

Una iniciativa de:



ACADEMIA ESPAÑOLA
DE DERMATOLOGÍA
Y VENEREOLOGÍA



FUNDACIÓN
PIEL SANA
ACADEMIA ESPAÑOLA
DE DERMATOLOGÍA
Y VENEREOLOGÍA

Con el patrocinio de:



AEDV 35^a
edición

HIGHLIGHTS

Viena

30sep - 3oct
2026

AEDV 35ª edición

HIGHLIGHTS

Viena
30sep - 3oct
2026

ENFERMEDADES AUTOINMUNES Y MEDICINA INTERNA PARTE I

Daniel Martín Torregrosa
Hospital de Sagunto

Una iniciativa de:



Con el patrocinio de:



AEDV ^{35ª}
edición

HIGHLIGHTS

Viena
30sep - 3oct
2026

**NO TENGO CONFLICTOS
DE INTERÉS**

Una iniciativa de:



Con el patrocinio de:



Completed Phase 3 Trials for Nonsegmental Vitiligo



Ritlecitinib[®]
(JAK3/TEC inhibitor)

Phase 3 Dose

50 mg
Once Daily



Ages
12+ years and adults



Phase 3 Trial Programme:
TRANQUILLO 1 & TRANQUILLO 2

abbvie

Upadacitinib[®]
(JAK1 inhibitor)

Phase 3 Dose

15 mg
Once Daily



Ages
12+ years and adults



Phase 3 Trial Programme:
VITI UP 1 & VITI UP 2



Povorcitinib[®]
(JAK1 inhibitor)

Phase 3 Dose

30 mg
Once Daily



Ages
Adults (18+ years)

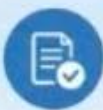


Phase 3 Trial Programme:
STOP-V 1 & STOP-V 2

Doses reflect the doses evaluated in Phase 3 trials for nonsegmental vitiligo.

Upadacitinib-systemic JAK1 inhibitor: 1st approved systemic treatment Upadacitinib in non-segmental vitiligo

EU approved in 2026



European Commission approval

- ✓ RINVOQ® (upadacitinib) 15 mg once daily
- ✓ Approved July 2026
- ✓ Adults and adolescents 12+ years
- ✓ For non-segmental vitiligo in patients who are candidates for systemic therapy
- ✓ First and only systemic medication approved in the EU for NSV

Data shown are topline phase 3 Viti-Up results; EU approval based on the Viti-Up programme.

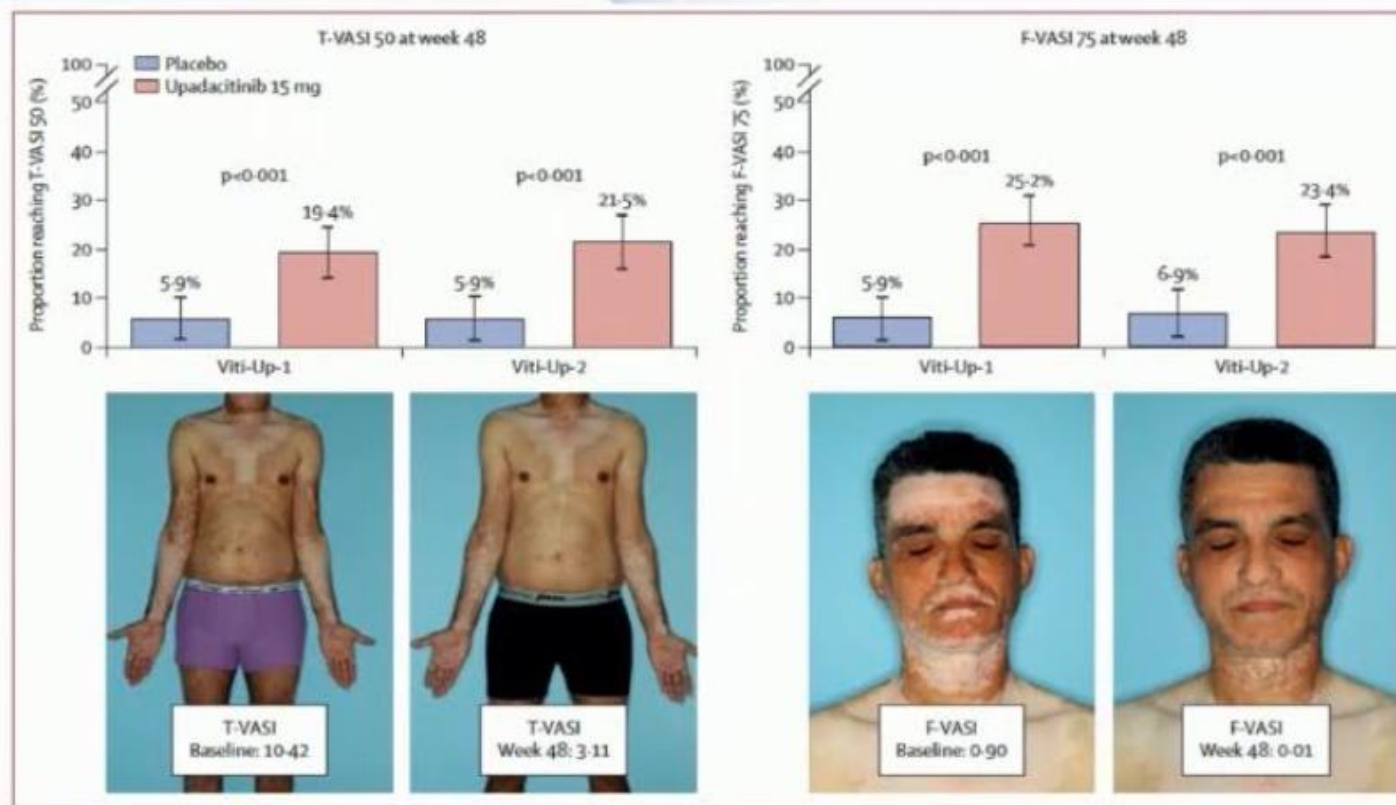
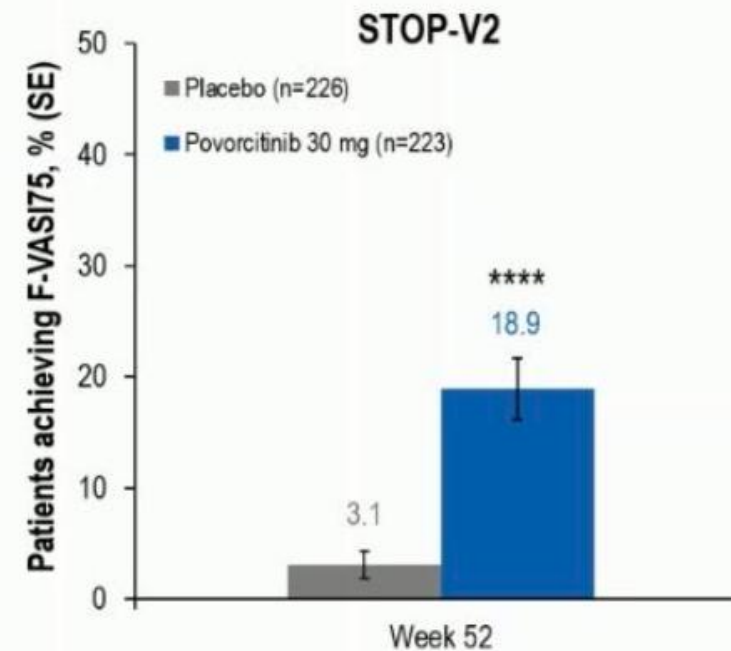
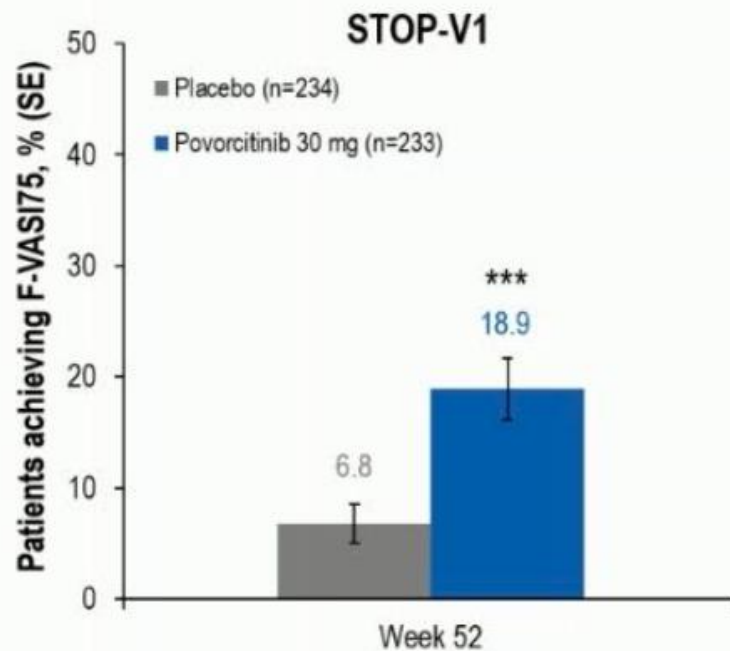


Figure 2: Proportions of patients who reached coprimary endpoints at week 48 and representative clinical images

Non-responder imputation while incorporating multiple imputation was the primary approach to handle missing data; however, as no missing data were observed that could be reasonably assumed to be missing at random, non-responder imputation was used instead. Patients were considered non-responders at visits affected by intercurrent events. F-VASI= Facial Vitiligo Area Scoring Index. T-VASI= Total Vitiligo Area Scoring Index.

Povorcitinib: Primary Endpoint

- Significantly more patients achieved F-VASI75 at Week 52 with Povorcitinib vs placebo in both studies



*** $P < 0.001$ or **** $P < 0.0001$ for povorcitinib vs placebo at Week 52 using the Cochran-Mantel-Haenszel test with stratification for F-VASI (<1.5 and ≥ 1.5), T-VASI (4–20 and >20), and Fitzpatrick skin type (I–II and III–VI). Patients with missing postbaseline values were imputed using modified nonresponder imputation at Week 52.

Povorcitinib: Achievement of T-VASI50

- Significantly more patients achieved T-VASI50 at Week 52 with povorcitinib vs placebo in both studies

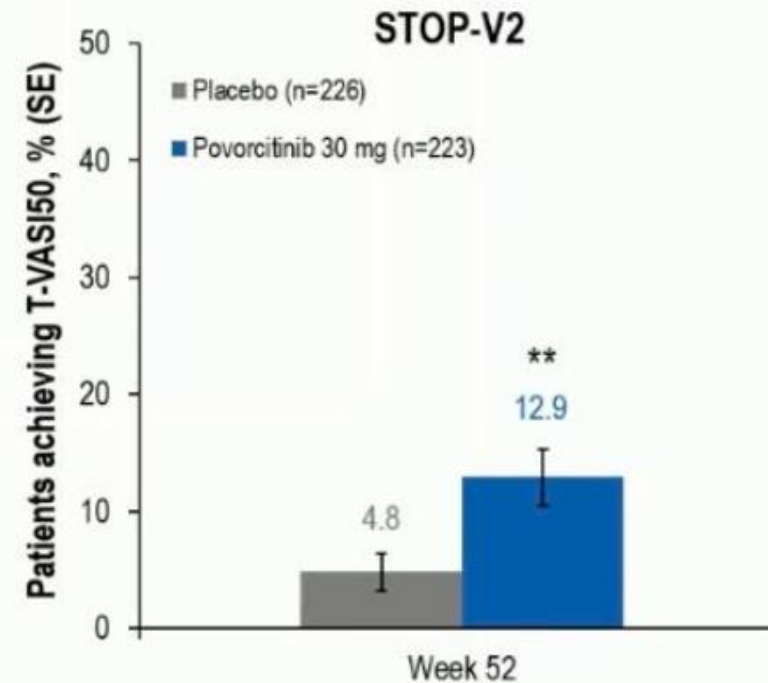
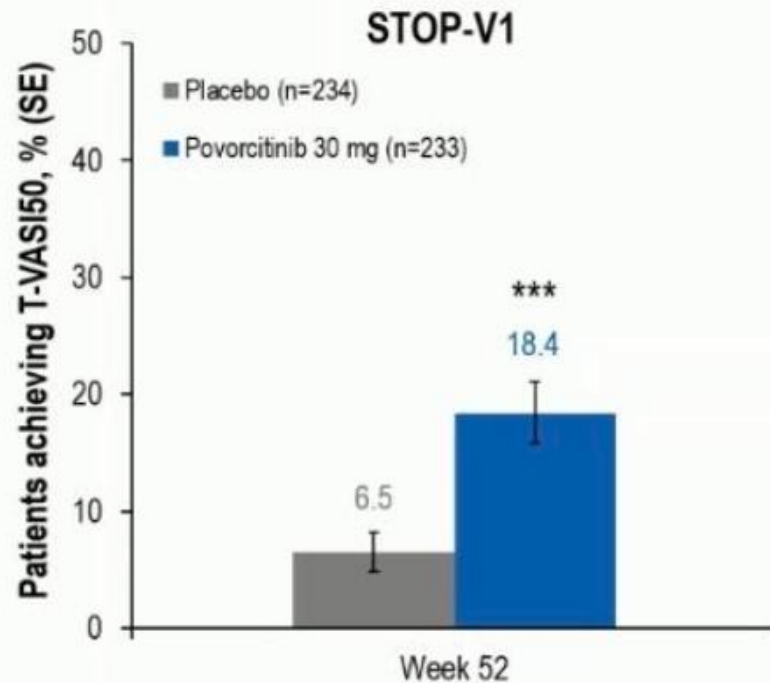
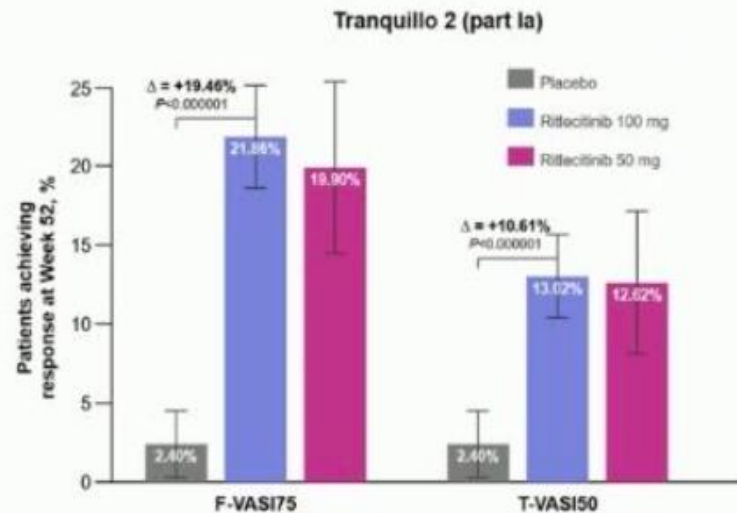
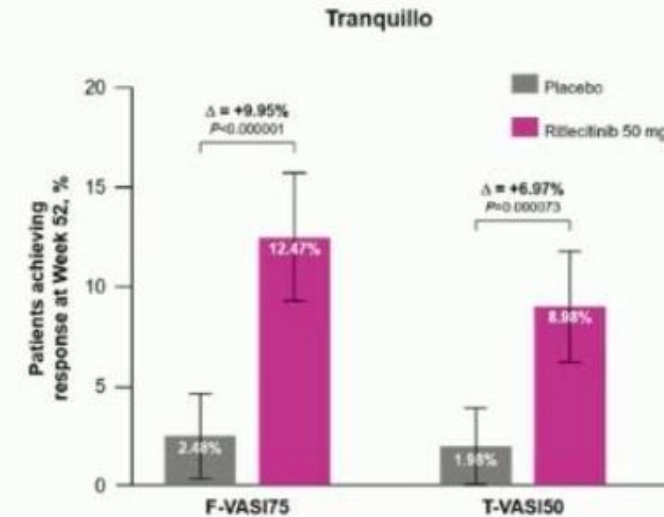


Figure 1. Co-primary endpoints (F-VASI75 & T-VASI50 at Week 52) for the (A) Tranquillo 2 Part Ia and (B) Tranquillo clinical trials

A. Tranquillo 2 Part Ia



B. Tranquillo



In Tranquillo 2 Part Ia, type I error for the ritlecitinib 100-mg group vs placebo was controlled at 2-sided alpha of 0.05; the comparison between ritlecitinib 50-mg dose vs placebo was not alpha controlled.

In Tranquillo, type I error for the ritlecitinib 50-mg group vs placebo was controlled at 2-sided alpha of 0.05.

Non-bullous pemphigoid (NBP)

> 20% of pemphigoid patients

- Underrecognized variant of pemphigoid
- Previously termed prodromal pemphigoid
- Pruritus with or without skin lesions
- Broad clinical spectrum of skin lesions
- Histopathology is not specific
- DIF and IIF microscopy are required
- Increased all-cause mortality risk
- NBP is not a variant with milder prognosis
- Predominantly anti-BP230 abs, **lower titers of anti-BP180**



A subset of patients with severe urticarial forms of BP have **IgE antibodies** against BP230 and BP180 (ELISA testing)

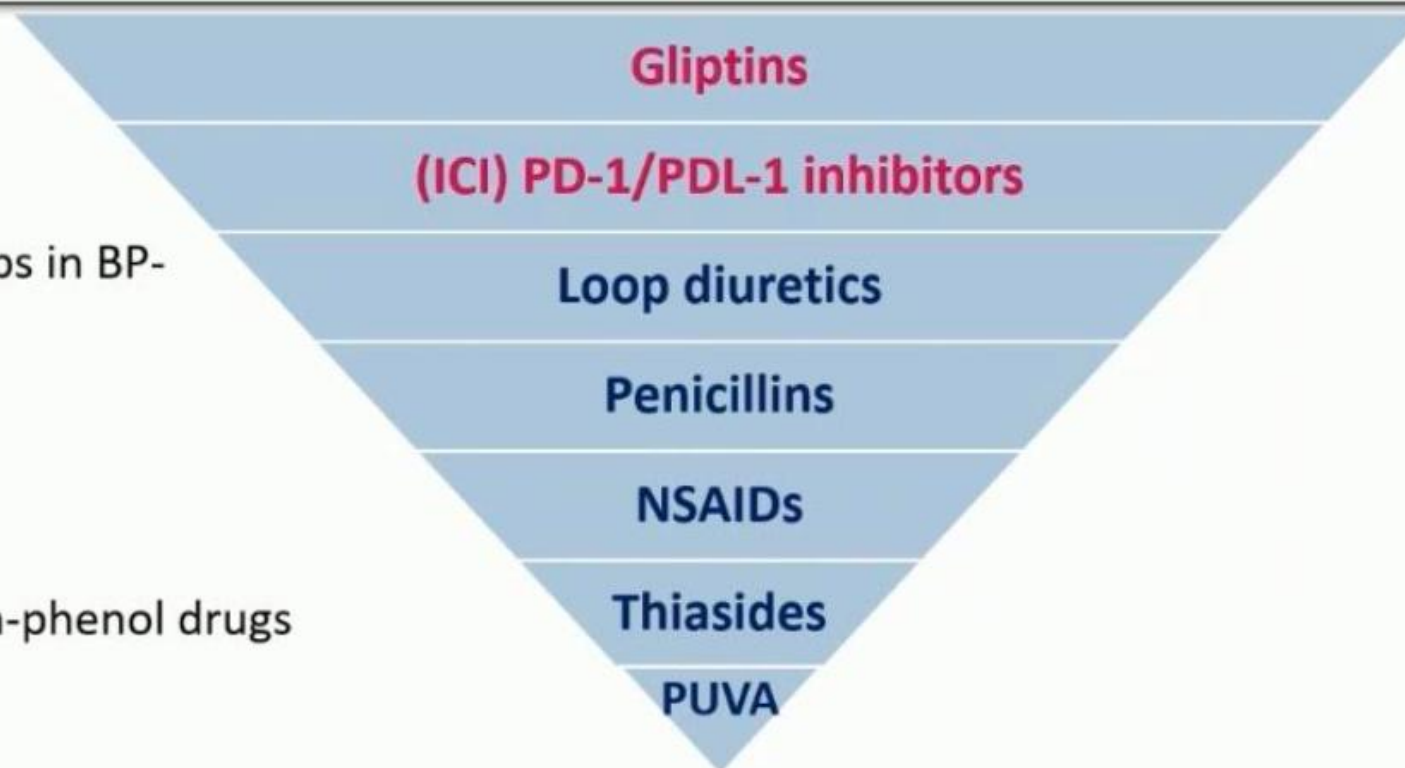
A Systematic Review of Drug-associated Bullous Pemphigoid

Matthew J. VERHEYDEN¹, Asli BILGIC^{2,3} and Dédée F. MURRELL^{2,4}

¹School of Medicine, University of Notre Dame, ²St George Hospital, Department of Dermatology, Sydney, Australia, ³Antalya Research and Training Hospital, Antalya, Turkey and ⁴Faculty of Medicine, University of New South Wales, Sydney, Australia

Functional groups in BP-inducing drugs:

- Thiol-drugs
- Phenol-drugs
- Non-thiol non-phenol drugs



Drugs Reported to Induce Bullous Pemphigoid

Dipeptidyl Peptidase-4 Inhibitors (DPP4i / “gliptins”) Induced Bullous Pemphigoid

DPP4i exposure - a 3.2-fold higher risk for BP

- **Vildagliptin x 10-fold**
- **Linagliptin x 6-fold**
- Sildagliptin non-significant association

Latency period ranging from a few months to several years (median > 1 year)

Favourable response to treatment

Younger patients

Patients have **fewer comorbidities**

Non-inflammatory phenotype

Extensive blistering – **higher BPDAI score**

Higher mucosal involvement

↓ blood and tissue eosinophilia

Autoantibodies:

- ✓ non-inflammatory DPP4i-BP - **full-length BP180 Abs**
- ✓ inflammatory DPP4i-BP - **BP180 NC16A Abs**
- ✓ **mucosal** involvement – **anti-BP180 C-terminus**

Immune Checkpoint Inhibitors (ICI) Associated BP

Both bullous and non-bullous phenotypes can be observed

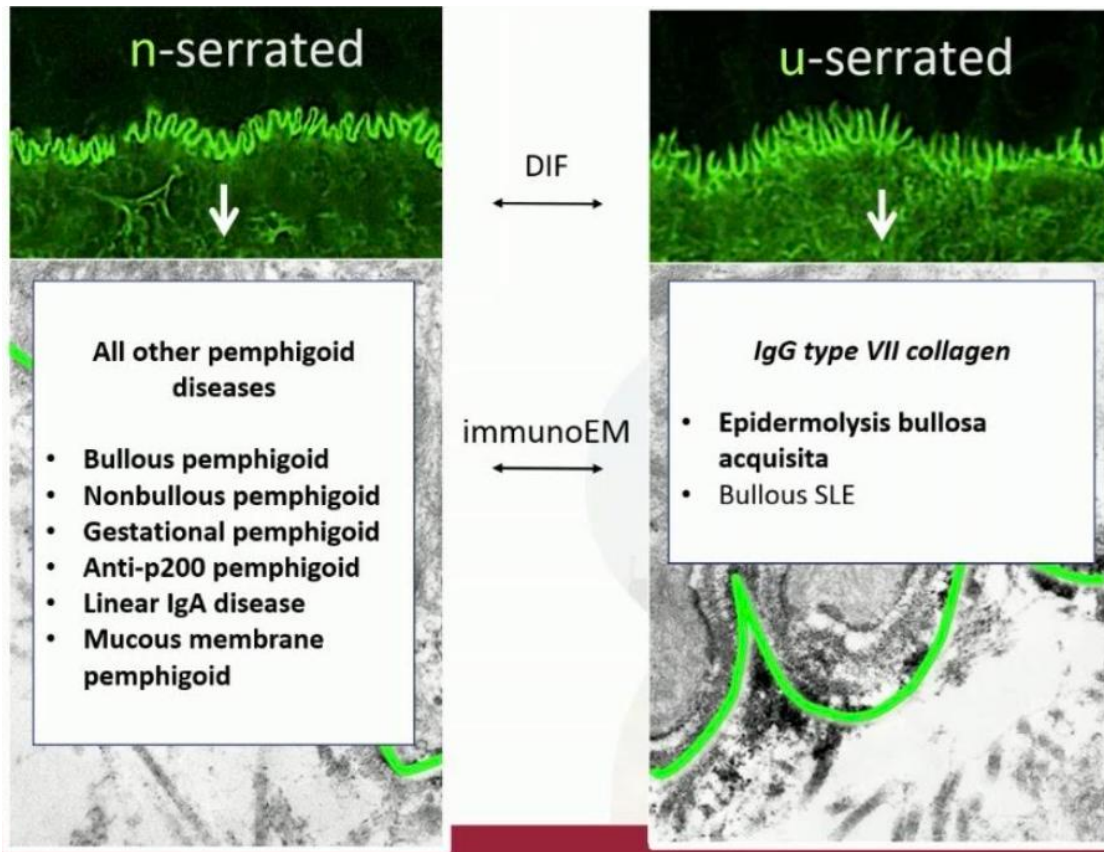
- ~ 0.3% to 1% of patients treated with ICI
- ~ 6-12 months post-treatment initiation (also after completion)
- Protracted prodromal pruritus
- Heterogeneous clinical phenotypes – bullous, nonbullous, nodular-erosive
- More frequent mucosal involvement
- Anti-**BP180 C-terminal epitope**
- **Higher BP180** and lower anti-BP230 Ab titers

A 72-y-o man with MM on pembrolizumab and BP



Dermatology Dept, Alexandrovskia Univ. Hospital





Serration pattern analysis: EADV MAXISPA study

MAXISPA conclusions

- **Multicenter validation:** MAXISPA validated DIF serration pattern analysis across European centers in routine diagnostics
- When you can see an n- or u-serrated pattern: **high agreement ($\kappa = 0.96$)**
- **No misclassification from n-serrated to u-serrated** in validation

Efficacy of Dupilumab in Bullous Pemphigoid

Evidence Synthesis

Phase 2/3 ADEPT Trial

Sustained remission: significant response vs. placebo at 36 weeks
18.2% vs. 4.0%

Rapid pruritus relief:
38.3% vs 10.5%

Steroid sparing: reduced total cumulative oral CS use
5.1 vs 4.1 g

Meta-Analyses

Disease control rate 95%
(95% CI: 92%-98%) across systematic reviews

Complete Response:
68% pooled CR rate;
63% as monotherapy

Favorable safety profile

Real-World Evidence

Rapid control:
53.4% complete remission within 4 weeks

Sustained response
with 95.7% CR at week 52

Steroid reduction:
82.1% reduced systemic CS use

- <https://clinicaltrials.gov/study/NCT04206553?tab=results>
- da Silva JON, et al. *An Bras Dermatol.* 2025;100:429
- Planella-Fontanillas N, et al. *Br J Dermatol.* 2025;192:501

- Zhao L, et al. *JAMA Dermatol.* 2023;159:953.
- Chen Y, et al. *Front Immunol.* 2026;17:1651543
- Abdat R. et al. *J Am Acad Dermatol.* 2020;83:46

Desmoglein Compensation Hypothesis in Pemphigus: A Bicentric Clinicopathological Evaluation

106 patients (93 PV · 13 PF) · PGIMER Chandigarh, India & University of Lübeck, Germany · Retrospective bicentric study

Clinical subtype	DCH prediction	Serology concordance	Histology concordance
PF n = 13 <i>Cutaneous only</i>	Anti-Dsg1 IgG only → Subcorneal split	62% 8/13 Dsg1 only	46% 6/13 subcorneal split
PV mucosal n = 16 <i>Mucosal only</i>	Anti-Dsg3 IgG only → Suprabasal split	37% 6/16 Dsg3 only	100% 16/16 suprabasal split
PV mucocutaneous n = 75 <i>Skin + mucosa</i>	Anti-Dsg1+Dsg3 IgG → Dual split	75% 56/75 Dsg1+Dsg3	9% 7/75 dual split
PV cutaneous n = 2 <i>Skin only</i>	Contradicts DCH <i>Cutaneous-only PV has no classical DCH-predicted phenotype</i>	Observed serology Anti-Dsg1+Dsg3 IgG both patients (2/2)	Observed histology Suprabasal split both patients (2/2)

Histopathological split pattern according to serological profile

Dsg1 only → Subcorneal split 33% 3 / 9	Dsg3 only → Suprabasal split 75% 15/20	Dsg1+Dsg3 → Dual split 9% 6/69
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Concordance: ● High ≥75% ● Partial 50–74% ● Low <50%

Pemphigus foliaceus and psoriasis

An emerging, mechanistically linked association

Rx Clinical association

- **Rare but increasingly reported comorbidity;** most cases are pemphigus foliaceus, arising on a background of pre-existing, often long-standing, chronic plaque psoriasis
- First population-based, large-scale study confirmed a statistically significant association between pemphigus and psoriasis
- **Phototherapy (PUVA/NBUVB) and other psoriasis therapies** have been reported as possible precipitants of pemphigus onset

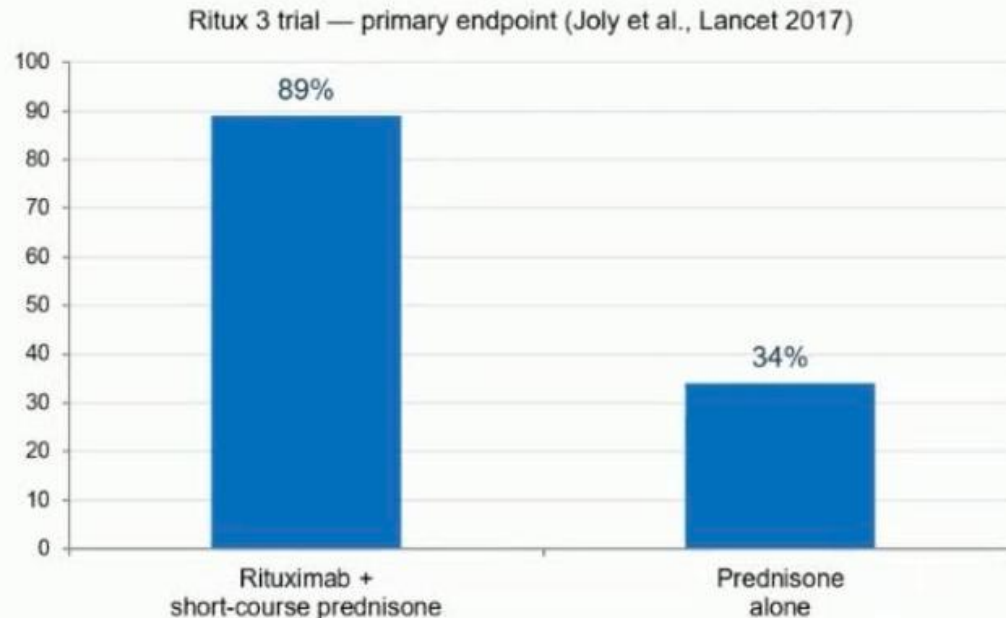
DNA Shared pathogenesis pathways

- **Epitope spreading** — chronic psoriatic keratinocyte damage/inflammation exposes cryptic desmoglein-1 epitopes, triggering secondary anti-Dsg1 autoantibody formation
- **Shared HLA class II susceptibility** — overlapping DRB1/DQB1 haplotypes implicated in both psoriasis and pemphigus, suggesting a common genetic predisposition
- **Th17 / IL-17 axis** — the central driver of psoriasis; IL-17-expressing cells are also elevated in pemphigus foliaceus lesional skin, pointing to a shared inflammatory circuit
- **Phototherapy-induced antigen exposure** — UVB/PUVA alters keratinocyte surface antigens, facilitating autoantibody–Dsg1 interaction

Kridin K, Zelber-Sagi S, Comaneshter D, Cohen AD. Association between pemphigus and psoriasis: a population-based large-scale study. J Am Acad Dermatol. 2017;77(6):1174–1175.

