New Topicals for AD and Psoriasis

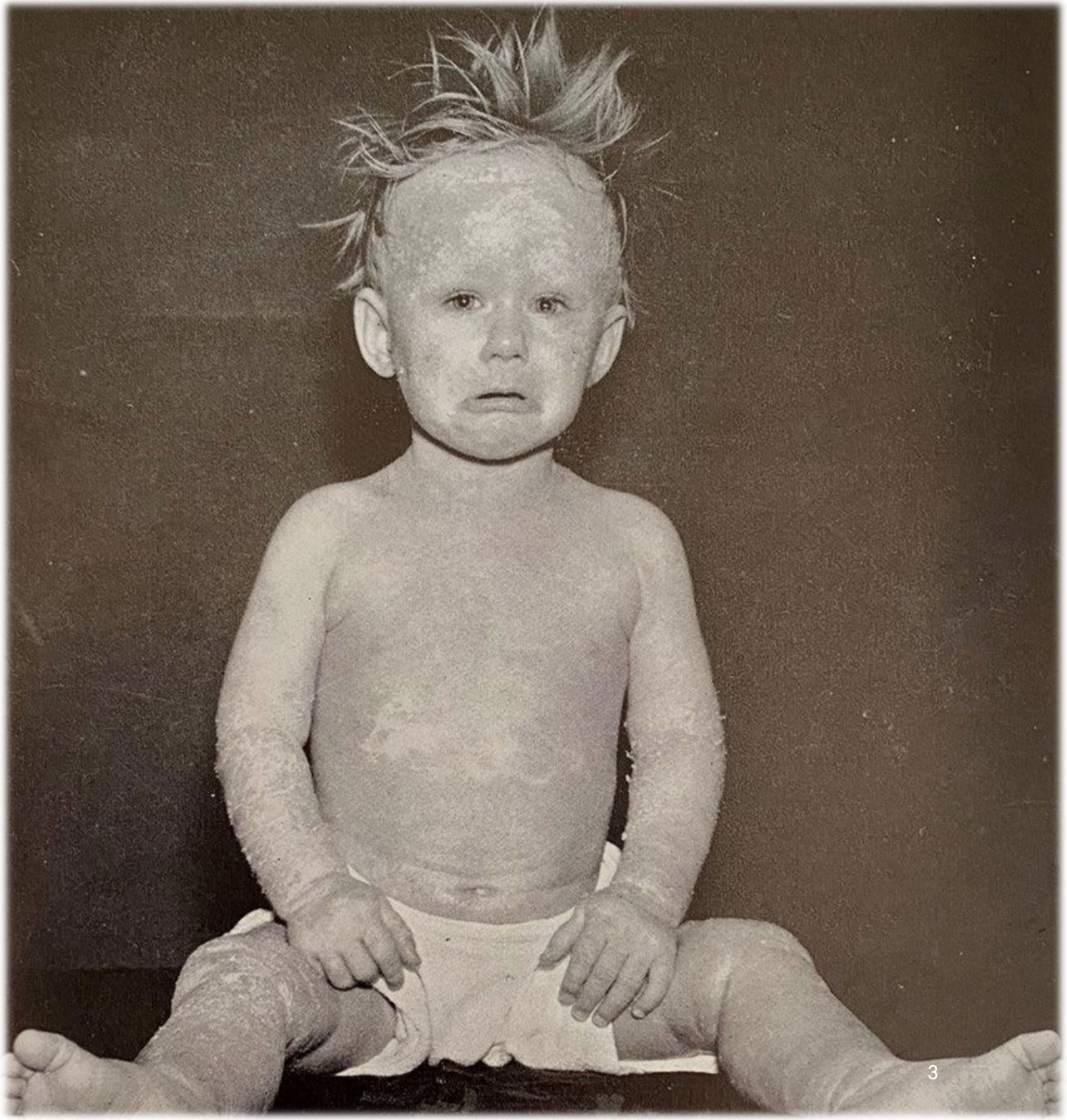
PETER LIO, MD

Relationship	Manufacturer
Speaker	AbbVie, Eli Lilly, Galderma, Hyphens Pharma, Incyte, La Roche-Posay/L'Oreal, Pfizer, Pierre-Fabre Dermatologie, Regeneron/Sanofi Genzyme
Advisory Board	Alphyn Biologics, AbbVie, Almirall, Amyris, ASLAN, Boston Skin Science, Bristol-Myers Squibb, Burt's Bees, Castle Biosciences, Codex Labs, Concerto Biosci, Dermavant, Eli Lilly, Galderma, Janssen, Johnson & Johnson, Kimberly Clark, LEO Pharma, Lipidor, L'Oreal, Merck, Micreos, MyOR Diagnostics, Regeneron/Sanofi Genzyme, Sibel Health, Skinfix, Sonica, Theraplex, UCB, Unilever, Verrica, Yobee Care
Research	AbbVie
Patent Holder	Theraplex AIM (Patent Pending)
Stock Options	Codex Labs, Concerto Biosci, Yobee Care

Disclosure

Misery

From: Pillsbury DM, Kligman AM, Shelley WB. A manual of cutaneous medicine, by Donald M. Pillsbury, Walter B. Shelley [and] Albert M. Kligman.
Philadelphia. Saunders, 1961.



Burden of AD

Increasing US Prevalence[1,2]

12% to 13% in children and adolescents and 7% in adults

- 90% of cases present by 5 years of age
- Among adults, 17% of cases develop after adolescence

Increasing Costs[3]

~$5.3 billion/year

- Doesn't include time, emotional cost, and presenteeism

Impact on QoL[4]

Greater than type 1 diabetes

- Not "just a rash"

Sleep Deprivation[2,3-6]

- Exhaustion
- Mood changes
- Impaired psychosocial functioning

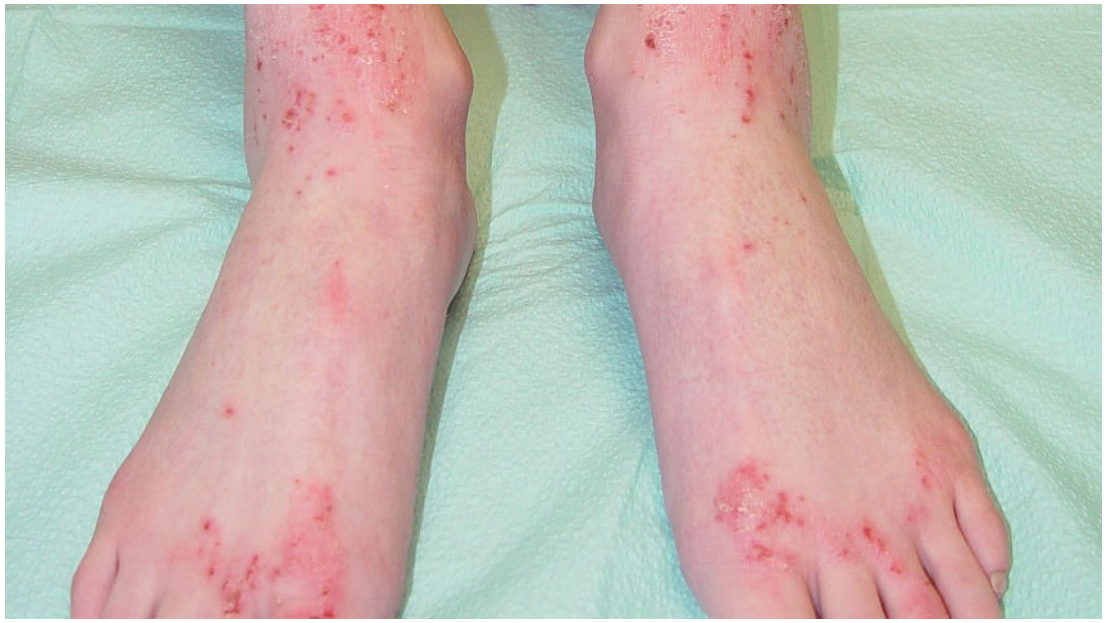
Social Isolation[2,3,5]

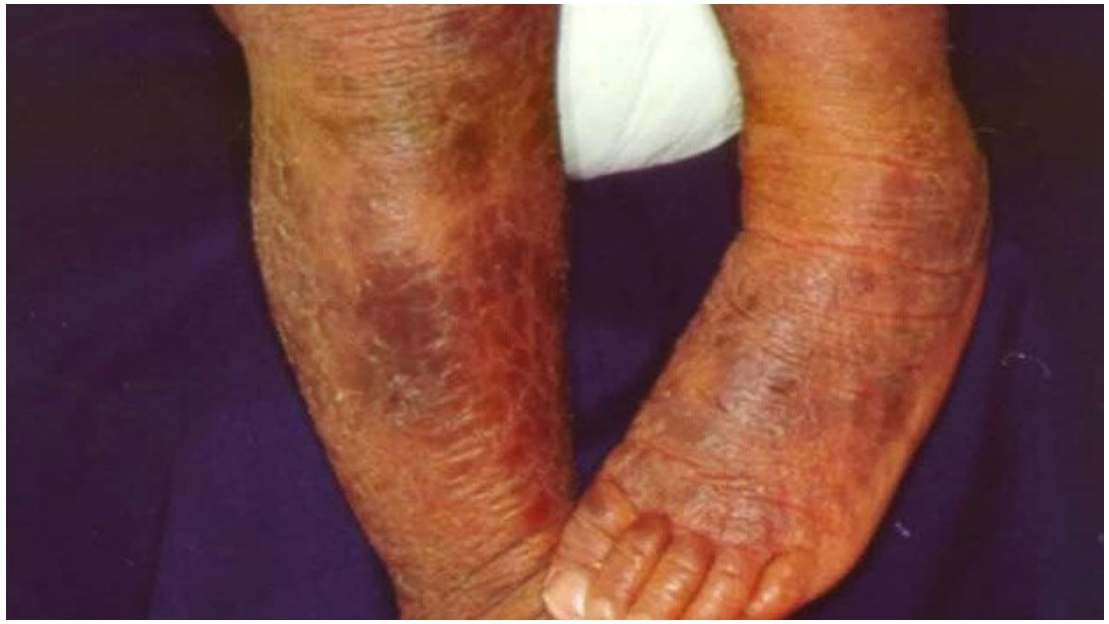
- School avoidance
- Depression

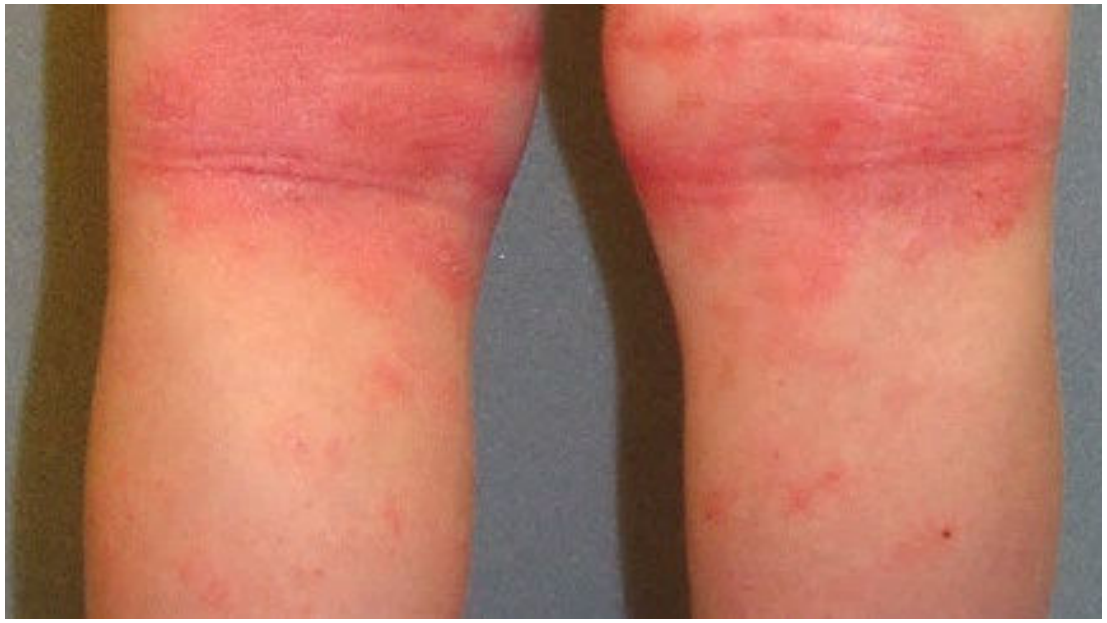
Restricted Choices[3,5]

