin and eosin, original magnification (a) × 2.5; (b) × 10; (c) × 40.

Moreno-Vílchez C, Fornons-Servent R, Penin RM, Cabo J, Jucglà A. Black cutaneous discharge: think metallosis. *Clin Exp Dermatol*. 2021;46(6):1135-1136

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highlights

¡Muchas gracias!

Una iniciativa de:

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

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