MANAGEMENT

Rituximab: First-line therapy for moderate–severe disease



Joly P, et al. First-line rituximab combined with short-term prednisone versus prednisone alone for the treatment of pemphigus (Ritux 3): a prospective, multicentre, parallel-group, open-label randomised trial. Lancet. 2017 May 20;389(10083):2031-2040.

Tedbirt B, et al. Sustained Remission Without Corticosteroids Among Patients With Pemphigus Who Had Rituximab as First-Line Therapy: Follow-Up of the Ritux 3 Trial. JAMA Dermatol. 2024 Mar 1;160(3):290-296.

- Rituximab (anti-CD20) depletes CD20+ B lymphocytes, removing the source of pathogenic autoantibody production
- Ritux 3: 90 patients with newly-diagnosed pemphigus, randomised to rituximab + short prednisone vs prednisone alone
- 7-year follow-up confirmed durable benefit: 93.5% vs 38.6% remained in corticosteroid-free complete remission

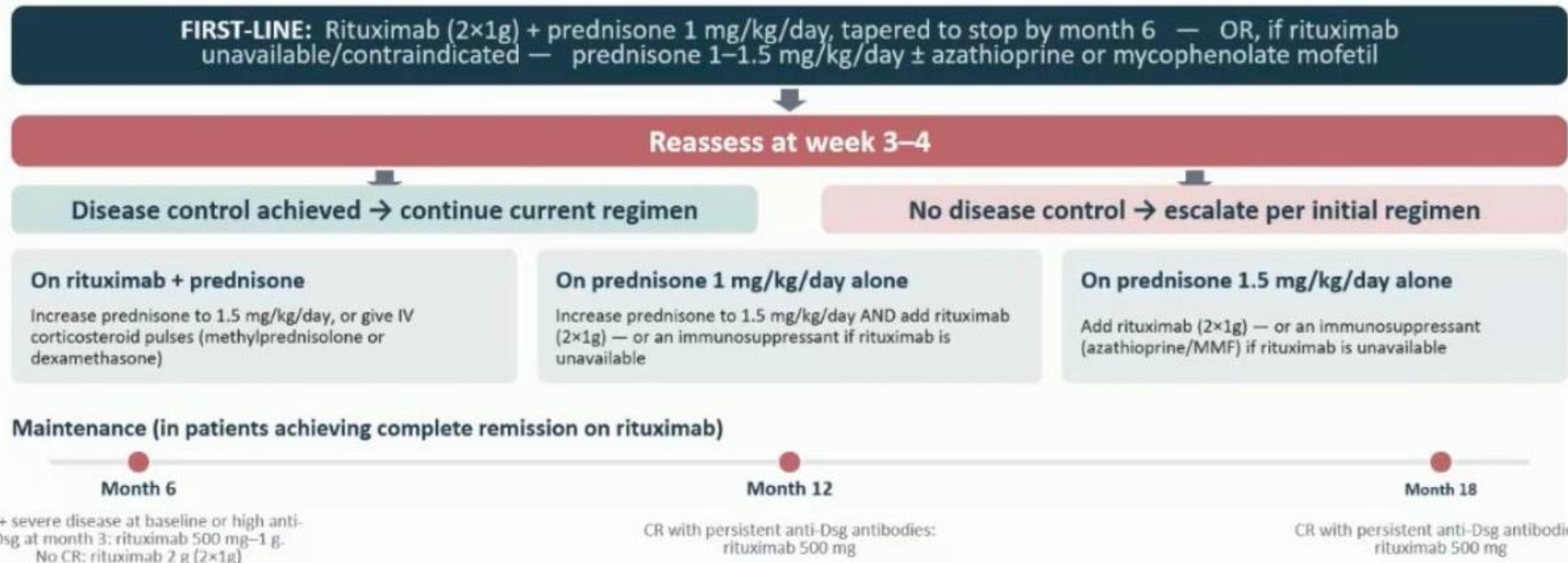
MANAGEMENT

Rituximab dosing protocols in pemphigus

Protocol	Regimen	Origin / Evidence
Lymphoma protocol	375 mg/m ² IV weekly × 4 doses	Adapted from oncology dosing; early pemphigus case series
Rheumatoid-arthritis (RA) protocol	1000 mg IV × 2, 2 weeks apart	Most widely used fixed-dose regimen internationally
Ritux 3 protocol	1000 mg D1 and D15, plus 500 mg maintenance at months 12 & 18	First-line RCT evidence (Joly et al., Lancet 2017)
Low-dose protocol	500 mg IV × 2, 2 weeks apart	Meta- analysis (Wang et al.) — comparable efficacy, lower cost, at the cost of shorter remission
Immunologically-guided ultra-low-dose	500 mg × 2 (induction) + 200 mg top-up only if CD19+ B cells repopulate	Prevent clinical relapse, cost effective compared to standard dose RA protocol with fixed time-point maintenance
Ultra-low-dose protocols		

MANAGEMENT · EADV S2K GUIDELINE

Treatment algorithm — moderate-to-severe PV / PF



MANAGEMENT · EADV S2K GUIDELINE

Treatment algorithm — mild pemphigus vulgaris

Mild pemphigus vulgaris — BSA < 5% + limited oral lesions not impairing food intake · PDAI ≤ 15

FIRST-LINE THERAPY

- Prednisone 0.5–1 mg/kg/day, with or without azathioprine (2 mg/kg/d) or mycophenolate mofetil (2 g/day)
- OR rituximab — two infusions of 1 g, two weeks apart — alone or with prednisone 0.5 mg/kg/day, tapered to stop by month 3–4

Started on corticosteroids alone — lesions persist

Second-line: add rituximab (2×1g); taper prednisone rapidly to stop by month 3–4

Started on corticosteroids + rituximab — lesions persist

Increase prednisone dose up to 1 mg/kg/day

Disease control achieved at any stage: continue the chosen regimen, tapering to stop corticosteroids by month 3–4 (faster if rituximab was used)

MANAGEMENT · EADV S2K GUIDELINE

Treatment algorithm — mild pemphigus foliaceus

Mild pemphigus foliaceus — BSA < 5% · PDAI ≤ 15

First-line therapy (any one option)

- Dapsone 50–100 mg/day (up to 1.5 mg/kg) combined with a topical corticosteroid
- Topical corticosteroid alone, for very limited lesions
- Prednisone 0.5–1 mg/kg/day
- Rituximab — two infusions of 1 g, two weeks apart — alone or with topical/oral corticosteroid

Disease control achieved

Continue the chosen therapy; taper to stop corticosteroids by month 3–4

Disease control NOT achieved

SECOND-LINE: add rituximab (2×1g) ± low-dose prednisone — or, if rituximab unavailable/contraindicated, prednisone 0.5–1 mg/kg/day ± azathioprine or mycophenolate mofetil

MANAGEMENT

Recognising and managing relapse

- Relapse: ≥ 3 new lesions in a month that fail to heal within a week, or extension of existing lesions, after remission was achieved
- Recent onset pruritus, if can not be explained by another cause, can precede clinical relapse
- Rising anti-Dsg3/Dsg1 ELISA titres or CD19+ B-cell repopulation, or a negative DIF becoming positive; all of these when serially monitored, often precede clinical relapse
- Re-treatment strategy should be individualised: repeat rituximab, prednisolone re-initiation or dose escalation
- 500 mg single infusion of rituximab upon mild-to-moderate relapse can re-induce remission (yet unpublished data)

De D, et al. Differences among Indian and European pemphigus patients based on demographics, clinical parameters and propensity for relapse: results of a prospective bicontinental cohort study. *Eur J Dermatol*. 2023 Dec 1;33(6):642-647.

De D, et al. Antidesmoglein 1 and 3 serum IgG and positivity by direct immunofluorescence microscopy is associated with relapse in pemphigus in a prospective bicontinental study. *JAAD Int*. 2025 Jan 20;19:67-74.

MANAGEMENT

Biomarker-guided retreatment: A cost-conscious model



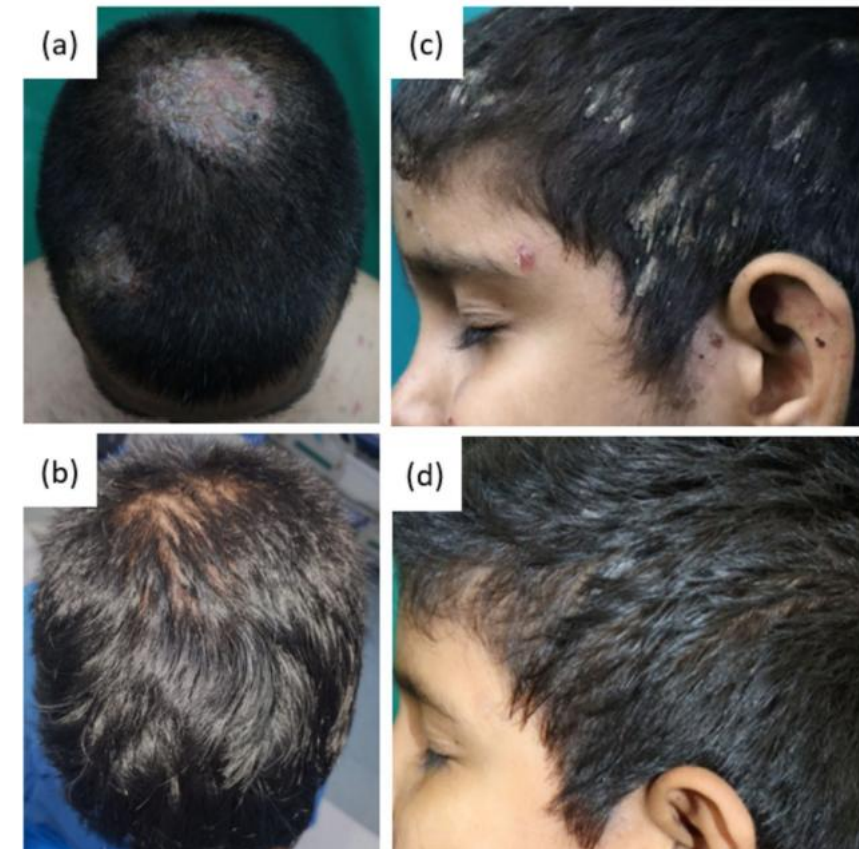
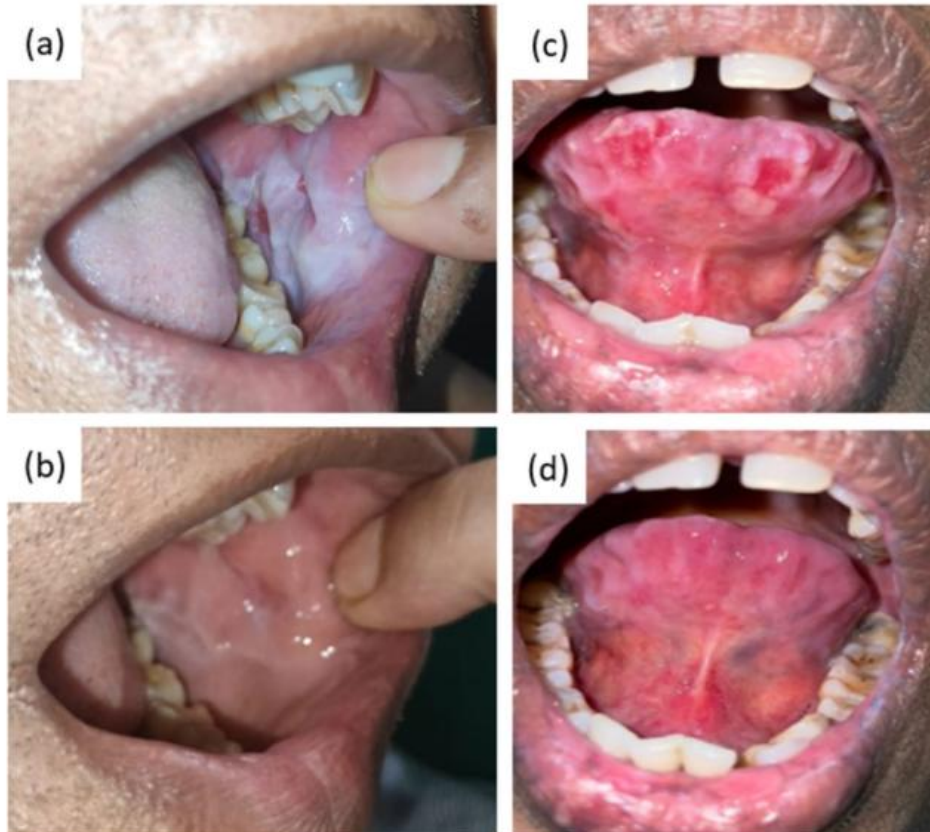
Why this may matter globally

- Removes fixed-timepoint maintenance dosing, cutting cumulative rituximab exposure and cost
- Particularly valuable where drug cost or infusion capacity is limited — but the logic applies to any health system seeking value-based care
- Access to flow-cytometry may be a limiting factor

Singh N, Handa S, Mahajan R, Sachdeva N, De D. Comparison of the efficacy and cost-effectiveness of an immunologically targeted low-dose rituximab protocol with the conventional rheumatoid arthritis protocol in severe pemphigus. Clin Exp Dermatol. 2022 Aug;47(8):1508-1516.

Intralesional Rituximab in Recalcitrant Oral and Scalp Lesions of Pemphigus: A Retrospective Study

Vishalakshi Viswanath  | Isha Kiran Kane  | Nupur Mukesh Sanklecha  | Pradnya Rushikesh Joshi 



Received: 6 October 2023

Accepted: 19 January 2024

DOI: 10.1111/jdv.19880

GUIDELINES



S2k guidelines on diagnosis and treatment of linear IgA dermatosis initiated by the European Academy of Dermatology and Venereology

Pharmacological treatments

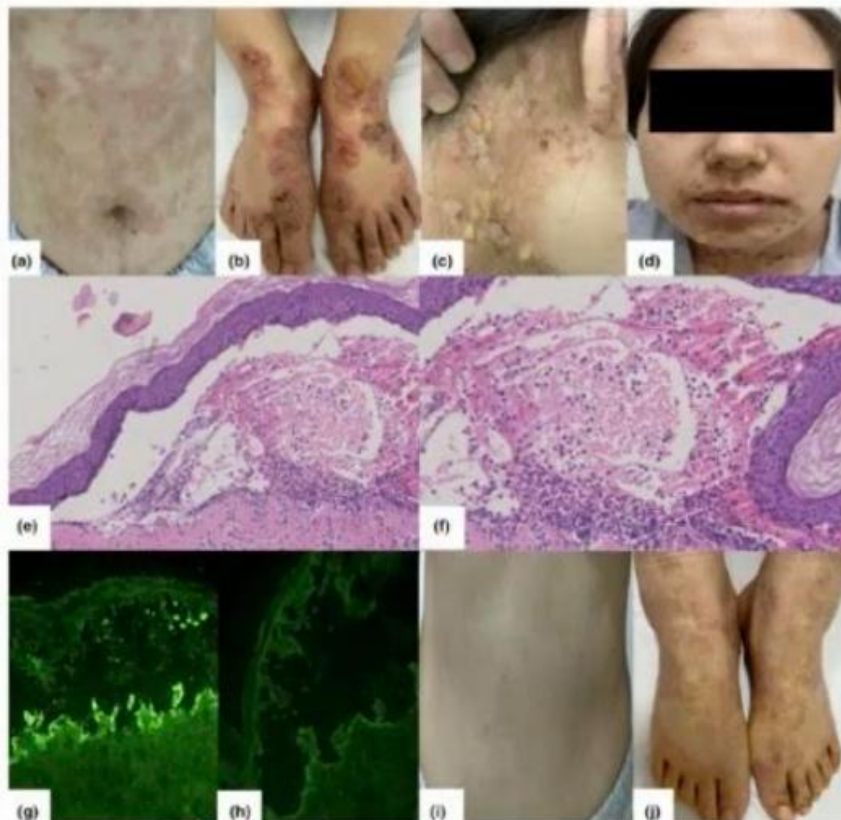
J Eur Acad Dermatol Venereol. 2024;38:1006–1023.

First line	Dapsone +/- topical corticosteroids			Third line	Sulfamethoxypyridazine*		
Second line	Sulfapyridine				Mycophenolates*		
	Sulfasalazine				Azathioprine*		
	Systemic corticosteroids*				IV immunoglobulins		
	Erythromycin		↑		Ciclosporin		
	Colchicine		↑↑		Methotrexate		
	Dicloxacillin		↑↑		Infliximab		↑↑
	Flucoxacillin		↑↑		Etanercept		↑↑
	Trimethoprim-sulfamethoxazole		↑↑		Rituximab		
	Tetracycline and niacinamide		↑↑		Omalizumab		↑
					Cyclophosphamide**		↑

- **Dupilumab:** series de casos exitosas tanto en adultos como en niños. Particularmente efectivo para reducir el prurito grave.
- **Omalizumab:** casos exitosos donde los pacientes mostraban altos niveles de IgE o eosinofilia.
- **Rituximab:** usado en casos refractarios. Puede inducir remisión cuando otras terapias de primera línea fallan. Múltiples cursos de tratamiento pueden ser requeridos.
- **Anticuerpos monoclonales anti-CD89.** Bloquean el receptor FcαRI (CD89) en los neutrófilos. **JJP-1212** se encuentra en desarrollo clínico.

Treatment of refractory, inflammatory epidermolysis bullosa acquisita with a combination of dupilumab and systemic glucocorticoid

J Dermatol. 2025;52:e308-e310.



After admission, she was treated with systemic prednisolone (1 mg/kg/day) for 9 days and intravenous immunoglobulin (IVIG) (0.4 g/kg/day for 5 days), with still more than 10 new vesicles observed daily. She declined immunosuppressants like cyclosporine because of concern about side effects. Afterwards, she was prescribed with dupilumab. Disease control (no new inflammatory lesions or bullae), complete healing of skin and mucous membrane were obtained in 3, 8, and 10 weeks respectively.

Recalcitrant epidermolysis bullosa acquisita treated with upadacitinib as a bridge to rituximab



JAAD Case Reports 2025;63:34-7.

Taha Rasul, MD, Anthony Concilla, DO, Michelle Militello, DO, Paola Torres, MD, and Angelia Stepien, DO



Fig 1. Initial presentation of extensive tense bullae, erosions, and crusting predominantly affecting the breasts (A) and extremities (B), consistent with mechanobullous EBA. EBA4, Epidermolysis bullosa acquisita.



Fig 2. A and B, Marked improvement of skin lesions following initiation of upadacitinib and subsequent rituximab therapy, with resolution of erosions. Postinflammatory hyperpigmentation and milia at sites of scarring can be seen.

CHARACTERISTICS OF EBA

Upadacitinib effectively bridged therapy to rituximab, providing rapid disease stabilization while awaiting rituximab's therapeutic effects. Oral JAKi may offer therapeutic benefits in EBA by targeting key inflammatory pathways with comparable monitoring compared to other immunomodulatory medications.⁸ By inhibiting cytokines such as interleukin-6, interferon-gamma, and granulocyte-macrophage colony-stimulating factor, JAKi can reduce neutrophil activation, autoantibody-driven inflammation, and tissue damage.⁶ JAKi may suppress B-cell activity, modulate Th1/Th17-mediated immune responses, and promote wound healing, highlighting the potential role of JAKi in managing refractory autoimmune blistering diseases, offering a promising avenue for patients with limited therapeutic options.^{9,10}

DERMOSCOPY: ACRAL PETECHIAE/PURPURA

- It may be clinically inconspicuous to the naked eye but rather frequent (~80%)
- Routine acral dermoscopy can increase suspicion in atypical DH

**Acral Purpura as Leading Clinical Manifestation of Dermatitis Herpetiformis: Report of Two Adult Cases with a Review of the Literature**

Honggang Tu^{a,c} Laurent Parmentier^b Marco Stieger^c Zoe Spanou^c Michael Horn^d
Helmut Beltraminelli^c Luca Borradori^c

^aShanghai Skin Disease Hospital, Shanghai, China; ^bUnit of Dermatology, Hôpital de Sierre, Sierre,
^cDepartment of Dermatology and ^dInstitute of Immunology, Inselspital – University Hospital of Bern, Bern, Switzerland



Limited gluten-free options

Gluten cross-contamination is common



<20 ppm

A person eating a typical “gluten-free” diet will consume between 6 and 10 mg of gluten per day

Medications (prescription or OTC) are not generally included in the FDA gluten-free labeling regulation

“...less than **1 ppm** level of gluten in foods is the level of exposure for individuals with CD on a GFD that protects the most sensitive individuals with CD and thus, also protects the most number of individuals with CD from experiencing any detrimental health effects from extended to long-term exposure to gluten”



GLUTEN TESTER for food, beverages, medications...

- Portable
- Sensitive (< **1 ppm**?, 0.01 ppm?)
- Cheap (< **\$1** ?)
- Fast (< **1 min** ?)
- Easy to use
- Limited available options
- Expensive
- Only one is portable and easy to use but it is expensive and not sensitive enough (20 ppm)



Pemphigoid Gestationis

First-Line & Escalation Therapy

Mild Disease

Topical high-potency corticosteroids plus oral antihistamines control pruritus and limit new blister formation

Treatment Success

No new blisters within 2 weeks — clinicians should then taper the corticosteroid dose

Moderate - Severe Disease (>10% BSA)

Oral prednisone/prednisolone 0.5 mg/kg/day

A total daily dose up to 20 mg is preferred

Nonresponsive Cases

Immunosuppressants (cyclosporine, dapsone, azathioprine) may be considered, watching for bone marrow suppression, preterm birth, or liver impairment

Pemphigoid Gestationis

Treatment options in refractory / relapsing cases

- **IVIG** is used alone or with other agents in refractory cases and has a better safety profile than classic immunosuppressants.
- **Dupilumab** (anti-IL-4Ra monoclonal antibody) has been used for refractory, corticosteroid-dependent disease, producing rapid remission and steroid weaning
- **Rituximab**, given preconceptually, has reportedly prevented recurrent PG; patients should avoid pregnancy for 12 months after the last infusion

Dupilumab as a novel steroid-sparing treatment for pemphigoid gestationis: A new case report and review of literature

Celine H. Phong, MD, Bonnie A. Lee, MD, and Sergei A. Grando, MD, PhD, DSc

JAAD CASE REPORTS
JUNE 2025



Fig 1. A, Before treatment with prednisone or dupilumab. Annular, coalescing dusky red papules and plaques with slight central clearing on the trunk and extremities. Patient at 23 weeks gestation. B, Two weeks into treatment with oral prednisone. Vesicles developing on the borders of annular plaques on the anterior aspect of the right thigh. Patient at 25 weeks gestation. C, A few days after the second dose of dupilumab. Thin annular coalescing hyperpigmented plaques in areas of prior rash and no active blisters. Patient at 31 weeks gestation.

J Eur Acad Dermatol Venereol. 2023;37:1207–1214.

Adverse Pregnancy Outcomes and anti BP180 Elisa Values

- 95 patients with PG
- 42 had one or more adverse pregnancy outcomes (preterm birth (n = 26), intrauterine growth restriction (IUGR) (n = 18) and small weight for gestational age at birth (n = 16))
- A threshold of 150 IU ELISA value was the most discriminating to differentiate between patients with or without intrauterine growth restriction
- The combination of blisters and ELISA values higher than 150 IU led to a 2.4-fold higher risk of all-cause APO (OR: 10.90; 95% CI: 2.33–82.3) relative to patients with blisters but lower values of anti-BP180 antibodies (OR of 4.54; 95% CI 0.92–34.2).

