What's hot in Rheum Derm?

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October 2024

University of Virginia Health System

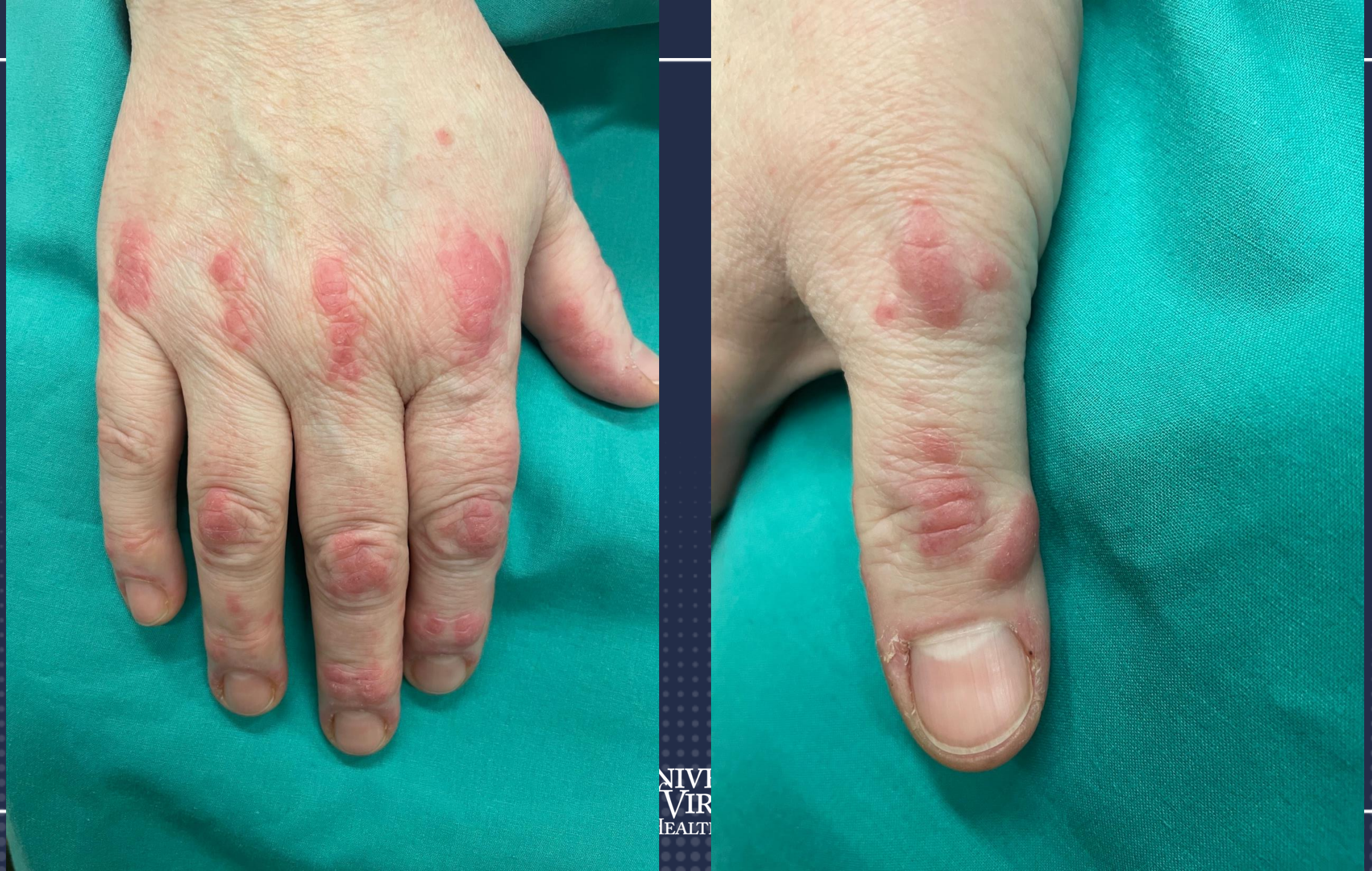
Talk outline

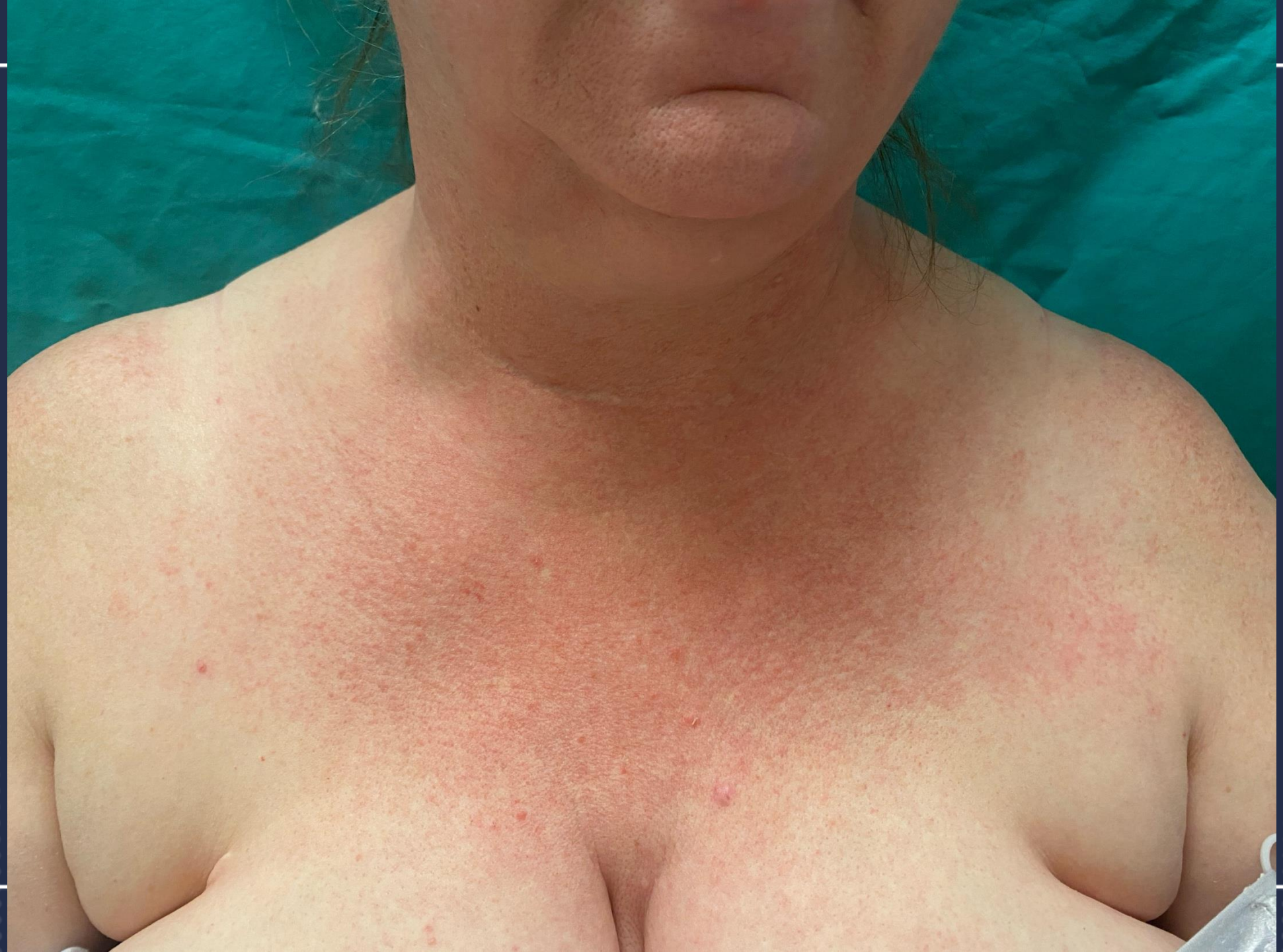
- 7 med derm cases, as they came
- Focus on new steps in work up and therapeutic management
- Bell ringers and cup fillers

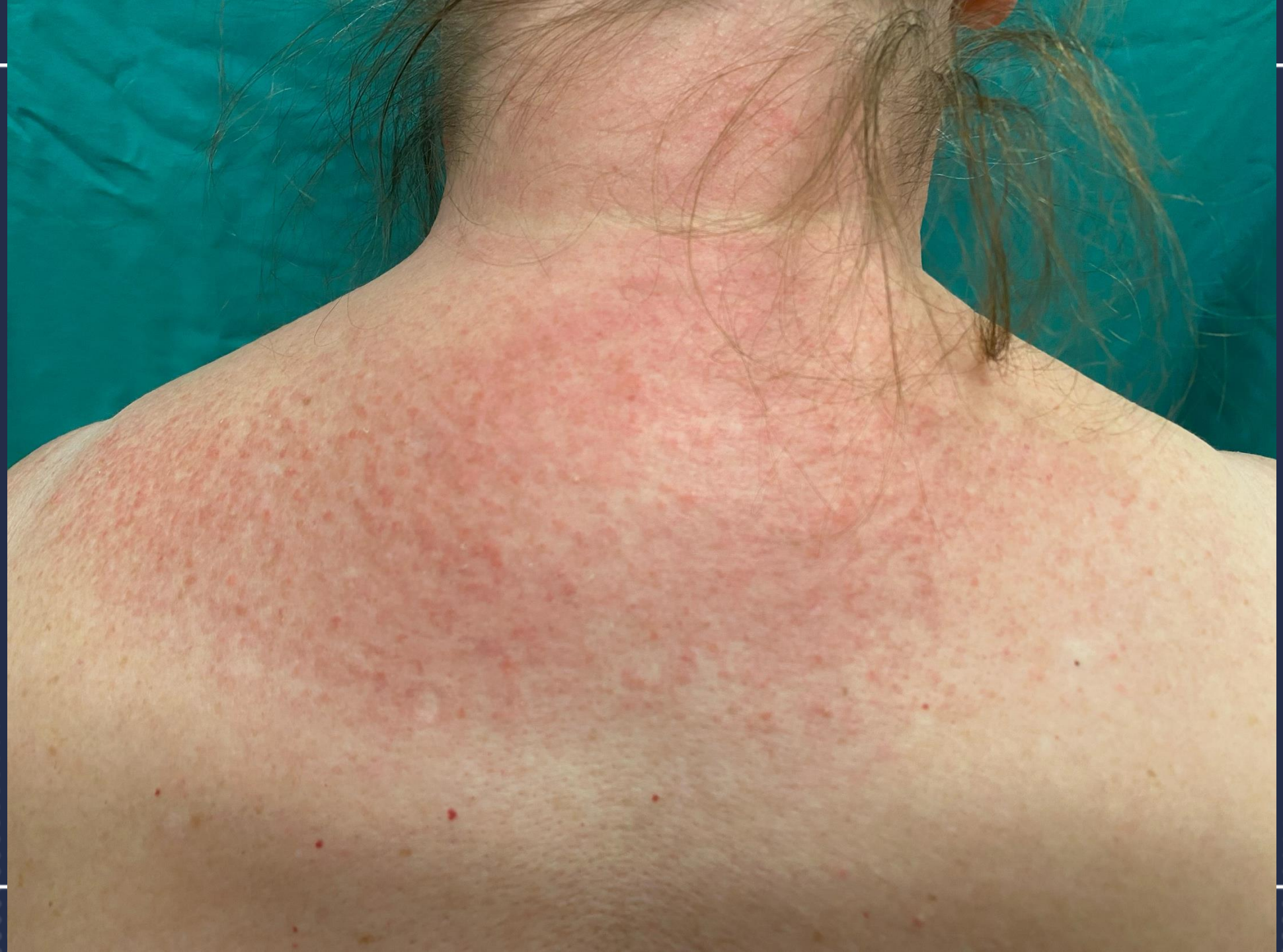
DISCLOSURES

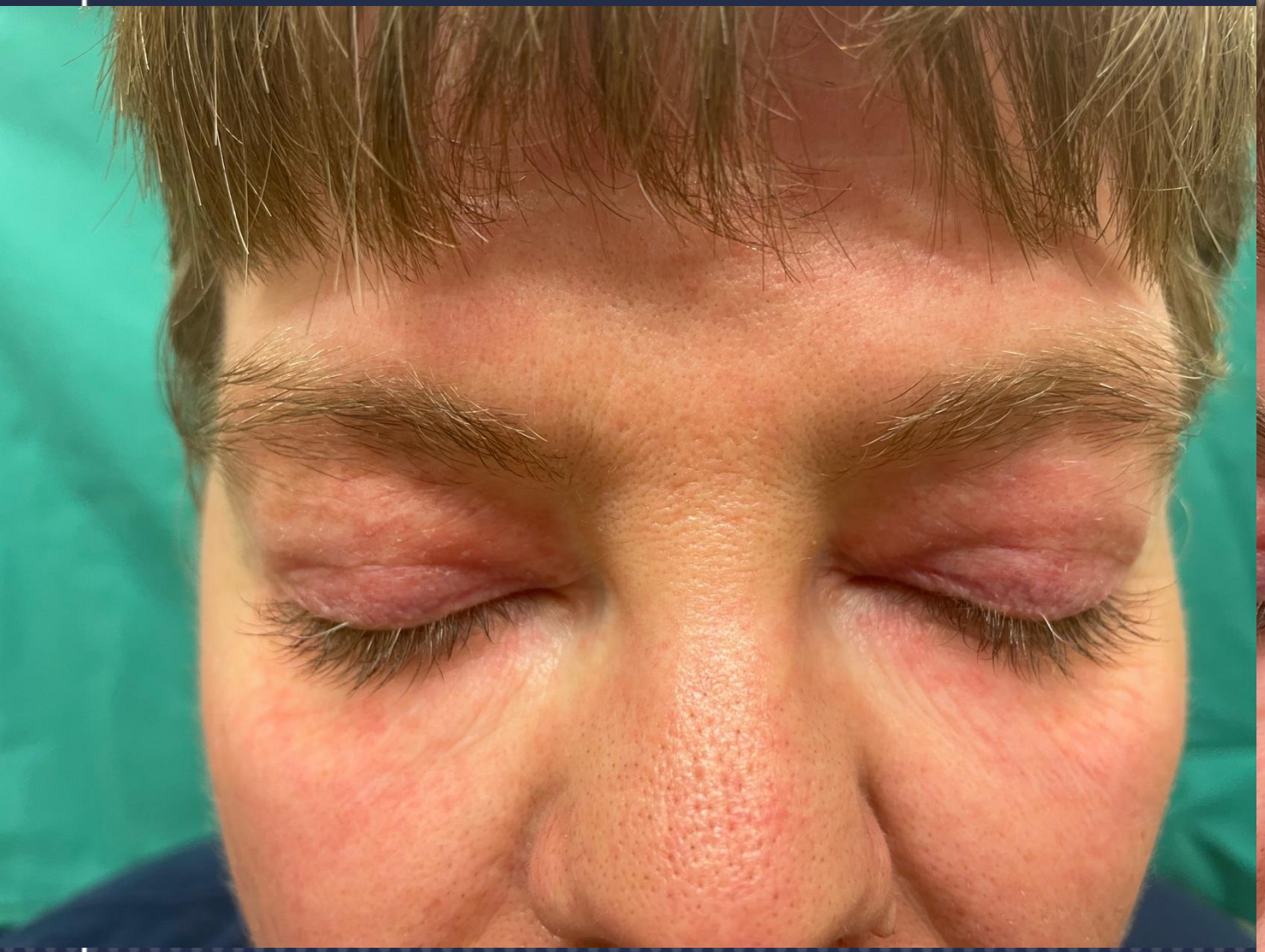
- Clinical trials for Abbvie, Regeneron, Acelyrin, Clinuvel, AstraZeneca, Sun Pharmaceuticals

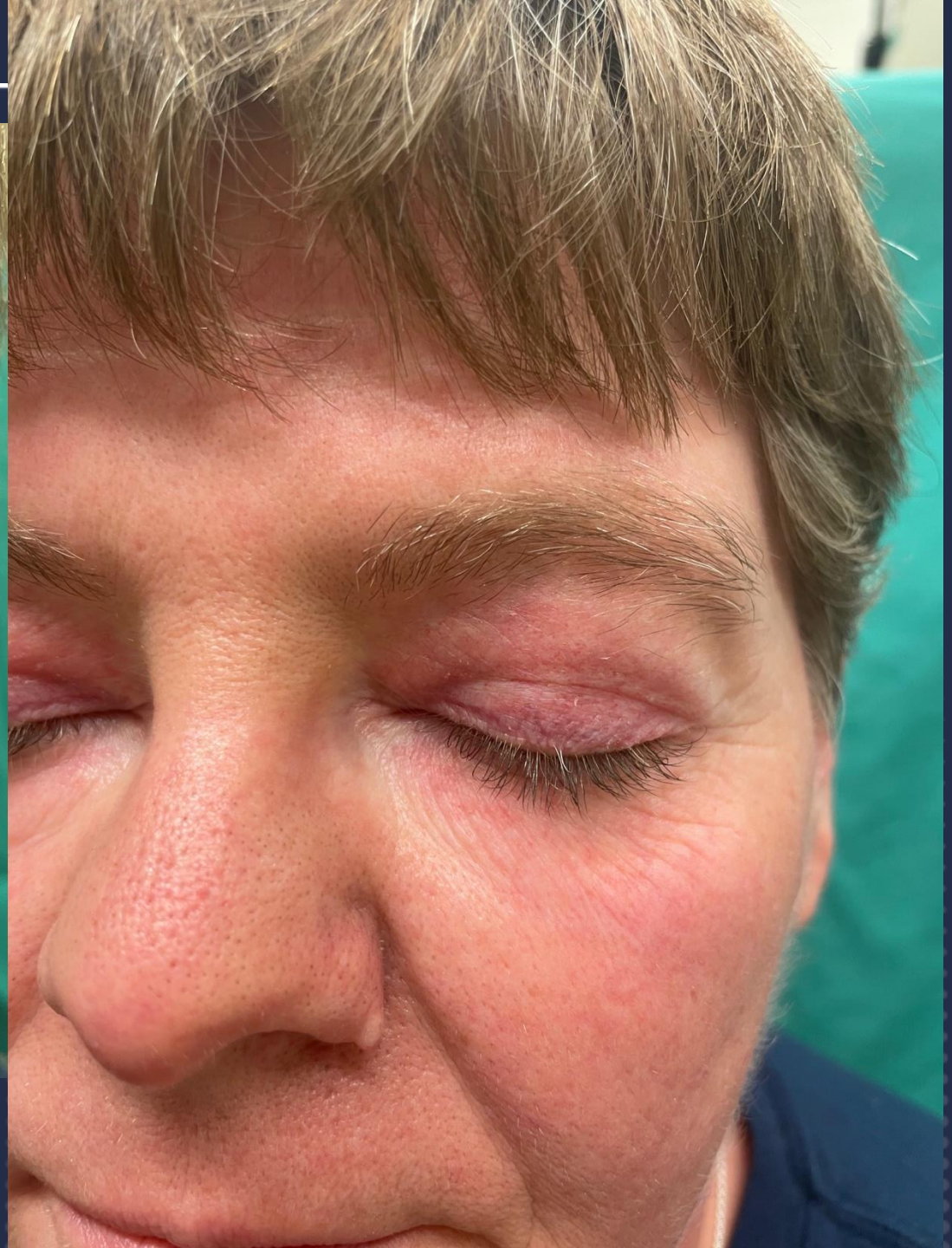
- Advisory Boards for Bristol Myers Squibb, Jannsen, Argenx











