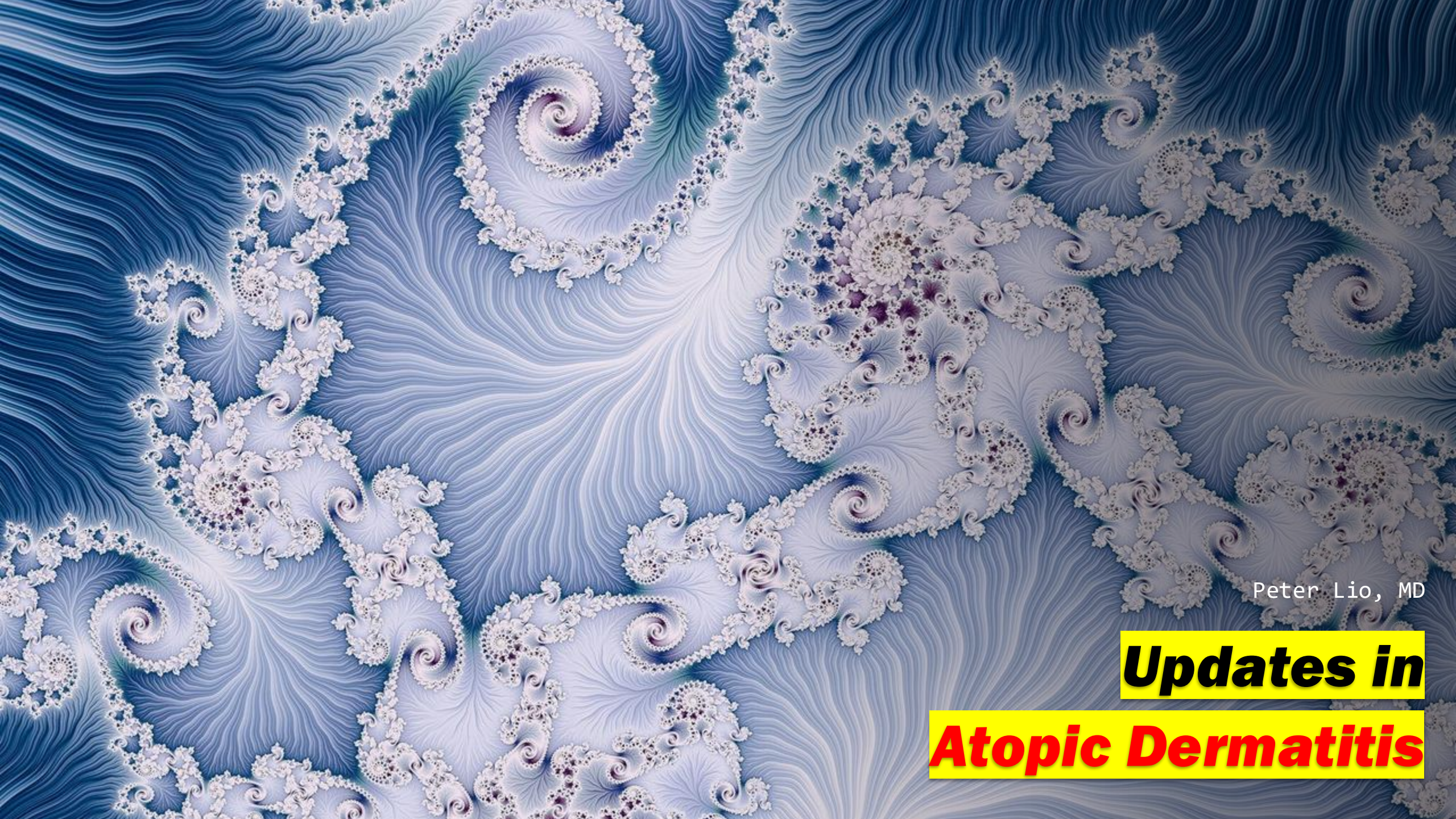


Peter Lio, MD

Updates in Atopic Dermatitis

DISCLOSURE

- Peter Lio, MD, FAAD

Relationship	Manufacturer
Speaker	AbbVie, Arcutis, Eli Lilly, Galderma, Hyphens Pharma, Incyte, La Roche-Posay/L'Oreal, MyOR Diagnostics, Pfizer, Pierre-Fabre Dermatologie, Regeneron/Sanofi Genzyme, Verrica
Advisory Board	Alphyn Biologics, AbbVie, Almirall, Amyris, Arcutis, ASLAN, Atria Therapeutics, Boston Skin Science, Bristol-Myers Squibb, Burt's Bees, Castle Biosciences, Codex Labs, Concerto Biosci, ClearRx, Dermavant, Eli Lilly, Galderma, Kenvue, LEO Pharma, Lipidor, L'Oreal, Merck, Midwest Bioprocessing, Micreos, MyOR Diagnostics, Nektar Therapeutics, Nia Health, Pelthos Therapeutics, Phyla, Regeneron/Sanofi Genzyme, Sibel Health, Skinfix, Soteri Skin, Stratum Biosciences, Theraplex, Thimble Health, Topaz Biosciences, UCB, Unilever, Verdant Scientific, Verrica, Yobee Care
Patent Holder	Theraplex AIM (Patent Pending)
Stock Options	Codex Labs, Concerto Biosci, LearnSkin/Learn Health, Medable, Modernizing Medicine, Suneco Technologies, Yobee Care, Verdant Scientific

A HETEROGENEOUS DISEASE

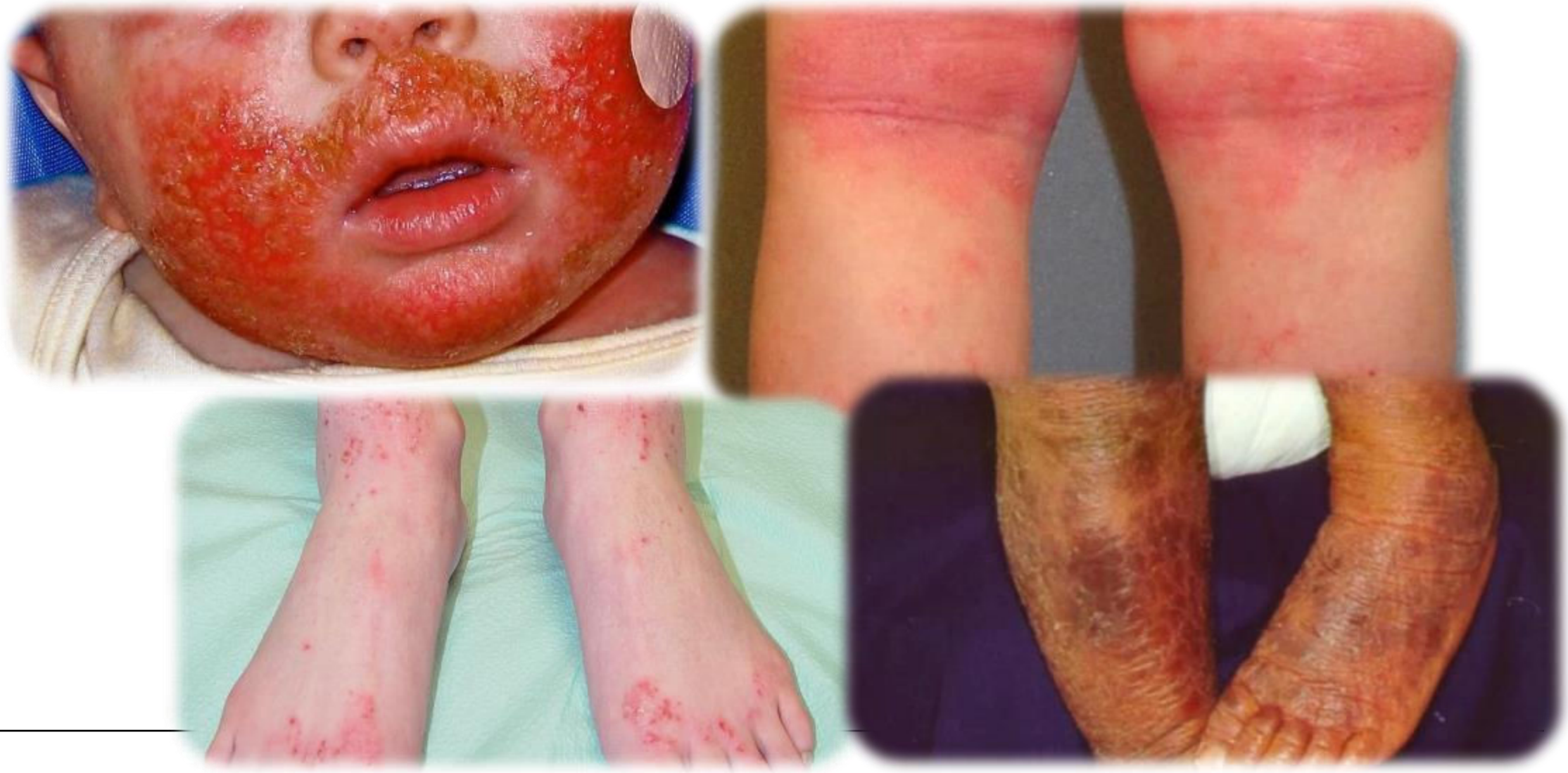
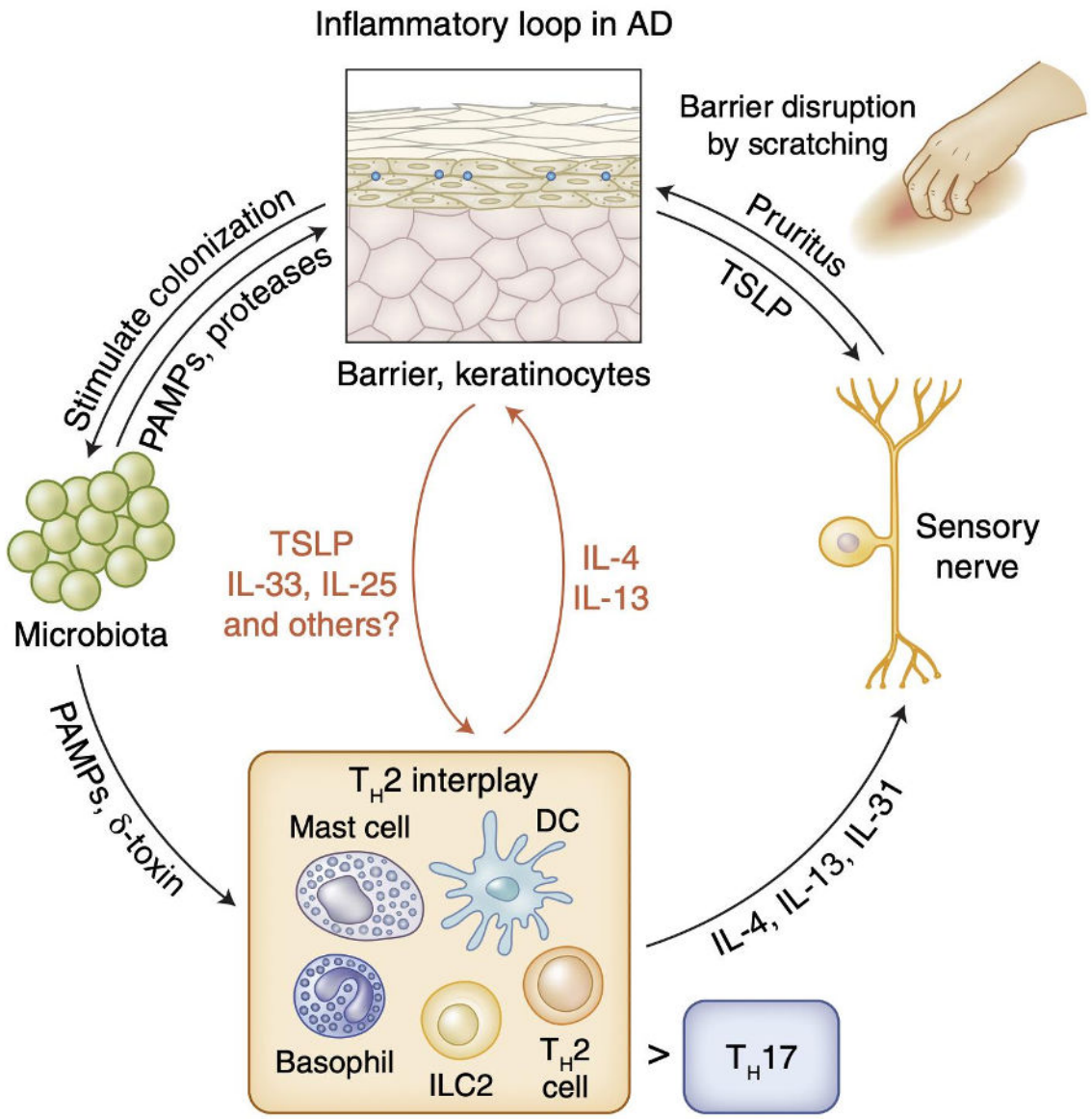