Pemphigus in pregnancy Treatment and Outcomes

Treatment

- Systemic corticosteroids (prednisone) remain first-line
- **IVIg**: proposed steroid-sparing option — 2 g/kg/cycle monthly, continued ≥ 4 months postpartum
- **azathioprine** is considered a safe immunosuppressive
- Rituximab, mycophenolate mofetil, methotrexate, cyclophosphamide are contraindicated

Maternal/fetal outcomes

- Live-birth rate: 92% overall
- Fetal mortality: 9.8% overall; stillbirth in 7%, postnatal death in 1.7%
- Mucocutaneous disease raises neonatal complication risk (OR 5.27-12.1)
- Delivery: ~ 37 weeks mean gestation; no significant vaginal vs cesarean difference

Neonatal Pemphigus

- Neonatal pemphigus results from transplacental transfer of maternal anti-Dsg IgG4 autoantibodies (predominantly anti-Dsg3 in PV)
- Neonatal skin, unlike adult skin, expresses both Dsg1 and Dsg3 throughout the epidermis — explaining why maternal antibodies against either desmoglein can cause extensive cutaneous blistering with minimal mucosal involvement in neonates

Medication Safety Across Blistering Diseases in Pregnancy

Drug	Pregnancy	Lactation
Topical corticosteroids	Safe at any potency for standard use	Safe; avoid direct nipple application
Systemic corticosteroids (prednisone)	Preferred; placental 11- β -HSD ~10:1 M:F ratio; keep ≤ 20 mg/day maintenance	Wait ≥ 4 h post-dose before feeding
Betamethasone/dexamethasone	Cross placenta readily — reserve for fetal lung maturation only	Limited data
Azathioprine	Relatively safe; ≤ 2 mg/kg/day	Probably safe; wait ≥ 4 h
Dapsone	Generally safe (Cat. B2); check G6PD first	AAP-compatible; monitor infant jaundice
Cyclosporine A	No clear teratogenicity; HTN/renal/preterm risk	Avoid — excreted in milk
IVIg	Safer option vs immunosuppressants	No major concerns
Methotrexate	CONTRAINDICATED — teratogenic/embryotoxic	CONTRAINDICATED
Mycophenolate mofetil	CONTRAINDICATED — known teratogen	CONTRAINDICATED
Cyclophosphamide	CONTRAINDICATED	CONTRAINDICATED
Rituximab	Avoid; delay conception ~12 months post-infusion	Not recommended

**S2k guidelines on the management of paraneoplastic pemphigus/
paraneoplastic autoimmune multiorgan syndrome initiated by the
European Academy of Dermatology and Venereology (EADV)**

- **Asociación con trastornos linfoproliferativos y otras enfermedades hematológicas:** LNH, LLC, Castleman, timoma, etc
- **Estomatitis erosiva grave,** afectación ocular, anogenital y GI
- **Afectación cutánea polimorfa** (tipo pénfigo, penfigoide, LP, EM, GVHD).
- **Bronquiolitis obliterante**



Histopathology

- In patients with suspected PNP/PAMS, light microscopy studies of skin/mucosa biopsy specimens are recommended (111), since they can provide important diagnostic clues
- Histopathological findings mainly reflect the clinical picture. As such, not only acantholysis can be seen but also lichenoid interface dermatitis and keratinocyte necrosis are frequently found
- Absence of acantholysis does not exclude the diagnosis of PNP/PAMS

**Direct immunofluorescence**

- It is recommended (111) to perform DIF on a perilesional specimen from skin or mucosa.
- Combination of epithelial intercellular and linear/ granular deposits along the epidermal-epithelial basement membrane zone of IgG and/or C3 is highly specific for the diagnosis of PNP/PAMS.
- Repeated DIF studies may be recommended (11). Negative DIF findings do not exclude the diagnosis of PNP/PAMS in presence of compatible clinical context, clinico-pathological features and/or immunoserological findings.

**Indirect immunofluorescence**

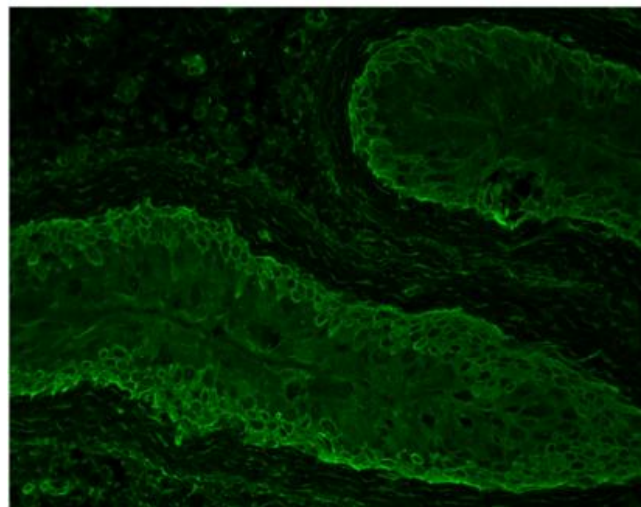
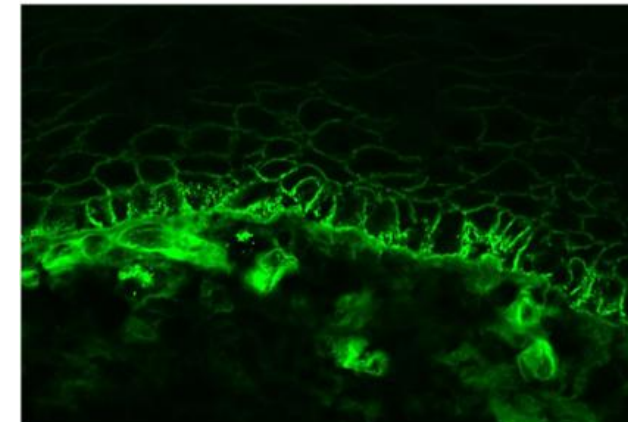
- It is recommended (111) that IIF is performed using rat bladder, the most sensitive and specific substrate for the diagnosis of PNP/PAMS
- Repeated DIF studies may be recommended (111) that IIF studies are concomitantly performed using monkey esophagus

**ELISA**

- It is recommended (111) that anti-envoplakin antibodies, which are highly specific for PNP/ PAMS, are searched by ELISA
- It is recommended (111) to also perform ELISAs for anti-desmoglein 1, anti-desmoglein 3, anti-BP230, and anti-BP180 antibodies which may be positive but exhibit low specificity in PNP/ PAMS.

**Immunoblotting / immunoprecipitation**

- IB and/or IP with keratinocytes or epidermal extracts are highly specific and sensitive tools for the detection and characterization of PNP/ PAMS autoantibodies and are available in specialized laboratories; it is recommended (111) that IB and/or IP are used as diagnostic tools, if available



The following treatment recommendations for PNP/PAMS are given:

- Treatment of underlying malignancy is recommended (↑↑↑);
- Treatment with oral systemic corticosteroids (prednisone or prednisolone) 0.5mg/kg to 1.5 mg/kg/day is recommended (↑↑↑);
- Topical treatment of skin and mucosal lesions, e.g. clobetasol propionate ointment, topical antiseptics, wound care is recommended (↑↑↑);
- In presence of B cell proliferative malignancies, B-cell depleting therapy as potentially effective therapy for both PNP/PAMS and the underlying malignancy is recommended (↑↑).



Additional options:

- Steroid-sparing agents (azathioprine, mycophenolate mofetil, cyclosporine, cyclophosphamide, methotrexate) may be recommended (↑↑);
- Immunoabsorption and plasmapheresis may be considered (↑), if available;
- High dose intravenous immunoglobulins may be considered (↑);
- Rituximab (anti-CD20) may be considered (↑) even in the absence of underlying B-cell malignancy, as it may be effective for PNP/PAMS
- It is recommended (↑↑↑) to discuss the additional options with a haematologist/ oncologist



Acanthosis palmaris/tripe palms

- Thickened skin of palms (rarely soles) with accentuated dermatoglyphics and velvety pattern (resembles intestinal lining = tripe)
- Males > females
- Associated malignancy in 90% of cases
 - Mostly lung (with clubbing) or gastric (with AN)
 - In 60% - associated with other paraneoplastic signs (AN, Leser-Trelat, cutaneous papillomatosis)
 - Usually precedes or coincides with malignancy
- Other associations: psoriasis, eczema, BP
- Pathogenesis: unknown; possibly related to the release of growth factors by tumor cells/stromal cells (TGF- α signaling through EGFR or IGF-1R)



Acrokeratosis paraneoplastica (Bazex syndrome)

- Males > females
- Several phases:
 - Violaceous discoloration of peripheries (ears, palms, soles, nose) with scaling (rarely bullae)
 - Hyperkeratosis developing into PPK
 - Generalized eruption (psoriasiform, eczematous)
- Nail dystrophy and paronychia
- Usually precedes (11 mo) mostly squamous cell carcinomas of the upper respiratory and gastrointestinal tract with metastasis to cervical LNs
- Disappears upon successful cancer treatment
- Pathogenesis: due to cancer-associated cytokine release (Th2 shift), release of growth factors or immune response to neoantigens



van Leersum and Liu, N Engl J Med, 2015

Other forms of acquired PPK associated with cancer

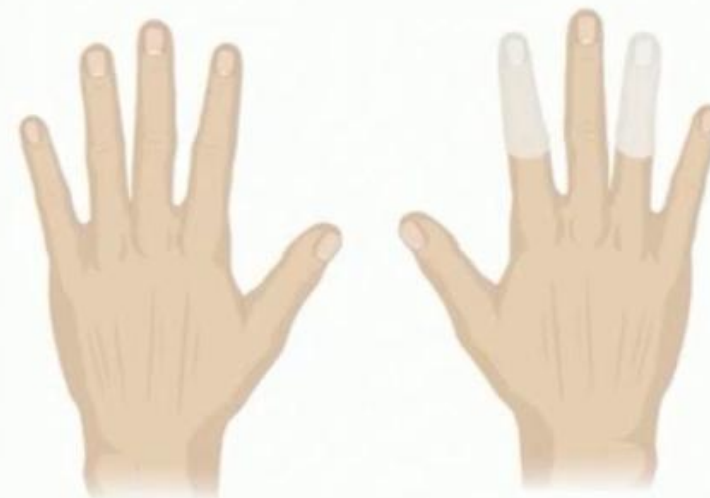
- Pityriasis rubra pilaris
- Diffuse PPK (lung)
- Filiform PPK (breast, colon, kidney)
- Arsenic-induced PPK (internal malignancies)



Corral et al, Dermatol Online J, 2020; Campbell et al, JAAD Case Reports, 2018; Tao and Wang, Skin Res Technol, 2024; Davis et al, JAAD Case Rep, 2022

Paraneoplastic Raynaud's phenomenon

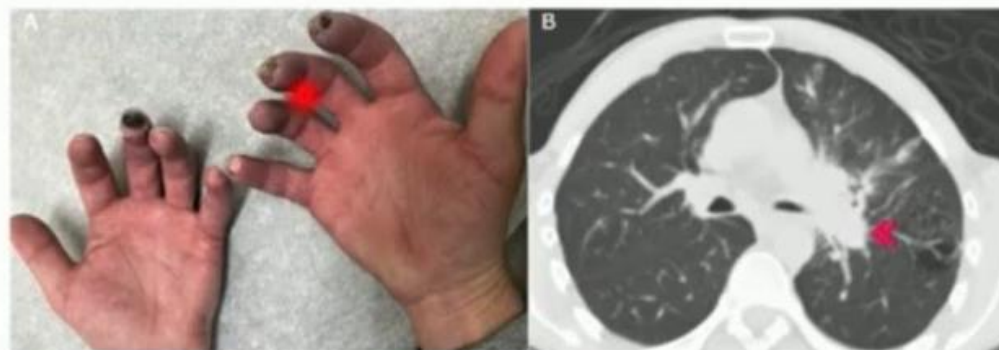
- It is a rare condition (PubMed has a total of 97 ref)
- No signs of a connective tissue disease
- **Elderly** – especially males
- **Asymmetrically distributed**, or with an odd presentation
- Often sudden onset
- Tissue loss (digital ulcers)
- Severe pain
- Aggressive/persistent



Paraneoplastic Raynaud's phenomenon

Whom should I suspect?

- New onset in an elderly
- Rapid progression with sudden onset, severe ischemia and loss of tissue
- Asymmetric presentation
- **LOOK FOR RED FLAGS**
 - Unexplained weight loss
 - Nightly fever
 - Anaemia, abnormal blood counts
 - Other paraneoplastic lesions



Paraneoplastic acral vascular syndrome (PAVS)

Lokineni et al. Eur J Case Rep Intern Med. 2021 Jul 9;8(7):002690

Malignancies associated with reports of Paraneoplastic Raynaud's phenomenon

- Lung cancer
- Breast cancer
- Ovarian cancer
- Gastric and other gastrointestinal cancers
- Lymphoma
- Multiple myeloma
- Leukaemia
- Pancreatic cancer
- And more.....

All of them

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HIGHLIGHTS

Viena

30sep - 3oct
2026

La Academia Española de Dermatología y Venereología expresa su agradecimiento al patrocinador UCB, por su especial apoyo y contribución con la actividad formativa Highlights 2026.

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HIGHLIGHTS

Viena
30sep - 3oct
2026

ENFERMEDADES AUTOINMUNES Y MEDICINA INTERNA PARTE II

Daniel Martín Torregrosa
Hospital de Sagunto

Una iniciativa de:



Con el patrocinio de:



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**NO TENGO CONFLICTOS
DE INTERÉS**

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From IFN Signatures to Clinically Accessible Biomarkers

Biomarker	Measured by	Clinical relevance
SIGLEC1 (CD169)	Flow cytometry on monocytes	Well-established surrogate of IFN-I pathway activation; associated with disease activity
MxA (MX1 protein)	IHC – particularly skin	Tissue marker of IFN-I activation; particularly relevant in CLE
CXCL10 (IP-10)	ELISA / multiplex assay	IFN-inducible chemokine associated with disease activity; relevant in SLE and CLE
IFN-α protein	Simoa ultrasensitive assay	Direct measurement of IFN- α ; sensitive but technically demanding

No single assay captures the entire IFN-I pathway.

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SIGLEC1 (CD169) - A Surrogate Biomarker of Type I IFN Activity

RHEUMATOLOGY

Concise report

Evaluation of SIGLEC1 in the diagnosis of suspected systemic lupus erythematosus

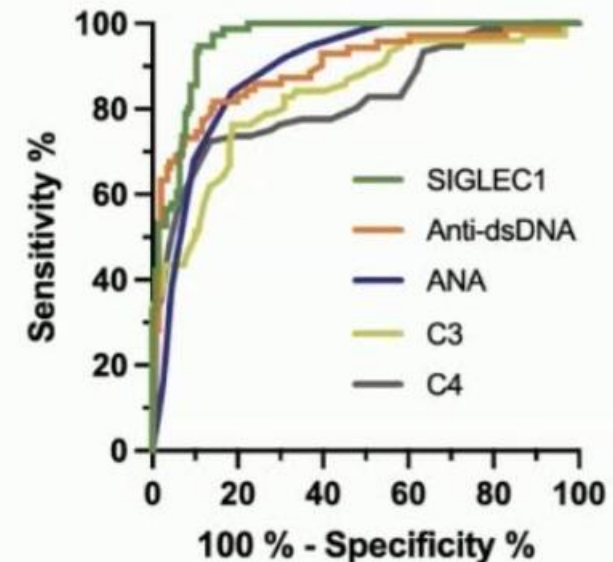
Lydia Zorn-Pauly¹, Anne Sae Lim von Stuckrad², Jens Kiotsche³, Thomas Rose¹, Tilmann Kallinich^{3,2}, Philipp Enghard⁴, Lennard Ostendorf^{3,4}, Marie Burns⁵, Thomas Doerner¹, Christian Meisel⁶, Udo Schneider¹, Nadine Unterwalder⁷, Gerd Burmester¹, Falk Hiepe¹, Tobias Alexander^{1,3,*} and Robert Biesen^{1,*}

SIGLECT (sialic acid-binding immunoglobulin-like lectin-1, CD169): an adhesion molecule restricted to cells of the monocyte lineage

Excellent diagnostic performance in suspected SLE

AUC 0.95 | NPV >99% in this diagnostic cohort

Fig. 1 ROC analysis



ROC curves analysis of ANA, SIGLEC1, anti-dsDNA antibodies, as well as C3 and C4 levels in a cohort of 76 newly diagnosed SLE patients and 156 SLE-mimicking conditions.

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Potential Cell-Bound Diagnostic Biomarkers in SLE

**CONVENTIONAL
COMPLEMENT BIOMARKERS**
↓ C3 and ↓ C4
soluble complement



**CELL-BOUND COMPLEMENT
ACTIVATION PRODUCTS**
TC4d
*cellular footprint of
complement activation*



Flow cytometry

TigG, BC4d and TC4d outperformed conventional biomarkers in distinguishing ANA+ SLE from other autoimmune rheumatic diseases (AUC 0.81, 0.80 and 0.79 vs 0.72 for anti-dsDNA)

TC4d: 58% sensitivity at 95% specificity vs conventional SLE-specific autoantibodies

In serologically inactive SLE: T-cell biomarkers identified 19% of all SLE patients missed by conventional serology and normal complement

• Within this serologically inactive subgroup, the combined T-cell biomarkers identified 53% of patients

Front Immunol. 2025 Feb 26;16:1518208.

Multi-centered clinical validation demonstrating superior precision in lupus diagnosis: T cell autoantibodies and TC4d outperform conventional lupus erythematosus biomarkers

Vasileios Kyttaris¹, Daniel J. Wallace², Arezou Khosroshahi³, Andrew Concoff⁴, Nicole Wilson⁵, Chau Ching Liu⁵, Susan Manzi⁵, Joseph Ahearn⁵, Sepehr Taghavi⁴, Toubia Warsi⁴, Stanley Park⁴, Christine Schleif⁴, Brittany D. Partain⁴ and Tyler O'Malley ^{6*}

Urinary Biomarkers in Lupus Nephritis - liquid biopsy

PATHOPHYSIOLOGIC PROCESS	URINARY BIOMARKER	MEASUREMENT (typical method)	KEY EVIDENCE / PERFORMANCE	POTENTIAL CLINICAL UTILITY
 Macrophage activation	sCD163	ELISA (normalized to urinary creatinine)	- Active LN: AUC >0.97 - Strongly associated with histological activity - Predicts impending flares and remission - Tracks treatment response	- Disease activity - Monitoring - Flare prediction
 Leukocyte activation / adhesion	ALCAM	ELISA (normalized to urinary creatinine)	- Correlates with histological activity index - Proliferative vs membranous LN: AUC 0.81	- Activity assessment - Prognosis
	VCAM-1	ELISA (normalized to urinary creatinine)	- Associated with renal activity - High baseline levels predict long-term renal function decline (OR 22.9)	
 Chemotaxis / monocyte recruitment	MCP-1 (CCL2)	ELISA / multiplex (normalized to urinary creatinine)	- Tracks renal activity longitudinally - AUC ~0.82-0.87; Sn ~90%, Sp ~79%	- Activity monitoring - Flare detection
 Tubular injury	NGAL	ELISA / immunoassay (normalized to urinary creatinine)	- Active LN: AUC 0.996; Sn 95%, Sp 100% - Levels decrease after treatment	- Activity assessment - Renal injury
 Cytokine signaling	TWEAK	ELISA (normalized to urinary creatinine)	- Reflects renal activity; peaks with flares - Month-3 level predicts response - Combined with proteinuria improves AUC to 0.83	- Activity monitoring - Response prediction
	BAFF	ELISA / multiplex	Identified by proteomics as a discriminator of active LN	

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Interferon-α Biological Activity Predicts Disease Activity and Flares in Cutaneous Lupus

Interferon-α biological activity is associated with disease activity and risk of flare in cutaneous lupus erythematosus: A monocentric study of 184 patients

Quiterio Mont de Morán, MD,¹ Clemente Martínez, MD,¹ Laura Pérez, MD,¹ Alicia Muñoz, MD,¹ Raquel Dargatzis, PhD,¹ Gey Guecho, MD, PhD,¹ Alexander Schindl, MD,¹ Carolina Trancón, MD,¹ Isabella Arriaga, MD, PhD,¹ Ismael Barba, MD, PhD,¹ Zoltan Kertész, MD, PhD,¹ Carolina Chacón, PhD,¹ and Francisco Chacón, MD, PhD¹

Study Cohort

- 184 CLE patients
- 102 with longitudinal follow-up (multiple serum samples)
- Routine testing, 3 batches/week, results within 7 days

Methodology

- Functional antiviral assay: patient serum → MDBK cells (cell culture) → infected with VSV → measure protection
- Higher IFN-α = stronger antiviral protection → activity in IU/mL (> 2 = positive)

Key Findings

- Confirms central role of type I interferon pathway in CLE
- Higher IFN-α biological activity correlates with active skin disease
- Patients with high IFN-α activity had significantly increased flare risk
- Positive IFN-α biological activity is associated with ~5x higher flare risk

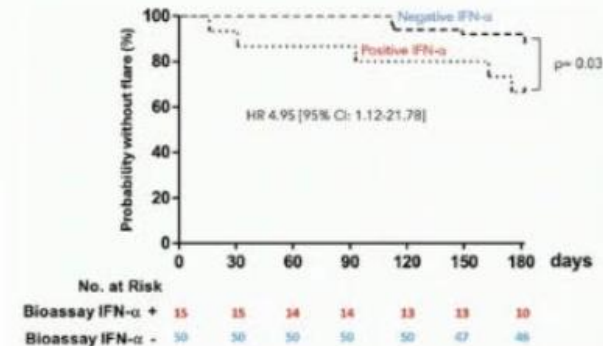
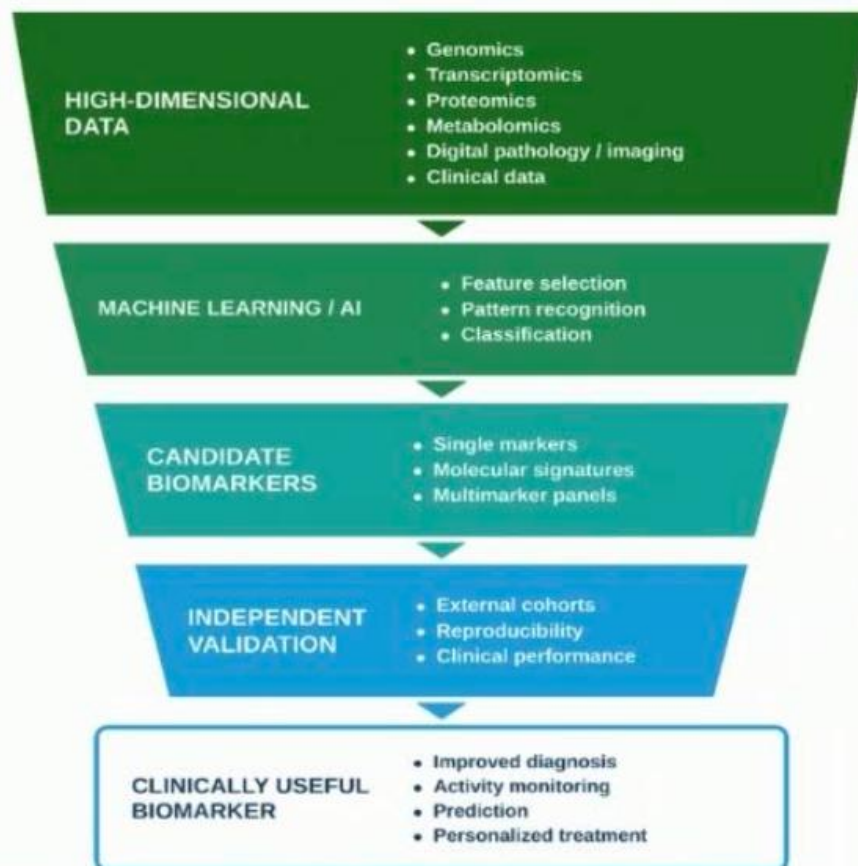


Fig 2. Time to CLE flare in the 6 months after first IFN-α sampling in the negative ($n = 50$) versus the positive IFN-α group ($n = 15$). Kaplan-Meier survival curves were computed using the log-rank test. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using univariable survival analysis. CLE remission was defined by CLASI-A = 0 and first flare by a new increase of 2 points of CLASI-A associated with a modification of CLE treatment. Times to first flare are expressed in days. CLE, Cutaneous lupus erythematosus; IFN-α, interferon-α; CLASI-A, cutaneous Lupus Erythematosus disease Area and Severity Index Activity.

AI and Machine Learning in Biomarker Discovery in SLE



Examples of AI-derived candidate biomarkers in SLE

Biomarker category	Candidate biomarkers	Potential clinical significance
Genetic (transcriptomic) <i>BMC Immunology, 2023; Front. Genet., 2022</i>	Five-gene signature: ABCB1, CD247, DSC1, KIR2DL3, MX2 Ten-gene signature: IFI44, IFI44L, EIF2AK2, IFIT3, IFITM3, ZBP1, TRIM22, PRIC285 (HELZ2), XAF1, PARP9	MX2 and IFI44 – high diagnostic accuracy (MX2 AUC: 0.907; IFI44 validated via RT-qPCR).
Proteomic <i>Arthritis Rheumatol. 2026 Online ahead of print</i>	SCARB2 (lysosome membrane protein 2), SOD2 (mitochondrial superoxide dismutase), CD302, Galectin-9 (LGALS9), GGT5.	Valuable for predicting disease and distinguishes proteomic profiles up to 3.4 years before clinical onset.
Metabolomic <i>Clin Immunol. 2024</i>	N-Methyl-L-glutamic acid, L-2-aminobutyric acid, Phosphoserine, L-Cystine, 5-Aminolevulinic acid, L-Lactic acid, Quinic acid, Oxoglutaric acid.	As an 8-metabolite panel, these metabolites distinguish SLE from healthy individuals with high accuracy (AUC > 0.95). Two of them – N-Methyl-L-glutamic acid and L-2-aminobutyric acid – were individually validated as SLE classifiers (AUC > 0.775) and correlate significantly with SLEDAI scores.