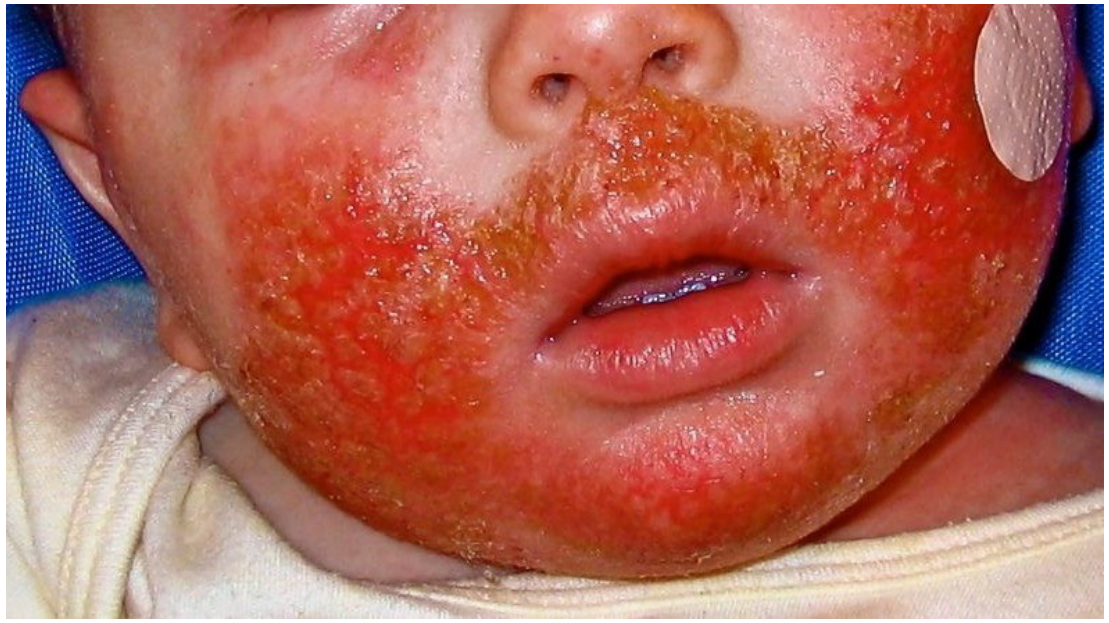
- Clothing, holidays, socializing, owning pets, and participating in sports

1. Avena-Woods C. *Am J Manag Care*. 2017;23(8 Suppl): S115-S123. 2. Silverberg JI. *Ann Allergy Asthma Immunol*. 2019;123(2):144-151. 3. Drucker AM eta l. *J Invest Dermatol*. 2017;137(1):26-30. 4. Silverberg JI et al. *Ann Allergy Asthma Immunol*. 2018;121(3):340-347. 5. Lewis-Jones S. *Int J Clin Pract*. 2006;60(8):984-992. 6. Arkwright PD et al. *J Allergy Clin Immunol Pract*. 2013;1(2):142-151.



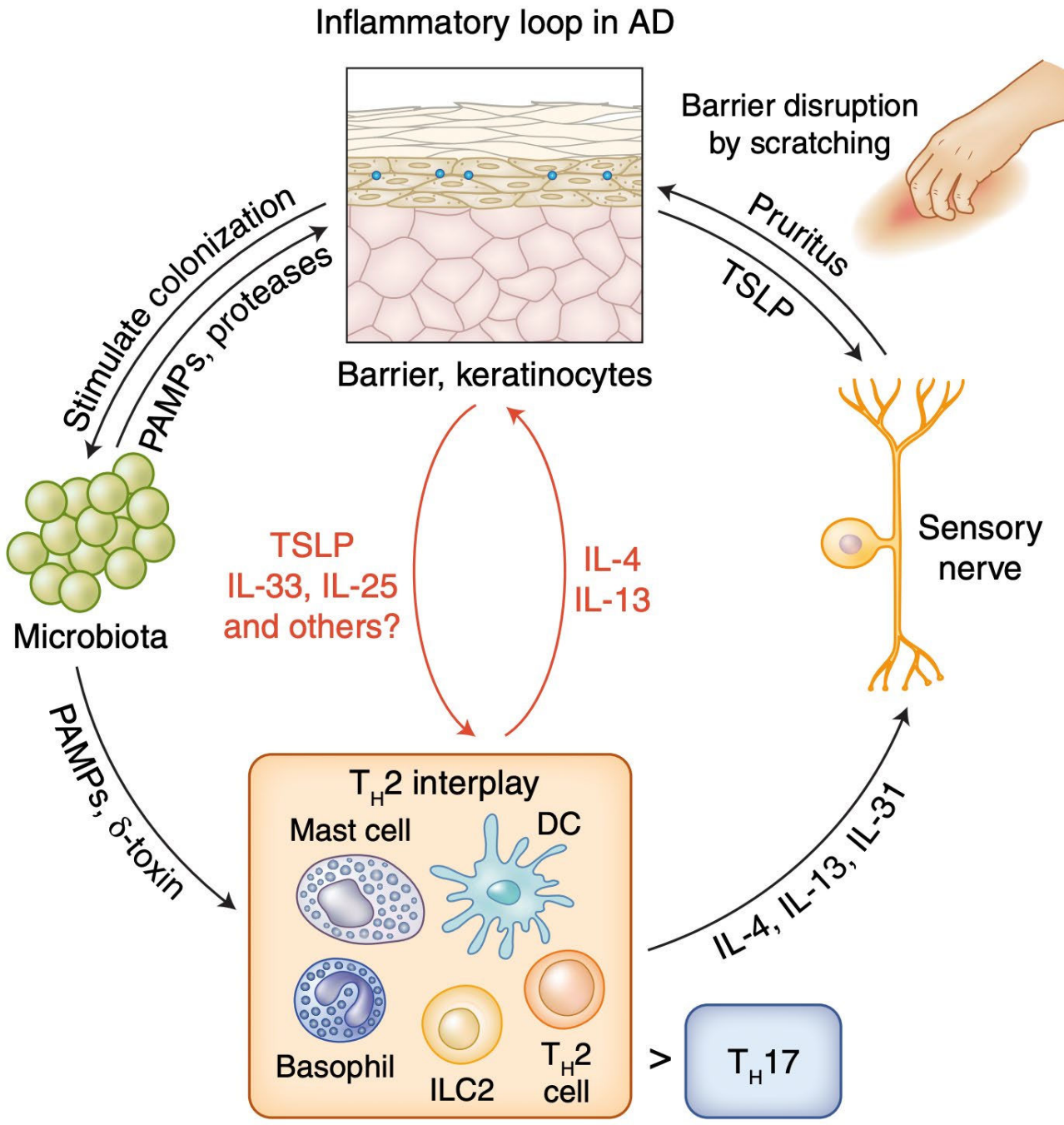






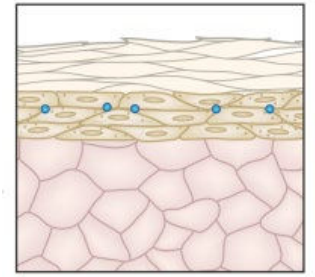
Photos courtesy of Peter Lio, MD. (Permission obtained and on file)

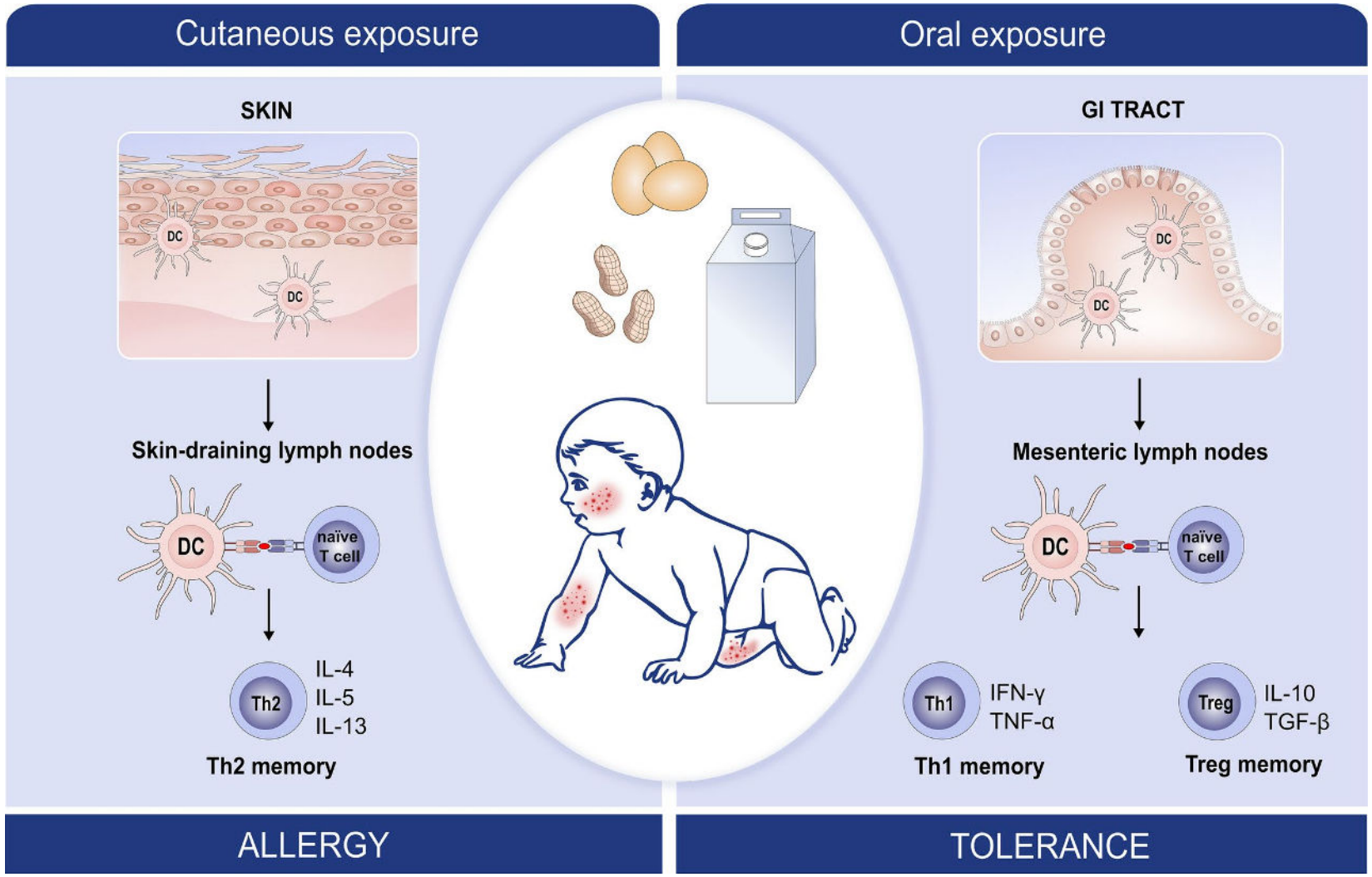
Loops



The epithelial immune microenvironment (EIME) in atopic dermatitis and psoriasis. Dainichi T, Kitoh A, Otsuka A, Nakajima S, Nomura T, Kaplan DH, Kabashima K. *Nat Immunol*. 2018 Dec;19(12):1286-1298.

