
AAD ANNUAL MEETING
AEDV
highlights
SAN DIEGO
8-12 MARZO
#AEDVENAAD2024
AEDV
1909
ACADEMIA ESPAÑOLA
DE DERMATOLOGÍA
Y VENEREOLOGÍA

DERMATOPATOLOGÍA

ACADEMIA ESPAÑOLA
DE DERMATOLOGÍA
Y VENEREOLOGÍA

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

AAD ANNUAL MEETING AEDV highlights SAN DIEGO 8-12 MARZO

Highligths en dermatopatología

María Dolores Mendoza Cembranos

Hospital Universitario Fundación Jiménez Díaz

dolores.mendoza@quironsalud.es

ACADEMIA ESPAÑOLA
DE DERMATOLOGÍA
Y VENEREOLOGÍA

AAD ANNUAL MEETING
AEDV highlights

SAN DIEGO
8-12 MARZO

NO TENGO CONFLICTOS DE INTERÉS para esta presentación

Sessiones resumidas

AAD ANNUAL MEETING AEDV highlights

SAN DIEGO 8-12 MARZO

U013 - Biopsies in Challenging Locations: a Review for the General Dermatologist

- Director: Amrit Greene, MD, FAAD
- Speakers: Molly A. Hinshaw, MD, FAAD; Kimberly Marie Ken, MD, FAAD

Description: Histopathologic evaluation has remained the gold standard for diagnosis of cutaneous disease from inflammatory conditions to neoplasias. There are several areas of the body that can be more challenging to obtain biopsy specimens. The purpose of this session is to review biopsy techniques in challenging anatomic locations such as the eyelid, oral mucosa and nails/soles for general dermatologists who want to become more comfortable working in these locations. Relevant anatomy will be reviewed as well as tips on anesthesia and appropriate surgical tools to yield the best biopsy results.

- Friday, March 8 | 7:30 AM - 8:30 AM
- Room 6F

F005 - Dermatopathology Case Challenge: Recognizing Mimics and Masqueraders

- Director: Rosalie Elenitsas, MD, FAAD
- Speakers: Tammie C. Ferringer, MD, FAAD; Alexandra Flamm, MD, FAAD; Kevin John Gaddis, MD, FAAD; Ronald P Rapini, MD, FAAD; Michi Shinohara, MD, FAAD

Description: Diagnostic mimics in dermatology and dermatopathology pose a potential pitfall in the accurate diagnostic interpretation of patient biopsies. This session intends to provide dermatopathologists, dermatologists, and those in training with enhanced awareness of both common and novel mimics that may be encountered in dermatopathology practice. An interactive case-based format will be utilized and speakers will describe masqueraders that they have faced, ancillary tools employed, and the lessons learned in reaching the correct interpretation. Dermatopathologists in a busy practice may not readily recognize entities that can serve as mimics. This may result in non-intentional diagnostic errors and delay of appropriate patient treatment.

- Friday, March 8 | 9:00 AM - 11:00 AM
- Room 3

F016 - Complex Medical Dermatology: Clinicopathologic Correlation

- Director: Daniela Kroshinsky, MPH, MD, FAAD
- Speakers: Adela Rambi G. Cardones, MD, FAAD; Allison Dobry, MD, FAAD; Stephanie Gallitano, MD, FAAD; Joanna L. Harp, MD, FAAD; Christopher Iriarte, MD, FAAD; Melodi Whitley, MD, PhD, FAAD; Scott Worswick, MD, FAAD

Description: This session will utilize a case-based format with biopsy review to present complex dermatologic scenarios. Through discussion of clinical and histologic clues, a differential diagnosis will be formulated and processed to reach a definitive diagnosis. This forum will provide dermatologists and dermatopathologists with a review and update of important skin disorders while highlighting the value of a collaborative and rewarding relationship between the dermatologist and dermatopathologist within the hospital setting. Available and emerging treatment options for these challenging conditions will also be reviewed.

- Friday, March 8 | 1:00 PM - 3:00 PM
- Room 29B

Saturday March 9th

S039 - What's New in Dermatopathology

- Director: Jeffrey P. North, MD, FAAD
- Speakers: Emily Y. Chu, MD, PhD, FAAD; Julia S. Lehman, MD, FAAD; Kiran Motaparthi, MD, FAAD; Anisha Patel, MD, FAAD; Michelle B Tarbox, MD, FAAD; Karolyn Wanat, MD, FAAD; Iwei Yeh, MD, PhD, FAAD

Description: This symposium provides information regarding advances in key areas of dermatopathology. Cutaneous neoplasia, inflammatory skin disease, dermoscopy, molecular techniques, translational research, and cutaneous infections will be covered. Attendees will leave the session with updated knowledge in dermatopathology.

- Saturday, March 9 | 1:00 PM - 4:00 PM
- Room 28B

Sessiones resumidas

AAD ANNUAL MEETING AEDV highlights

SAN DIEGO 8-12 MARZO

F073 - Transformation of Dermatology through Digital Dermatopathology: Practice Opportunities and Challenges

- Director: Olayemi Sokumbi, MD, FAAD
- Co-Director: Nneka I. Comfere, MD, FAAD
- Speakers: Anil Parwani MD; Margot S. Peters, MD, FAAD; Curtis T. Thompson, MD

Description: Innovations in whole slide scanning technology, artificial intelligence and access to big data are resulting in dramatic shifts in the practice of dermatopathology. However, few laboratories are utilizing digital dermatopathology at scale. Our session aims to highlight opportunities and challenges associated with the implementation of digital dermatopathology, algorithms to support dermatopathology diagnosis, 'real-life' scenarios encountered in a fully transformed digital dermatopathology practice, and perspectives reflecting the spectrum of expertise provided by our diverse expert speaker panel.

- Saturday, March 9 | 3:30 PM - 5:30 PM
- Room 25B

Novedades ISDP (cortesía Dra Mar Llamas)

International Society of Dermatopathology

BIOPSIAS EN LOCALIZACIONES ESPECIALES

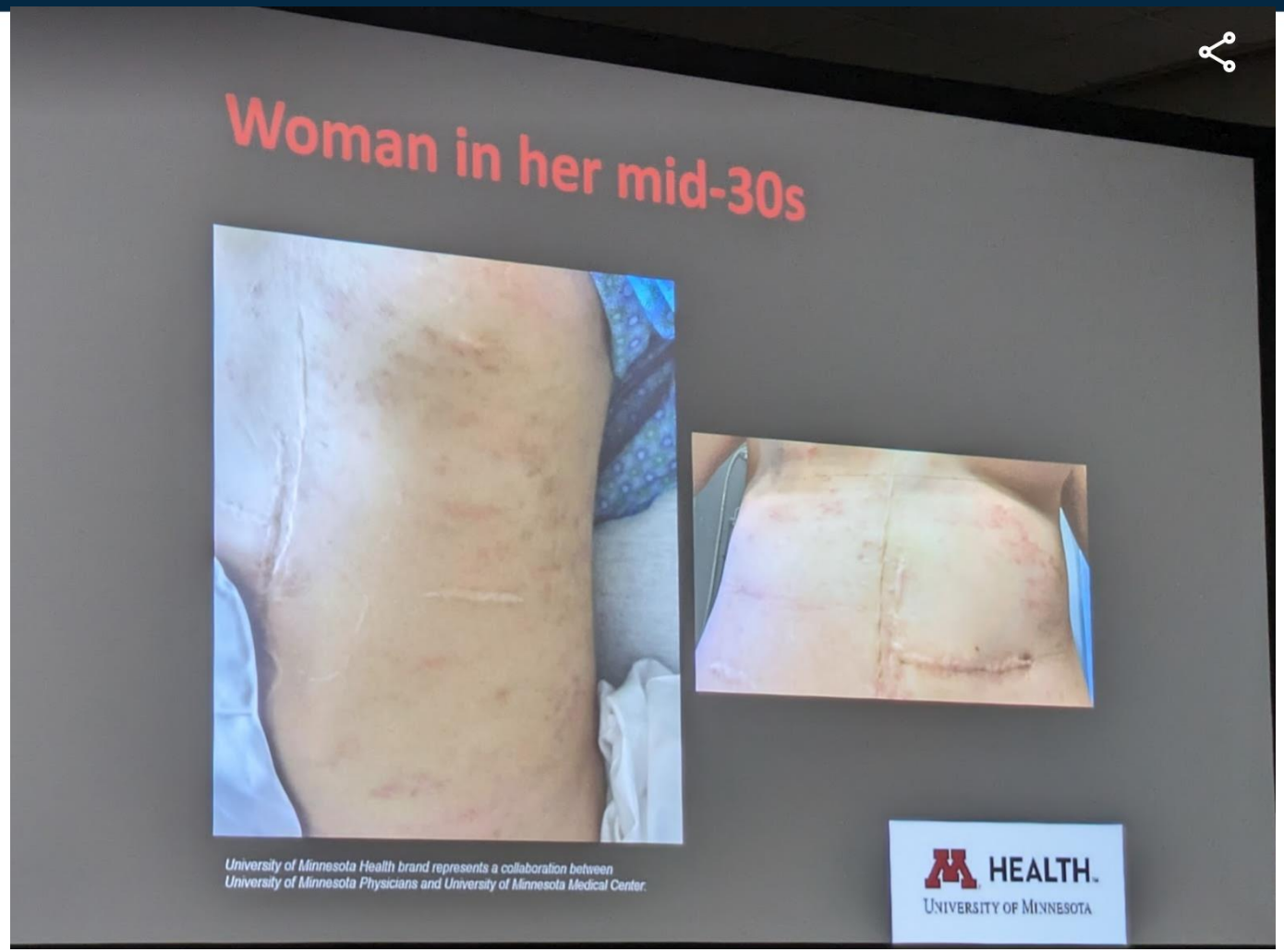
Pre-Operative Exam Guides Surgical Approach

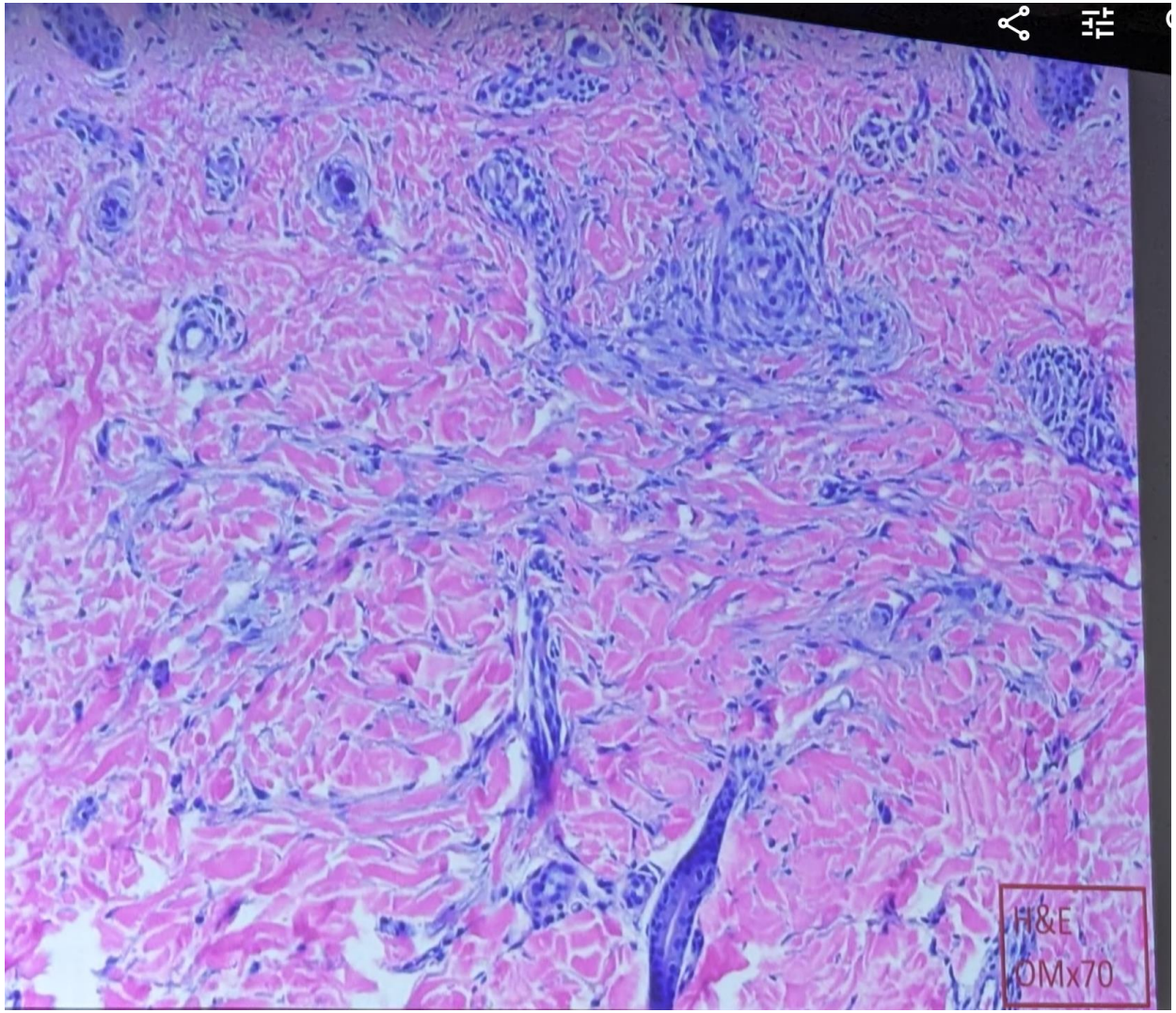
- If avulsion needed, do partial avulsion
- Do not force the avulsion
- Do replace plate
- Delineate erythronychia pre-anesthesia with skin marker; may not be visible post-anesthesia
- Erythronychia typically due to distal matrix +/- bed lesion & longitudinal shave bx is useful
- Longitudinal melanonychia=matrix lesion

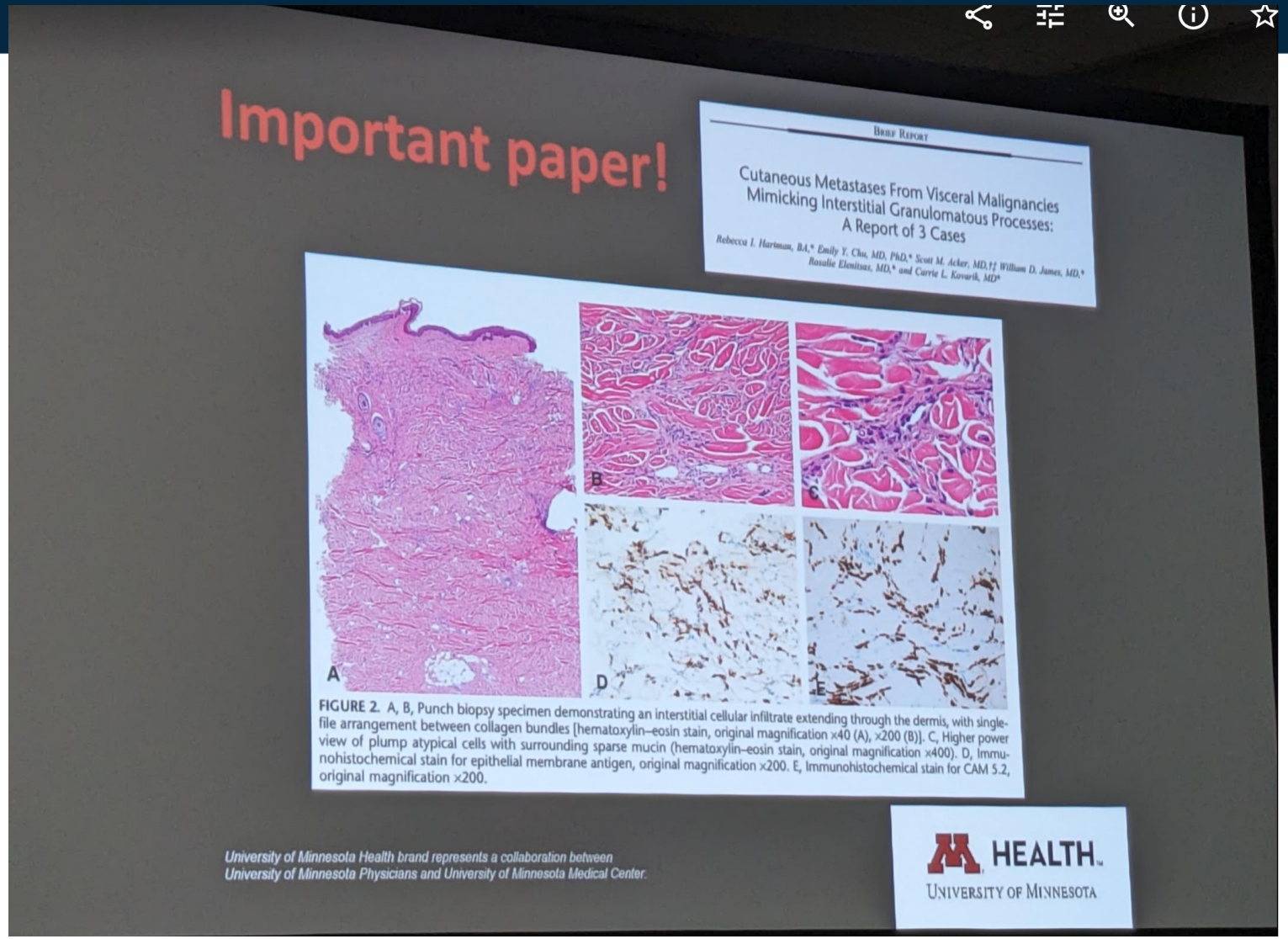
Figure 34-10. (A) Distal partial avulsion. (B) Proximal partial avulsion. (C) Lateral longitudinal partial avulsion. (D) Trap door avulsion. In each instance, the nail plate is freed with a freer elevator, cut transversely with an English anvil nail splitter, and rolled laterally, then replaced after the surgical specimen is harvested. (E) A wide variety of partial avulsion patterns are possible.

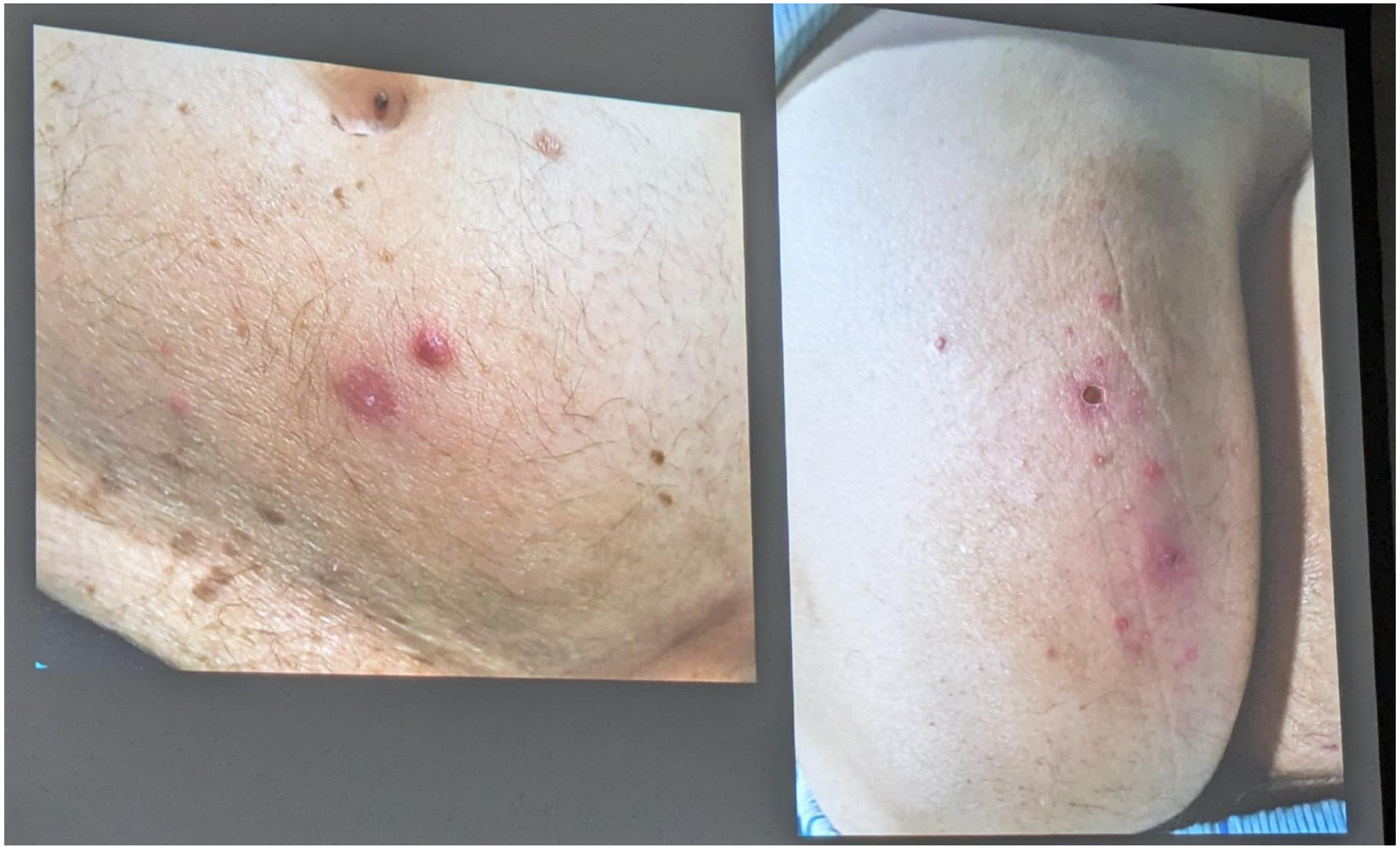
Hinshaw MA, Garrity K, Richert B. Ch. 34 Nail Surgery. In: Dermatologic Surgery. Eds Albertini JG et al. McGraw Hill 2018

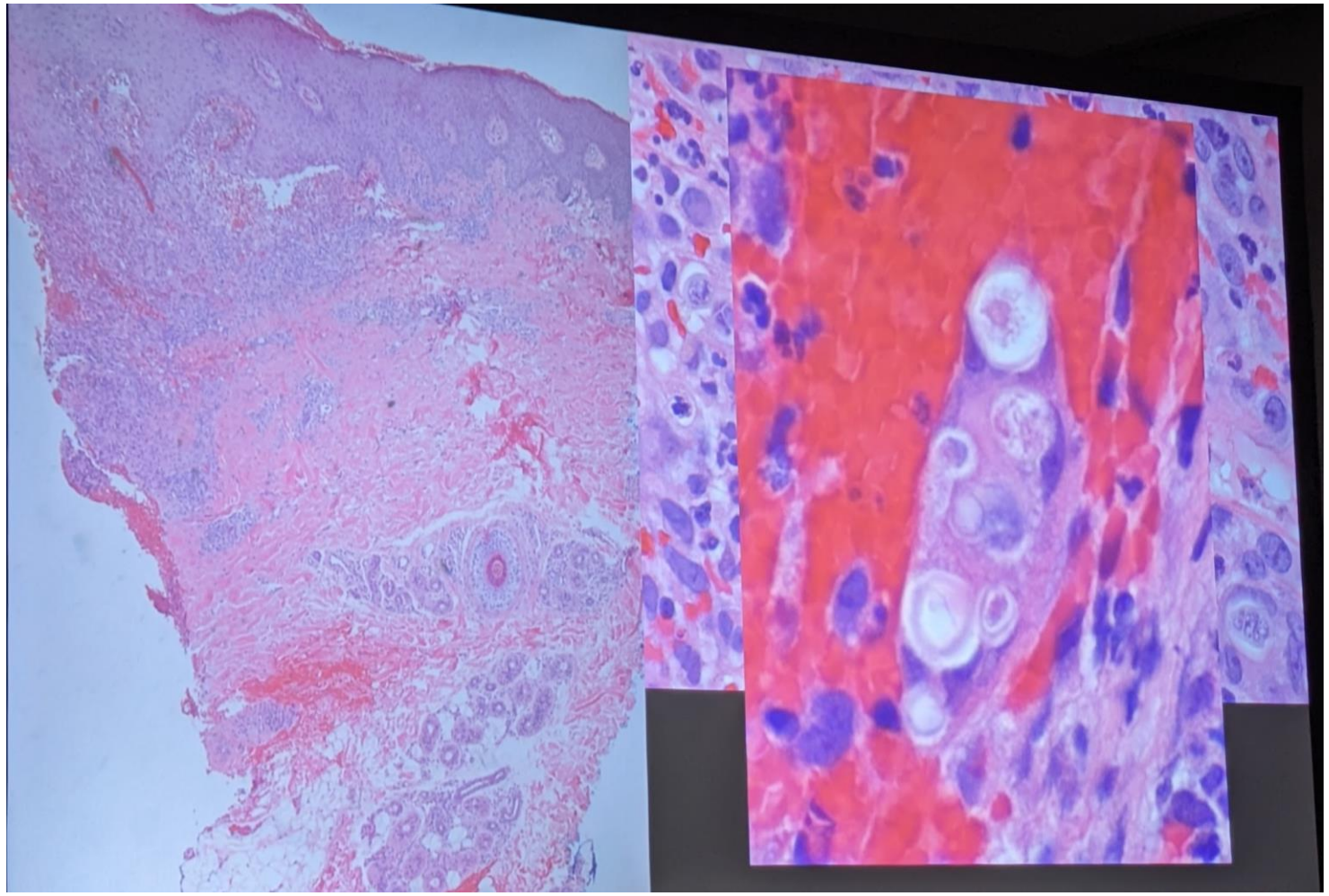
Hematoxilina/eosina frente a IHQ

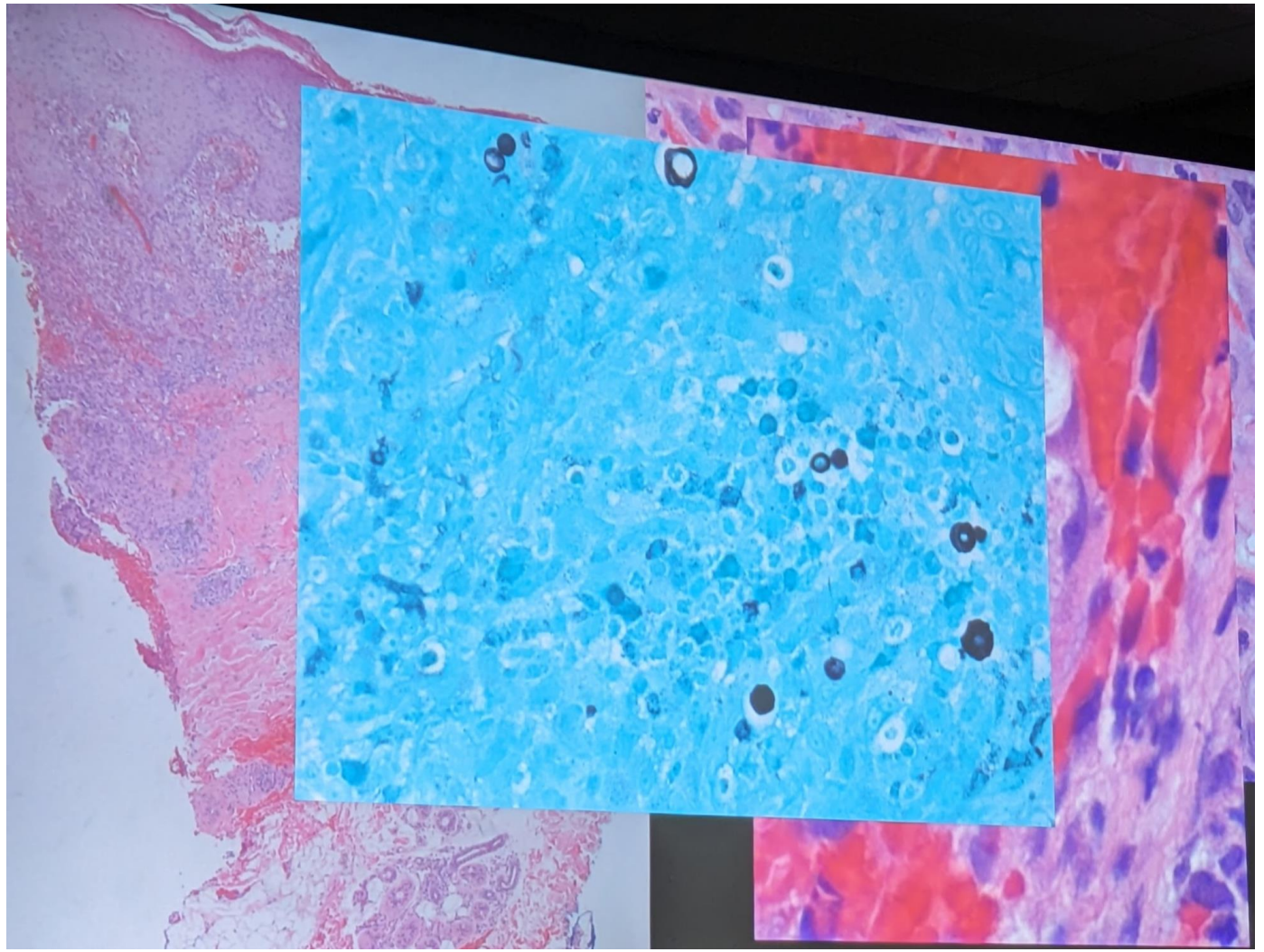

Woman in her mid-30s
University of Minnesota Health brand represents a collaboration between
University of Minnesota Physicians and University of Minnesota Medical Center.
HEALTH
UNIVERSITY OF MINNESOTA

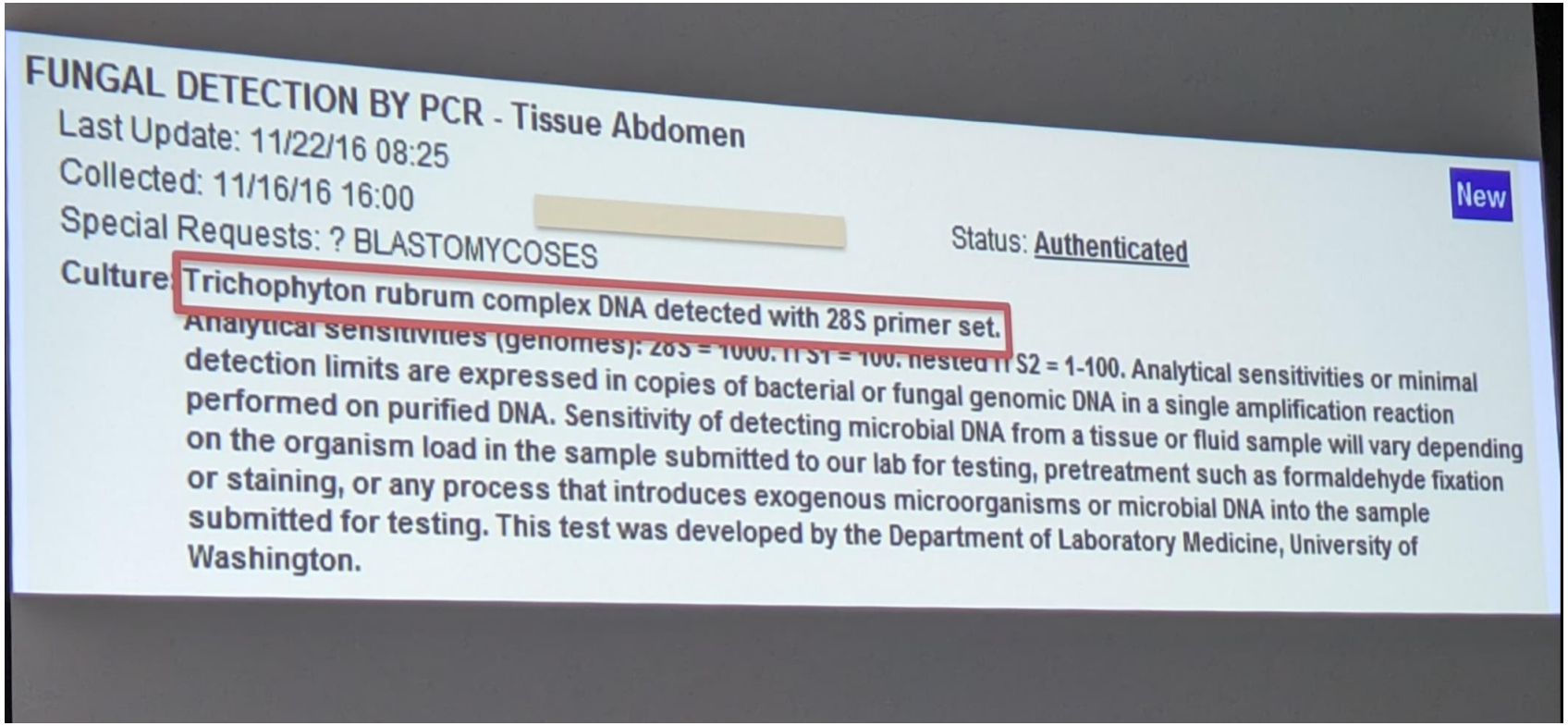

H&E
OMx70

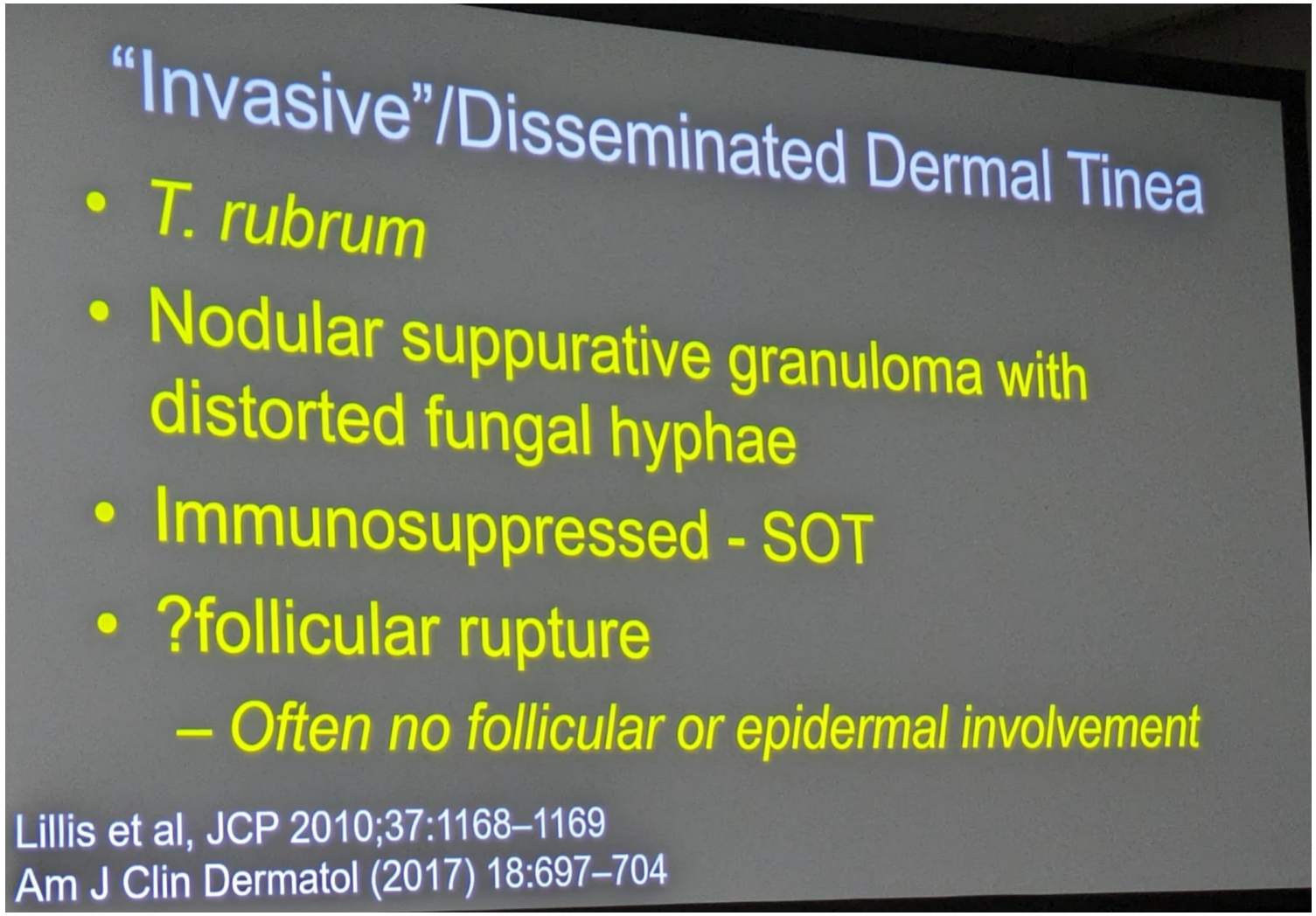

Important paper!
BRIEF REPORT
Cutaneous Metastases From Visceral Malignancies Mimicking Interstitial Granulomatous Processes: A Report of 3 Cases
Rebecca I. Hartman, BA,* Emily Y. Chu, MD, PhD,* Scott M. Acker, MD,†‡ William D. James, MD,* Rosalie Elenitsas, MD,* and Carrie L. Kovarik, MD*
A
B
C
D
E
FIGURE 2. A, B, Punch biopsy specimen demonstrating an interstitial cellular infiltrate extending through the dermis, with single-file arrangement between collagen bundles [hematoxylin–eosin stain, original magnification ×40 (A), ×200 (B)]. C, Higher power view of plump atypical cells with surrounding sparse mucin (hematoxylin–eosin stain, original magnification ×400). D, Immunohistochemical stain for epithelial membrane antigen, original magnification ×200. E, Immunohistochemical stain for CAM 5.2, original magnification ×200.
University of Minnesota Health brand represents a collaboration between
University of Minnesota Physicians and University of Minnesota Medical Center.
HEALTH
UNIVERSITY OF MINNESOTA