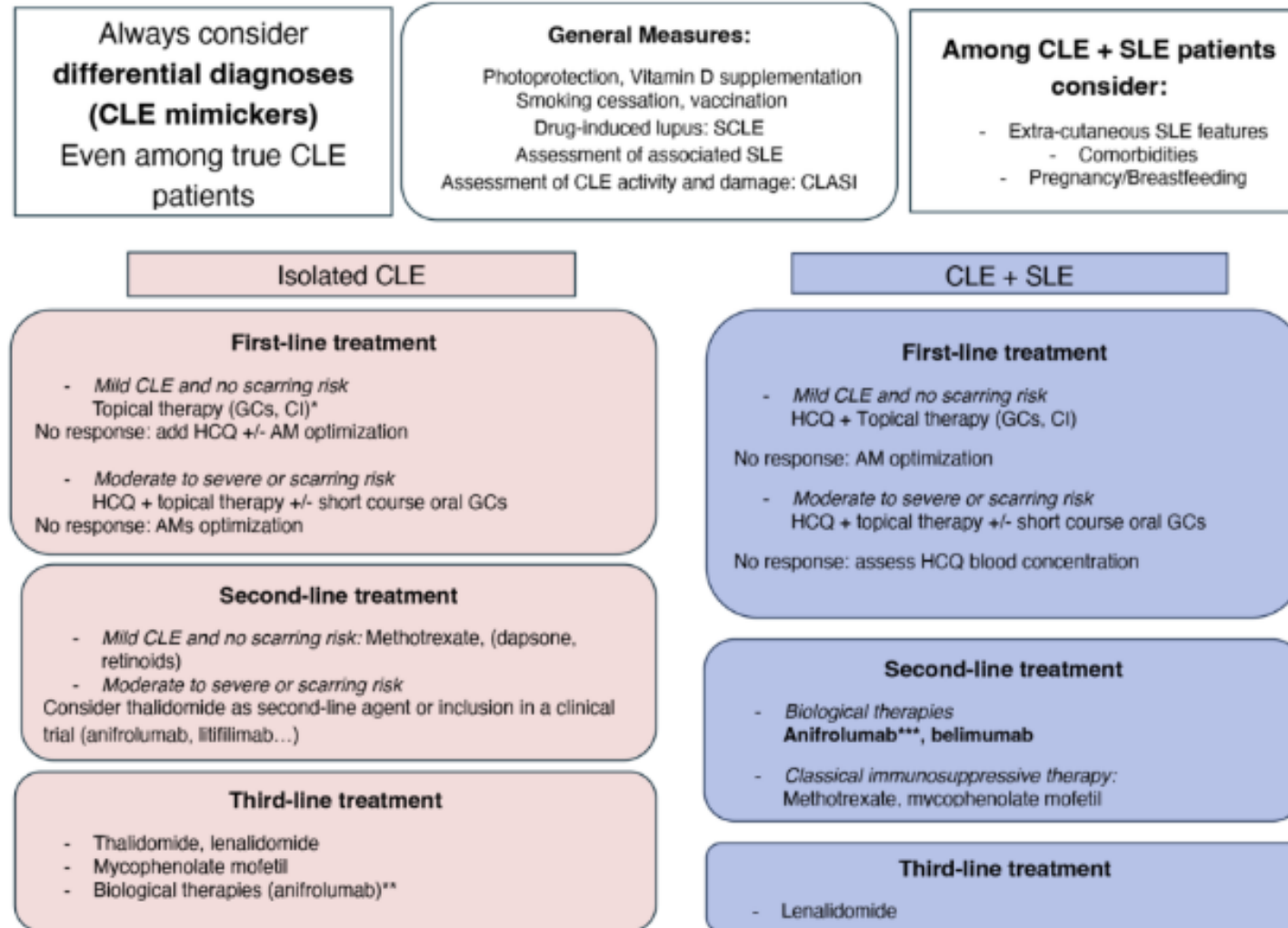


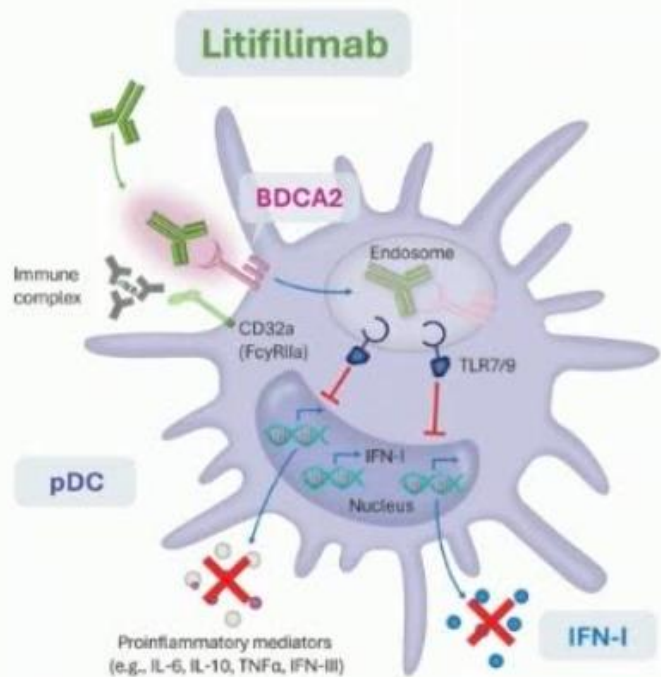
TABLE 4 Emerging therapies for cutaneous lupus erythematosus.

Category	Molecule	Pathway	Preliminary results	Stage of development in CLE
pDC-targeted therapies	Litifilimab (BIIB059)	Humanized IgG1 monoclonal antibody targeting BDCA-2	Phase 2: dose-dependent reduction in CLASI-A scores. -24.3 to -33.4 percentage points reduction in CLASI-A compared to placebo.	Phase 3, ongoing (NCT05531565)
	Daxidilimab (HZN-7734)	IgG1λ monoclonal antibody against ILT7	Phase 1: CLASI-A decrease and pDC depletion correlation	Phase 2, terminated (NCT05591222)
	KK4277	Humanized anti-protein tyrosine phosphatase receptor type S (PTPRS) antibody	Improvement of CLASI-A in some subjects	Phase 1, completed (NCT05411016)
JAK/STAT inhibitors	Deucravacitinib (BMS-986165)	TYK2 inhibitor	Phase 2: CLASI-50 responses in 69.6% versus 16.7% with placebo ($p < 0.001$)	Phase 3, ongoing (NCT05620407)
Topical JAK/STAT inhibitors	Ruxolitinib 1.5% cream	JAK1/2 inhibitor (topical)	Phase 2 (open label): 30.2% CLASI-A decrease at week 12	Phase 2, ongoing (NCT06261021); completed (NCT04908280)
	Delgocitinib cream	Pan-JAK inhibitor	Case reports show improvement in refractory lupus lesions	Phase 2, terminated (NCT03958955)
TLR7/8 inhibitors	Afimetoran (BMS-986256)	TLR7/8 inhibitor	CLASI-A 50 reached in 5/8 patients	Phase 1b, completed (NCT04493541)
	Enpatoran (M5049)	TLR7/8 inhibitor	Phase 2: up to 91.3% of patients achieving CLASI-50, and up to 60.9% CLASI-70 at week 16 (vs 38.5% and 11.5% for placebo)	Phase 2, completed (NCT05162586), ongoing (NCT05540327)
	SOF-SKN	Topical ultra-short oligonucleotide inhibiting TLR7		Early phase 1, ongoing (NCT07072611)
B-cell & FcRn modulators	IMVT-1402	Fully human monoclonal antibody targeting the neonatal Fc receptor (FcRn)		Phase 2b, ongoing (NCT06980805)
	DR-0201/SAR448501	Bispecific antibody engaging myeloid cells to deplete B cells via targeted phagocytosis		Phase 1, ongoing (NCT06647069)
Interferon/cytokine pathway	Dazukibart (PF-06823859)	Humanized IgG1 monoclonal antibody neutralizing IFN-β (type I IFN)	Promising results in a phase 2 trial for dermatomyositis	Phase 2, ongoing (NCT05879718)
	Anifrolumab (Saphnelo)	Fully human monoclonal antibody targeting type I interferon receptor subunit IFNAR1	Approved for moderate-to-severe SLE. CLASI-50 achieved for 49% of patients (vs 25% in the placebo group).	Phase 3, ongoing (NCT06015737)
Other mechanisms	Eclitasertib (SAR443122)	Inhibitor of receptor-interacting serine/threonine-protein kinase 1 (RIPK1)	Phase 2: CLASI-50 achieved for 44.74% of patients (vs 45% in placebo group).	Phase 2, completed (NCT04781816)
	BMS-986326	IL-2/CD25 fusion protein	In vitro and healthy volunteers Treg expansion	Phase 1b, ongoing (NCT06013995)
	Edecisertib (GS-5718)	Inhibitor of interleukin-1 receptor-associated kinase 4 (IRAK4)		Phase 2a, ongoing (NCT05629208)
	Iberdomide (CC-220)	Cereblon modulator causing proteasomal degradation of Ikaros/Aiolos transcription factors.	Phase 2: CLASI-A 50 at week 24 versus placebo achieved for 91.7% patients with subacute (9 vs 52.9%, $p = 0.035$) and 62.1% with chronic (vs 27.8%; $p = 0.029$) CLE but not for the overall population (55.6% vs 44.6%) or patients with baseline CLASI-A ≥ 8 (66.7% vs 50.0%).	Phase 2, completed (NCT03161483)
Topical metabolic modulators	Tapinarof cream	Aryl hydrocarbon receptor (AhR) agonist (topical)		Early phase 1, ongoing (NCT06661213)

Abbreviations: CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; JAK/STA, janus kinase-signal transducer and activator of transcription; pDC, plasmacytoid dendritic cell; TLR, Toll like receptor; TYK, tyrosine kinase.

Efficacy and Safety of Litifilimab in Cutaneous Lupus Erythematosus (CLE): 52-week results of the Phase 2 Study, AMETHYST Part A

Joseph F. Merola,^{1,2,3} Victoria P. Werth,^{4,5} Benjamin F. Chong,¹ Filippa Nyberg,⁶ Eric F. Morand,⁷ David Fivenson,⁸ Qianyun Li,⁹ Michael Schindelar,⁹ Hua Carroll,⁹ Erica Camargo Faye,⁹ Effie Pournara,¹⁰ Weihong Yang,⁹ Francois Chasset¹¹



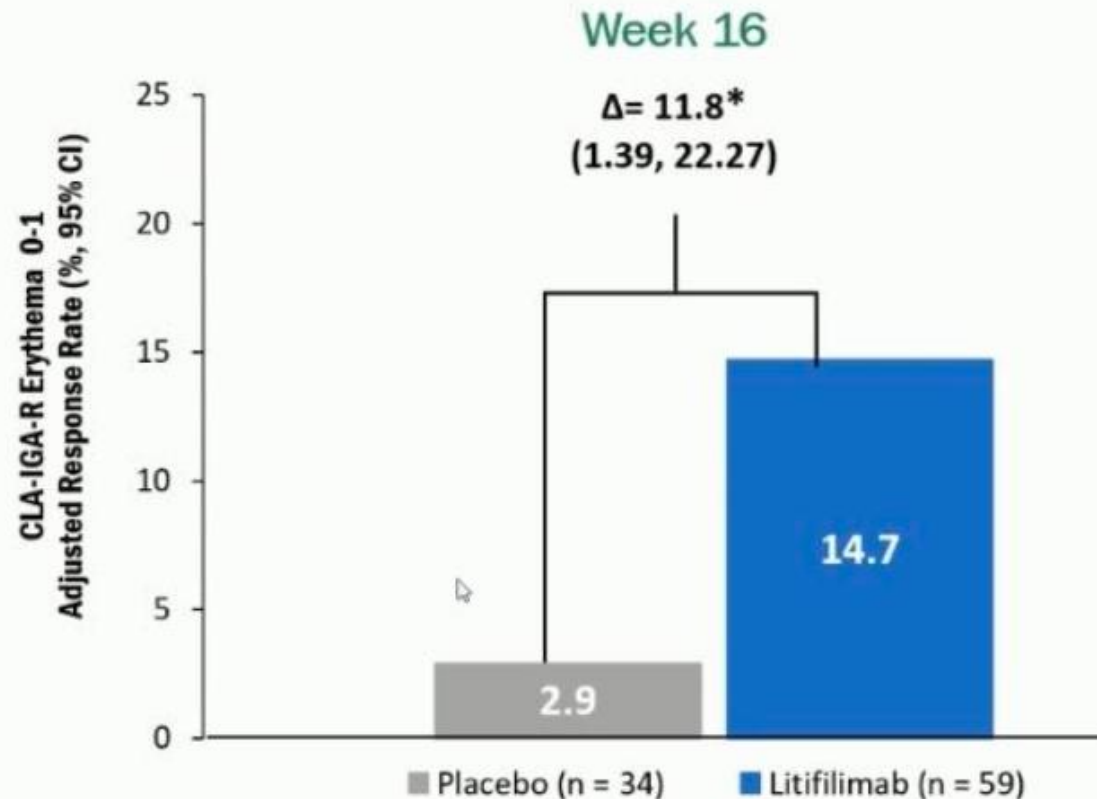
Litifilimab is a monoclonal antibody that selectively binds to BDCA2, a receptor expressed on pDCs, and inhibits proinflammatory mediators, including IFN-I.²⁻⁸

		Litifilimab treated: participant number and CLE subtype ²		
	Timepoint	5 SCLE	7 ACLE	8 DLE
MxA area epidermis	Day -1	58.4%	21.0%	34.3%
	Week 4	0.1%	2.2%	1.0%
MxA histology	Day -1			
	Week 4			
CLASI-A score	Day -1	9	6	10
	Week 4	0	2	6
CLASI response		R	R	R

In the Phase 1 study, IFN expression in skin lesions was reduced after a single IV dose of litifilimab 20 mg/kg.²

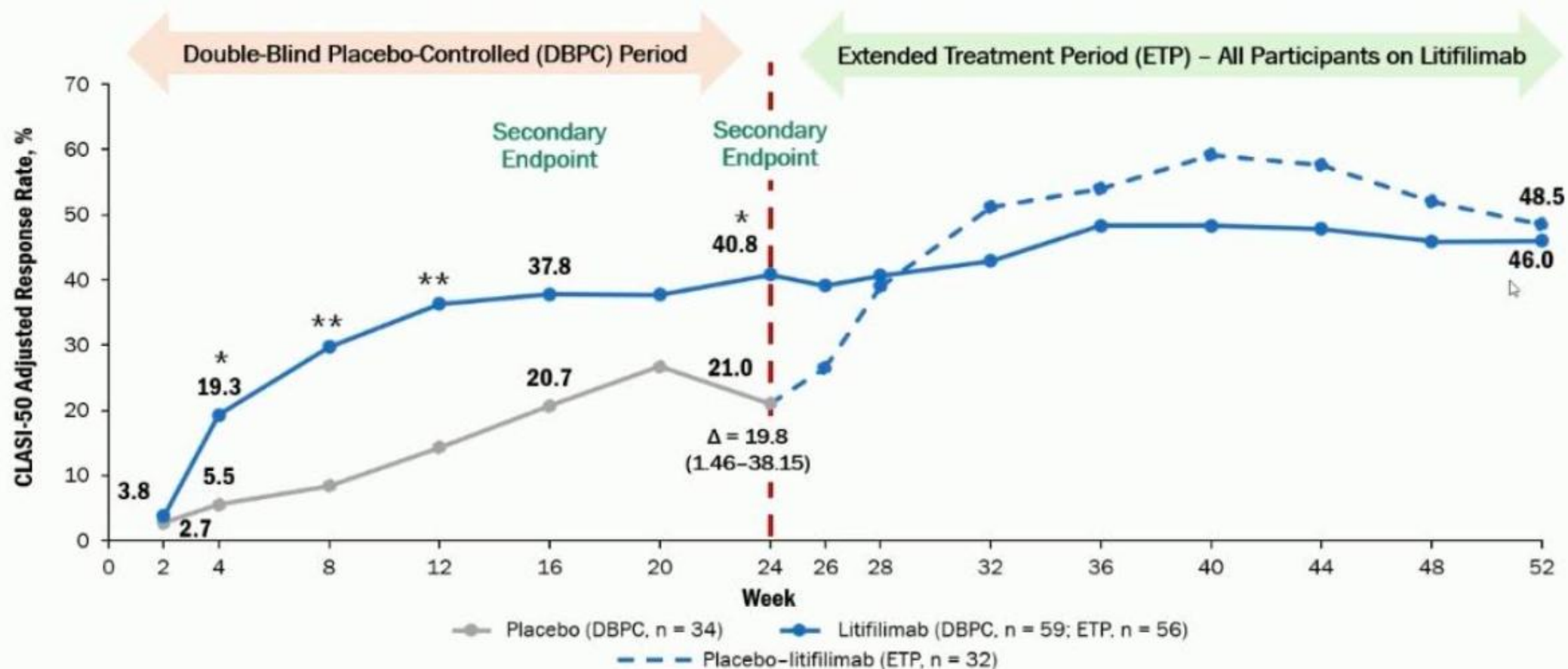
Primary Endpoint Met: CLA-IGA-R Erythema 0-1 (Clear/Almost Clear)

More participants treated with litifilimab achieved clear/almost clear skin¹ at Week 16



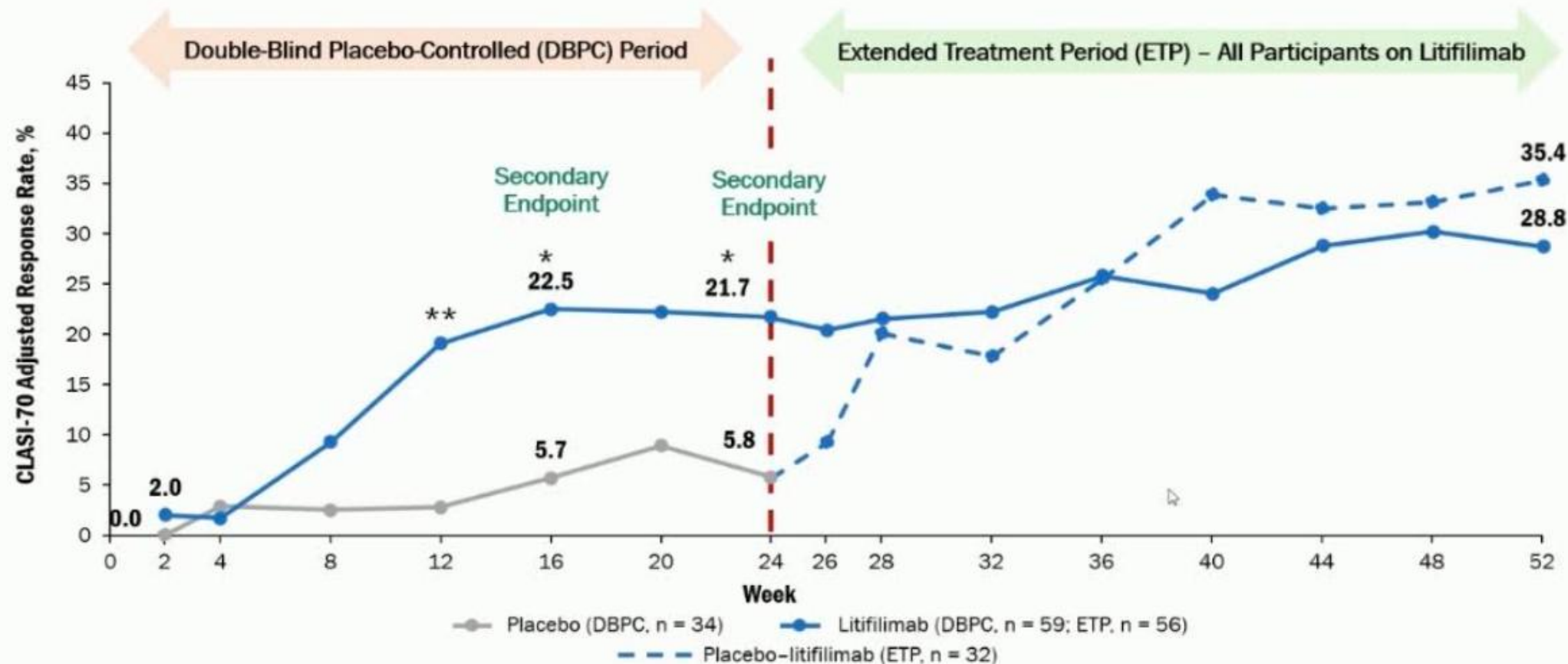
CLASI-50

Response rates continuously improved through Week 52 in litifilimab-treated participants



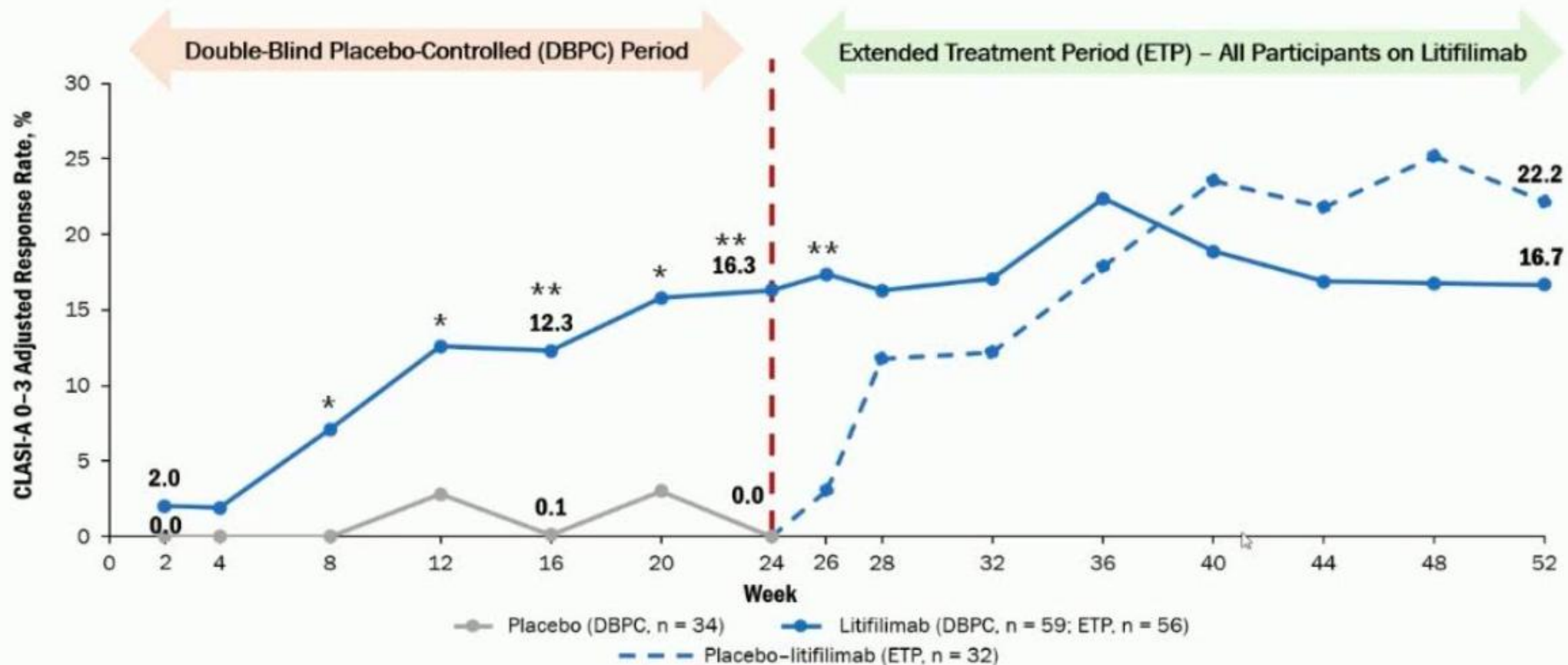
CLASI-70

Response rates continuously improved through Week 52 in litifilimab-treated participants



CLASI-A 0-3: No or Minimal Disease Activity

Response rates continuously improved through Week 52 in litifilimab-treated participants



Safety Outcomes through Week 52

Litifilimab was generally well tolerated

Weeks 0-24 (DBPC)			Weeks 24-52 (ETP)		
Events, % (n)	Litifilimab (n = 59)	Placebo (n = 34)	Events, % (n)	LITI-LITI (n = 56)	PBO-LITI (n = 32)
Any event ^a	74.6 (44)	64.7 (22)		76.8 (43)	78.1 (25)
Mild	54.2 (32)	41.2 (14)		48.2 (27)	46.9 (15)
Moderate	18.6 (11)	20.6 (7)		26.8 (15)	31.3 (10)
Severe	1.7 (1)	2.9 (1)		1.8 (1)	0
Related event ^b	20.3 (12)	26.5 (9)		14.3 (8)	21.9 (7)
Serious event ^c	6.8 (4)	2.9 (1)		3.6 (2)	3.1 (1)
Most common event (≥ 5% in LITI [DBPC]; ≥ 5% in LITI total group ^d [ETP])					
Nasopharyngitis	6.8 (4)	14.7 (5)	Nasopharyngitis	8.9 (5)	6.3 (2)
Upper respiratory tract infection	5.1 (3)	8.8 (3)	Influenza	3.6 (2)	9.4 (3)
Back pain	5.1 (3)	0	Arthralgia	7.1 (4)	6.3 (2)
Diarrhea	5.1 (3)	5.9 (2)			
Nausea	5.1 (3)	2.9 (1)			
Pyrexia	5.1 (3)	0			

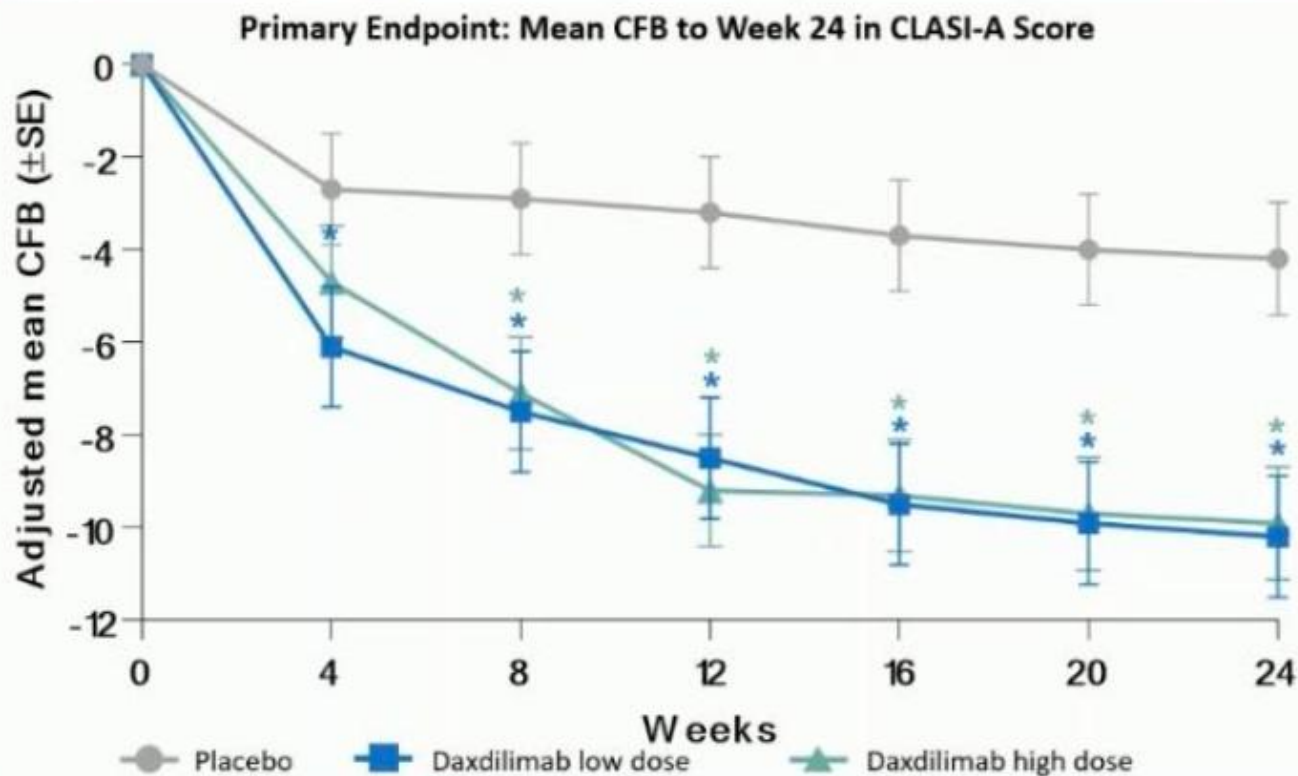
Safety Outcomes through Week 52: Viral Infections

Weeks 0-24 (DBPC)			Weeks 24-52 (ETP)		
Events, % (n)	Litifilimab (n = 59)	Placebo (n = 34)	Events, % (n)	LITI-LITI (n = 56)	PBO-LITI (n = 32)
Viral infections occurring in > 1 participant in either group ^a					
COVID-19	3.4 (2)	0	Influenza	3.6 (2)	9.4 (3)
Oral herpes	3.4 (2)	2.9 (1)	Herpes zoster	1.8 (1)	6.3 (2)
Viral upper respiratory tract infection	1.7 (1)	5.9 (2)			