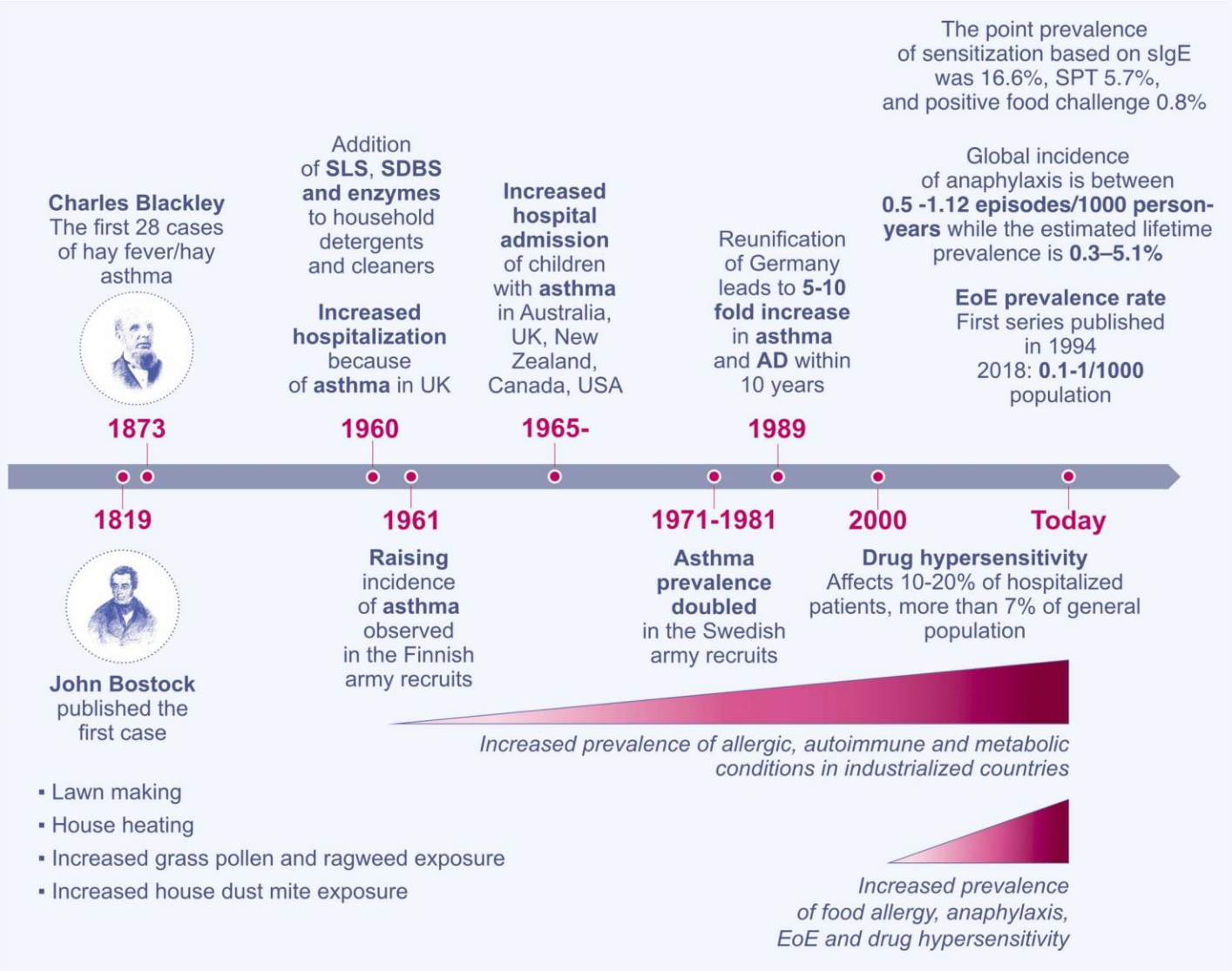
Photo courtesy of Peter Lio, MD (Consent on file)

LOOP



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.

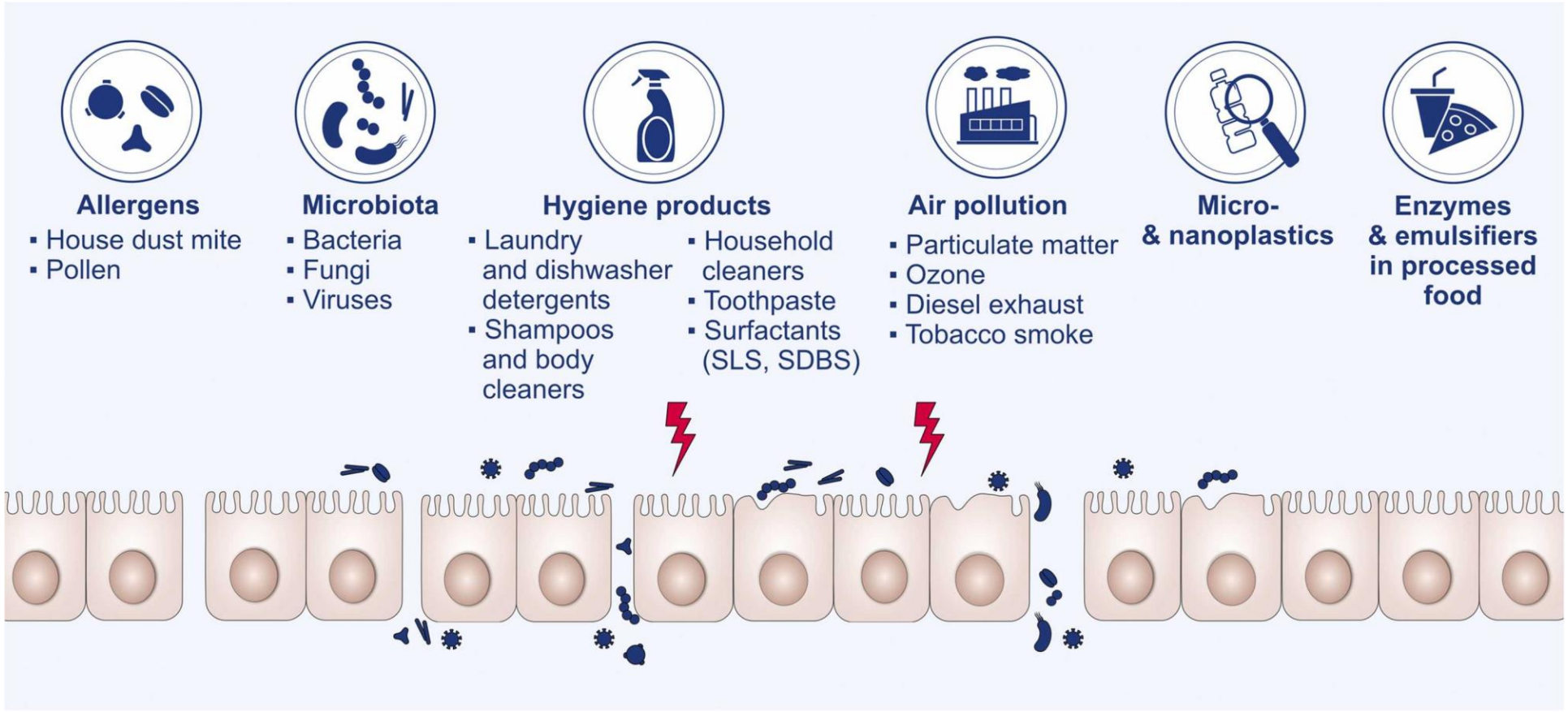
THE RISE OF ALLERGY



- SLS = sodium lauryl sulfate, SDBS = sodium dodecyl benzene sulfonate; SPT = skin prick test; EoE = eosinophilic esophagitis.
  Yazici D, et al. *Semin Immunol*. 2023;70:101846.

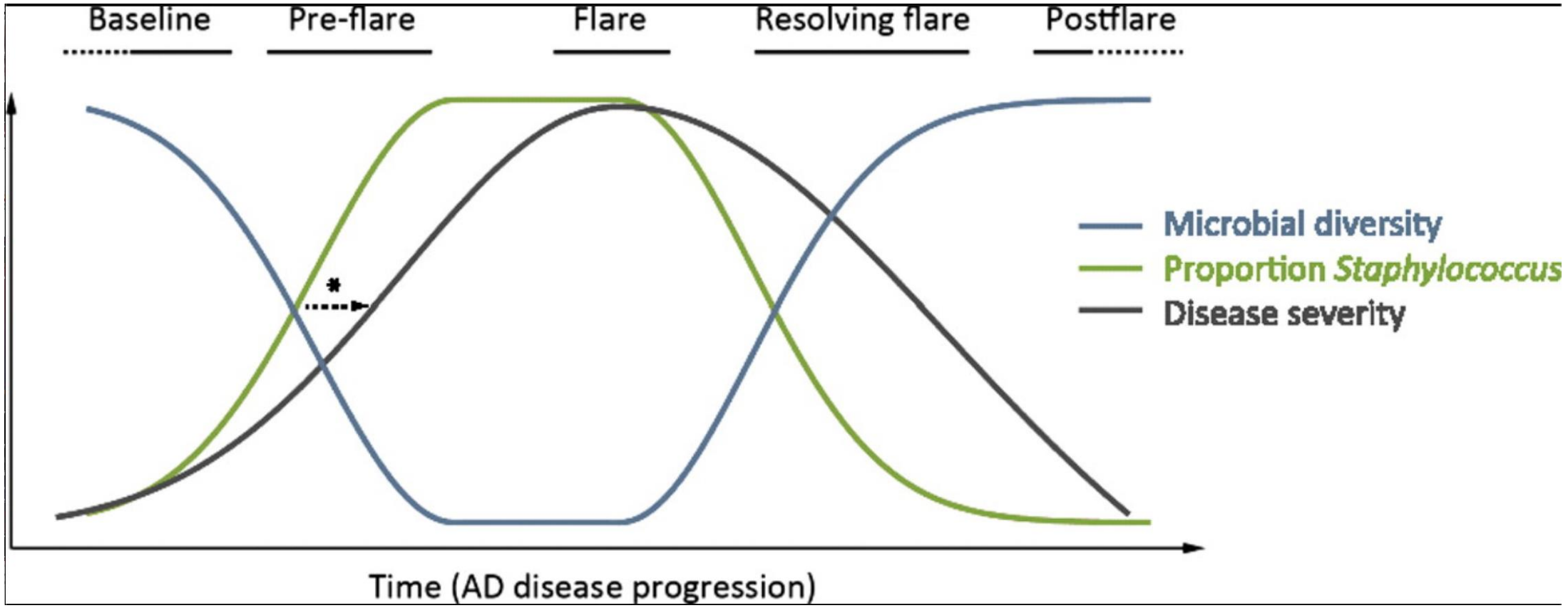
EPITHELIAL BARRIER HYPOTHESIS

- Industrialization, urbanization and Westernized lifestyle have a devastating impact on the epithelial barriers of the skin, airways, and gut mucosa as proposed by the Epithelial Barrier Theory



- Yazici D, et al. *Semin Immunol*. 2023;70:101846.