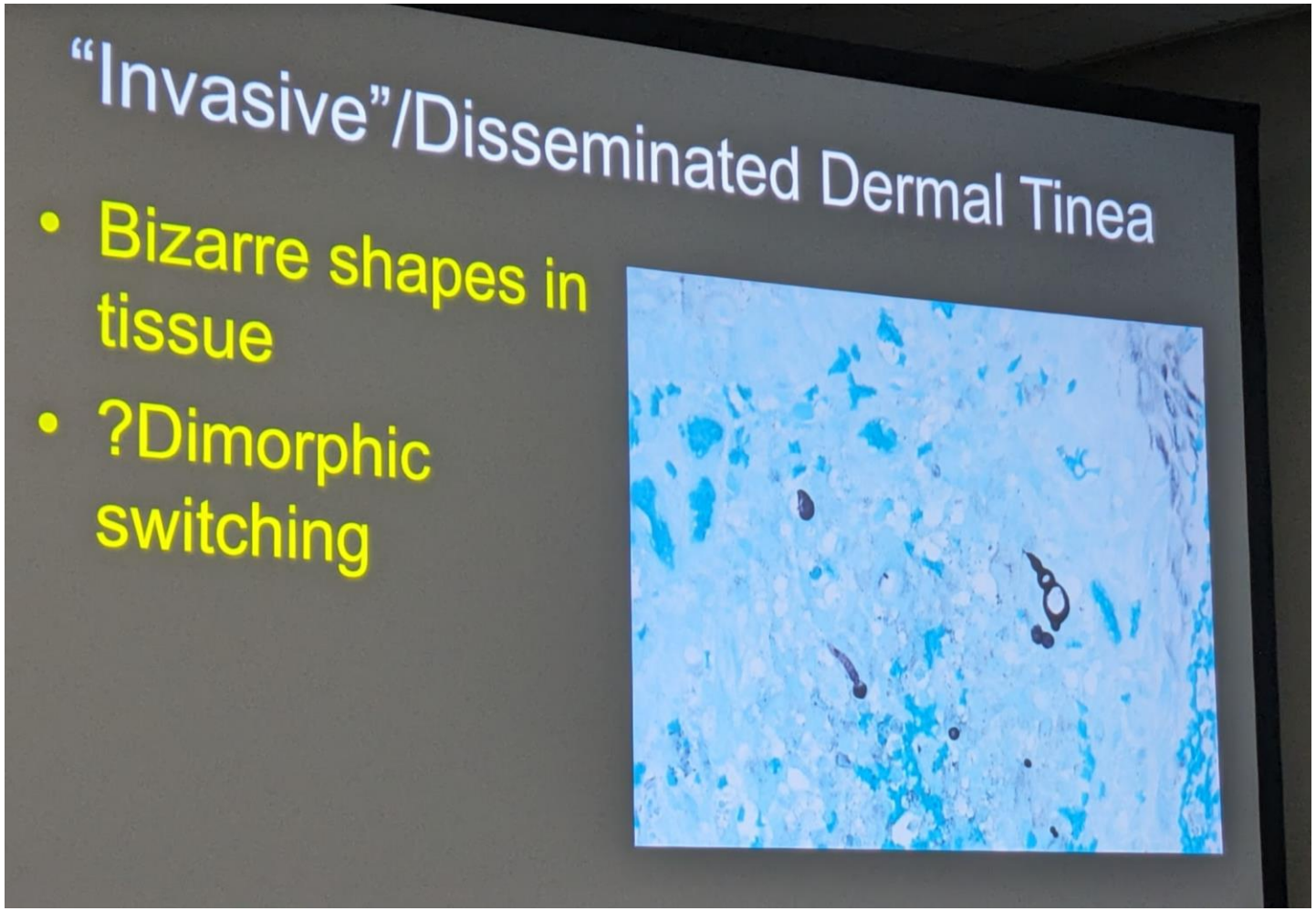


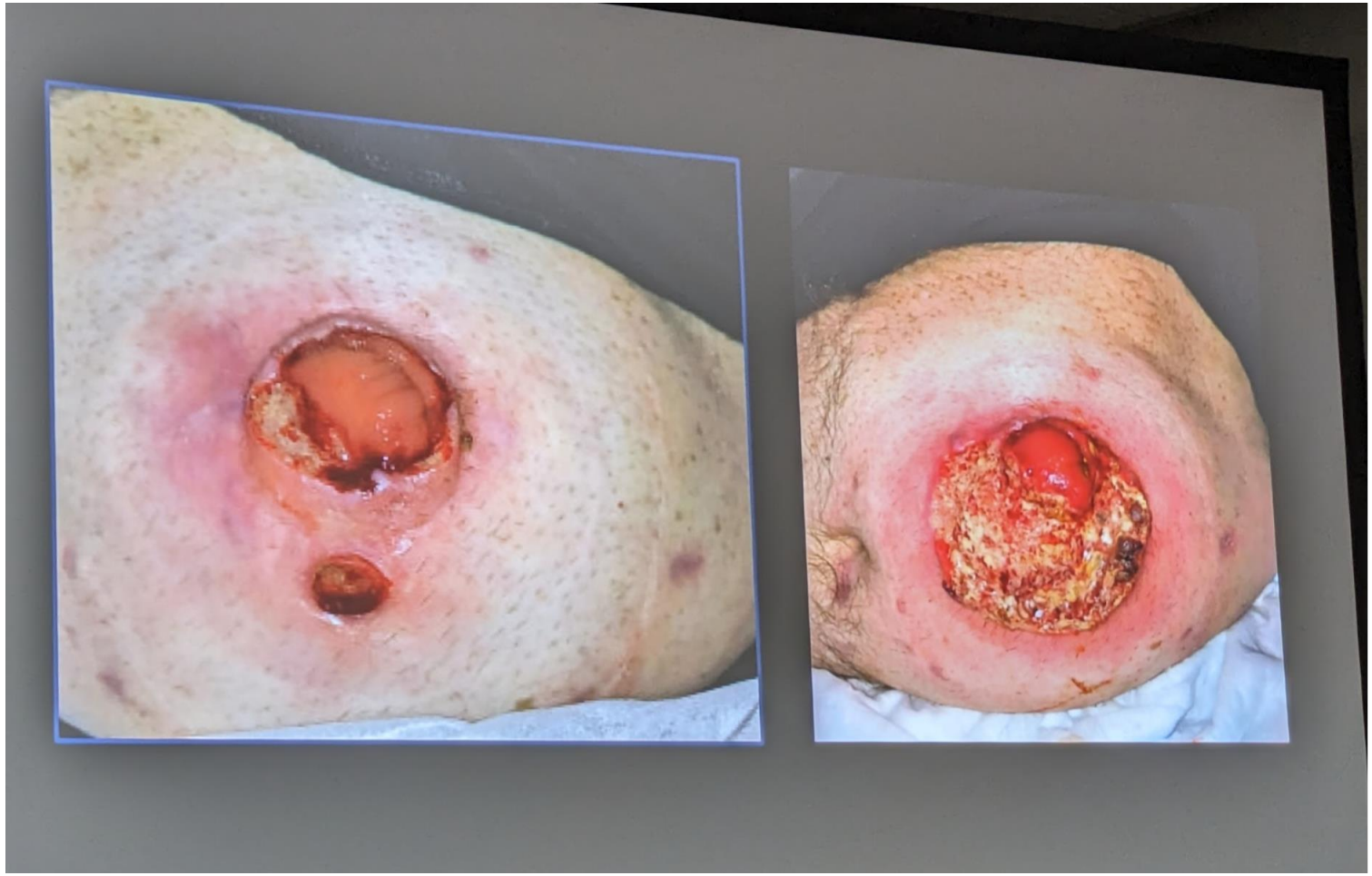


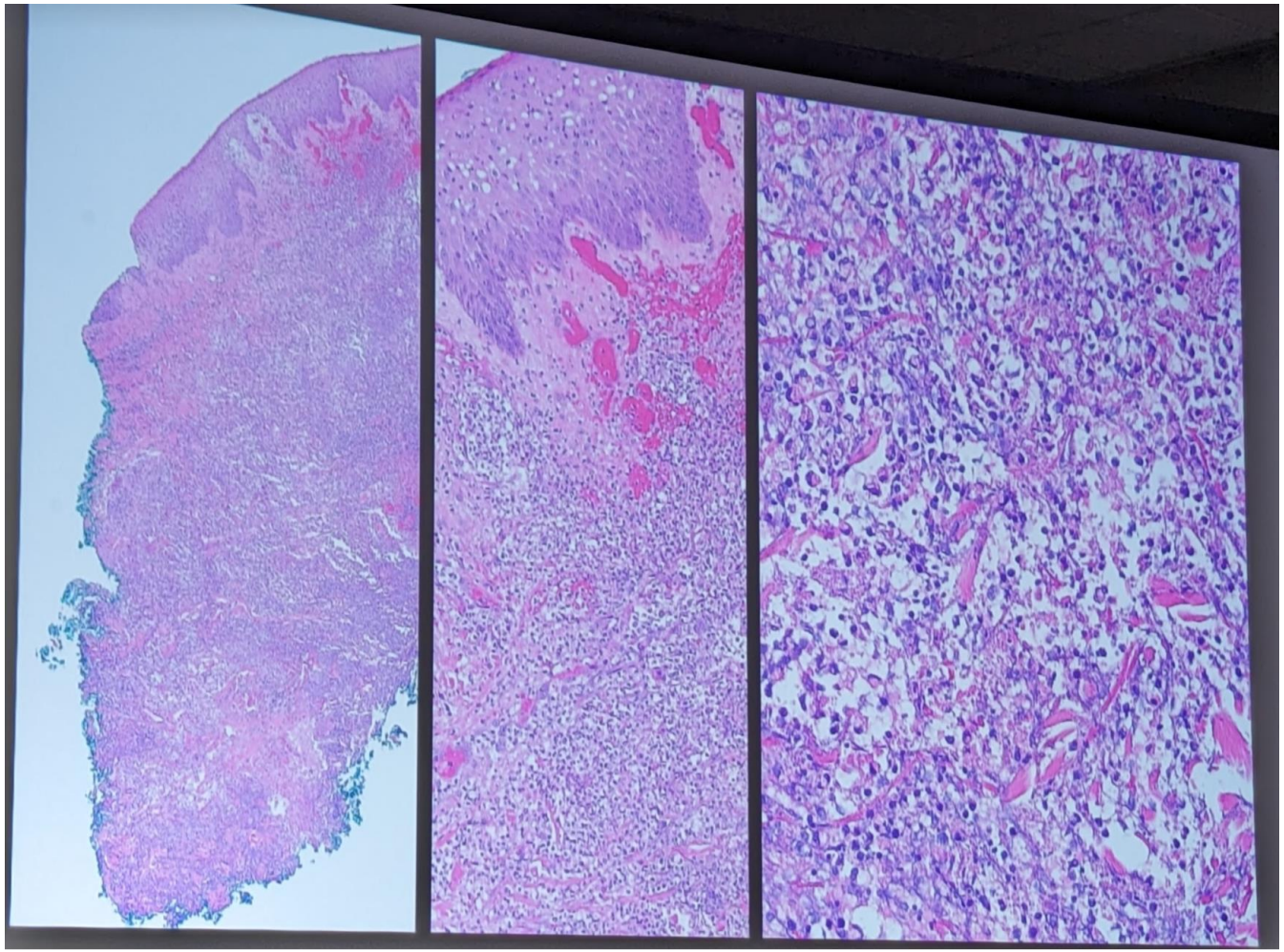



FUNGAL DETECTION BY PCR - Tissue Abdomen
Last Update: 11/22/16 08:25
Collected: 11/16/16 16:00
Special Requests: ? BLASTOMYCOSES
New
Status: Authenticated
Culture: Trichophyton rubrum complex DNA detected with 28S primer set.
Analytical sensitivities (genomes): 28S = 1000; ITS1 = 100; nested ITS2 = 1-100. Analytical sensitivities or minimal detection limits are expressed in copies of bacterial or fungal genomic DNA in a single amplification reaction performed on purified DNA. Sensitivity of detecting microbial DNA from a tissue or fluid sample will vary depending on the organism load in the sample submitted to our lab for testing, pretreatment such as formaldehyde fixation or staining, or any process that introduces exogenous microorganisms or microbial DNA into the sample submitted for testing. This test was developed by the Department of Laboratory Medicine, University of Washington.

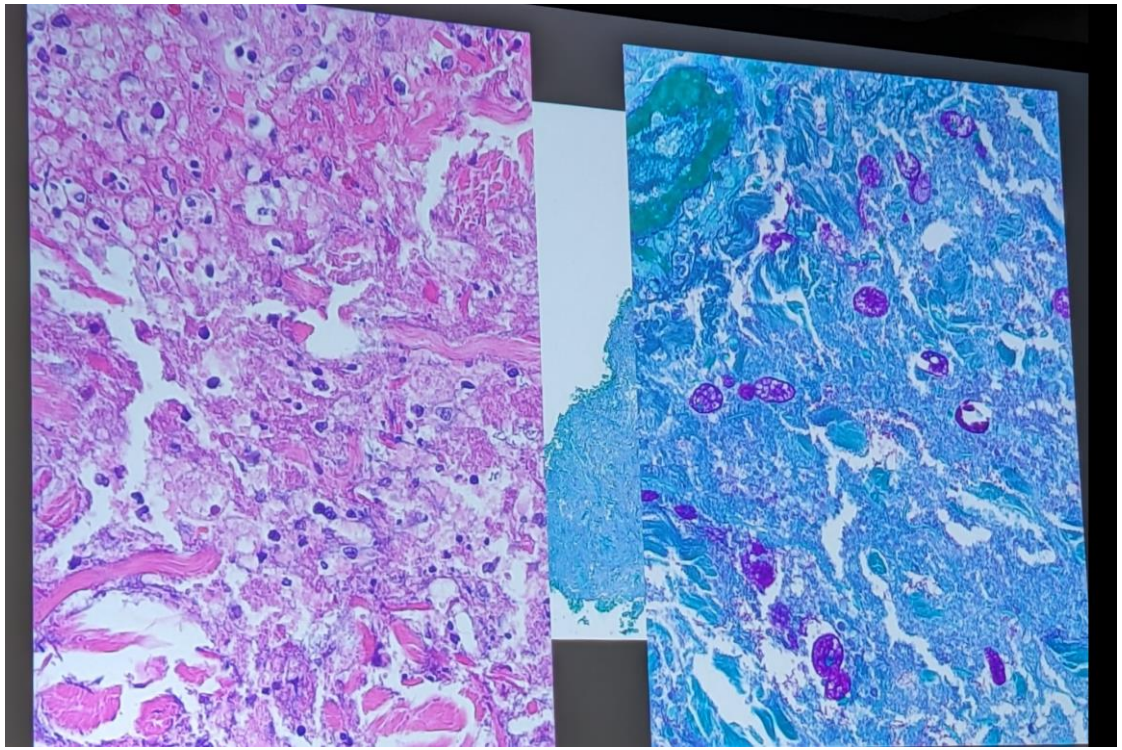

"Invasive"/Disseminated Dermal Tinea
• T. rubrum
• Nodular suppurative granuloma with distorted fungal hyphae
• Immunosuppressed - SOT
• ?follicular rupture
– Often no follicular or epidermal involvement
Lillis et al, JCP 2010;37:1168–1169
Am J Clin Dermatol (2017) 18:697–704

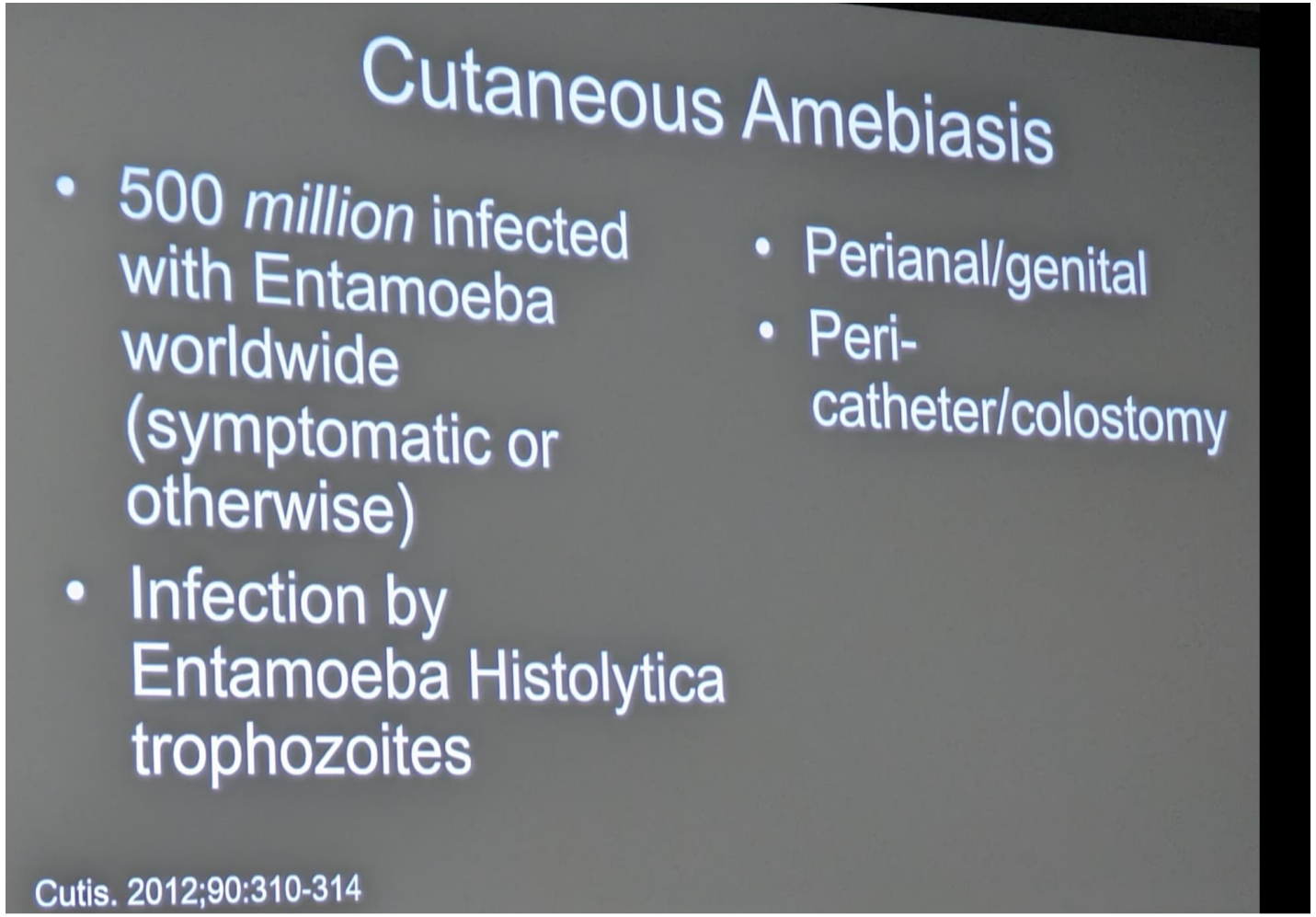

"Invasive"/Disseminated Dermal Tinea
• Bizarre shapes in tissue
• ?Dimorphic switching

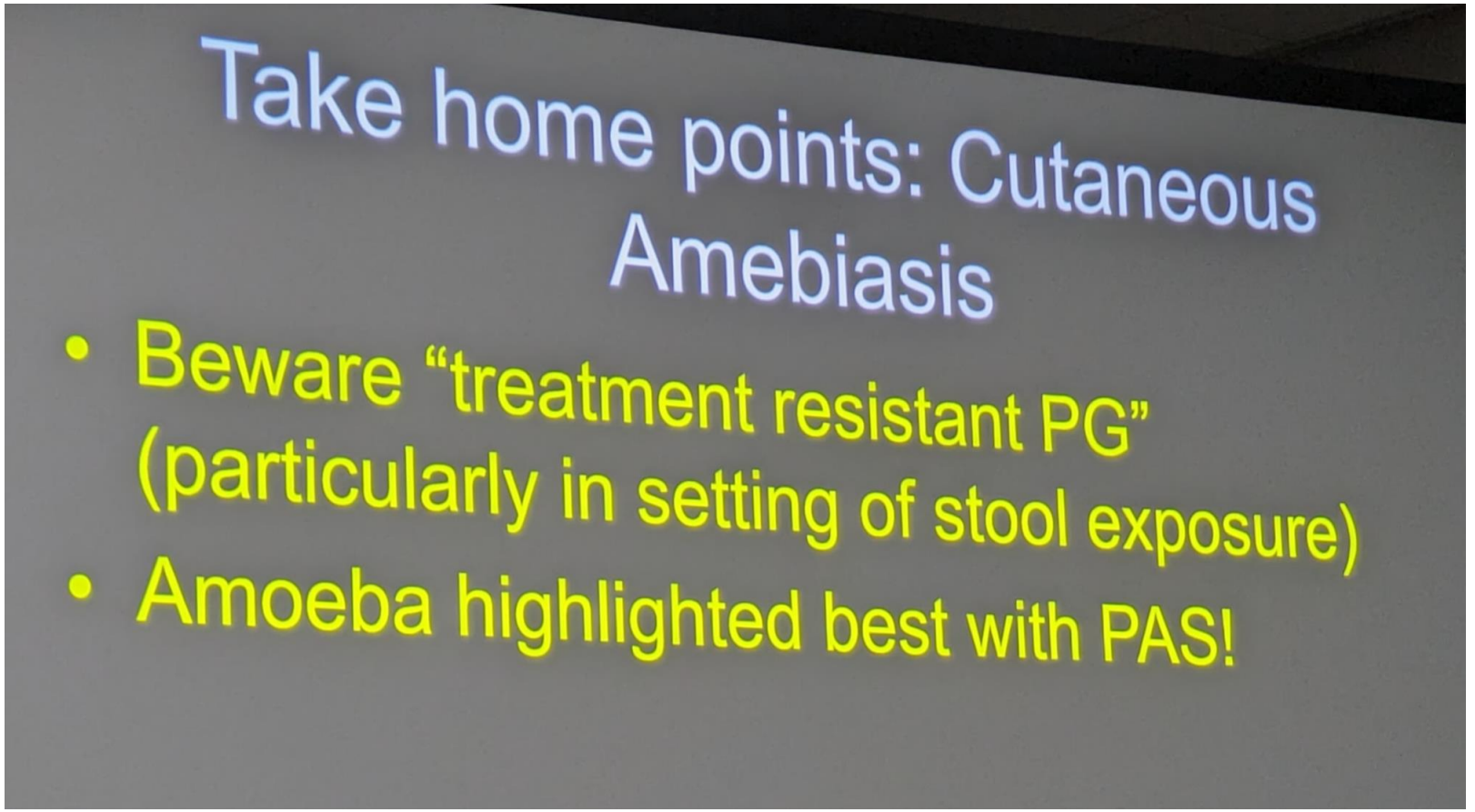




Stool PCR: +*Entamoeba histolytica*




Cutaneous Amebiasis
• 500 *million* infected with Entamoeba worldwide (symptomatic or otherwise)
• Infection by Entamoeba Histolytica trophozoites
• Perianal/genital
• Peri-catheter/colostomy
Cutis. 2012;90:310-314


Take home points: Cutaneous Amebiasis
• Beware "treatment resistant PG" (particularly in setting of stool exposure)
• Amoeba highlighted best with PAS!

Novedades en enfermedades ampollosas

AAD ANNUAL MEETING AEDV highlights SAN DIEGO 8-12 MARZO

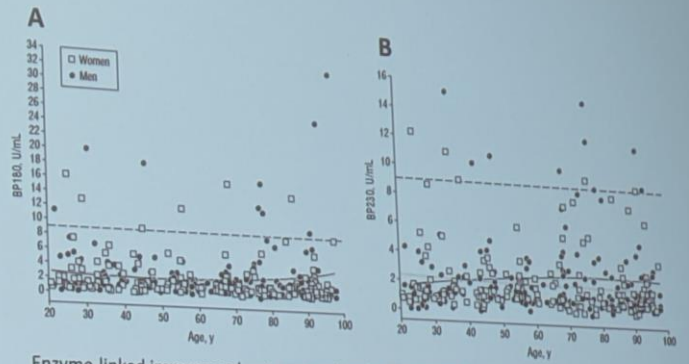
- Se identifican 3 “gaps” en el diagnóstico de enfermedades ampollosas autoinmunes
- Se dan soluciones para estos “gaps”

- Limitaciones de la histopatología: No es específica, overlap con otras entidades
- Limitación depende de la evolución de las lesiones
- Limitaciones de la IFD: Puede darnos fasos positivos y falsos negativos
- Limitaciones de la IIF: Falsos positivos (anticuerpos ABO→ patrón de superficie)

Falsos negativos (poca actividad de la enfermedad, penfigoide de mucosas)

ELISA - LIMITATIONS

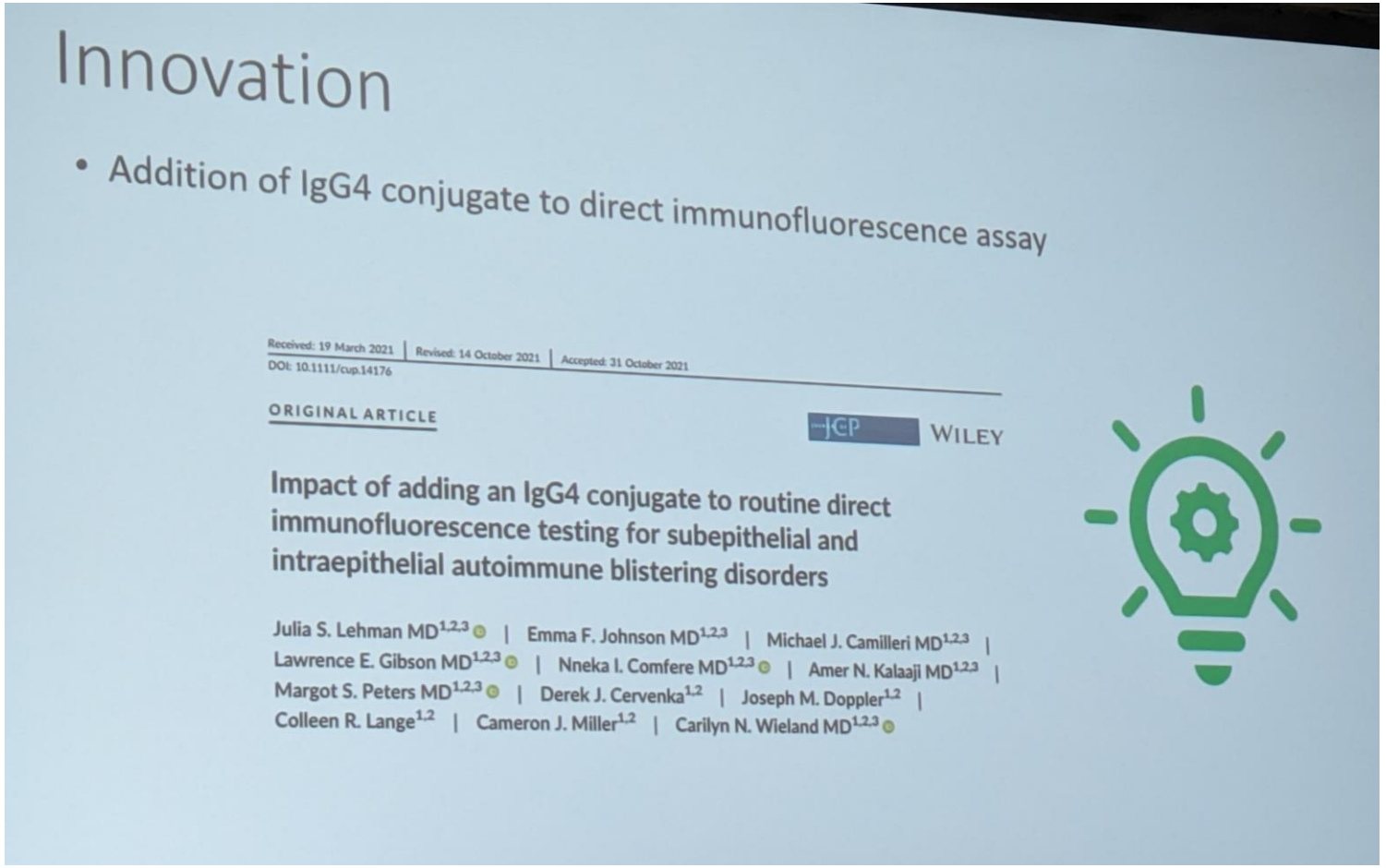
- False-positives
- False-negatives
  - Specific antigens only

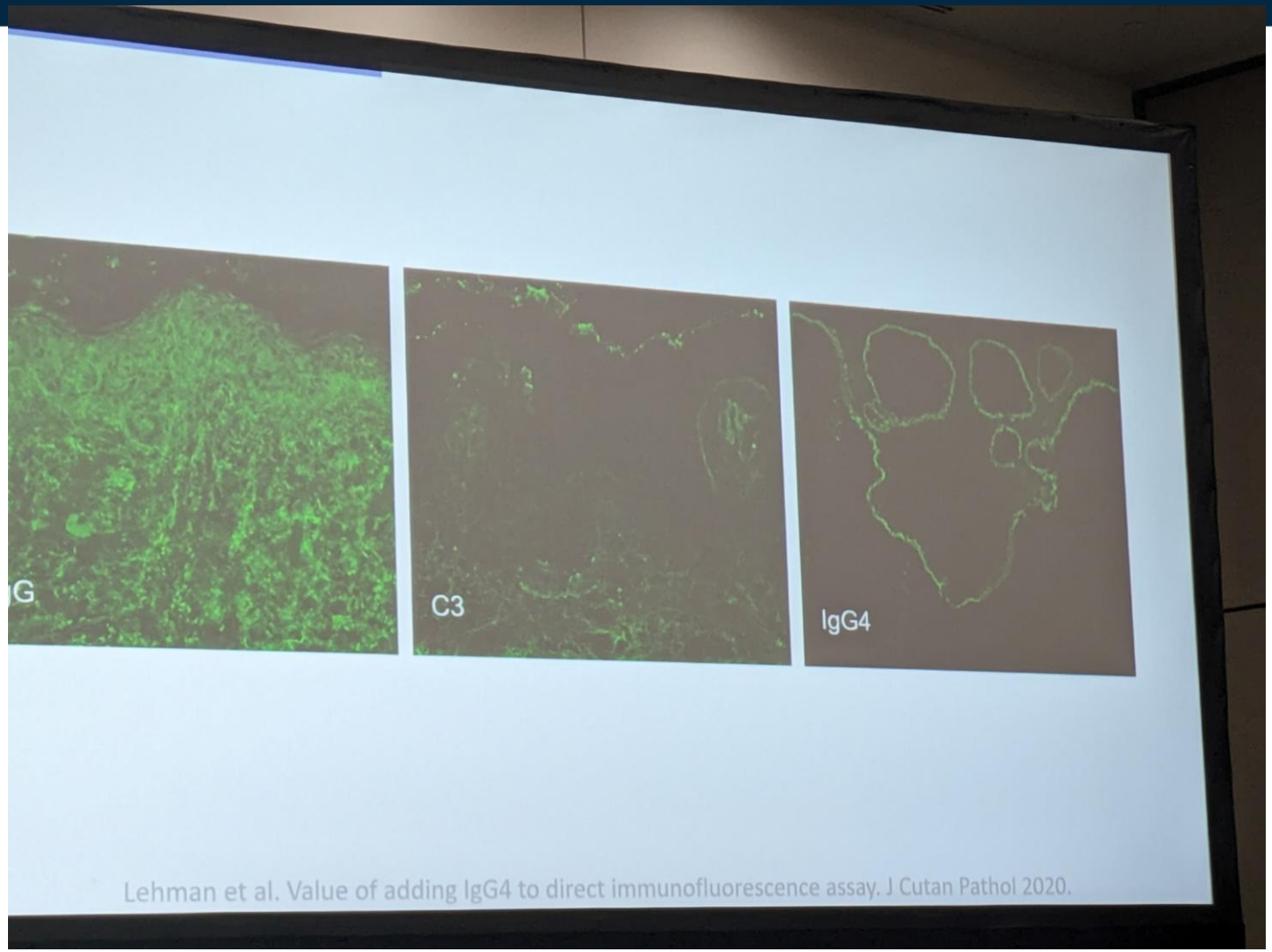


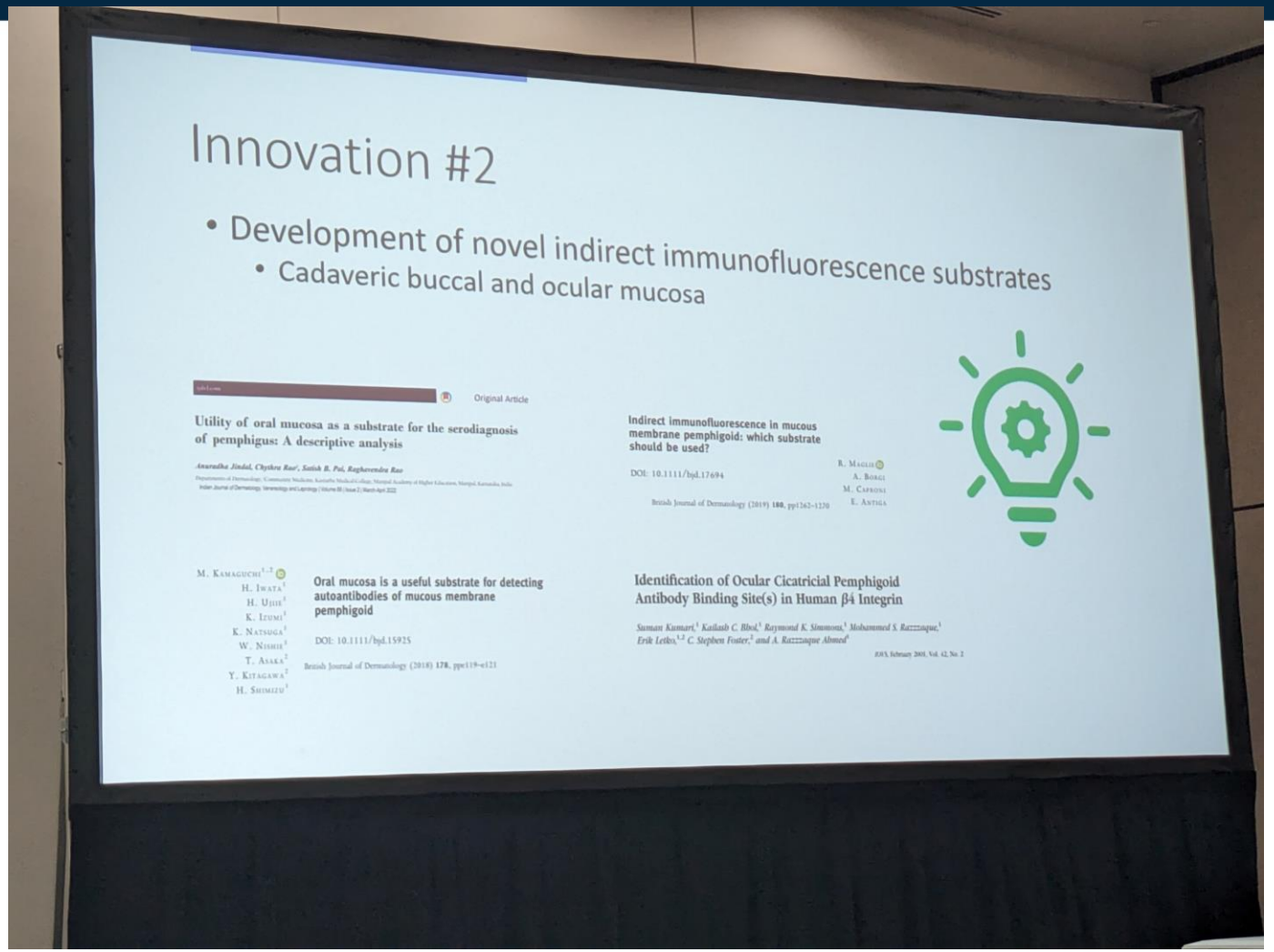
Enzyme-linked immunosorbent assay value for BP180 (BP antigen II) (A) and BP230 (BP antigen I) (B) autoantibodies vs patient age. Smooth curves were fit separately for men (solid line) and women (dotted line). Dashed line shows the cutoff value of 9 U/mL for a positive result (≥9 U/mL).