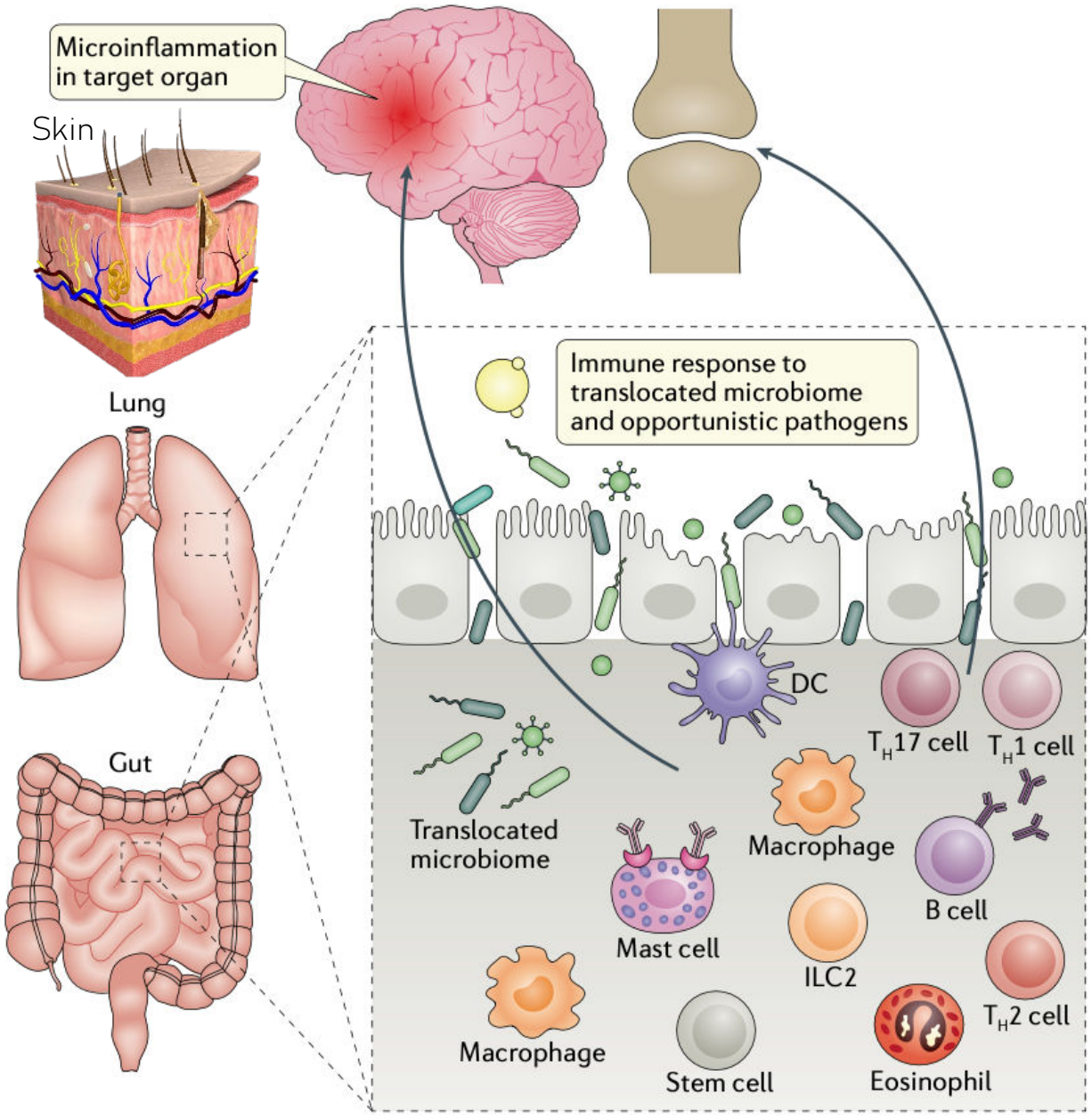
Epicutaneous Sensitization


Barrier, keratinocytes



Allergy. 2020;75(9):2185–2205. doi: 10.1111/all.14304.

Far-Reaching Effects of Leaky Epithelia



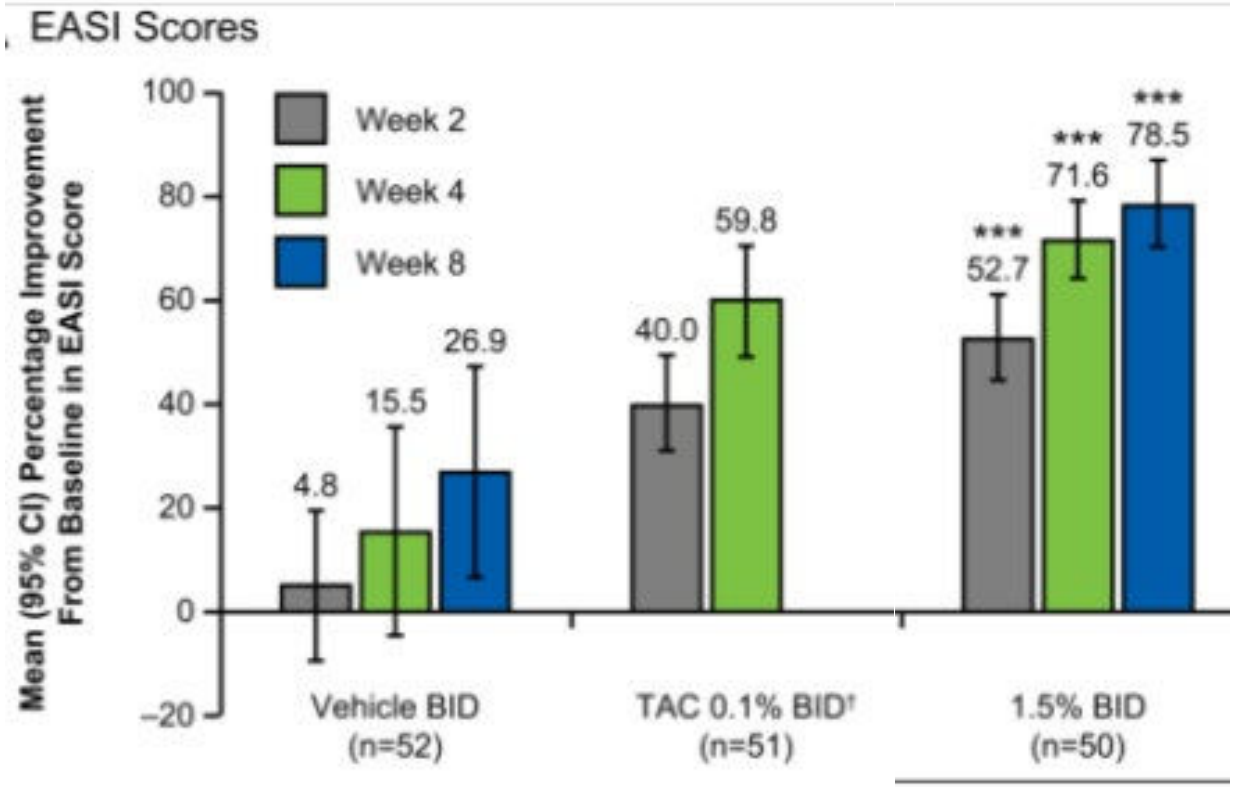
Akdis, C.A. Does the epithelial barrier hypothesis explain the increase in allergy, autoimmunity and other chronic conditions?. *Nat Rev Immunol*. 2021. https://doi.org/10.1038/s41577-021-00538-7

Conventional Topical Therapies

Agent/class	Recommended use[1–3]	Considerations[3]
Corticosteroids (TCS) Up to twice daily	• After inadequate response to good basic management • At lowest effective dose to achieve disease control	Risk of localized skin changes (eg, atrophy, striae, acne) with long-term use Rare risk of systemic absorption with suppression of the HPA axis "Steroid phobia" leading to underutilization Withdrawal after prolonged use (eg, erythema, burning, or itch)[4]
Calcineurin inhibitors (TCI) Up to twice daily	• After inadequate response or contraindication to other topical prescription treatments • Short-term and intermittent	Application-site burning and irritation Boxed warning regarding hypothetical increase in long-term cancer risk • No increased cancer risk shown in recent studies[5,6]
Crisaborole 2% ointment twice daily	• Mild-to-moderate disease • Patients averse to using TCS or TCI	Application-site irritation, burning, and stinging reported more frequently in clinical practice than clinical trials[7]

1. EICHENFIELD LF ET AL. J AM ACAD DERMATOL. 2014;71:116-132; 2. BOGUNIEWICZ M ET AL. ANN ALLERGY ASTHMA IMMUNOL. 2018;120:10-22.E2; 3. KLEINMAN E ET AL. AM J CLIN DERMATOL. 2022;23:595-603; 4. HWANG J, LIO PA. J DERMATOLOG TREAT. 2022;33:1293-1298; 5. ASGARI MM ET AL. JAMA DERMATOL. 2020;156:1066-1073; 6. PALLER AS ET AL. J AM ACAD DERMATOL. 2020;83:375-381; 7. LYNDE CW ET AL. SKIN THERAPY LETTER. 2020;25. HTTPS://WWW.SKINTHERAPYLETTER.COM/DERMATOLOGY/TOPICAL-CRISABOROLE-DERMATITIS-TREATMENT/. ACCESSED AUGUST 1, 2023.

Treatment of AD With Ruxolitinib Cream or Triamcinolone Cream



Kim BS, Howell MD, Sun K, et al. *J Allergy Clin Immunol*. 2020;145(2):572-582. doi:10.1016/j.jaci.2019.08.042

Ruxolitinib Safety

INDICATIONS AND USAGE

OPZELURA is a Janus kinase (JAK) inhibitor indicated for the topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. (1)

Limitation of Use

Use of OPZELURA in combination with therapeutic biologics, other JAK inhibitors or potent immunosuppressants such as azathioprine or cyclosporine is not recommended. (1)

DOSAGE AND ADMINISTRATION

- Apply a thin layer twice daily to affected areas of up to 20% body surface area. Do not use more than 60 grams per week. (2)
- For topical use only. (2)
- Not for ophthalmic, oral, or intravaginal use. (2)

WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE), AND THROMBOSIS

See full prescribing information for complete boxed warning.