STAPH



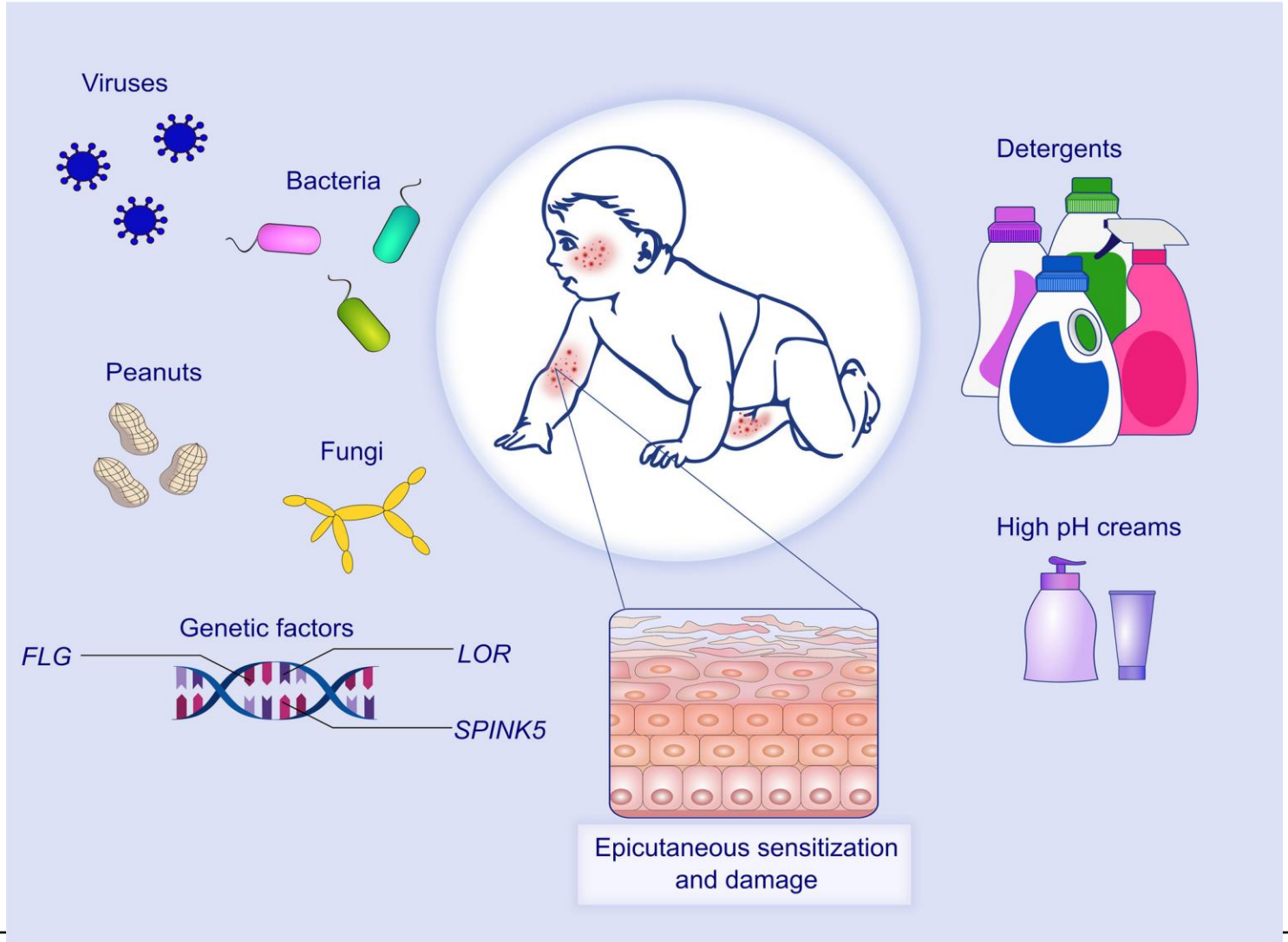
- Kong HH, et al. *Genome Res*. 2012;22(5):850-9.

Table 1. *Staphylococcus aureus* Proteins That Contribute to Atopic Dermatitis

S. aureus proteins	Possible role in AD
Clumping factor B	Adhesion to corneocytes in stratum corneum via loricrin or other ligands
Fibronectin-binding proteins	Adhesion to fibronectin that is present at high levels in the upper strata of epidermis and stratum corneum of AD skin
Protein A	Proinflammatory. Binds to TNFR-1 on keratinocytes
Lipoproteins	Proinflammatory. Activate TLR-2 on keratinocytes
α-Toxin	Membrane damage/lysis of keratinocytes
δ-Toxin	Mast cell degranulation. Synergy with IgE. Allergic skin inflammation
Phenol-soluble modulins	Trigger proinflammatory responses associated with AD in keratinocytes at sublytic concentrations
Enterotoxins and TSST-1	Excessive T cell cytokine production and toxicity. Allergens. Enterotoxins might trigger mast cell degranulation directly
Staphopain Aureolysin	Inactivation of antimicrobial peptides
V8 serine protease	Epidermal barrier dysfunction in hairless mice
Serine protease-like proteins	Potent allergens in idiopathic asthma following *S. aureus* colonization. Similar role in AD?

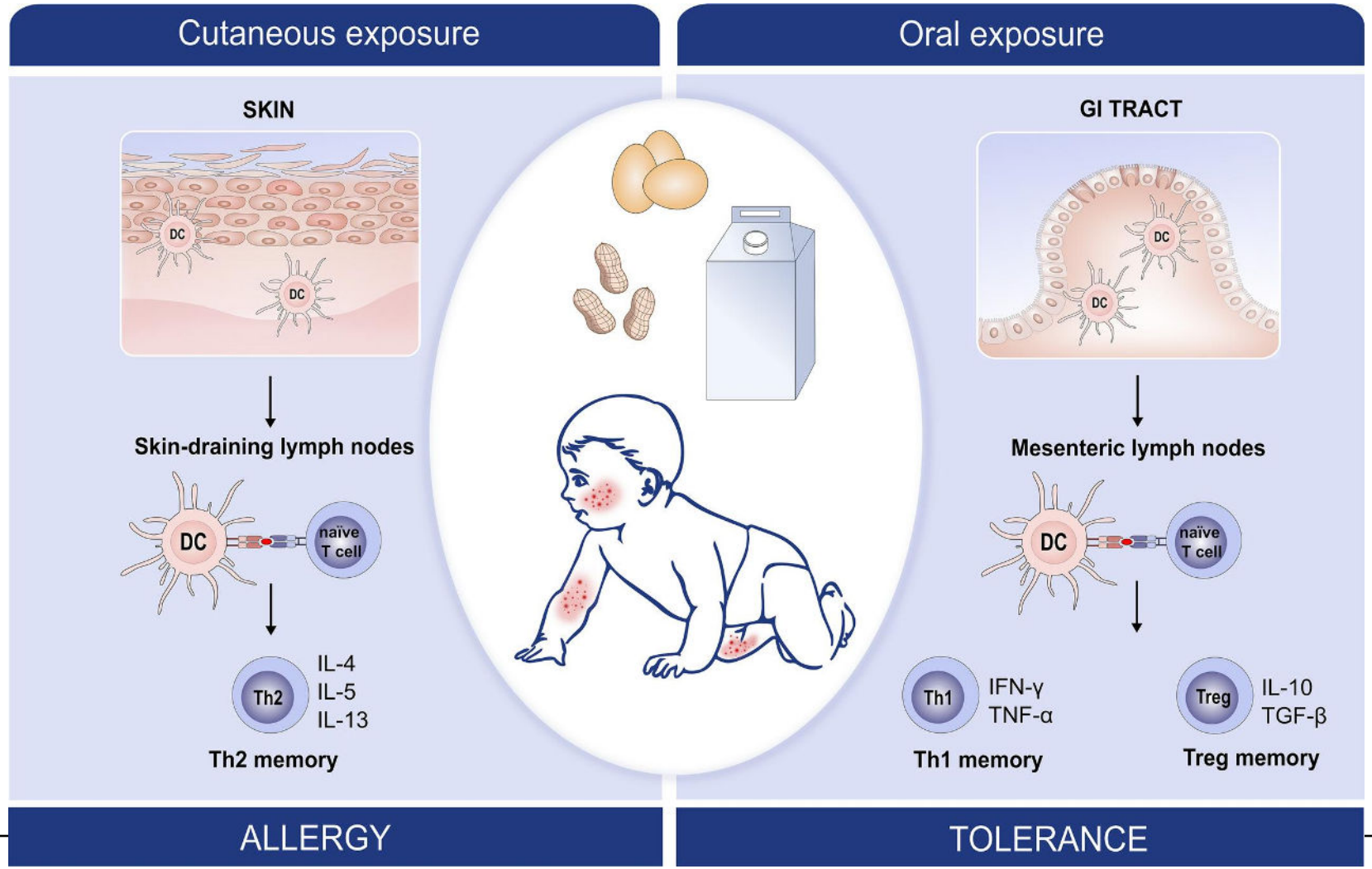
- Geoghegan JA, et al. *Trends Microbiol*. 2018;26(6):484-497.

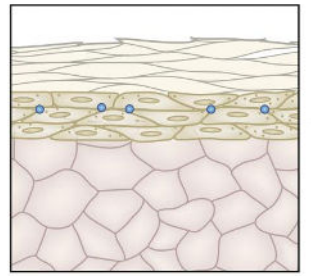
Environmental and genetic factors leading to epicutaneous damage



- Brough HA, et al. *Allergy*. 2020;75(9):2185-2205.