Carilyn N Wieland, MD; Nneka I Comfere, MD; Lawrence E Gibson, MD; Amy L Weaver, MS; Patricia K Krause, BS, MBA; Joseph A Murray, MD
Anti-Bullous Pemphigoid 180 and 230 Antibodies in a Sample of Unaffected Subjects.
Arch Dermatol. 2010;146(1):21-25

- GAP 1: basa sensibilidad/ especificidad de la IFD
- Solución



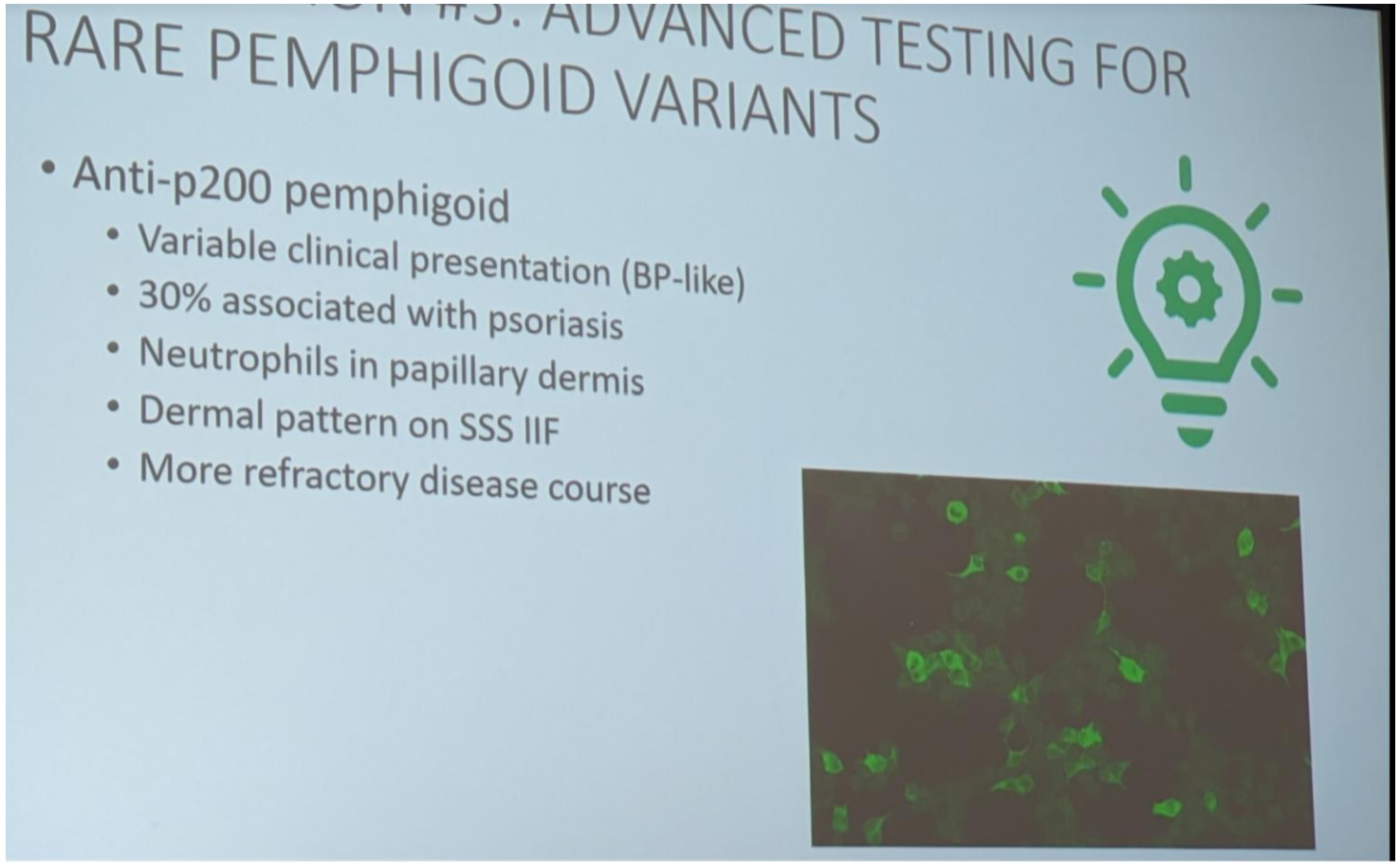

C3
IgG4
Lehman et al. Value of adding IgG4 to direct immunofluorescence assay. J Cutan Pathol 2020.


Innovation #2
• Development of novel indirect immunofluorescence substrates
• Cadaveric buccal and ocular mucosa
Original Article
Utility of oral mucosa as a substrate for the serodiagnosis of pemphigus: A descriptive analysis
Anuradha Jindal, Chythra Rao, Satish B. Poi, Raghavendra Rao
Indirect immunofluorescence in mucous membrane pemphigoid: which substrate should be used?
DOI: 10.1111/bjd.17694
R. Maglie
A. Borgi
M. Caproni
E. Antiga
British Journal of Dermatology (2019) 180, pp1262–1270
M. Kamaguchi
H. Iwata
H. Ujiie
K. Izumi
K. Natsuga
W. Nishie
T. Asaka
Y. Kitagawa
H. Shimizu
Oral mucosa is a useful substrate for detecting autoantibodies of mucous membrane pemphigoid
DOI: 10.1111/bjd.15925
British Journal of Dermatology (2018) 178, ppe119–e121
Identification of Ocular Cicatricial Pemphigoid Antibody Binding Site(s) in Human β4 Integrin
Suman Kumari, Kailash C. Bhol, Raymond K. Simmons, Mohammed S. Razzaque, Erik Lehto, C. Stephen Foster, and A. Razzaque Ahmed

Indirect immunofluorescence with IgG4

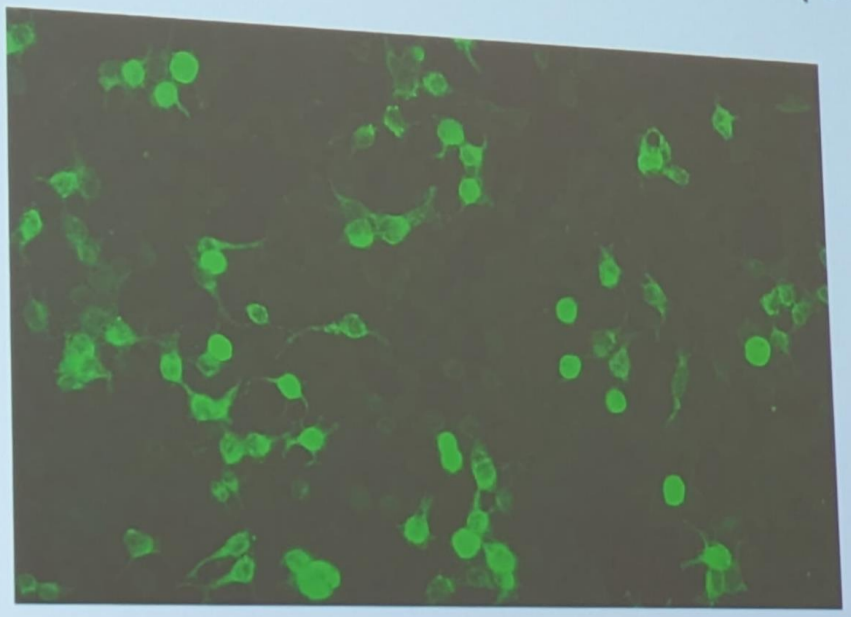
		IIF-IgG positive samples n (%)	IIF-IgG4 Positive Samples n (%)	Additional cases detected by IIF-IgG4 n (%)
Study group 1 (n=99)	IIF-IgG Negatives	0	8 (8)	8 (8%)
Study group 2 (n=71)	BP180/BP23 Positives (n=23)	0	5 (22%)	5 (22%)
	DSG1/DSG3 Positives (n=24)	0	10 (42%)	10 (42%)
	DIF Positives (n=24)	0	16 (67%)	16 (67%)
Study group 3 (n=61)	MMP	12 (20%)	27 (33%)	15 (25%)

Credit: Anatilde Gonzalez Guerrico , PhD; Mayo Clinic Developer


RARE PEMPHIGOID VARIANTS
• Anti-p200 pemphigoid
• Variable clinical presentation (BP-like)
• 30% associated with psoriasis
• Neutrophils in papillary dermis
• Dermal pattern on SSS IIF
• More refractory disease course

Additional data

- Indirect immunofluorescence with transfected cells (laminin-332):

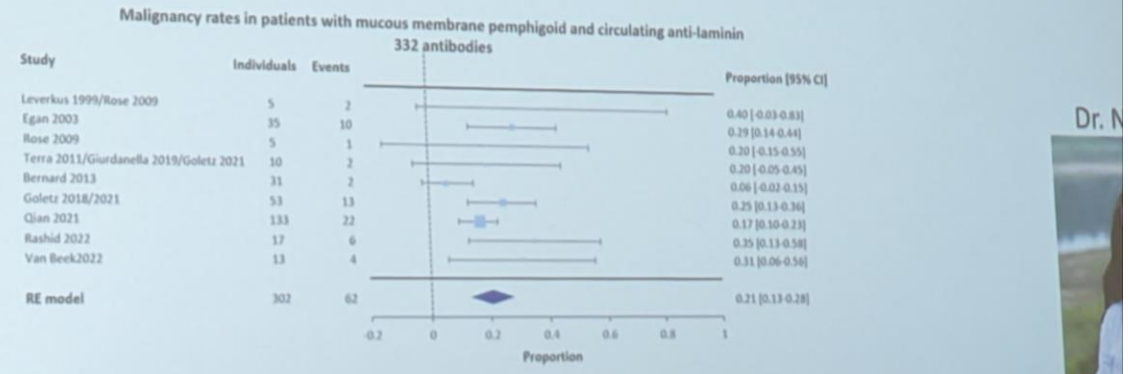


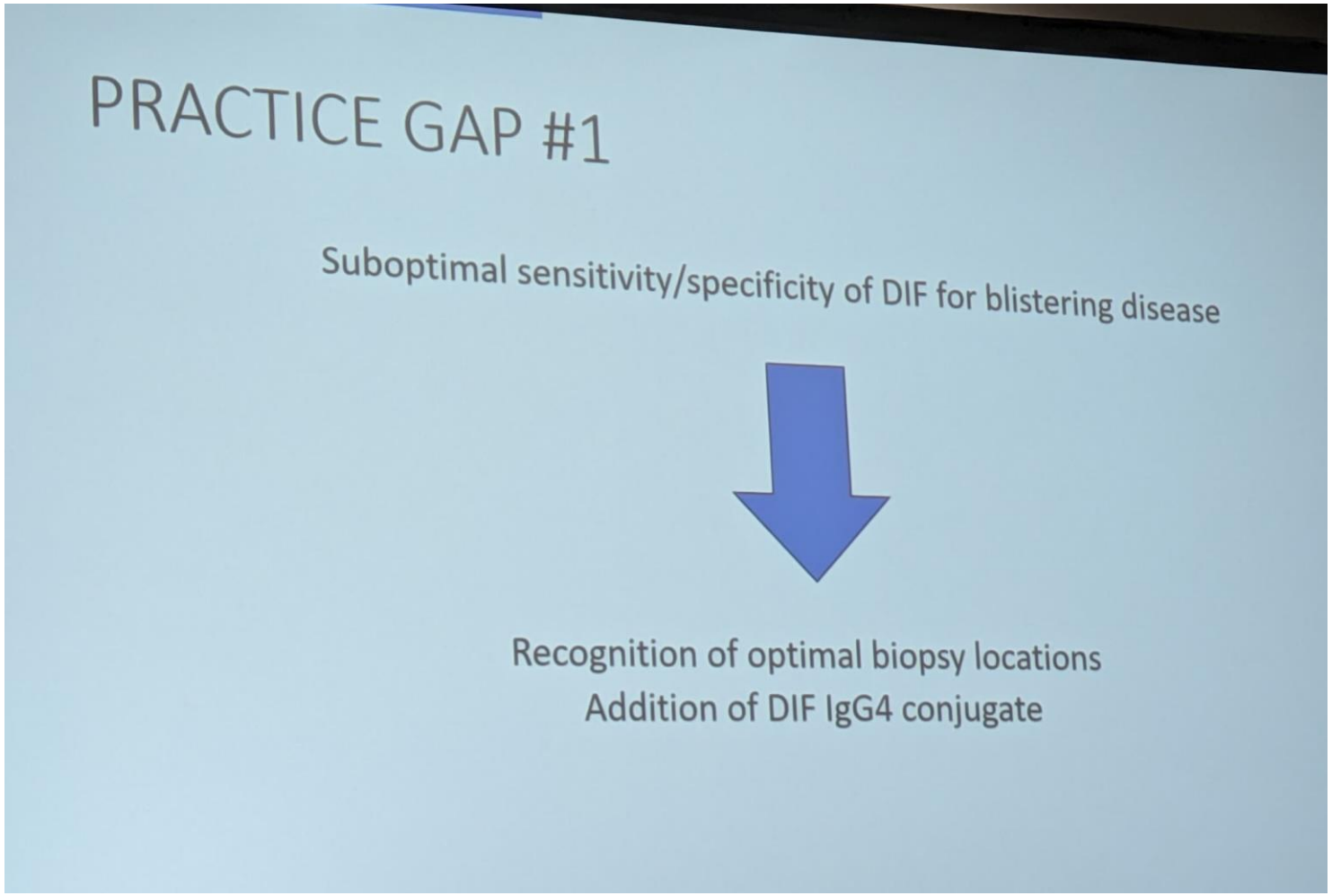
Penfigoide de mucosas y riesgo de malignización

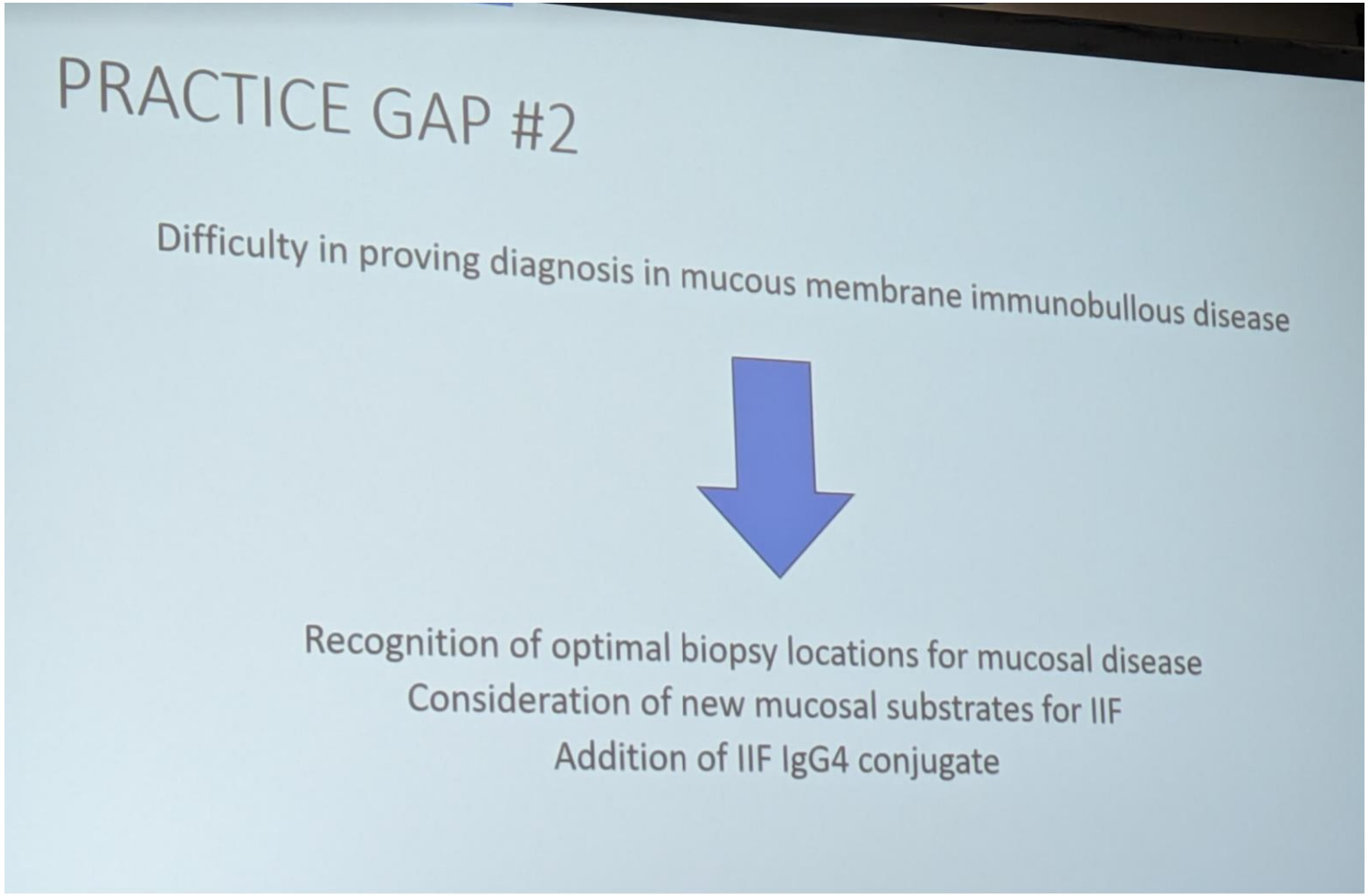
AAD ANNUAL MEETING AEDV highlights

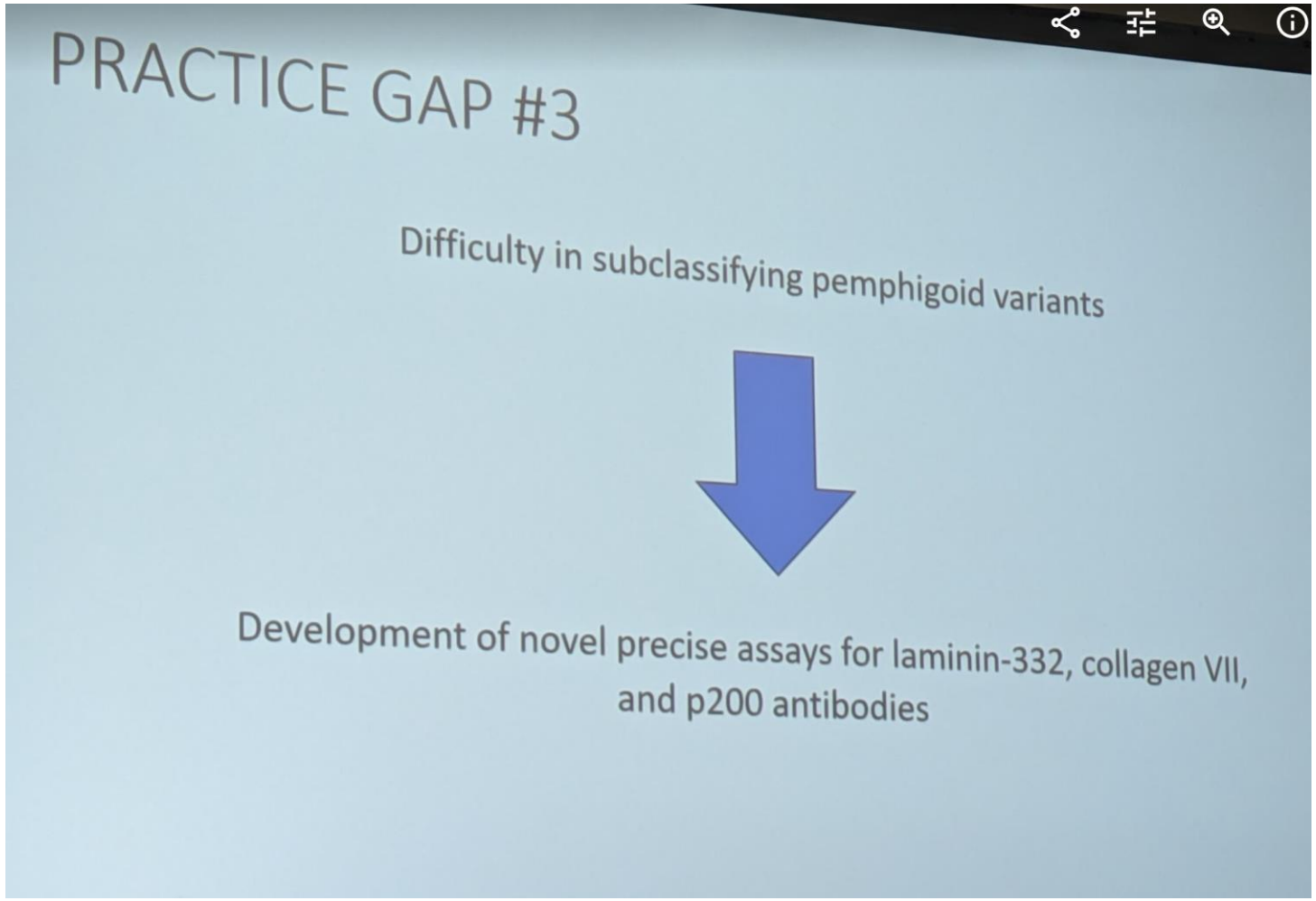
SAN DIEGO 8-12 MARZO

- Systematic review and meta-analysis of >1400 MMP patients
  - 15% with malignancy overall
  - Laminin-332 antibodies or ocular involvement increase risk considerably




PRACTICE GAP #1
Suboptimal sensitivity/specificity of DIF for blistering disease
Recognition of optimal biopsy locations
Addition of DIF IgG4 conjugate


PRACTICE GAP #2
Difficulty in proving diagnosis in mucous membrane immunobullous disease
Recognition of optimal biopsy locations for mucosal disease
Consideration of new mucosal substrates for IIF
Addition of IIF IgG4 conjugate


PRACTICE GAP #3
Difficulty in subclassifying pemphigoid variants
Development of novel precise assays for laminin-332, collagen VII, and p200 antibodies

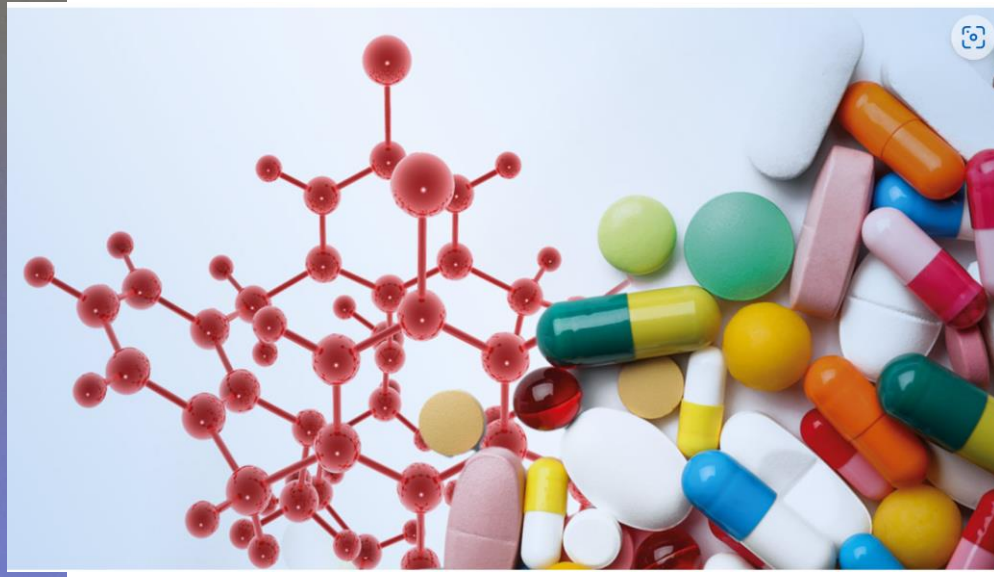
Novedades en toxicodermias

AAD ANNUAL MEETING AEDV highlights

SAN DIEGO 8-12 MARZO

Updates in Cutaneous Drug Reactions

- Dupilumab-associated lymphoid reactions
- Mogamulizumab-associated reactions
- Immune checkpoint inhibitor-associated reactions



Progression of CTCL following dupilumab

- 4 patients with clinically presumed atopic dermatitis
  - Initial ↓ in BSA in all 4 patients, 3 with ↓ pruritus
  - All eventually diagnosed with CTCL (tx duration: 8-27 months)
- 3 patients with CTCL and severe pruritus
  - Initial ↓ pruritus 2/3 patients
  - All with progression of disease to Sezary syndrome

Table I. Patient characteristics and response to dupilumab therapy

Case	Sex/age, years	Diagnosis before dupilumab	Total treatment time with dupilumab, months	Concomitant therapies	Length of time improved with dupilumab, months; description of initial improvement	Worsening with dupilumab	Sézary cell count	Outcome on discontinuation of dupilumab
1	M/64	Presumed AD (retrospectively diagnosed as CTCL-NOS stage Ib)	8	Azathioprine (PO), diphenhydramine (PO), gabapentin (PO), glucocorticoids (T), prednisone (PO)	1; decrease in BSA (40% to 32%[‡]) and pruritus	Palmoplantar desquamation, severe skin burning/pruritus, development of erythroderma (BSA 95%), impetiginization with *Staphylococcus aureus*	N/A	PD (CTCL-NOS stage IIIa), improvement with radiation, bexarotene, and interferon-α
2	M/72	Presumed AD	4	Methotrexate (PO)	1.5; decrease in BSA (80% to 60%) and pruritus	Thickening of plaques with superimposed papules	N/A	MF stage Ib, improveme with NBUVB and topi corticosteroids
3	F/59	Presumed AD	27	Gabapentin (PO), glucocorticoids (T), nonmedication emollient (T), tacrolimus (T)	8; decrease in BSA neck down (40% to 5%), decreased pruritus	Enlargement of facial plaque and onset of fatigue and weight loss	N/A	MF stage Ia, dupilumab continued at longer intervals (300 mg ev 3.5 wk), given patie preference and atop benefits
4	F/40	Presumed AD	15	Pantoprazole (PO), montelukast (PO), mirabegron (PO)	4; decrease in BSA (unclear %)	Development of erythroderma and blepharoconjunctivitis, worsening pruritus	N/A	MF stage IIIa, improve with prednisone ta triamcinolone, methotrexate, and NBUVB
5	M/67	MF stage IIIb	3	Bexarotene (PO), hydroxyzine (PO), interferon-γ (IM), glucocorticoids (T), prednisone (PO), pregabalin (PO)	2; decrease in BSA (80%[*] to 60%[*]), decreased pruritus	Palmoplantar desquamation, increase in BSA (100%), LAD, worsening pruritus, fatigue, impetiginization with *S aureus*	575/μL,[†] 1022/μL[§]	PD (MF/SS stage IVa and death
6	M/58	MF stage IIa	3	Bexarotene (PO), mechlorethamine (T), immunoglobulin (IV), glucocorticoids (T), tacrolimus (T)	1.75; improved asthma and mild decrease in BSA (15%[*] to 13%[*])	Increase in BSA (60%[*]), development of LAD, worsening pruritus, fatigue	⩽100/μL,[†] 6000/μL,[†] 9000/μL[§]	PD (MF/SS stage IV and death
7	F/77	MF stage Ib	3	Nonmedication emollient (T), Glucocorticoids (T)	0; N/A	Development of erythroderma (BSA 80%) and LAD, worsening pruritus	1150/μL,[†] 1296/μL[§]	PD (MF/SS stage endocarditis, p response with romidepsin

Dupilumab-associated cutaneous atypical lymphoid infiltrates

- 7 cases in which an "atypical lymphoid infiltrate" or MF was diagnosed on biopsy following treatment with dupilumab for biopsy-supported refractory AD
- 5 cases with pre-dupilumab slides available for review
  - One case with IHC staining
  - None had TCR gene rearrangement studies

TABLE 2. Histopathologic Findings of Predupilumab Biopsies

Patient	Histopathologic Features	Distribution of Cellular Infiltrate	Density and Composition of Cellular Infiltrate	Final Diagnosi
1	Biopsy 1: focal folliculotropism, vessel ectasia, wiry collagen, and lymphocyte tagging	Perivascular and perifollicular	Mild; lymphocytes and histiocytes	Mild superficial, peri inflammation
	Biopsy 2: wiry collagen and vessel ectasia	Perivascular	Mild; lymphocytes and histiocytes	Urticarial tissue re
2	Biopsy 1: spongiosis	Perivascular	Moderate; lymphocytes, histiocytes, and cosinophils	Subacute spongiotic with mixed dermal in
	Biopsy 2: ulcer	Lichenoid and perivascular	Moderate; lymphocytes, histiocytes, and cosinophils	Focal lichenoid and dermatitis with foca
3	Biopsy 1: lymphocyte tagging, mild epidermotropism, spongiosis, and vessel ectasia	Perivascular	Mild; lymphocytes, histiocytes, and neutrophils	Spongiotic derm superficial peri inflammat
	Biopsy 2: lymphocyte tagging, mild epidermotropism, spongiosis, vessel ectasia, and wiry collagen	Perivascular	Mild; lymphocytes, histiocytes, and eosinophils	Spongitoic derm perivascular
4	Mild epidermotropism, psoriasiform, spongiotic, and wiry collagen	Perivascular	Mild; lymphocytes and histiocytes	Chronic psoriasif
5	Biopsy 1: mild epidermotropism, lymphocyte tagging, spongiotic, and wiry collagen	Perivascular	Mild; lymphocytes and histiocytes	Subacute spong
	Biopsy 2: mild epidermotropism, lymphocyte tagging, spongiotic, psoriasiform, and wiry collagen	Lichenoid and perivascular	Moderate; lymphocytes and histiocytes	Spongiotic and derm

Patients 6 and 7 did not have predupilumab biopsy available for review.

Sokumbi et al., Am J D

Histopathologic features in post-dupilumab biopsies

- All diagnosed as MF or atypical lymphoid infiltrate
- TCR PCR revealed a clonal population in only 1/7 patients

TABLE 3. Histopathologic Findings of Postdupilumab Biopsies

Patient	Time to Biopsy After Dupilumab (mo)	Histopathologic Features	Distribution of Cellular Infiltrate	Density and C of Infil
1	1.2	Biopsy 1: severe epidermotropism, with Pautrier microabscess	Dense lichenoid infiltrate	Heavy; lymphocyt
		Biopsy 2: moderate folliculotropism	Perivascular and perifollicular	Moderate; lyn histi
2	2	No epidermotropism, wiry collagen	Lichenoid	Moderate; lymph and co
3	24	Lymphocyte tagging, mild epidermotropism, vessel ectasia, and wiry collagen	Lichenoid	Moderate; ly hist
4	14	Biopsy 1: lymphocyte tagging, moderate epidermotropism, spongiosis, and wiry collagen	Lichenoid	Moderate; l his
		Biopsy 2: lymphocyte tagging, mild epidermotropism, and wiry collagen	Focal lichenoid	Mild; lymphoc superfic
		Biopsy 3: moderate folliculotropism	Perivascular and perifollicular	Moderate; h
5	1	Moderate epidermotropism, Pautrier microabscess, medium-size neoplastic T-cell lymphocytes, vessel ectasia, and wiry collagen	Lichenoid	Moderate
6*	12	Rare lymphocyte tagging, mild epidermotropism, Pautrier microabscess, psoriasiform, and wiry collagen	Lichenoid	Moderate; ly neutrophil
7*	14	Parakeratosis, inflamed serum crust, and spongiosis. Lymphocyte tagging at DEJ, mild epidermotropism, mild lymphocyte atypia with notching, spongiosis, and wiry collagen	Focal lichenoid	Mild to mo

Sokumbi et al., Am J

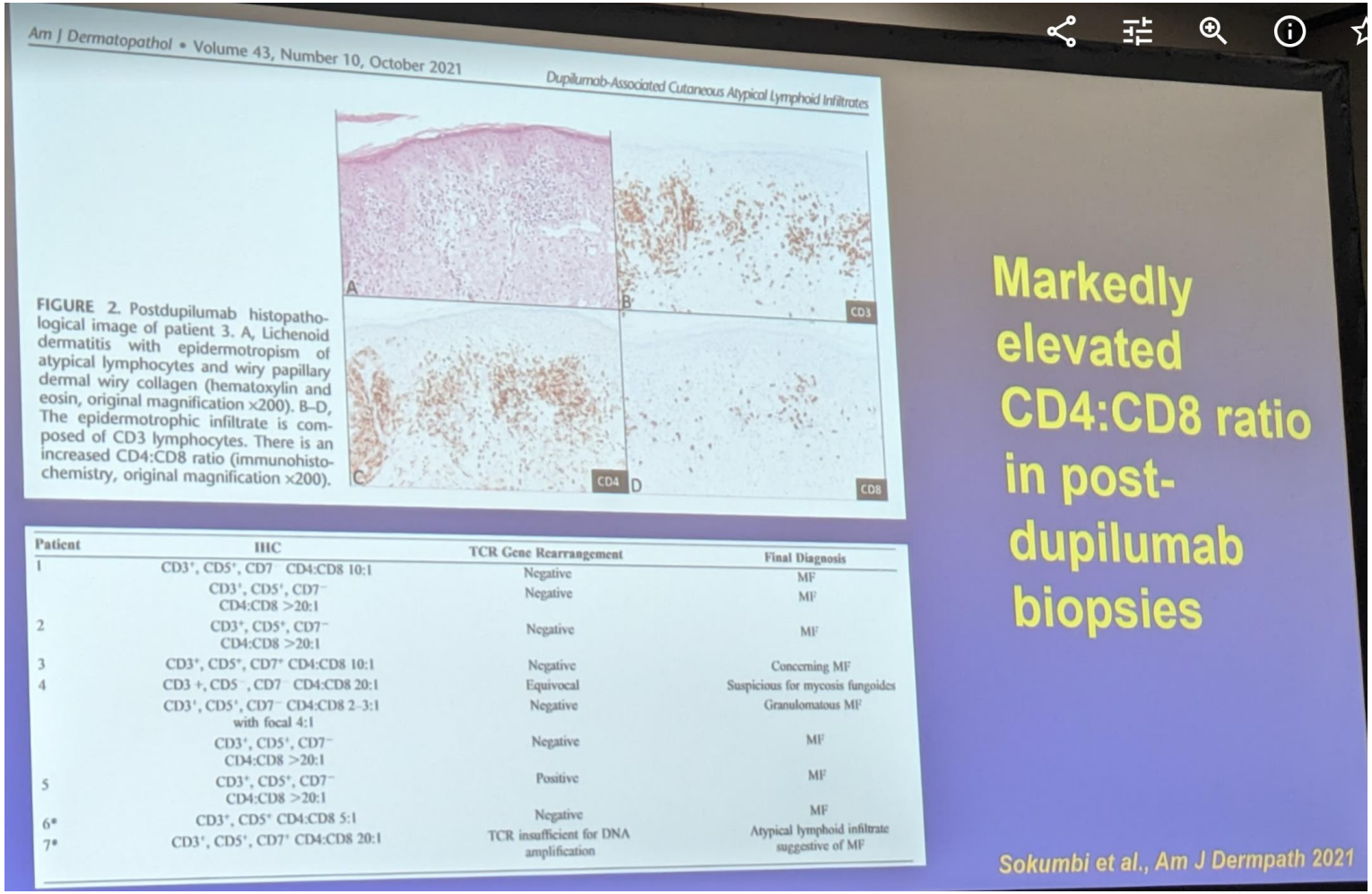
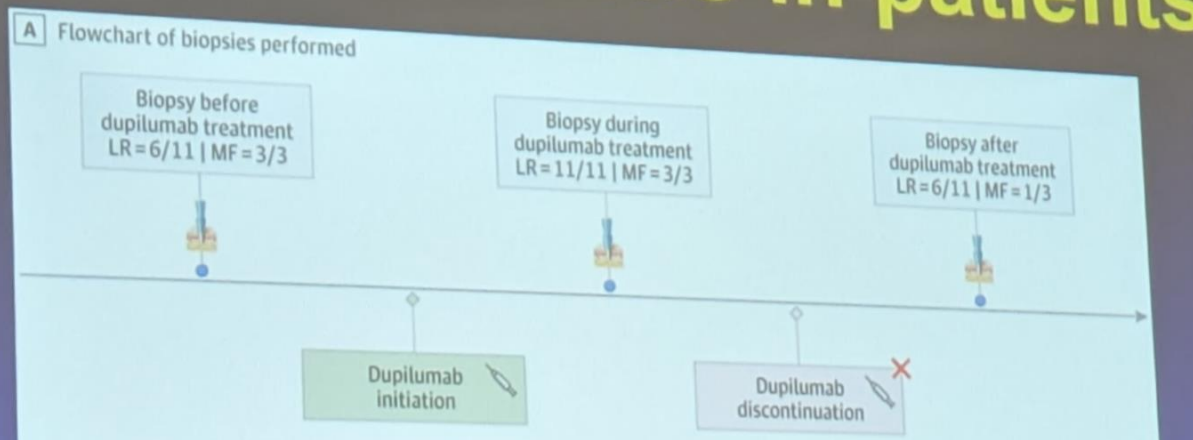


FIGURE 2. Postdupilumab histopathological image of patient 3. A, Lichenoid dermatitis with epidermotropism of atypical lymphocytes and wiry papillary dermal wiry collagen (hematoxylin and eosin, original magnification ×200). B–D, The epidermotrophic infiltrate is composed of CD3 lymphocytes. There is an increased CD4:CD8 ratio (immunohistochemistry, original magnification ×200).