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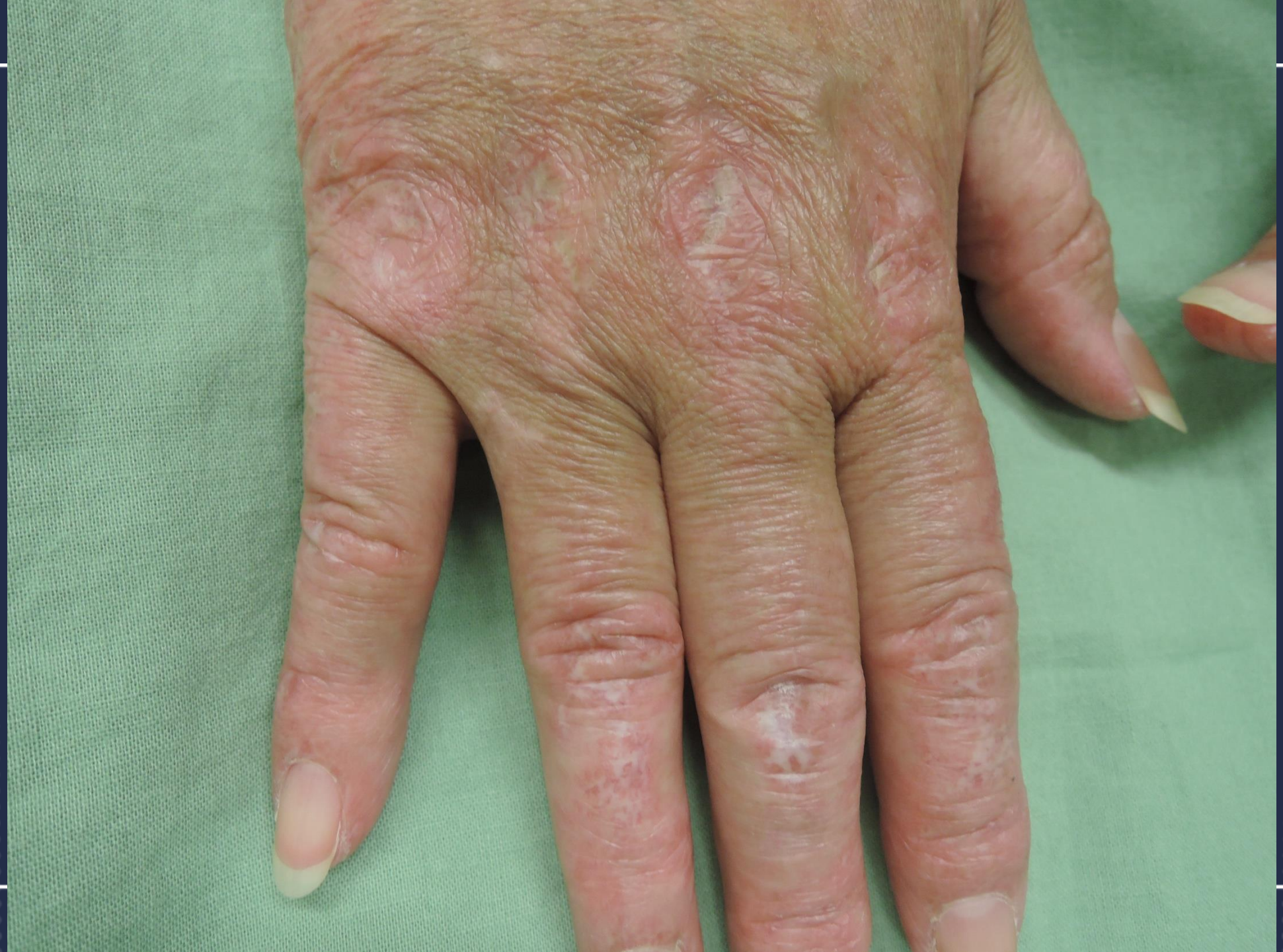

Treatment of cutaneous DMM

- Myocutaneous discordance: often treating skin disease CADM or "post-myopathic"
    - 51/49% (classic/CADM) at UPenn cohort of 269
        - 40% of classic became postmyopathic
        - Of those, 45% had CDASI-A scores > 14 (mod-severe)
- Skin symptoms often >>>> clinically evident disease
- Worst organ involved should dictate treatment
    - HCQ, apremilast will not help muscles

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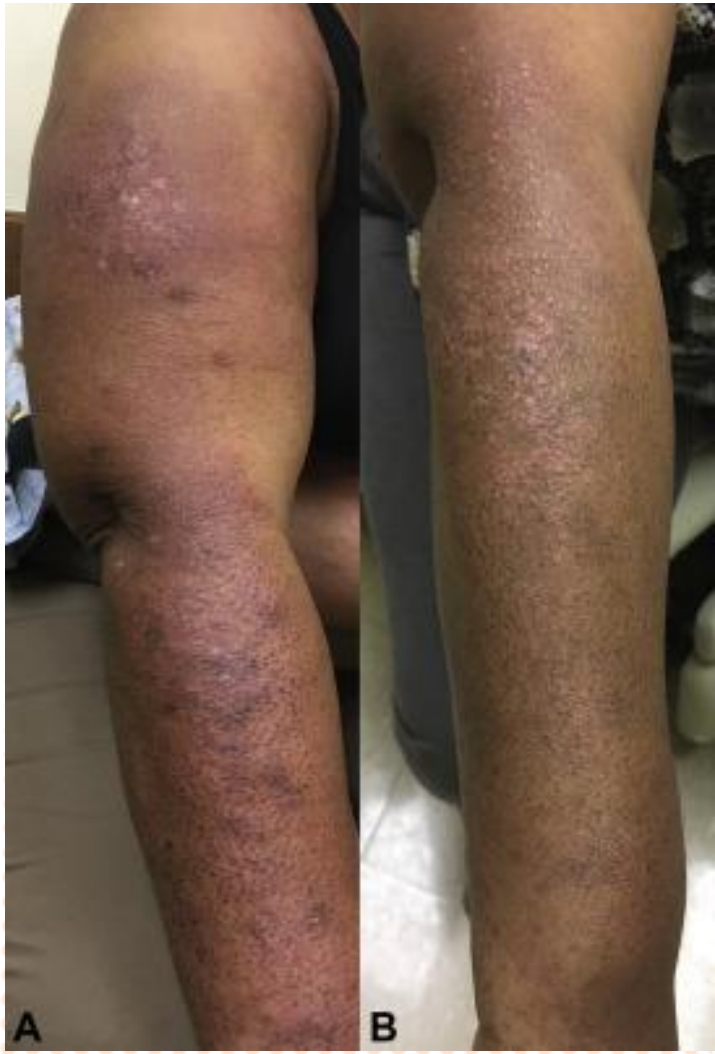
Pandya et al. JAAD. 2024 Jul 1;91(1):31-6.

Hydroxychloroquine

- Monotherapy for mild disease
- Non-immunosuppressive; stackable
- Generally better as adjunctive
- Better with IS agents (JAAD Oct 2021)
- Flares assoc with SAE-1 + (JAMA Derm Oct 2018)

Apremilast

- 8 pt with refractory cutaneous dermatomyositis (no active muscle)
- Failed OCS, multiple steroid-sparing agents (median 5 agents)
  - Mean dz duration of 5.5 years
- 7 of 8 saw meaningful improvement in CDASI at 3 mo
  - 2 pt tapered steroids; 1 pt stopped steroid sparing agent



Bitar et al. JAMA Derm. Dec 2022; 158(12):1357-1366.
Bitar et al. JAAD Case Reports. 2019 Feb 1;5(2):191-4.

Conventional immunosuppressive agents

- **MTX**
- **AZA**
- **MMF**
- **Calcineurin inhibitors**

* No particular cutaneous phenotypes where these agents are preferred

Newer (more effective) therapies

- **IVIG**
- **JAK inhibitors**
- **IFN-inhibitors**

Newer (more effective) therapies

- **IVIG**
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- **IFN-inhibitors**

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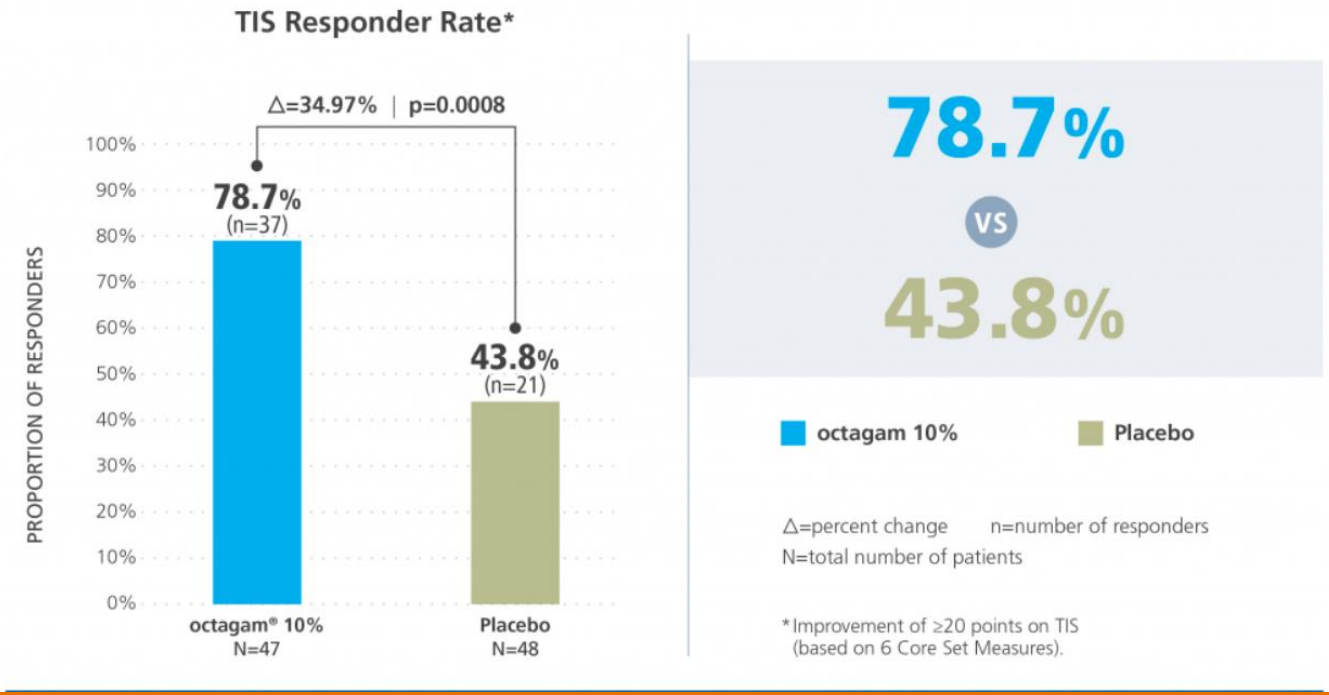
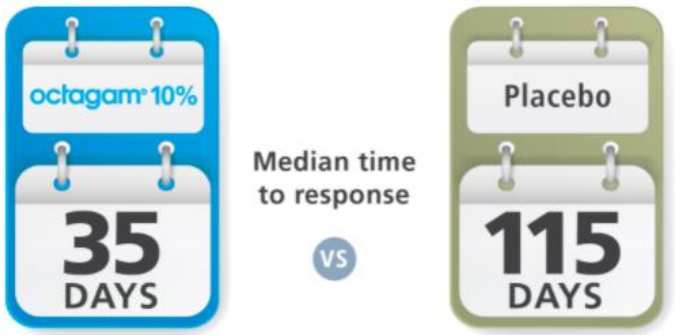
ProDerm Trial

- Double blind, placebo controlled, switch arm + 6 mo open label extension
- 95 adults, 10 countries
- Inclusion: DMM per Bohan and Peter, active disease, +/- other therapy





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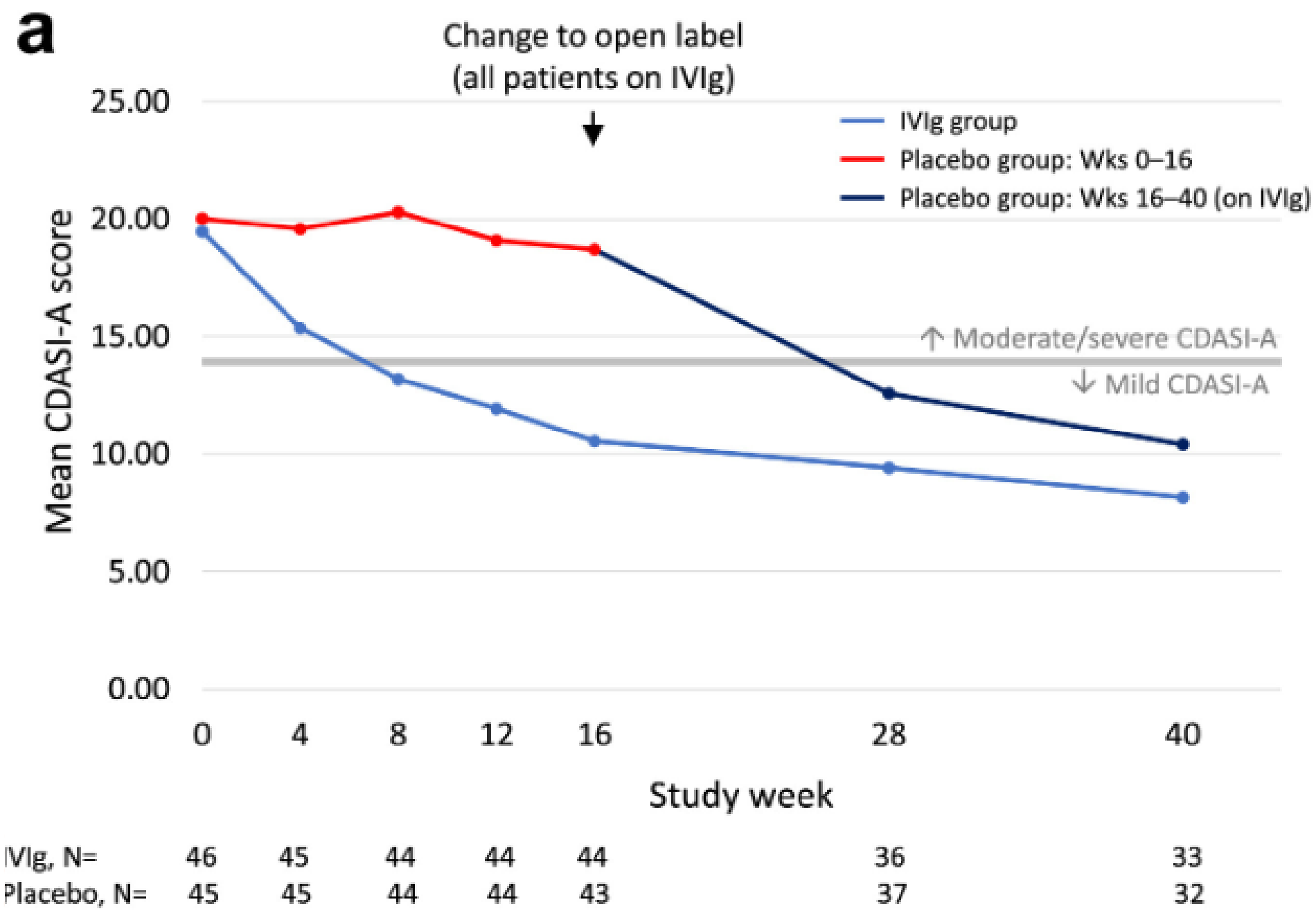
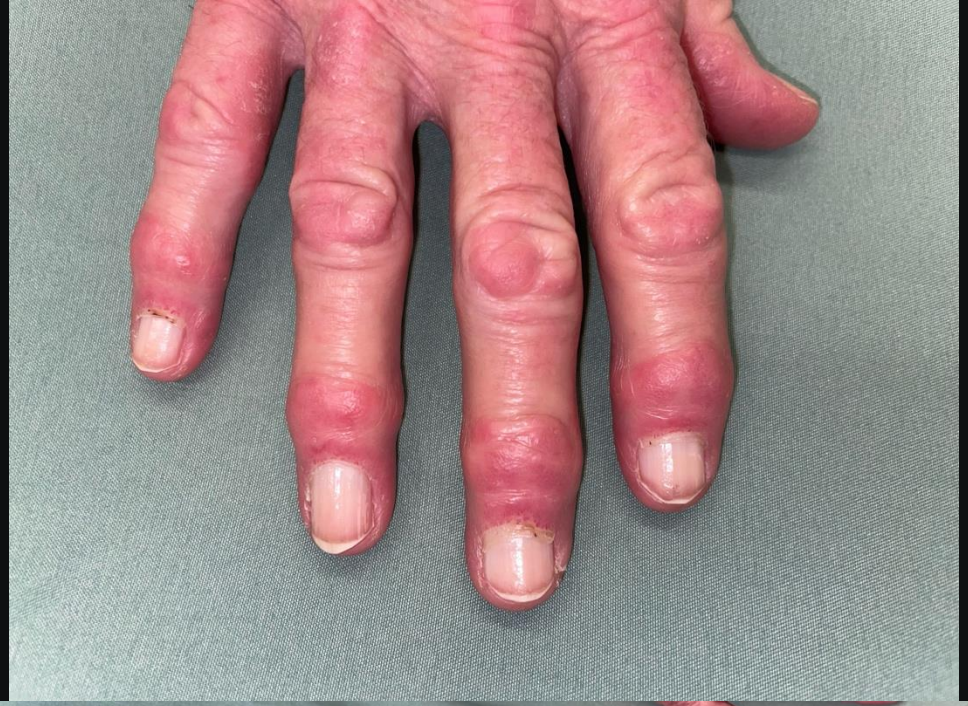
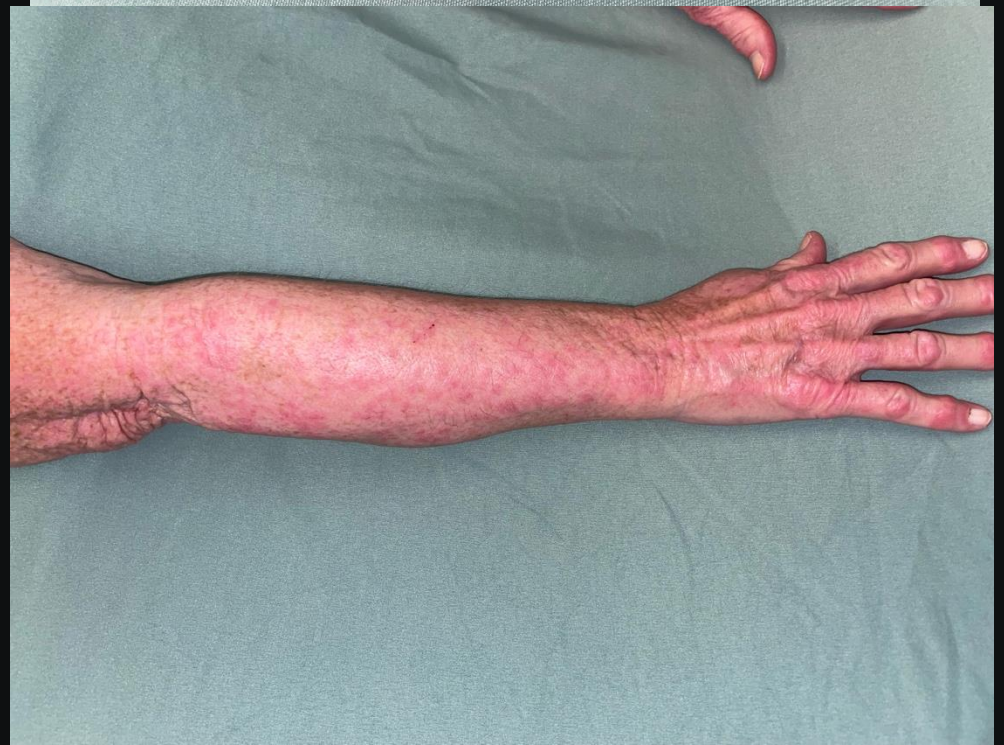


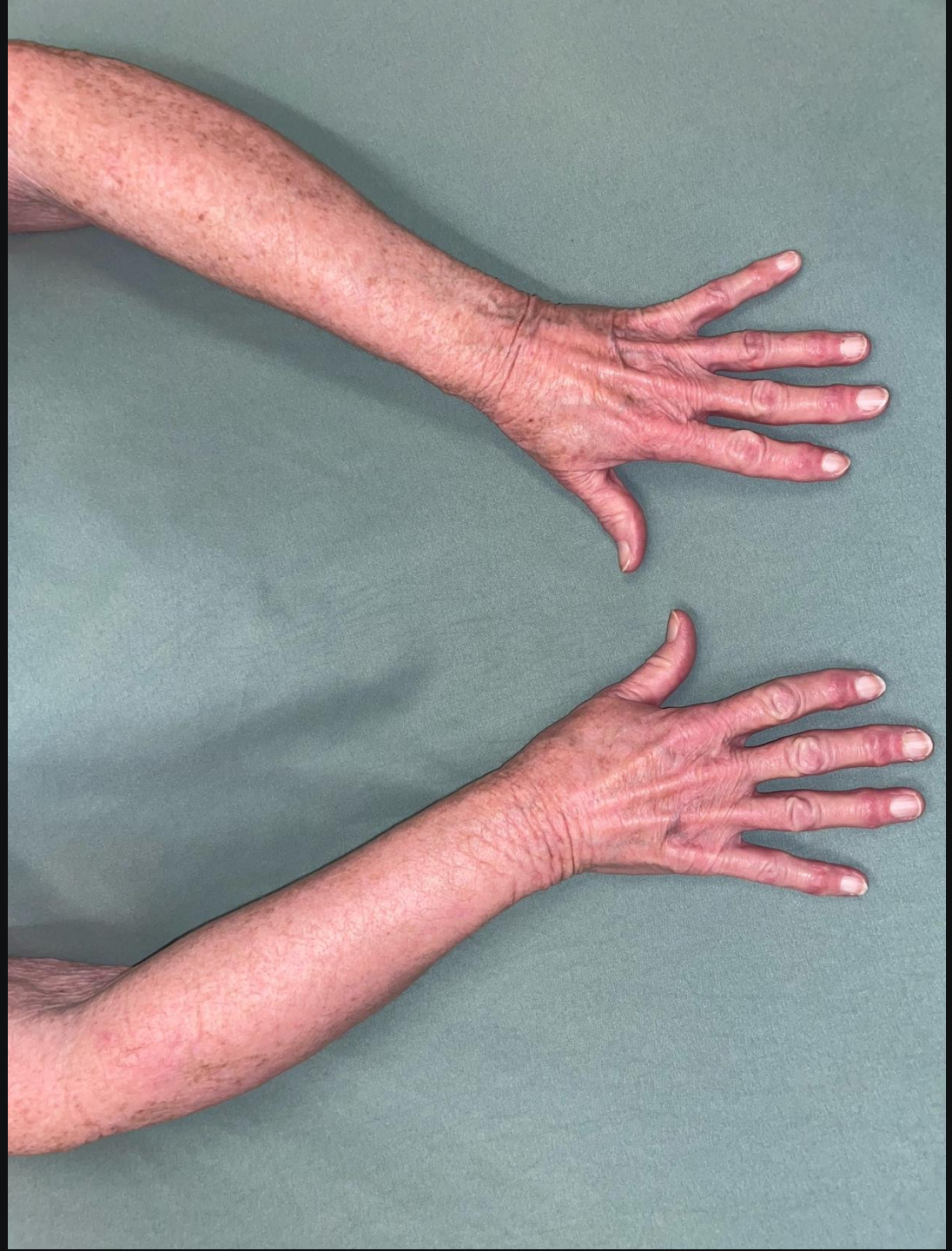
Werth et al. EClinicalMedicine. 2023 Oct 1;64.