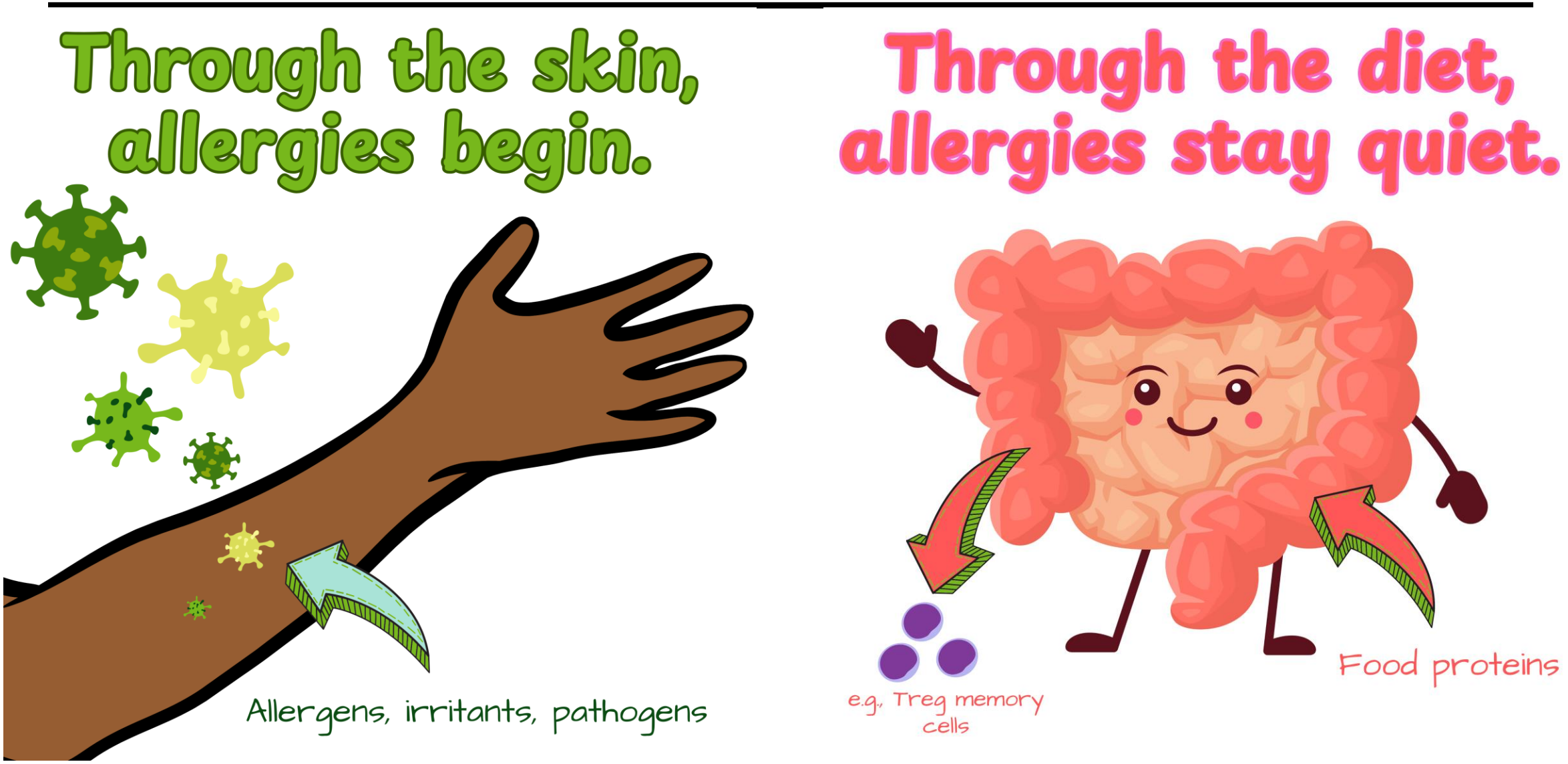
EPICUTANEOUS SENSITIZATION



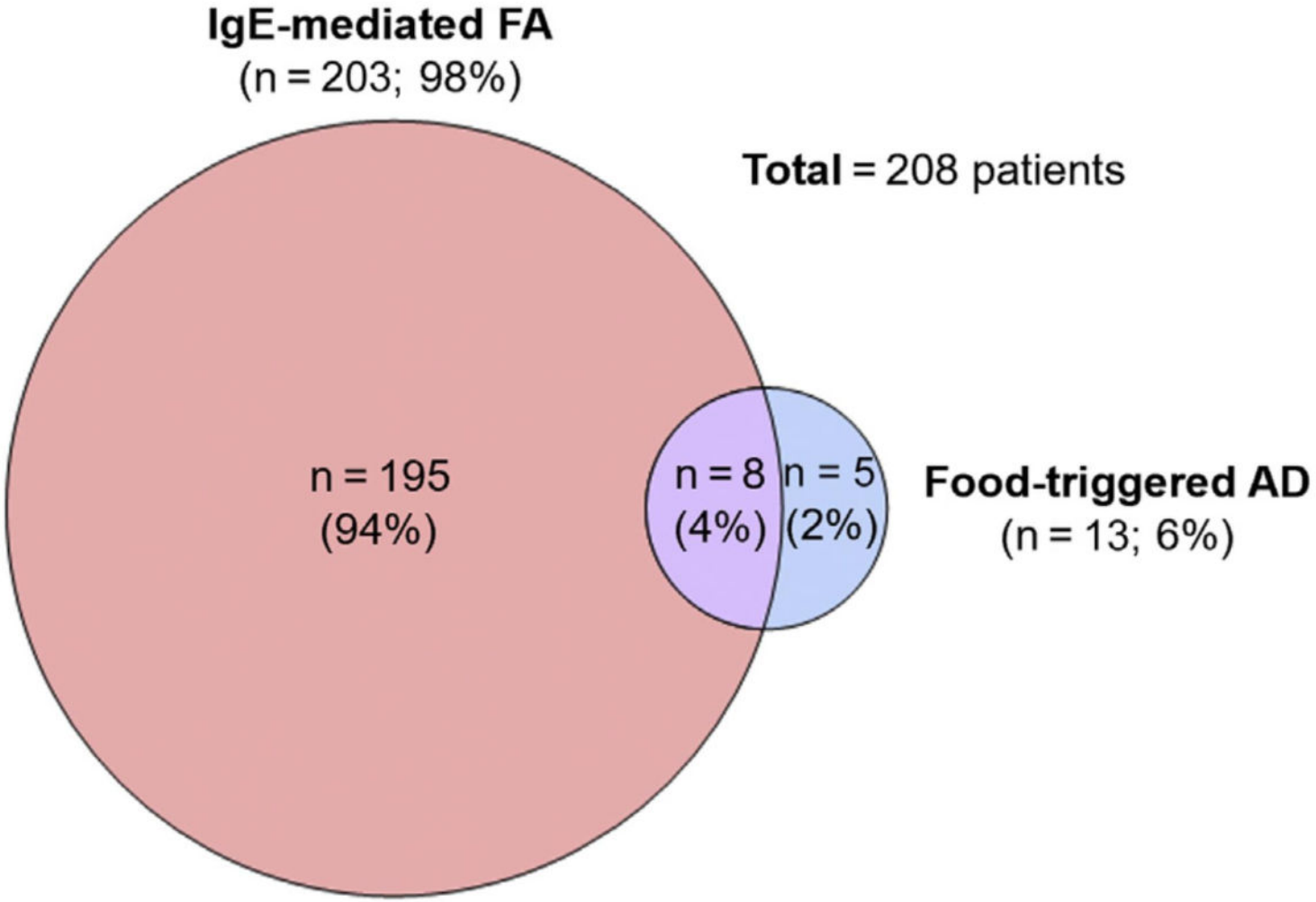


Barrier, keratinocytes

- Brough HA, et al. *Allergy*. 2020;75(9):2185-2205.

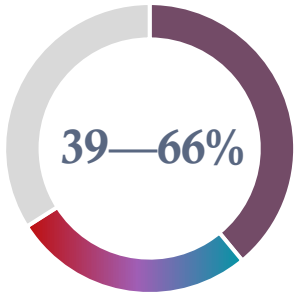


- Figures: originals by Peter Lio, MD. Quote attributed to Ruchi Gupta, MD

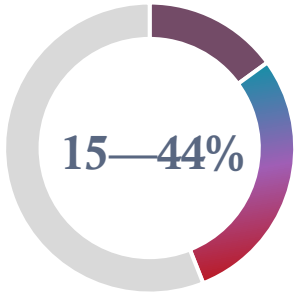


Li JC, Arkin LM, Makhija MM, Singh AM. Prevalence of food allergy diagnosis in pediatric patients with atopic dermatitis referred to allergy and/or dermatology subspecialty clinics. The Journal of Allergy and Clinical Immunology: In Practice. 2022 Sep 1;10(9):2469-71.

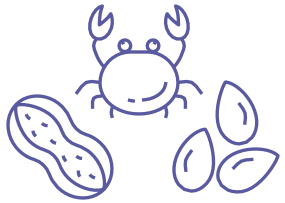
PREVALENCE OF FOOD SENSITIZATION AND FOOD ALLERGY IS HIGH IN PATIENTS WITH AD[1-3]



Prevalence of **food sensitization** in children with AD[1]



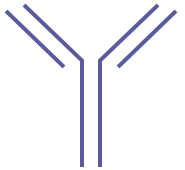
Prevalence of **food allergy** in children with AD[1]



FOOD ALLERGY

- Defined as a food hypersensitivity reaction mediated by immunology mechanisms

FOOD ALLERGY VS FOOD SENSITIZATION



FOOD SENSITIZATION

- Refers to the production of food-allergen-specific IgE
- Is a prerequisite for food allergy

The prevalence of food allergy is higher in children with moderate to severe AD[2]

AD, atopic dermatitis; IgE, immunoglobulin E.

1. Tsakok T, et al. *J Allergy Clin Immunol.* 2016;137(4):1071-1078. 2. Fleischer DM, et al. *J Allergy Clin Immunol Pract*. 2021;9(1):22-43.e4. 3. Papapostolou N, et al. *J Clin Med*. 2022;11(14):4232.

GOALS

1. Get clear
2. Keep clear – safely
3. Keep it up

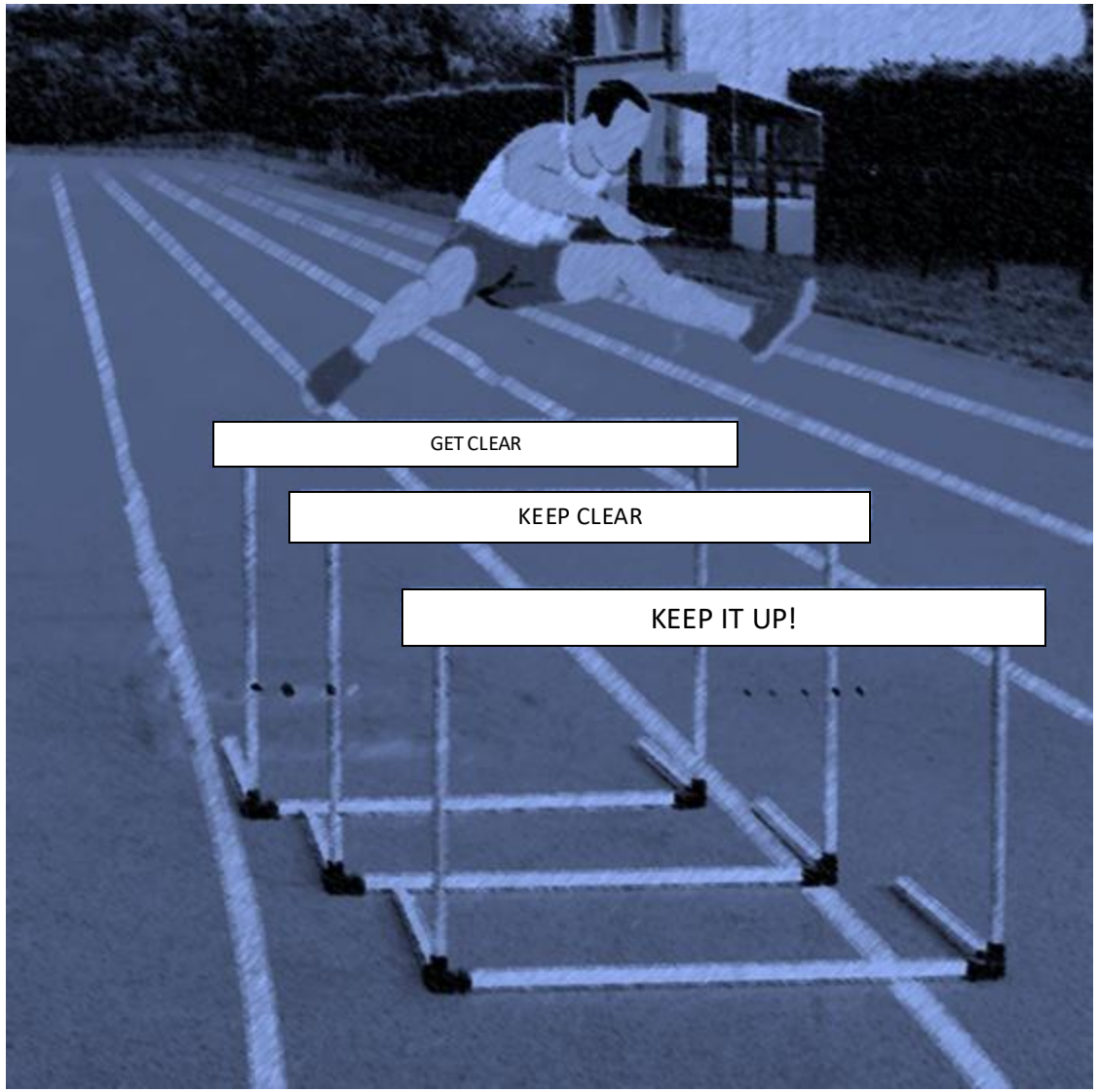
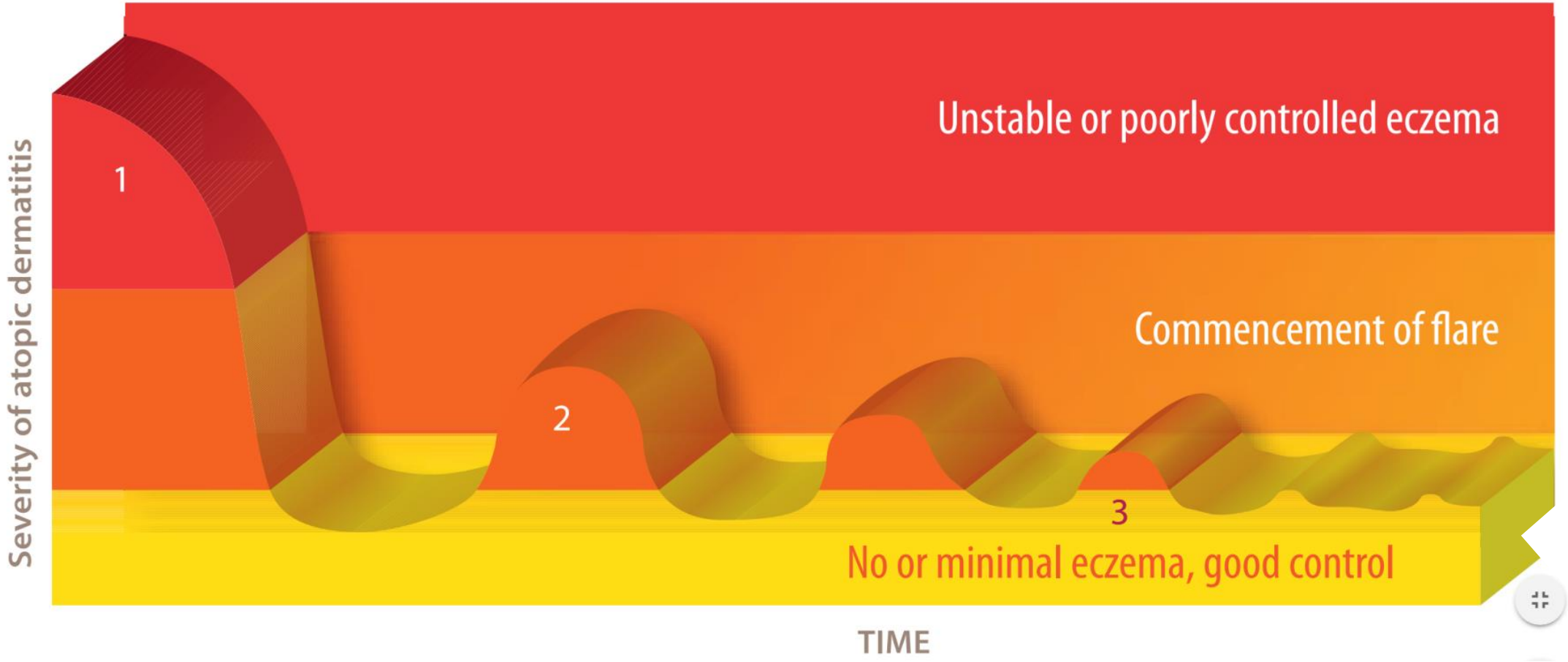