Patient	IHC	TCR Gene Rearrangement	Final Diagnosis
1	CD3⁺, CD5⁺, CD7⁻ CD4:CD8 10:1	Negative	MF
	CD3⁺, CD5⁺, CD7⁻ CD4:CD8 >20:1	Negative	MF
2	CD3⁺, CD5⁺, CD7⁻ CD4:CD8 >20:1	Negative	MF
3	CD3⁺, CD5⁺, CD7⁺ CD4:CD8 10:1	Negative	Concerning MF
4	CD3 +, CD5⁻, CD7⁻ CD4:CD8 20:1	Equivocal	Suspicious for mycosis fungoides
	CD3⁺, CD5⁺, CD7⁻ CD4:CD8 2–3:1 with focal 4:1	Negative	Granulomatous MF
	CD3⁺, CD5⁺, CD7⁻ CD4:CD8 >20:1	Negative	MF
5	CD3⁺, CD5⁺, CD7⁻ CD4:CD8 >20:1	Positive	MF
6*	CD3⁺, CD5⁺ CD4:CD8 5:1	Negative	MF
7*	CD3⁺, CD5⁺, CD7⁺ CD4:CD8 20:1	TCR insufficient for DNA amplification	Atypical lymphoid infiltrate suggestive of MF

Dupilumab-associated lymphoid reactions in patients with AD



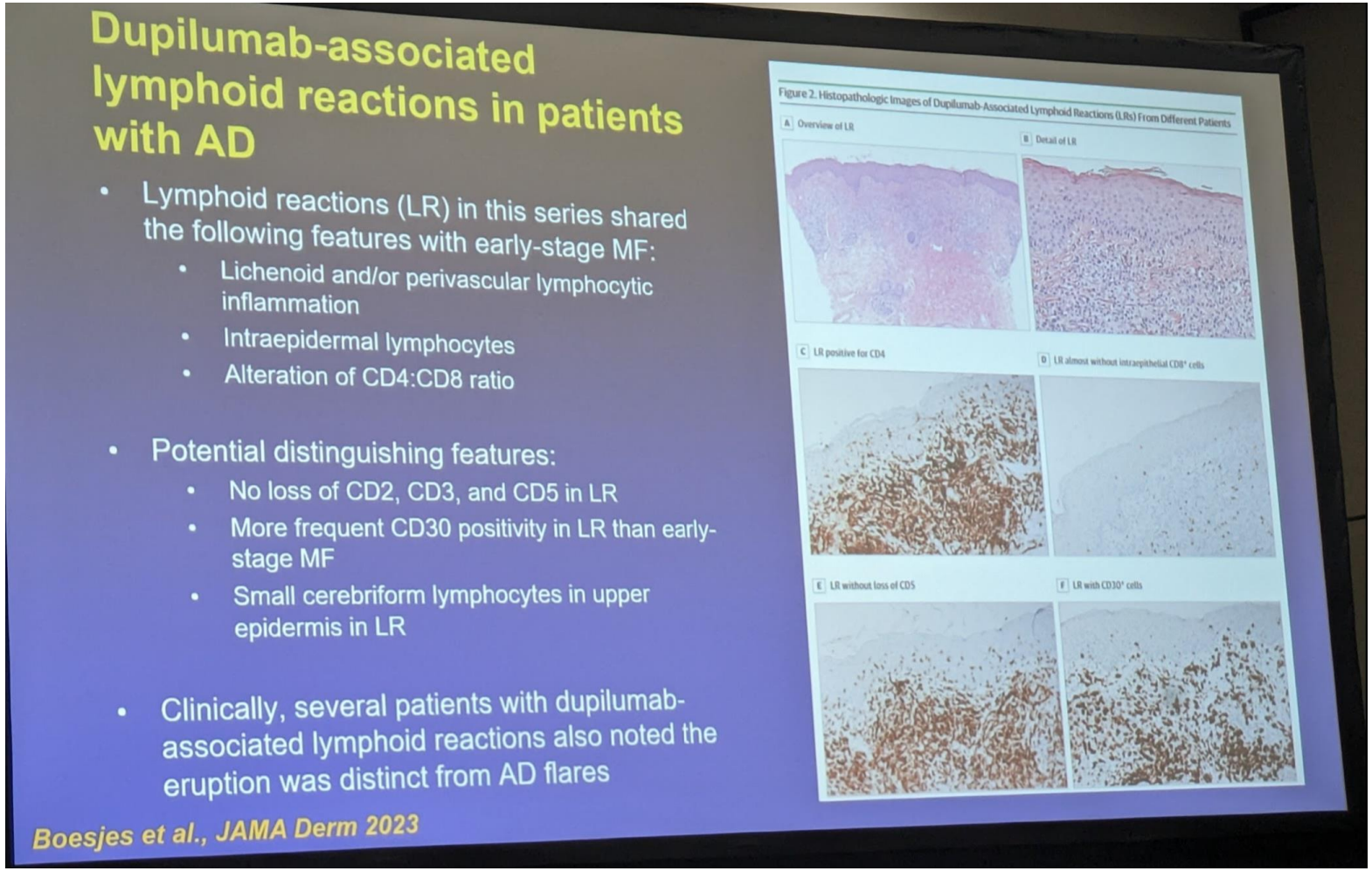
- Retrospective study of 14 adult patients with AD
  - Clinically suspected to have CTCL during dupilumab treatment
- 3 patients diagnosed with MF during treatment
  - Pre-treatment biopsies retrospectively diagnosed as MF
- 11 diagnosed with "lymphoid reactions"

Boesjes et al., JAMA De

Reacción linfomatoide inducida por Dupilumab en pacientes con dermatitis atópica

AAD ANNUAL MEETING AEDV highlights

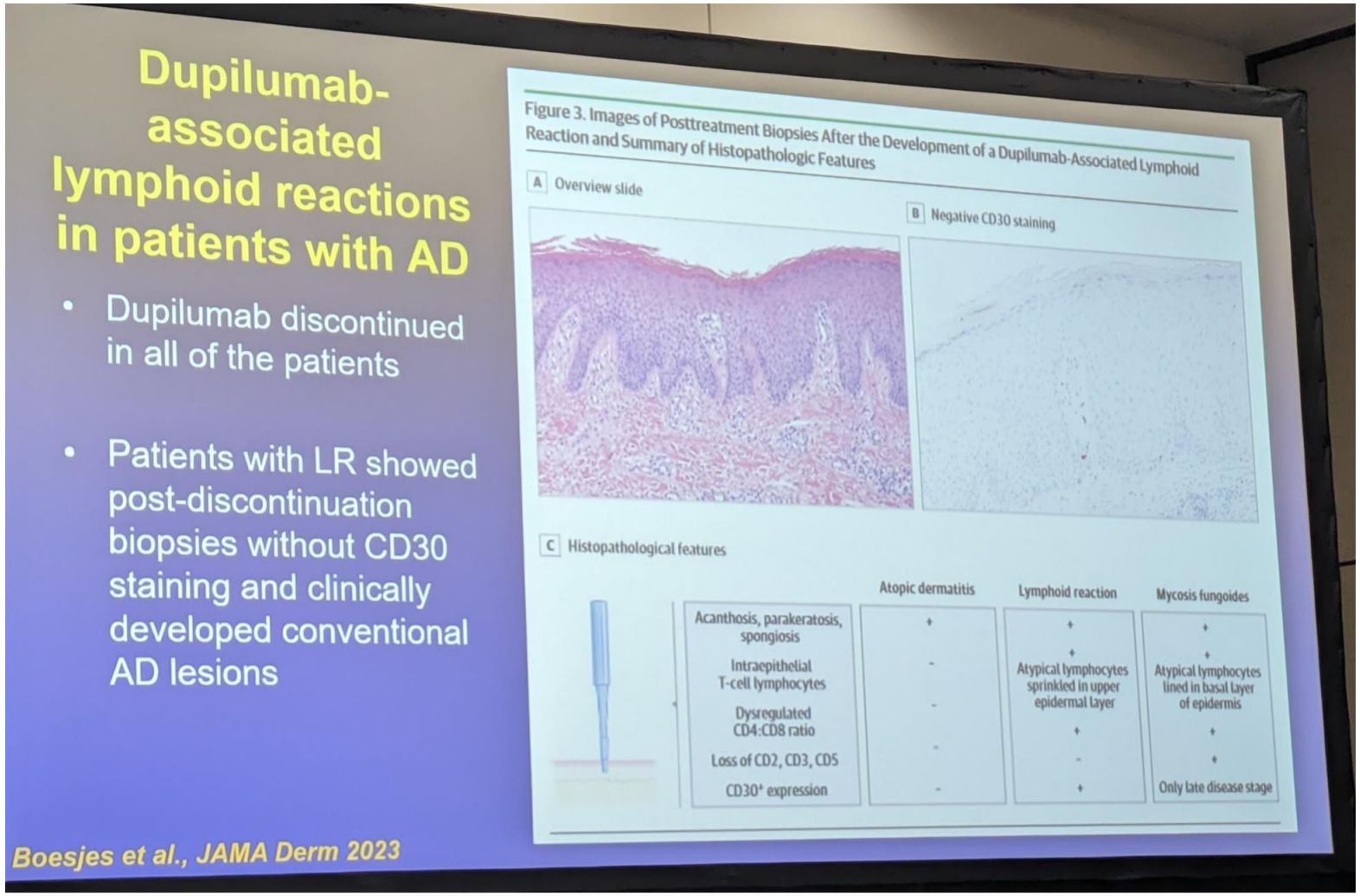
SAN DIEGO 8-12 MARZO



Reacción linfomatoide inducida por Dupilumab en pacientes con dermatitis atópica

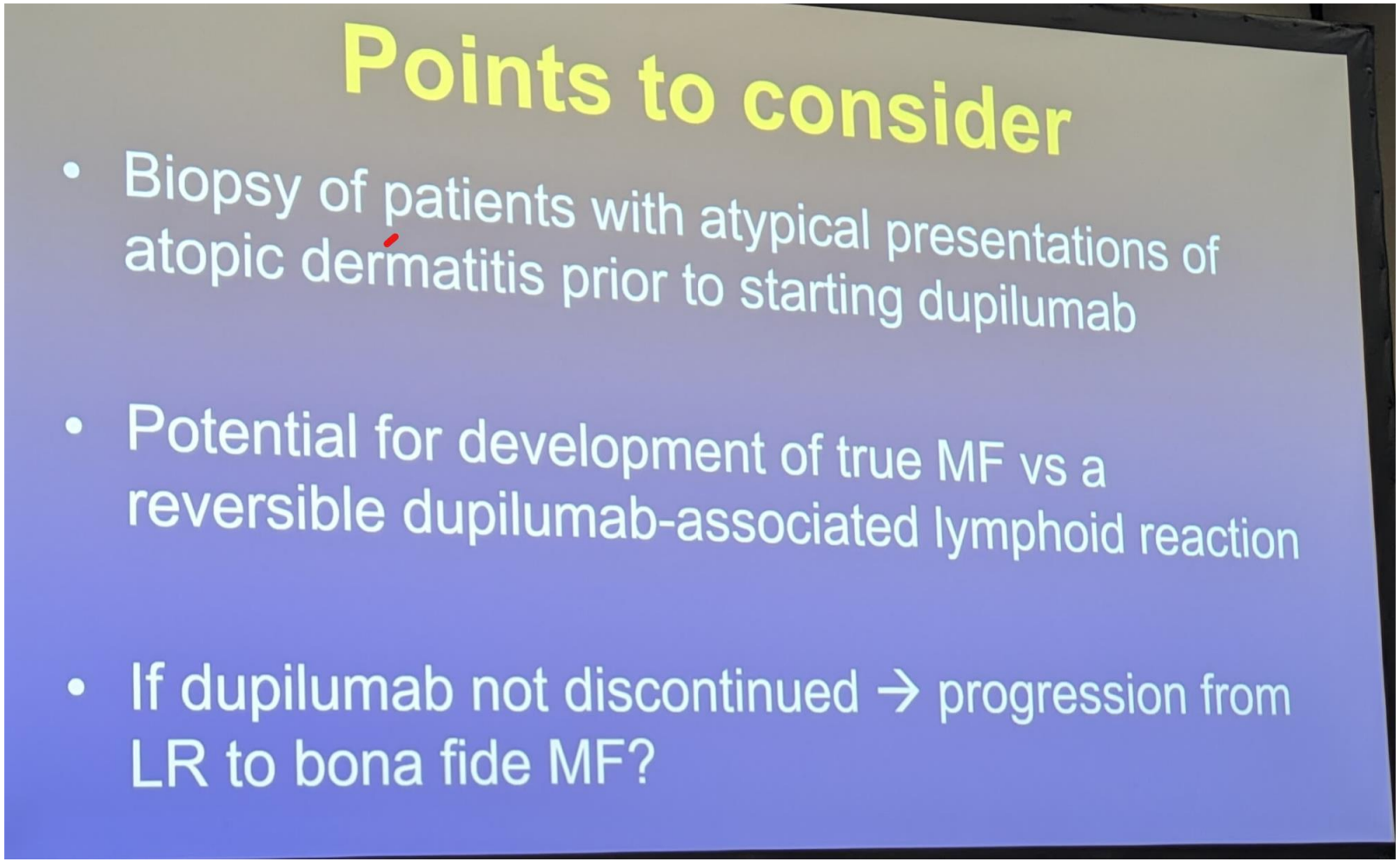
AAD ANNUAL MEETING AEDV highlights

SAN DIEGO 8-12 MARZO

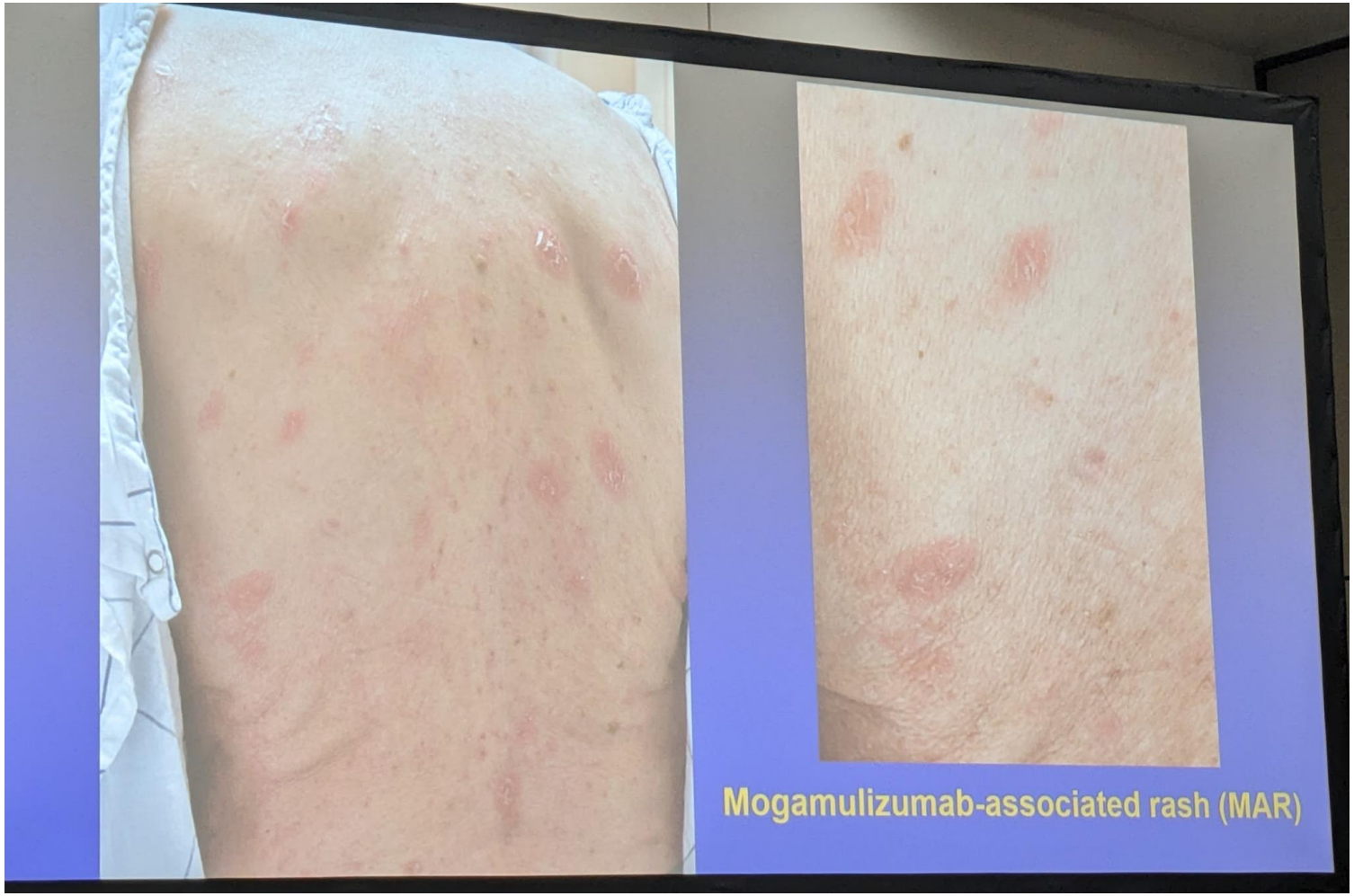


Puntos a tener en cuenta…

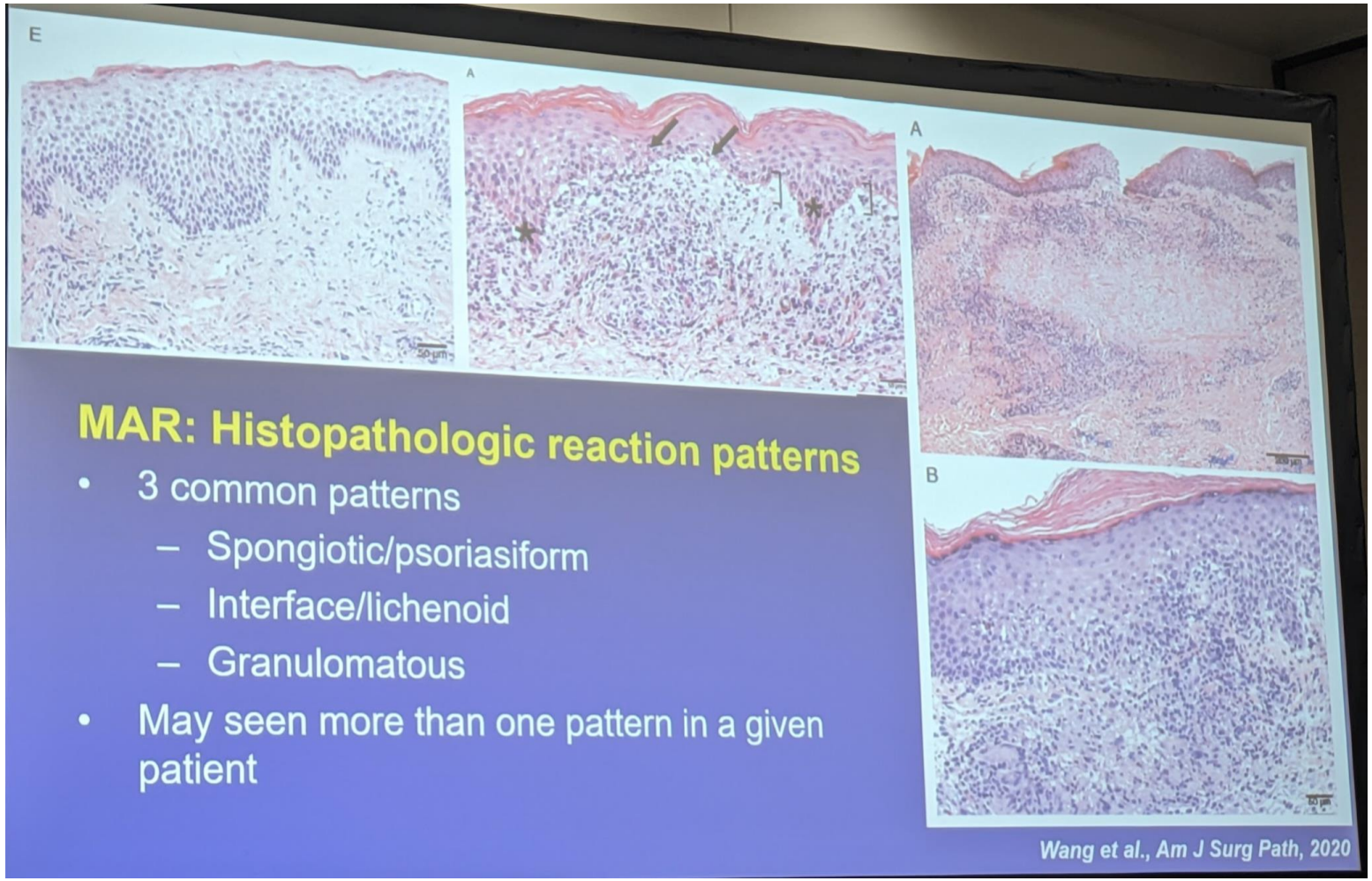
AAD ANNUAL MEETING AEDV highlights SAN DIEGO 8-12 MARZO



Rash asociado a Mogalizumab

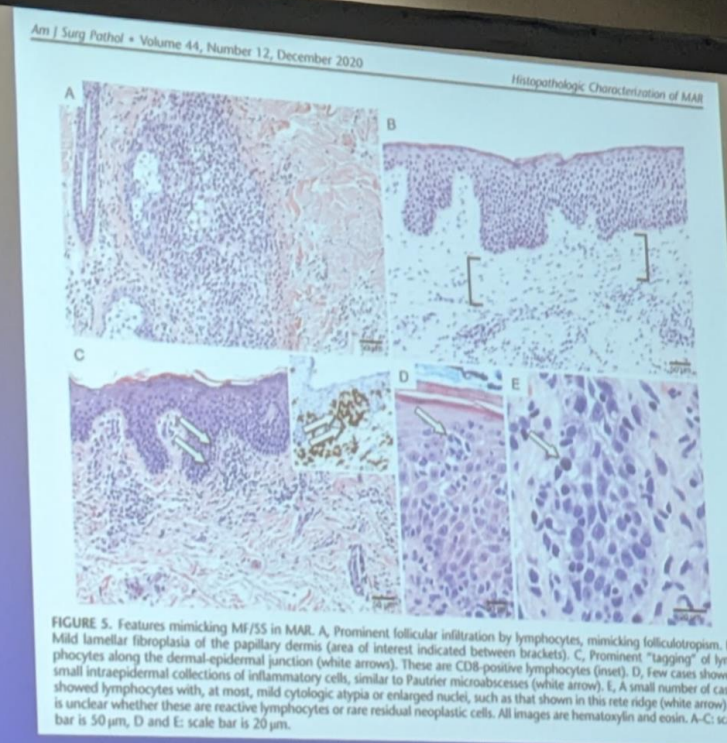


Rash asociado a mogalizumab



Rash asociado a mogalizumab

MAR may exhibit overlapping histopathologic features of MF/SS, but an inverted or normalized CD4:CD8 ratio helps to distinguish MAR from MF/SS



Am J Surg Pathol • Volume 44, Number 12, December 2020 — Histopathologic Characterization of MAR

FIGURE 5. Features mimicking MF/SS in MAR. A, Prominent follicular infiltration by lymphocytes, mimicking folliculotropism. B, Mild lamellar fibroplasia of the papillary dermis (area of interest indicated between brackets). C, Prominent "tagging" of lymphocytes along the dermal-epidermal junction (white arrows). These are CD8-positive lymphocytes (inset). D, Few cases showed small intraepidermal collections of inflammatory cells, similar to Pautrier microabscesses (white arrow). E, A small number of cases showed lymphocytes with, at most, mild cytologic atypia or enlarged nuclei, such as that shown in this rete ridge (white arrow). It is unclear whether these are reactive lymphocytes or rare residual neoplastic cells. All images are hematoxylin and eosin. A-C: scale bar is 50 μm, D and E: scale bar is 20 μm.

	Total (N)	Ratio <1:1	Ratio = 1:1	Ratio > 1:1
Immunohistochemistry				
CD4:CD8 in epidermis	43	31 (72)	7 (16)	5 (12)
CD4:CD8 in dermis*	43	4 (9)	13 (30)	26 (60)
CD4:CD8 in follicles	14	1 (7)	6 (43)	7 (50)

Wang et al., Am J Surg Path, 2020

Rash asociado a mogalizumab

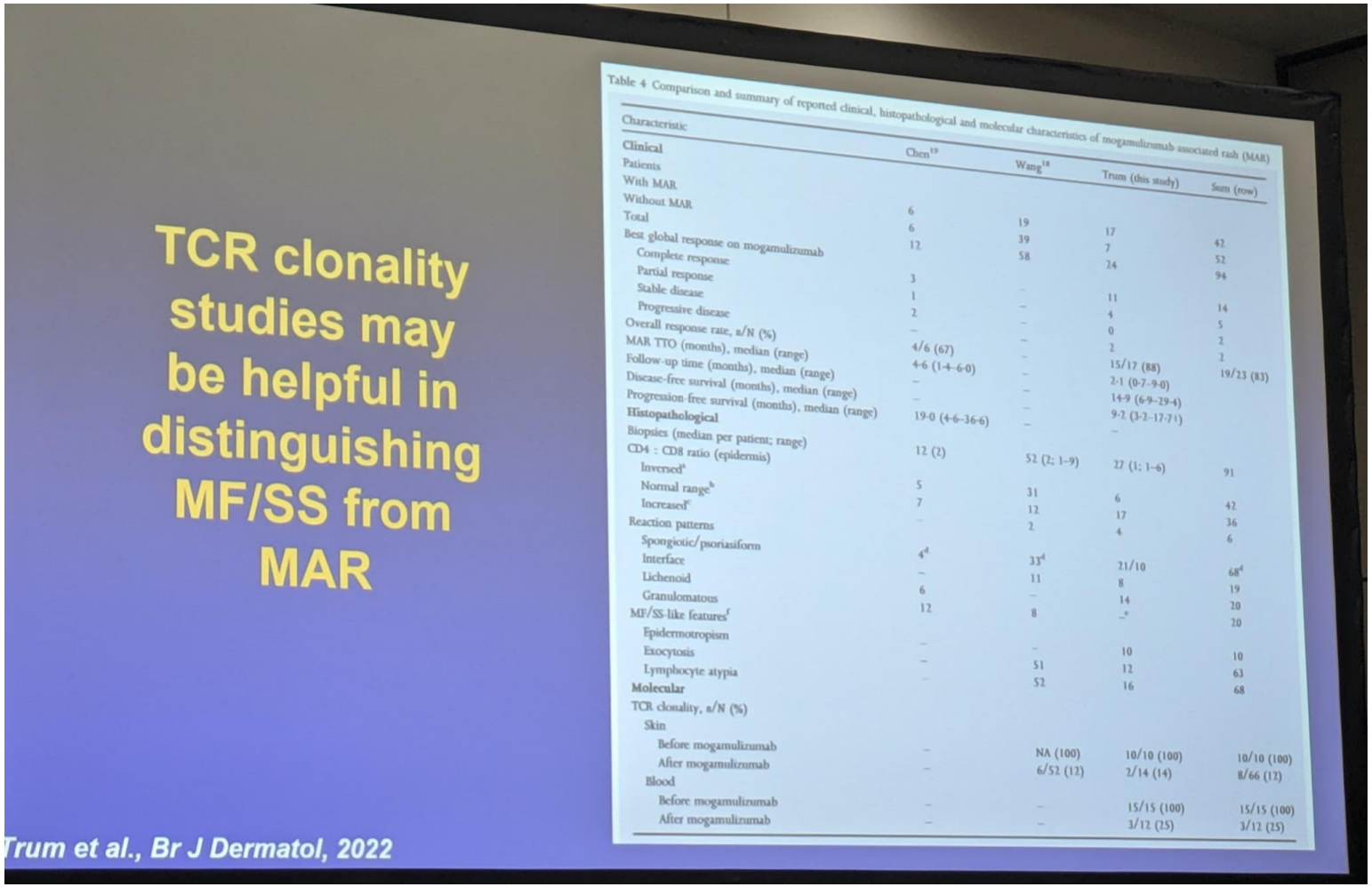


Table 4 Comparison and summary of reported clinical, histopathological and molecular characteristics of mogamulizumab associated rash (MAR)

Characteristic	Chen[19]	Wang[18]	Trum (this study)	Sum (row)
Clinical				
Patients				
With MAR	6	19	17	42
Without MAR	6	39	7	52
Total	12	58	24	94
Best global response on mogamulizumab				
Complete response	3	–	11	14
Partial response	1	–	4	5
Stable disease	2	–	0	2
Progressive disease	–	–	2	2
Overall response rate, n/N (%)	4/6 (67)	–	15/17 (88)	19/23 (83)
MAR TTO (months), median (range)	4·6 (1·4–6·0)	–	2·1 (0·7–9·0)	
Follow-up time (months), median (range)	–	–	14·9 (6·9–29·4)	
Disease-free survival (months), median (range)	–	–	9·2 (3·2–17·71)	
Progression-free survival (months), median (range)	19·0 (4·6–36·6)	–	–	
Histopathological				
Biopsies (median per patient; range)	12 (2)	52 (2; 1–9)	27 (1; 1–6)	91
CD4 : CD8 ratio (epidermis)				
Inversed[a]	5	31	6	42
Normal range[b]	7	12	17	36
Increased[c]	–	2	4	6
Reaction patterns				
Spongiotic/psoriasiform	4[d]	33[d]	21/10	68[d]
Interface	–	11	8	19
Lichenoid	6	–	14	20
Granulomatous	12	8	–[e]	20
MF/SS-like features[f]				
Epidermotropism	–	–	10	10
Exocytosis	–	51	12	63
Lymphocyte atypia	–	52	16	68
Molecular				
TCR clonality, n/N (%)				
Skin				
Before mogamulizumab	–	NA (100)	10/10 (100)	10/10 (100)
After mogamulizumab	–	6/52 (12)	2/14 (14)	8/66 (12)
Blood				
Before mogamulizumab	–	–	15/15 (100)	15/15 (100)
After mogamulizumab	–	–	3/12 (25)	3/12 (25)

Granulomatous MAR may be associated with favorable tumor response

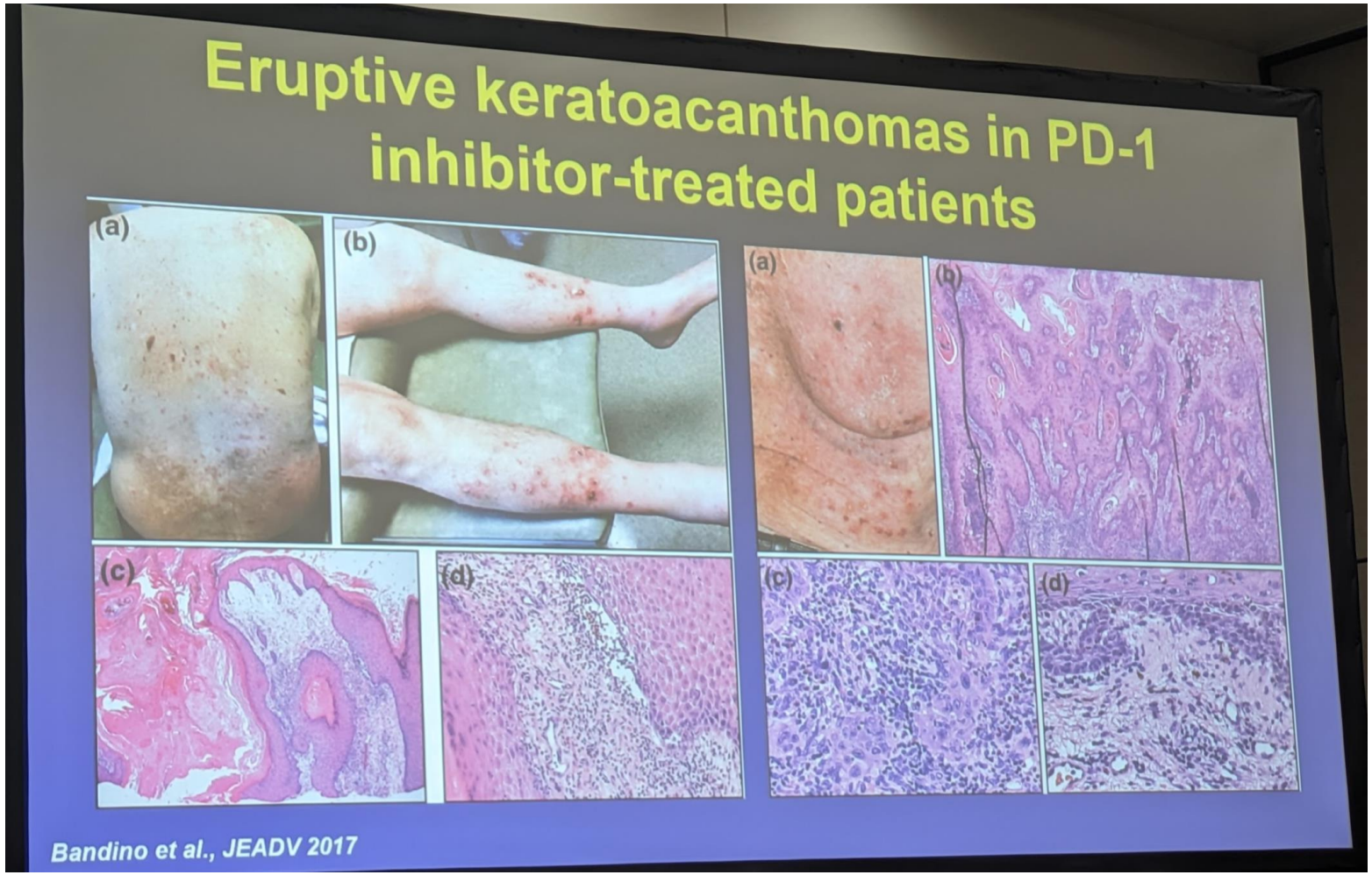
Table. Clinical and Histologic Characteristics of Mogamulizumab-Associated CGDE

Characteristic	Patient No. 1	2	3	4	5	6
Prior therapies	α-Interferon, bexarotene, methotrexate, and romidepsin	Photopheresis, romidepsin, and vorinostat	α-Interferon, bexarotene, photopheresis, and vorinostat	α-Interferon, bexarotene, methotrexate, and vorinostat	Methotrexate and vorinostat	Methotrexate and vorinostat
TTO, mo	1.4	3.9	6.0	4.6	4.6	5.5
Clinical presentation	Erythematous macules	Scaly erythematous plaques	Scaly erythematous plaques	Scaly erythematous plaques	Scaly erythematous plaques	Scaly erythematous papules
Distribution of lesions	Arms	Scalp, trunk, extremities, groin, and buttocks	Trunk, extremities, groin, and buttocks	Face, neck, arms, trunk, and groin	Scalp, trunk, and groin	Face, groin, and foot
Best response						
Blood	SD	CR	CR	CR	CR	CR
Skin	PR	CR	CR	PR	CR	CR
Lymph nodes	SD	PR	CR	SD	CR	CR
Global	SD	PR	CR	SD	CR	CR
Reason for discontinuation	PD (blood)	AE (CGDE, study protocol)	AE (CGDE, study protocol)	AE (CGDE, study protocol)	AE (CGDE, patient withdrew consent)	AE (infection, patient withdrew consent)
PFS, mo	4.6	12.2[a]	36.6[a]	11.3[a]	28.3	25.8
Histologic findings	Moderate superficial granulomatous infiltrates with scattered multinucleated giant cells	Spongiotic dermatitis and dense superficial and deep granulomatous infiltrates with numerous eosinophils and multinucleated giant cells	Lichenoid dermatitis with dyskeratosis and moderate superficial granulomatous infiltrates with scattered eosinophils	Lichenoid dermatitis with focal dyskeratosis and mild superficial granulomatous infiltrates with numerous eosinophils and rare trinucleated cells	Spongiotic dermatitis and dense superficial and deep granulomatous infiltrates with numerous eosinophils and scattered multinucleated giant cells	Lichenoid dermatitis with focal dyskeratosis and mild superficial granulomatous infiltrates with rare eosinophils
CD4:CD8 ratio of CGDE	Normal	Normal or decreased	Normal or decreased	Normal or decreased	Decreased	Normal
CD4:CD8 ratio of SS	Increased	Markedly increased	Increased	Increased	Markedly increased	Markedly increased
TCR-PCR of CGDE	Polyclonal	Polyclonal	No amplification	No amplification	Polyclonal	Clonal at 158 and 191 bp[b]
T-bet, %[c]	NA	32	75	48	46	NA
Decrease in Treg cells, %[d]	NA	NA	65	68	NA	NA