IVIG for DMM

- Highly effective agent for cDMM
- Usual dosing at 2 g/kg divided over 2 days
- Monthly dosing, goal to decrease frequently over time



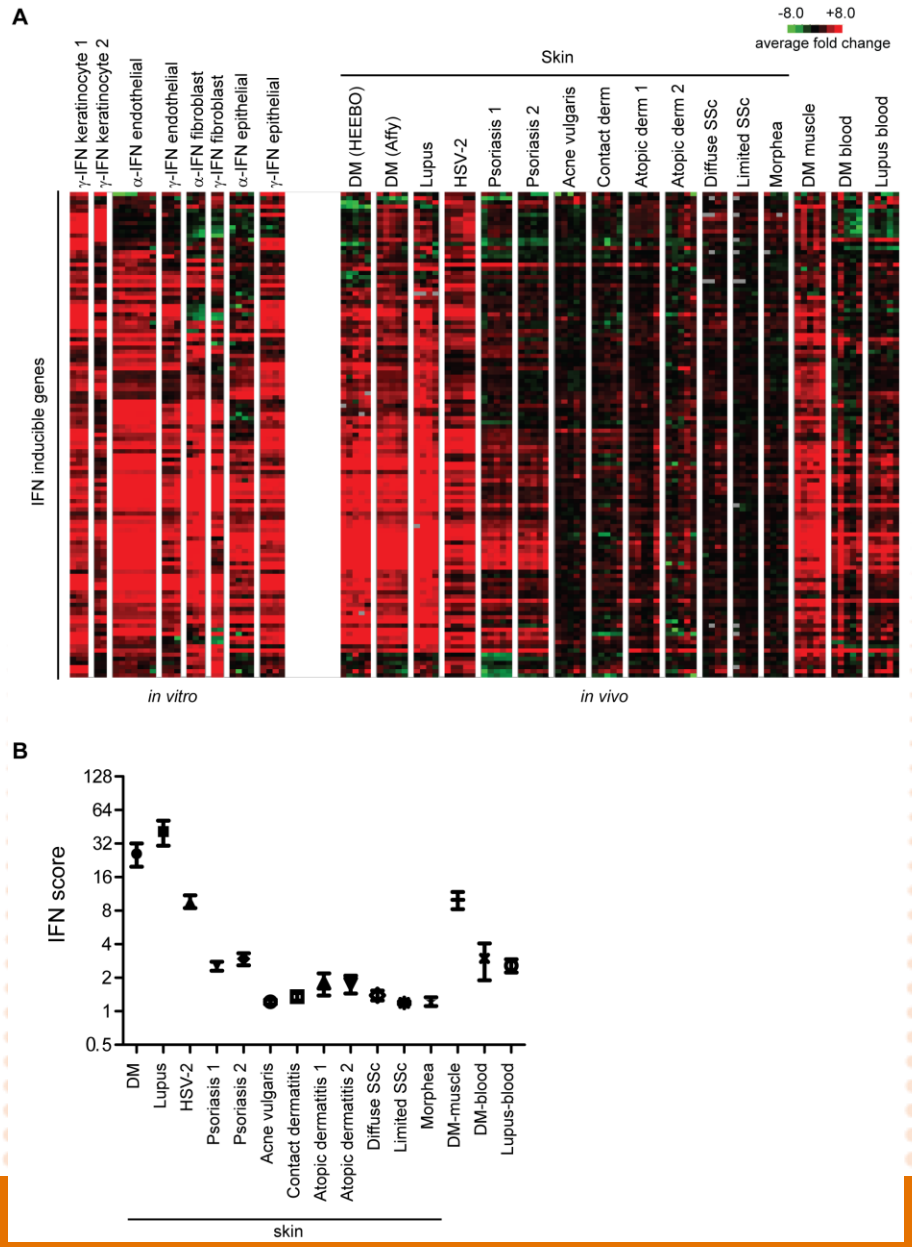




Newer (more effective) therapies

- **IVIG**
- **JAK inhibitors**
- **IFN-inhibitors**

Dermatomyositis as an “acquired interferonopathy”



- Type I IFN genes overexpressed in blood, skin, muscles in DMM pt

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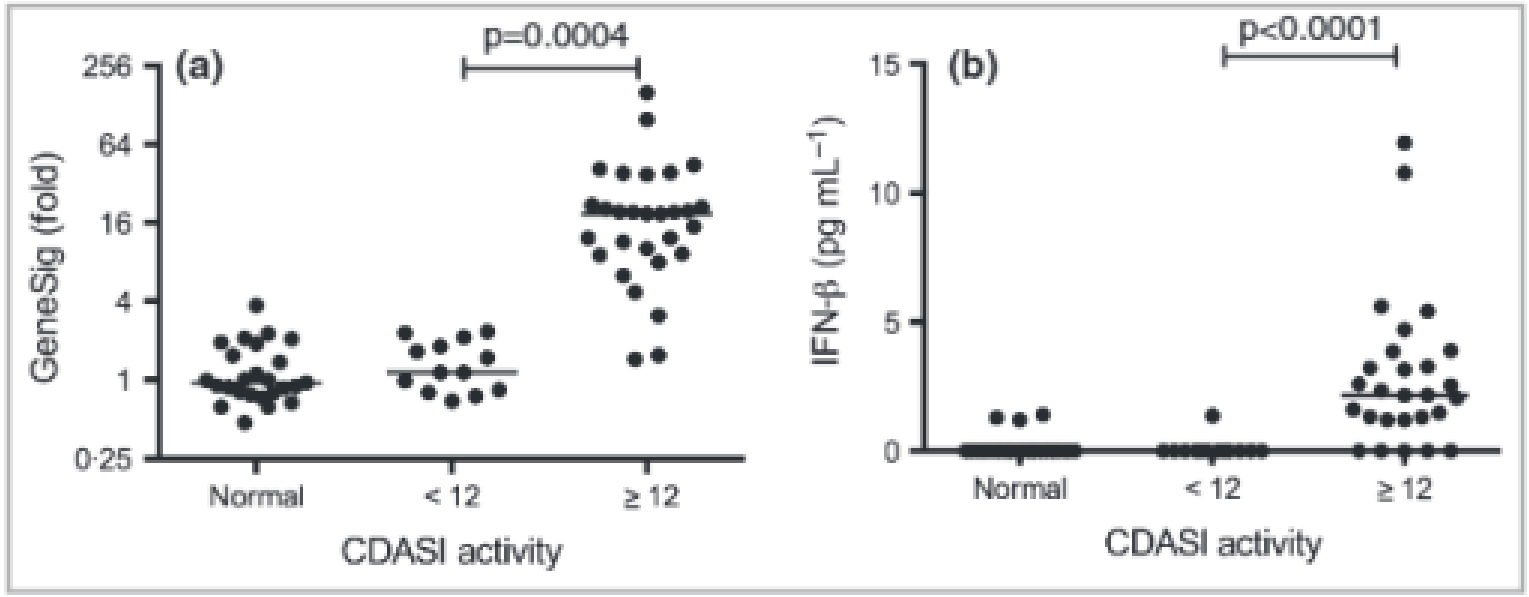
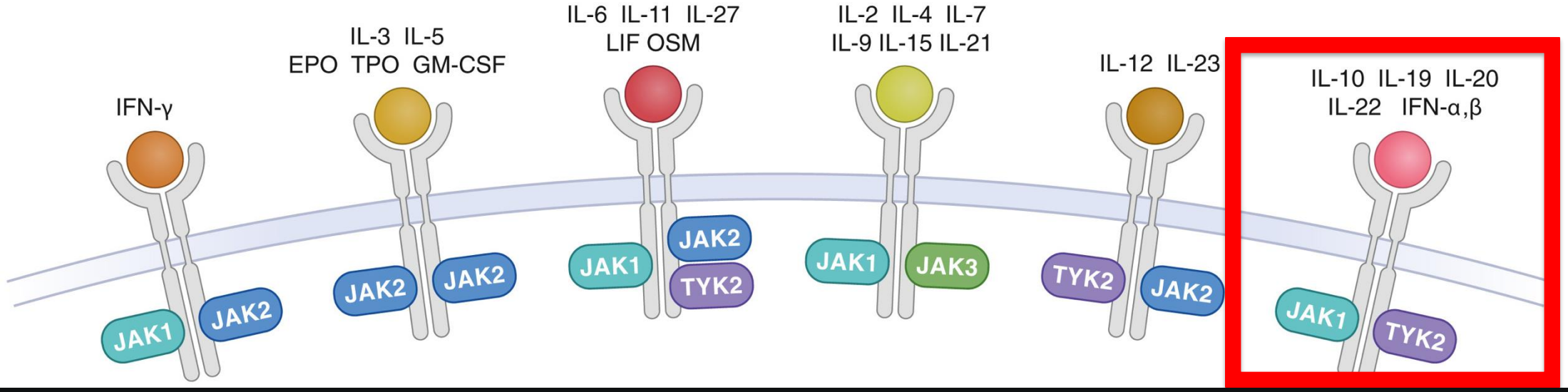
Wong et al. PloS one. 2012 Jan 3;7(1):e29161.

Dermatomyositis as an “acquired interferonopathy”

- IFNβ is highly correlated with skin dz activity



Huard et al. BJD. 2017 May 1;176(5):1224-30.



Jensen et al. EBioMedicine. 2023 Nov 1;97.

Oral JAK inhibitors in dermatomyositis: systematic review

- 48 publications of 145 unique patients (adult DM, n=84; JDM, n=61)
- 61 of 84 adults (73%) had refractory skin disease at baseline
  - 61 of 61 saw improvement
- 57 of 61 JDM pt saw improvement in skin disease
- 16 of 16 saw improvement in muscle symptoms
- 31 of 33 (94%) with ILD improved

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Paik et al. Clin Exp Rheum. 2022 Jun 28;41(2):348.

Baricitinib for cutaneous DMM

- 12 pt on 2 mg BID x 12 weeks
- Improvements in 9 of 12 in CDASI-A
- Pred taper in 5 of 6

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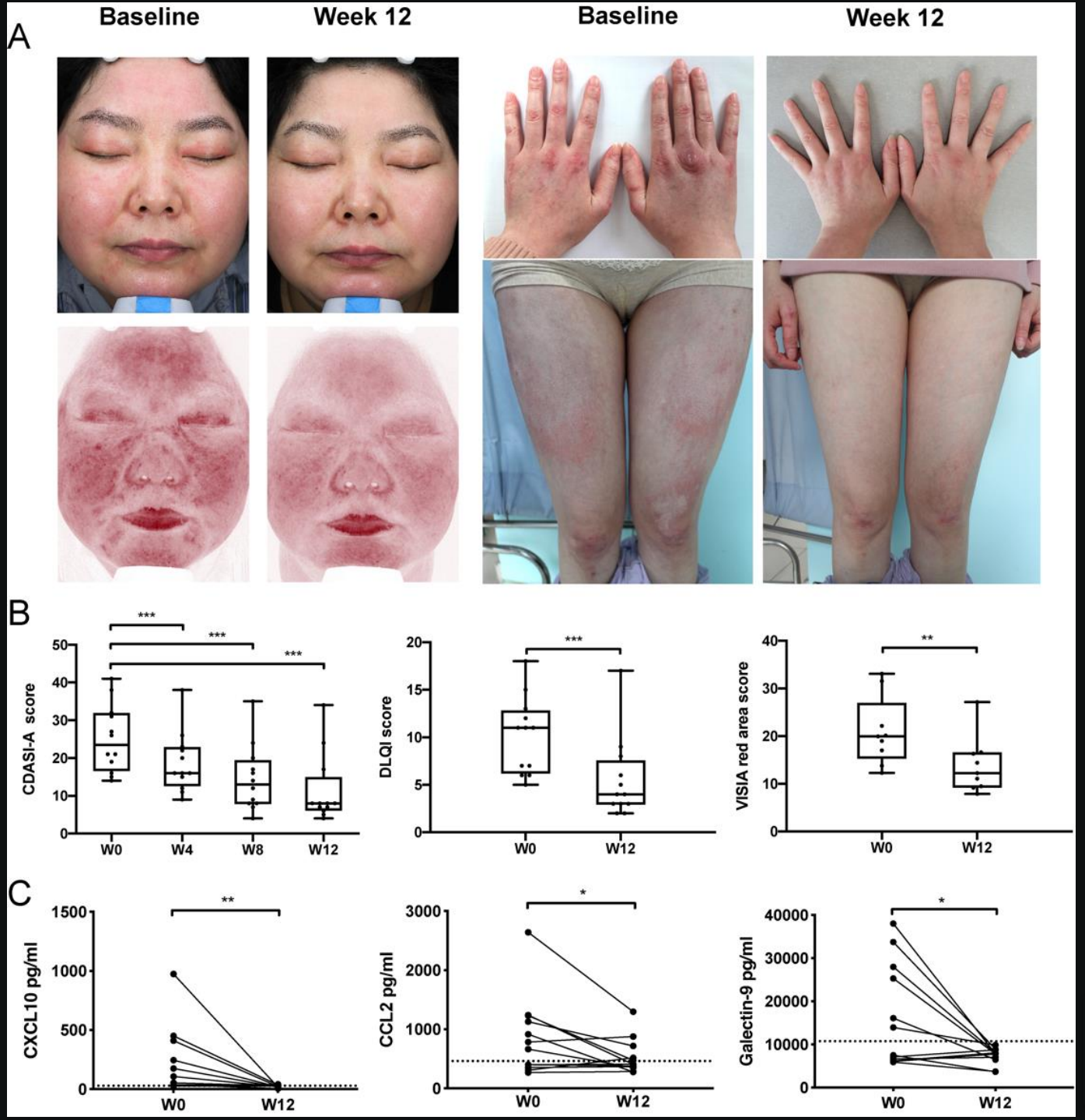
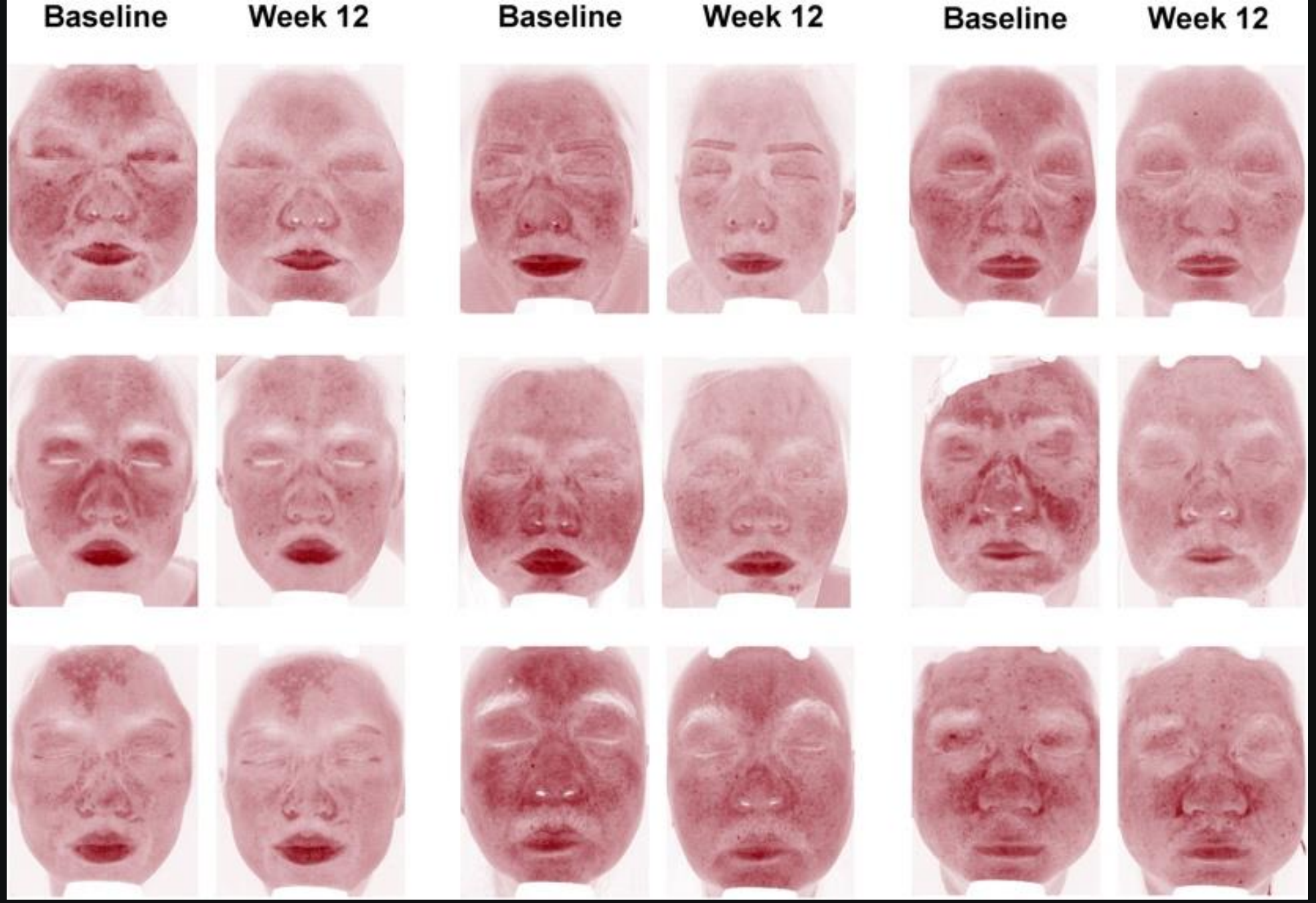
Zhao et al. JAAD. Dec 2022; 87(6): 1374-75.



Zhao et al. JAAD. Dec 2022; 87(6): 1374-75.