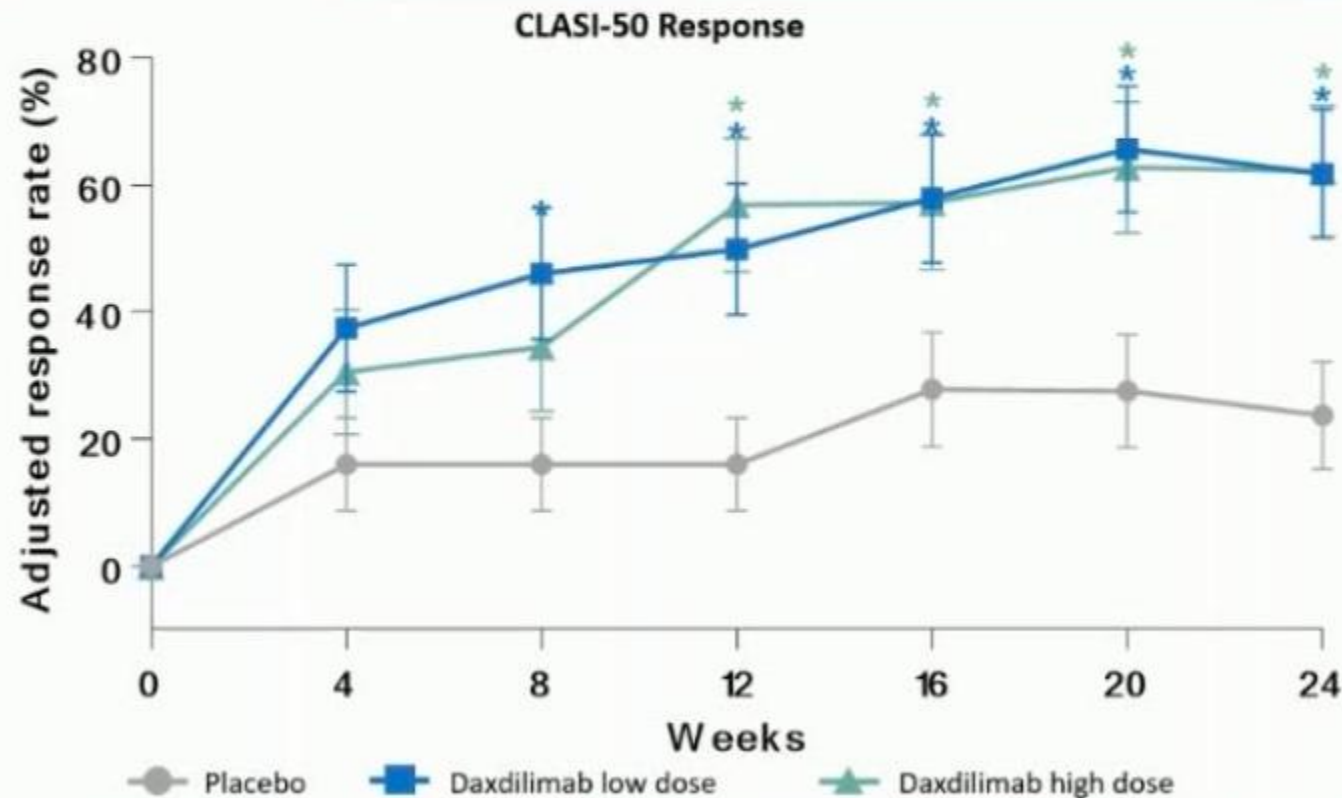
Daxdilimab in Moderate-to-Severe Discoid Lupus Erythematosus: Efficacy and Safety Results from a Phase 2, Randomised, Placebo-Controlled Trial

- **Daxdilimab** is a human IgG1 mAb targeting ILT7 expressed on pDCs, resulting in targeted reduction in the number of pDCs in the tissue and blood²

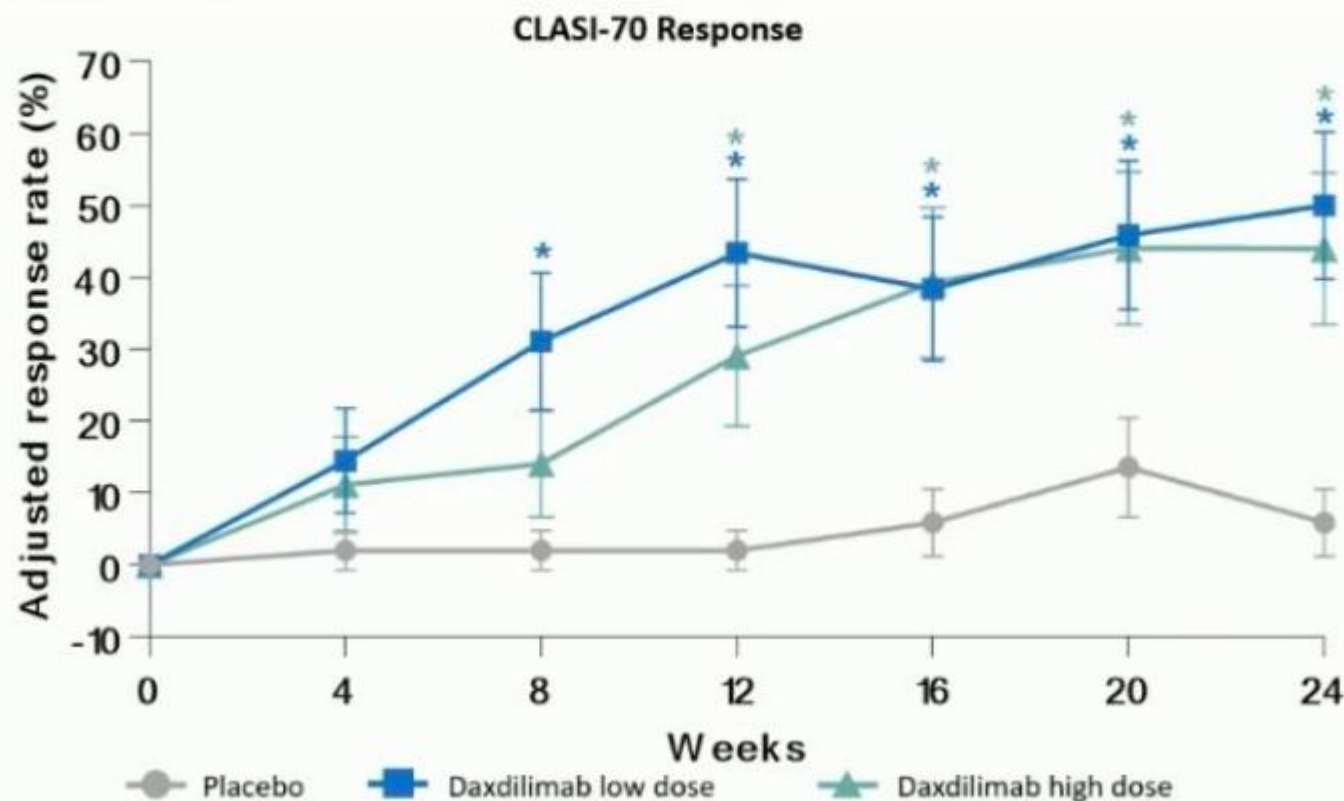
Both daxdilimab doses met the primary endpoint, significantly reducing CLASI-A vs placebo at Week 24, with responses evident as early as Week 4



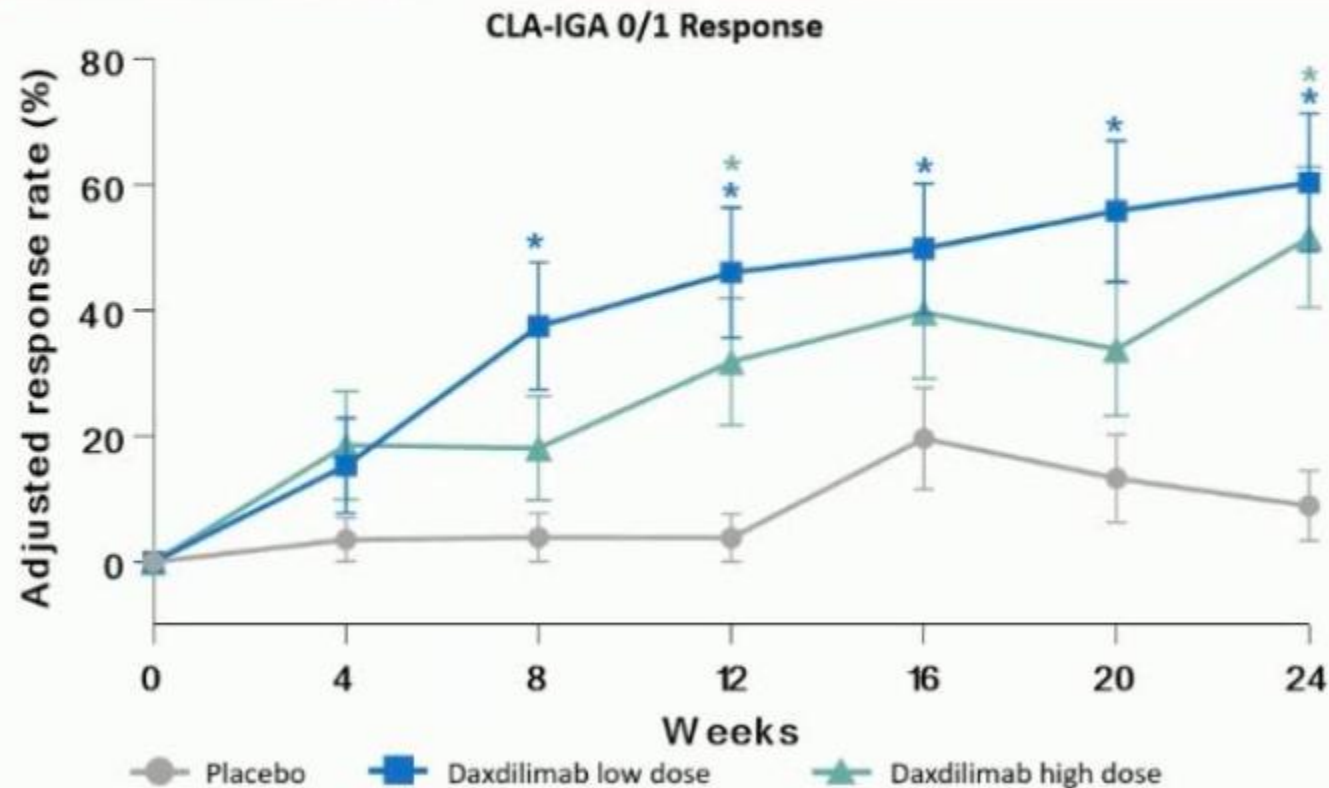
A higher proportion of patients achieved CLASI-50 with both daxdilimab doses versus placebo, with responses evident by Week 4



A higher proportion of patients achieved a CLASI-70 response with both doses of daxdilimab versus placebo



A higher proportion of patients achieved CLA-IGA 0/1 with both daxdilimab doses versus placebo, with responses evident by Week 4 and increasing through Week 24



Daxdilimab was well tolerated through Week 24 with no cases of zoster (cont)

n (%)*	Placebo (N = 25)	Daxdilimab low dose (N = 24)	Daxdilimab high dose (N = 23)	Total Daxdilimab (N = 47)
Most Frequent TEAEs (≥5%)				
Headache	0 (0.0)	4 (16.7)	1 (4.3)	5 (10.6)
Cough	0 (0.0)	2 (8.3)	1 (4.3)	3 (6.4)
Diarrhoea	0 (0.0)	0 (0.0)	3 (13.0)	3 (6.4)
Upper respiratory tract infection	1 (4.0)	3 (12.5)	0 (0.0)	3 (6.4)
Injection site pain	0 (0.0)	2 (8.3)	0 (0.0)	2 (4.3)
Nausea	0 (0.0)	0 (0.0)	2 (8.7)	2 (4.3)
Nasopharyngitis	4 (16.0)	1 (4.2)	0 (0.0)	1 (2.1)
Seasonal allergy	2 (8.0)	1 (4.2)	0 (0.0)	1 (2.1)
Hypertension	2 (8.0)	0 (0.0)	1 (4.3)	1 (2.1)
Influenza	2 (8.0)	0 (0.0)	0 (0.0)	0 (0.0)

Autoantibody Positivity Rates in Classic and Clinically Amyopathic Dermatomyositis

Xiwei Yang, BA^{1,2}; Shae Chambers, BA^{1,2}; Aretha On, BS^{1,2}; [et al](#)

Table 2. Positivity Rates of MSA, MAA, and ANA by DM Subtype

Positivity status	DM subtype, No./total No. (%)		P value
	Classic (n = 198)	Clinically amyopathic (n = 122)	
Any MSA positive	94/198 (47)	49/122 (40)	.20
Any MAA positive	48/168 (29)	26/100 (26)	.65
Any ANA positive	90/143 (63)	42/85 (49)	.045
Either MSA or MAA positive	118/198 (60)	63/122 (52)	.16
Both MSA and MAA negative	80/198 (40)	59/122 (48)	.16
Both MSA and MAA negative but ANA positive	26/53 (49)	13/36 (36)	.23

Evaluation of Dermatomyositis (DM)

- History
 - Use of meds that can exacerbate DM (hydroxyurea, TNF blockers, statins, checkpoint inhibitors)
 - Immunostimulatory herbs
 - Timing of onset or flares with both COVID infection and COVID vaccination

Herbal supplement use in DM

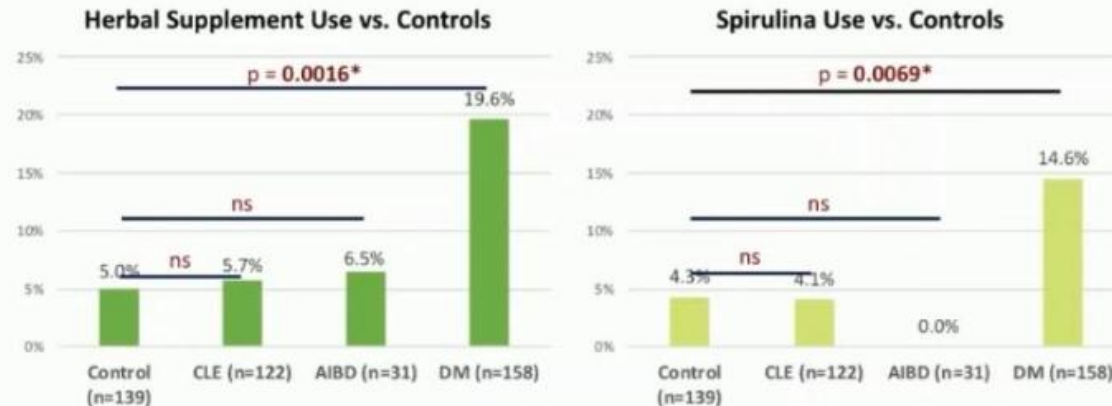


- Herbal supplement use is increasing in US.
- IsaLean weight-loss powder associated with DM onset or flare (Zeidi et al, 2019)
 - Herbalife has many of same ingredients
- Herbs stimulate the immune system, as determined by both in vitro and in vivo studies (Chakka et al, 2020)
 - *Spirulina platensis*
 - *Aphanizomenon flos-aqua* (Blue-Green Algae)
 - *Chlorella*
 - *Echinacea*
 - *Alfalfa*
 - *Elderberry*
 - *Ashwaganda*

Zeidi M, Chansky PB, Werth VP. Acute onset/flare of dermatomyositis following ingestion of IsaLean herbal supplement: Clinical and immunostimulatory findings. Journal of the American Academy of Dermatology. 2019;80(3):801-4.

*Chakka S, *Concha JSS, *Bax CE, Zeidi M, Werth VP. The effects of immunostimulatory herbal supplements on autoimmune skin diseases. Journal of the American Academy of Dermatology. 2020.

Immunostimulatory herbal supplement use among dermatology patients at Penn



Herbal supplement use is **3.47x** more common in DM than in CLE & AIBD ($p = 0.0032$) and **4.0x** more common in DM than in healthy controls ($p = 0.0016$).

Spirulina use **3.63x** more common in DM than in healthy controls ($p = 0.0069$) and **4.92x** more common in DM than in CLE and AIBD ($p = 0.0027$).

Immunostimulatory herbs

They may be found in:

- BOLTHOUSE FARM
- HEALTH-ADE KOMBUCHA
- SYNERGY KOMBUCHA
- NAKED JUICE
- SUJA
- RAW JUICE GURU
- SMARTFRUIT
- JUICE PLUS
- ROBITUSSIN
- MELATONIN
- AND MANY OTHER PRODUCTS!

Neutrofol

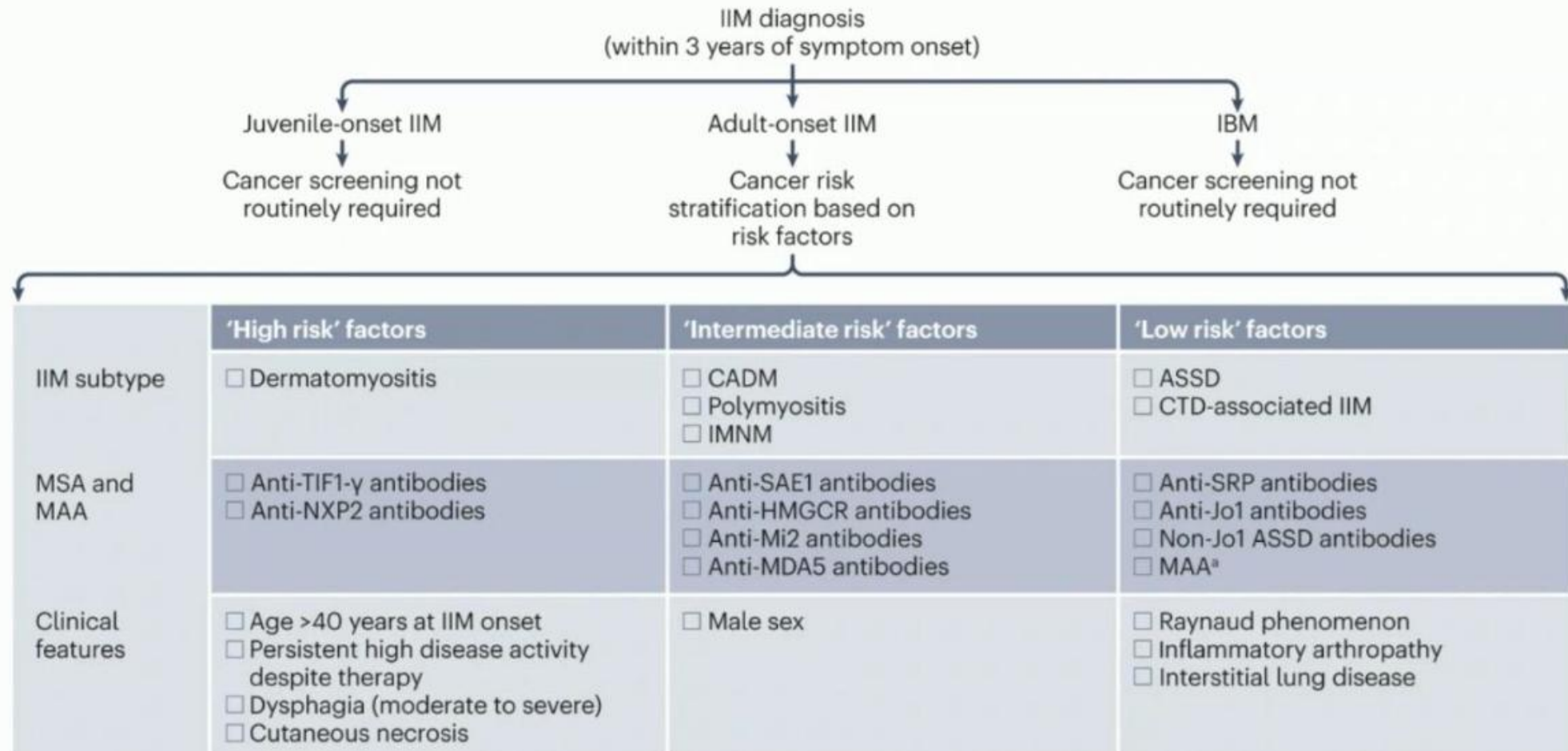


Weiner JD, et al. *Lupus Sci Med.* 2025 Dec 31;12(2):e001803.

1. Zeidl M, Chansky PB, Werth VP. Acute onset/flare of dermatomyositis following ingestion of IsaLean herbal supplement: clinical and immunostimulatory findings. *Journal of the American Academy of Dermatology*, 2018
2. Barak V, Halperin T, Kalickman I. The effect of Sambucol, a black elderberry-based, natural product, on the production of human cytokines: I. Inflammatory cytokines. *European Cytokine Network*, 2001

*Nature Reviews
Rheumatology* 19:805–
817, 2023

Stratification of Cancer Risk



Screening Recommended based on risk

Basic screening panel

- Comprehensive history
- Comprehensive physical examination
- Complete blood count
- Serum liver function tests
- Serum ESR and/or plasma viscosity
- Serum CRP
- Serum protein electrophoresis
- Urinalysis
- Plain chest X-ray radiograph

Enhanced screening panel:

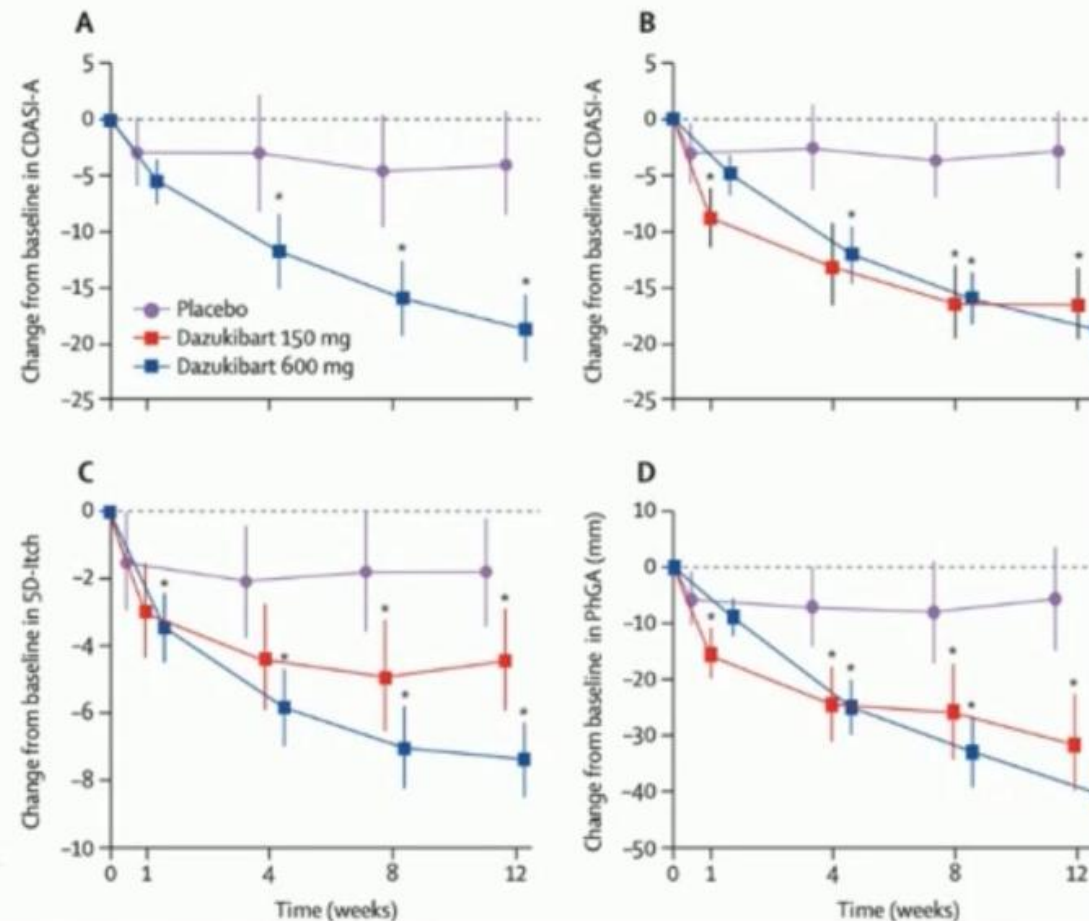
- CT scan of the neck, thorax, abdomen and pelvis
- Cervical screening^b
- Mammography^b
- Prostate-specific antigen^b
- CA-125
- Pelvic or transvaginal ultrasonography for ovarian cancer
- Faecal occult blood^b

Dazukibart (Anti-IFN β monoclonal antibody)

- Multicenter double-blinded randomized placebo-controlled phase 2 trial
- 75 patients, 15 to 150 mg, 37 to 600 mg, 23 to placebo
- Initial skin cohort, then smaller muscle cohort
- CDASI primary outcome
- Dazukibart resulted in a pronounced reduction in disease activity

Dazukibart (Anti-IFN β monoclonal antibody)

Mean change
in CDASI



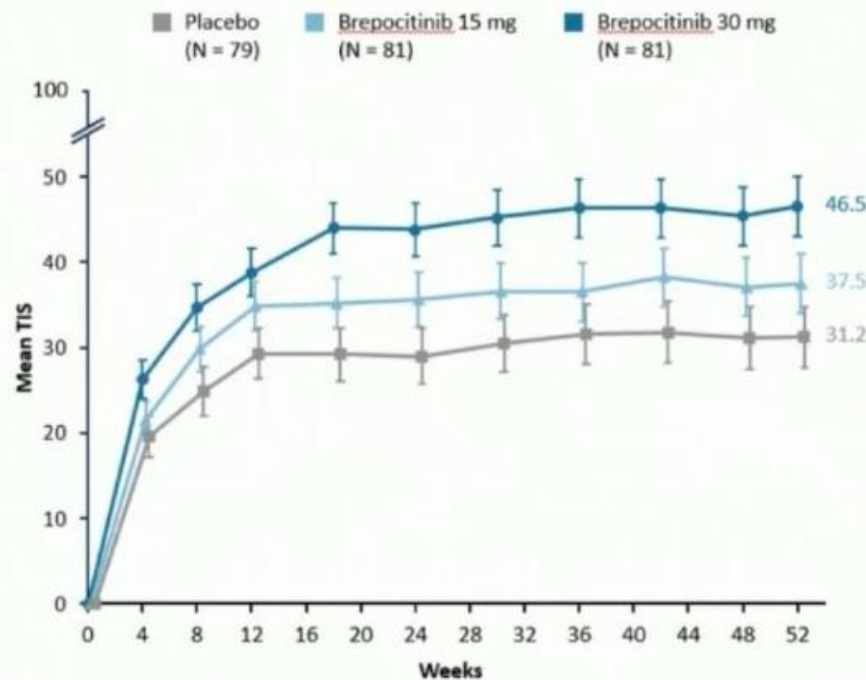
FDA NEWS RELEASE

FDA Approves First Oral Drug Indicated to Treat Dermatomyositis in Adults

Brepocitinib (TYK2/JAK1 inhibitor)

- Data from phase 3 reported out recently, led to approval by the FDA a month ago
- 241 participants were randomized: 81 to brepocitinib 30 mg, 81 to brepocitinib 15 mg, and 79 to placebo.
- At week 52, mean TIS was 46.5, 37.5, and 31.2 for the brepocitinib 30 mg, brepocitinib 15 mg, and placebo groups, respectively (difference, brepocitinib 30 mg vs. placebo, 15.3 points; 95% confidence interval, 6.7–24.0; P=0.0006).
- Benefit across all nine key secondary endpoints, with improvement evident by week 4.