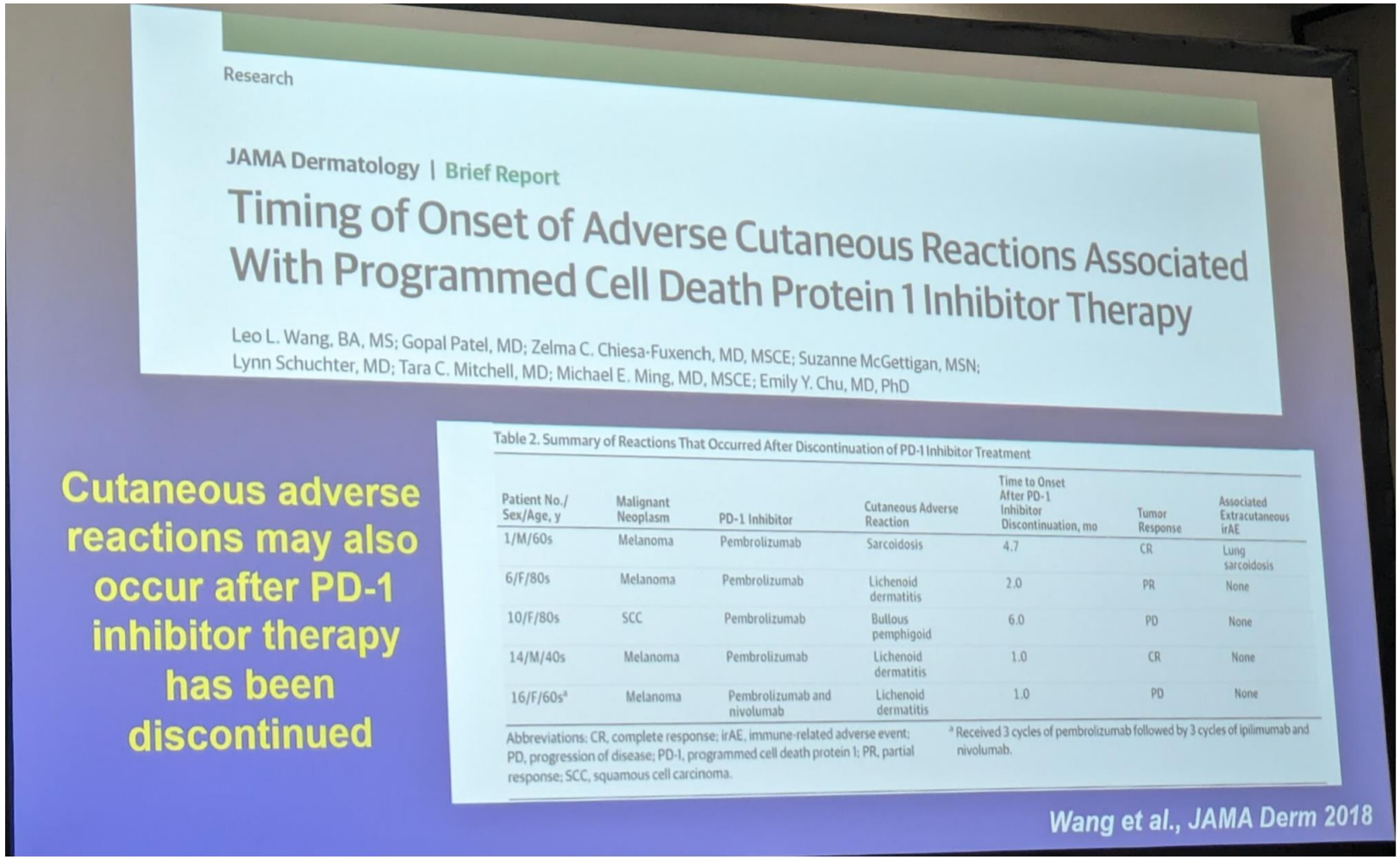
Chen et al., JAMA Derm 2019

Reacciones asociadas a pembrolizumab

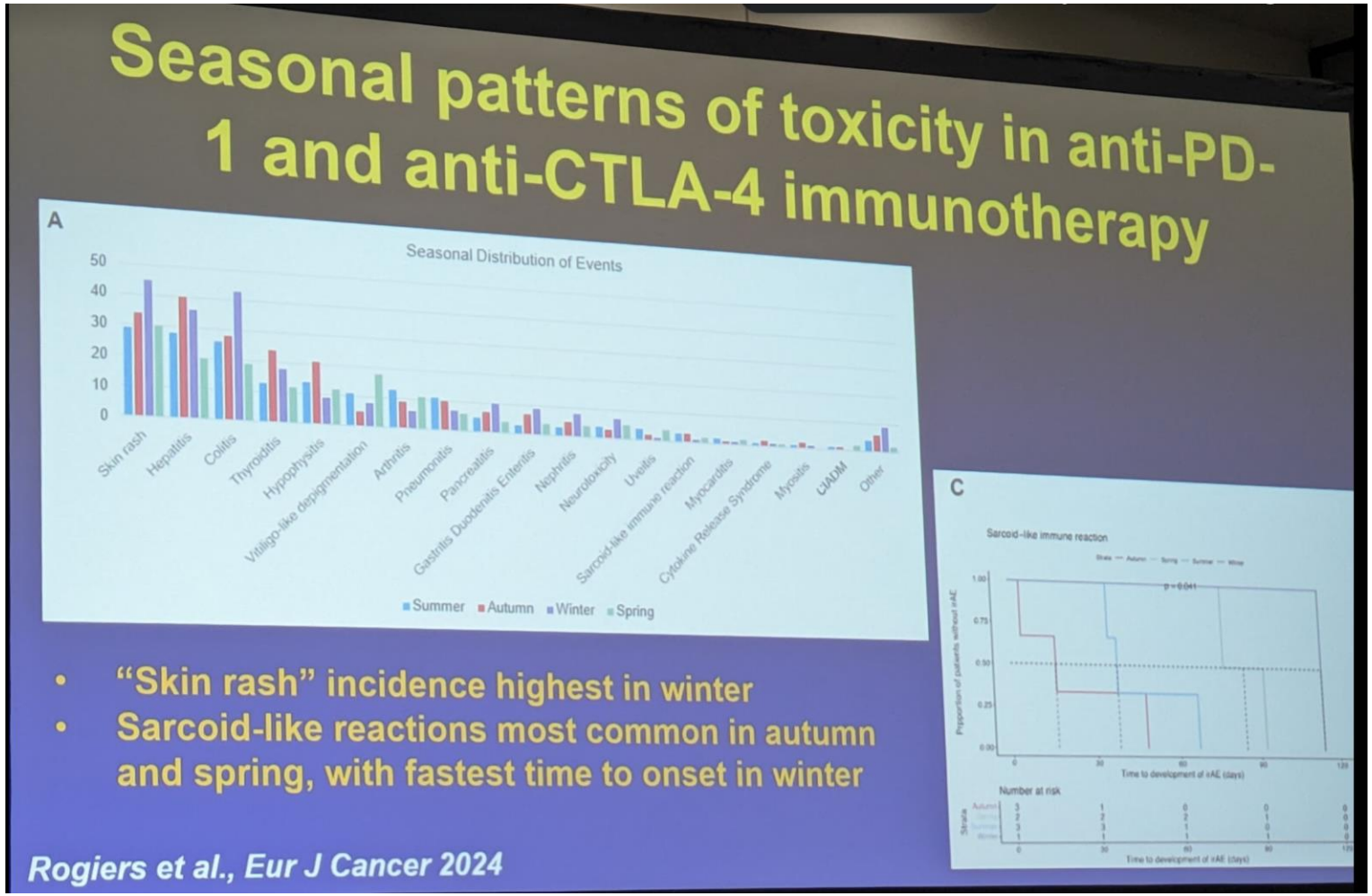
Querartoacantomas eruptivos



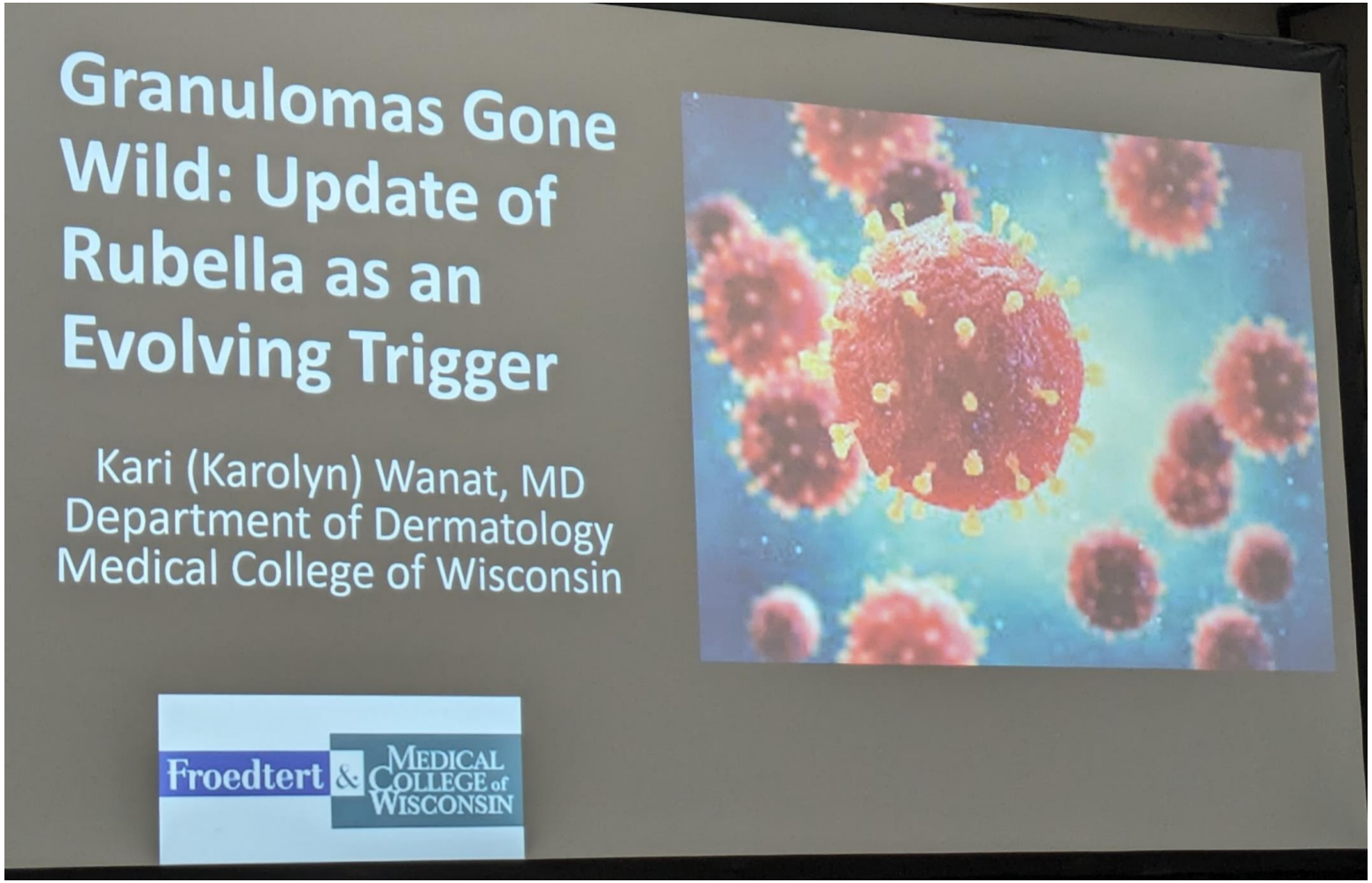
Efectos adversos pueden suceder tras suspensión



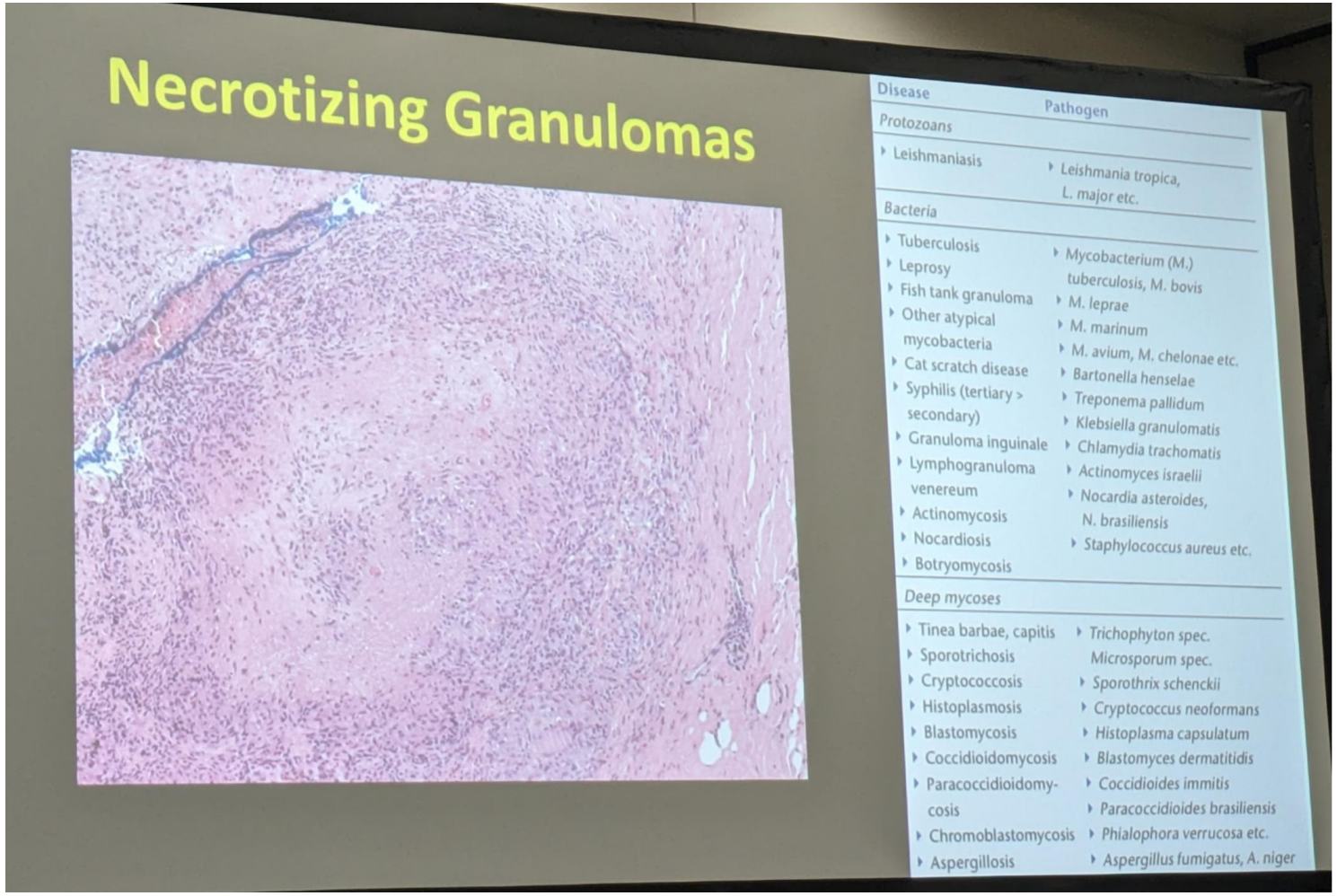
Toxicidad estacional por anti-PD1 anti CTLA-4

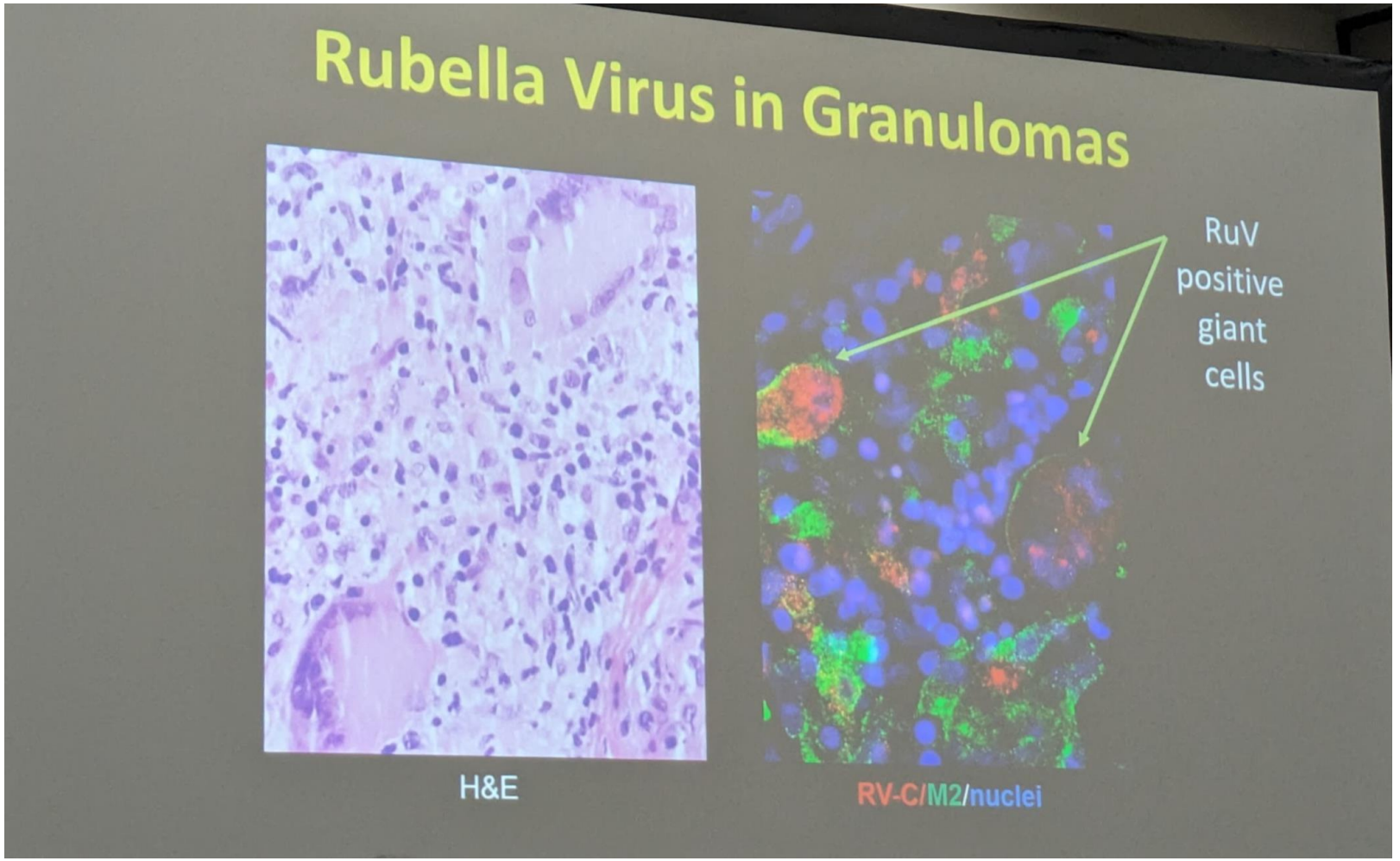


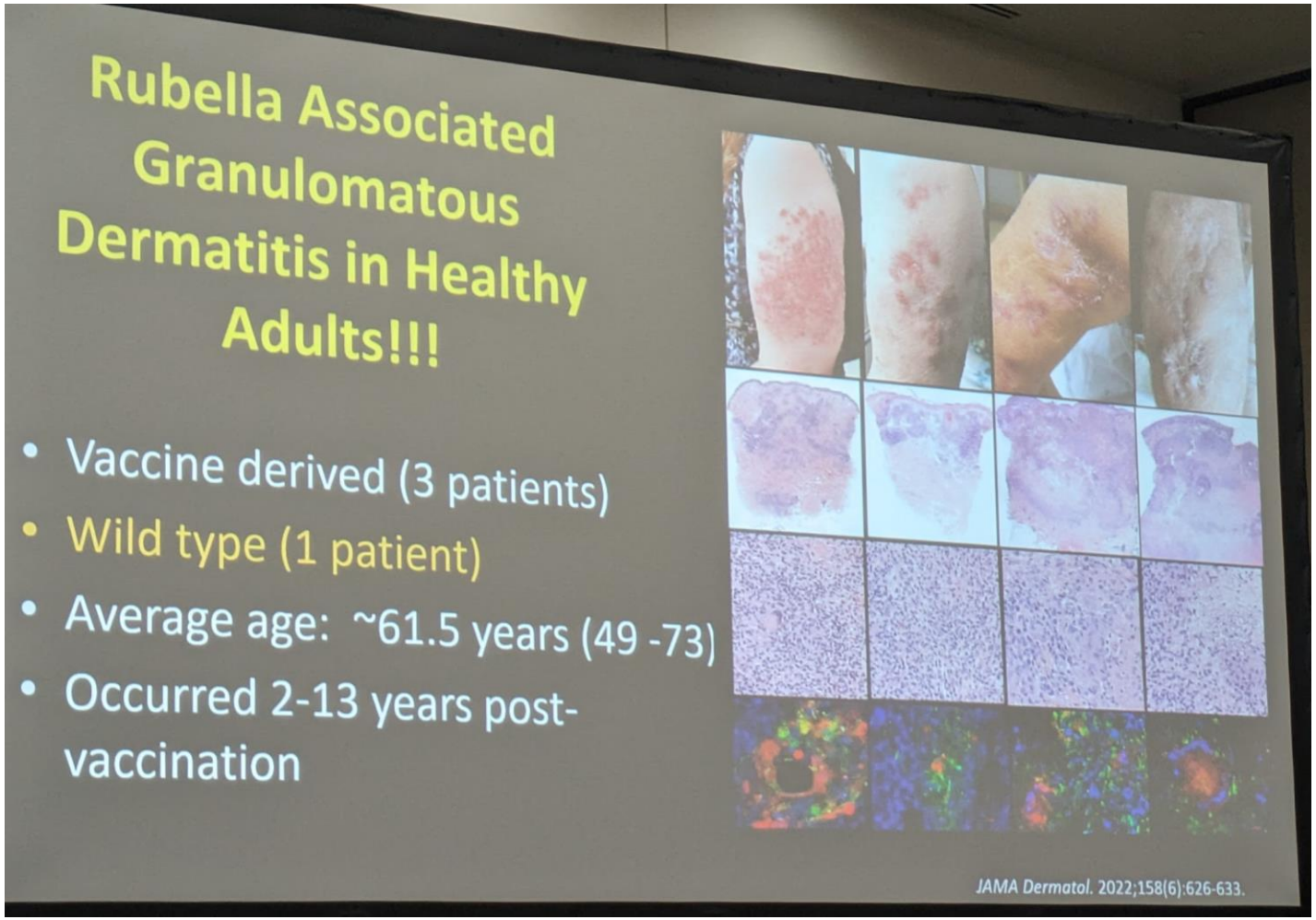
Procesos granulomatosos secundarios a rubeola

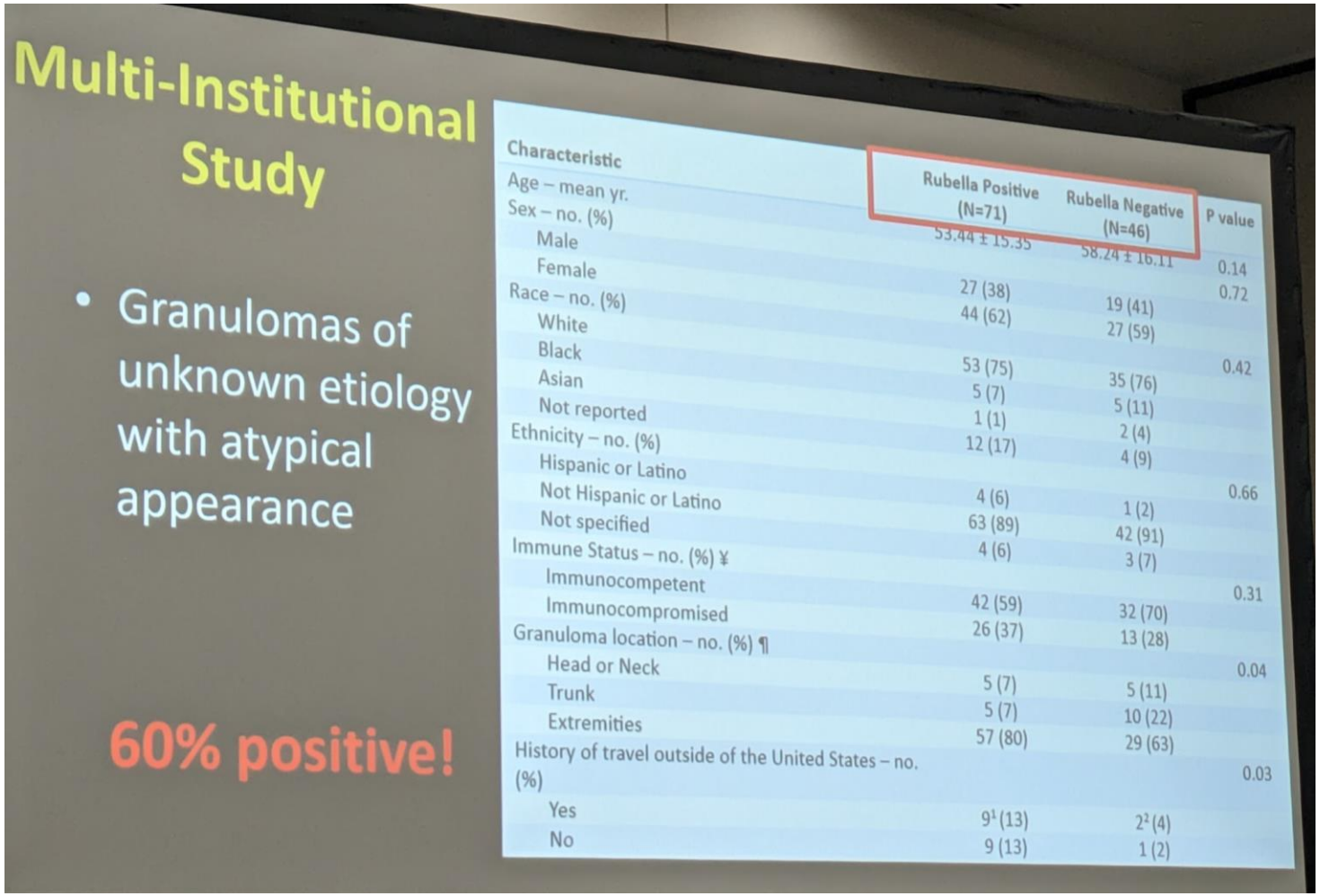


Granuloma necrotizante.. infección

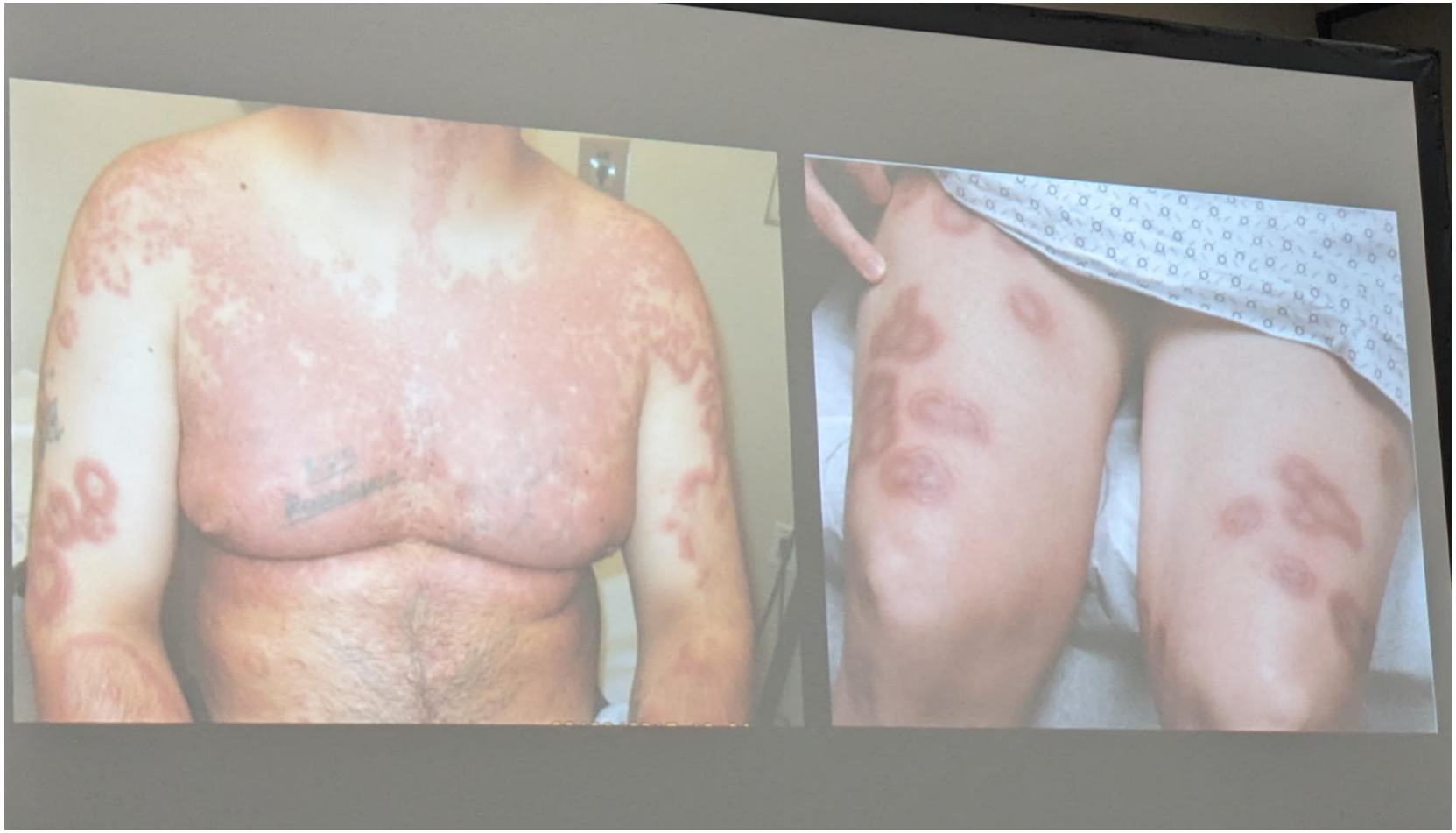


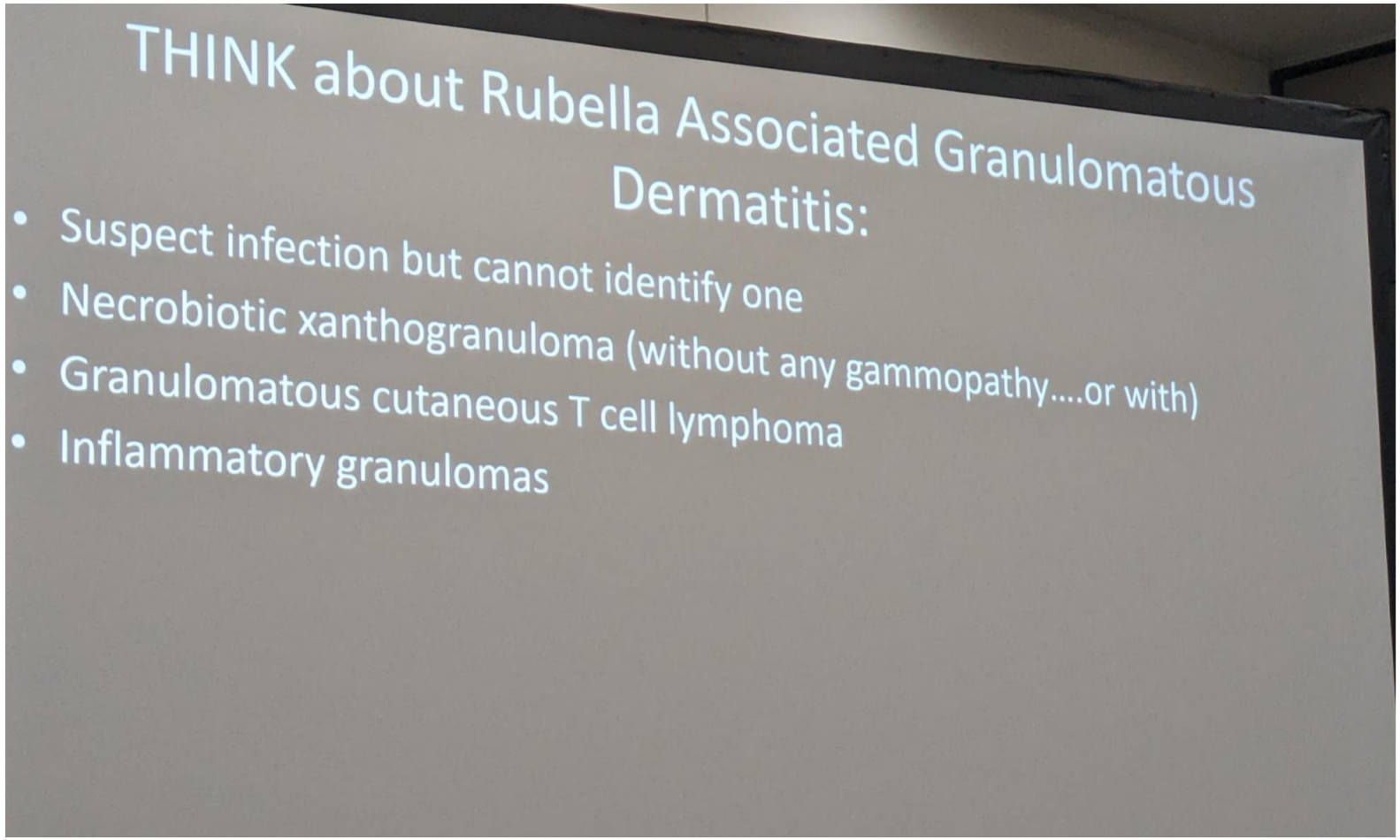

Rubella Virus in Granulomas
RuV positive giant cells
H&E
RV-C/M2/nuclei

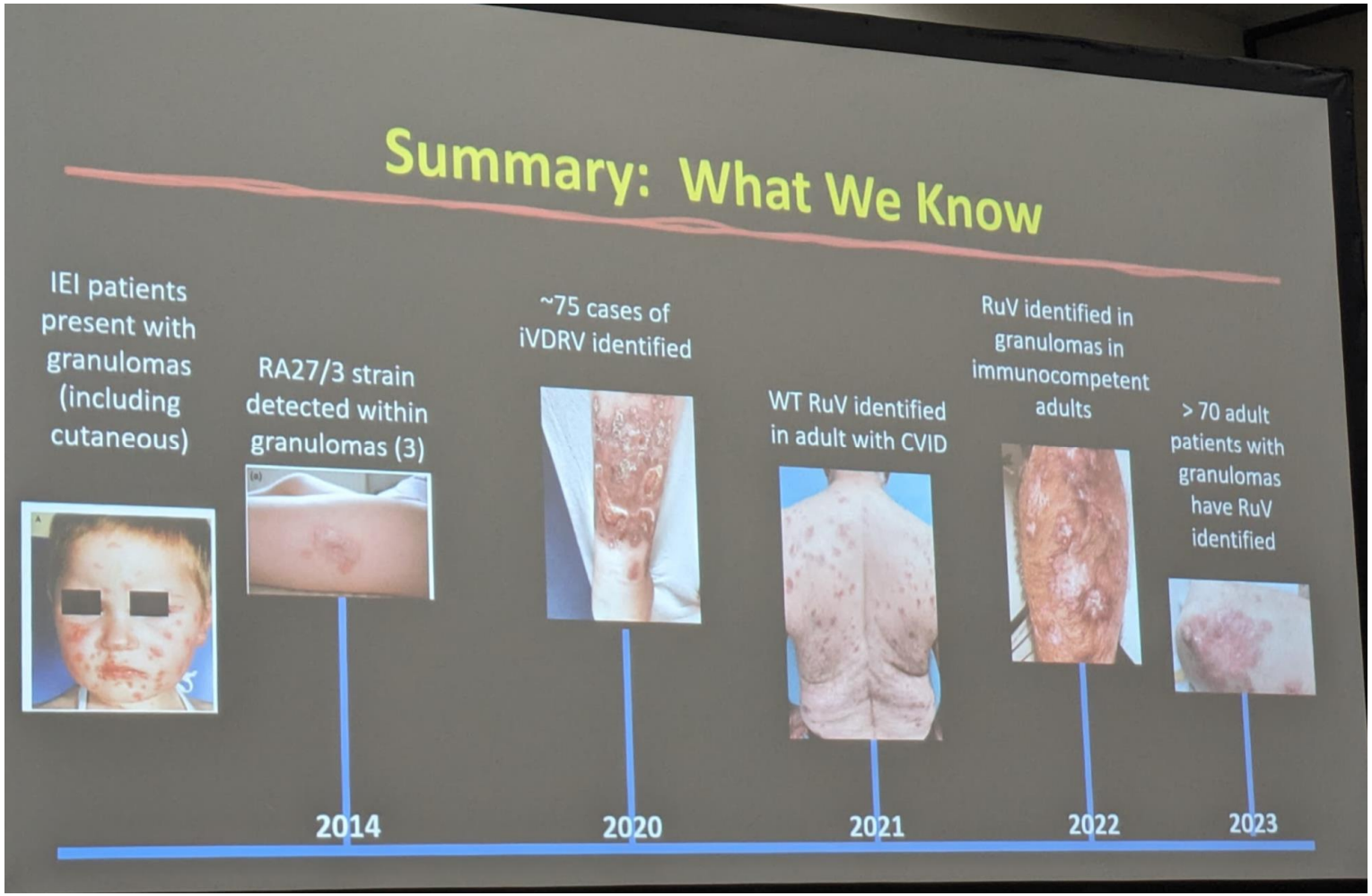

Rubella Associated Granulomatous Dermatitis in Healthy Adults!!!
• Vaccine derived (3 patients)
• Wild type (1 patient)
• Average age: ~61.5 years (49 -73)
• Occurred 2-13 years post-vaccination
JAMA Dermatol. 2022;158(6):626-633.