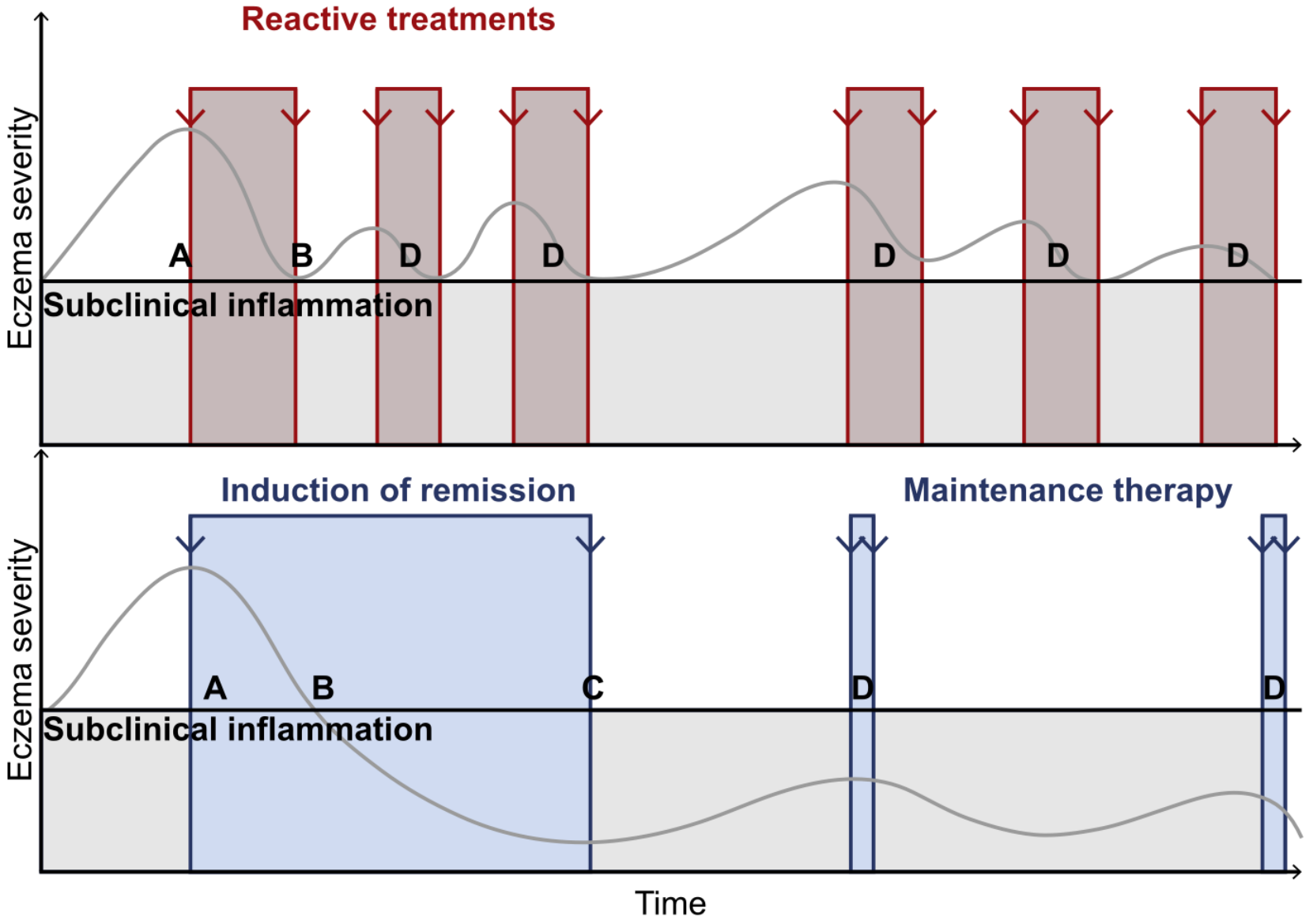
Image credit: Peter Lio, MD

Treatment Goal



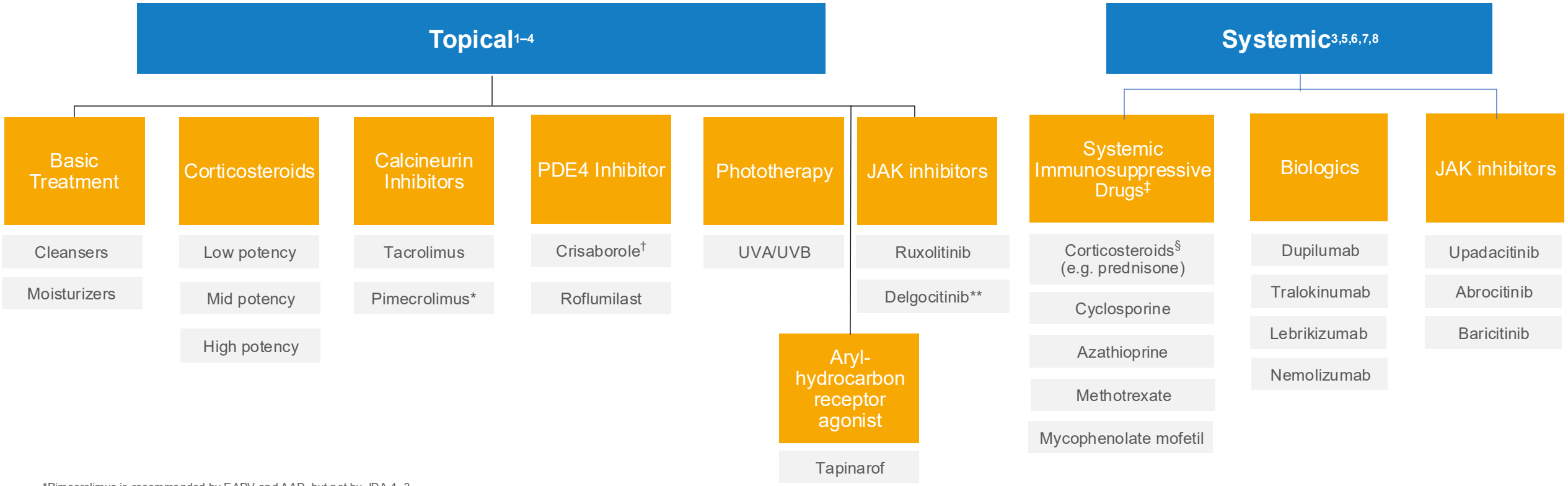
Rubel D, et al. *J Dermatol*. 2013;40(3):160-171.

JTF Guidelines

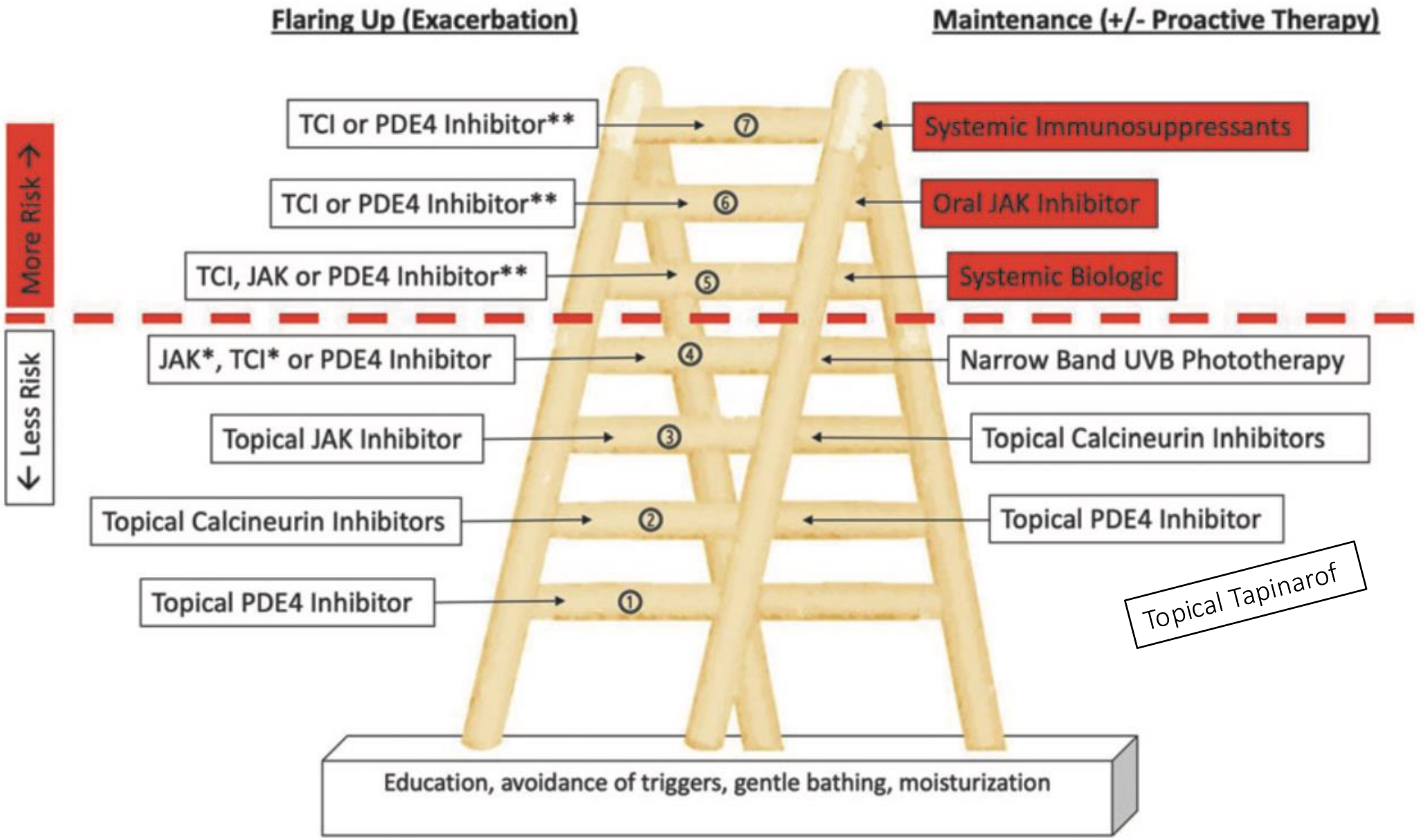


AAAAI/ACAAI JTF Atopic Dermatitis Guideline Panel; Chu DK, Schneider L, Asiniwasis RN, Boguniewicz M, De Benedetto A, Ellison K, Frazier WT, Greenhawt M, Huynh J, Kim E, LeBovidge J, Lind ML, Lio P, Martin SA, O'Brien M, Ong PY, Silverberg JI, Spergel JM, Wang J, Wheeler KE, Guyatt GH; Patient Groups, Global Parents for Eczema Research; Capozza K; National Eczema Association; Begolka WS; Evidence in Allergy Group; Chu AWL, Zhao IX, Chen L, Oykhman P, Bakaa L; AAAAI/ACAAI Joint Task Force on Practice Parameters; Golden D, Shaker M, Bernstein JA, Greenhawt M, Horner CC, Lieberman J, Stukus D, Rank MA, Wang J, Ellis A, Abrams E, Ledford D, Chu DK. Atopic dermatitis (eczema) guidelines: 2023 American Academy of Allergy, Asthma and Immunology/American College of Allergy, Asthma and Immunology Joint Task Force on Practice Parameters GRADE- and Institute of Medicine-based recommendations. Ann Allergy Asthma Immunol. 2023 Dec 15:S1081-1206(23)01455-2. doi: 10.1016/j.anai.2023.11.009. Epub ahead of print. PMID: 38108679.

Treatment Landscape



*Pimecrolimus is recommended by EADV and AAD, but not by JDA.1–3
**Delgocitinib is approved for Chronic Hand Eczema only.
†In 2016, the FDA approved crisaborole for the topical treatment of mild-to-moderate AD in patients aged ≥3 Months.
‡Cyclosporine is the only approved systemic immunosuppressive drug for AD (approved in most European countries and Japan).3,7 Off-label use of cyclosporine is recommended by AAD.
5 Off-label use of azathioprine, methotrexate, and mycophenolate mofetil is recommended by AAD and EADV.5,6
§Treatment guidelines recommend oral/injectable corticosteroids for the short-term treatment of acute flare in patients with severe AD.3,5,6
FDA, US Food and Drug Administration; PDE4, phosphodiesterase 4; UVA, ultraviolet A; UVB, ultraviolet B.
1. Eichenfield LF et al. J Am Acad Dermatol 2014;71:116–132. 2. Ring J et al. J Eur Acad Dermatol Venereol 2012;26:1045–1060. 3. Saeki H et al. J Dermatol 2016;43:117–1145. 4. FDA. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm533371.htm. 5. Sidbury R et al. J Am Acad Dermatol 2014;71:327–349. 6. Ring J et al. J Eur Acad Dermatol Venereol 2012;26:1176–1193.
7. Bieber T, Straeter B. Allergy 2015;70:6–11; 8. Gooderham M et al. JCMS 2017;21:31-39.