- **Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving Janus kinase inhibitors for inflammatory conditions. (5.1)**
- **Higher rate of all-cause mortality, including sudden cardiovascular death have been observed in patients treated with Janus kinase inhibitors for inflammatory conditions. (5.2)**
- **Lymphoma and other malignancies have been observed in patients treated with Janus kinase inhibitors for inflammatory conditions. (5.3)**
- **Higher rate of MACE (including cardiovascular death, myocardial infarction, and stroke) has been observed in patients treated with Janus kinase inhibitors for inflammatory conditions. (5.4)**
- **Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis, some fatal, have occurred in patients treated with Janus kinase inhibitors for inflammatory conditions. (5.5)**

WARNINGS AND PRECAUTIONS

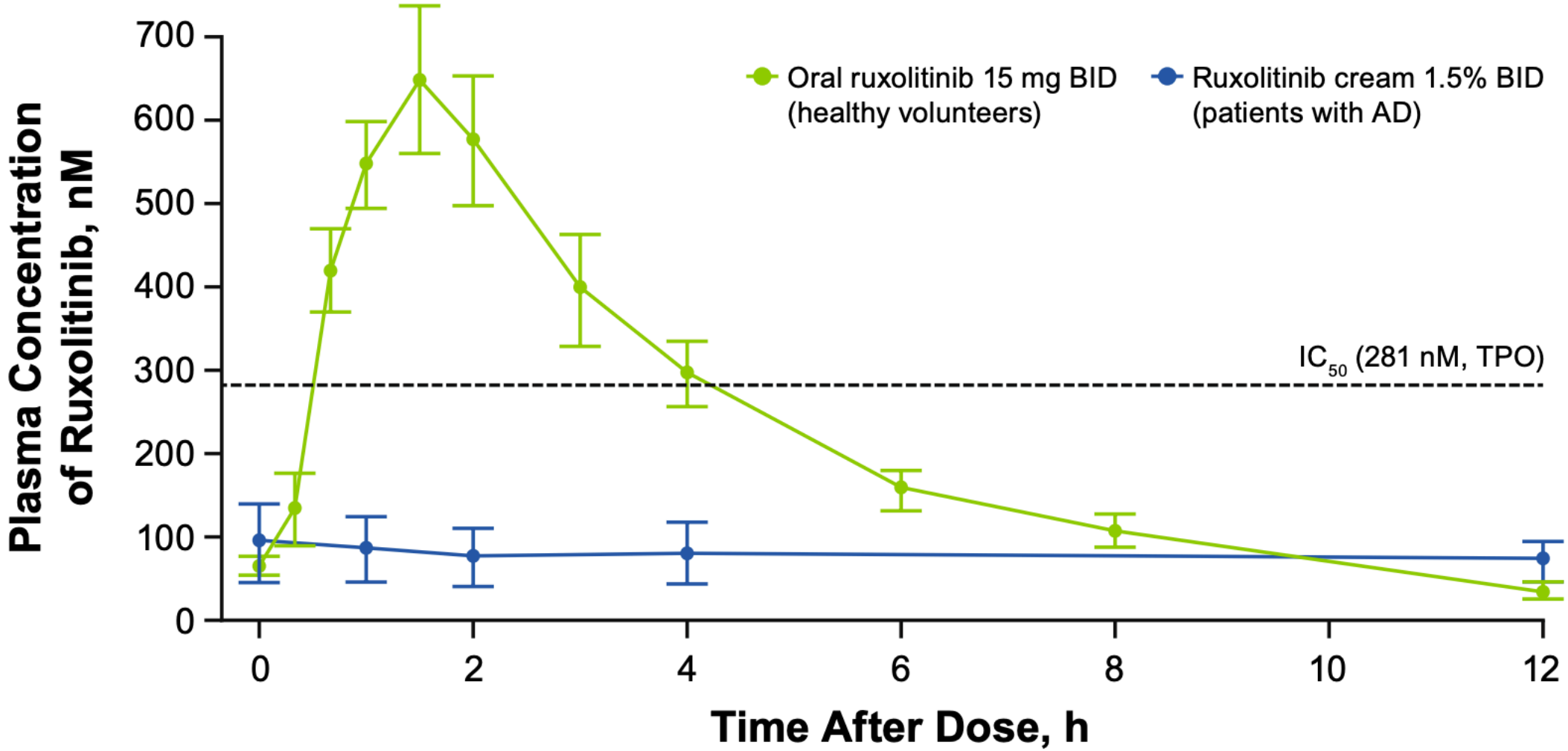
- *Serious Infections:* Serious bacterial, mycobacterial, fungal and viral infections have occurred. Regularly monitor patients for infection and manage it promptly. (5.1)
- *Non-melanoma Skin Cancers.* Basal cell and squamous cell carcinoma have occurred. Perform periodic skin examinations during treatment and following treatment as appropriate. (5.3)
- *Thrombosis.* Thromboembolic events have occurred. (5.5)
- *Thrombocytopenia, Anemia and Neutropenia:* Thrombocytopenia, anemia and neutropenia have occurred. Perform CBC monitoring as clinically indicated (5.6).

ADVERSE REACTIONS

- The most common adverse reactions (incidence ≥1%) are nasopharyngitis, diarrhea, bronchitis, ear infection, eosinophil count increased, urticaria, folliculitis, tonsillitis, and rhinorrhea. (6)

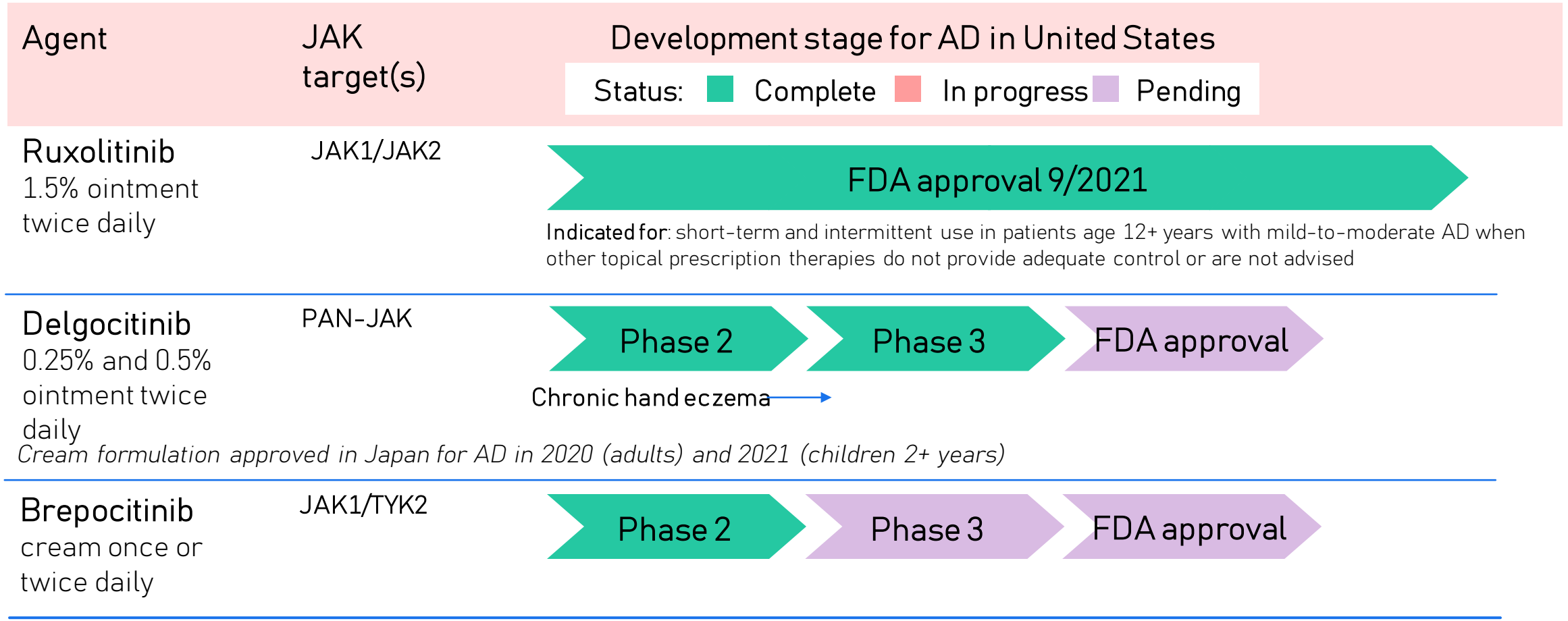
From: https://www.opzelura.com/prescribing-information.pdf

Ruxolitinib



Bissonnette R, Call RS, Raoof T, Zhu Z, Yeleswaram S, Gong X, Lee M. A Maximum-Use Trial of Ruxolitinib Cream in Adolescents and Adults with Atopic Dermatitis. American Journal of Clinical Dermatology. 2022 Apr 4:1-0.

Newer and Emerging Topical JAK Inhibitors



CLINICALTRIALS.GOV. ACCESSED OCTOBER 19, 2022; FDA. HTTPS://WWW.ACCESSDATA.FDA.GOV/SCRIPTS/CDER/DAF/. ACCESSED AUGUST 1, 2023;
Japan Tobacco. https://www.jt.com/media/news/2021/pdf/20210323_E1.pdf. Accessed August 1, 2023.

Roflumilast Cream in Adults and Adolescents With Mild-to-Moderate AD

Approved in for psoriasis in US

Phase 2 proof-of-concept study

- 136 patients randomized 1:1:1 to roflumilast 0.05%, 0.15%, or vehicle control once daily for 4 weeks
- Age ≥12 years; BSA: 1.5–35%; EASI >5

Efficacy at week 4

Endpoint	Roflumilast 0.05%	Roflumilast 0.15%	Vehicle
EASI absolute change from baseline (primary)	−6.0 (NS)	−6.4 (NS)	−4.8
EASI-75 response, %	59.1	52.3	31.1
vIGA-AD score of clear/almost clear, %	50.0 (NS)	52.3	31.1

P<0.05 vs vehicle unless otherwise indicated

Adverse events

Treatment-emergent AEs (TEAE), %	Roflumilast 0.05%	Roflumilast 0.15%	Vehicle
Any TEAE	21.7	26.7	13.3
	All mild or moderate in severity		
Application site pain	2.2	0	2.2
Worsening AD	0	0	2.2
Any treatment-related TEAE	4.3	0	4.4
TEAE leading to discontinuation	2.2[a]	0	2.2

[A] MODERATE APPLICATION-SITE PAIN (N=1).

BSA, body surface area; vIGA-AD, Validated Investigator Global Assessment for Atopic Dermatitis; NS, not significant.

Gooderham MJ et al. *J DRUGS DERMATOL*. 2023;22:139-147.