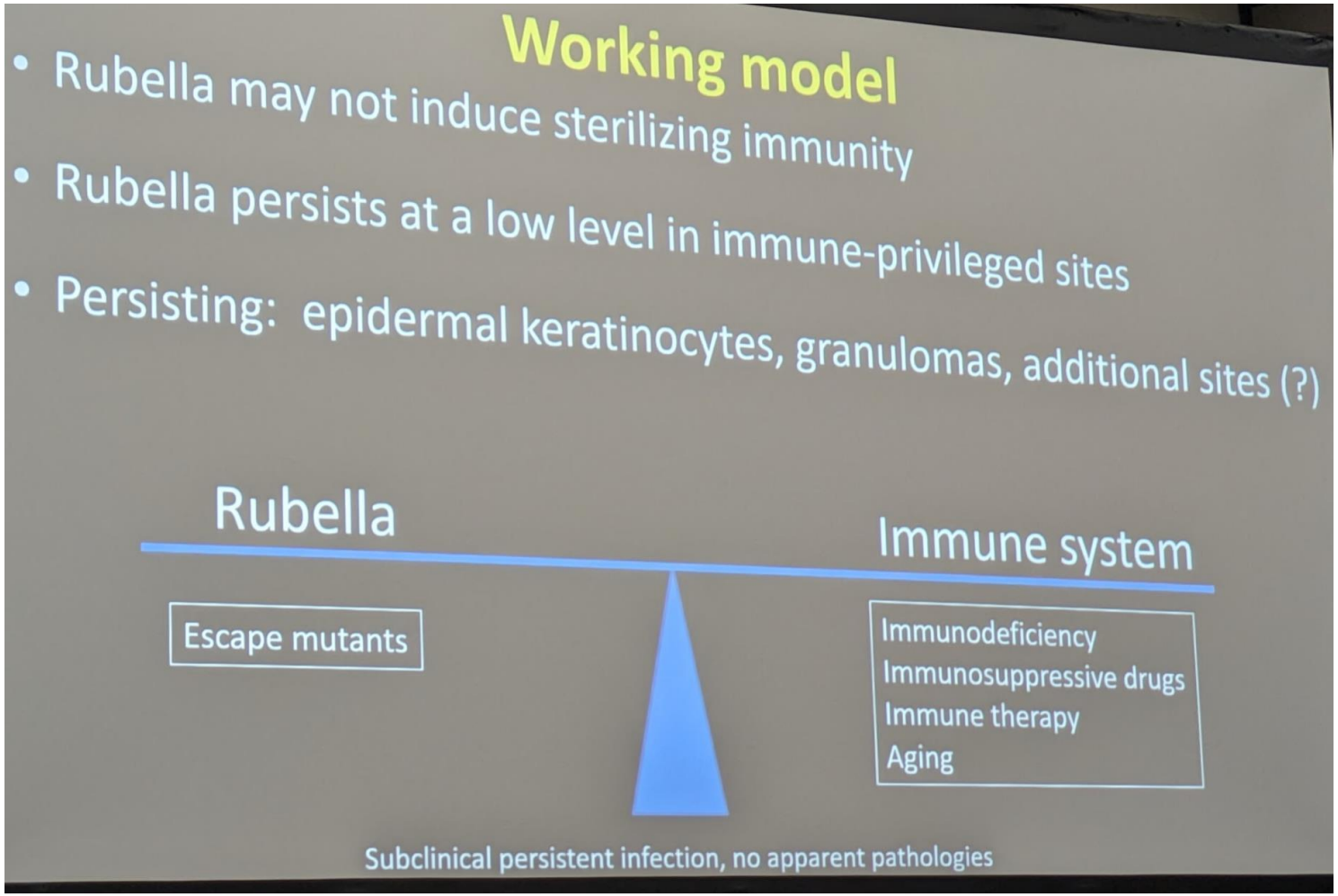


Characteristic	Rubella Positive (N=71)	Rubella Negative (N=46)	P value
Age – mean yr.	53.44 ± 15.35	58.24 ± 16.11	0.14
Sex – no. (%)			0.72
Male	27 (38)	19 (41)	
Female	44 (62)	27 (59)	
Race – no. (%)			0.42
White	53 (75)	35 (76)	
Black	5 (7)	5 (11)	
Asian	1 (1)	2 (4)	
Not reported	12 (17)	4 (9)	
Ethnicity – 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[2] (4)	
No	9 (13)	1 (2)	




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

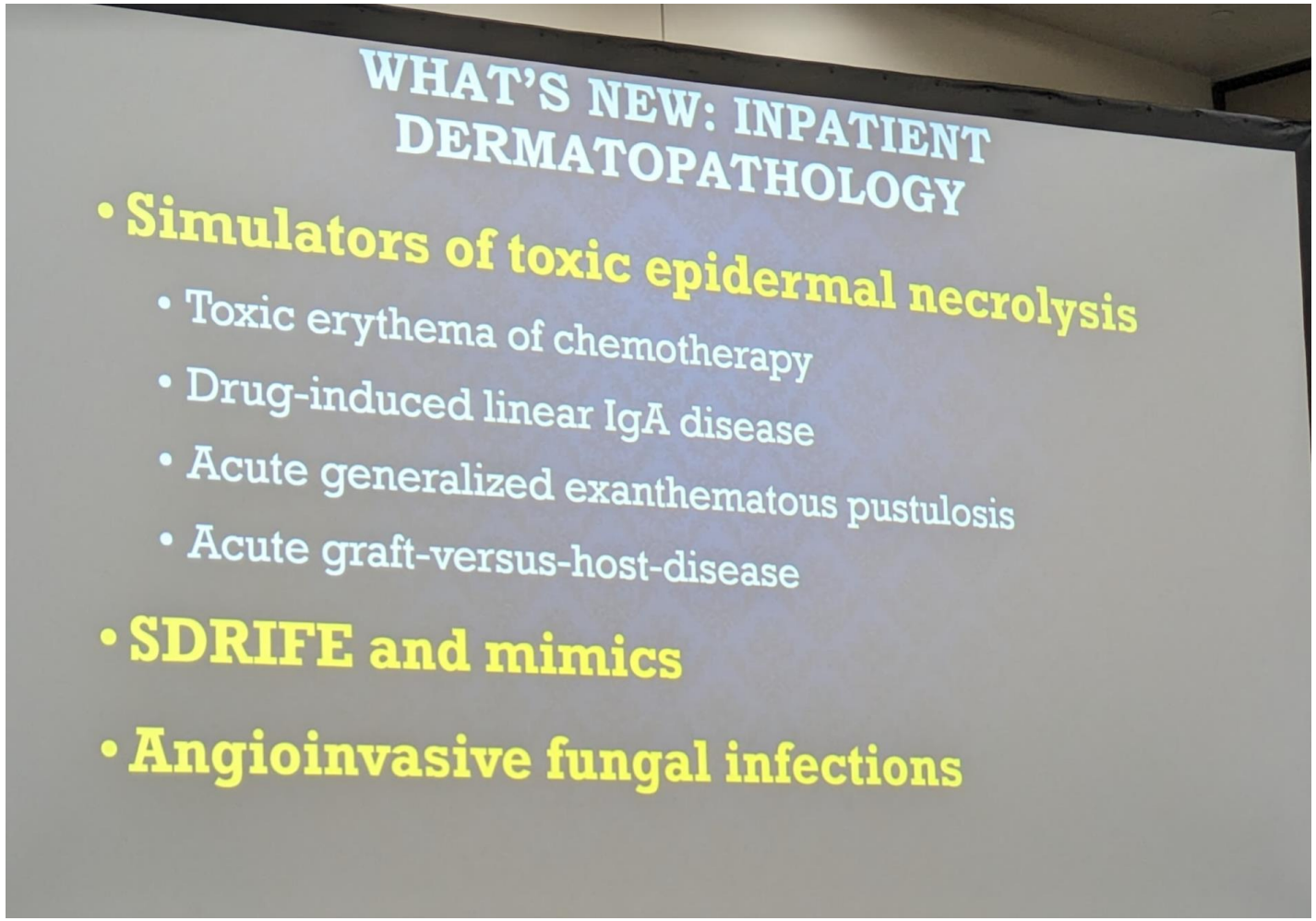

Summary: What We Know
IEI patients present with granulomas (including cutaneous)
RA27/3 strain detected within granulomas (3)
~75 cases of iVDRV identified
WT RuV identified in adult with CVID
RuV identified in granulomas in immunocompetent adults
> 70 adult patients with granulomas have RuV identified
2014
2020
2021
2022
2023


Working model
• Rubella may not induce sterilizing immunity
• Rubella persists at a low level in immune-privileged sites
• Persisting: epidermal keratinocytes, granulomas, additional sites (?)
Rubella
Immune system
Escape mutants
Immunodeficiency
Immunosuppressive drugs
Immune therapy
Aging
Subclinical persistent infection, no apparent pathologies

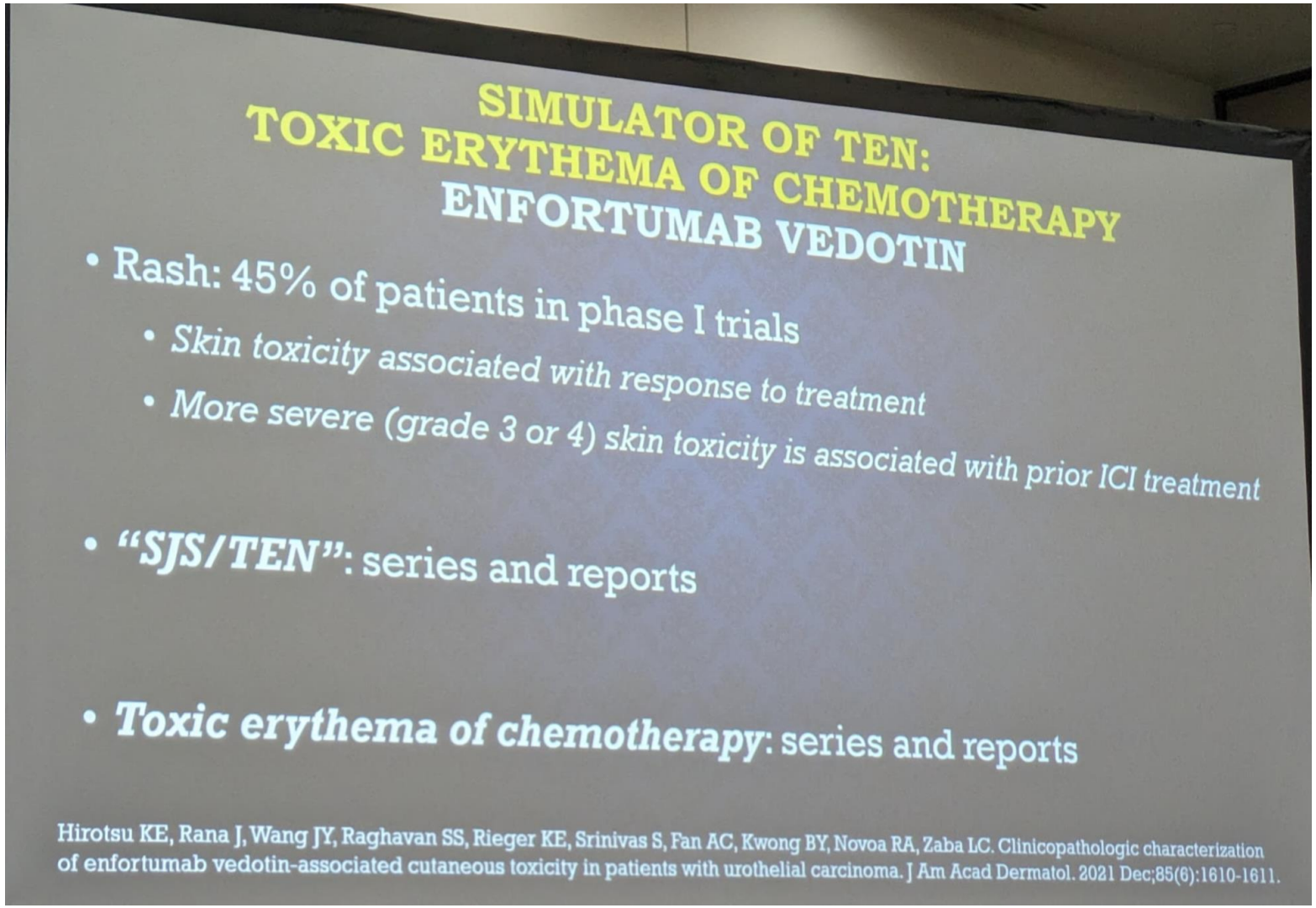
Novedades en toxicodermias y simuladores

AAD ANNUAL MEETING AEDV highlights

SAN DIEGO 8-12 MARZO



Simuladores de NET: Enfortumab vedotin



Anti-nectina 4 mAb

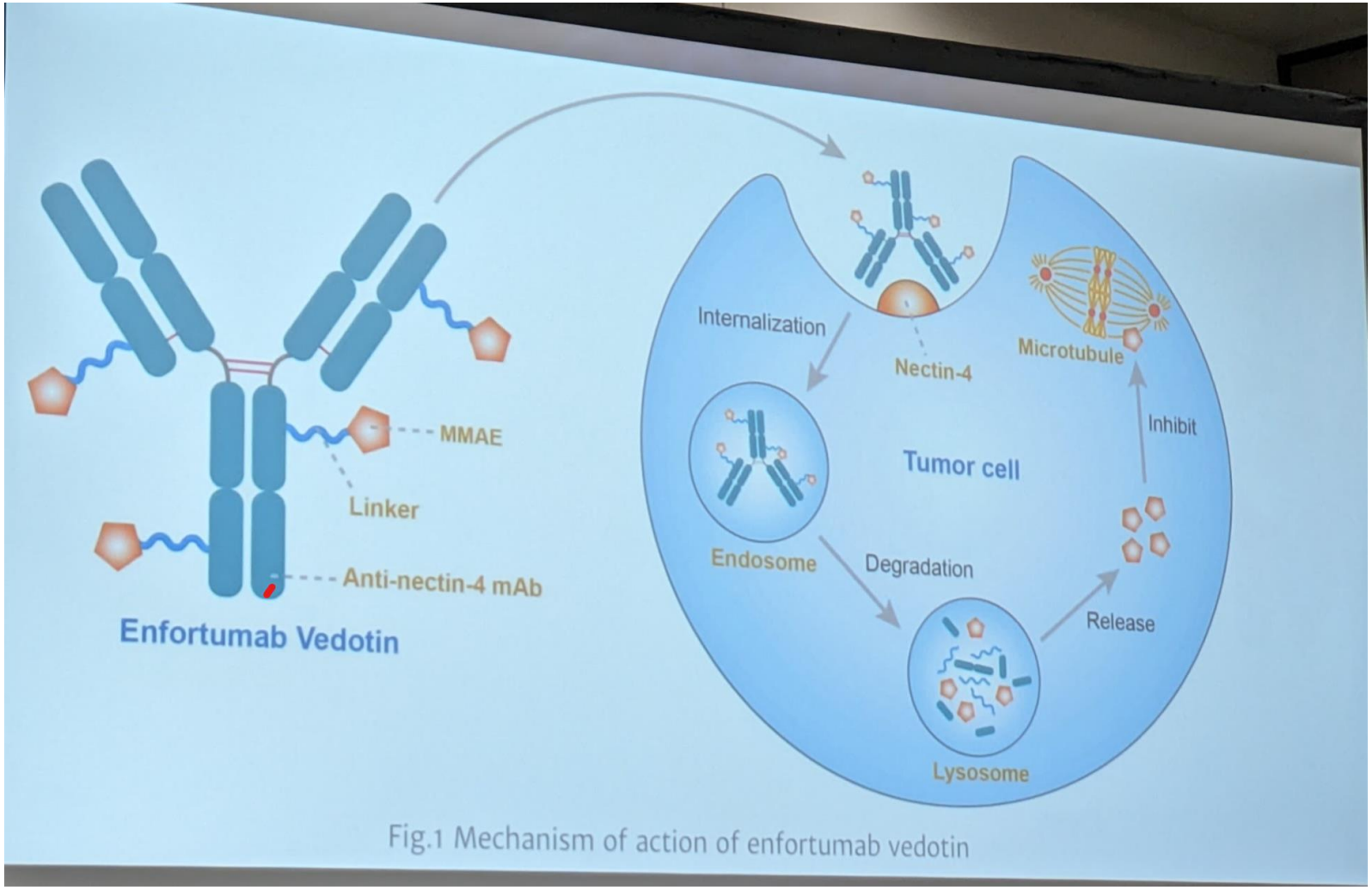
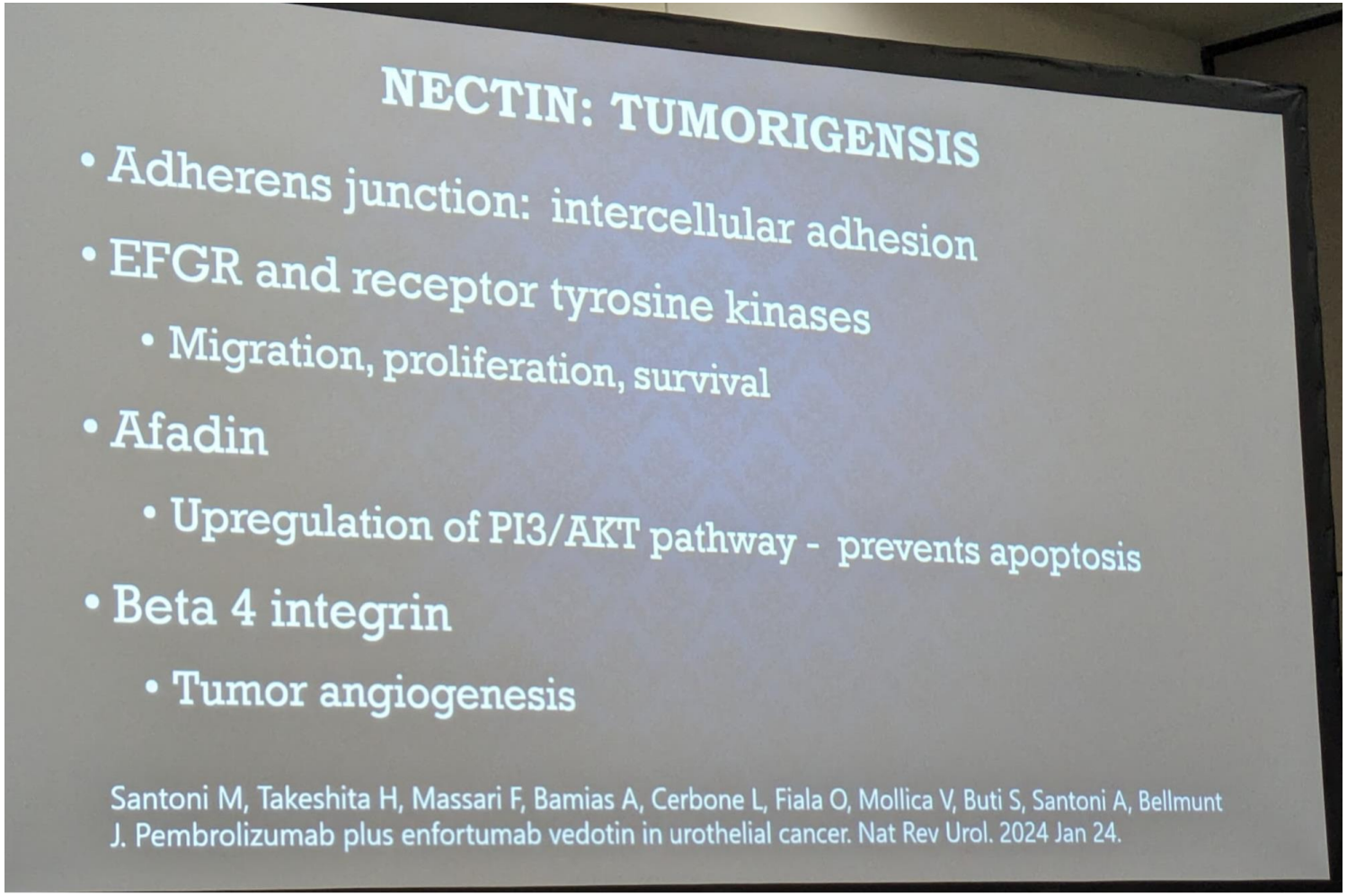
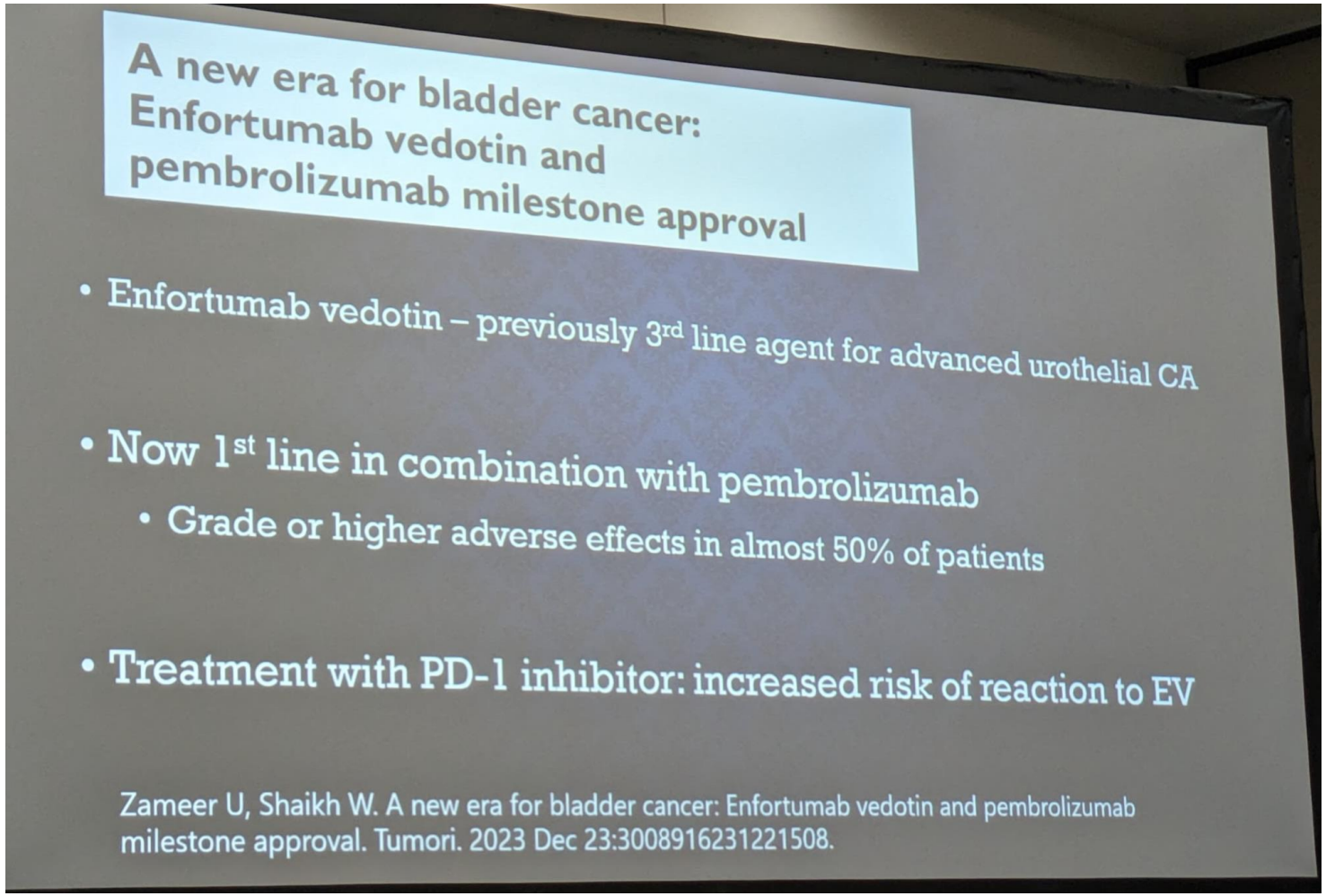