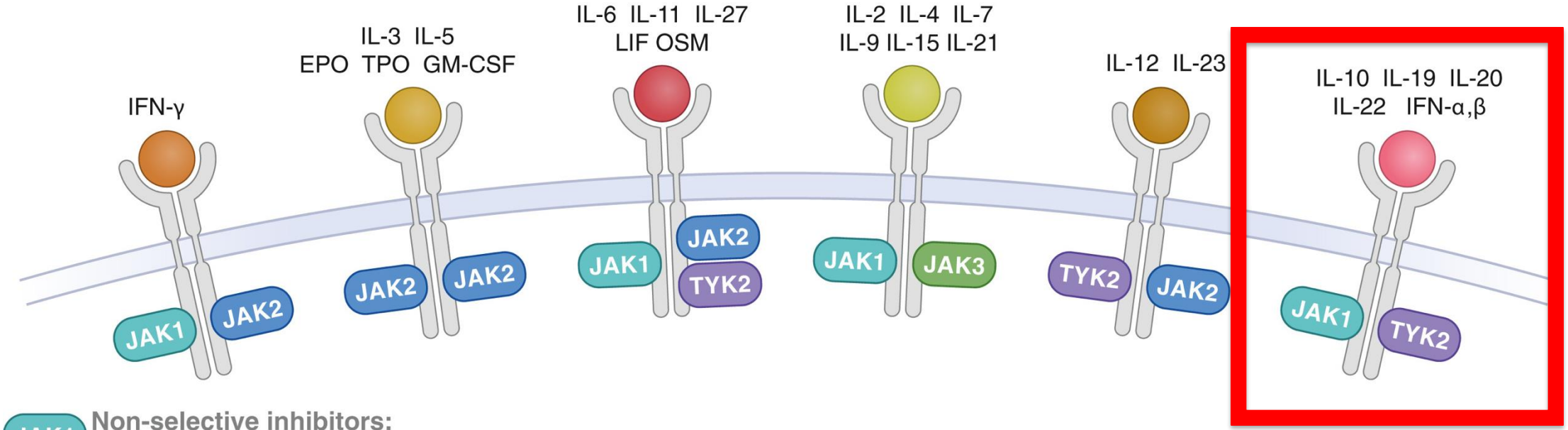


Zhao et al. JAAD. Dec 2022; 87(6): 1374-75.

Beprocitinib for DMM

- Selective JAK1/TYK2 inhibitor

Paik et al. Clin exp rheum. 2025.



Non-selective inhibitors:

JAK1 JAK2 JAK3	Ruxolitinib (MF, PV, GVHD, AD*, VI*)	Tofacitinib (RA, UC, JIA, PSA, JPSA, AS)	Baricitinib (RA, AA, AD, COVID-19)	Peficitinib (RA)	Delgocitinib (AD)
TYK2	Ruxolitinib (PN, COVID-19, PC, HLH, ALL)	Tofacitinib (AA, PSO, TAK, GB, COVID-19, GPA, DM)	Baricitinib (SSc, SLE, JIA, UV, DM, P)		Delgocitinib (Ecz)

JAK1 inhibitors:	JAK2 inhibitors:	JAK3 inhibitors:	TYK2 inhibitors:
Upadacitinib (RA, PSA, AS, nr-axSpA, UC, AD) Filgotinib (RA, UC) Abrocitinib (AD)	Fedratinib (MF) Pacritinib (MF)	Ritlecitinib (AA)	Deucravacitinib (PSO)
Upadacitinib (JIA, CD, TAK, AA, SLE, HS, GCA) Filgotinib (AS, CD, PSA)		Ritlecitinib (VI)	Deucravacitinib (PP, SS, SLE, PSA)

Jensen et al. EBioMedicine. 2023 Nov 1;97.

Beprocitinib for DMM

- Selective JAK1/TYK2 inhibitor
- Completed P2 and now P3 trials for DMM
- Data expected later this year
  - ?First JAKi approved for DMM

Newer (more effective) therapies

- **IVIG**
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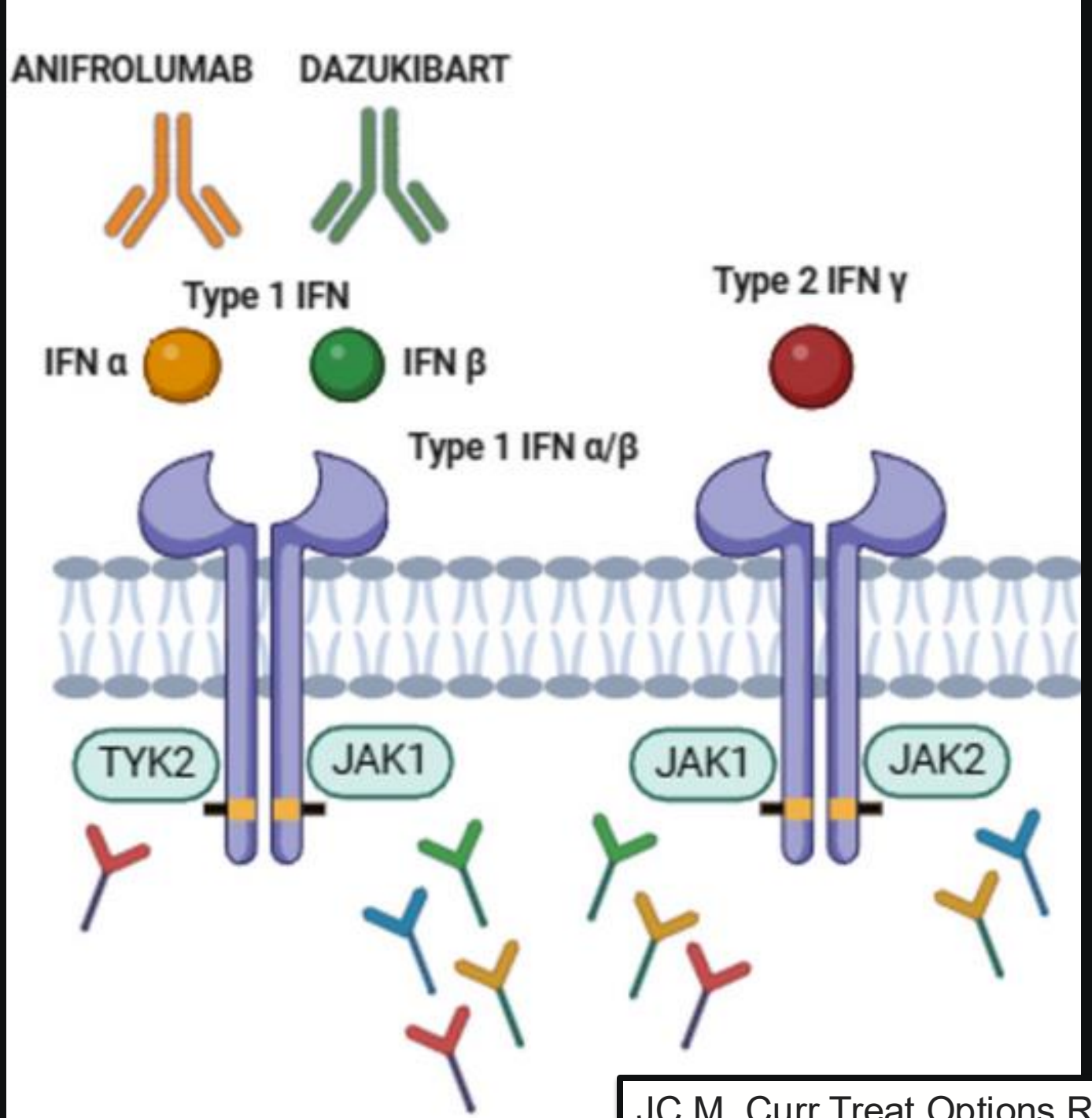
- **IFN-inhibitors**



JC M. Curr Treat Options Rheum. 2025 Dec;11(1):1-2.

Anifrc

- Mab aga
- Approve
- Numero

Anifrolumab in recalcitrant cutaneous **dermatomyositis**: A multicenter retrospective cohort study

KS Shaw, KB Hashemi, RL Castillo, E Rainone… - Journal of the American …, 2024 - Elsevier

… in cutaneous disease activity after 89 initiating **anifrolumab** (Figure 1). Mean decrease […] **anifrolumab**, respectively. 91 For those patients who had received at least 4 doses of **anifrolumab** …

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[HTML] Refractory **dermatomyositis** responsive to **anifrolumab**

PS Ang, E Ezenwa, K Ko, MD Hoffman - JAAD Case Reports, 2024 - Elsevier

… In this report, we present an individual with DM whose refractory skin disease responded to **anifrolumab**, a monoclonal antibody blocking IFN-α receptor-1. … We report an individual with …

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[PDF] A Novel Treatment for Skin Manifestations in **Dermatomyositis**: A Case Report

MS Murthy, A Haikal - Cureus, 2024 - cureus.com

… **Anifrolumab** has additionally been shown to have a … **anifrolumab** for treating DM skin manifestations, especially in refractory cases. More research is needed to guide where **anifrolumab** …

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[CITATION] A Novel Treatment for Refractory **Dermatomyositis**: A Systematic Review of **Anifrolumab** and **Dermatomyositis**

A Srivatsa, W Rehman, R Rehman, M Moossavi… - Journal of the American …, 2025 - Elsevier

… **Dermatomyositis** is a severe systemic autoimmune disease with an estimated 5% 32 … **anifrolumab** and **dermatomyositis**. Of the 50 articles screened, six met the criteria for inclusion …

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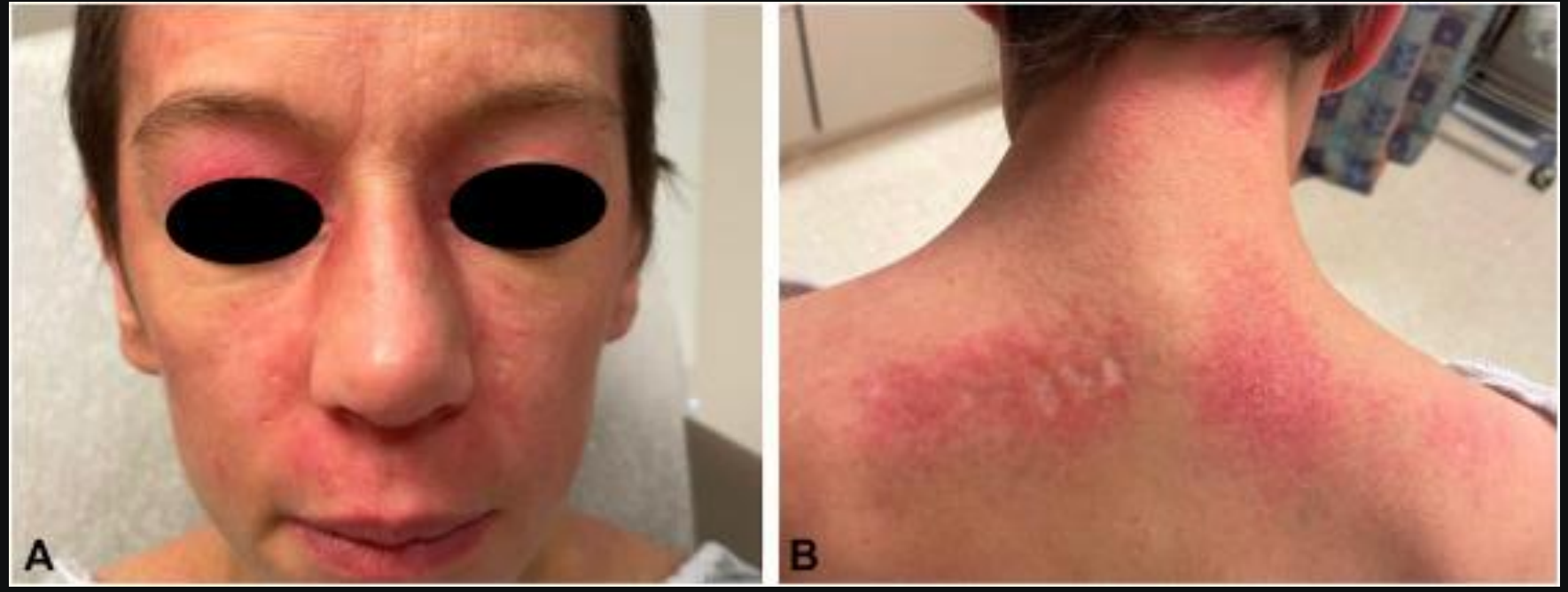
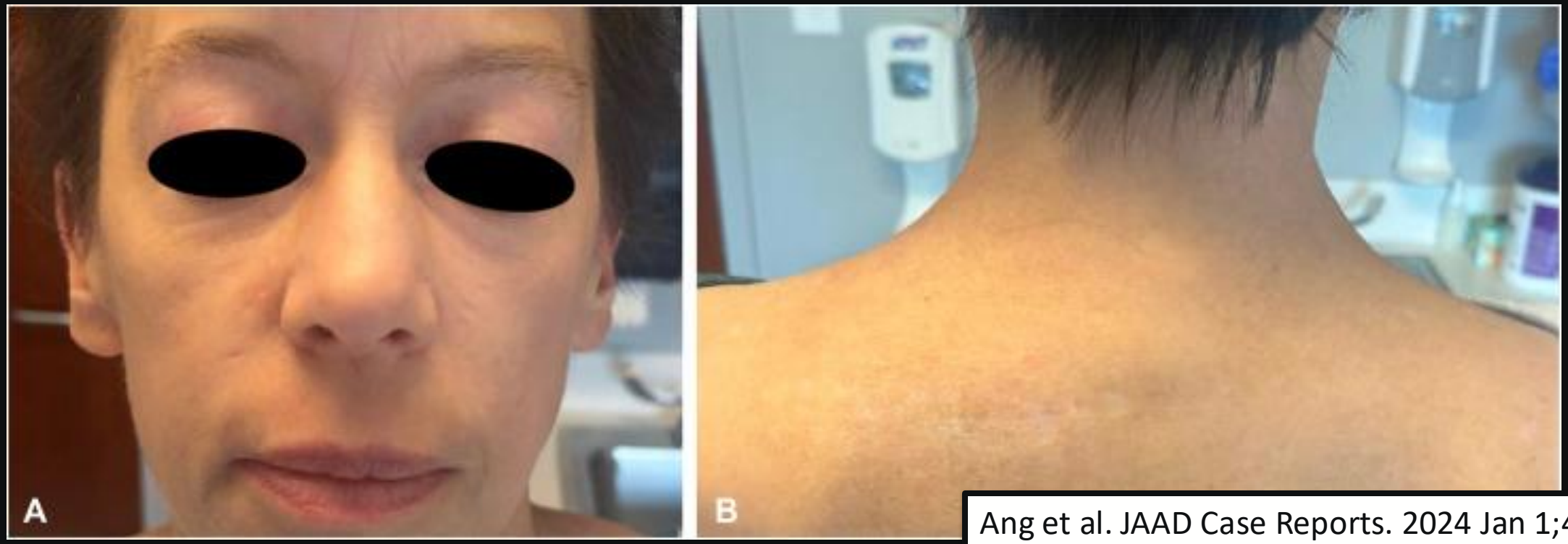
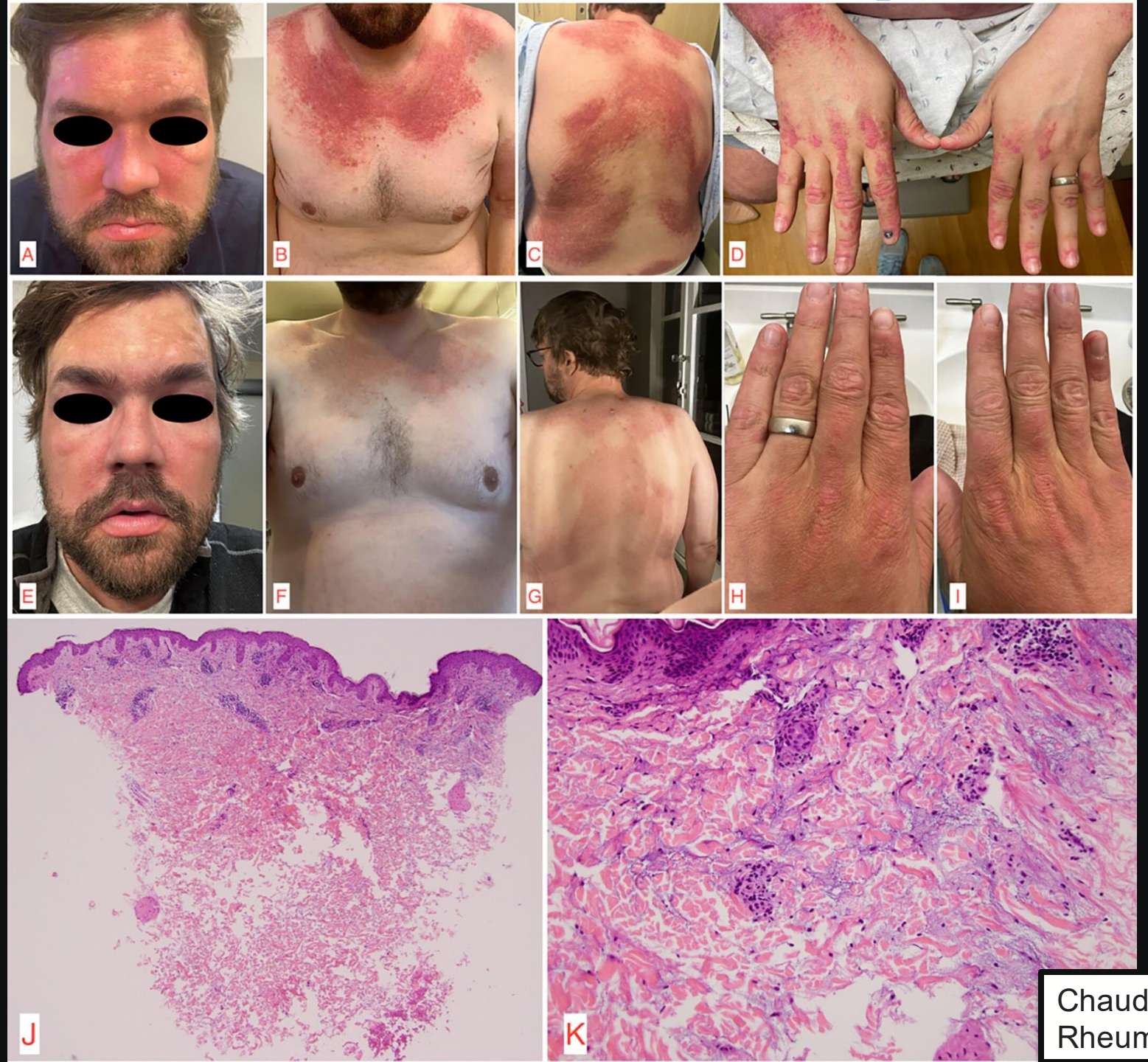




Ang et al. JAAD Case Reports. 2024 Jan 1;43:27-9.



Chaudhary et al. ACR Open Rheum. 2025 Jan;7(1):e11792.

Dazukibart for DMM

- RCT at 25 sites in Europe and US
- Adults 18–80 years with skin-predominant mod-severe DMM (P1-2a) and muscle predominant (P3) enrolled
- Failed one additional treatment
- Enrolled to dazukibart 150, 600 or PBO

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Fiorentino et al. The Lancet. 2025 Jan 11;405(10473):137-46.

Dazukibart for DMM

- 75 patients enrolled and treated

- Treatment-emergent adverse events occurred in 12 (80%) of 15 patients in the dazukibart 150 mg group versus 30 (81%) of 37 in the dazukibart 600 mg group versus 18 (78%) of 23 in the placebo group, with the most common being infections and infestations (two [13%] *vs* 12 [32%] *vs* seven [30%]).