Brepocitinib: TIS at week 52 and GC reduction



Corticosteroid Reduction Outcomes (Prednisone-Equivalent Dose)

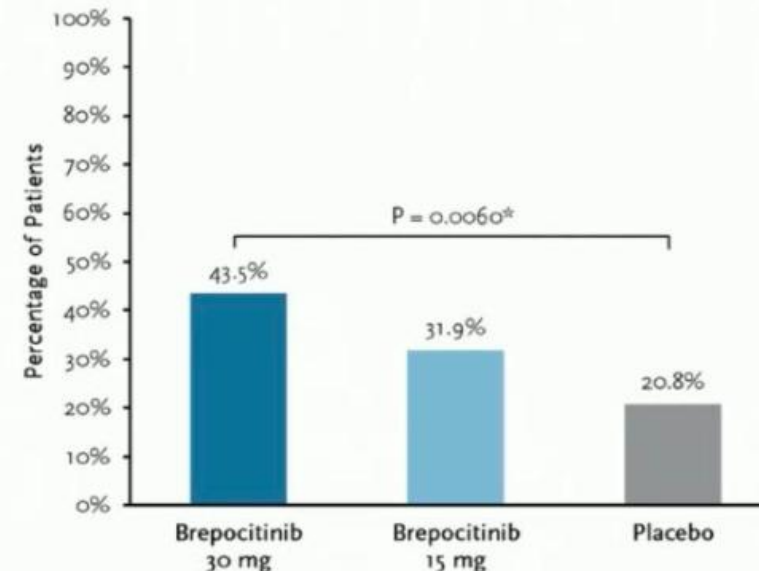
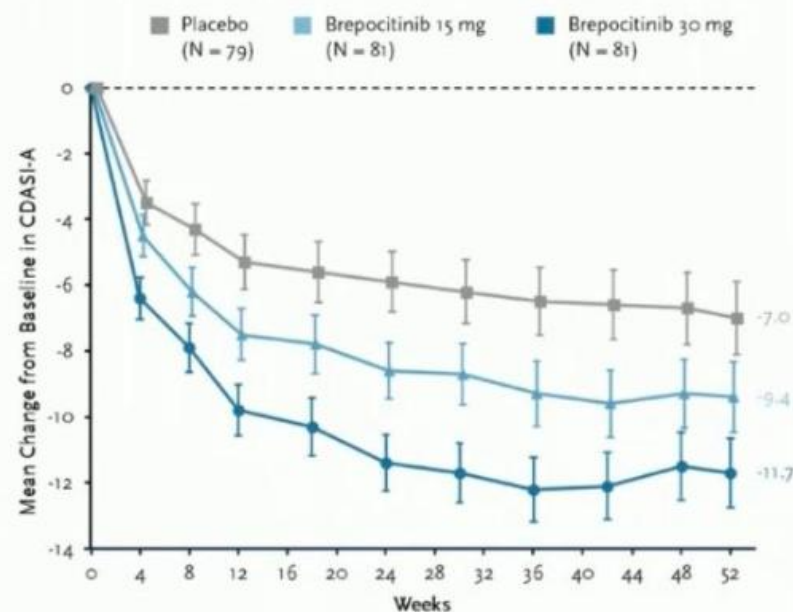
Treatment Group	Baseline steroid dose (mg/day), mean (SD)	Proportion achieving ≤ 2.5 mg/day by weeks 48-52	Proportion achieving 0 mg/day by weeks 48-52
Brepocitinib 30 mg (N* = 60)	12.2 (5.7)	62%	42%
Brepocitinib 15 mg (N* = 58)	10.7 (6.2)	41%	31%
Placebo (N* = 64)	11.3 (5.9)	34%	23%

*Number of patients on corticosteroids at baseline

Brepocitinib: CDASI Change

Change in CDASI-A Score
from Baseline to week 52

CDASI-A ≤ 5 by week 52 in
moderate to severe skin disease



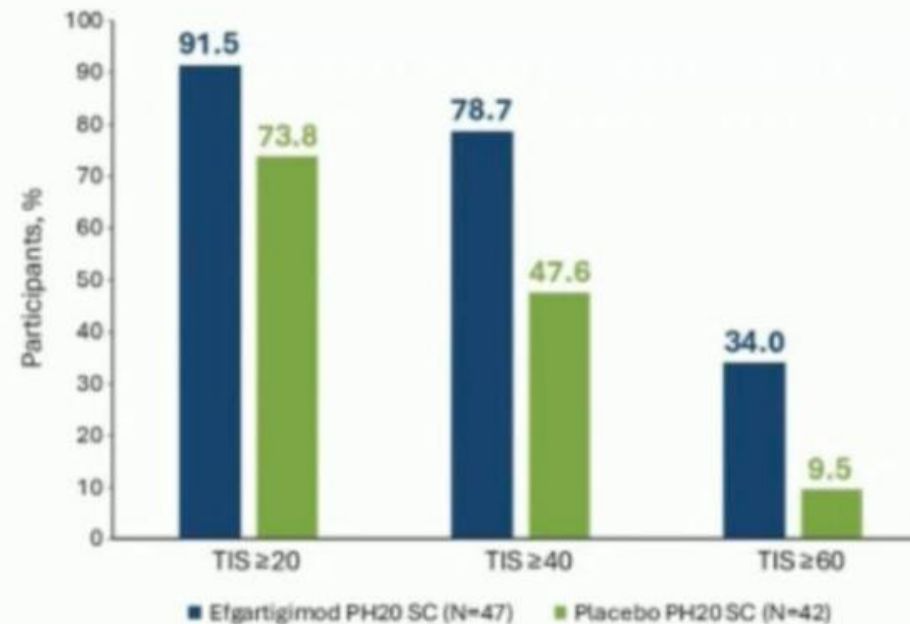
Efgartigimod (FcRn Antibody)

- ALKIVIA Phase 2/3 study evaluated three myositis subtypes (IMNM, ASyS, DM)
- Data from Phase 2 show significant improvement in muscle strength and physical function when treated with efgartigimod.
- TIS improvement was observed in a majority of efgartigimod-treated patients across all six core measures, and the primary endpoint was met.

Efgartigimod (FcRn Antibody)

- ALKIVIA Phase 3 study evaluated three myositis subtypes (IMNM, ASyS, DM)
- **Study met its primary endpoint ($p=0.0011$)**
- In the combined immune-mediated necrotizing myopathy (IMNM) and dermatomyositis (DM) population, patients treated with efgartigimod demonstrated statistically significant and clinically meaningful 15.4-point greater improvement in mean Total Improvement Score (TIS) at Week 52 versus placebo (47.95 vs 32.56).

Efgartigimod (FcRn Antibody): Proportion with TIS levels



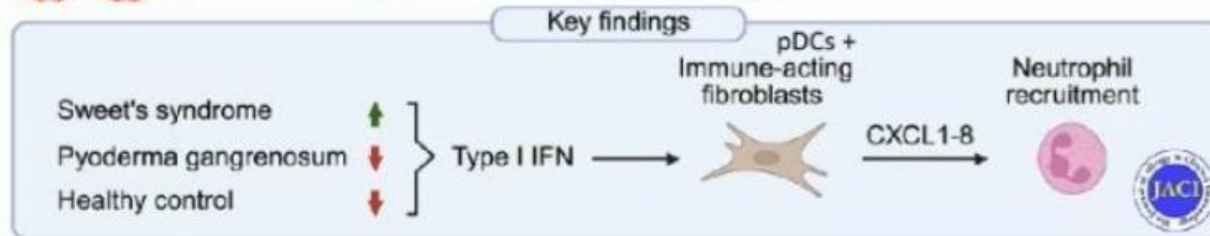
Ongoing/Future studies

- Anti-Interferon- β (Phase 3 ongoing)
- Anifrolumab (Phase 3)
- Efgartigimod (Phase 3)
- CD19-CAR T cells (RESET-Myositis)
- JAK1/TYK2 inhibitor (Brepocitinib)- just approved by FDA
- Many ongoing studies: All in classic DM

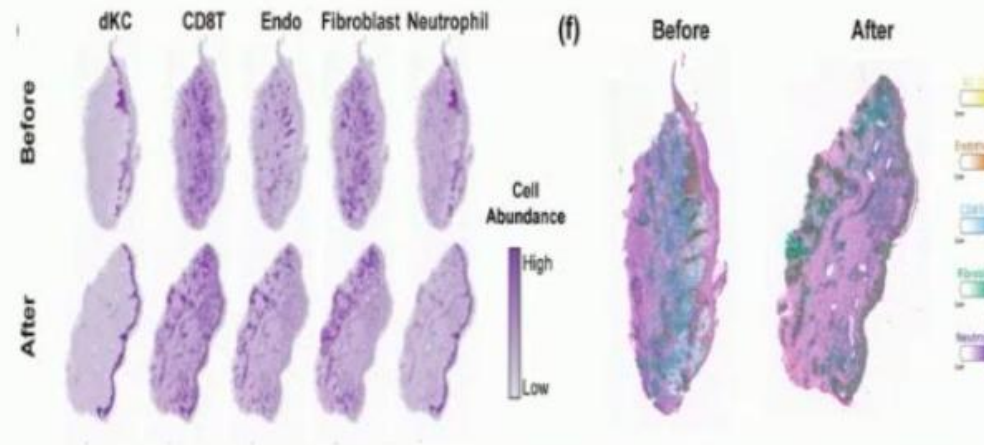
Neutrophil – Fibroblast interaction



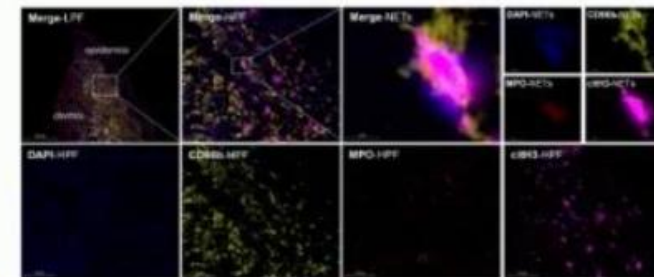
Positionally distinct interferon-stimulated dermal immune-acting fibroblasts promote neutrophil recruitment in Sweet's syndrome



Cavagnero et al., 2025



Extracellular traps

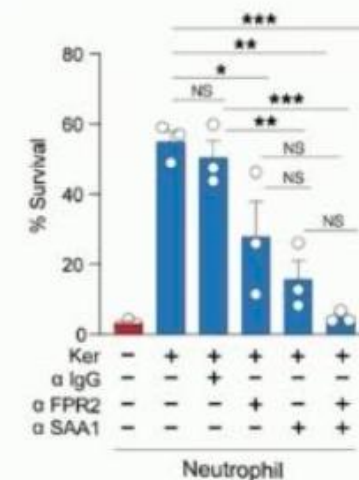
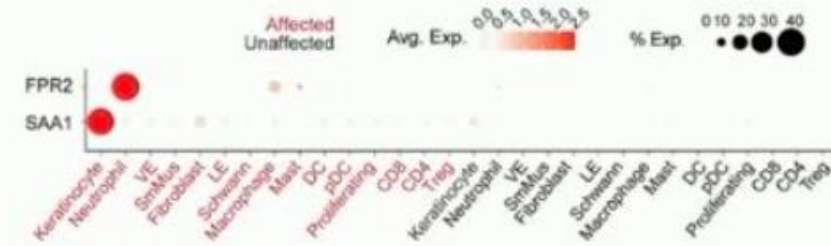
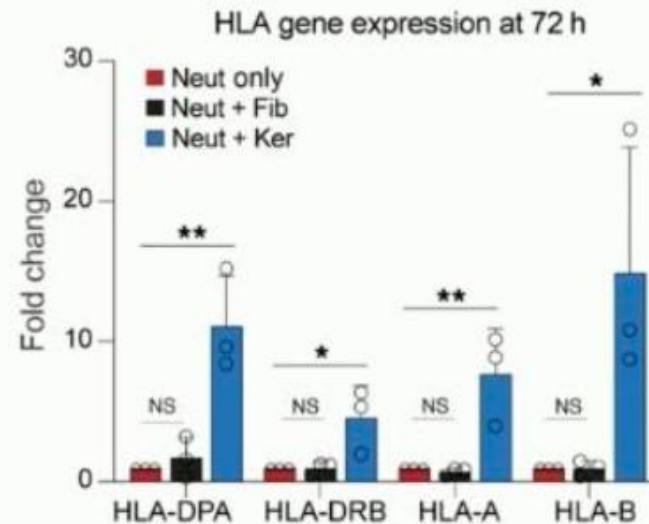
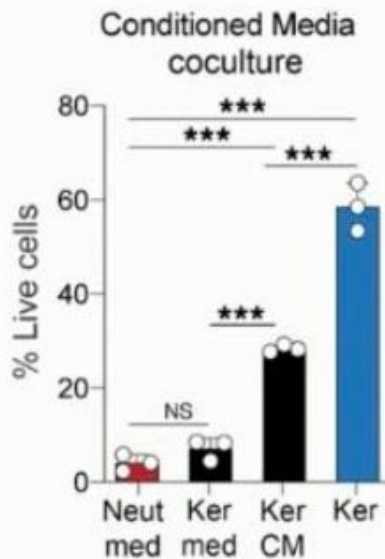


Fu et al. 2026



Neutrophil – Keratinocyte interaction

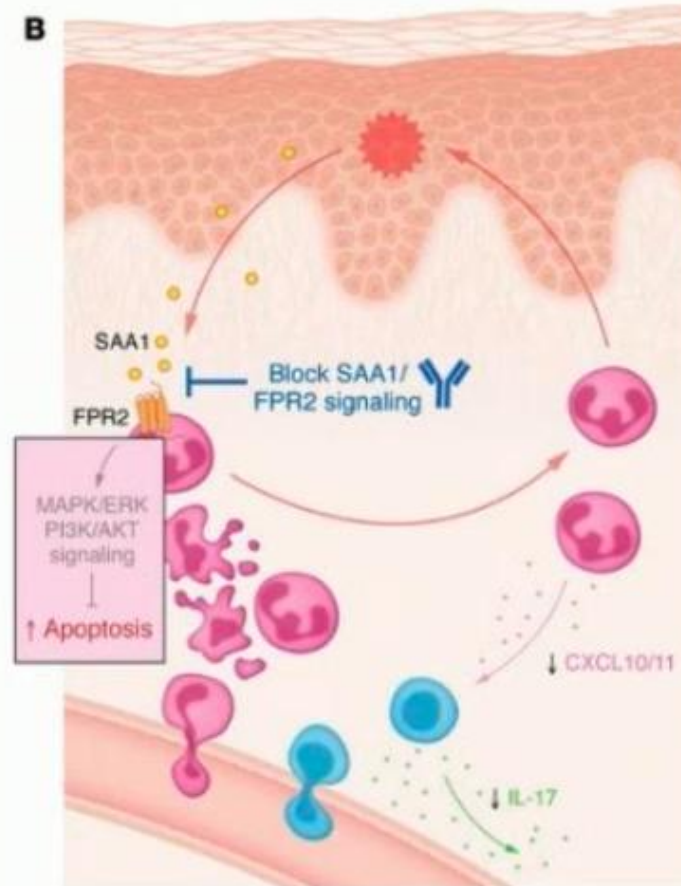
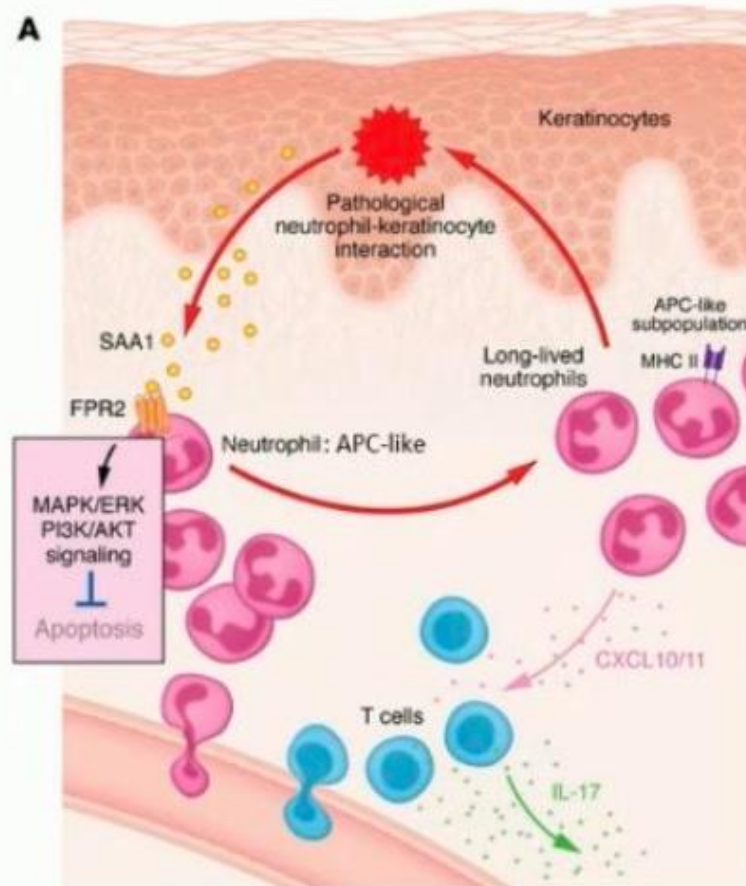
Tahara et al. 2025



Neutrophils in Sweet's live x10 longer, 30% of neutrophils display antigen processing (APC)-like phenotype



Neutrophil – Keratinocyte interaction



Dual inhibition?



Treatment of Sweet Syndrome

- Corticosteroids
- Dapsone
- Colchicine
- Potassium Iodine
- Interferon Pathways
- Spesolimab
- JAK-Inhibitors
- SAA1/FPR2-Inhibitors

?

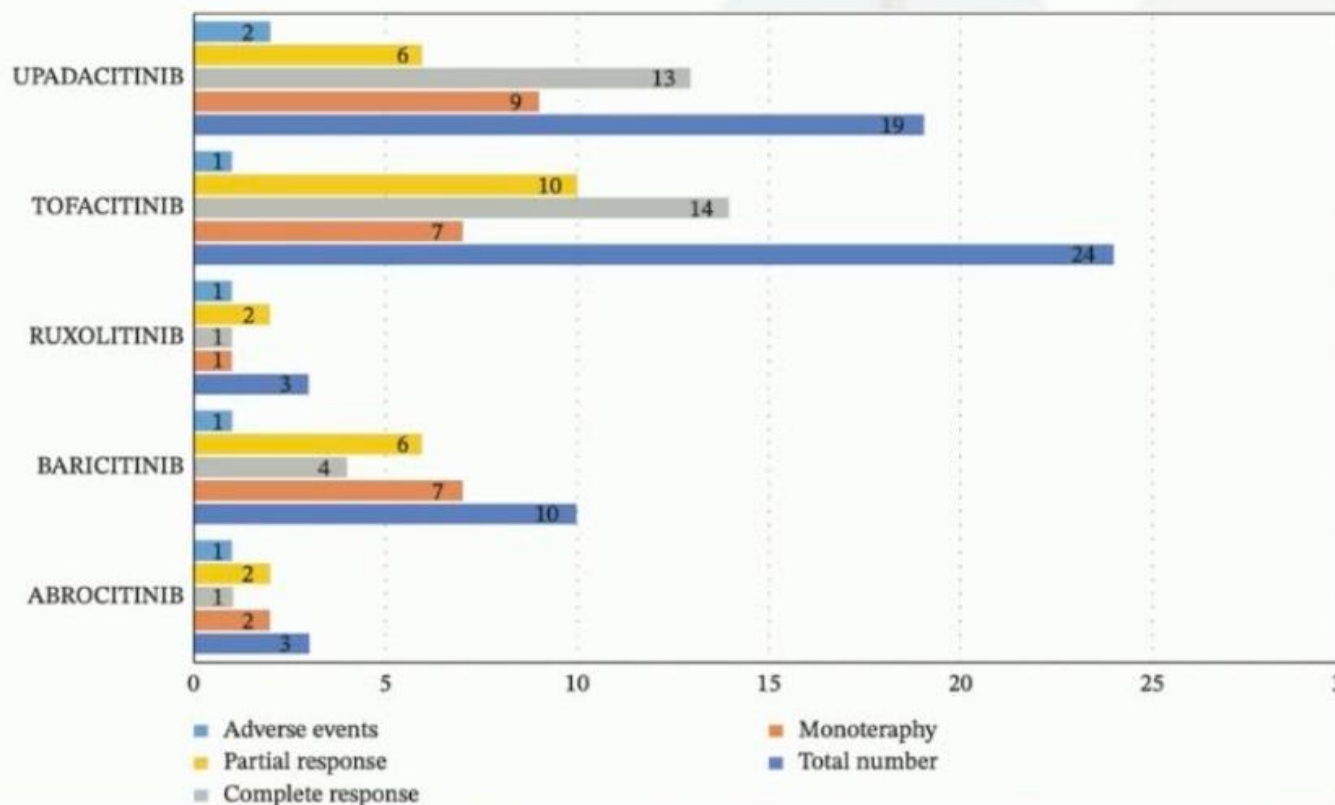
TREATMENT – IL-23i refractory PG

- Retrospective, n=18 (lesions n=52) refractory PG (median of 4 prior treatments)
- Guselkumab (n=11), Risankizumab (n=6), Tildrakizumab (n=1)
- Concurrent oral corticosteroids (n=16)
- IBD 16.7%, hematologic disorders 16.7%
- Classic PG (77.8%), pustular/ulcerative (16.7%), vegetative (5.6%)
- **Progressive significant reduction** from month 1 or 3 onward: total ulcer area (mean 95cm² (22-700) at baseline – 9cm² at month 12 (0-88)), number of active ulcers, ulcer depth, IGAPg, pain intensity, seroid-sparing effect.



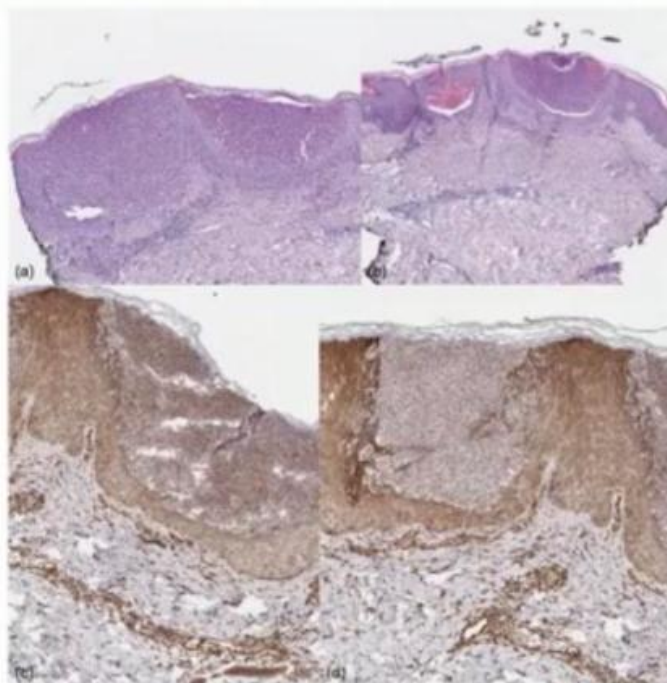
TREATMENT – JAK inhibitors (Systematic review)

- **59 patients:** Tofa (n=24), Upa (n=19), Bari (n=10), Abro (n=3), Ruxo (n=3)
- **55.9% complete response**, mean time to response 4.56 months
- **44.1% partial response**, mean time to response 2.78 months
- Comorbidities: 86.4% ≥ 1 (23.7% IBD, 18.6% RA, 10.1% malignancy)
- **44.1% monotherapy JAK**
- **10.1% adverse events** (high blood pressure, mild anemia, decreased renal function, acneiform eruption)



Subcutaneous Spesolimab for Amicrobial Pustulosis of the Folds

Angelo Valerio Marzano^{1,2} | Luca Bettolini¹ | Federica Derlino¹ | Luisa Sarno¹ | Stefano Buffon¹ | Giovanni Genovese¹ |
Francesca Laura Boggio³ | Chiara Moltrasio^{1,2} | Annapaola Pilliu^{1,2} | Marco Brevi⁴ | Carlo Alberto Maronese^{1,2}



The Japanese
Dermatological Association

Amicrobial pustulosis of the folds (APF)

EADV CONGRESS
VIENNA 2026
30 SEP-3 OCT**Amicrobial Pustulosis of the Folds Successfully Treated With Apremilast: Report of Two Cases and Review of the Literature**Luca Bettolini^{1,2} | Carlo Alberto Maronese^{1,3} | Stefano Bighetti² | Giovanni Genovese¹ | Luisa Sarno¹ | Stefano Buffon^{1,3} | Francesca Laura Boggio⁴ | Federica Derlino¹ | Angelo Valerio Marzano^{1,3}

F, 19 with a 5-year history of undifferentiated connective tissue disease and SLE-like features (arthralgias, positive ANA and anti-SSA antibodies)
Pustular eruption that had first manifested 3 years earlier



BEHÇET-LIKE SYNDROMES

Symptoms similar to BD (OA, GU, pustules, joint, intestinal, vascular, fever...)

Monogenic immune defects

Myeloproliferative diseases

Infections

Medications

MYELOPROLIFERATIVE; Trisomy 8

- ❑ Common in hematological diseases (MDS, CML)
- ❑ Also autoinflammatory condition
- ❑ *NRAS*, *JAK2*, *MEFV*, *PTPN11*, *SALL1* genes
- ❑ Activation of the NF- κ B pathway;

Overexpression of IL-6, IL-7R, TGF- β , IL-18 pathway genes
Neutrophil & Monocyte hyper-reactivity

EA CONGRESS
DV 2026MIMICS
MEDICATIONS**Secukinumab**-Induced Delayed **Behcet**-Like Reaction in a Patient with Plaque Psoriasis: A Case Report.

Wei Y, Zhang P, Chuan J, Ye J, Liu T.

Clin Cosmet Investig Dermatol. 2026 Jan 8;19:567115. doi: 10.2147/CCID.S567115. eCollection 2026.

Secukinumab induced paradoxical worsening of mucocutaneous features of **Behcet's disease**.

Goyal A, Meshram AS, Gupta V.

Indian J Dermatol Venereol Leprol. 2025 Apr 12:1-3. doi: 10.25259/IJDVL_1883_2024. Online ahead of

Paradoxical **Behcet's Disease** after Ixekizumab: A Case Report and Literature Review.

Ren YK, Ren L, Sun W, Liu HY, Guo SP.

Indian J Dermatol. 2025 Jan-Feb;70(1):42-46. doi: 10.4103/ijdd.719_24. Epub 2024 Dec 30.

Review > Rheumatol Int. 2026 Mar 2;46(3):57. doi: 10.1007/s00296-026-06096-2.