Fig.1 Mechanism of action of enfortumab vedotin

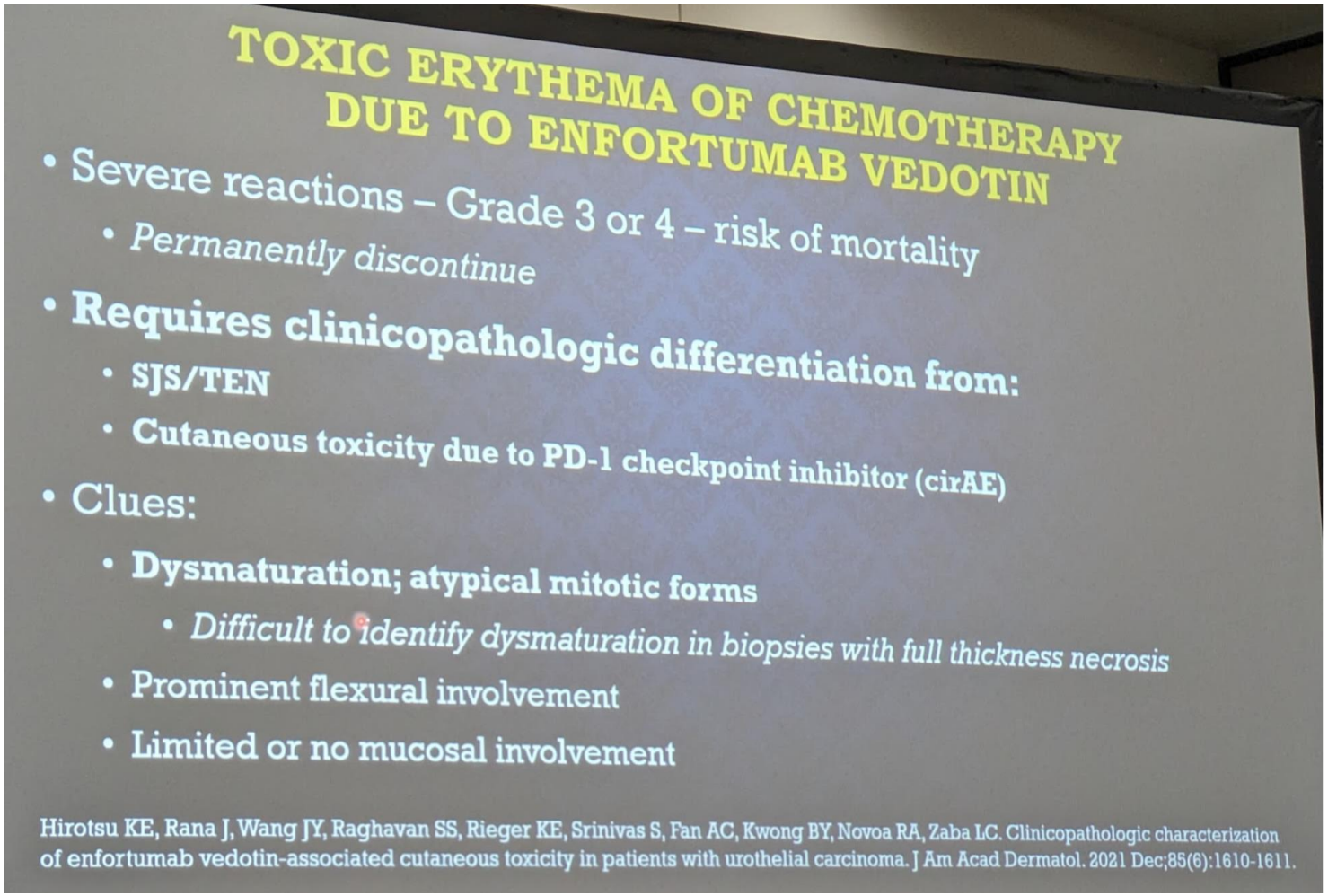
Nectina: Tumorigénesis



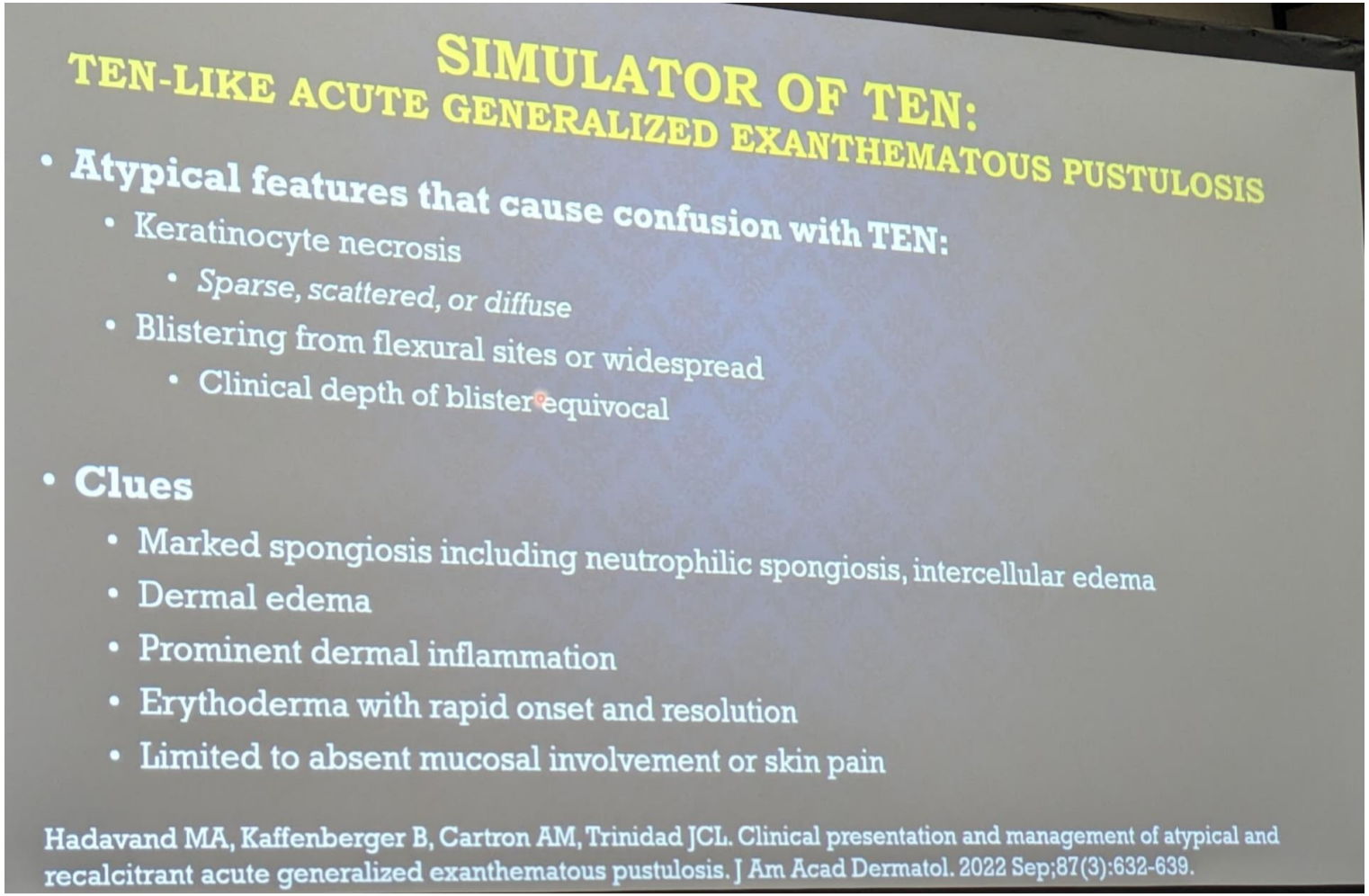
Primera línea de tratamiento



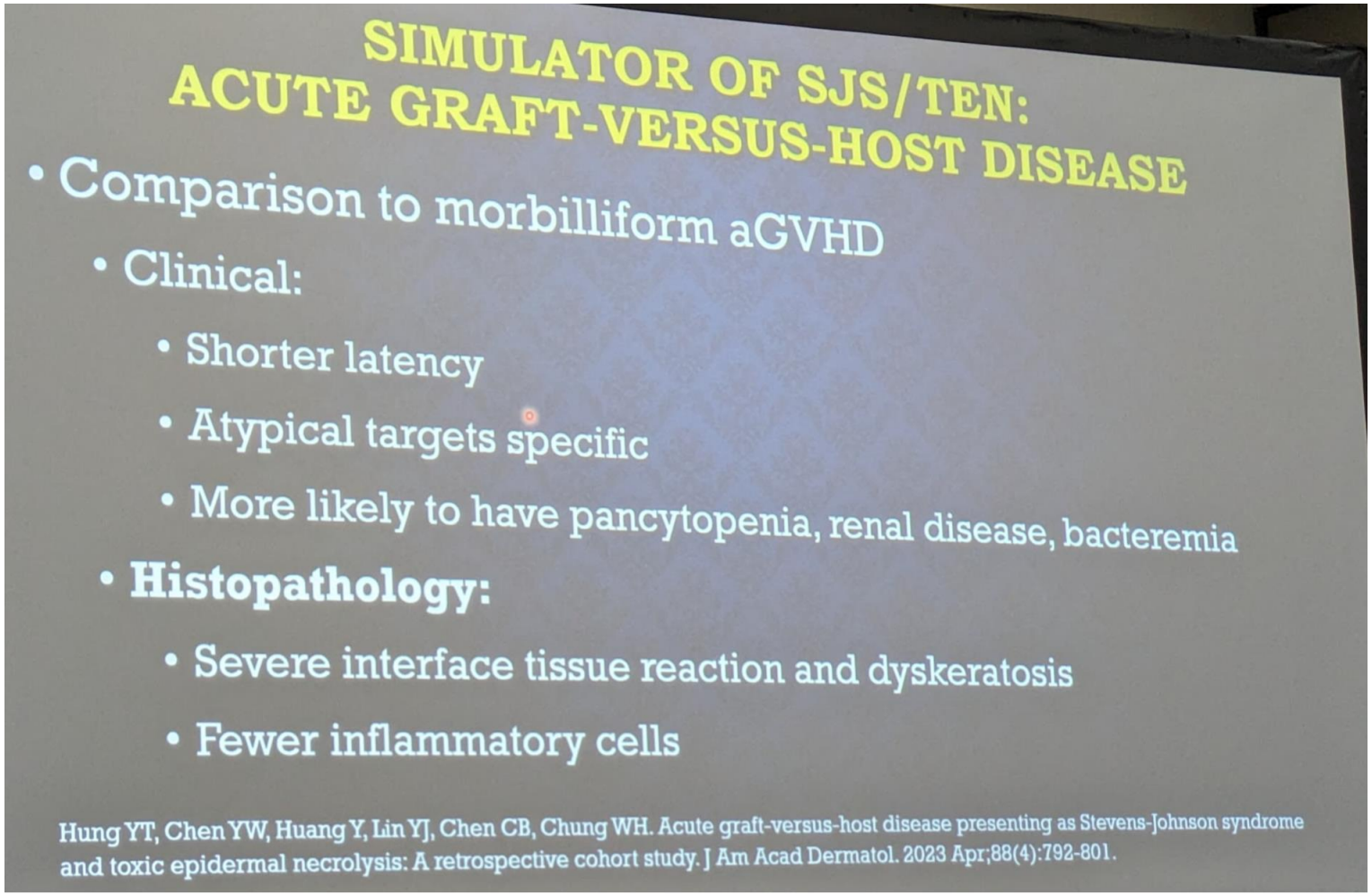
Eritema tóxico por enfortumab vedotin



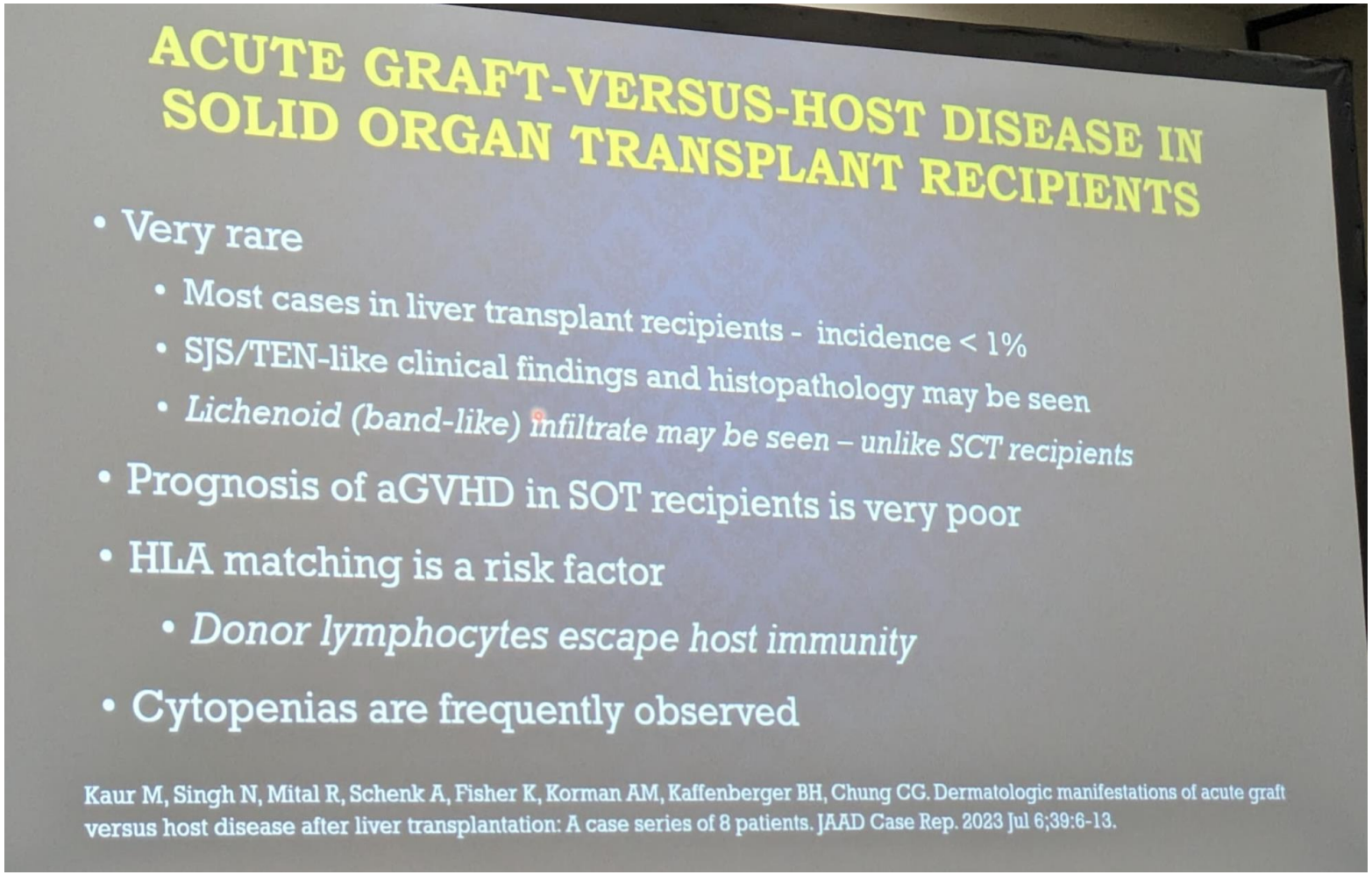
Simuladores de NET: PEGA NET LIKE



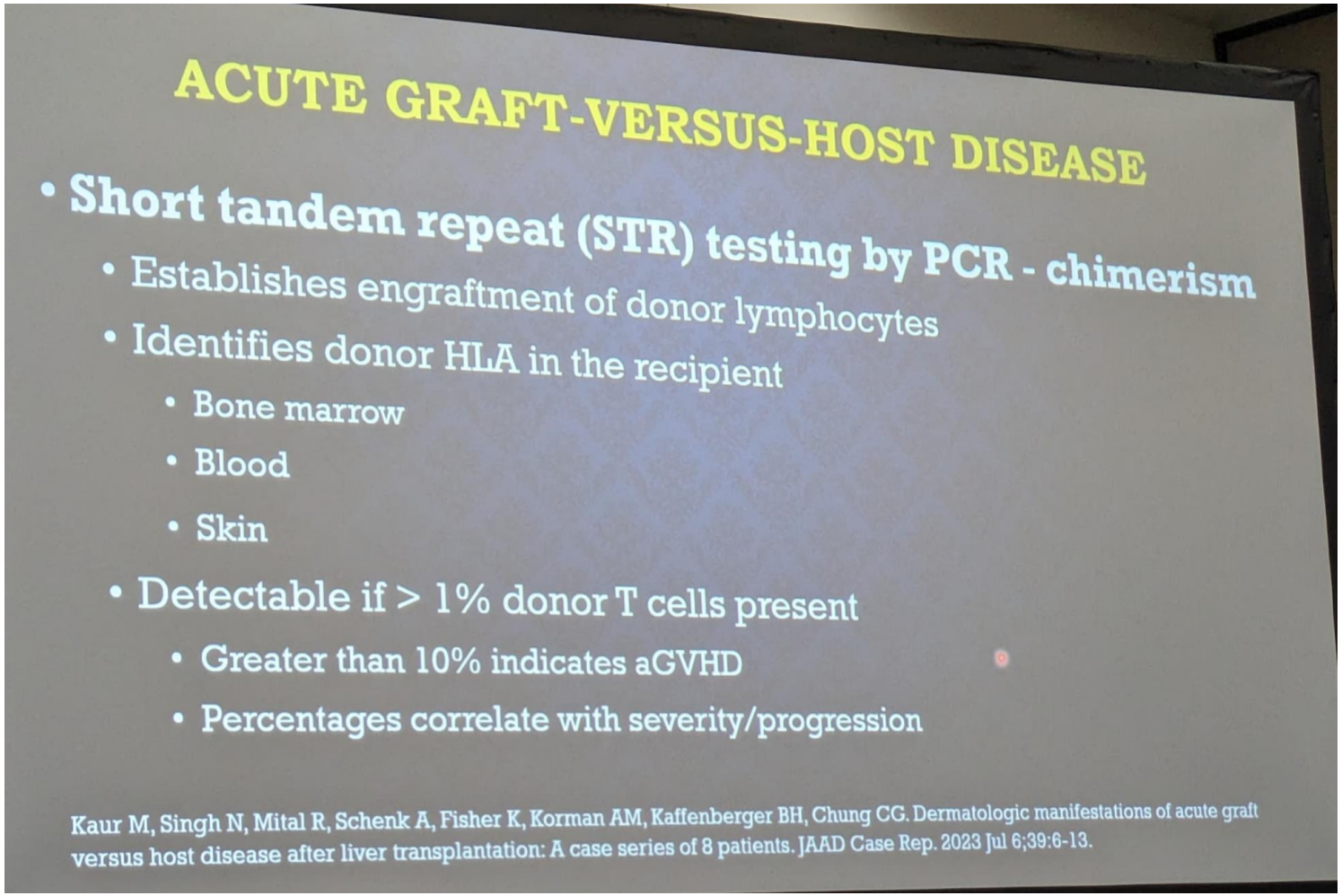
EICH simulando NET



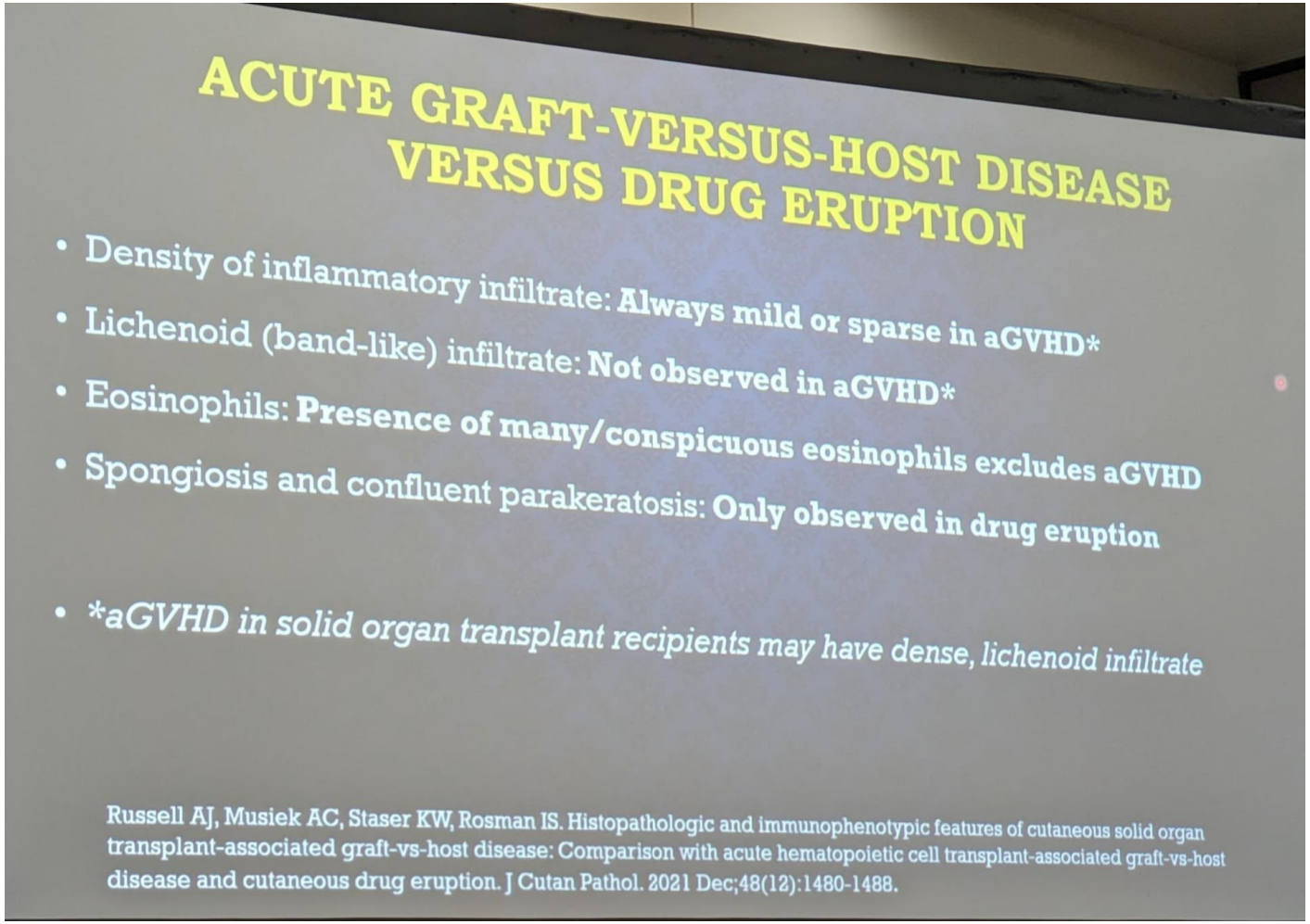
EICH en Trasplantados de órgano sólido



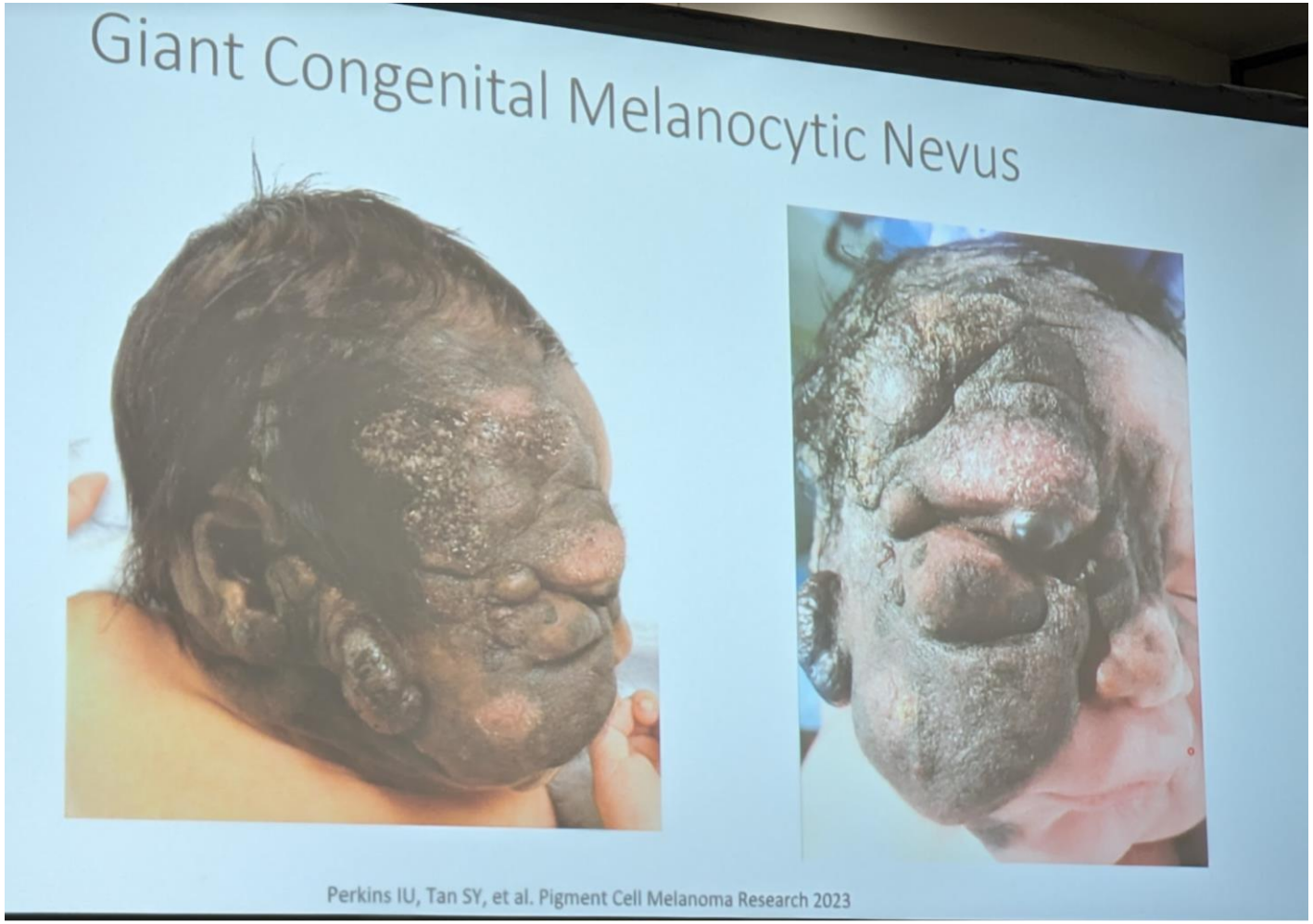
EICH

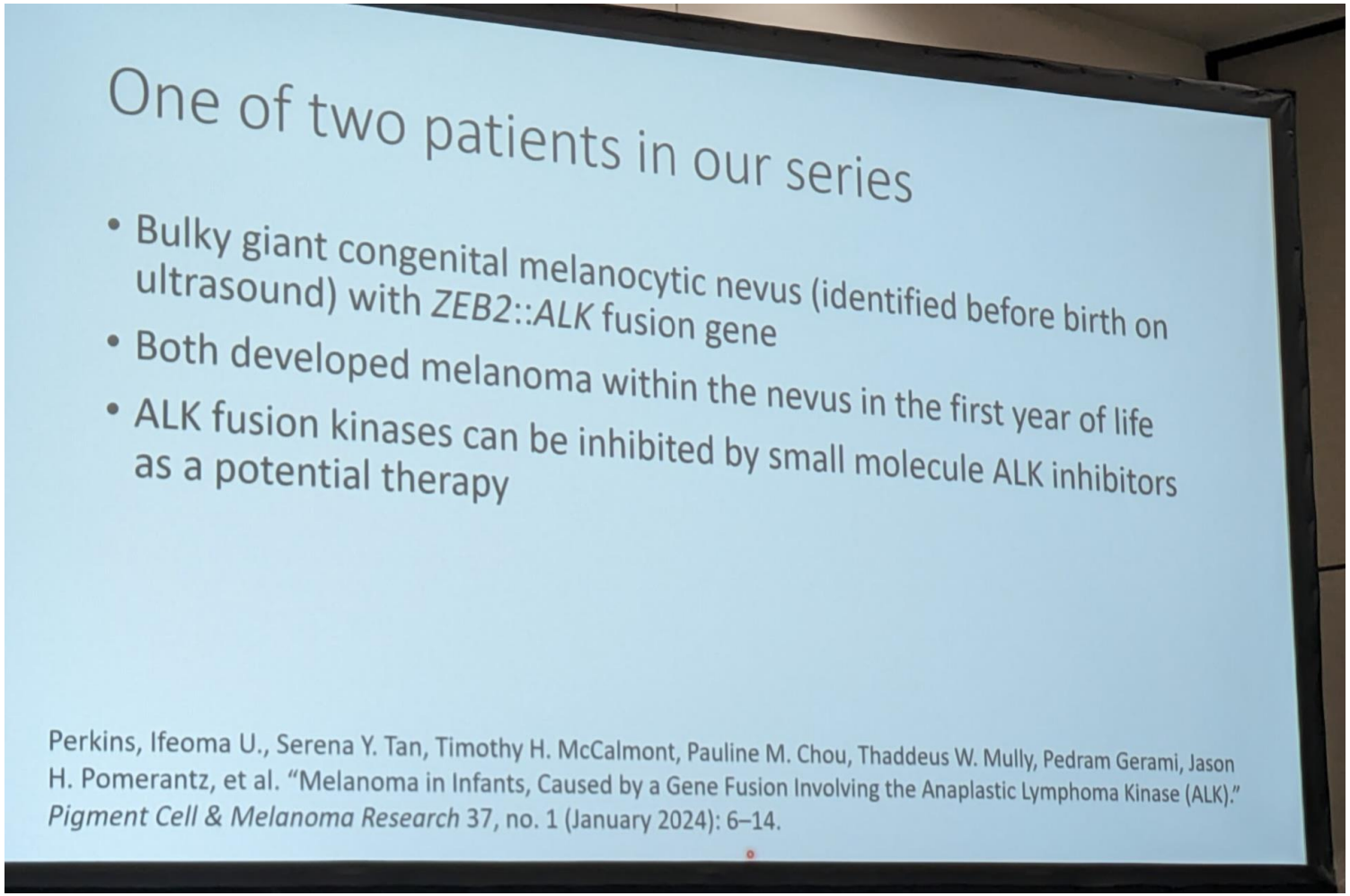

ACUTE GRAFT-VERSUS-HOST DISEASE
• Short tandem repeat (STR) testing by PCR - chimerism
• Establishes engraftment of donor lymphocytes
• Identifies donor HLA in the recipient
• Bone marrow
• Blood
• Skin
• Detectable if > 1% donor T cells present
• Greater than 10% indicates aGVHD
• Percentages correlate with severity/progression
Kaur M, Singh N, Mital R, Schenk A, Fisher K, Korman AM, Kaffenberger BH, Chung CG. Dermatologic manifestations of acute graft versus host disease after liver transplantation: A case series of 8 patients. JAAD Case Rep. 2023 Jul 6;39:6-13.

EICH vs toxicodermia



Melanocíticas




One of two patients in our series
• Bulky giant congenital melanocytic nevus (identified before birth on ultrasound) with *ZEB2*::*ALK* fusion gene
• Both developed melanoma within the nevus in the first year of life
• ALK fusion kinases can be inhibited by small molecule ALK inhibitors as a potential therapy
Perkins, Ifeoma U., Serena Y. Tan, Timothy H. McCalmont, Pauline M. Chou, Thaddeus W. Mully, Pedram Gerami, Jason H. Pomerantz, et al. "Melanoma in Infants, Caused by a Gene Fusion Involving the Anaplastic Lymphoma Kinase (ALK)." *Pigment Cell & Melanoma Research* 37, no. 1 (January 2024): 6–14.

Genomic Analysis of Pigmented Epithelioid Melanocytomas Reveals Recurrent Alterations in *PRKAR1A*, and *PRKCA* Genes

Jarish N. Cohen, MD, PhD, Nancy M. Joseph, MD, PhD,*†‡ Jeffrey P. North, MD,‡§‖ Courtney Onodera, PhD,† Artur Zembowicz, MD, PhD,¶ and Philip E. LeBoit, MD*‡§*

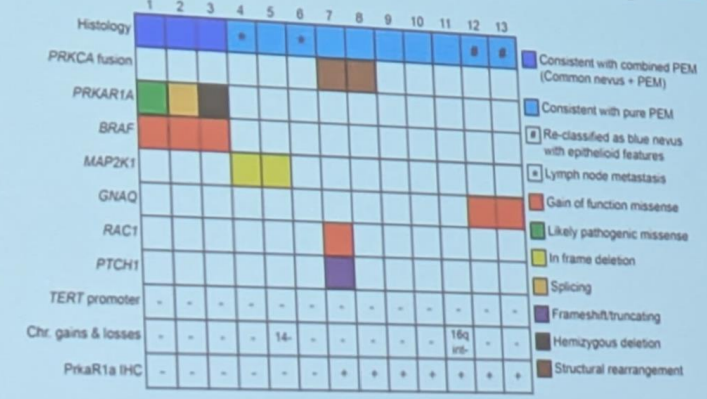
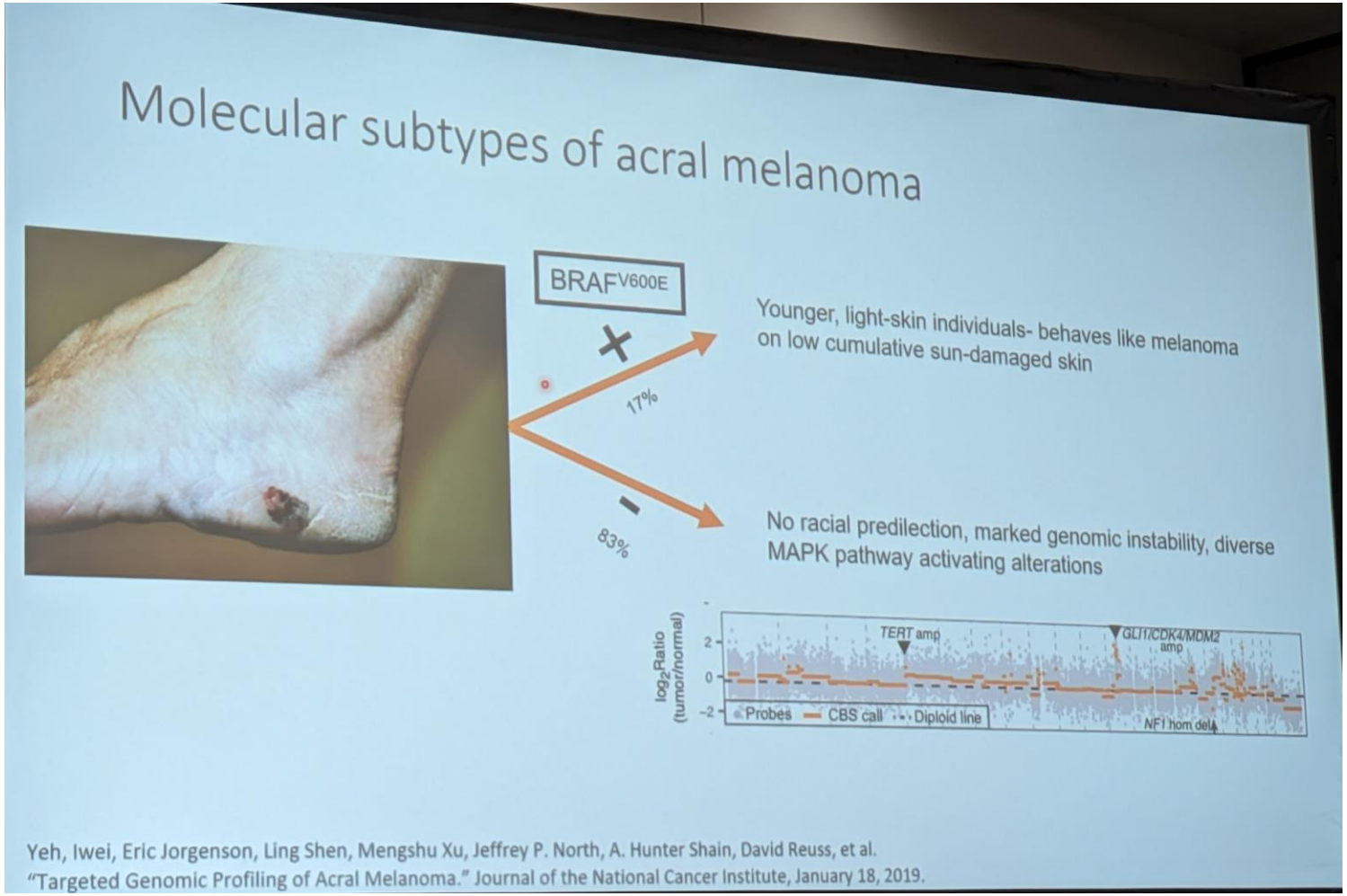
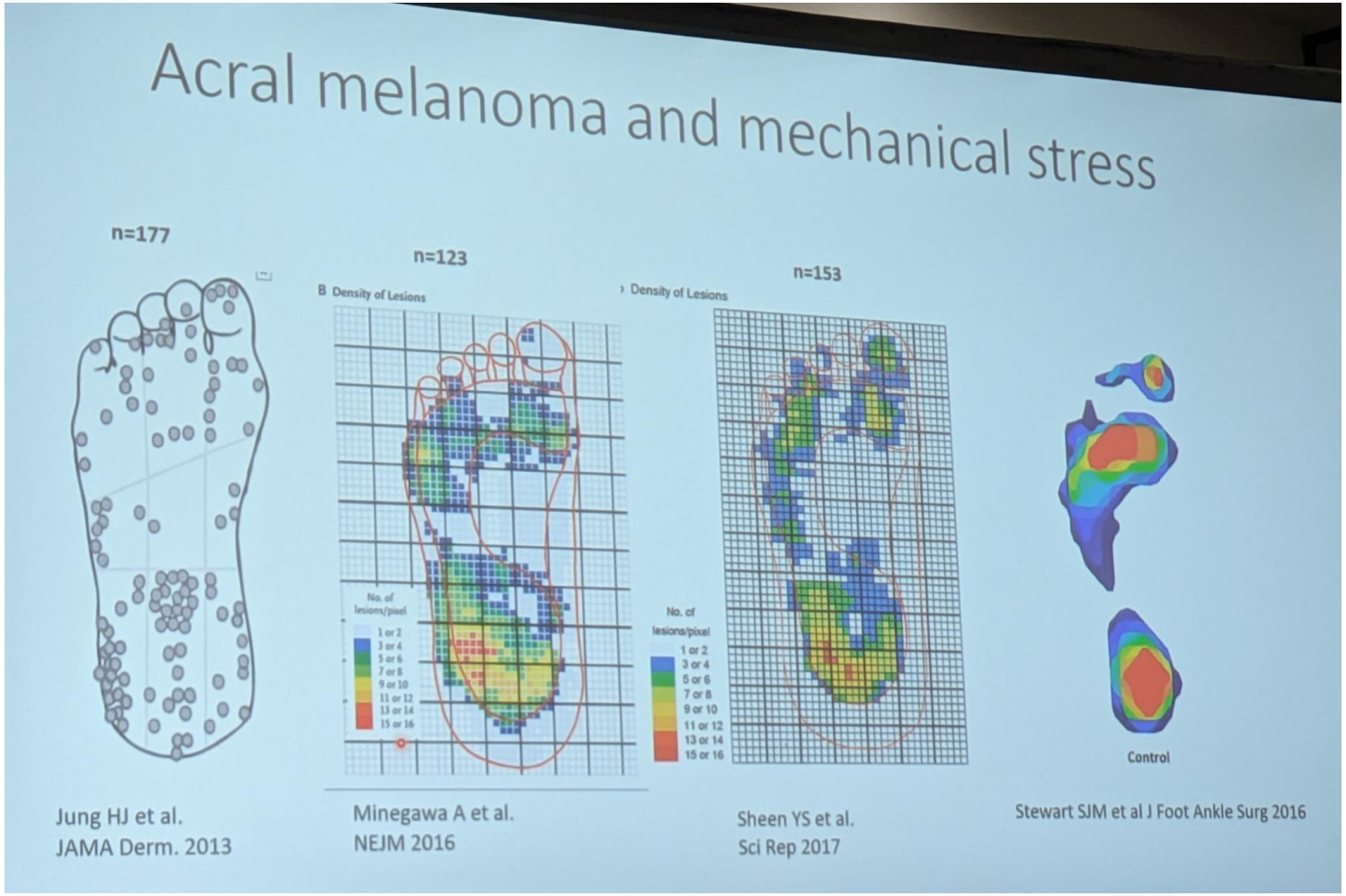


FIGURE 1. Summary of pathogenic genomic aberrations identified in PEM. Chr indicates chromosomal; IHC, immunohistochemistry; int, interstitial; LN, lymph node; (–) deletion or negative immunohistochemical staining; (+) positive immunohistochemical staining.

Subtipos moleculares de melanoma acral



Melanoma acral y estrés mecánico



Inteligencia artificial en dermatopatología

AAD ANNUAL MEETING AEDV highlights

SAN DIEGO 8-12 MARZO

Why Should pathology Invest in Digital Workflow/AI?

INCREASED PRODUCTIVITY

- Improved information management and workflow distribution
- Integration of data

IMPROVED QUALITY/BETTER MEDICINE

- Quality assurance
- Rapid second review and easier access to sub-specialists

INCREASE REVENUES

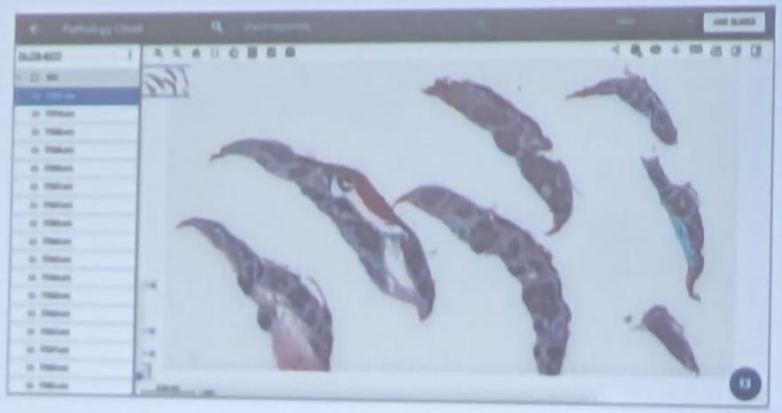
- Insourcing (digital consults)
- Pull-Through revenues

COST SAVINGS

- Consolidations
- Reduced costs from moving slides around

BECOME AN INNOVATION LEADER

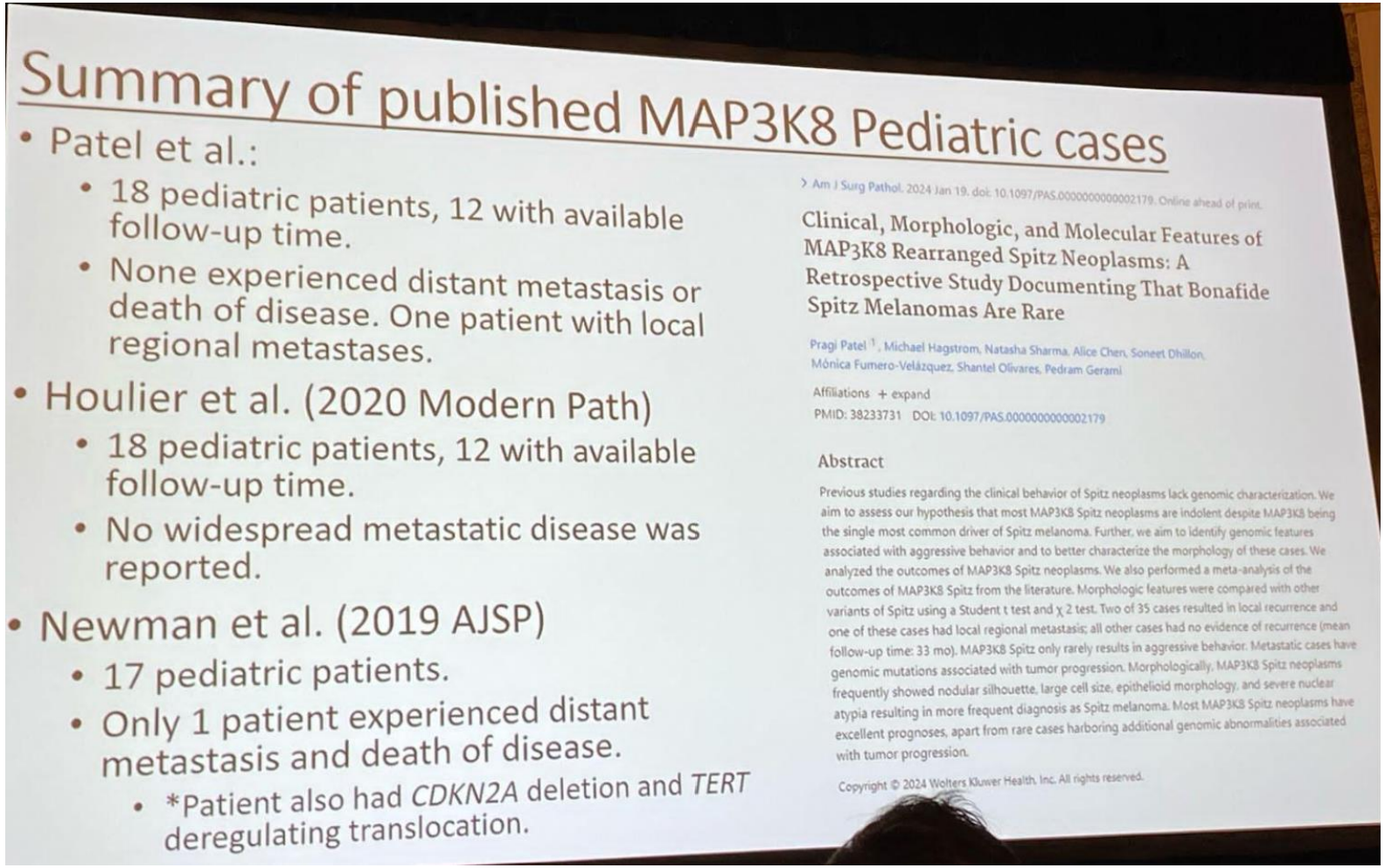
- Image analysis/Workflow algorithms
- AI enabled predictive tools



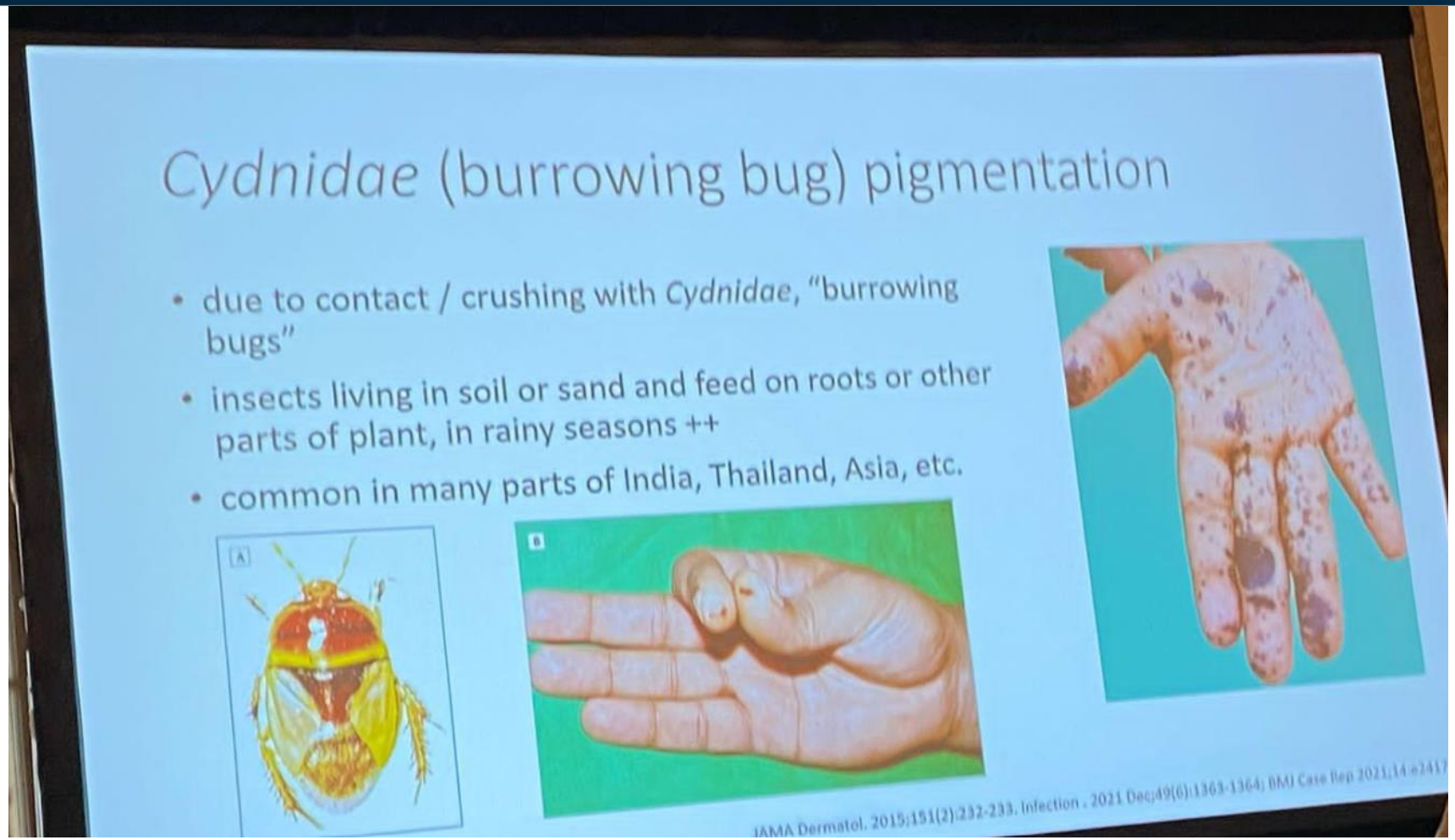
International Society of Dermatopathology