- Four (11%) patients in the dazukibart 150 mg group and one (4%) in the placebo group reported serious adverse events. One patient in stage 3 received dazukibart 600 mg then placebo and died during follow-up due to HLH/MAS

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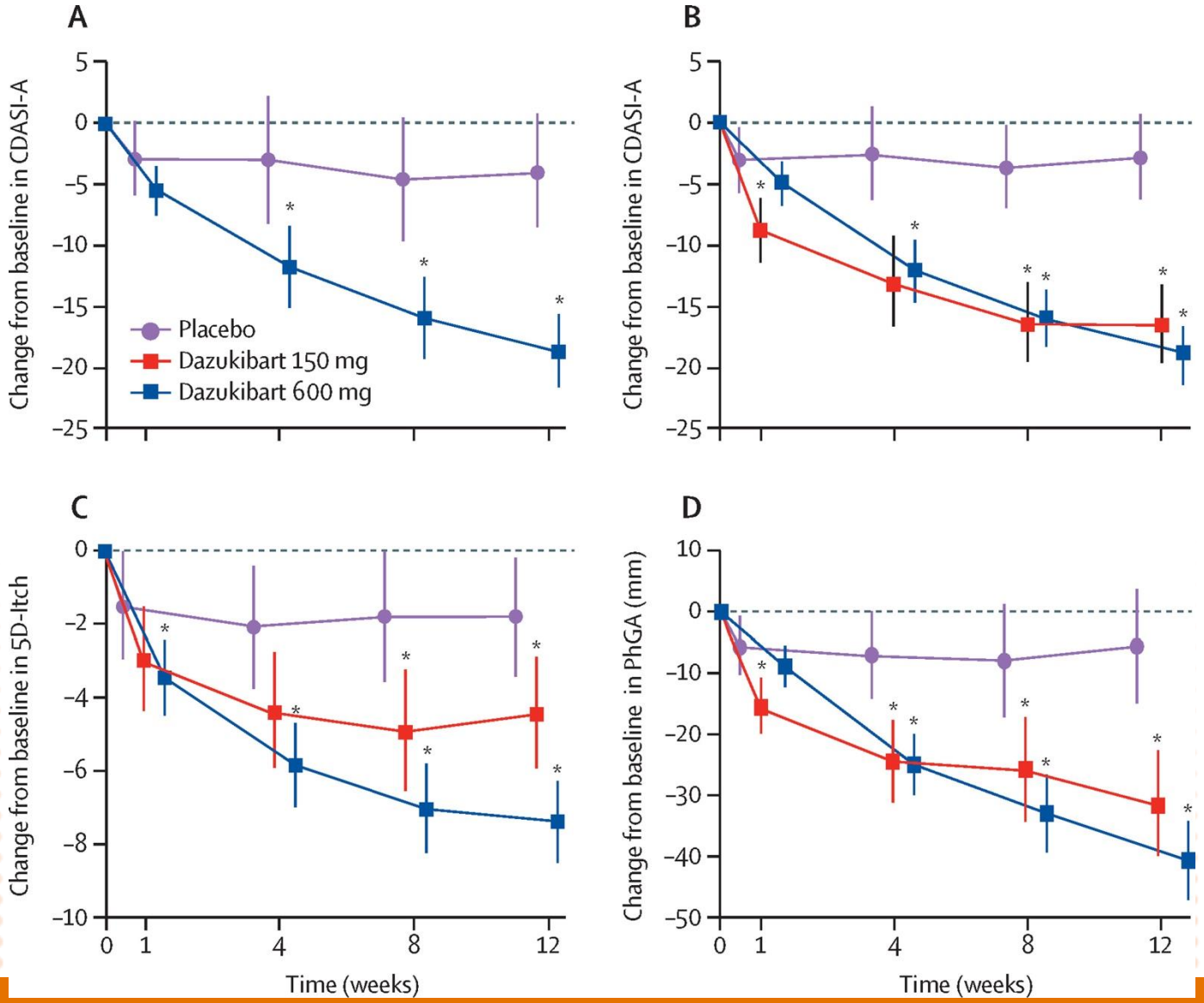
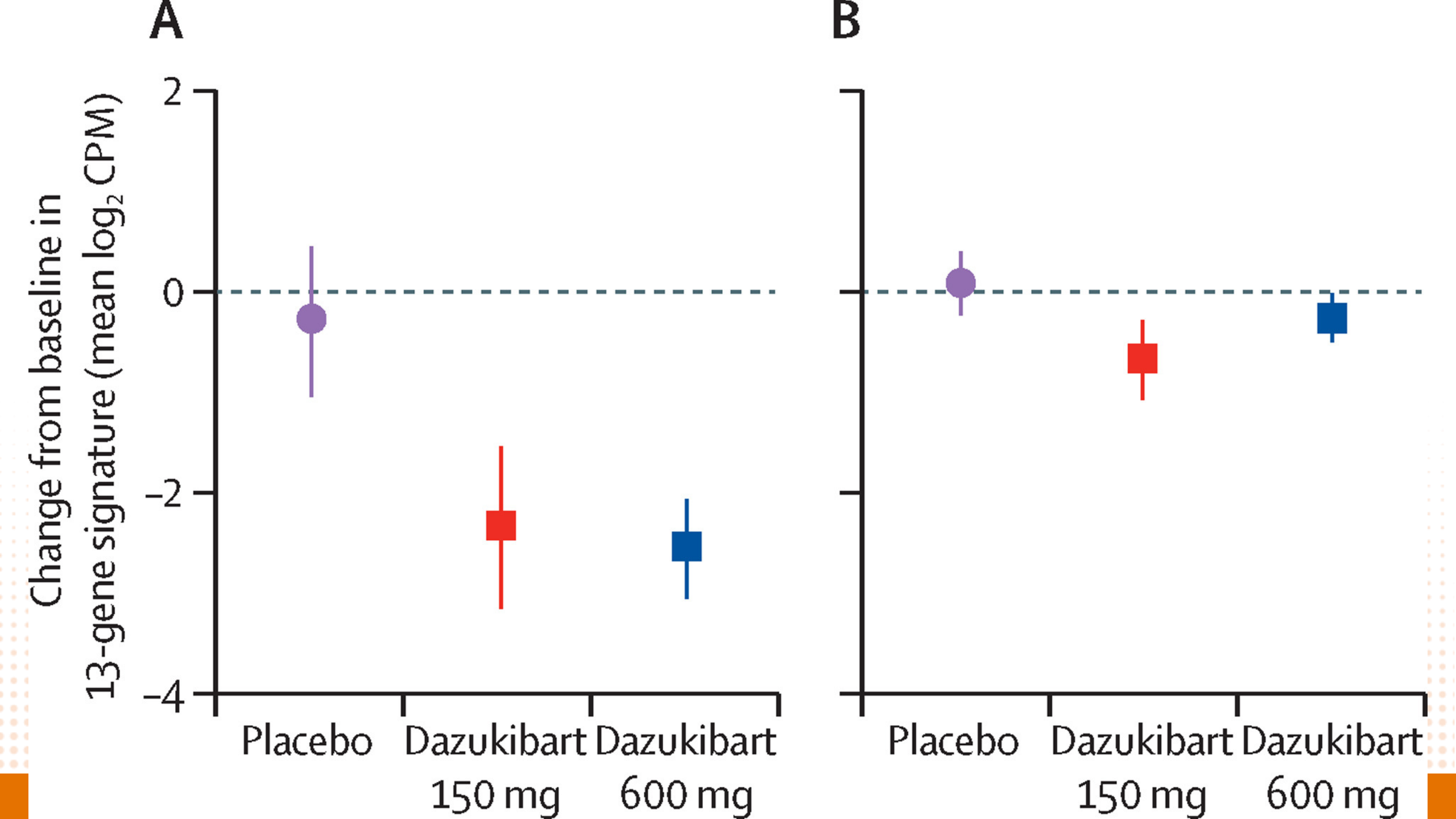
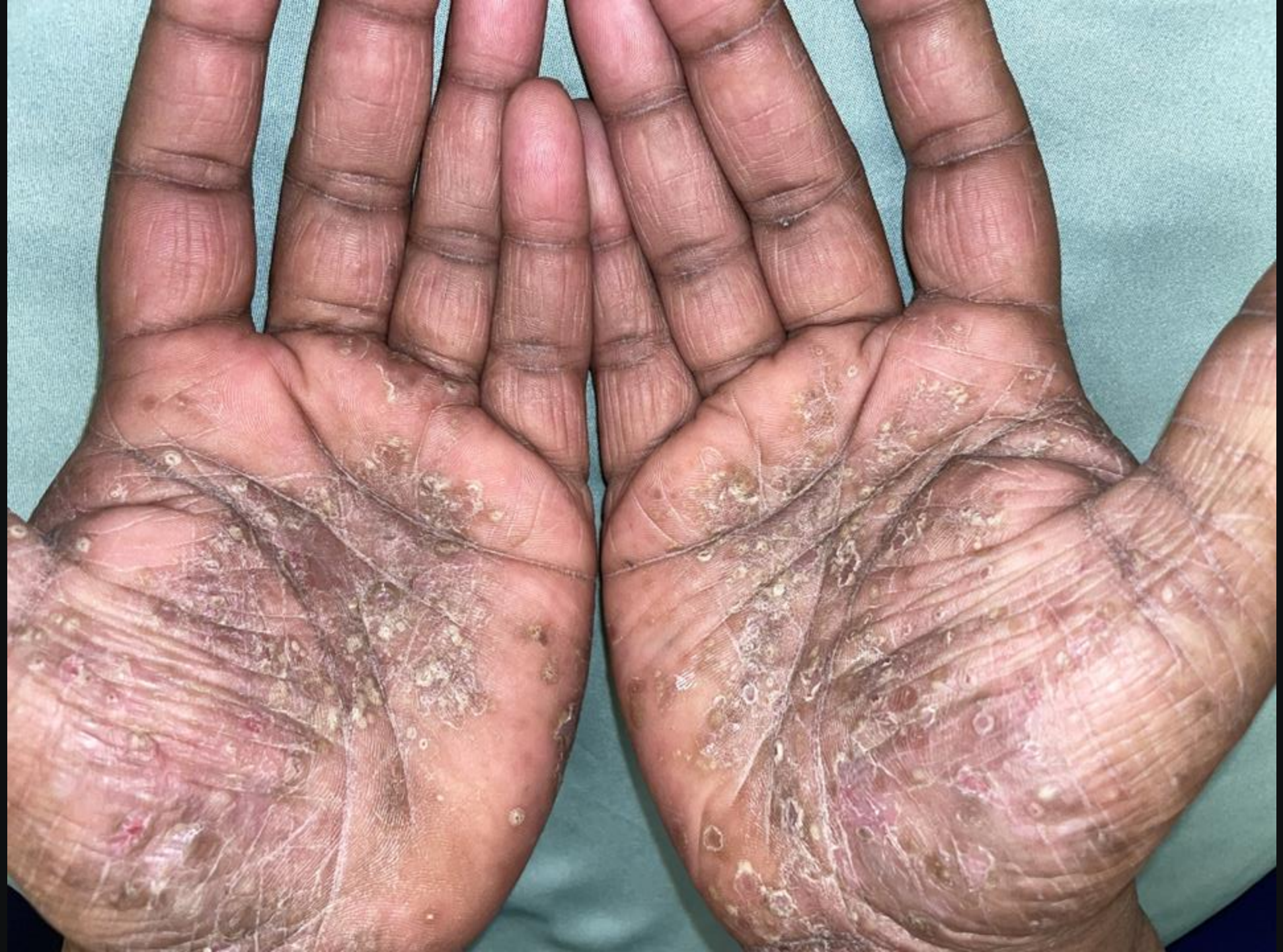
Fiorentino et al. The Lancet. 2025 Jan 11;405(10473):137-46.

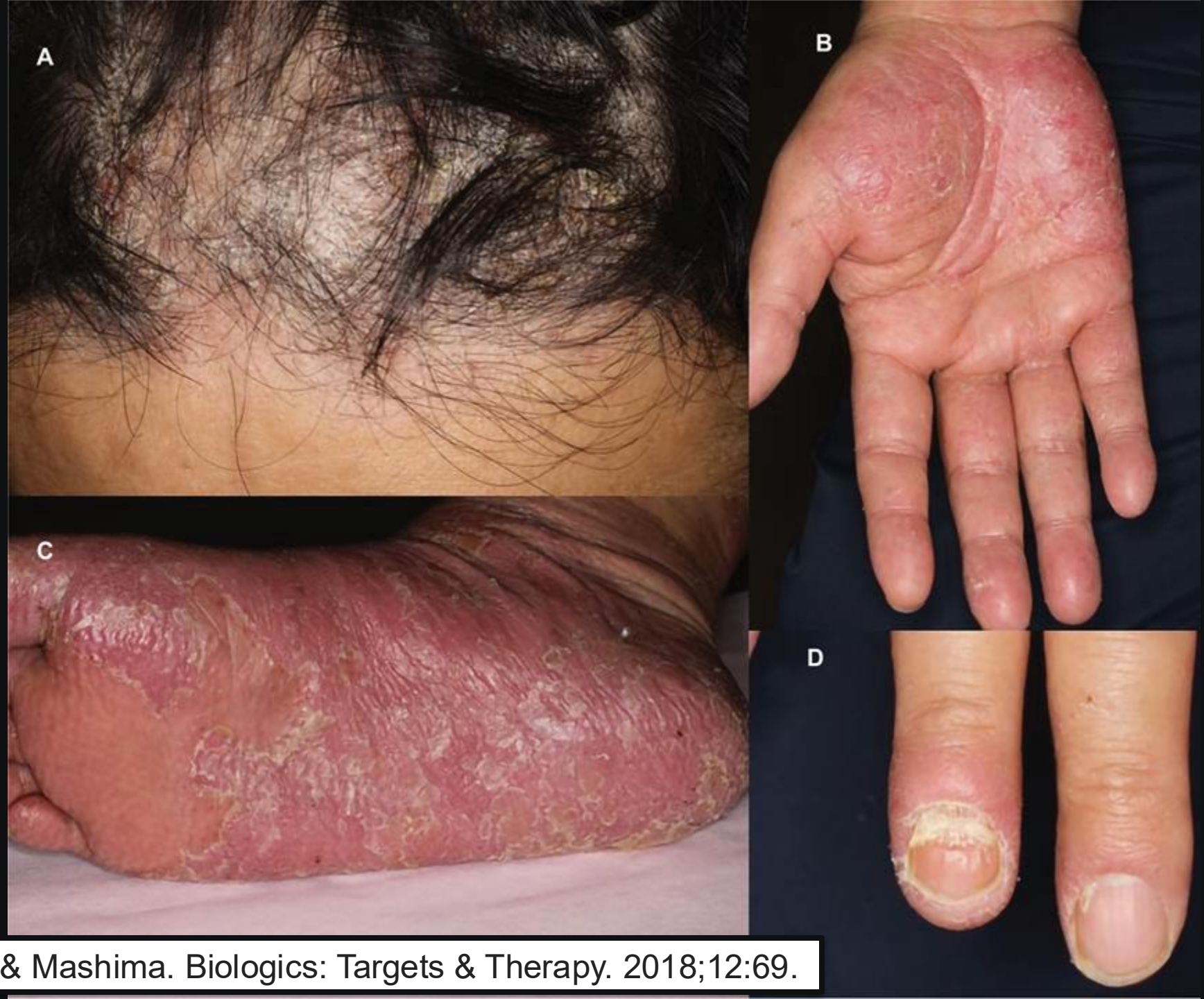
IFN-inhibition for cutaneous DMM



Fiorentino et al. The Lancet. 2025 Jan 11;405(10473):137-46.


A
B
Change from baseline in 13-gene signature (mean log2 CPM)
2
0
−2
−4
Placebo
Dazukibart 150 mg
Dazukibart 600 mg
Placebo
Dazukibart 150 mg
Dazukibart 600 mg



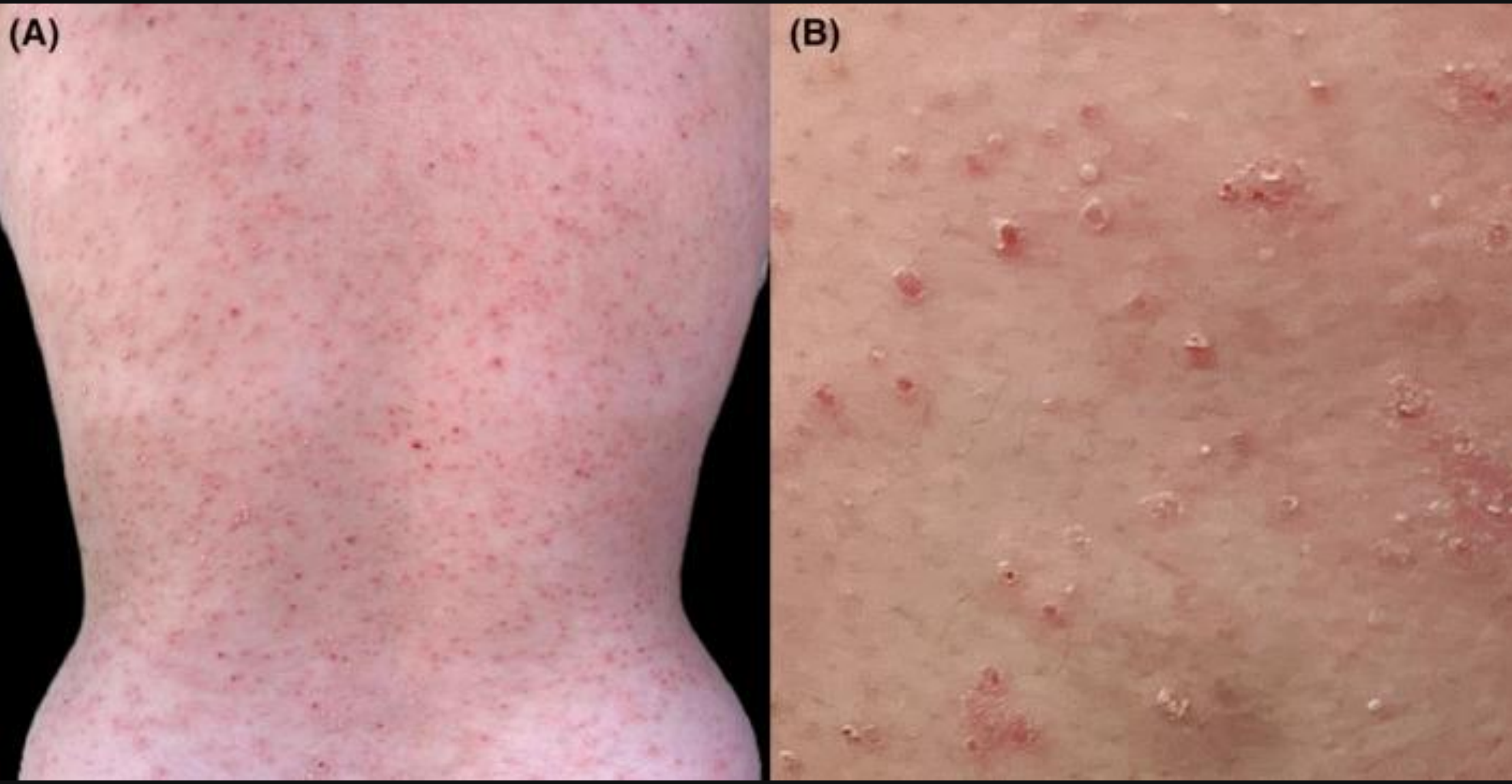


Matsumoto & Mashima. Biologics: Targets & Therapy. 2018;12:69.