Behçet's disease occurred after brodalumab initiation in a patient with chronic non-bacterial osteitis: a case-based literature reviewKoji Suzuki ¹, Mitsuhiro Akijama ², Koichi Saito ¹, Yuko Kaneko ³

- Onset of paradoxical reactions ;1 week-10 months
- Microbial dysbiosis?
- Compensatory ↑ in IL-23 → stimulation

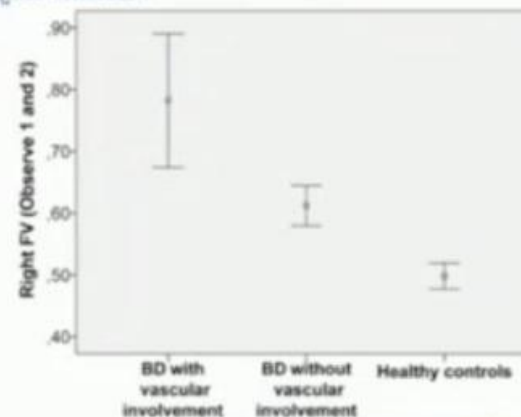
EA CONGRESS
DV 2026

DIAGNOSIS

- BD patients have ↑ FV thickness
- Healthy individuals, RAS, AS, Crohn, systemic vasculitides, venous insufficiency, APAS, deep vein thrombosis
- Sensitivity; >90%, specificity ; >80%
- Diagnostic sensitivity and the specificity rates > 80% for the cut-off value ≥ 0.5 mm

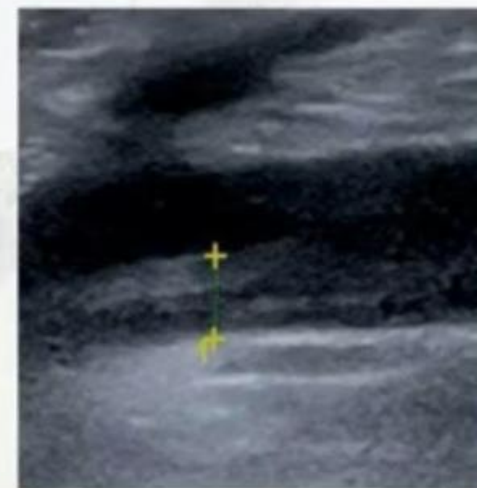
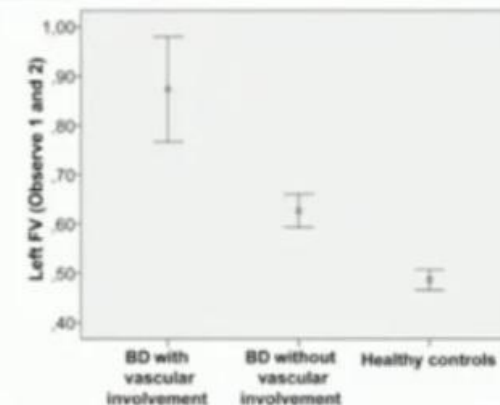
> Rheumatology (Oxford). 2021 Jan 5;60(1):288-296. doi: 10.1093/rheumatology/keaa264.

Femoral vein wall thickness measurement: A new diagnostic tool for Behçet's disease

Fatma Alibaz-Oner¹, Rabia Ergelen², Yasin Yıldız³, Mustafa Aldag⁴, Ayten Yazıcı⁴, Ayşe Cefle⁴, Ertan Koç⁵, Bahar Artım Esen⁶, Gonca Mumcu⁷, Tulin Ergun⁸, Hristina Nisic⁹

> Rheumatology (Oxford). 2024 Mar 1;63(3):e86-e87. doi: 10.1093/rheumatology/kead476.

Common femoral vein wall thickness measurement as a diagnostic test in suspected Behçet's disease

Fatma Alibaz-Oner¹, Rabia Ergelen², Seda Kuluğ-Ağaçkaran³, Fatma Temiz⁴, Tulin Ergun⁵, Haner Direskeneli⁶



Clinical Trial > Ann Rheum Dis. 2026 Jul;85(7):1425-1435. doi: 10.1016/j.ard.2026.01.014.

Epub 2026 Feb 25.

Efficacy and safety of mufemilast in patients with Behçet's syndrome: a phase 2 randomised clinical trial

Clinical Trial > Arthritis Res Ther. 2026 Mar 3;28(1):83. doi: 10.1186/s13075-026-03778-x.

Upadacitinib for refractory Behçet's syndrome: a multi-centre, single-arm trial

Nat Commun. 2026 Jan 7;17:1344. doi: [10.1038/s41467-025-68100-w](https://doi.org/10.1038/s41467-025-68100-w)

Efficacy and safety of low-dose interleukin 2 for Behçet's syndrome: a randomized, placebo-controlled, double-blind, phase 2 clinical trial

Review > Semin Arthritis Rheum. 2026 Oct;80:153040. doi: 10.1016/j.semarthrit.2026.153040.

Epub 2026 Jul 6.

Efficacy and safety of Janus kinase inhibitors in Behçet's disease: A systematic literature review

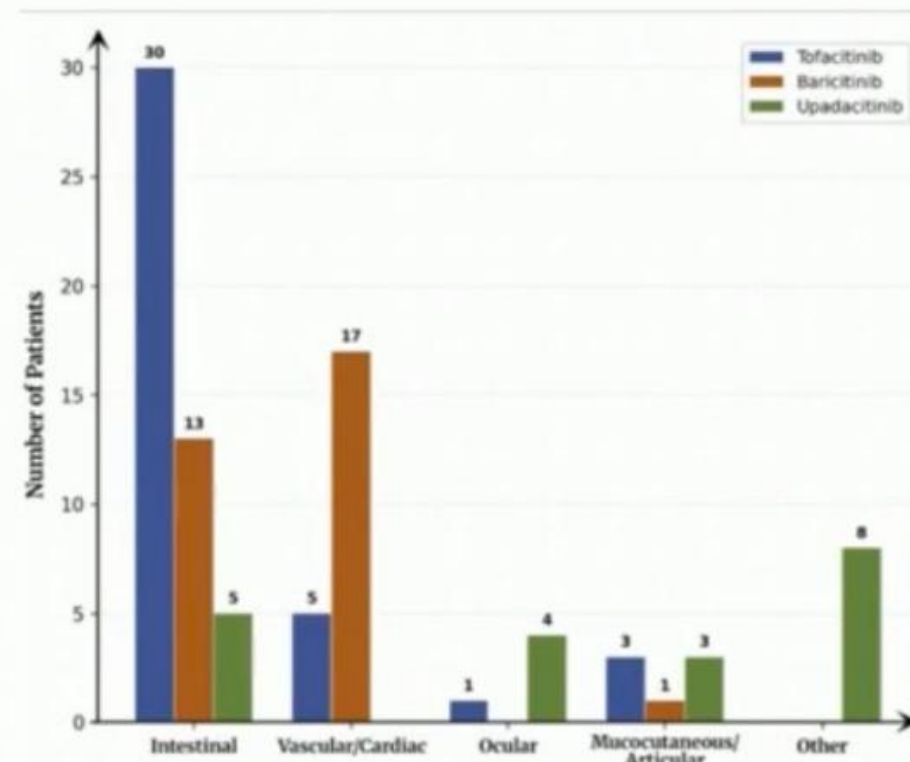
17 studies comprising 99 BD patients;

- Tofacitinib, n: 32; 2X5 mg/d
- Baricitinib, n: 31; 2-4 mg/d
- Upadacitinib, n: 36; 15-45 mg/d

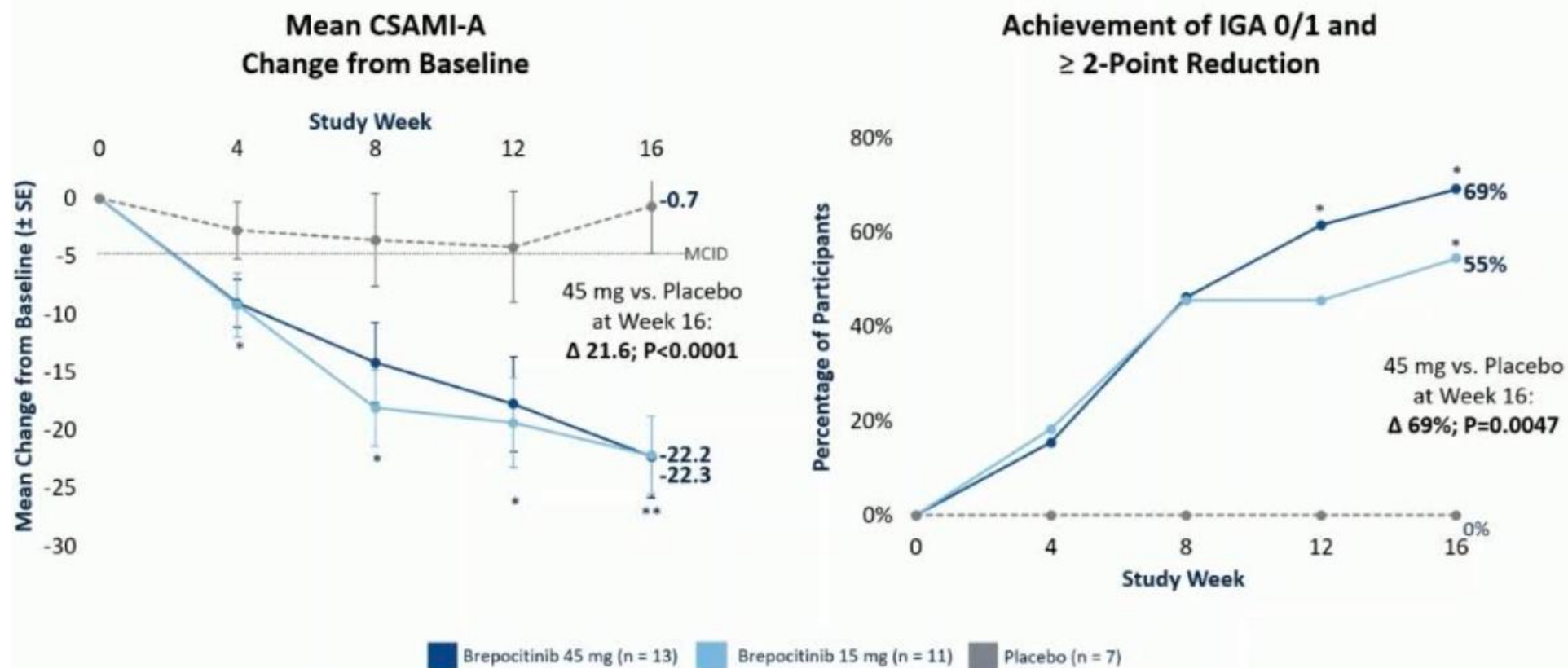
UPA: Overall response rate 85.2%

BARI: Overall response rate 76.5%

Infections, H. Zoster, ↑liver enzymes, lipids
No thrombotic risk



Brepocitinib Achieved Rapid, Deep, Sustained Benefit on Cutaneous Sarcoidosis Disease Activity Over 16 Weeks



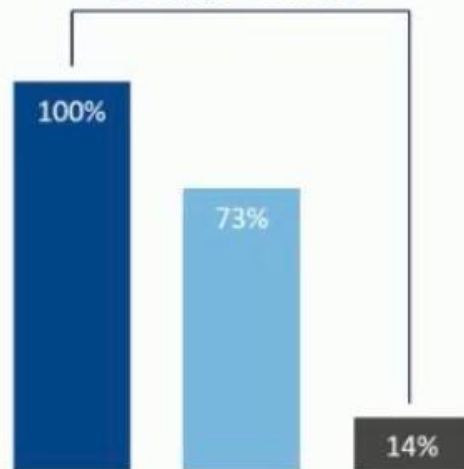
* $P < 0.05$; ** $P < 0.0001$

CSAMI-A: Cutaneous Sarcoidosis Activity and Morphology Instrument-Activity Score; MCID: minimal clinically important difference; IGA: Investigator's global assessment

Dose-dependent Benefit of Brepocitinib Seen on High-Bar Clinical Endpoints

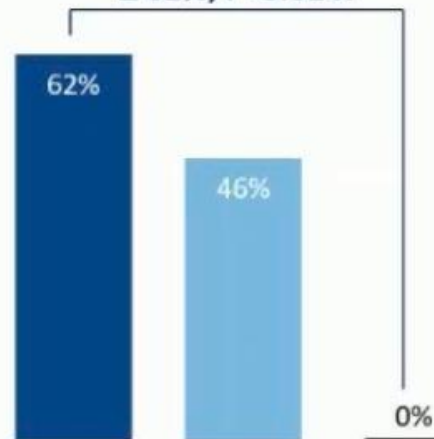
**Achievement of CSAMI-A
≥ 10-point Reduction at Week 16**

45 mg vs. Placebo:
Δ 86%; P=0.0002



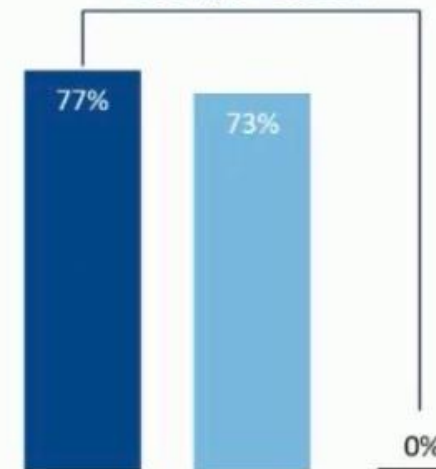
**Achievement of CSAMI-A < 5
(Functional Remission) at Week 16**

45 mg vs. Placebo:
Δ 62%; P=0.0147



**Achievement of CSAMI-A
≥ 50% Reduction from Baseline at Week 16**

45 mg vs. Placebo:
Δ 77%; P=0.0031



■ Brepocitinib 45 mg (n = 13) ■ Brepocitinib 15 mg (n = 11) ■ Placebo (n = 7)

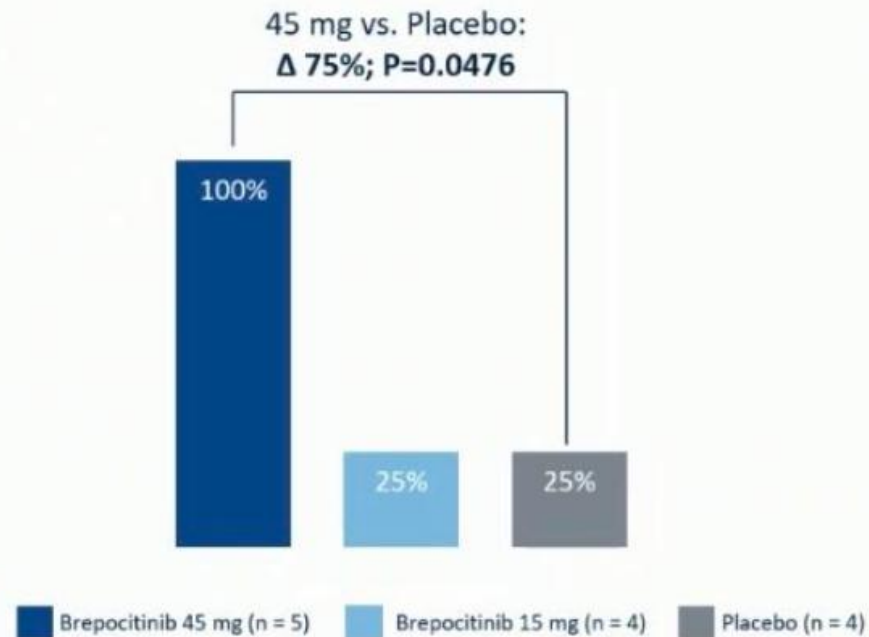
100% of Participants With Lupus Pernio Achieved CSAMI-A Response With Brepocitinib 45 mg

All 45 mg participants with lupus pernio achieved ≥ 10 -point CSAMI-A improvement by Week 16

Baseline Lupus Pernio Participant



Achievement of CSAMI-A ≥ 10 -point Reduction at Week 16 in Patients with Lupus Pernio



All P values are nominal.

CSAMI-A: Cutaneous Sarcoidosis Activity and Morphology Instrument-Activity Score; MCID: minimal clinically important difference

Brepocitinib Was Well-Tolerated During Treatment Period, with No SAEs and All AEs Graded Mild or Moderate In Severity

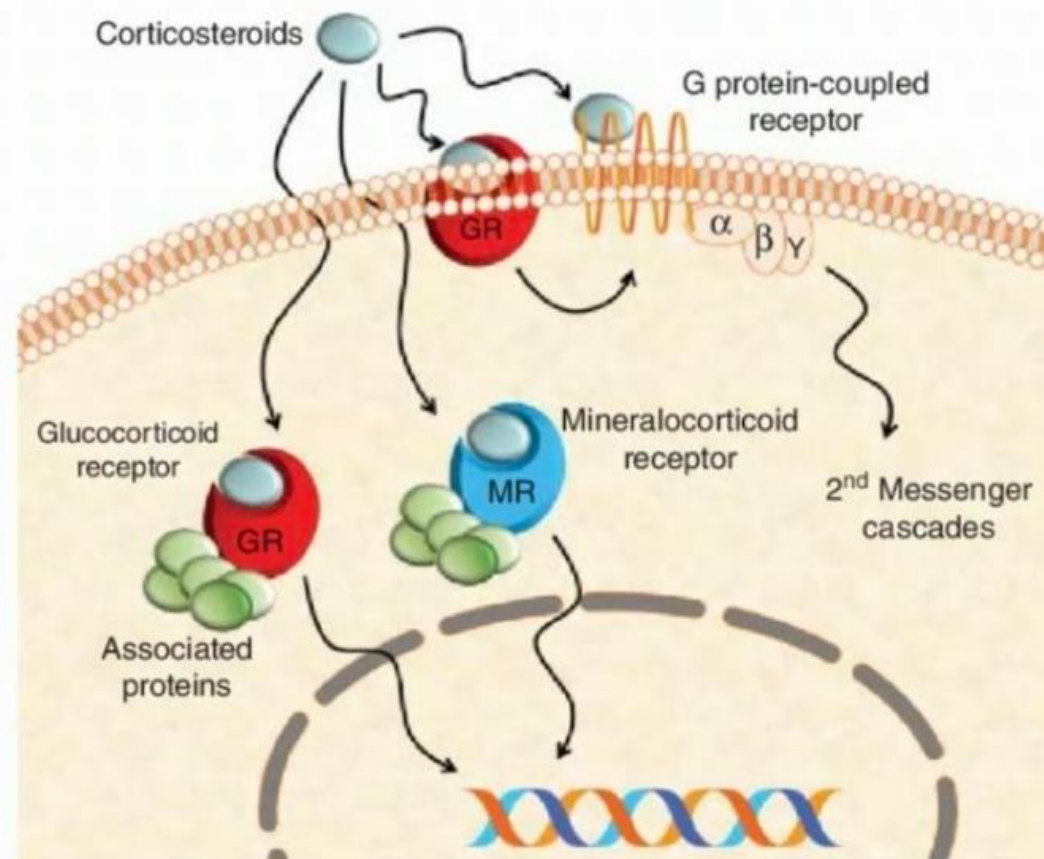
	Brepocitinib 45 mg QD (N=13)	Brepocitinib 15 mg QD (N=11)	Placebo (N=7)
Participants with:			
Adverse Events (AEs)	12 (92%)	6 (55%)	6 (86%)
Death	0	0	0
AEs graded as severe	0	0	0
Serious Adverse Events (SAEs)	0	0	0
AEs leading to treatment discontinuation	1 (8%)	1 (9%)	1 (14%)
AEs leading to study discontinuation	0	0	0
Adverse Events of Special Interest (AESI):			
Creatine Kinase (CK) Increased	1 (8%)	0	0
Anemia	1 (8%)	0	0
Viral reactivation	0	0	0
Malignancy	0	0	0
Major adverse cardiovascular event	0	0	0
Venous thromboembolism	0	0	0
Liver enzyme elevation	0	0	0
Other AESIs	0	0	0



van Lümig PPM, Pasch MC. SAD 2018;4:156-9
Nail Sarcoidosis Presenting with Longitudinal Erythronychia

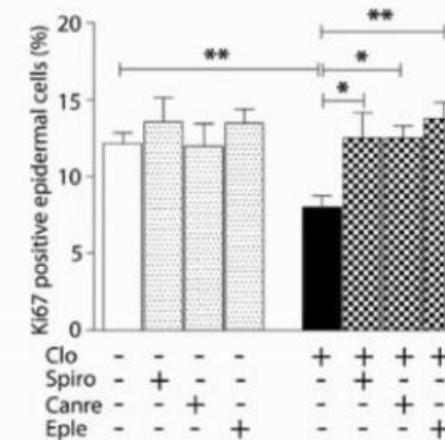
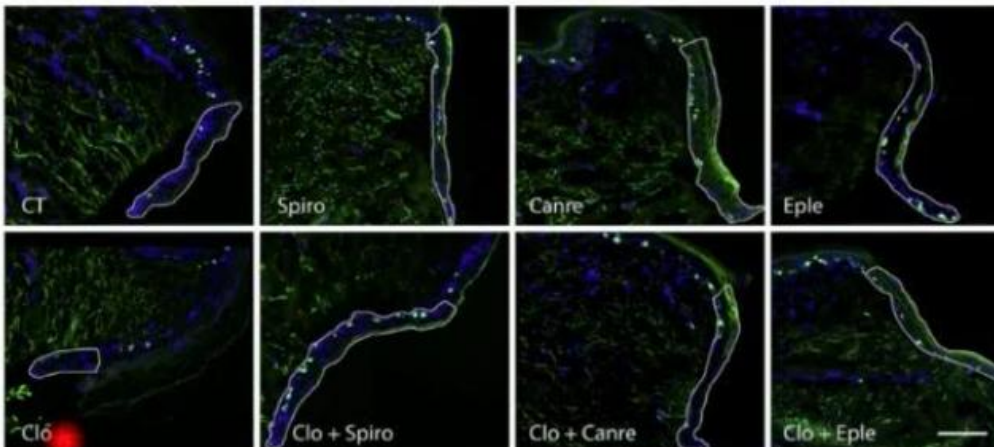
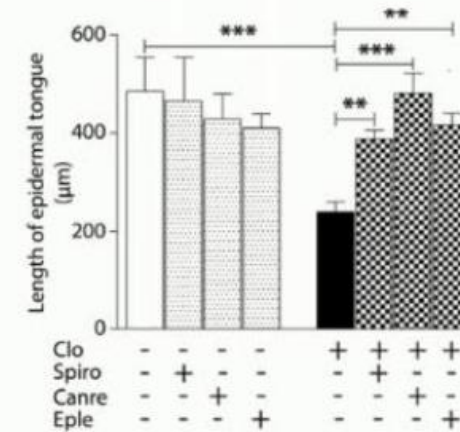
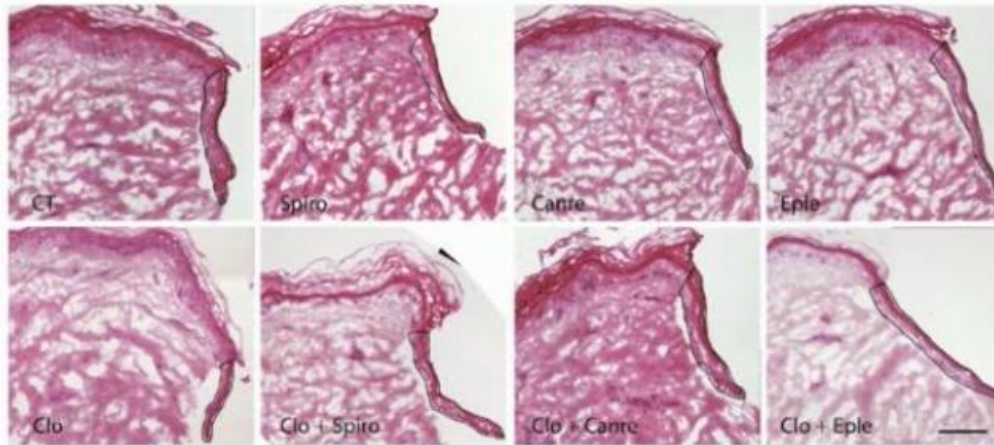


Cortisol binds receptors: GR but also MR



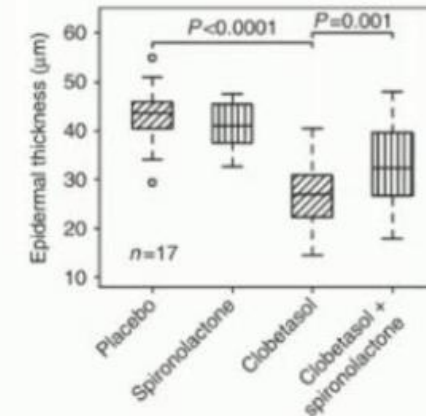
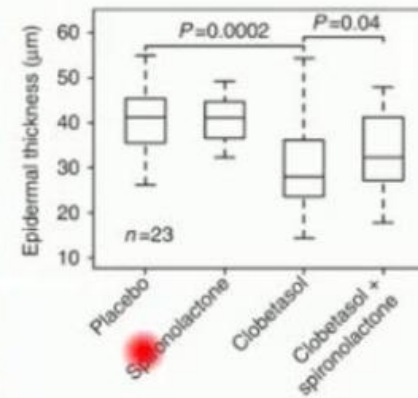
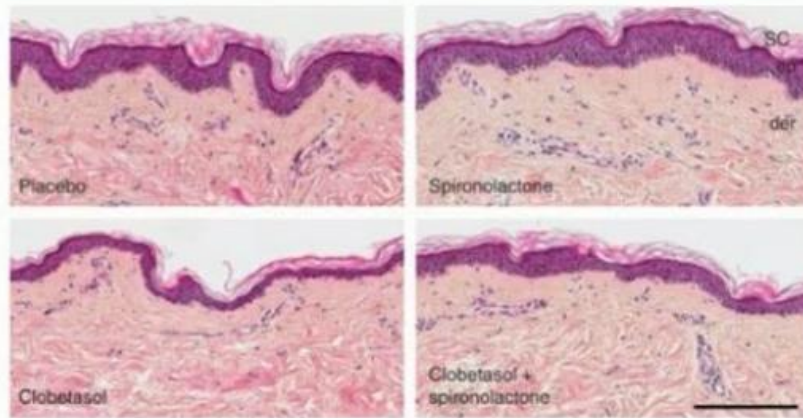
Jeffrey G. Tasker et.al., 2015

MR antagonism rescues the defect of epidermal outgrowth induced by GC in human skin explants

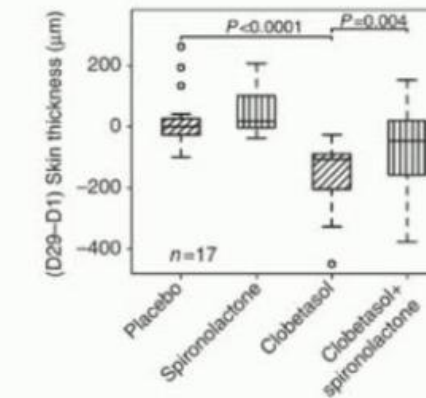
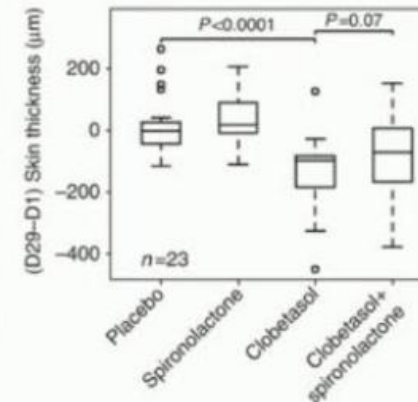
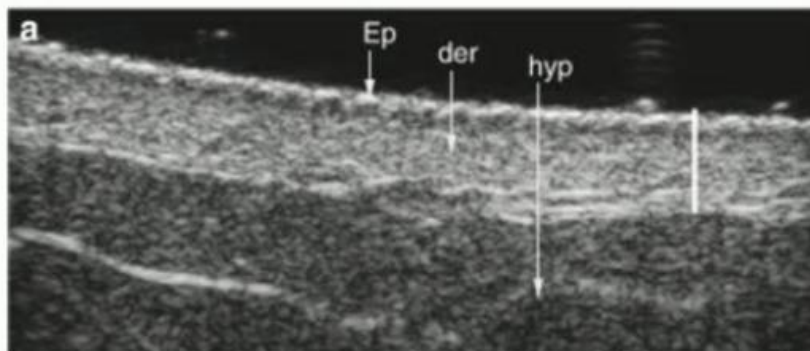


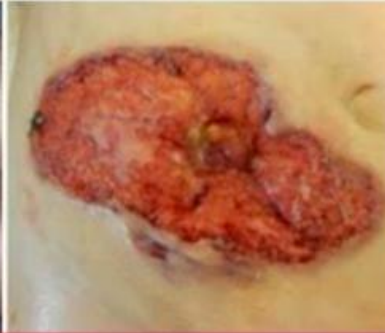
SPIREPI clinical trial: topical administration of the MR antagonist spironolactone limit GC-induced skin atrophy in healthy volunteers

Histological sections



Ultrasound



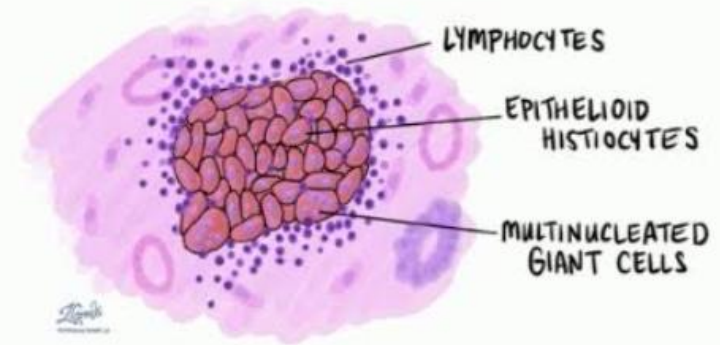
Specific manifestations	Disorders associated with inflammatory bowel disorders	Reactive manifestations	Muco-cutaneous conditions secondary to treatment of inflammatory bowel disorders	Cutaneous manifestations secondary to nutritional malabsorption
Continuous/contiguous Crohn's disease Metastatic Crohn's disease	Aphthous stomatitis Erythema nodosum Psoriasis Epidermolysis bullosa acquisita	Pyoderma gangrenosum Sweet's syndrome Bowel-associated dermatosis-arthritis syndrome Aseptic abscess ulcers Pyodermatitis-pyostomatitis vegetans SAPHO syndrome PAPA syndrome	Adverse muco-cutaneous reactions (injection site reactions, infusion reactions, paradoxical reactions, eczematiform and psoriasiform reaction, life-threatening disorders) Cutaneous infections Cutaneous malignancies	Stomatitis Glossitis Angular cheilitis Pellagra Scurvy Purpura Acrodermatitis enteropathica Phrynoderma Seborrheic-type dermatitis Hair and nail abnormalities
				

EA CONGRESS
DV 2026

“Metastatic” Crohn’s disease or non-contiguous cutaneous CD

SPECIFIC MANIFESTATIONS

- Today, the more accurate term is **non-contiguous cutaneous CD** rather than “metastatic” Crohn’s disease (Mountain, 1970)
- Characterized by non-caseating cutaneous granulomas distant from the site of intestinal disease
- **Sites:** any skin site (including the **genitals**); the most frequent are the **lower limbs** and **intertriginous areas**
- **No correlation with CD disease course** (more frequently associated with **colorectal forms**)



EA CONGRESS
DV 2026

“Metastatic” Crohn’s disease or non-contiguous cutaneous CD

SPECIFIC MANIFESTATIONS

Children

Genital lesions predominate (~90 % of cases¹):

type of skin lesions	%
swelling	82.0
nodules/plaques	4.9
ulcers	4.9

Non-genital skin lesions (in up to 16 % of cases¹):

papules/nodules/plaques	8.2
swelling	4.9
ulcers	3.3

Special features

rarely ulcers in the intertriginous area

rarely skin tags/nodules on the genitals

Adults

Genital manifestations (in up to 60 % of cases²):

type of skin lesions	%
fissures/ulcers	37.0
swelling	35.0
papules/nodules/plaques	2.1

Non-genital skin lesions (~53 % of cases²):

papules/nodules/plaques	28.6
fissures/ulcers	25.0
swelling	0.7

intertriginous ulcers tend to display a fissured, rhagadiform-like appearance

skin tags/nodules on the genitals possible

DDx: erysipelas, cellulitis, hidradenitis suppurativa, etc.
→ history and physical examination are essential

Epub 2021 May 7.