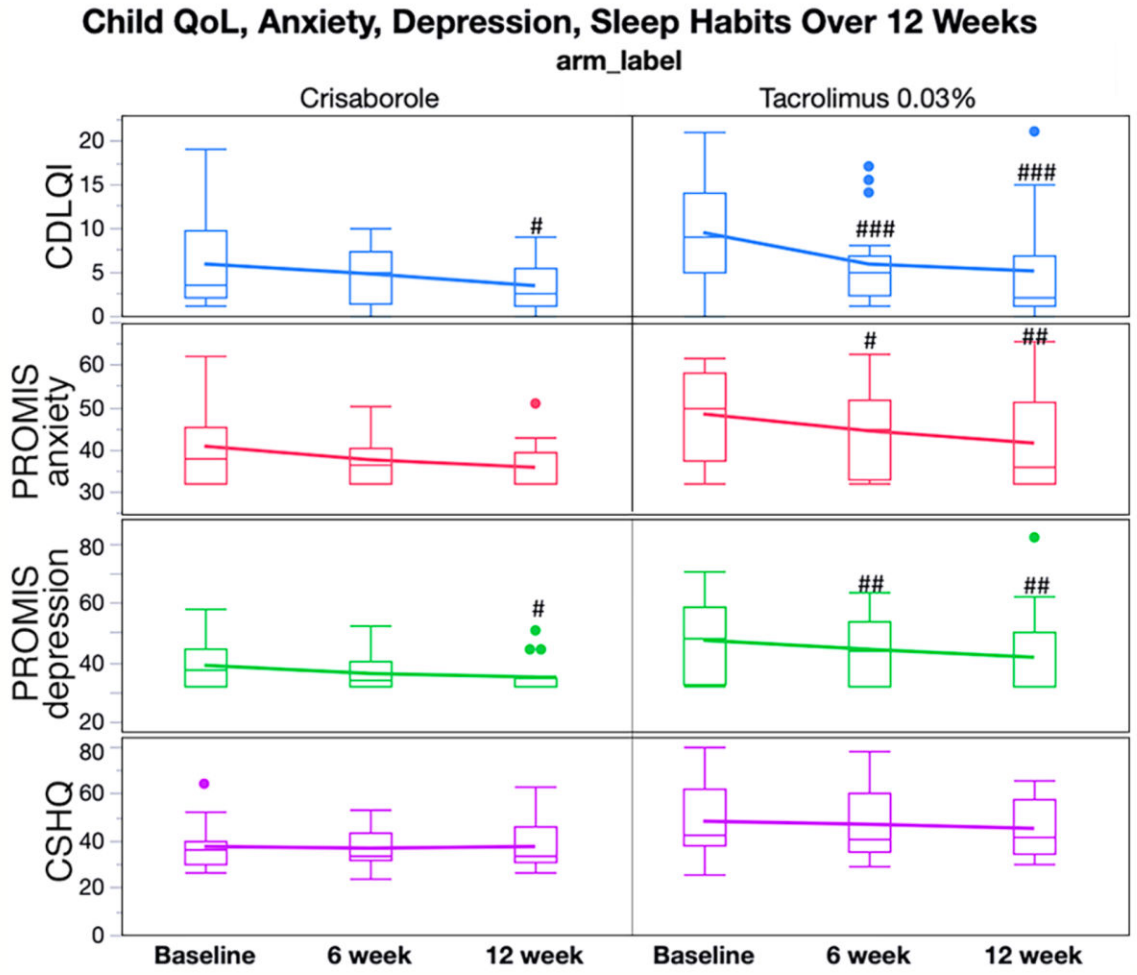


Ch'en PY, Lio PA. Nonsteroidal Approaches for Atopic Dermatitis: A Clinical Update. Dermatitis®. 2024 Feb 6.

Tacrolimus vs. Crisaborole

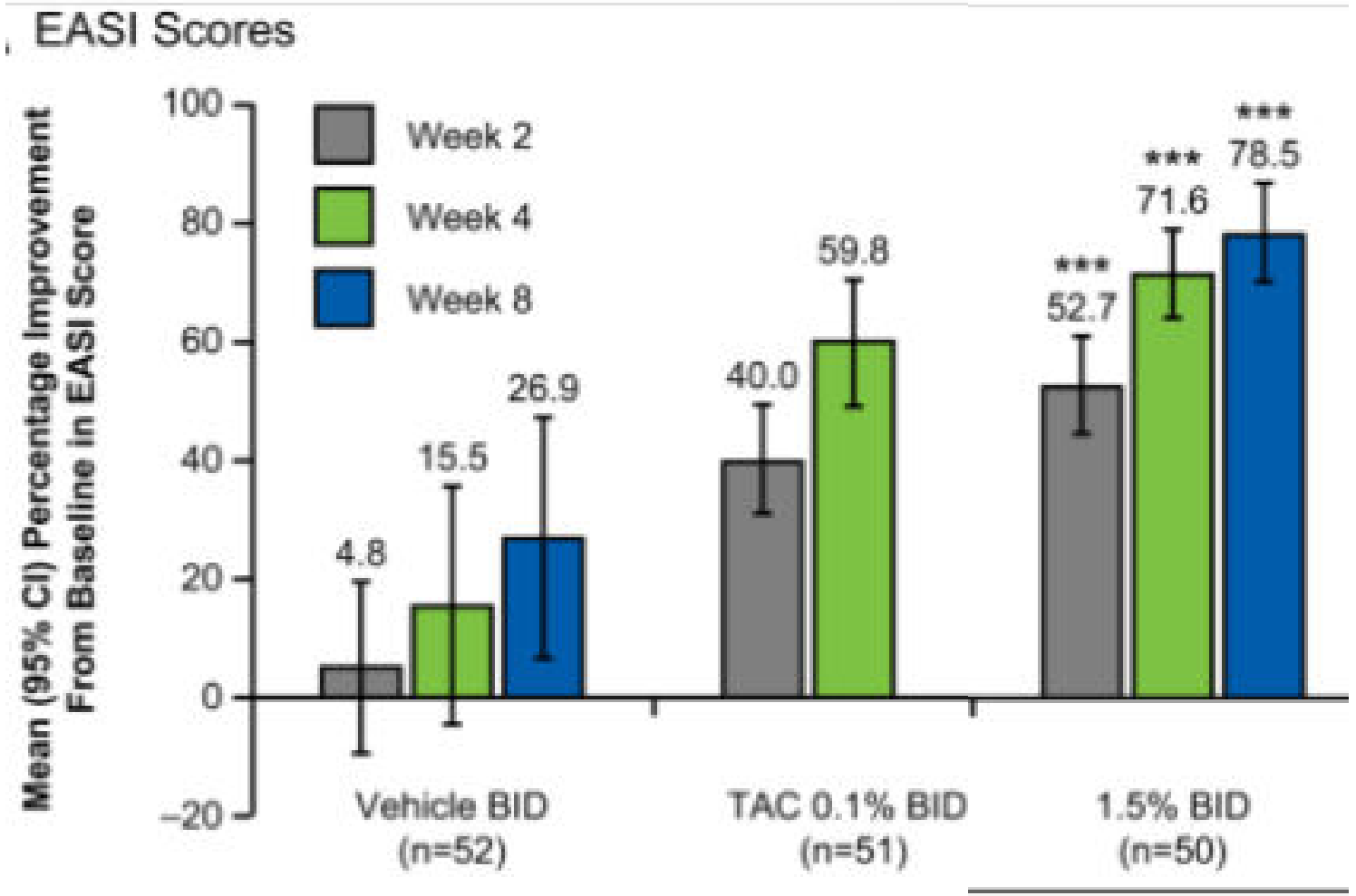
- Analyses showed no difference in 12-week change scores for itch and pain interference between arms
- TAC improved more outcome measures at 12weeks than CRIS
- Additionally, CRIS was associated with more reports of burning throughout the study

"Our results suggest that TAC may be the better overall treatment for mild AD based on patient and caregiver perspectives."



Ryan Wolf J, Chen A, Wieser J, Johnson B, Baughman L, Lee G, Pope E, Franco A, Love T, Beck LA. Improved patient-and caregiver-reported outcomes distinguish tacrolimus 0.03% from crisaborole in children with atopic dermatitis. Journal of the European Academy of Dermatology and Venereology. 2024.

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)
- Click to edit Master text styles

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).

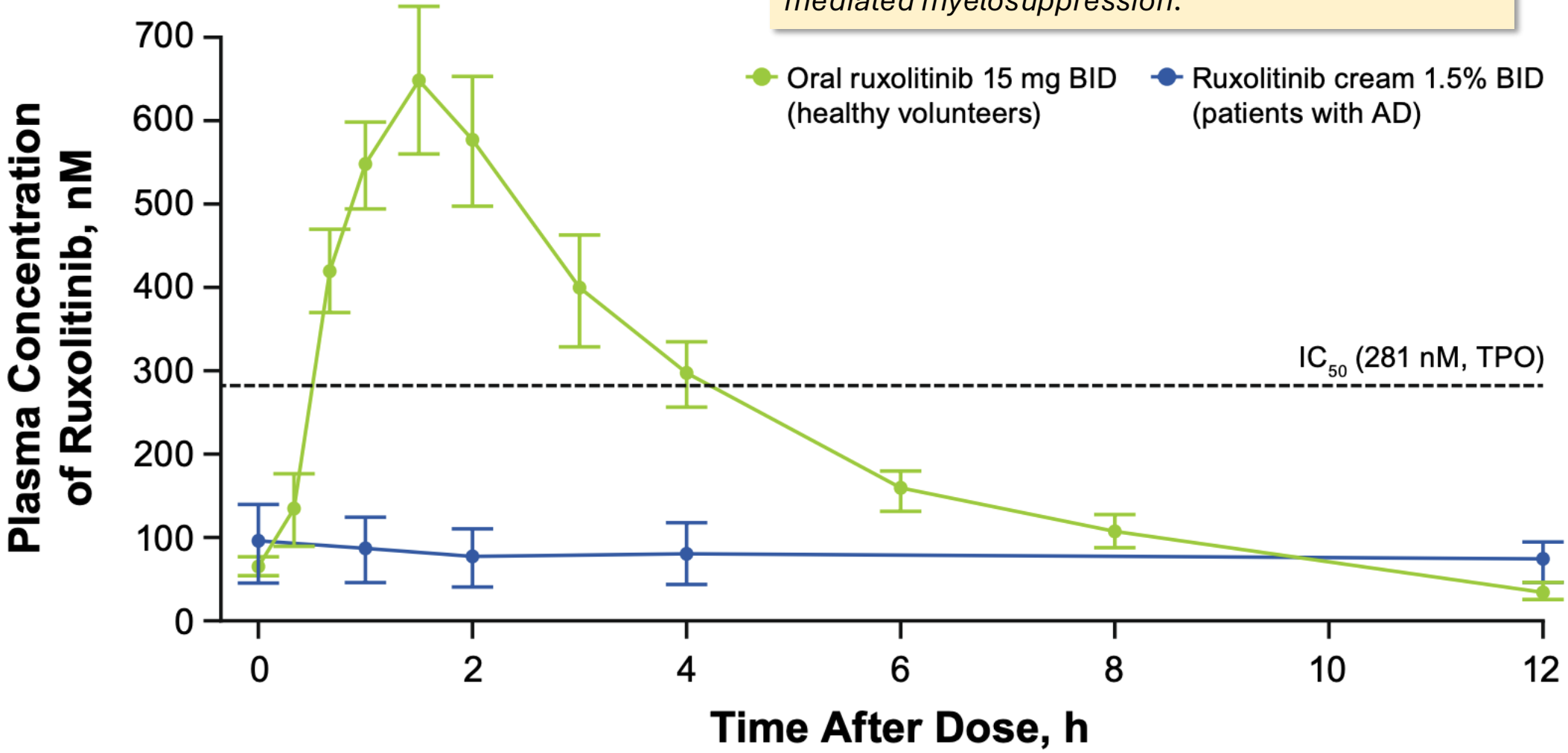
ADVERSE REACTIONS

- 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

"The mean steady-state plasma concentration of ruxolitinib remained consistently below the half-maximal inhibitory concentration of Janus kinase-mediated myelosuppression."