Difamilast Ointment in Adults and Children With Mild-to-Moderate AD

Approved in Japan for AD in 2021: age 2+ years

Efficacy

IGA success at week 4

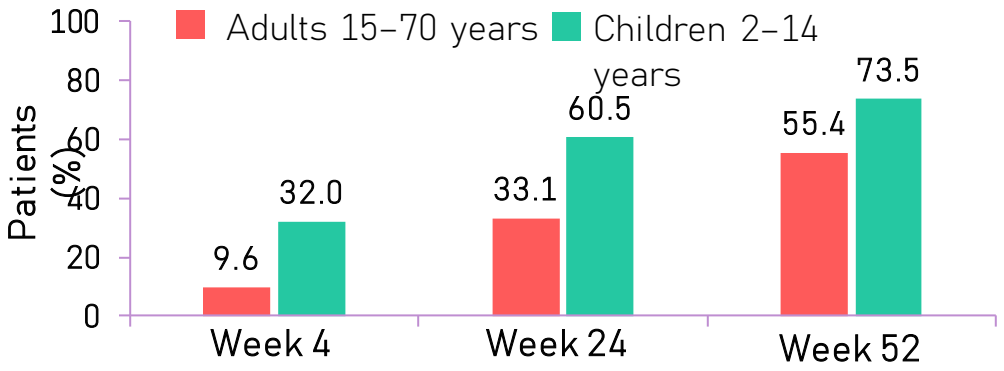
Randomized, double-blind, vehicle-controlled trials[1-3]

Population (study phase; location)	Difamilast 0.3%	Difamilast 1%	Vehicle
15–70 years (3; Japan)	NA	38.5%	12.6%
2–14 years (3; Japan)	44.6%	47.1%	18.1%
10–70 years (2; US+)	14.6% (NS)	20.9%	2.7%

P<0.05 vs vehicle unless otherwise specified

EASI-75 cumulative success rates

(long-term, open-label study)[4]



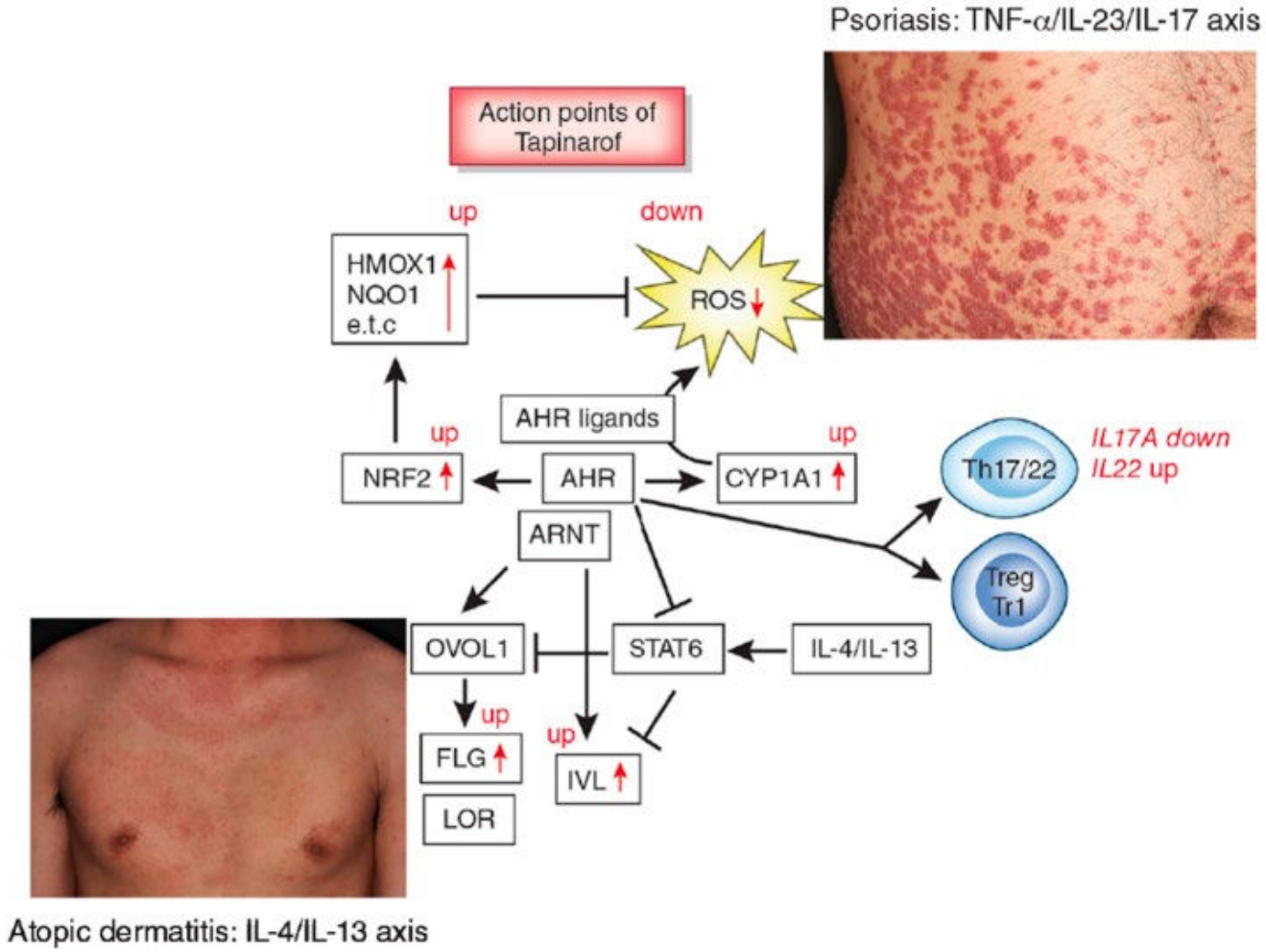
Safety and tolerability

- Low incidence of application-site reactions in difamilast groups
  - None in Japanese phase 3 trials; 1 case each in phase 2 and open-label studies (both adults)
- No serious treatment-related events or clinically relevant safety issues reported[1-4]

IGA success defined as a score of 0 or 1 with ≥2-grade improvement; EASI-75 success rates defined as the percentages of patients achieving ≥75% improvement in overall EASI score.

NA, not applicable; NS, not significant. 1. Saeki H et al. *J Am Acad Dermatol.* 2022;86:607-614; 2. Saeki H et al. *Br J Dermatol.* 2022;186:40-49; 3. Hanifin JM et al. *J Am Acad Dermatol.* 2016;75:297-305; 4. Saeki H et al. *Dermatol Ther (Heidelb).* 2022;12:1589-1601.

Aryl Hydrocarbon Receptor Modulation in AD



Approved by FDA for the treatment of plaque psoriasis in May 2022 (tapinarof 1% cream once daily)

AHR, aryl hydrocarbon receptor; ARNT, AHR-nuclear translocator; CYP1A1, cytochrome P450 1A1; FLG, filaggrin; HMOX1, heme oxygenase 1; ILV, involucrin; LOR, loricrin;
NQO1, NAD(P)H dehydrogenase, and quinone 1; NRF2, nuclear factor-erythroid 2-related factor-2; OVOL1, OVO-like 1; ROS, reactive oxygen species.

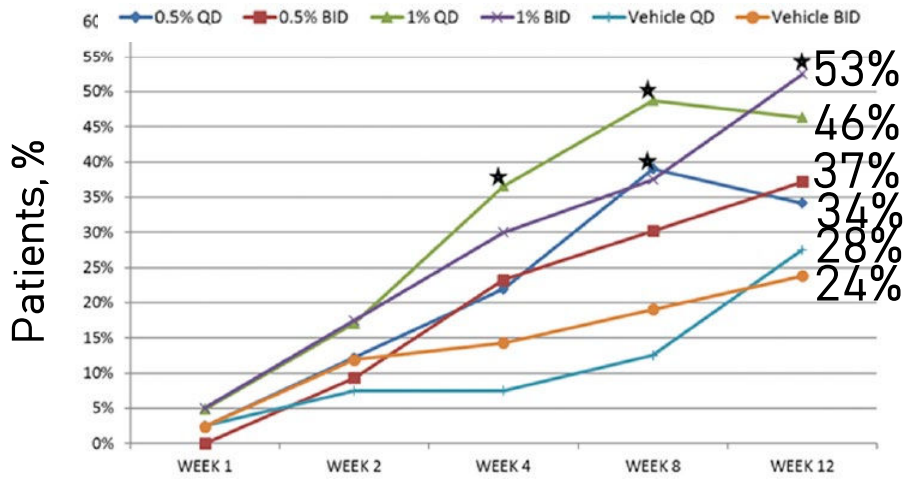
FURUE M ET AL. *INT J MOL SCI.* 2019;20:5424.

Tapinarof: Efficacy in Atopic Dermatitis

Phase 2b trial

- 247 patients randomized 1:1:1:1:1:1 to tapinarof cream 0.5% or 1% once or twice daily or vehicle once or twice daily for 12 weeks
- Age 12–65 years (30% adolescents); BSA: ≥5–35%; IGA ≥3 (91% moderate severity)

IGA treatment success[1,2]



Key efficacy endpoints

(Tapinarof 1% QD[a] vs vehicle QD at week 12)

Primary endpoint	
IGA treatment success rate	46% vs 28%
Secondary and post-hoc endpoints	
EASI-75 response rate	51% vs 25%*
EASI-90 response rate	27% vs 5%*
≥3-point improvement in itch NRS from week 2	32% vs 15%
Change in BSA from baseline	−48% vs −5%*

Improvements were maintained for 4 weeks after last application in most patients

1. Peppers J et al. *J Am Acad Dermatol*. 2019;80:89-98; 2. Paller AS et al. *J Am Acad Dermatol*. 2021;84:632-638.

Safety and Tolerability of Tapinarof

- AEs related to tapinarof treatment (no cases reported with vehicle control)
  - Folliculitis (7%)
  - Impetiginous eczema (2%)
  - Hyperkeratosis follicularis et parafollicularis (2%)
- Application site reactions
  - 2% vs 3%
- Discontinuation due to treatment-emergent AE
  - 0% vs 5%
- No serious treatment-related AEs reported

Phase 3 trials of tapinarof 1% QD in patients age 2+ years are completed (NCT05014568 and NCT05032859)

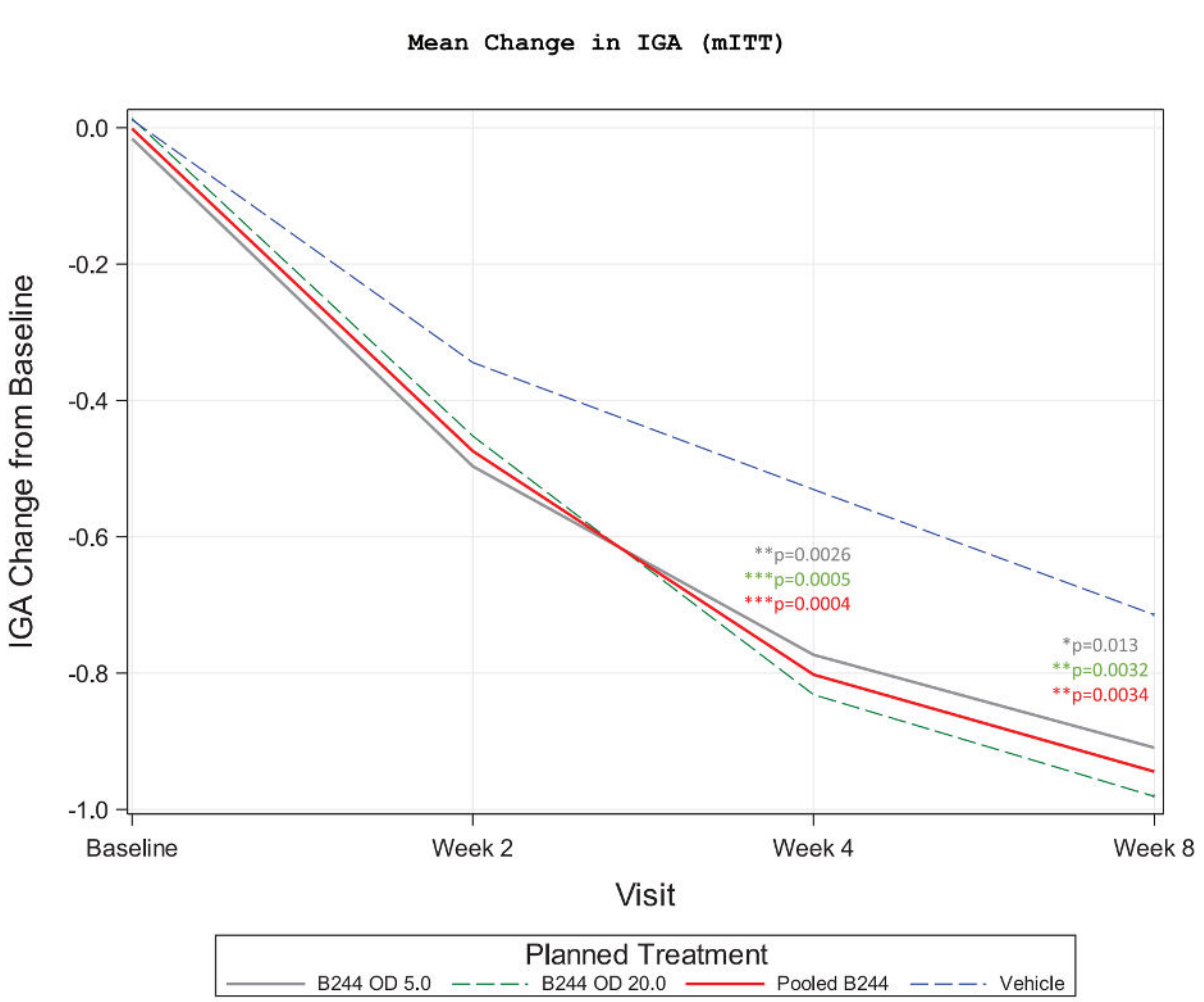
Peppers J et al. *J Am Acad Dermatol*. 2019;80:89-98; Clinicaltrials.gov. Accessed August 7, 2023