Metastatic Crohn's disease: an underestimated entity

Franziska Ickrath ¹, Johanna Stoevesandt ¹, Lena Schulmeyer ¹, Caroline Glatzel ¹,
Matthias Goebeler ¹, Andreas Kerstan ¹

EA CONGRESS
DV 2026

“Metastatic” Crohn’s disease or non-contiguous cutaneous CD

SPECIFIC MANIFESTATIONS



Epub 2021 May 7.

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Matthias Goebeler ¹, Andreas Kerstan ¹



2026

*The **p-i** concept*

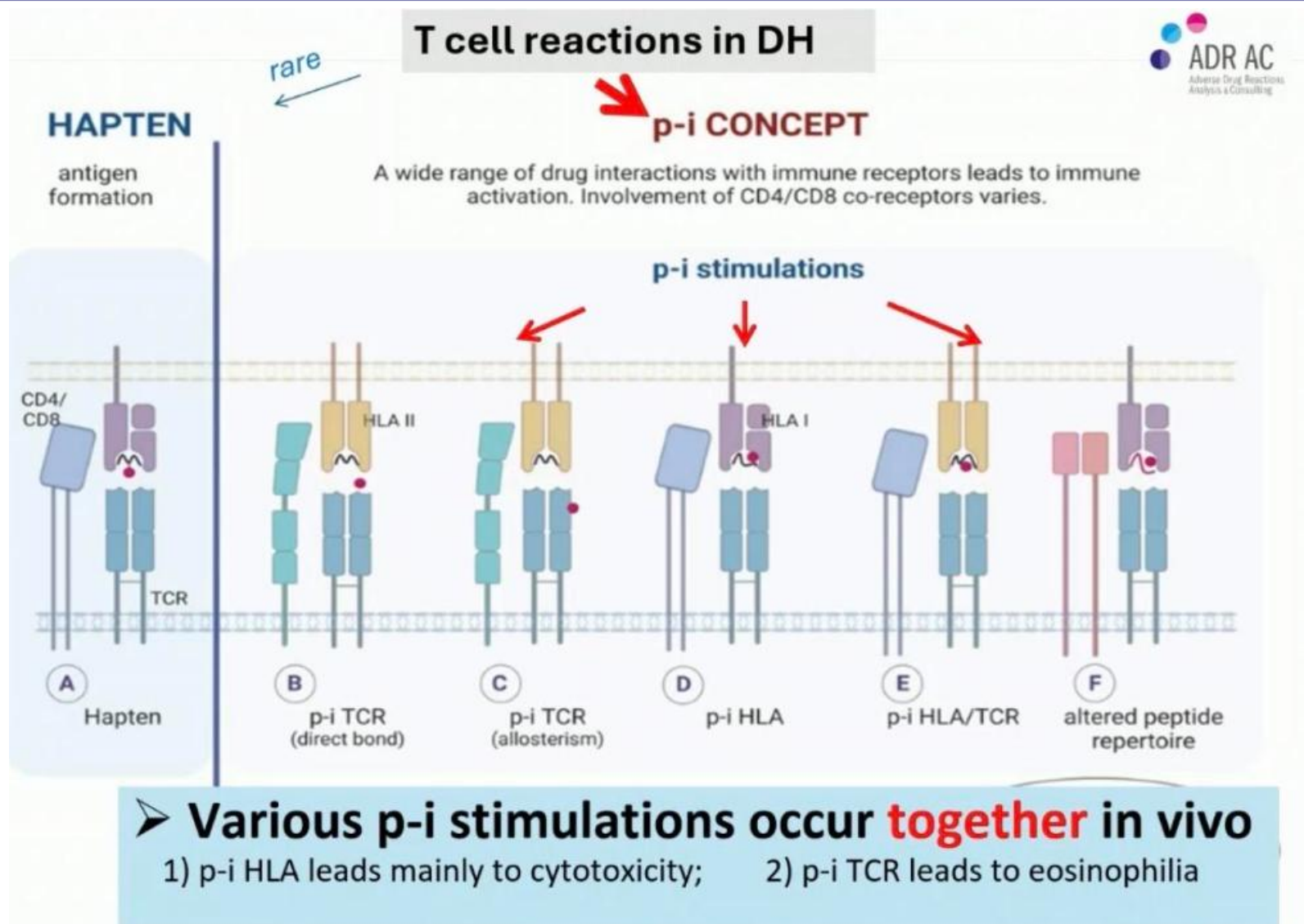
Pharmacological Interaction with Immune Receptors

A chemically inert drug shows an «**off target**» activity (non-covalent binding) with some of the highly variable TCR and/or HLA molecules

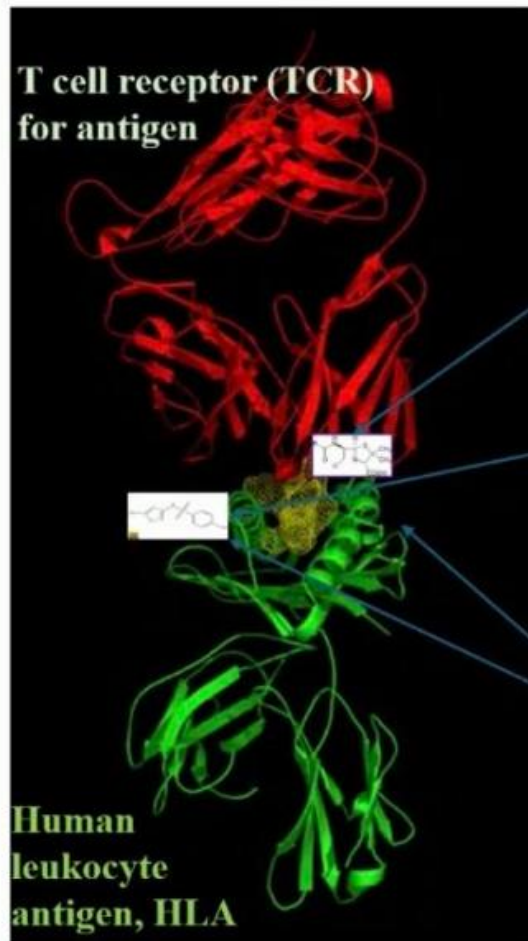
p-i concept: This drug binding (= **p**harmacology) to the (**TCR**>_{peptide}<**HLA**) **complex** can lead to activation and expansion of T cells (= **i**mmunology)

The p-i concept follows **p**harmacological rules (dose dependence, affinity, competition, cross-reactivity, ...) and results in **i**mmune activation (= **p**harmacology is transformed into **i**mmunology)

- The p-i stimulation **differs** from antigen driven immune stimulations with T1, T2 activation and maturation
 - p-i has features of **allo- or superantigen** stimulations
- the p-i stimulated T cells show **cytotoxicity**, high **IFN γ** and often increased **IL-5** production (→ **eosinophilia**)



P-i: the affinity, localization, structure of drug determine the functional outcome



According to **p-i**, the drug can

- 1) **alter the HLA structure:** making self HLA looking foreign (abc model) → **CYTOTOXICITY** in T cells
- 2) Allow more *affine* drug / immune receptor interactions which do not need **co-receptor (CD4, CD8) engagement:** thus Lck mediated signalling is changed → IL-5↑, **EOSINOPHILIA**
- 3) **type of drug** → bias to more IL-5/IL13 vs IFN γ /GrzB/GL production (data in preparation)

✓

(✓)

(✓)

Patch testing is safe in patients with SCAR

CUTANEOUS ALLERGY

BJD
British Journal of Dermatology

A multicentre study to determine the value and safety of drug patch tests for the three main classes of severe cutaneous adverse drug reactions

A. Barbaud,¹ E. Collet,² B. Milpied,³ H. Assier,⁴ D. Staumont,⁵ M. Avenel-Audran,⁶ A. Grange,⁷ S. Amarger,⁸ P. Girardin,⁹ M.-T. Guinépain,¹⁰ F. Truchetet,¹¹ A. Lasek¹² and J. Waton¹ on behalf of the Toxidermies group of the French Society of Dermatology

▪ DRESS	64% (46/72)	} limited by low sensitivity
▪ AGEP	58% (26/45)	
▪ SJS/TEN	24% (4/17)	



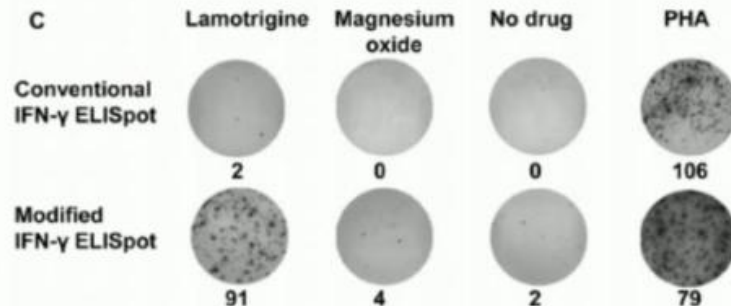
Contents lists available at ScienceDirect

Journal of Dermatological Science

journal homepage: www.jdsjournal.com

Novel interferon- γ enzyme-linked immunoSpot assay using activated cells for identifying hypersensitivity-inducing drug culprits

Kenichi Kato^{a,1}, Asami Kawase^{c,1}, Hiroaki Azukizawa^{a,b,c,*}, Takaaki Hanafusa^{a,d}, Yukinobu Nakagawa^a, Hiroyuki Murota^a, Shimon Sakaguchi^{b,e}, Hideo Asada^c, Ichiro Katayama^a



JOURNAL ARTICLE

In vitro test to confirm diagnosis of allopurinol-induced severe cutaneous adverse reactions [Get access >](#)

J. Klaewsongkram , P. Thantiworasit, N. Suthumchai, P. Rerknimitr, C. Sukasem, P. Tuchinda, L. Chularojanamontri, Y. Srinoulprasert, T. Rerkpattanapipat, K. Chanprapaph, W. Disphanurat, P. Chakkavittumrong, N. Tovanabutra, C. Srisuttiyakorn

British Journal of Dermatology, Volume 175, Issue 5, 1 November 2016, Pages 994–1002, <https://doi.org/10.1111/bjd.14701>

Published: 01 November 2016

Allopurinol-induced SCAR:

- 13 DRESS, 11 SJS/TEN
- 21 controls
- IFN- γ ELISpot + anti-PD-L1

79,2% sensitivity and 95,2% specificity

The phytotherapeutic fenugreek as trigger of toxic epidermal necrolysis



MANUFACTUM.
Es gibt sie noch, die guten Dinge.



Allergy pass:

- aminophenole
- arylpropionic acid
- pyrazolone
- fenugreek

S3 guideline: Diagnosis and treatment of epidermal necrolysis (Stevens-Johnson syndrome and toxic epidermal necrolysis) – Part 1: Diagnosis, initial management, and immunomodulating systemic therapy

S3 guideline: Diagnosis and treatment of epidermal necrolysis (Stevens-Johnson syndrome and toxic epidermal necrolysis) – Part 2: Supportive therapy of EN in the acute and post-acute stages



No 4	Consensus-based recommendation
EC Strong consensus	A dermatological examination shall be performed within 24 hours if EN is suspected. In cases of a clinically probable diagnosis of EN, an ophthalmological examination shall be performed within 24 hours. If possible, within 48 hours, but no later than within the first week, a gynecological and/or urological evaluation should also be performed for all patients. Depending on the clinical presentation, (repeated) consultative evaluations by the following specialities should be performed during the course of the acute treatment phase: nutritional medicine, gastroenterology, otolaryngology, infectious diseases, nephrology, and pulmonology. Psychotherapeutic support shall be offered to clinically stable and responsive patients. Patients shall receive physiotherapy if needed. Patients with pain, regardless of the pain level, may be offered a consultation with a pain specialist. For a pain level $\geq 4/10$ on the numerical rating scale (NRS) despite provision of standard analgesic measures, a pain specialist shall be consulted.

No 2	Consensus-based recommendation
EC Strong consensus	To detect parainfectious events, an infection-focused investigation consisting of urine status and chest X-ray (or, if necessary, chest computed tomography) shall be performed in the presence of clinical signs of infection and elevated CRP.

- approx. 70% of EN-cases are drug-induced
- in children less than 50%
- many of the non-drug related EN-cases are induced by an infectious condition, mostly viral

No 3	Consensus-based recommendation
EC Strong consensus	Potential causative drugs (for identification of causative drugs see box "Notes on identification/narrowing of possible causative drugs" of the AWMF long version) shall be discontinued. Medications taken for less than 4 days, or more than 28 days may generally be continued. Drugs from the group of "suspected" or "highly suspected" drugs shall be considered as possible triggers and discontinued, even if their use began within the last 12 weeks. If the causative drug remains unclear, all non-essential medications (see background text) shall be discontinued. Other active substances from the same substance group as the likely causative drug may be administered (for exceptions, see background text).

No 10	Consensus-based recommendation
EC Strong consensus	Therapy should be initiated immediately after diagnosis. Any comorbidities (see background text) shall be considered when selecting the therapy.
No 11	Consensus-based recommendation
EC Strong consensus	If EN has already persisted for several days and no progression of the skin (see Statement 12) or mucous membranes has been observed for over 24 hours, the expected benefit of initiating a new systemic therapy should be critically evaluated.
No 12	Consensus-based statement
EC – Statement Strong consensus	Progression is defined as further spreading of redness, possibly with blister formation/skin detachment. New blister formation on/detachment of already reddened skin is not considered progression. To determine the extent of erythema, marking the boundaries of redness with a skin marker is helpful; regular photographic documentation over time is required.



No 13	Evidence-based recommendation
Grade of recommendation 0 Strong consensus	In addition to supportive and organ-oriented therapy for EN, a systemic monotherapy with corticosteroids may be considered.

No 14	Evidence-based recommendation
Grade of recommendation 0 Consensus	A systemic monotherapy with intravenous immunoglobulins (off-label) for the treatment of EN cannot be conclusively evaluated .

No 16	Evidence-based recommendation
Grade of recommendation 0 Consensus	In addition to supportive and organ-oriented therapy for EN, a systemic monotherapy with etanercept (off-label) may be considered.

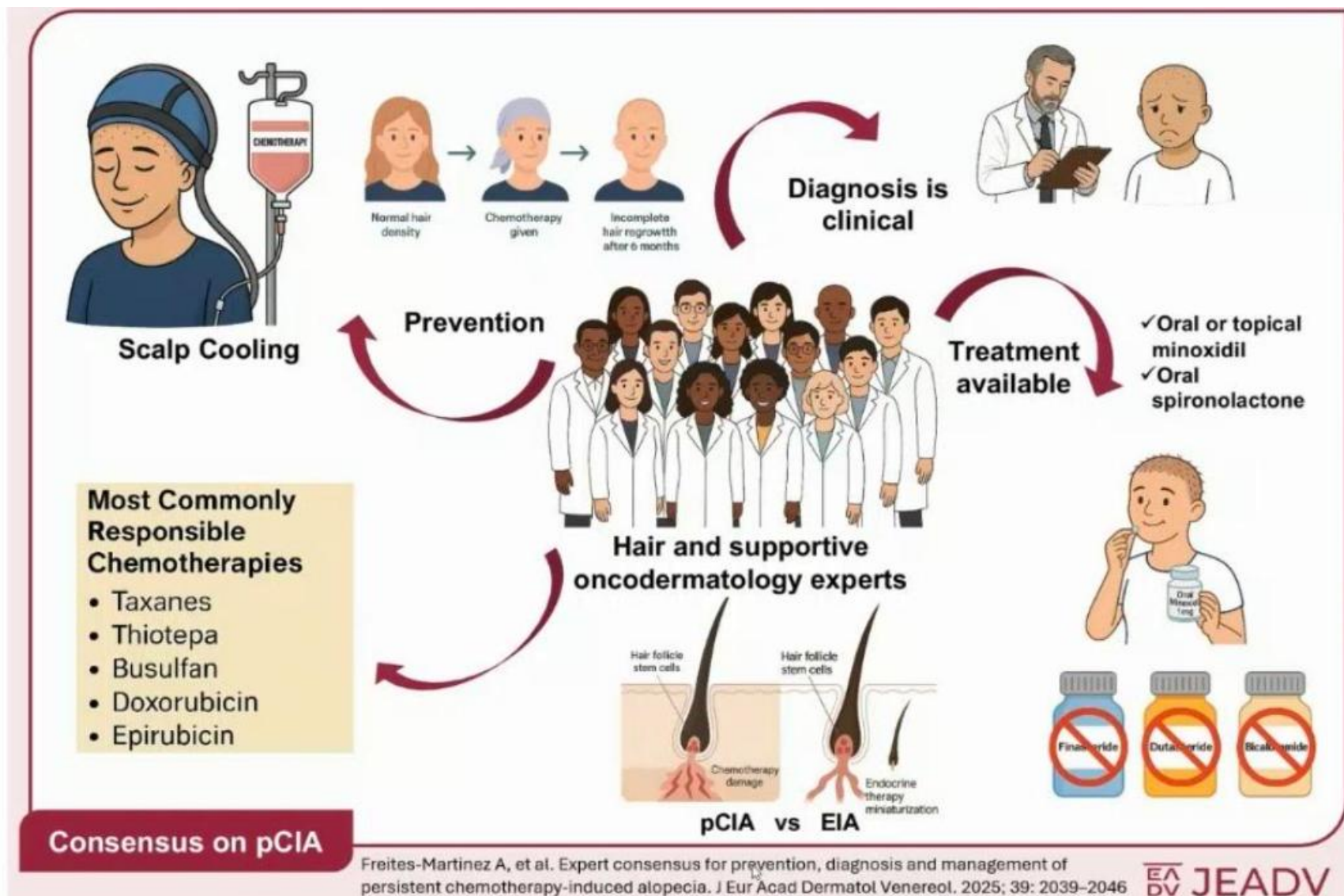
No 15	Evidence-based recommendation
Grade of recommendation 0 Strong consensus	In addition to supportive and organ-oriented therapy for EN, a systemic monotherapy with cyclosporine A (off-label) may be considered.
GRADE Very low (⊕○○○) to moderate (⊕⊕⊕○)	Comparison of CsA versus other therapies (supportive, CS, IVIG); evidence from prospective or retrospective comparative observational studies; for detailed study characteristics and results see <i>evidence report</i> .
Low (⊕⊕○○)	<i>Mortality:</i> CsA versus supportive: no statistically significant difference (RR 1.5, 95% CI: 0.27–8.46; 1 observational study, n = 74)
Low (⊕⊕○○)	CsA versus CS: no statistically significant difference (RR 0.45, 95% CI: 0.11–1.82; 2 observational studies, n = 62)
Moderate (⊕⊕⊕○)	CsA versus IVIG: <u>statistically significant advantage for CsA</u> (RR 0.18, 95% CI: 0.05–0.56; 2 observational studies, n = 91)

Differentiating generalized pustular psoriasis from acute generalized exanthematous pustulosis

Mika Yamanaka-Takaichi, MD, PhD^a · Miki Watanabe, MD^b · Nneka I. Comfere, MD^{a,c} · ... · Sho Hiroyasu, MD, PhD^b · Daisuke Tsuruta, MD, PhD^b · Afsaneh Alavi, MD^a  ... Show more

Table I. Statistically significant clinical variables used to distinguish GPP from AGEPS*

Variable	OR (univariate) predicting AGEPS (95% CI)	OR (univariate) predicting GPP (95% CI)	P value
Causative drug	109.33 (25.16-799.32)	0.01 (0.00-0.04)	<.001
Time from drug administration to onset of disease, d	0.94 (0.89-0.98)	1.06 (1.02-1.13)	.02
Recurrence	0.21 (0.04-0.75)	4.81 (1.33-22.99)	.03
History of psoriasis or current psoriasiform plaques	0.07 (0.02-0.20)	14.62 (4.96-50.88)	<.001
Plasma cells	0.20 (0.06-0.59)	4.96 (1.70-16.18)	.005
Density of dermal infiltrate cells	0.35 (0.13-0.89)	2.88 (1.13-7.83)	.03
Density of dermal infiltrate neutrophils	0.35 (0.16-0.74)	2.82 (1.35-6.45)	.009



ICI-associated pruritus: practical management

Escalate according to CTCAE severity — while preserving effective immunotherapy whenever possible

GRADE 1 • MILD / LOCALIZED

Skin-directed therapy

- Fragrance-free moisturizers + soap-free cleansers
- Potent topical corticosteroid

Systemic / ICI

- Consider a non-sedating antihistamine
- Withdraw antihistamine if ineffective after 1 week

CONTINUE ICI at current dose

GRADE 2 • MODERATE

Skin-directed therapy

- Moisturizers + soap-free cleansers
- Potent / superpotent topical corticosteroid

Escalate anti-itch therapy

- Non-sedating antihistamine
- Consider replacing with a GABA analogue
Gabapentin 100–300 mg TID or
pregabalin 50–100 mg TID (titrate)

CONTINUE ICI at current dose

PERSISTENT G2 / GRADE 3

Steroid-sparing escalation

- DUPILUMAB: 600 mg SC loading, then 300 mg SC every 2 weeks
- OR omalizumab 300 mg SC every 4 weeks

If Grade 3

- Potent/superpotent topical steroid
- GABA analogue
- Consider prednisone 0.5–1 mg/kg/day, 14-day taper
- Multidisciplinary decision on holding ICI

KEY MESSAGE • ICI can be continued in most patients. For refractory Grade 2 or severe pruritus, consider targeted steroid-sparing therapy — particularly dupilumab.

JAMA ONCOLOGY • 2026

A new steroid-sparing signal for severe ICI dermatitis?

Upadacitinib 15 mg/day for 28 days in a prospective phase 2, single-arm trial

33 patients • Grade 3–4 ICI-related dermatitis • 78.8% maculopapular • 100% with pruritus • No concomitant corticosteroids, immunosuppressants or antihistamines



SPEED OF RESPONSE



PROMISING SIGNAL • Rapid control of both rash and itch without concomitant glucocorticoids — potentially allowing ICI continuation.

CAUTION • Single-center, nonrandomized, n=33; no comparator and no long-term follow-up.

Systemic Treatment of Immune Checkpoint Inhibitor (ICI)-Induced Psoriasis



Multidisciplinary
expert panel
(n=15)



Delphi
process



Inference-based approach
considered the **totality of**
direct and indirect evidence

Inference-Based Guidance

- All treatment decisions should be made on a **case-by-case basis** after an **informed discussion** between the treating physicians (dermatologist and oncologist) and the patient, considering the below factors:

Cancer Type &
Prognosis

Response to ICI

Time since ICI Initiation

Psoriasis Severity

Comorbid Diseases

Previous Psoriasis
Therapy

ICI treatment interruption

A short-term ICI treatment interruption (i.e., 1–2 dose cycles) in response to severe ICI-Ps has a **low to negligible risk** of impairing ICI effectiveness. Short term interruption is unlikely to improve ICI-Ps.

Systemic Agents for the Treatment of Psoriasis

Agents are ordered by expert panel-rated support for the agent being **unlikely** to impair ICI efficacy. Ratings are not meant to be hierarchical, see full text for details.

Higher-
Rated
Agents

Systemic
Retinoid

Systemic PDE-4
inhibitor

IL-17 inhibitor

TNF inhibitor

Lower-
Rated
Agents

IL-23 inhibitor

IL-12/23 inhibitor

Methotrexate

TYK2 inhibitor

Decision Framework

Una iniciativa de:



ACADEMIA ESPAÑOLA
DE DERMATOLOGÍA
Y VENEREOLOGÍA



FUNDACIÓN
PIEL SANA
ACADEMIA ESPAÑOLA
DE DERMATOLOGÍA
Y VENEREOLOGÍA

Con el patrocinio de:



AEDV 35ª
edición

HIGHLIGHTS

Viena

30sep - 3oct
2026

La Academia Española de Dermatología y Venereología expresa su agradecimiento al patrocinador UCB, por su especial apoyo y contribución con la actividad formativa Highlights 2026.

Una iniciativa de:



ACADEMIA ESPAÑOLA
DE DERMATOLOGÍA
Y VENEREOLOGÍA



FUNDACIÓN
PIEL SANA
ACADEMIA ESPAÑOLA
DE DERMATOLOGÍA
Y VENEREOLOGÍA

Con el patrocinio de:



AEDV 35ª
edición

HIGHLIGHTS

Viena

30sep - 3oct
2026

GRACIAS