IC_{50} half-maximal inhibitory concentration, *TPO* thrombopoietin

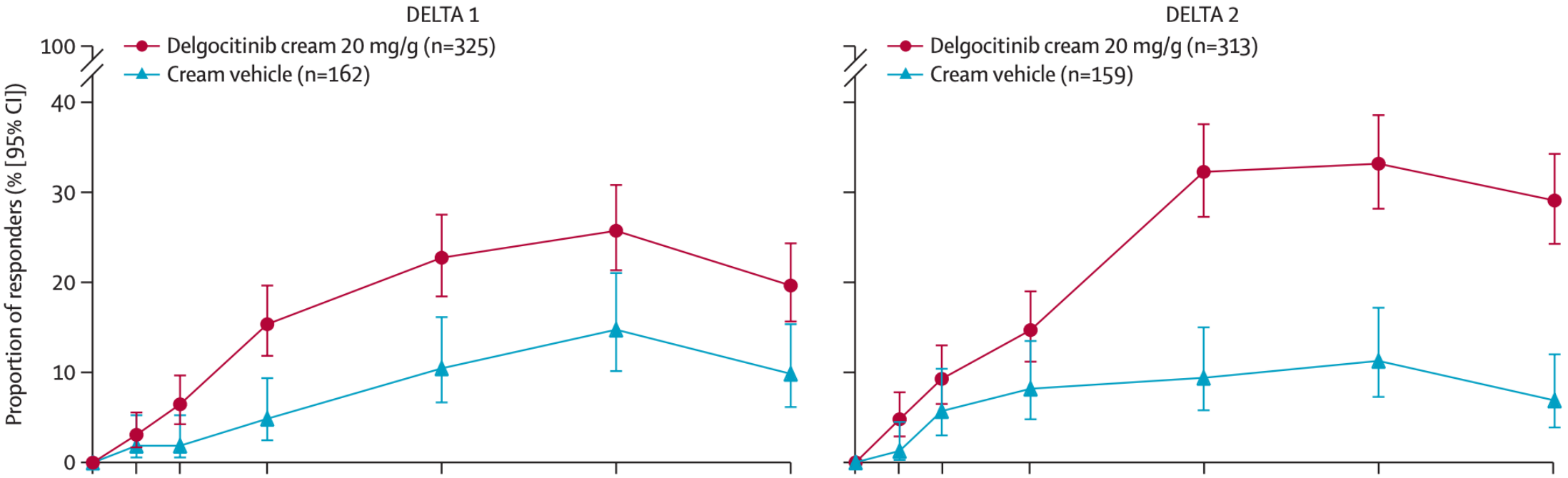
Bissonnette R, Call RS, Raoof T, Zhu Z, Yeleswaram S, Gong X, Lee M. A Maximum-Use Trial of Ruxolitinib Cream in Adolescents and Adults with Atopic Dermatitis. American Journal of Clinical Dermatology. 2022 Apr 4:1-0.

Delgocitinib

Pan-JAK inhibitor cream
Approved on 7/23/25 for the topical treatment of moderate-to-severe chronic hand eczema (CHE) in adults

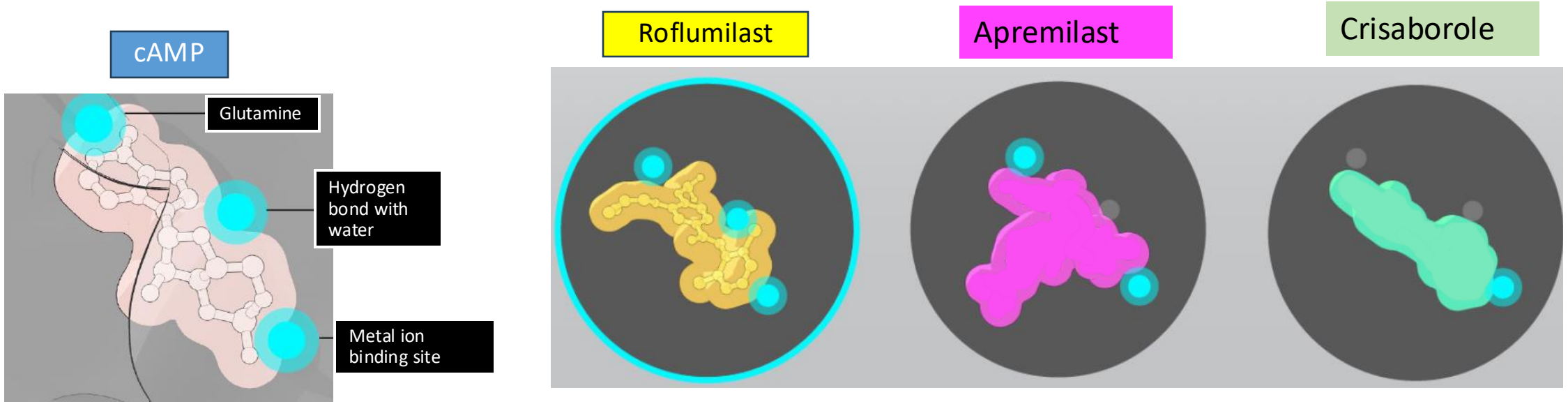
Chronic hand eczema subtype‡	
Atopic hand eczema	217 (45%)
Allergic contact dermatitis	84 (17%)
Hyperkeratotic eczema	77 (16%)
Irritant contact dermatitis	75 (15%)
Vesicular hand eczema (pompholyx)	34 (7%)

IGA 0 or 1



Bissonnette R, Warren RB, Pinter A, Agner T, Gooderham M, Schuttelaar ML, Crépy MN, Stingeni L, Serra-Baldrich E, Baranowski K, Korn S. Efficacy and safety of delgocitinib cream in adults with moderate to severe chronic hand eczema (DELTA 1 and DELTA 2): results from multicentre, randomised, controlled, double-blind, phase 3 trials. The Lancet. 2024 Aug 3;404(10451):461-73.

PDE4 inhibitors are molecularly distinct



Roflumilast has not been studied in head-to-head clinical trials and the comparative clinical significance is unknown.
Efficacy and safety cannot be derived from these data.

Wang J, et al. International Societies for Investigative Dermatology (ISID) Meeting 2023.

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

Approved on 7/9/24 in the 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 (AEs)

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

Gooderham MJ et al. SKIN. 4(6):s93.
https://jofskin.org/index.php/skin/article/view/1063.

Treatment-emergent adverse events (at least 1.0%) in INTEGUMENT 1 and 2

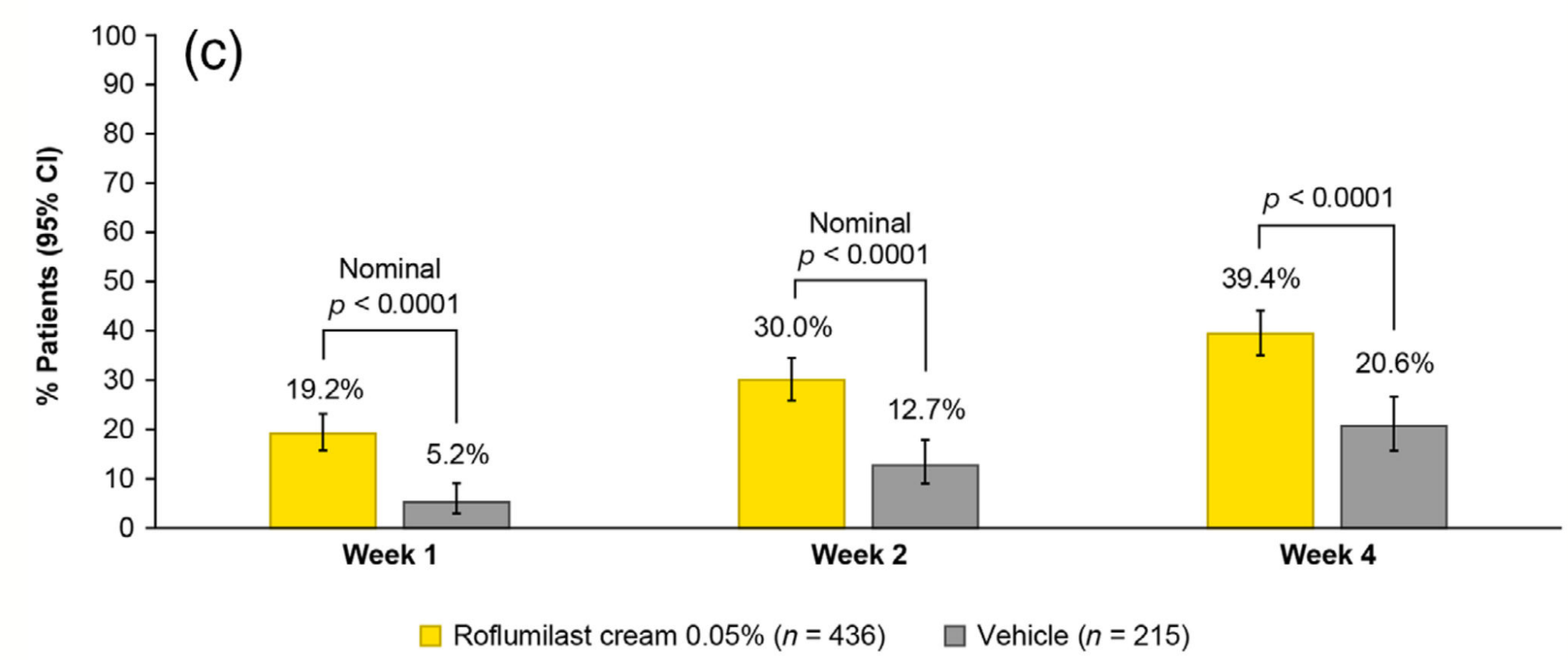
	Roflumilast (n=885)	Vehicle (n=451)
Headache	26 (2.9%)	4 (0.9%)
Nausea	17 (1.9%)	2 (0.4%)
Application site pain	13 (1.5%)	3 (0.7%)
Diarrhea	13 (1.5%)	2 (0.4%)
Vomiting	13 (1.5%)	2 (0.4%)

- Stinging or burning: 1.6% with roflumilast vs 2.0% with vehicle after first application

Prescribing information. Arcutis Biotherapeutics, Inc; 2024.
Bunick CG, et al. Poster presented at: Fall Clinical Dermatology Conference Meeting; October 19-22, 2023; Las Vegas, NV

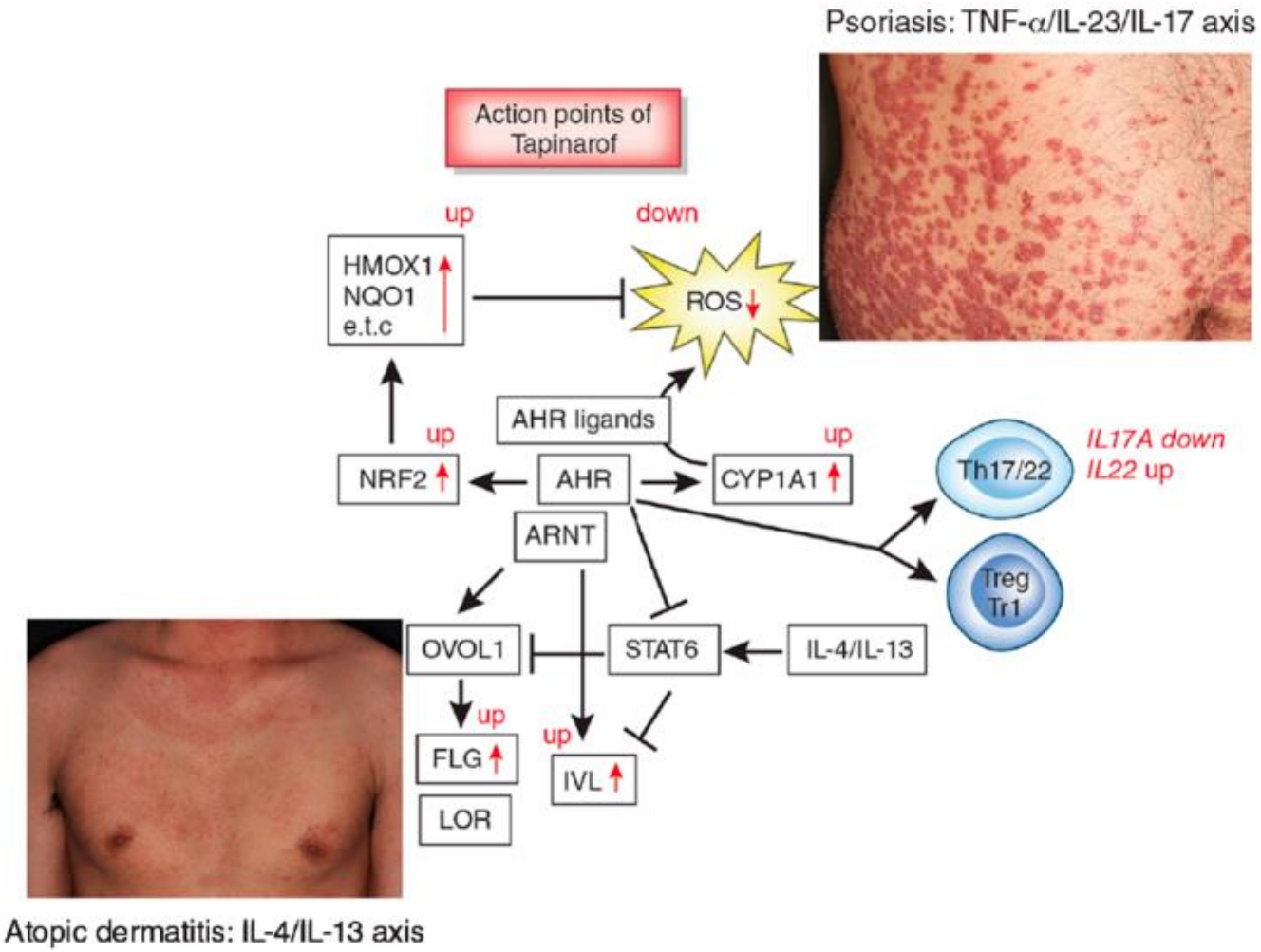
- 0.15% daily for ages 6 years+
- **<u>0.05% daily for ages 2-5 years: October 6, 2025</u>**

Proportion of patients achieving EASI- 75. Intent- to- treat population.