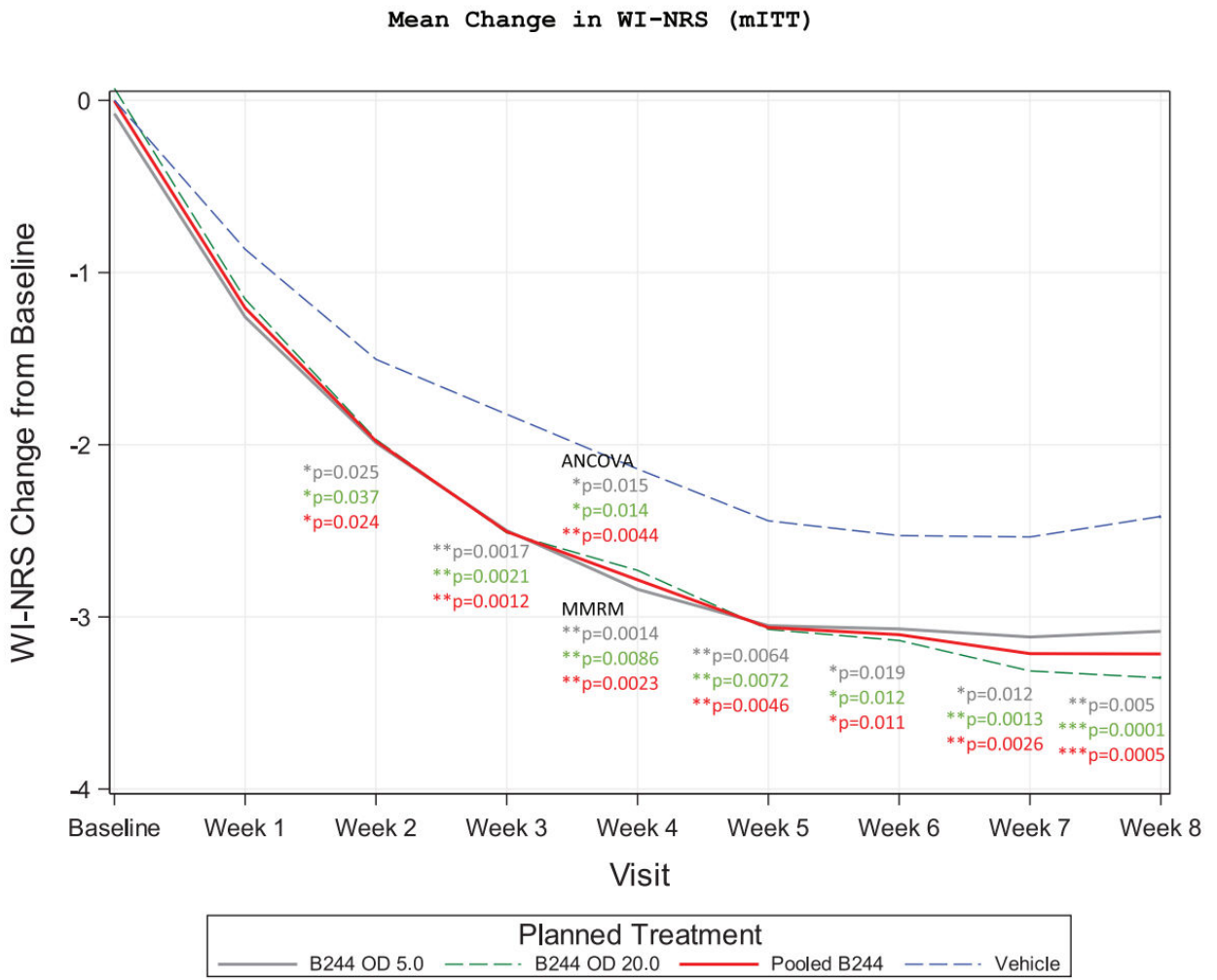
Topical Probiotic Spray: Nitrosomonas eutropha (B244)

- RDBCT Phase 2b trial of 18–65 years w/ mild-to-moderate AD and moderate-to-severe pruritus
- Randomized 1:1:1 into a low-dose (optical density at 600 nm [OD] 5.0), high-dose (OD 20.0), or vehicle group for the 4-week treatment period and a 4 week follow-up to apply the topical spray twice daily
- B244 was well tolerated and demonstrated improved efficacy compared to vehicle in all endpoints: WI-NRS (itch), POEM, IGA, 5-D Pruritus Scale, and EASI

Silverberg JI, Lio PA, Simpson EL, Li C, Brownell DR, Gryllos I, Ng-Cashin J, Krueger T, Swaidan VR, Bliss RL, Kim HD. Efficacy and safety of topically applied therapeutic ammonia oxidising bacteria in adults with mild-to-moderate atopic dermatitis and moderate-to-severe pruritus: a randomised, double-blind, placebo-controlled, dose-ranging, phase 2b trial. eClinicalMedicine 2023; 102002. Published Online https://doi.org/10. 1016/j.eclinm.2023.

Topical Probiotic Spray





Silverberg JI, Lio PA, Simpson EL, Li C, Brownell DR, Gryllos I, Ng-Cashin J, Krueger T, Swaidan VR, Bliss RL, Kim HD. Efficacy and safety of topically applied therapeutic ammonia oxidising bacteria in adults with mild-to-moderate atopic dermatitis and moderate-to-severe pruritus: a randomised, double-blind, placebo-controlled, dose-ranging, phase 2b trial. eClinicalMedicine 2023; 102002. Published Online https://doi.org/10. 1016/j.eclinm.2023.

Knowledge Gaps in Microbiome Research

Topics	Gaps
Microbial interactions	• How do different species of microorganisms influence each other's colonization and function? • How do the different species of microorganisms collaborate to maintain a host's homeostasis? What are the mechanisms that contribute to skin dysbiosis? • How does the skin microbiome reestablish new homeostasis once some commensals are removed or changed?
Interaction between microbiome and host	• What are the age-, sex-, location-, or hormone-specific commensals? What are the underlying mechanisms? • What is the role of the host immune system during a change of commensals' colonization? How do commensals interact with the innate and adaptive immune components? • How does a human body sense different commensal antigens? What are the receptors, the antigens, the antigen-presenting cells and the key signaling pathways?
Microbiome transmission and dynamics	• How are commensals shared between family members, roommates, or between humans and pets? What are the benefits and potential harms? • What roles do the host and environmental factors have during this process? • How does microbiome transmission affect the dynamics and stability of microbiota?
Microorganisms and skin conditions	• How do changes in cutaneous microbiota alter the skin microenvironment? • How does fungal or parasitic skin microorganisms modulate skin inflammatory di ses? • Would antibiotic treatment be a useful additional therapy for skin inflam atory, para tic or gal infe ous seases?
Implementing integration of strains in vivo	• How can we induce sufficient production and directional diffus of a icrobial prod t of inte ith the proper size and function? • What is the composition of the differen bial spe s c nizing t human bodysp;? Why do they colonize different areas? How can specific commensals be colonized i reas of i erest • How can colonization resist ce of the skin m obiom e overcome at a sufficient density and reproducibly while heeding strain diversity? • Can we use components of the skin mic biome as therapeutic strategies to decolonize pathogens?

STAY TUNED...

Liu Q, Ranallo R, Rios C, Grice EA, Moon K, Gallo RL. Crosstalk between skin microbiota and immune system in health and disease. Nature Immunology. 2023 Apr 20:1-4.