TNF-α inhibitor induced psoriasis

- Palmoplantar > flexural pustular eruptions
- Scalp (~50%), postauricular, face, umbilicus
- Impetiginization common ("dirty psoriasis")
- Up to 10% of peds pt w IBD treated with TNF-inhibitor
  - Mean onset 10-20 months after starting tx
  - Tx change in ~20%
  - ~50% recur with another TNF-inhibitor

1. Ossio et al J Cutan Med Surg. 2020
2. Sridhar et al Inflam Bowel Dis 2018
3. Perman et al Ped Derm 2012
4. Sherlock et al J Ped Gastr Nutr 2015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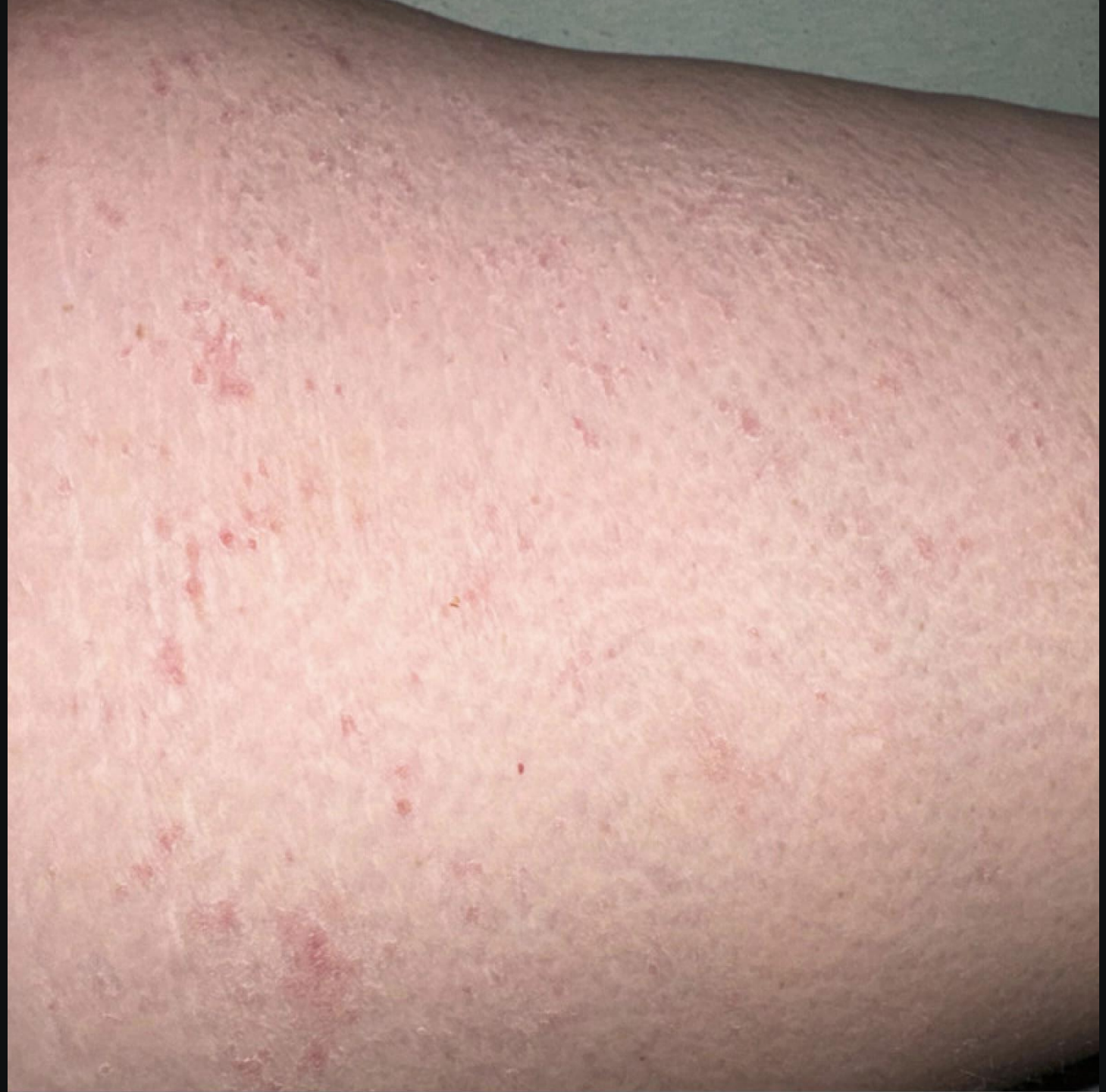

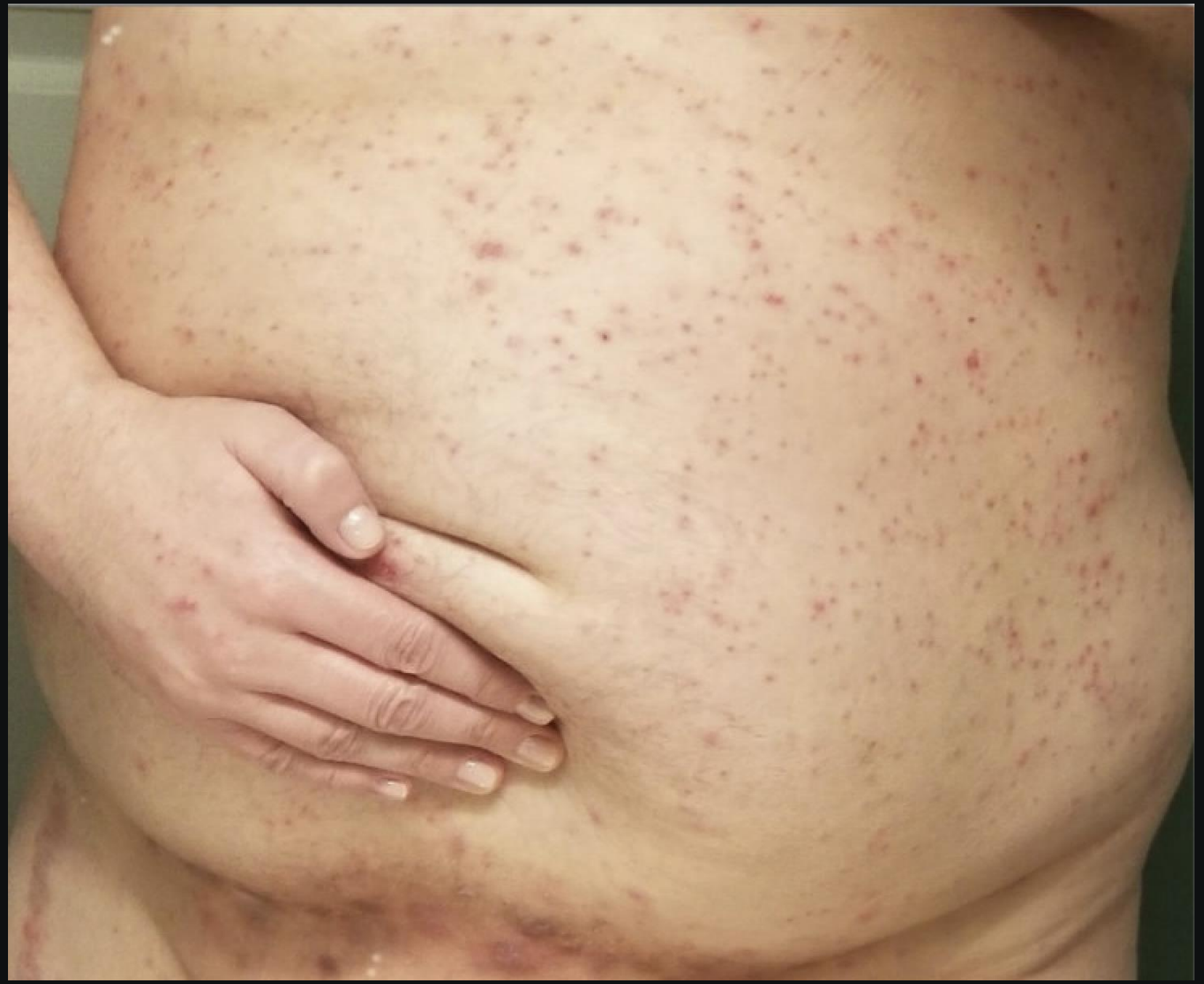

“Psoriasis punctata” is also typical of TNF induced disease

- 93 patients with TNF inhibitor-induced psoriasis at UVA
- 21 patients (22.6%) dx with “psoriasis punctata”
  - Two thirds with concurrent plaque psoriasis
  - Often **perifollicular** and may show clinical and histologic overlap with **pustular** variants of psoriasis
- Vs "other” group
  - **Younger** average age: 31 vs 38 yo
  - Shorter onset (NS): 19 vs 27 months
  - No major differences in TNF inhibitor, underlying disease, sex, % with prior psoriasis

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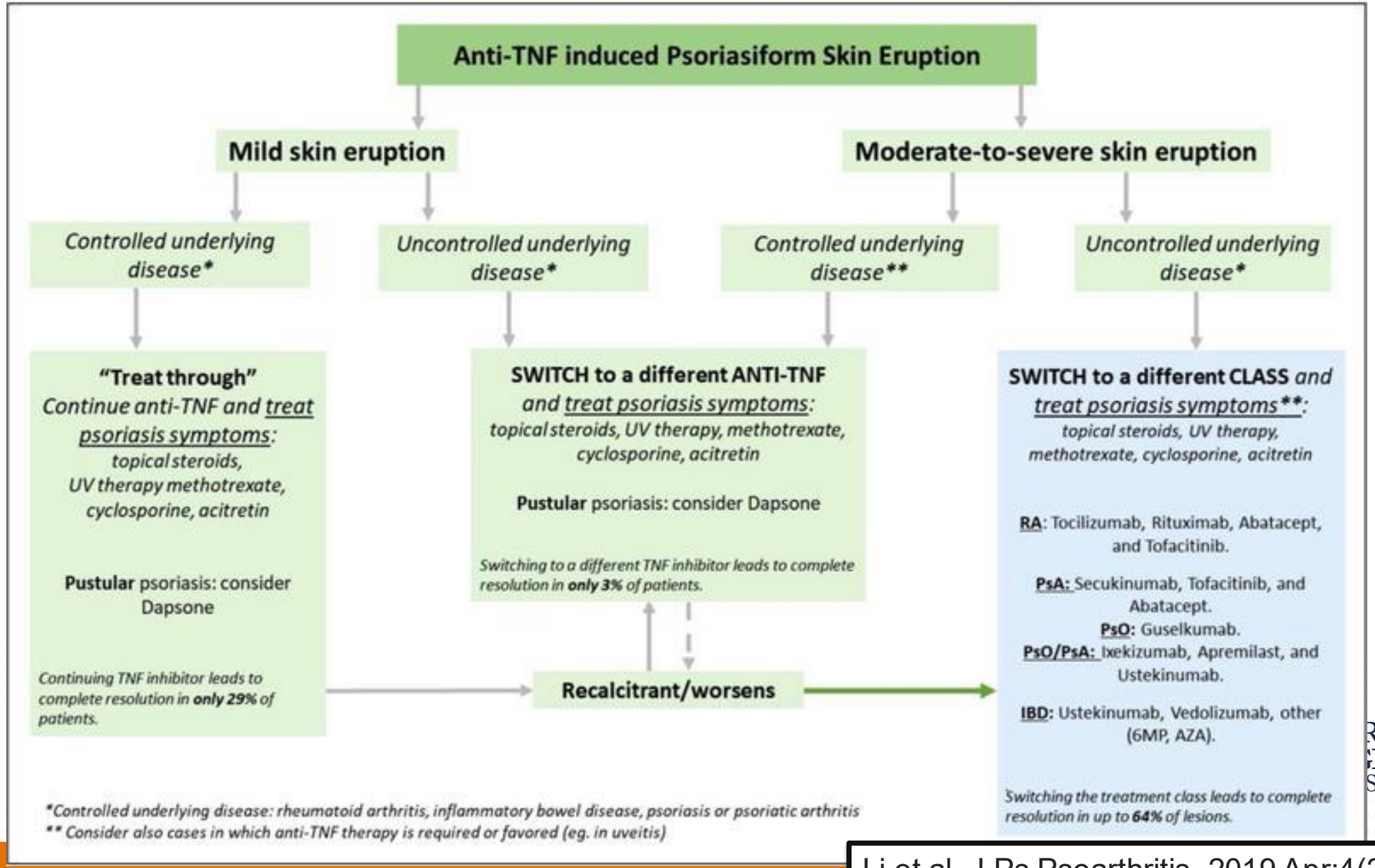
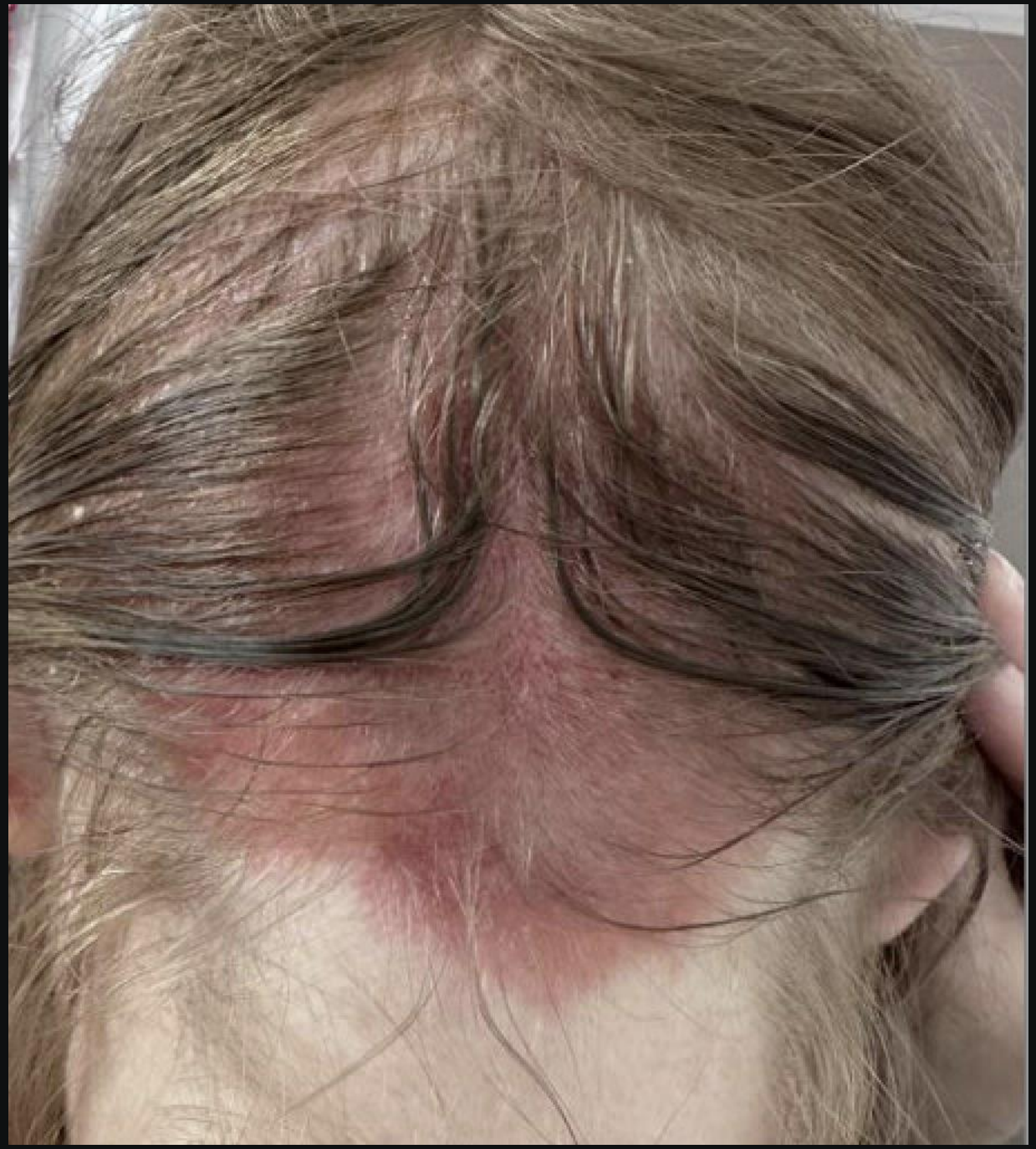
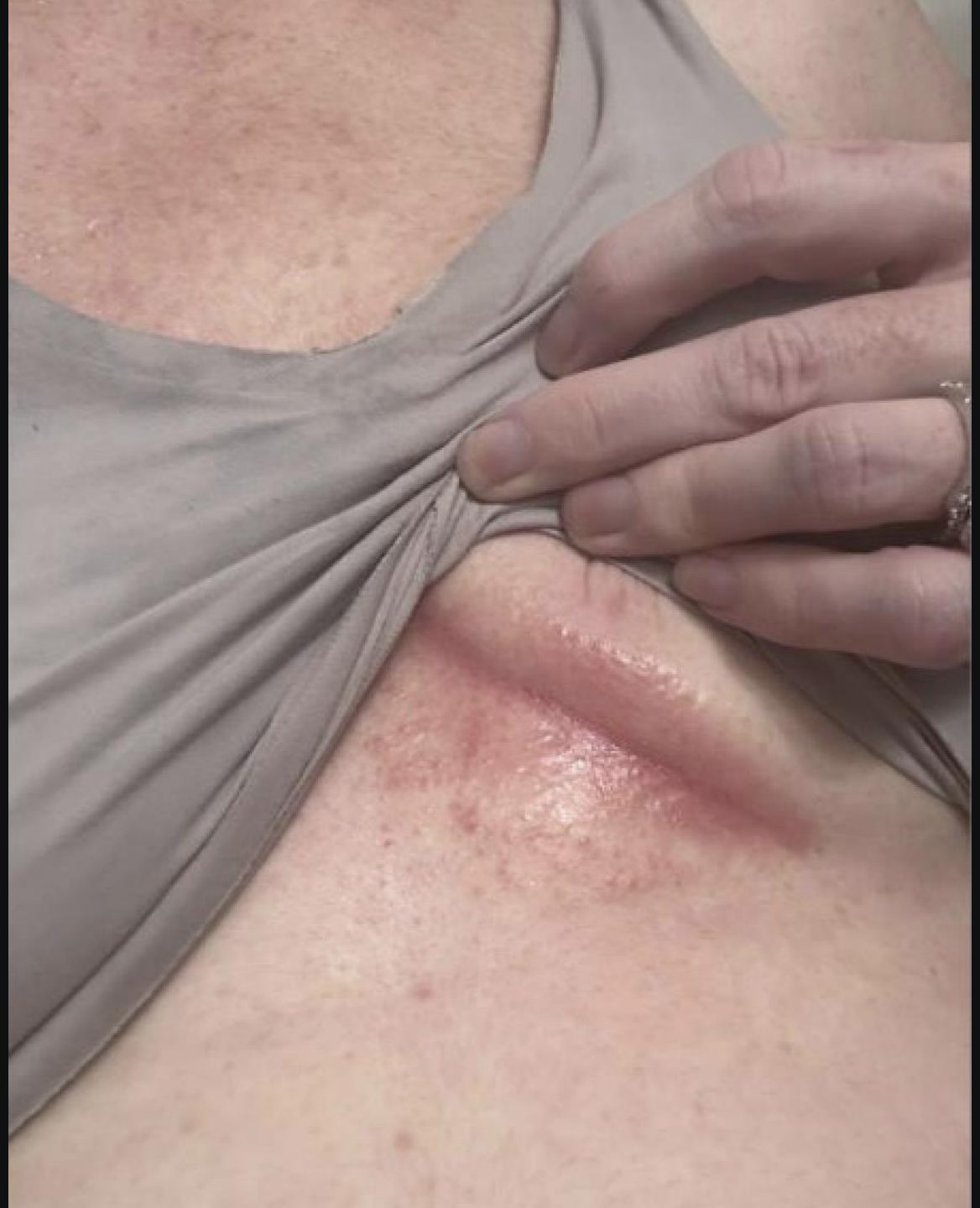
Im et al. Australasian J Derm. 2025 Jan 30;66(1):42.



Li et al. J Ps Psoarthritis. 2019 Apr;4(2):70-80.