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

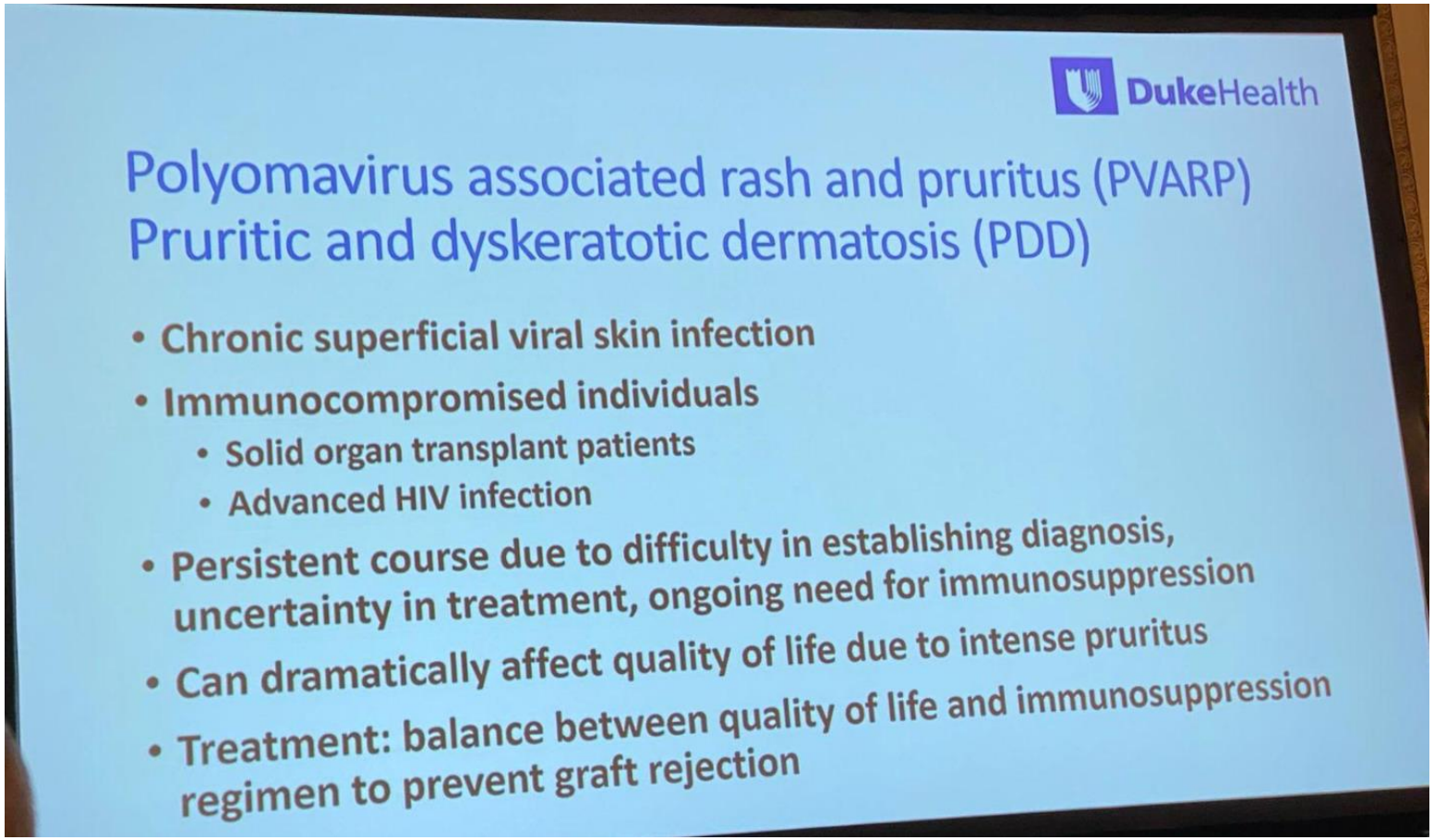
Neoplasias spitzoides MAP3K8



Pigmentación secundaria a “chinche excavador” Cydnidae

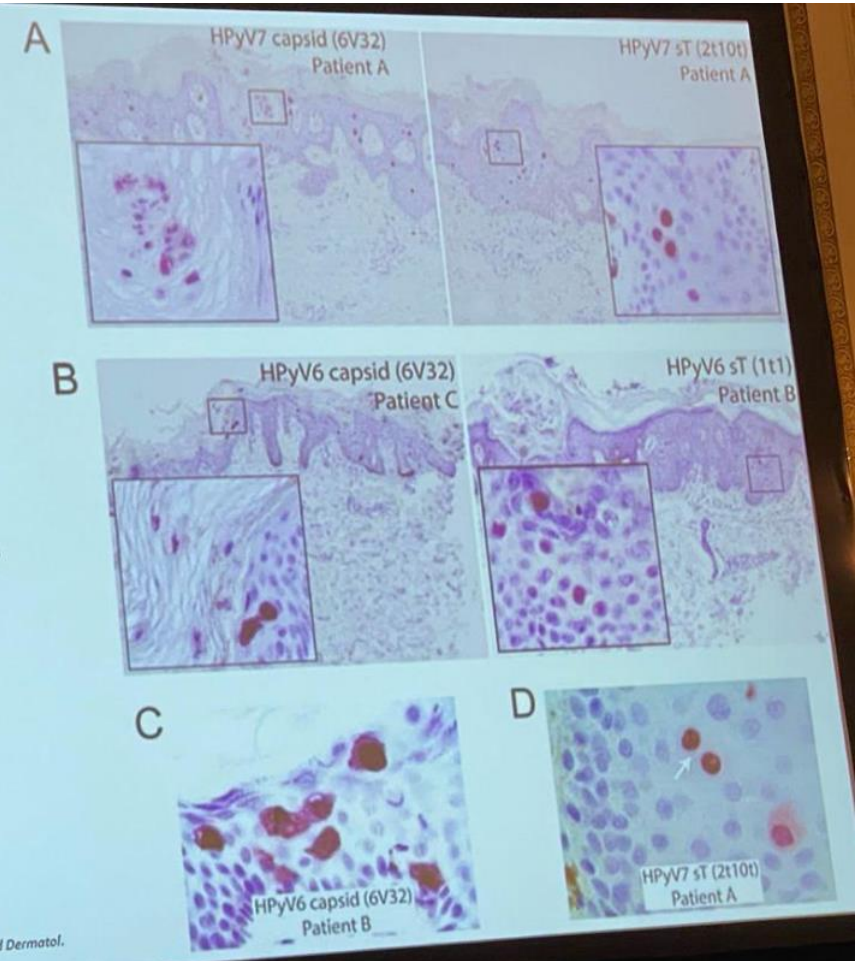


Erupción asoiciada a polyomavirus



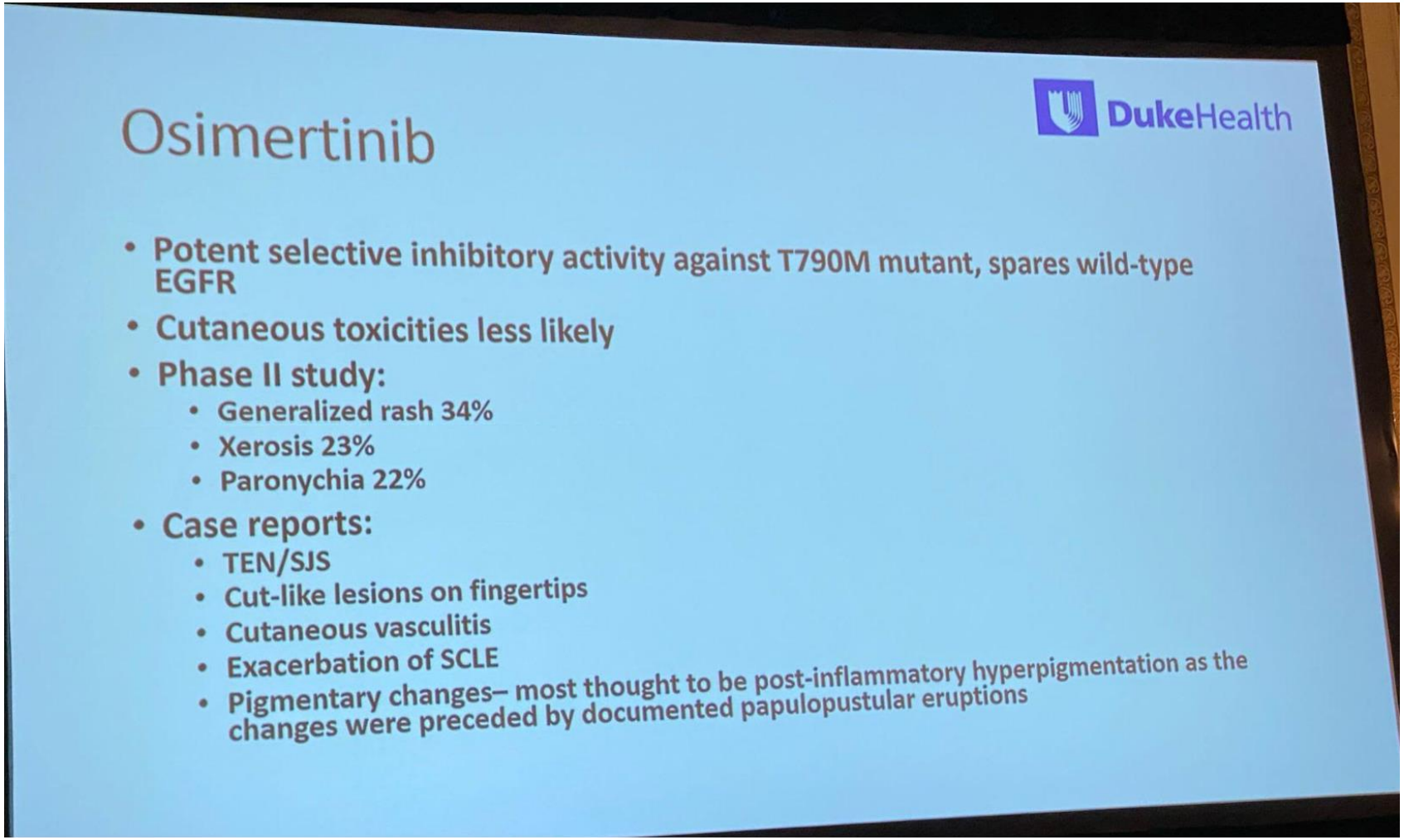
PVARP/PDD

- Immunohistochemistry against HPyV6 and HPyV7 viral proteins
- Definitively identify HPyV7 targeting non-follicular keratinocytes
- Patient B had persistent HPyV6 detection despite resolution of the eruption
- How latency is maintained is unclear
- As case numbers are small, establishing definitive causation is not possible
- Histology is distinctive, though not necessarily pathognomonic
- Clinical context is important



Lee EE, Yue Y, et al. Human polyomavirus 6 and 7 are associated with pruritic and dyskeratotic dermatoses. *J Am Acad Dermatol.*

Osimertinib



PÓSTERS

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

PÓSTERS

AAD ANNUAL MEETING AADV highlights

SAN DIEGO 8-12 MARZO

Memorial Sloan Kettering Cancer Center

Pre-procedure second-opinion histopathologic confirmation

Sarah Ghadersohi BS*, Michael J Davis MD*, Nick Kurtansky*, Klaus Busam MD*, Elizabeth A Quigley MD**, Karen L Connolly MD*
*No relevant disclosures; **Honoraria from UpToDate

Memorial Sloan Kettering Cancer Center

Background

- Pre-procedure confirmation of histopathologic review is the standard of care in many surgical specialties
  - Prevents unnecessary surgeries, patient morbidity, and costs
  - Not routine for dermatologic surgeries
- A prior study showed that 2.3% of 5,629 general surgery pathology cases had diagnostic discrepancies with 51.5% of those cases calling for a change in clinical management
  - Dermatopathology specimens have been found to be among the groups with the highest percentage of inaccurate diagnoses (1)
- In the literature, the rate of diagnostic discrepancy ranges widely from 2% to 35%
  - The rate of discrepancy impacting treatment options ranges from 4% to 13% (2-5)
- Costs of second opinion pathology review
  - Monetary
  - Added work for dermatopathology team
  - Delays in care
- Effects on surgical care
  - 87.5% of dermatopathology cases in which second opinion changed treatment resulted in cancellation of surgery (4)

Objectives

1. Describe incidence of diagnostic discrepancies after pre-procedure confirmation of histopathologic review at MSKCC
1. Describe incidence of diagnostic discrepancies affecting treatment plan
1. Define associated characteristics of specimens with diagnostic discrepancies impacting management

Methods

- Institutional search performed to identify external pathology reports reviewed Jan 2022 through Dec 2022 that underwent pre-procedure confirmation of histopathologic review at MSKCC
- Included 6 Mohs/dermatologic surgeons at MSKCC
- Outside and internal 2nd review pathology reports were compared
- Exclusion criteria:
  - Cases with incomplete data/ missing outside pathology reports in EMR

Note:
SCC = Squamous cell carcinoma
BCC = Basal cell carcinoma
M = Melanocytic
H = high risk
L = low risk
MSKCC = Memorial Sloan Kettering Cancer Center

Acknowledgement: Research reported in this poster was supported under award number 5R25CA020449.

Methods (cont.)

	Low Risk	High Risk
BCC	**BCCL:** BCC unspecified, superficial BCC, nodular BCC	**BCCH:** BCC infiltrative, morpheaform, perineural invasion
SCC	**SCCL:** SCC in situ, SCC well differentiated	**SCCH:** SCC moderately or poorly differentiated, deeply invasive, infiltrative growth pattern, or perineural invasion
M	**ML:** dysplastic nevus, atypical intraepidermal, melanocytic proliferation	**MH:** melanoma in situ, melanoma
Other malignant	sebaceous carcinoma, seborrheic keratosis, adnexal tumors	

Data Collected

- Demographic Information
  - Age at time of biopsy
  - Sex
- Anatomic site - Face, Scalp, Trunk, Extremities, Genitals
- Referring provider type and practice setting
- Outside pathologist specialty and practice setting
- Outside diagnosis and – when documented – treatment recommendation
- Number of slides submitted, special stains
- MSKCC pathological diagnosis and treatment recommendation

Common Diagnostic Discrepancies – Examples

	Melanocytic	BCC	SCC
Discrepancy Impacting Treatment	Melanoma in situ → Microinvasive melanoma Dysplastic Nevus → Melanoma	BCC superficial → BCC nodular and infiltrative	SCCIS → Actinic keratosis or Seborrheic keratosis SCC invasive → Keratoacanthoma
Discrepancy *Not* Impacting Treatment	Dysplastic nevus with mild atypia → moderate atypia	BCC nodular on nose → BCC infiltrative	SCC → SCC mod differentiated on nose

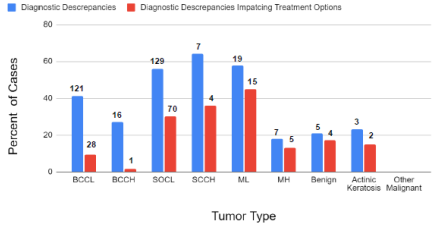
Results

- Reviewed 800 consecutive cases; 710 met inclusion criteria (90 excluded)
- 46% Male (n=327), 54% Female (n=383)
- Mean Patient Age = 72 years (63, 80)
- Pathologist Specialty: 98% (n=687) Dermatopathology, 1.4% (n=10) General Pathology, 0.7% (n=5) Dermatology, 0.1% (n=1) Hematopathology, 7 Unknown

Results (cont.)

- Frequency of Tumor Type, based on outside diagnosis (N=710):
  - BCCL – 296 Cases (42%)
  - BCCH – 60 Cases (8.5%)
  - SCCL – 230 Cases (32%)
  - SCCH – 11 Cases (1.5%)
  - ML – 33 Cases (4.6%)
  - MH – 40 Cases (5.6%)
  - Benign – 24 Cases (3.4%)
  - Pre-cancerous – 13 Cases (1.8%)
  - Other malignant – 3 Cases (0.4%)

Diagnostic Discrepancies by Tumor Type



→ **43%** - Diagnostic discrepancy (307/710 cases)

→ **18%** - Discrepancy impacting treatment options (129/710 cases)

Limitations

- Misrepresentation of the lesion due to number and type of slides reviewed for confirmation, such as only recuts or a single slide reviewed
- Tertiary care center case referral bias

Conclusions

- The incidence of diagnostic discrepancies that have a potential to impact treatment is 18%. Therefore, consideration of pre-procedure second-opinion histopathologic confirmation can impact treatment. Physicians should be aware of higher risk scenarios that can impact treatment, such as SCCL, SCCH, and ML.
- Significant findings:
  - **SCCL** – 56% diagnostic discrepancies, **30%** impacted management
  - **SCCH** – 64% diagnostic discrepancies, **36%** impacted management
  - **BCCL** – 41% diagnostic discrepancies, **9.5%** impacted management
  - **ML** – 58% diagnostic discrepancies, **45%** impacted management

References

1. Marion, E., Cohen, M. B., & Weydert, J. (2008). Mandatory second opinion in surgical pathology referral material: clinical consequences of major disagreements. The American journal of surgical pathology, 32(5), 732–737. https://doi.org/10.1097/PAS.0b013e31815a0415
2. Hawryluk, E. B., Sober, A. J., Pitts, A., Nazarian, R. M., Hoang, M. P., Tsao, H., Mihm, M. C., Jr, & Duncan, L. M. (2012). Histologically challenging melanocytic tumors referred to a tertiary care pigmented lesion clinic. Journal of the American Academy of Dermatology, 67(4), 727–735. https://doi.org/10.1016/j.jaad.2012.02.036
3. Johnson, S. M., Samuelski, T. D., O'Connor, S. M., Smith, S. V., Funkhouser, W. K., Broaddus, R. R., & Calhoun, B. C. (2021). Clinical and Financial Implications of Second-Opinion Surgical Pathology Review. American journal of clinical pathology, 156(4), 659–668. https://doi.org/10.1093/ajcp/aqaa263
4. Lohman, M. E., Green, R. C., North, J. P., & Neuhaus, I. M. (2021). Impact of second-opinion dermatopathology reviews on surgical management of malignant neoplasms. Journal of the American Academy of Dermatology, 84(6), 1585–1592. https://doi.org/10.1016/j.jaad.2020.12.022
5. Butler, S. T., Youker, S. R., Mandrell, J., Flanagan, K. H., & Fraker, D. W. (2005). The importance of reviewing pathology specimens before Mohs surgery. Dermatologic surgery : official publication for American Society for Dermatologic Surgery [et al.], 31(3), 407–412. https://doi.org/10.1111/j.1524-4725.2005.31056.x

Histopathologic Features of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

Emily Ehsan, BA, Corey Georgesen, MD
Department of Dermatology, University of Nebraska Medical Center, Omaha, NE 68198

Background

- DRESS Syndrome is a severe, life-threatening cutaneous adverse reaction that can occur two to eight weeks after a new medication.
- Common culprits: allopurinol, certain anticonvulsants, and antibiotics.
- Presenting symptoms: rash, fever, lymphadenopathy, facial edema, and internal organ involvement
- RegiSCAR clinical scoring system is a diagnostic tool that includes ***"biopsy suggestive of DRESS"***, a criterion which lacks clarity.
- Histopathological distinctions from maculopapular reactions include more dyskeratotic cells, spongiosis, and interface vacuolization. Eosinophilia, despite peripheral elevation, may be absent in skin biopsies.
- Given the life-threatening nature of DRESS, identifying histopathologic features with clinical criteria is vital for prompt diagnosis and treatment. This study aims to correlate pathologic features in DRESS patients with clinical manifestations and disease severity, potentially enhancing prognosis and treatment guidance.

Methods

- Identified 55 patients diagnosed with DRESS Syndrome at Nebraska Medicine from 2014 to 2023 by electronic health record search using the ICD-10-CM code for DRESS (D72.12).
- Confirmed cases had culprit drug within two months of onset and a RegiSCAR score of >2. Inclusion criteria mandated patients aged 18 or older with a clinical DRESS diagnosis and skin biopsy at time of presentation.
- Patient data encompassed demographics, histopathologic features, culprit medications, comorbidities, immunosuppressant details, treatment outcomes, duration, and disease severity. Severe outcomes include organ injury, cardiopulmonary manifestations, multiorgan dysfunction, and mortality.
- 15 patients were identified and the dermatopathological features were assessed by a pre-defined scoring system a board-certified dermatopathologist.
- Histopathological features were graded on a scale (0 to 4+) for various predefined scoring criteria and compared to a matched control group of 15 patients with maculopapular exanthematous drug rash, identified by ICD-10 code L27.0.
- Statistical analysis: Fisher's exact probability test (Freeman-Halton extension), ANOVA one-way test, correlation testing.

Results

Histopathological findings	Average score in DRESS patients	DRESS patients with 2+ score, N = 15 (%)	MDR patients with 2+ score, N = 15 (%)	OR (95% CI)	P - value
Spongiosis	1.1	5 (33.33)	4 (26.67)	1.375 (0.29, 6.6)	0.33
Interface dermatitis	**1.7**	**8 (53.33)**	**4 (26.67)**	**3.143 (0.68, 14.5)**	**0.043***
Lichenoid dermatitis	**2.05**	**12 (80)**	**2 (13.33)**	**26 (3.69, 183.4)**	**0.00068***
Perivascular dermatitis	2.55	13 (86.67)	11 (73.33)	2.364 (0.36, 15.5)	0.41
Periadnexal inflammation	1.55	7 (46.67)	4 (26.67)	2.406 (0.52, 11.1)	0.074
Parakeratosis	1.05	6 (40)	2 (13.33)	4.333 (0.71, 26.5)	0.29
Epidermal pustules	0.65	3 (20)	0 (0)	indeterminate	0.224
Acanthosis	1	6 (40)	1 (6.67)	9.333 (0.96, 90.9)	0.099
Dyskeratotic keratinocytes	1.4	8 (53.33)	3 (20)	4.571 (0.93, 23.1)	0.18
Pigment incontinence	0.95	6 (40)	1 (6.67)	9.333 (0.96, 90.9)	0.035*
Periadnexal interface dermatitis	**0.95**	**6 (40)**	**0 (0)**	**indeterminate**	**0.002***
Vasculitis	0	0 (0)	0 (0)	indeterminate	1
Lymphocytes	3.05	15 (100)	13 (86.67)	indeterminate	0.483
Histiocytes	1.5	8 (53.33)	4 (26.67)	3.143 (0.68, 14.5)	0.161
Eosinophils	1.05	7 (46.67)	6 (40)	1.313 (0.31, 5.59)	0.796
Neutrophils	1.15	7 (46.67)	4 (26.67)	2.406 (0.52, 11.1)	0.642

Table 1. Comparison of histological findings amongst DRESS patients OR, odds ratio; CI, confidence interval; * denotes statistical significance ($p < 0.05$). Some histopathological features had an indeterminate odds ratio in which all DRESS patients or none of the maculopapular drug rash control patients had a specific feature.

DRESS compared to MDR patients had statistically significant interface dermatitis, lichenoid dermatitis, pigment incontinence, and periadnexal interface dermatitis. Periadnexal interface dermatitis was observed in biopsies of all DRESS patients who suffered mortality and severe visceral organ damage. None of the MDR patient biopsies exhibited lymphocytic periadnexal interface dermatitis, the most prominent feature being perivascular eosinophil rich dermatitis

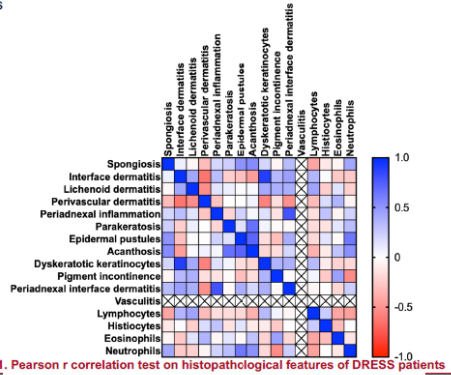


Figure 1. Pearson r correlation test on histopathological features of DRESS patients

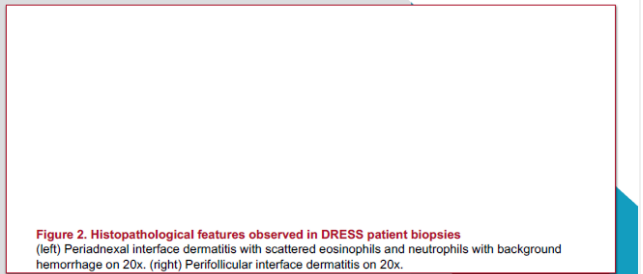


Figure 2. Histopathological features observed in DRESS patient biopsies
(left) Periadnexal interface dermatitis with scattered eosinophils and neutrophils with background hemorrhage on 20x. (right) Perifollicular interface dermatitis on 20x.

Conclusions

- All DRESS patients had ***prominent lymphocyte infiltration***, with 80% exhibiting prominent lichenoid dermatitis, making it the most prevalent reaction pattern.
- Statistically significant histopathologic DRESS features: ***interface dermatitis, lichenoid dermatitis, pigment incontinence, and periadnexal interface dermatitis***.
- Interface dermatitis was more common and severe in DRESS than in non-DRESS drug reactions, appeared to signify a more severe disease course.
- Eosinophilic inflammation was infrequent in DRESS biopsies, despite serologic eosinophilia being a diagnostic feature on RegiSCAR. Neutrophils, uncommon in conventional drug rashes, were notably common in DRESS biopsies.
- ***Periadnexal interface dermatitis*** associated with severe outcomes in all DRESS patients.
- Perivascular dermatitis showed an inverse correlation with features linked to more severe manifestations of DRESS, such as interface, lichenoid, and periadnexal interface dermatitis.
- The diverse and distinct histopathologic profile of DRESS, suggest potential implications of biopsy at onset for diagnosis, prognosis and severity assessment.

References

1. Chi MH, Hui RC, Yang CH, et al. Histopathological analysis and clinical correlation of drug reaction with eosinophilia and systemic symptoms (DRESS). Br J Dermatol. 2014;170(4):866-873. doi:10.1111/bjd.12783
2. Jindal R, Chugh R, Chauhan P, Shirazi N, Bisht YS. Histopathological Characterization of Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) and Comparison with Maculopapular Drug Rash (MPDR). Indian Dermatol Online J. 2022;13(1):32-39. Published 2022 Jan 24. doi:10.4103/idoj.idoj_452_21
3. Lee JW, Lee SR, Kim MJ, et al. Skin manifestations and clinical features of drug reaction with eosinophilia and systemic symptoms: a retrospective multicentre study of 125 patients. J Eur Acad Dermatol Venereol. 2022;36(9):1584-1592. doi:10.1111/jdv.18100

University of Nebraska Medical Center

Clear Cell Acanthoma: An Etiological Enigma

Marina Kristy Ibraheim, MD[1]; Michael T Tetzlaff, MD, PhD[2]; Jeffrey P North, MD[2]

[1] Loma Linda University, Department of Dermatology

[2] University of California San Francisco, Departments of Dermatology and Pathology

The authors have no conflicts of interest to disclose

LOMA LINDA UNIVERSITY HEALTH

UCSF University of California San Francisco

Background

Clear cell acanthoma (CCA) is considered by most to be a benign neoplasm characterized by psoriasiform acanthosis, parakeratosis, and pale keratinocytes with sharp demarcation from the adjacent unaffected epidermis.[1] In addition, CCA may contain neutrophils scattered in the epidermis as single cells and Munro microbascess-like collections of neutrophils in the parakeratotic cornified layer resembling psoriasis. Some postulate that CCA represents an inflammatory reaction given its histopathologic similarities to psoriasis or an epidermal reaction pattern given the overlap in features between CCA and other neoplasms such as seborrheic keratoses with "clear cell acanthosis." Overlapping features with eczematous eruptions on the nipple have also been described.[2-6] Prior studies have highlighted comparable histologic and immunostaining patterns between CCA and psoriasis.[3,5]

Interleukin (IL)-36, a pro-inflammatory cytokine in the Th17 inflammatory pathway that is highly expressed in the epidermis of psoriatic skin, induces abnormal cornification and epithelial hyperplasia, increases production of pro-inflammatory cytokines such as IL-12 and IL-23, and augments activity of the Th1 and Th17 pathways.[7] Interleukin-36 immunostaining can assist in distinguishing between psoriasis and eczema.[8-10]

We conducted a study assessing expression of IL-36 in the epidermis of CCA biopsies in order to investigate if CCA represents an inflammatory reaction with features of psoriasis.

Methods

20 cases of CCA identified → 5 cases excluded → 15 cases identified, stained with H&E and IL-36 immunostain

IL-36 Grading (Cohen et al)[8]	Interpretation
0	Negative
1	Focal weak
2	Diffuse weak
3	Focal strong
4	Diffuse strong

Histopathology and Immunohistochemistry

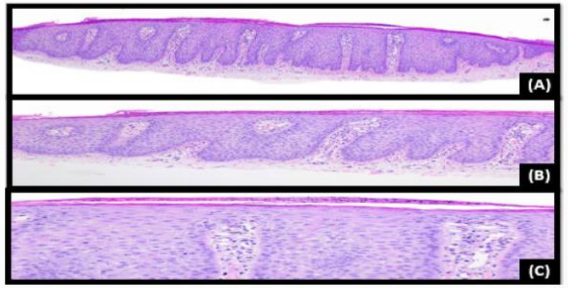


Figure 1. Representative H&E of CCA (A) Features of CCA including psoriasiform acanthosis, parakeratosis, and pale keratinocytes with sharp demarcation from the adjacent unaffected epidermis at 40x magnification. (B) Features at 100x magnification. (C) Features at 400x magnification.

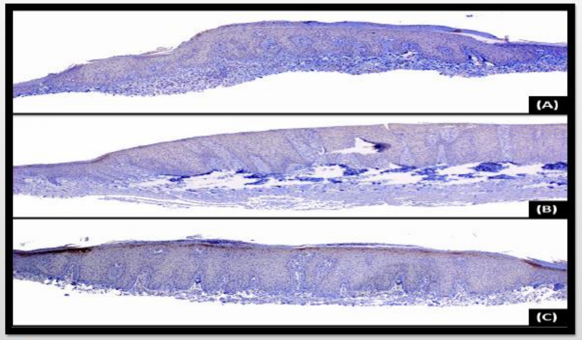


Figure 2. IL-36 Immunostaining Pattern of CCA. IL-36 immunostain scoring as described by Cohen et al and Aquino et al. (A) 0, negative in this case of CCA at 20x magnification. (B) 1, focal weak in this case of CCA at 40x magnification. (C) 2, diffuse weak in this case of CCA at 40x magnification.

Results

Grading of IL-36 Immunostaining	Clear Cell Acanthoma (n=15)
Negative (0-2)	15 (100%)
0	2
1	11
2	2
Positive (3-4)	0 (0%)

All 15 cases stained negative for IL-36 expression.

Discussion and Key Points

Psoriatic skin highly expresses IL-36 compared to skin afflicted by non-Th17-mediated dermatoses.[8-10] Cohen et al demonstrated that IL-36 is avidly expressed in psoriasis compared to eczematous/spongiotic dermatitis.[8] Expression of IL-36 in palmoplantar psoriasis is also increased when compared to palmoplantar eczema.[10] Increased IL-36 expression can also assist in distinguishing among other psoriasiform variants including lichen simplex chronicus, mycosis fungoides, pemphigus foliaceous, and syphilis.[8] Taken together, IL-36 can serve as an effective marker of a psoriasis inflammatory pattern.

The profound absence of immunostaining with IL-36 in every case examined in this study refutes the notion that CCA represents a psoriasis-like inflammatory reaction. Clear cell acanthoma likely represents a neoplastic process that overlaps histopathologically with psoriasis.

CONCLUSION: This study is the first to assess the IL-36 immunostaining pattern of CCA, demonstrating that IL-36 is not expressed in CCA. While our results do not rule out the possibility of CCA representing an inflammatory process, we deem that to be unlikely given the IL-36 staining results and lack of significant spongiosis or interface changes in CCA. Future molecular studies may help to definitively identify this controversial entity's etiology.

References

PÓSTERS

AAD ANNUAL MEETING AADV highlights

SAN DIEGO 8-12 MARZO

What Do Clinicians Mean When Submitting a Biopsy as "Rule Out Eczema"?`

COCKERELL DERMATOPATHOLOGY

Kaycee Nguyen BS[1], Clay J. Cockerell MD MBA JD[2,3]

[1]Texas A&M School of Medicine, Dallas, TX; [2]Cockerell Dermatopathology, Dallas, TX;
[3]Departments of Dermatology and Pathology, UT Southwestern Medical Center, Dallas, TX

Results

Dermatosis	Number of Respondents
Atopic dermatitis	52
Nummular eczema	41
Dyshidrotic eczema	34
Contact dermatitis	32
Neurodermatitis	14
Seborrheic dermatitis	9
Psoriasis	3
Mycosis fungoides	3
Tinea infection	2
Cutaneous T-cell lymphoma	1
Scabies	1
Chronic atopic dermatitis	1
Drug dermatitis	1
Connective tissue disease	1
Benign eczematous conditions	1
Psoriasiform dermatitis	1
Dermal hypersensitivity reaction	1

Conditions considered under the term "rule out eczema"

- Atopic dermatitis: 83%
- Nummular eczema: 65%
- Dyshidrotic eczema: 54%
- Contact dermatitis: 51%
- Neurodermatitis: 22%
- Seborrheic dermatitis: 14%
- Other: 25%

Table 1. Dermatological conditions considered by clinicians when submitting a biopsy to "rule out eczema"

Completion of requisition forms

- By medical assistants: 51%
- By dermatologists: 43%

Primary Individual	Number of Respondents
Medical assistant	32
Dermatologist	27
Physician assistant	1
Nurse practitioner	1
Resident physician	1
Software system	1

Table 2. Primary individual responsible for completing dermatopathology requisition form

Personal Modifications Made	Number of Respondents
Yes	48
No	11
N/A*	4

*Includes no response, users of handwritten paper requisition forms, or those not utilizing an automated EMR system

Customization of EMR diagnostic phrases prior to submission

- Yes: 81%
- No: 19%

Table 3. Modification status of EMR-automated phrases for differential diagnoses prior to submission to dermatopathologist

Discussion

- "Rule out eczema" is often used broadly by clinicians to cover a range of conditions like atopic dermatitis, nummular eczema, and others, highlighting the necessity for clear clinical indications on requisition forms.
- Eczema, a term often used interchangeably with atopic dermatitis, encompasses various conditions, not all related to IgE-mediated sensitivity. This broad usage can lead to overlooking non-atopic forms like contact dermatitis.
- Accurate clinical impressions on requisition forms are important for correct histopathological diagnoses, especially when diagnosing conditions like eczema where histology alone may be insufficient. This issue is exacerbated when forms lack clinical images, provider notes, or customized EMR phrases, forcing pathologists to depend only on the limited information provided.
- Ambiguous terms like "dermatitis unspecified" and "rule out eczema" offer limited diagnostic value and can lead to misdiagnosis or diagnostic delays, impacting patient treatment and outcomes.

Conclusion

To enhance diagnostic accuracy, it is recommended that the phrase "rule out eczema" be discarded in favor of specifying which disorder the clinician is presumptively diagnosing clinically.

References

1. Abdou Y, Lohse C, Comfere NI. Use of the term "rule out" in requisition forms may cause diagnostic delays in dermatopathology practice. International Journal of Dermatology. 2017;56(8):867-71. doi:https://doi.org/10.1111/ijd.13403
2. Williams HC. Atopic Dermatitis. New England Journal of Medicine. 2005;352(22):2314-2324. doi:10.1056/NEJMcp042903
3. Johansson SGO, Bieber T, Dahl R, et al. Revised nomenclature for allergy for global use: Report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. Journal of Allergy and Clinical Immunology. 2004;113(5):832-836. doi:10.1016/j.jaci.2003.12.591
4. Chimenti LA, Umsawadi N, Murphy B, Vivia KV, Amin B. The dermatopathology requisition form: attitudes and practices of dermatologists. J Am Acad Dermatol. Feb 2015;72(2):353-5. doi:10.1016/j.jaad.2014.10.031
5. Romano RC, Novotny PJ, Sloan JA, Comfere NI. Measures of Completeness and Accuracy of Clinical Information in Skin Biopsy Requisition Forms: An Analysis of 249 Cases. Am J Clin Pathol. Dec 2018;94(6):727-735. doi:10.1093/ajcp/aqw186

Improving patient comfort with waiting for contact from clinicians regarding skin biopsy results

MAYO CLINIC

Jennifer Coias, M.D.[1,4], Olivia Crum, M.D.[1,4], Chelsea Handfield, M.D.[1,4], Hasina Maredia, M.D.[1,4], Thomas Trischman, M.D.[1,4], Jacob Reinhart, M.D.[1,4], Nasro Isaq, M.D.[1,4], Sydney Proffer, M.D.[1,4], Donald Neal, M.D.[1,4], Emma Johnson, M.D.[2,3,4]

[1]Department of Graduate Medical Education, [2]Department of Dermatology, [3]Department of Laboratory Medicine and Pathology

[4]Author has no relationships to disclose.

INTRODUCTION

BACKGROUND

An information sharing rule from the 21st Century Cures Act requires that healthcare providers give patients access to their health information, allowing patients to download their test results, medication lists, referral information, and clinical notes in electronic formats, on request and free of charge[1]

To comply with this policy, the simultaneous release of skin biopsy results to the Mayo Clinic patients and clinicians began in January of 2022

In anticipation of this change, the patients were provided with written and verbal counseling during their dermatology visit with instructions to await contact from their clinician before reaching out with questions and concerns about the results

Despite this, total patient communications to the nurse triage team regarding biopsies increased by 204% after January of 2022

Most of these contacts regarding biopsies were from patients who had seen their results but had not allowed the clinician adequate time to provide further guidance

Contacts from patients who had seen their results prior to clinician contact increased from 2 contacts/week to 15 contacts/week, an overall 650% increase in this category of communications

PURPOSE AND AIM

This quality improvement project sought to improve patient comfort with waiting for clinician contact following the release of skin biopsy result communications

We aimed to reduce this category of communications to the dermatology nurse triage team by at least 25% by January of 2023 without increasing perceived clinician/nurse burden associated with expectation-setting discussions

1. Salmi L, Blease C, HÃ¤gglund M, Walker J, DesRoches C M. US policy requires immediate release of records to patients BMJ 2021; 372 :n426 doi:10.1136/bmj.n426

FIGURE 1

Dear [redacted]

During your recent dermatology visit a skin biopsy was performed. Biopsy results usually take from 1 to 3 weeks to return. Your biopsy results will be released to the patient portal at the same time as they are released to your dermatology clinician. Please allow a full 3-5 business days for your clinician to contact you before reaching out with questions or concerns regarding the results. If multiple tests or biopsies have been performed, you will be contacted when ALL results are available.

In most cases, the dermatology clinician will send you a letter outlining the diagnosis and any recommended next steps. Result letters can be found in the portal under the "Letters" section. In some cases, your clinician may decide to call you about the results.

Please click here to find helpful information about healing after your skin biopsy: Healing After Your Skin Biopsy

We greatly appreciate your patience and value your trust in Mayo Clinic for your dermatology care.

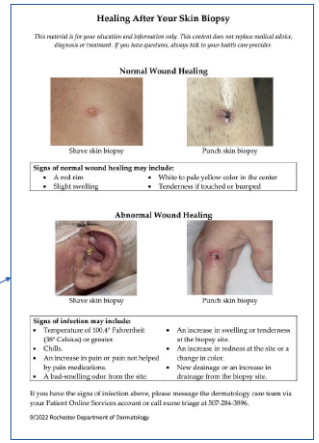


Figure 1: Message sent to patients who had a skin biopsy with a link to information regarding wound healing after biopsy.

METHODS

- Within 2 business days of having a skin biopsy, dermatology patients were sent a standardized online patient portal message outlining the anticipated timeline for biopsy results release (figure 1)
- The message specifically asked patients to allow for 3-5 business days for their clinician to contact them regarding the biopsy results
- The message also included information for how to locate letters from clinicians within the patient portal application and information about normal wound healing
- Feedback from nurses and patients was collected during and after the intervention and adaptations to the patient letter were implemented in real time
- The nurse triage team collected pre- and post-intervention data regarding the reasons for all calls or messages pertaining to biopsies for 5 business days
- The data was compared to evaluate intervention efficacy

RESULTS

- Pre-intervention data demonstrated 44 biopsy related contacts in one week (figure 2 - blue)
  - Of these 44 contacts, seeing the results before the provider had contacted them was the most common reason patients called; 34% of contacts
- Post-intervention data demonstrated 30 biopsy related contacts in one week (figure 2 - orange)
- There was an overall reduction in total contacts about biopsies from 44 contacts/week to 30 contacts/week; a 32% reduction in total contacts
- The number of contacts from patients who had seen the results before clinician contact dropped from 15 contacts/week to 8 contacts/week; a 47% reduction in this category of communications

FIGURE 2

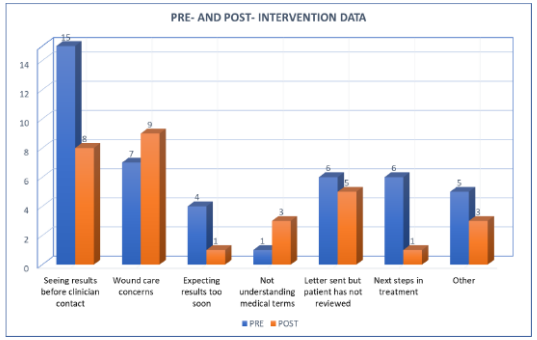


Figure 2: Blue bars represent pre-intervention categories of communications. Orange bars represent post-intervention categories of communications.

LESSONS LEARNED

- Patients are overloaded with new information during their dermatology visits, especially when a procedure is performed
- When patients have increased access to medical records, which are often written in complex medical language, there can be unforeseen effects such as increased uncertainty and discomfort with the knowledge
- The CURES Act changes in skin biopsy records release resulted in increased calls and messages to our nurse triage team from patients who had concerns about the results but had not yet received contact from their clinician
- Messages clearly delineating the departmental protocols and providing **anticipatory** guidance to patients reduced this category of communications to nurse triage, demonstrating improved patient comfort with waiting for their clinician to contact them regarding their skin biopsy results

AAD Annual Meeting
March 8, 2024; San Diego, CA

AAD **ANNUAL** MEETING

AEDV highlights

SAN DIEGO
8-12 MARZO

La Academia Española de Dermatología y Venereología expresa su agradecimiento al patrocinador UCB, por su especial apoyo y contribución con la actividad formativa Highlights 2024.

AAD **ANNUAL** MEETING

AEDV highlights

SAN DIEGO
8-12 MARZO

AEDV 1909

ACADEMIA ESPAÑOLA
DE DERMATOLOGÍA
Y VENEREOLOGÍA

GRACIAS