Psoriasis

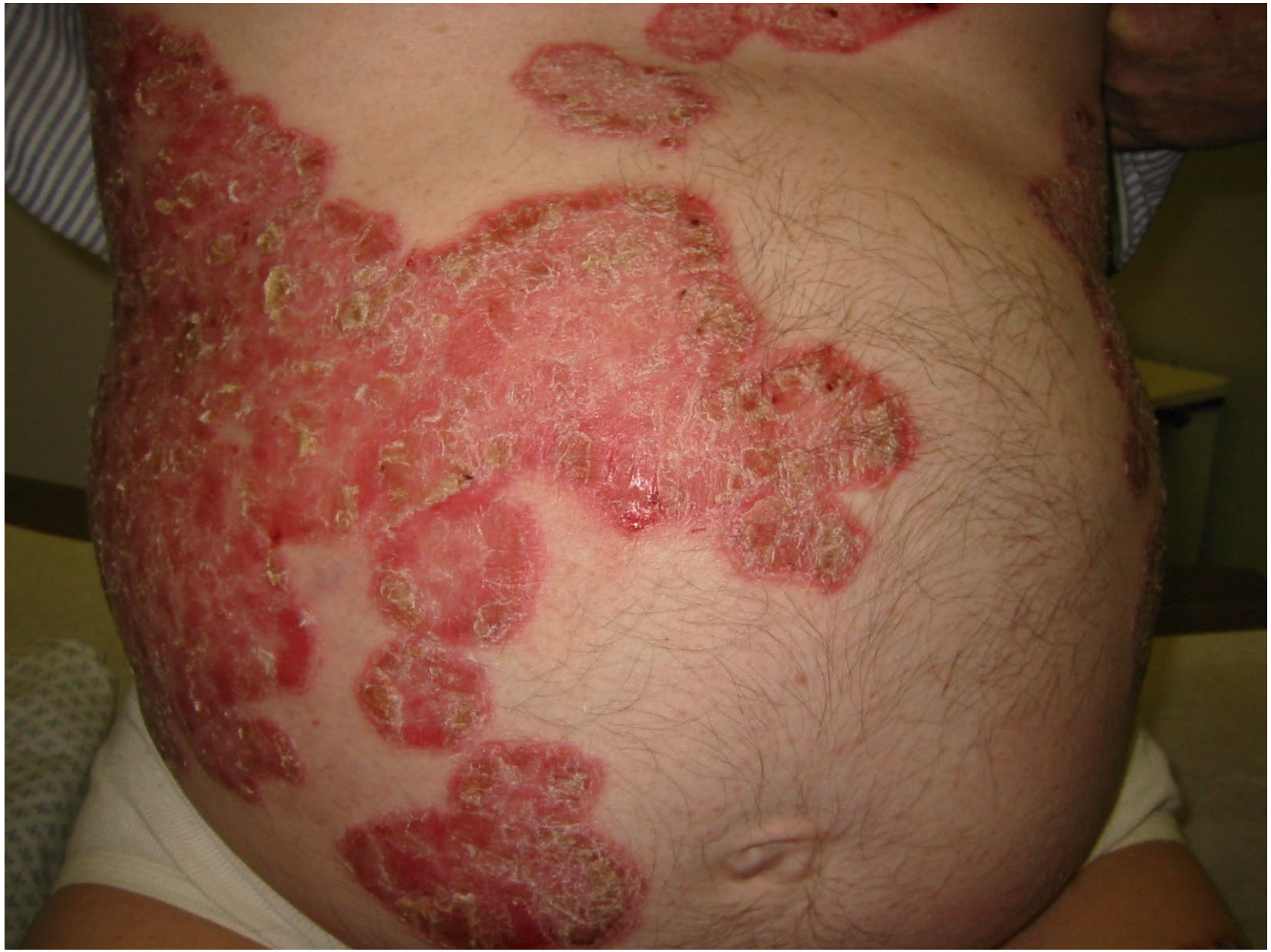
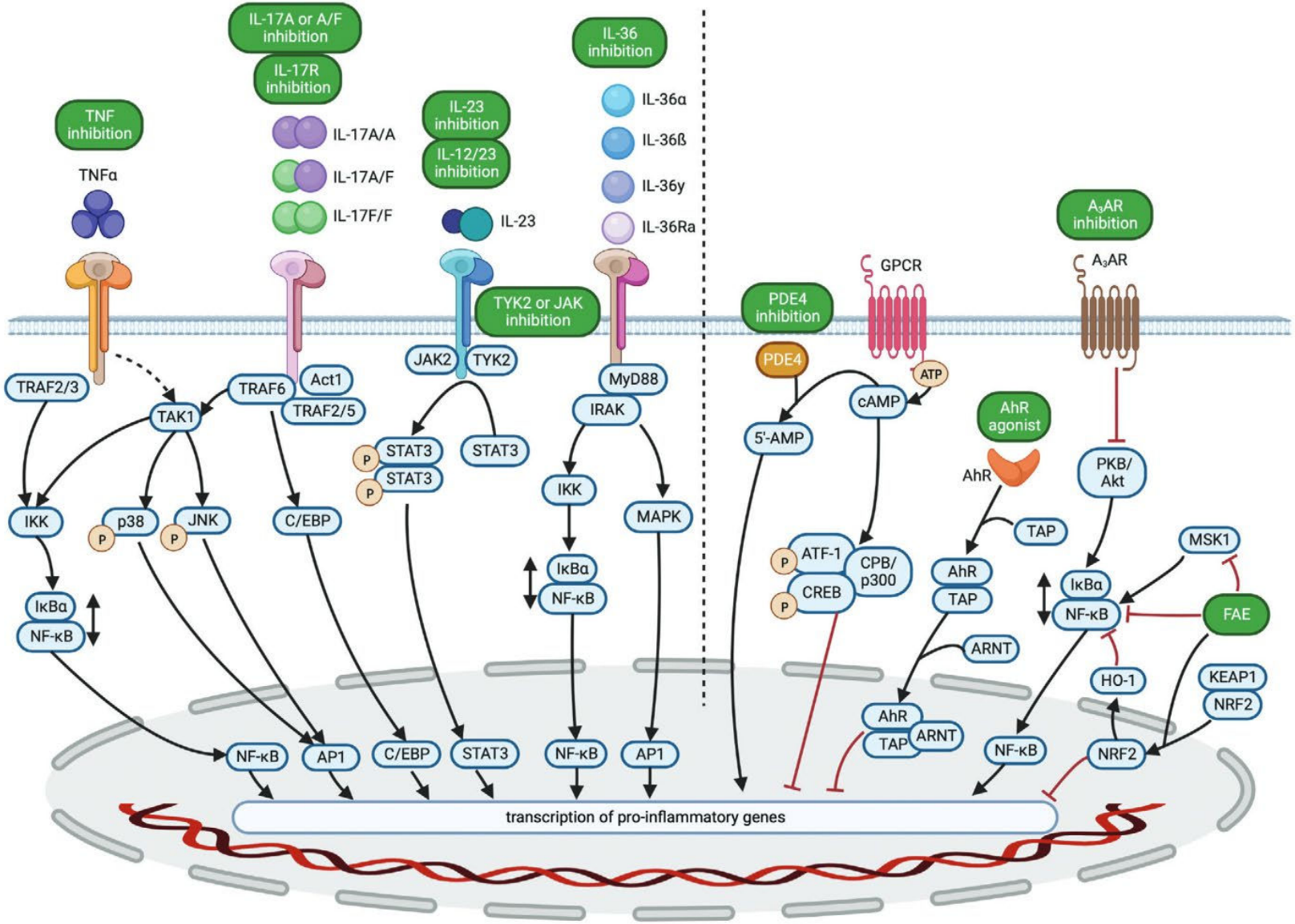


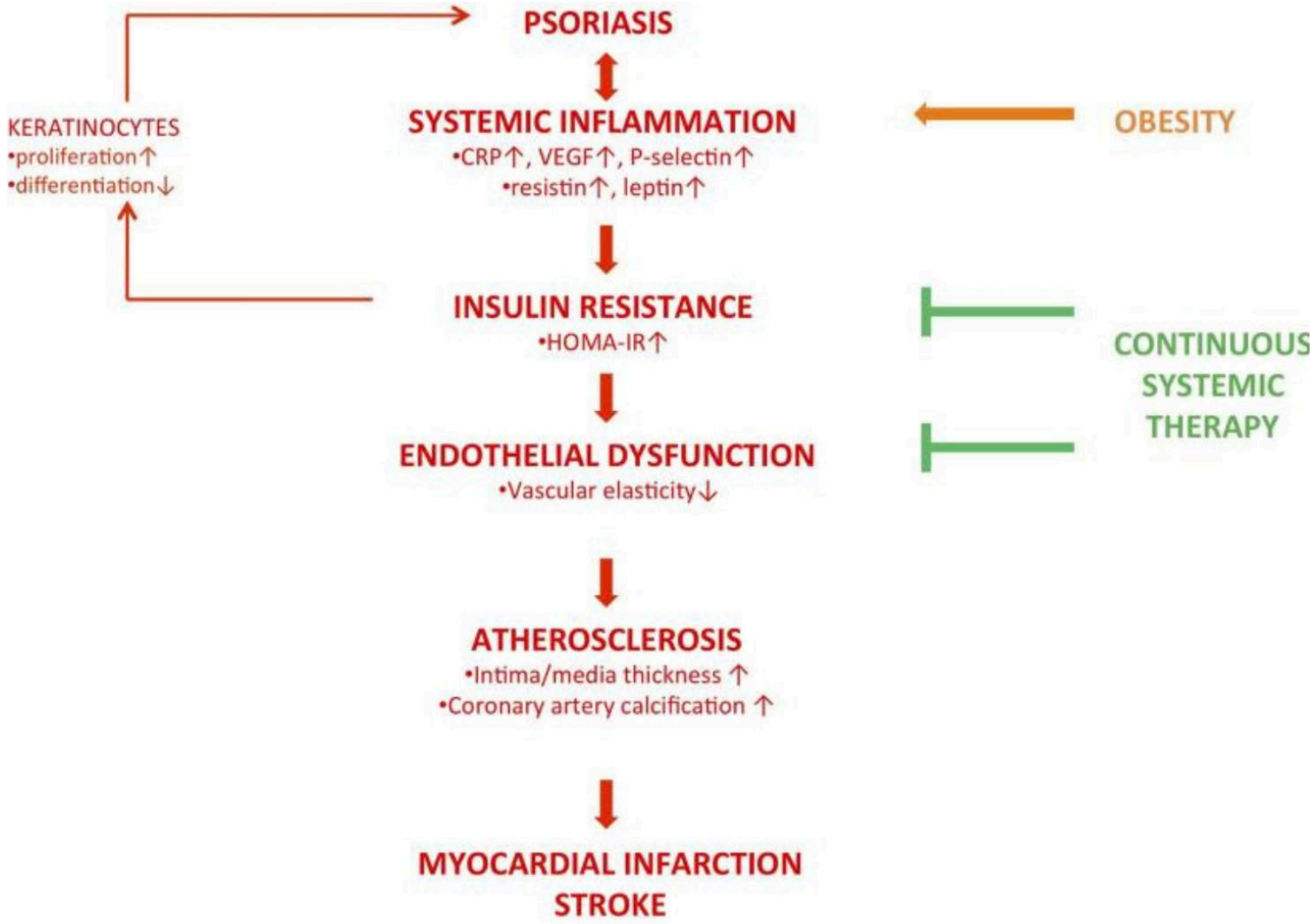
Photo courtesy of Peter Lio, MD, Consent on File

Psoriasis



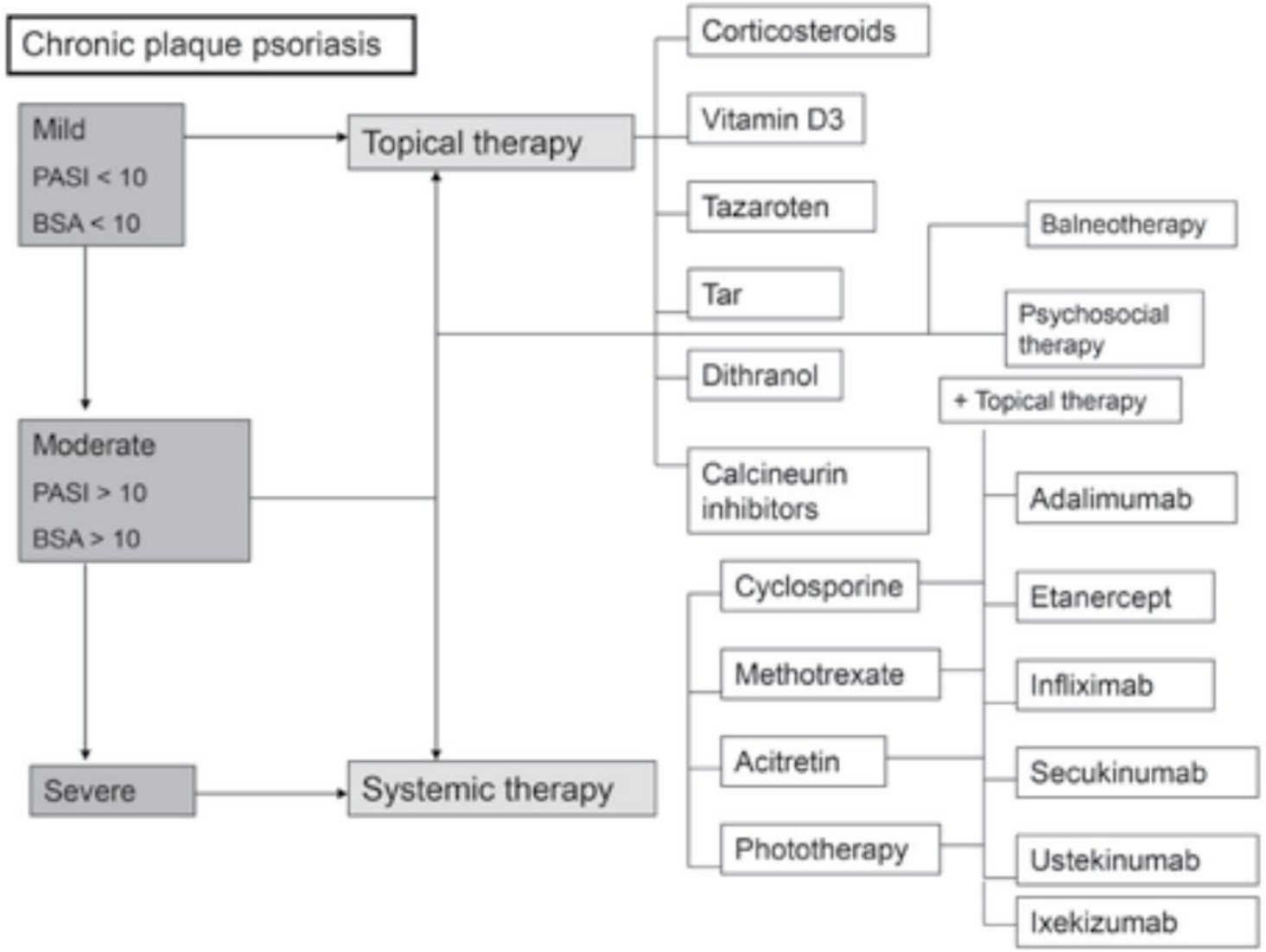
Schön MP, Wilsmann-Theis D. Current developments and perspectives in psoriasis. JDDG: Journal der Deutschen Dermatologischen Gesellschaft. 2023 Apr 5.