[PDF] Atopic-like **dermatitis** after **secukinumab** injection: a case report

M Burlando, E Cozzani, R Russo, A Parodi - Dermatol Ther, 2019 - academia.edu

… Six months after the first dose of **Secukinumab** was … nose-**dermatitis**, 4 days after every **Secukinumab** injection. … An atopic **dermatitis** eczema-like was diagnosed and **Secukinumab** …

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New onset of psoriasis **induced** by **secukinumab** in a patient with ankylosing spondylitis: a case report

D Currado, DPE Margiotta, C Conforti… - Scandinavian Journal …, 2020 - Taylor & Francis

… in the safety profiles of **secukinumab** compared with other … after swapping from infliximab to **secukinumab**. A 54-year-old … , such as seborrhoeic **dermatitis**, acute spongiotic eczema, …

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Secukinumab-induced paradoxical pustular psoriasis

S Dogra, A Bishnoi, T Narang… - Clinical and experimental …, 2019 - academic.oup.com

… tered by subcutaneous injections of **secukinumab** 300 mg (by … administered the 14th dose of **secukinumab** and after 3 days, … Psoriasis and pustular **dermatitis** triggered by TNF-{alpha} …

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Treatment of **Secukinumab-induced** Atopic **Dermatitis**-like Lesions Using Upadacitinib: A Case Report

W Xiang, X Lin, Q Li, W Zheng - Indian Journal of Dermatology, 2025 - journals.lww.com

… weekly **Secukinumab** therapy at … **Secukinumab**, he noticed a small number of erythematic papules on his hands. Despite discontinuing **Secukinumab** for two weeks, his atopic **dermatitis**-…

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Morphologic Switch From Psoriasiform to Eczematous Dermatitis After Anti-IL-17 Therapy

A Case Series

Francis Yi Xing Lai, MBBS (Hons)[1]; Eleanor Higgins, MRCPI[1]; Catherine H. Smith, FRCP[1] ; et al

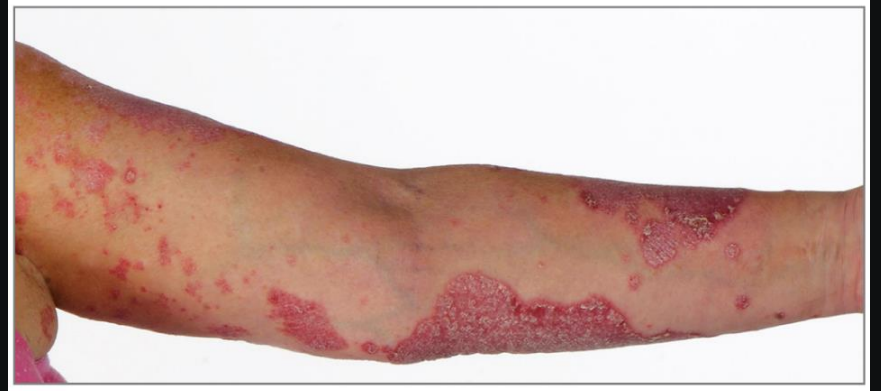
Table. Clinical Characteristics of the 4 Cases and Therapeutic Response

Case No./Sex/ Age, y	Psoriasis Subtype	Prior Psoriasis Therapies	Prior Atopy	PASI Following Secukinumab (Baseline PASI)	Anatomical Distribution of Eczema	Duration of Secukinumab Therapy Before Eczema Onset	Investigations	Eczema Response
1/F/30s	CPP	UV-B, MTX, adalimumab, ustekinumab	Asthma	PASI 100 (PASI 19.4)	Flexural	12 weeks (8 weeks after reintroduction)	NA	Controlled with potent topical steroids
2/F/50s	CPP	UV-B, MTX, CsA, adalimumab, etanercept, infliximab, ustekinumab	Eczema	80% improvement (PASI 30.0)[a]	Facial/flexural	5 weeks (12 weeks for ustekinumab)	IgE 1577 (normal, 0-81 kU/L) European Baseline Series patch test-negative	Severe and recalcitrant, persisted after secukinumab cessation and with the introduction of methotrexate and apremilast; patient continued to require day hospital admissions
3/F/30s	CPP	UV-B, MTX, CsA, adalimumab	Asthma	80% improvement (PASI 18.4)	Generalized/ dyshidrotic	5 weeks	Histologic examination results: acute spongiotic dermatitis with eosinophils	Severe and generalized, requiring cessation of secukinumab to resolve; etanercept introduced and PASI 100 achieved
4/F/50s	CPP	UV-B, MTX, CsA	Asthma, eczema	PASI 100 (PASI 11.0)	Flexural/ generalized	4 weeks	NA	Severe and generalized, requiring cessation of secukinumab to resolve; mild recurrence of psoriasis (PASI 3.6); cyclosporine, 4 mg/kg introduced

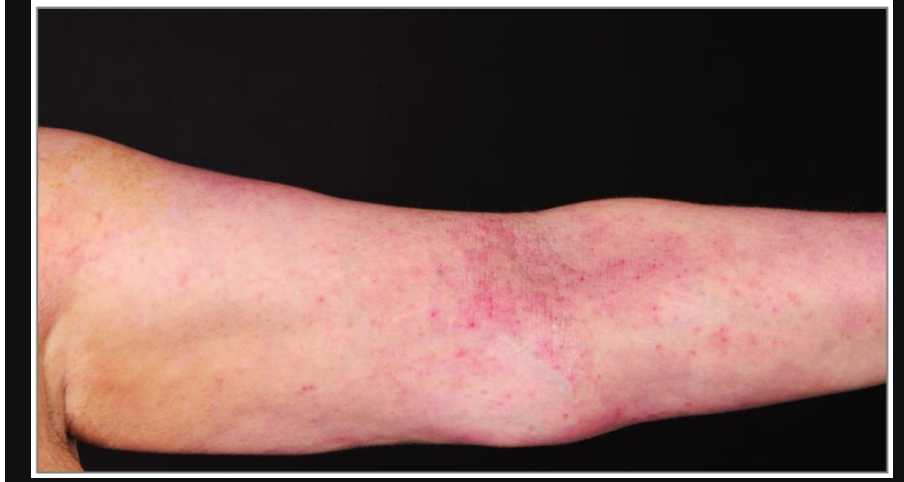
Abbreviations: CPP, chronic plaque psoriasis; CsA, cyclosporine; IgE, immunoglobulin E; MTX, methotrexate; NA, not applicable; PASI, Psoriasis Area and Severity Index; UV-B, ultraviolet B.

[a] 80% improvement refers to an 80% reduction of the baseline PASI score.

A Clinical image of plaque psoriasis



B Development of eczema following secukinumab therapy



Lai et al. JAMA derm. 2019 Sep 1;155(9):1082-4.

What's new in psoriasis?

- Topical therapies
- Injectable therapies
- Oral therapies

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

An Oral Interleukin-23–Receptor Antagonist Peptide for Plaque Psoriasis

Robert Bissonnette, M.D., Andreas Pinter, M.D., Laura K. Ferris, M.D., Ph.D., Sascha Gerdes, M.D., Phoebe Rich, M.D., Ronald Vender, M.D., Megan Miller, M.P.H., Yaung-Kaung Shen, Ph.D., Arun Kannan, Ph.D., Shu Li, Ph.D., Cynthia DeKlotz, M.D., and Kim Papp, M.D., Ph.D.

Bissonnette et al. NEJM. 2024;390:510-21

Do we really need another psoriasis systemic?

- Pt often prefer oral agents to injections, esp children and needle-phobic
- Apremilast has limited efficacy and is sometimes intolerable
- Deucravacitinib carries concerns about safety of JAK/TYK2 inhibition
  - Two oral TYK2 inhibitors in P3: TAK-279, ESK-001
  - Oral IL17A inhibitor with positive P1 data: DC-806

Bissonnette et al. NEJM. 2024;390:510-21

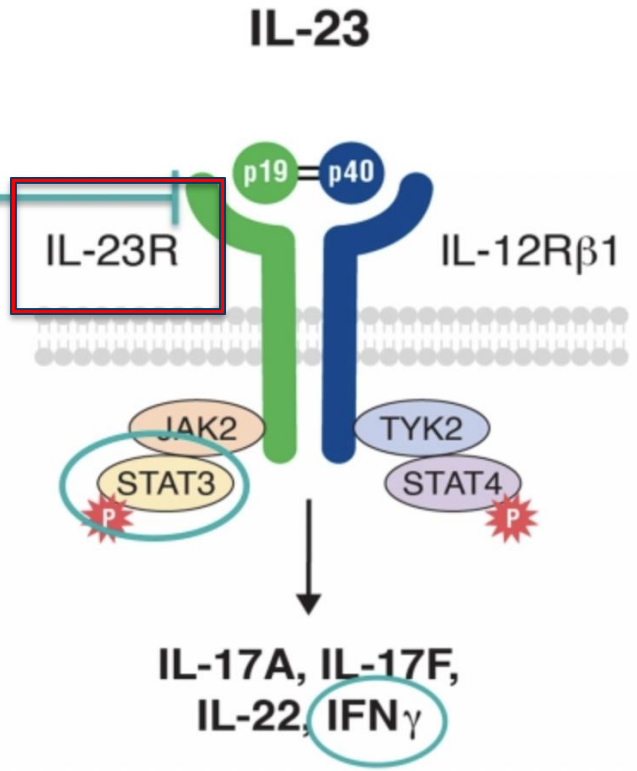
JNJ-77242113 (2113)

- JNJ-2113 is a competitive peptide antagonist that binds with high affinity to IL-23R, and selectively inhibits IL-23 proximal signaling and downstream cytokine production with high potency

- Binds with high affinity (K_D 2 pM) to human IL-23R (SPR)

- Potently inhibits (IC_{50} 6 pM) IL-23-induced proximal signaling (human PBMC pSTAT3)
- No inhibition of IL-12-induced pSTAT4

- Potently inhibits IL-23-induced IFNγ in human NK cells (IC_{50} 18 pM) and human whole blood (IC_{50} 11 pM)
- Similar IC_{50} range in blood from PsO patients



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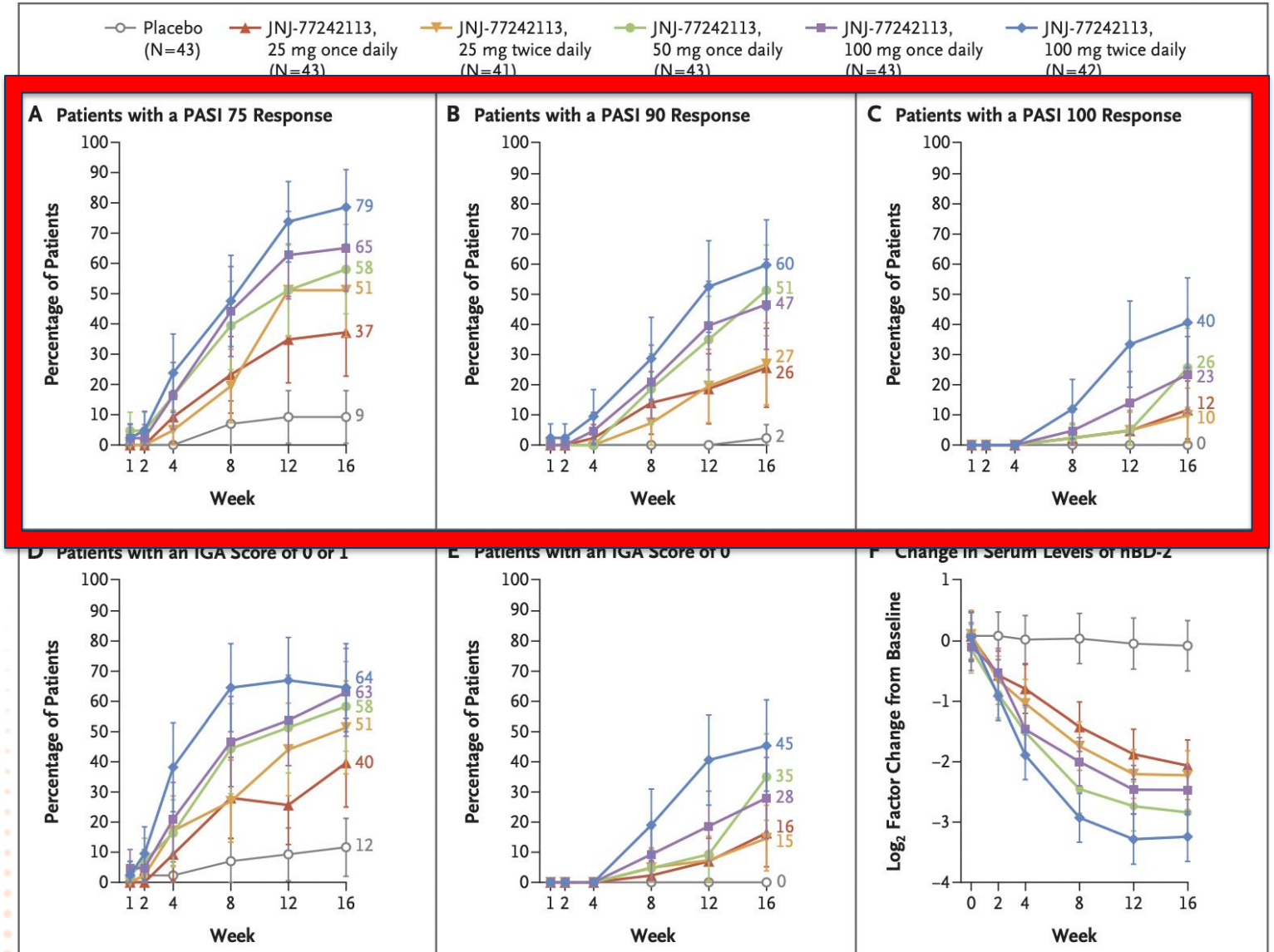

Figure 1. Efficacy End Points According to Trial Group from Week 1 through Week 16.

Scores on the Psoriasis Area and Severity Index (PASI) range from 0 to 72, with higher scores indicating greater extent or severity of psoriasis. PASI 75 response, PASI 90 response, and PASI 100 response refer to reductions from baseline of at least 75%, 90%, and 100%, respectively, in the PASI score. Scores on the Investigator's Global Assessment (IGA) range from 0 (clear skin) to 4 (severe disease); a score of 1 indicates minimal disease. I bars denote 95% confidence intervals. For serum levels of human β-defensin 2 (hBD-2), I bars indicate linear mixed-effect model–based 95% confidence intervals. The widths of the confidence intervals have not been adjusted for multiplicity and should not be used to infer definitive effects of JNJ-77242113 for the secondary end points.

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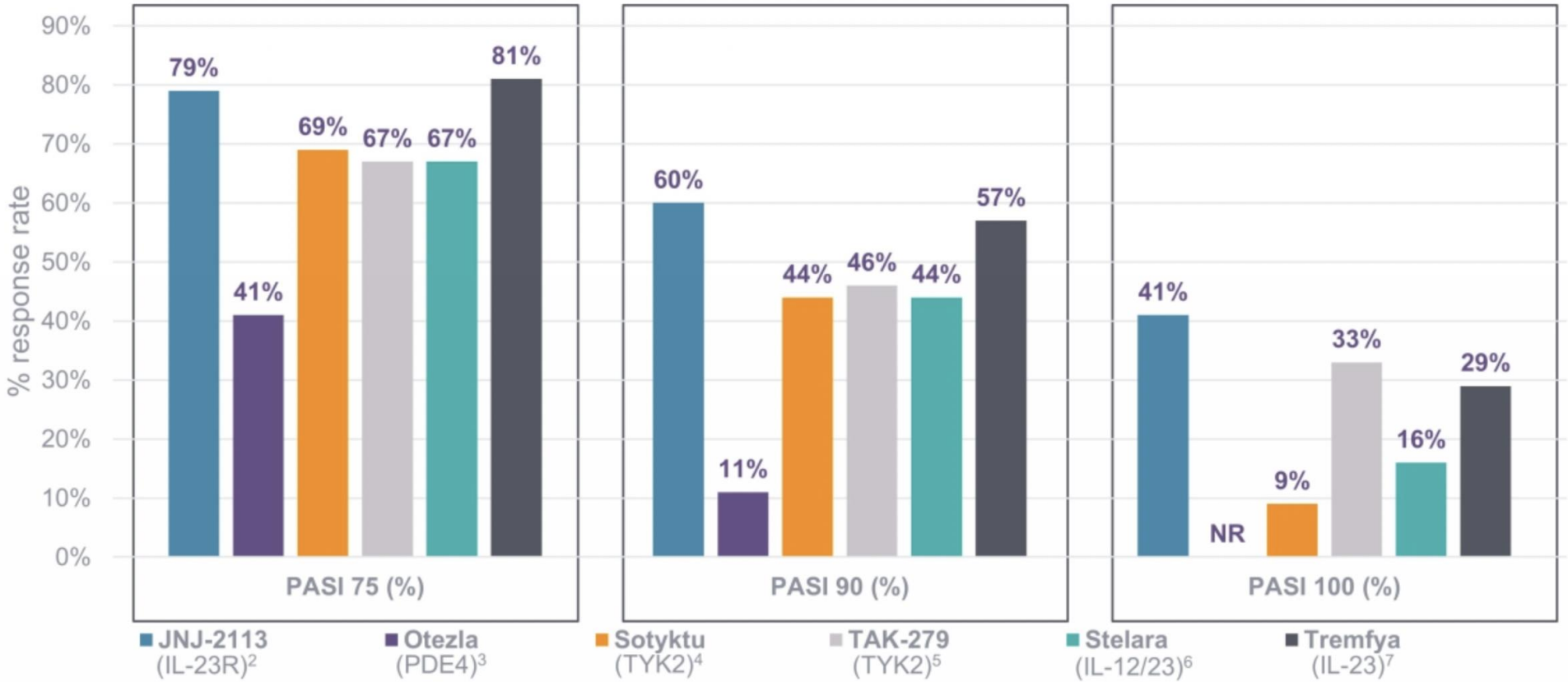
Bissonnette et al. NEJM. 2024;390:510-21

Cross-Study Comparison of JNJ-2113 to Clinically Relevant Phase 2 Benchmarks[1]



1. Cross trial (not head-to-head) comparisons
2. JNJ2113 100 mg bid dose. Wk 16 endpoint (Placebo: PASI 75: 9.3%, PASI 90: 2.3%, PASI 100: 0%)
3. Otezla 30 mg qd approved dose. Week 16 primary endpoint. Papp K et al. Lancet 2012; 380: 738–46. (Placebo: PASI 75: 5.7%, PASI 90: 1.1%, PASI 100: NR)
4. Sotyktu 3 mg bid dose (6 mg qd dose approved). Wk 12 primary endpoint. Papp K et al. N Engl J Med 2018; 379:1313-1321. (Placebo: PASI 75: 7%, PASI 90: 2%, PASI 100: 0%)
5. TAK-279 30 mg qd dose (Expected phase 3 dose). Wk 12 primary endpoint. AAD 2023. (Placebo: PASI 75: 5.8%, PASI 90: 0%, PASI 100: 0%)
6. Stelara 45 mg wkly x 4 (~approved 90 mg week 0 and 2 approved dose). Wk 12 primary endpoint. Krueger et al. N Engl J Med 2007;356:580-92. (Placebo: PASI 75: 2%, PASI 90: 2%, PASI 100: 0%)
7. Tremfya 200 mg wk 0, 4, then q 8 wks (approved dose 100 mg wk 0, 4 then q 8 wks). Wk 16 primary endpoint. Gordon KB et al. N Engl J Med 2015;373:136-44. (Placebo: PASI 75: 5%, PASI 90: 2%, PASI 100: 0%)

Protagonist Therapeutics

Table 3. Adverse Events after Initiation of JNJ-77242113 or Placebo in the Safety Analysis Set.*

Variable	Placebo (N=43)	JNJ-77242113 25 mg Once Daily (N=43)	JNJ-77242113 25 mg Twice Daily (N=41)	JNJ-77242113 50 mg Once Daily (N=43)	JNJ-77242113 100 mg Once Daily (N=43)	JNJ-77242113 100 mg Twice Daily (N=42)	JNJ-77242113 Dose Groups (N=212)
Mean duration of follow-up — wk	15.0	15.7	16.2	15.8	16.1	15.8	15.9
Adverse events — no. (%)†	22 (51)	20 (47)	20 (49)	26 (60)	19 (44)	26 (62)	111 (52)
Infections and infestations	12 (28)	15 (35)	14 (34)	17 (40)	7 (16)	11 (26)	64 (30)
Covid-19	5 (12)	5 (12)	8 (20)	3 (7)	3 (7)	4 (10)	23 (11)
Nasopharyngitis	2 (5)	1 (2)	3 (7)	8 (19)	1 (2)	2 (5)	15 (7)
Upper respiratory tract infection	1 (2)	3 (7)	0	0	0	2 (5)	5 (2)
Gastrointestinal disorders	5 (12)	3 (7)	4 (10)	6 (14)	4 (9)	7 (17)	24 (11)
Diarrhea	1 (2)	2 (5)	2 (5)	4 (9)	1 (2)	1 (2)	10 (5)
Nervous system disorders	1 (2)	0	2 (5)	3 (7)	3 (7)	2 (5)	10 (5)
Headache	1 (2)	0	1 (2)	1 (2)	3 (7)	1 (2)	6 (3)
Respiratory, thoracic, and mediastinal disorders	1 (2)	1 (2)	0	1 (2)	3 (7)	2 (5)	7 (3)
Cough	0	1 (2)	0	1 (2)	3 (7)	1 (2)	6 (3)
Serious adverse events — no. (%)	0	0	0	1 (2)	2 (5)	0	3 (1)
Infections and infestations	0	0	0	1 (2)	1 (2)	0	2 (1)
Covid-19	0	0	0	0	1 (2)	0	1 (<1)
Infected cyst	0	0	0	1 (2)	0	0	1 (<1)
Psychiatric disorders	0	0	0	0	1 (2)	0	1 (<1)
Suicide attempt	0	0	0	0	1 (2)	0	1 (<1)

* The safety analysis set included the same patients as the full analysis set. Covid-19 denotes coronavirus disease 2019.
† Adverse events with an incidence of at least 5% (on the basis of the preferred term) in any trial group through the end of the trial are shown.

- 684 patients (456 to treatment, 228 to PBO)
- Endpoint was PASI 90 and IGA 0/1
- 65% of those in the icotrokinra cohort attained IGA 0/1 compared to only 8% of those given a placebo.
- 50% achieved PASI 90 versus just 4% in the placebo arm (both $P < .001$).
- 33% attaining an IGA score of 0 and 27% a PASI 100 score (1% for PBO)
- 24 weeks: 74% IGA 0/1 and 65% PASI 90
- Similar Aes to placebo, including 6% GI Ses of patients in both cohorts

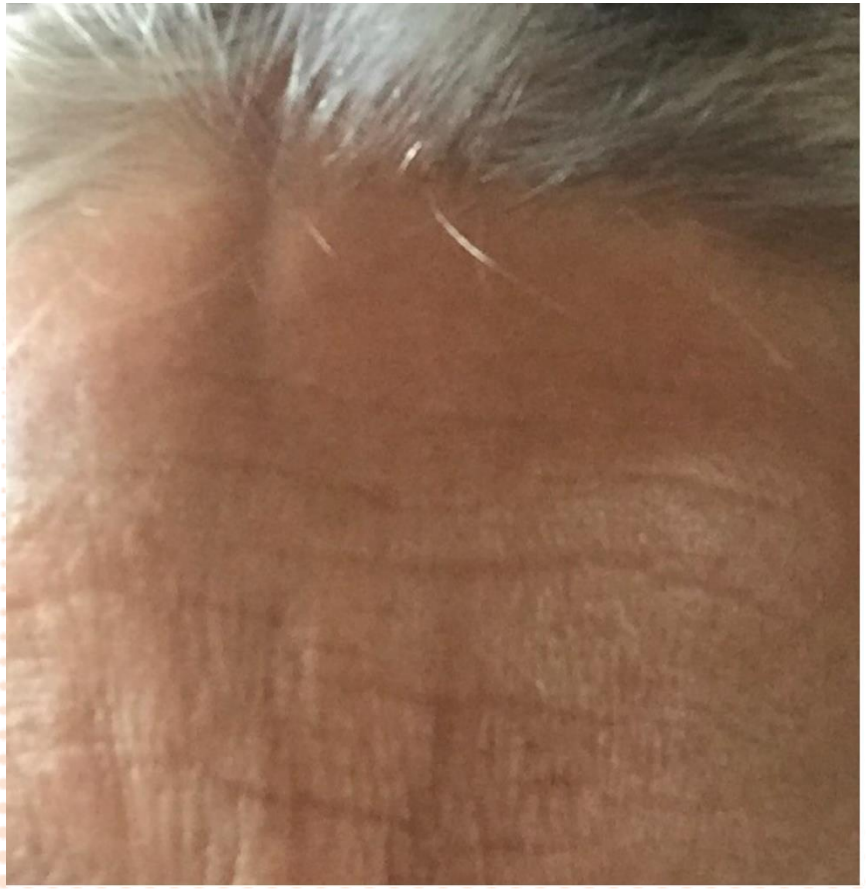
- Healthy 56 yo F with two years of depressed frontal scalp/forehead plaques with pulling and itching sensation

- Biopsy unremarkable, possibly early morphea

- Started methotrexate for presumed linear en coup de sabre morphea at 15 mg weekly

Case History

- 34 yo F presented with 1 week of tender leg and arm lesions
- No recent fevers, chills, infections, new medications, cough/SOB
- Also knee and elbow pain
- Breast lesion as well x 4 mo: painful
    - Recently underwent mammogram which was negative for cancer
    - Bx pending



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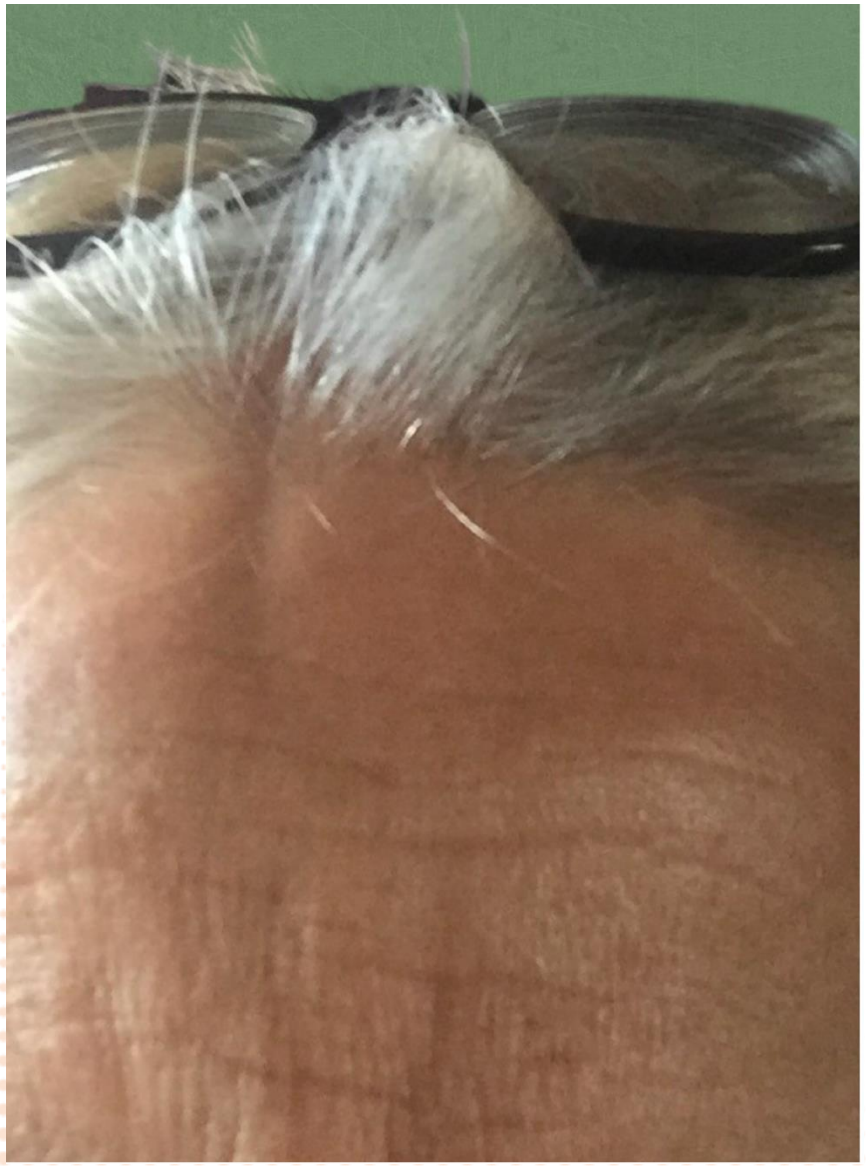


Pressure induced localized lipoatrophy

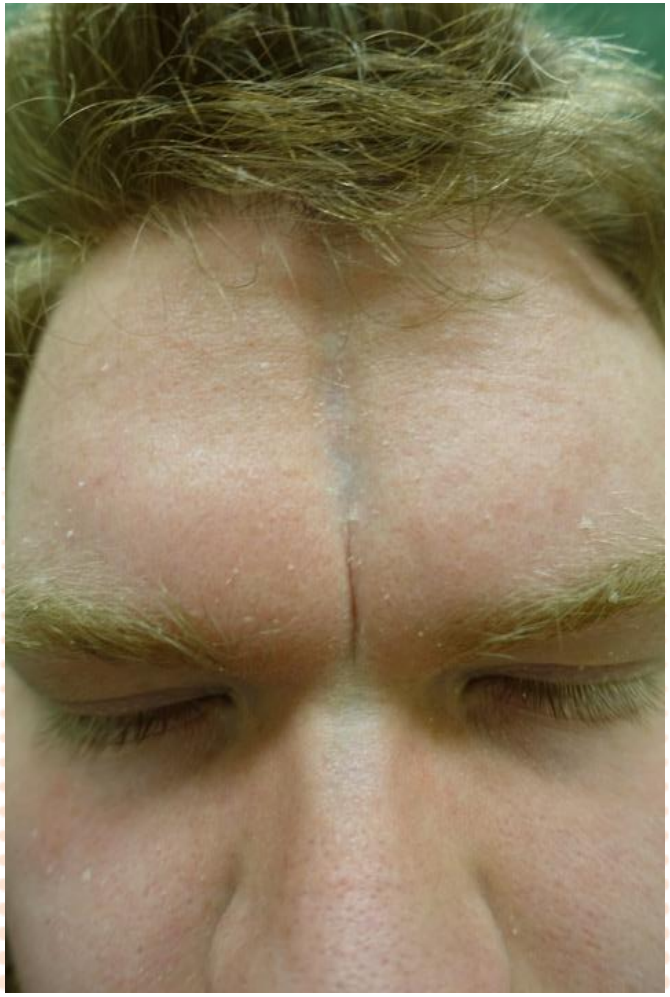
Loss of SQ adipose tissue secondary to repeated microtrauma and reduced perfusion

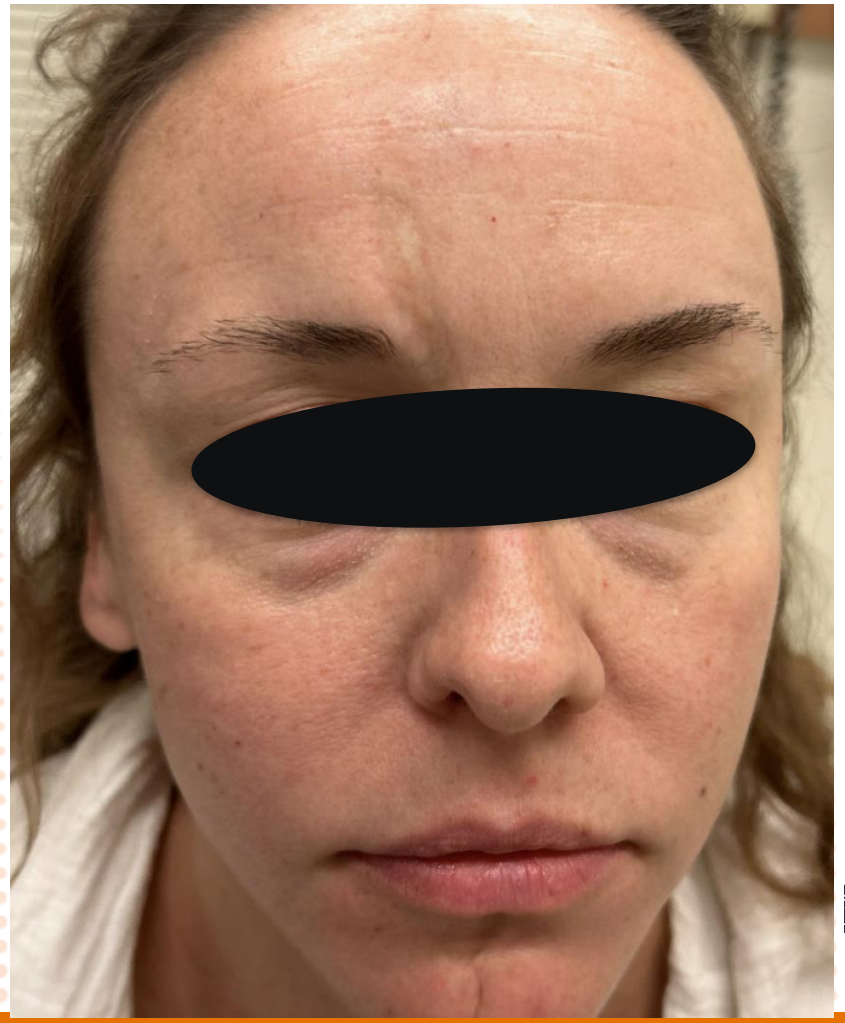
- Localized lipoatrophy
  - Lipoatrophia semilunaris of the thigh
  - Lipoatrophy from elbow compression

- Either rare or underrecognized/underreported

- Biopsy shows normal to complete loss of fat without signs of panniculitis

“En coup de sabre”





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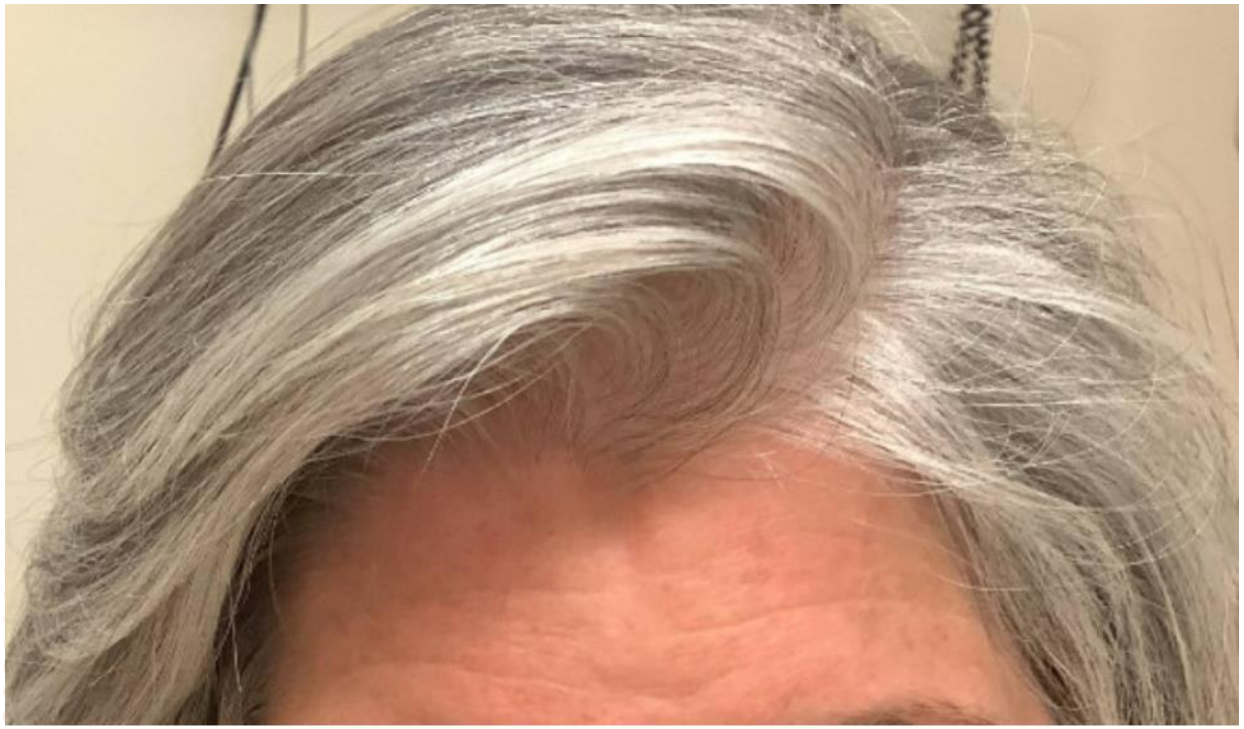
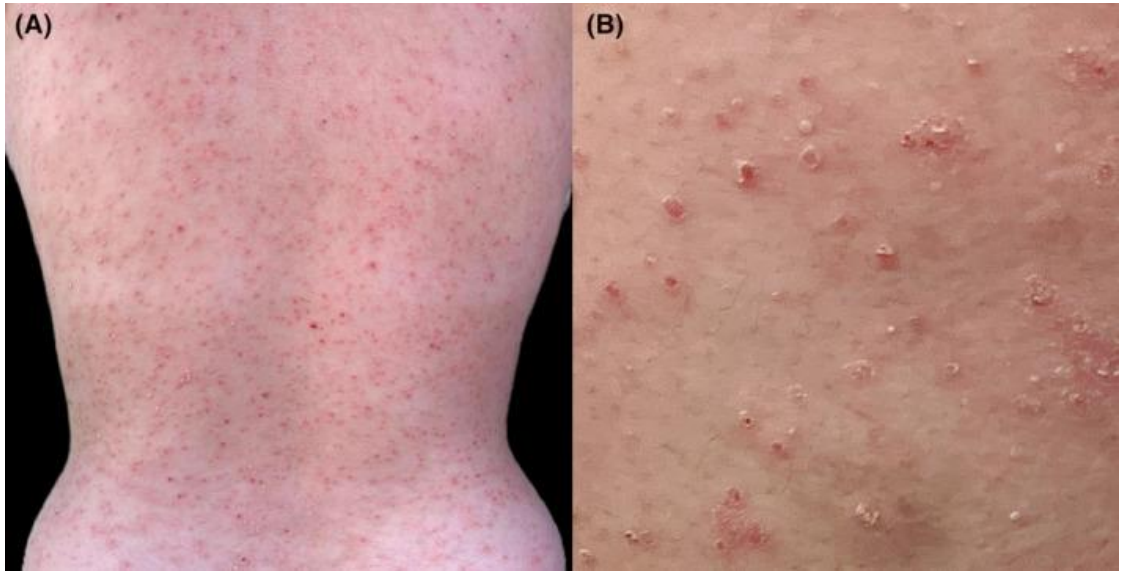
“En coup de lunnettes”



Teaching points

- “Psoraisis punctata” is a morphologic clue for TNF inhibitor induced psoriasis
- ***
- Morphea may arise post radiation; consider HCQ or apremilast in select pt



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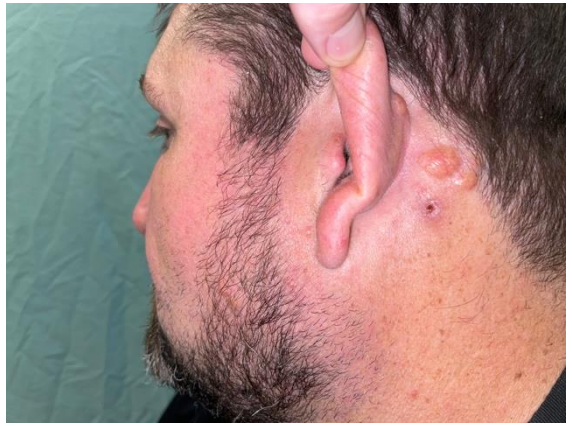
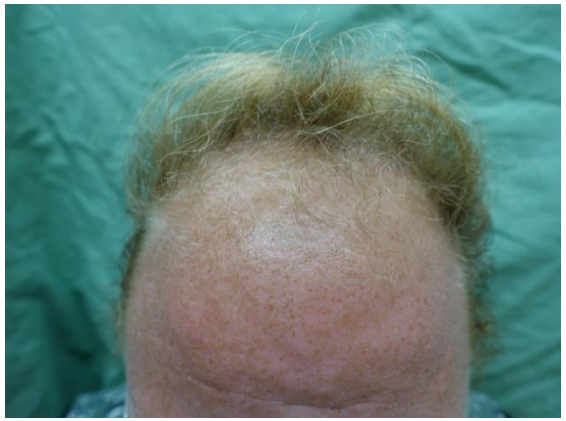
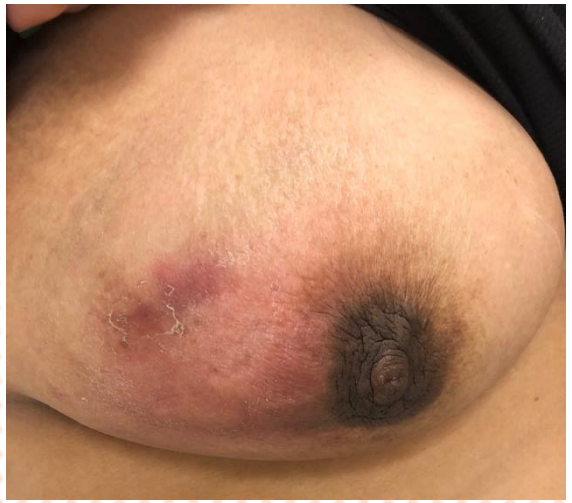
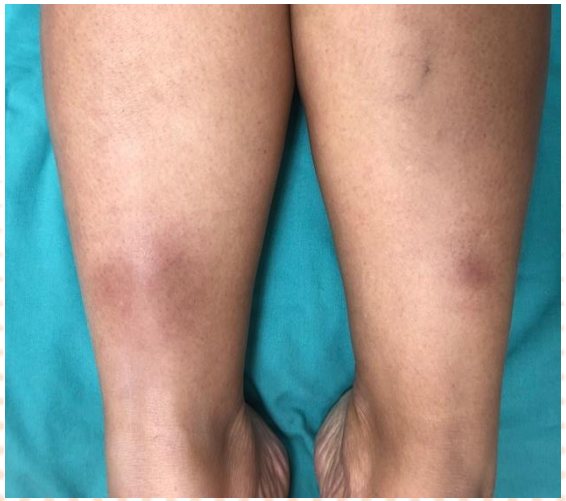
Teaching points

- Nodular amyloid is assoc with Sjogren's and systemic amyloidosis
- Free testosterone is most important test for HMSD; know when to get labs
- Granulomatous mastitis is an inflammatory condition assoc with erythema nodosum (and arthritis)

University of Virginia Health System

The end, thanks!

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