Psoriasis is a systemic disease



Boehncke W-H, Front Immunol. 2018; 9: 579.

Conventional Approach



Mijušković, Željko P., Kandolf-Sekulović, Lidija, Tiodorović, Danica, Nikolić, Miloš, Jovanović, Marina, Škiljević, Dušan, Gajinov, Zorica and Zečević, Radoš D.. "Serbian Association of Dermatovenereologists' Guidelines for the Diagnosis and Treatment of Psoriasis" Serbian Journal of Dermatology and Venereology, vol.8, no.2, 2017, pp.61-78. https://doi.org/10.1515/sjdv-2016-0006

Conventional Approach

- The most popular topical treatment in psoriasis is steroids
- Foam formulas have been used steroids and they may be superior
- Yet, hydroethanolic base of some foams can cause dryness and irritation
- Newer formulations are water-based and appear to be safer and more tolerable while still delivering the active agent, such as roflumilast

Kwiatkowska D, Reich A. Seeking new topical therapies in psoriasis. British Journal of Dermatology. 2023 Oct;189(4):359-60.

Psoriasis

Target	Compound	Indication – approval	Dosage (s.c.) in psoriasis vulgaris (PV) or psoriatic arthritis (PsA) in adults
Biologics			
TN-α	Adalimumab# (h IgG1 AB)	PV*, PsA, RA, JIA, AS HS, CD, UC, UV	80 mg wk. 0, 40 mg wk. 1 then every 2 wks. 40 mg; on wk. 16 40 mg q1w /80 mg q2w possible in case of nonresponse; in PsA 40 mg every 2 wk. – (hl ca. 2 wks.)
	Golimumab (h IgG1 AB)	PsA, RA, JIA, AS, UC	Once monthly 50 mg always on the same day of the month, if weight > 100 kg consider 100 mg every 4 wks. – (hl ca. 12 d)
	Etanercept (h FSP)	PV+*, PsA, RA, JIA, AS	2 × 25 mg/wk. or 1 × 50 mg/wk. (alternatively in PV: 2 × 50 mg/wk. for 12 wks., then as described as before) – (hl ca. 70 hrs.)
	Infliximab (chimeric IgG1 AB)	PV+, PsA, RA, AS[1], CD, UC	5 mg/kg Infusion i.v. wk. 0, 2, 6 then every 8 wks. or 5 mg/kg Infusion i.v. wk. 0, 2 then from wk. 6 120 mg s.c. q2W – (hl ca. 9.5 d)
	Certolizumab pegol# (hs Fab-Fragment)	PV, PsA, RA, AS	400 mg (2 × 200 mg) wk. 0, 2, 4 then every 2 wks. 200 mg or 400 mg (PV); in PsA 400 mg every 4 wks. – (hl ca. 14 d)
IL-17	Bimekizumab (IL-17 A/A, F/F, A/F) (hs IgG1 AB)	PV	320 mg (2 × 160 mg) wk. 0, 4, 8, 12, 16 then every 8 wks. or every 4 wks. if weight ≥ 120 kg – (hl ca.23 d)
	Ixekizumab (IL-17 A/A, A/F) (hs IgG4 AB)	PV*, PsA, AS	160 mg (2 × 80 mg) wk. 0 then 80 mg wk. 2, 4, 6, 8, 10, 12 then every 4 wks.; PsA 160 mg wk. 0 then 80 mg every 4 wks. – (hl ca. 13 d)
	Secukinumab (IL-17 A/A) (h IgG1 AB)	PV*, PsA*, JIA, AS	300 mg wk. 0, 1, 2, 3, 4 then monthly; 300 mg every 2 wks. possible if weight > 90 kg; in PsA and TNF-naive: initial 150 mg in wk. 0, 1, 2, 3, 4 then 150 mg monthly – (hl ca. 27 d)
IL-17RA	Brodalumab (h IgG2 AB)	PV	210 mg wk. 0, 1, 2 then every 2 wks. – (hl ca. 11 d)
IL-23	Guselkumab (h IgG1 AB)	PV, PsA	100 mg wk. 0, 4 then every 8 wks. or every 4 weeks in severe PsA – (hl ca. 15–18 d)
	Tildrakizumab (hs IgG1 AB)	PV	100 mg wk. 0, 4 then every 12 wks.; if weight ≥ 90 kg or high disease burden - 200 mg possible – (hl ca. 23 d)
	Risankizumab (hs IgG1 AB)	PV, PsA	150 mg wk. 0, 4 then every 12 wks. – (hl ca. 29 d)
IL-12/23	Ustekinumab (h IgG1 AB)	PV+*, PsA, CD, UC	45 mg wk. 0, 4 then every 12 wks.; 90 mg if weight > 100 kg – (hl ca. 15–32 d)
IL36R	Spesolimab (hs IgG1 AB)	relapses of GPP (no approval for PV)	Infusion i.v. 900 mg (2 × 450 mg), repetition after 1 wk. in case of persistence possible – (hl ca. 25.5 d)
CD80/86	Abatacept (FSP)	PsA, RA, JIA	Infusion i.v. weight adapted 500–1000 mg wk. 0, 2, 4 then every 4 wks. or 125 mg s.c. 1qw – (hl ca. 13.1 d)

Small molecules	Compound	Indication/ Approval	Dosage (p.o.) in psoriasis vulgaris (PV) or psoriatic arthritis (PsA) in adults	Binding affinity on JAK subtypes
JAK-inhibitor α-group	Tofacitinib	PsA, RA, JIA, AS[1], UC	Twice daily 5 mg alternatively 11 mg/d sustained release tablet – (hl ca. 0.5–1 hrs. or 4 hrs.)	JAK1, JAK3 > JAK2 >> TYK2
JAK-inhibitor β-group	Deucravacitinib	PV *(no EU approval)*	twice daily 6 mg (FDA-approval) – (hl ca. 7.4–13 hrs.)	TYK2
	Upadacitinib	PsA, RA, AS[1], AS, UC, AD	Once daily 15 mg – (hl ca. 2 - 4 hrs.)	JAK1 >> JAK2/JAK3
PDE4-inhibitor	Apremilast	PV+, PsA, Behçet's disease	Start with 10 mg/d and increase of 10 mg every d to 60 mg/d then maintenance: 30 mg twice daily – (hl ca. 6–9 hrs.)	Not applicable
PDE4-inhibitor	Roflumilast	PV from 12 years of age *(no EU approval)*	Topical application – cream 0.3 % once daily	Not applicable
Aryl hydrocarbon receptor agonist	Tapinarof	PV *(no EU approval)*	Topical application – cream 1 % once daily	Not applicable

Schön MP, Wilsmann-Theis D. Current developments and perspectives in psoriasis. JDDG: Journal der Deutschen Dermatologischen Gesellschaft. 2023 Apr 5.

Psoriasis Summary

Name	Class of medication	US FDA approval for psoriasis	Efficacy (vs vehicle)	Adverse events
Roflumilast 0.3% cream	PDE-4 inhibitor	Age ≥ 12 years	**DERMIS 1 and 2 (phase III)** ≥ 2 years, QD, 8 weeks IGA response: 37.5% vs 6.1%, 42.4% vs 6.9% I-IGA response: 68.1% vs 13.8%, 71.2% vs 18.5% PASI-75: 39.0% vs 5.3%, 41.6% vs 7.6% WI-NRS response: 67.5% vs 26.8%, 69.4% vs 35.6% PSD change: − 49.3 vs − 19.2, − 50.1 vs − 22.8 **PK and safety trials (phases I-II)** Phase II, 2–5 years, QD, 4 weeks Phase II, 6–11 years, QD, 4 weeks Phase I, ≥12 years, QD, 2 weeks (MUSE) Status: in progress (NCT04746911, NCT04655313, NCT04279119) **DERMIS-OLE (phase III)** 2–11 years, QD, 24 weeks Status: in progress (NCT04286607)	Diarrhea, headache, hypertension, nasopharyngitis
Roflumilast 0.3% foam	PDE-4 inhibitor	Age ≥ 12 years	**Safety and efficacy trial (phase II)** ≥ 12 years, QD, 8 weeks S-IGA response: 59.1% vs 11.4% B-IGA response: 40.3% vs 6.8% PSSI-75: 67.2% vs 21.8% PSSI-90: 46.7% vs 3.4% SI-NRS response: 71.0% vs 18.5% PSD change: − 55.0 vs − 27.5 **ARRECTOR (phase III)** ≥ 12 years, QD, 8 weeks Status: in progress (NCT05028582)	
Halobetasol propionate 0.05% foam	Corticosteroid	Age ≥ 12 years	**Safety and efficacy trial (phase III)** ≥ 18 years, BID, 2 weeks IGA response 25.3% vs 3.9%, 30.7% vs 7.4% Safety and efficacy trial (phase IV) 12–17 years, BID, 2 weeks IGA response: 54% HPA suppression: 26.1% (no clinical symptom, normalized 4 weeks after discontinuation) Adrenal suppression and absorption study (phase IV) 12–17 years, BID, 2 weeks Status: results submitted for review (NCT03992261)	Burning, stinging, skin atrophy, telangiectasia, HPA-axis suppression
Tapinarof 1% cream	AhR modulator	Age ≥ 18 years	**PSOARING 1 and 2 (phase III)** ≥ 18 years, QD, 12 weeks PGA response: 35.4% vs 6.0%, 40.2% vs 6.3% PSOARING 3 (phase III) ≥ 18 years, QD, 44 weeks Complete clearance: 40.9% PGA response: 58.2% Mean remittive effect: ~4 months **Pediatric trial (phase III)** 2–17 years, QD, 12 weeks + optional 40 weeks extension Status: in progress (NCT05172726)	Contact dermatitis, folliculitis, headache

AhR aryl hydrocarbon receptor, *BID* twice daily, *FDA* Food and Drug Administration, *HPA* hypothalamic-pituitary-adrenal, *IGA* Investigator's Global Assessment, *B-IGA* body IGA, *I-IGA* intertriginous IGA, *S-IGA* scalp IGA, *PDE-4* phosphodiesterase type 4, *PASI* Psoriasis Area and Severity Index, PGA Physician's Global Assessment, *PK* pharmacokinetic, *PSD* Psoriasis Symptom Diary, *PSSI* Psoriasis Scalp Severity Index, *QD* once daily, *SI-NRS* Scalp Itch Numeric Rating Scale, *WI-NRS* Worst Itch Numeric Rating Scale

Lie E, Choi M, Wang SP, Eichenfield LF. Topical Management of Pediatric Psoriasis: A Review of New Developments and Existing Therapies. Pediatric Drugs. 2023 Oct 17:1-0.

Treatment Considerations

- Location and extent of skin Involvement
- Presence of joint involvement
- Psychosocial impact
- Patient preference/FEARS
- TREAT TO TARGET
- Patient tolerance for different treatment options
- Cost
- Time…

Thank You!