Eichenfield LF, Serrao R, Prajapati VH, Browning JC, Swanson L, Funk T, Gonzalez ME, Hebert AA, Lee M, Boguniewicz M, Simpson EL. Efficacy and Safety of Once-Daily Roflumilast Cream 0.05% in Pediatric Patients Aged 2–5 Years With Mild-to-Moderate Atopic Dermatitis (INTEGUMENT-PED): A Phase 3 Randomized Controlled Trial. Pediatric dermatology. 2025 Mar;42(2):296-304.

Therapeutic Aryl Hydrocarbon Receptor Modulation in AD With Tapinarof Cream



Approved by FDA for the treatment of plaque psoriasis in adults May 2022 and for adults and children down to age 2 years with AD in Dec 2024 (tapinarof 1% cream once daily)

Furue M et al. *Int J Mol Sci.* 2019;20:5424

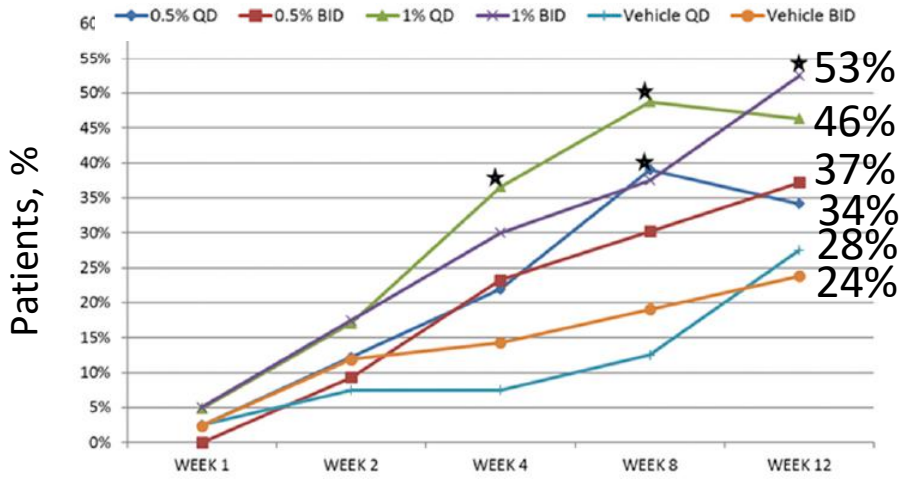
Tapinarof: Efficacy in Atopic Dermatitis

Approved on 12/24 down to 2-year-olds!

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

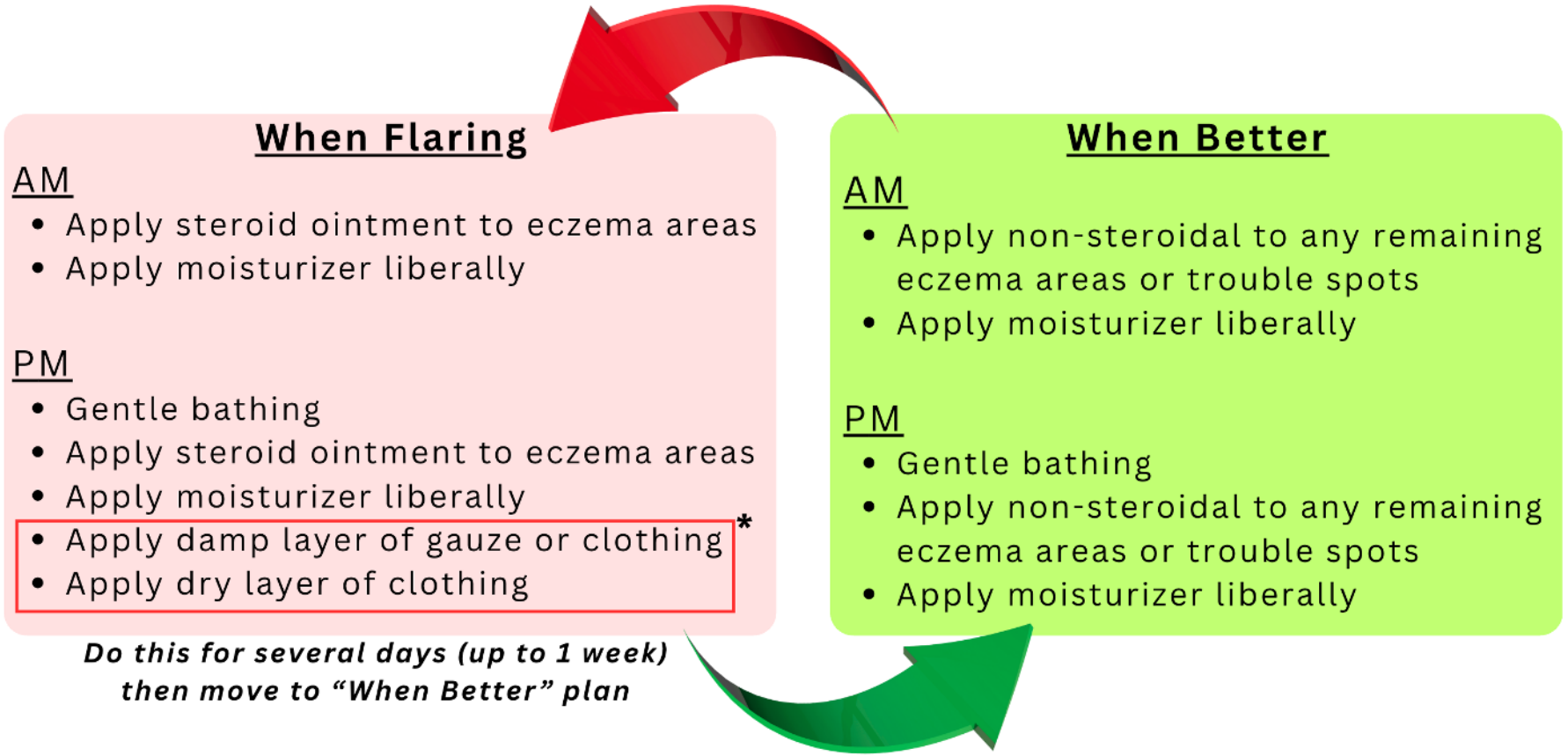
1. Peppers J et al. J Am Acad Dermatol. 2019;80:89-98; 2. Paller AS et al. J Am Acad Dermatol. 2021;84:632-638.

Safety and Tolerability of Tapinarof

- AEs related to tapinarof treatment
  - Follicular events (~10%)
- No serious treatment-related AEs reported

Silverberg JI, Eichenfield LF, Hebert AA, Simpson EL, Gold LS, Bissonnette R, Papp KA, Browning J, Kwong P, Korman NJ, Brown PM. Tapinarof Cream 1% Once Daily: Significant Efficacy in the Treatment of Moderate to Severe Atopic Dermatitis in Adults and Children Down to 2 Years of Age in the Pivotal Phase 3 ADORING Trials. Journal of the American Academy of Dermatology. 2024 May 20.

ECZEMA ACTION PLAN TEMPLATE



*Optional wet-wrap therapy

HOW TO APPLY WET WRAPS

Wet wraps can help put water back in the skin and calm the skin. They also help to decrease the itch and help you sleep. You can use wet wraps after bathing and applying the medications and moisturizers (see below).

All you need for wet wraps are something to be the damp layer and then a dry layer. This can be gauze, cotton pajamas, cotton gloves, or socks.

MEDICATION: _____

MOISTURIZER: _____

1. Take one pair of onesies, pajamas, gloves, and/or socks and soak it in warm water.

2. Wring out the onesies, pajamas, gloves, or socks until they are only slightly damp.

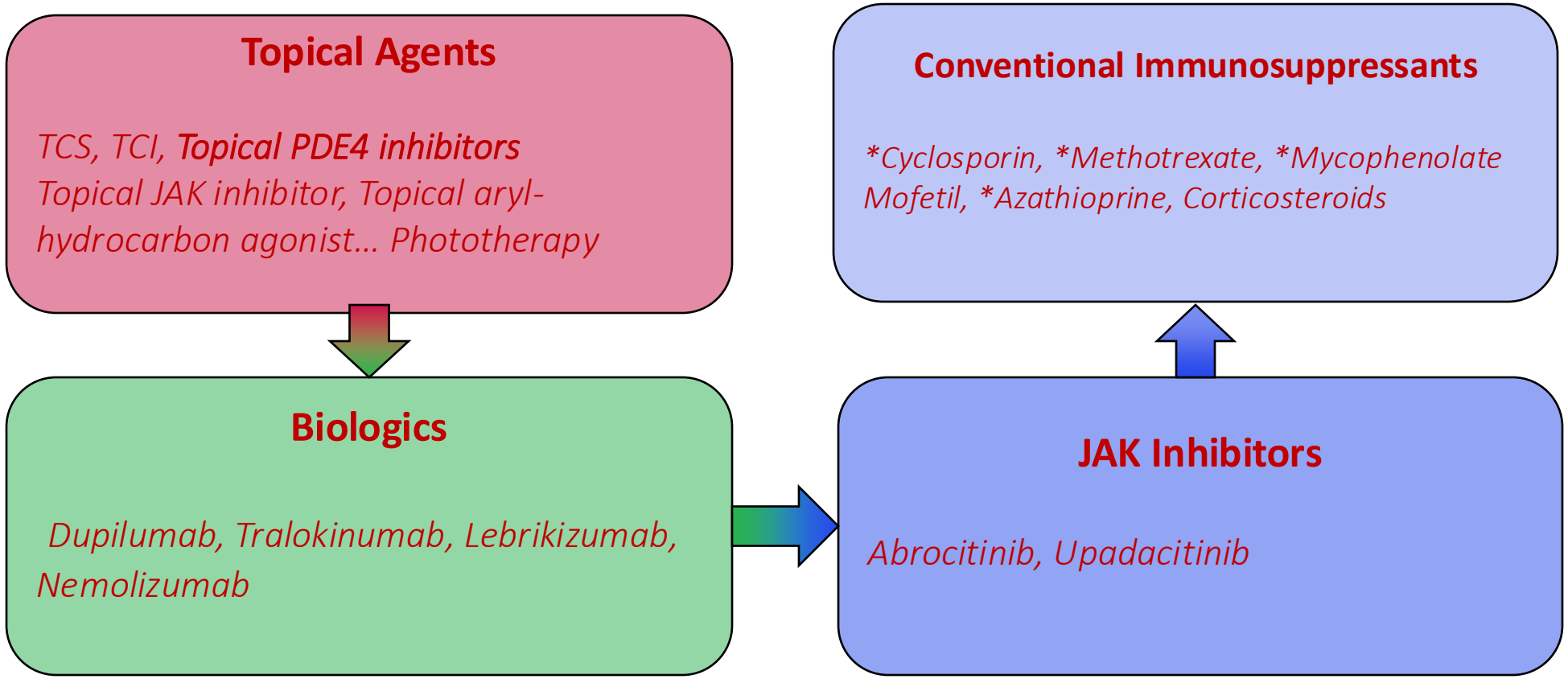
3. Put the damp onesies, pajamas, gloves, or socks on. Then put the dry onesies, pajamas, gloves, or socks on top of the damp layer.

4. Make sure the room is warm enough before you go to sleep.

When can I stop treatment?

Once the itchy, red, or scaly rash has significantly improved, you can stop. Usually wet wraps are applied only 3-5 days at a time. However, since atopic dermatitis is a long term condition, it is important to follow your Eczema Action Plan daily to help prevent things from flaring up again.

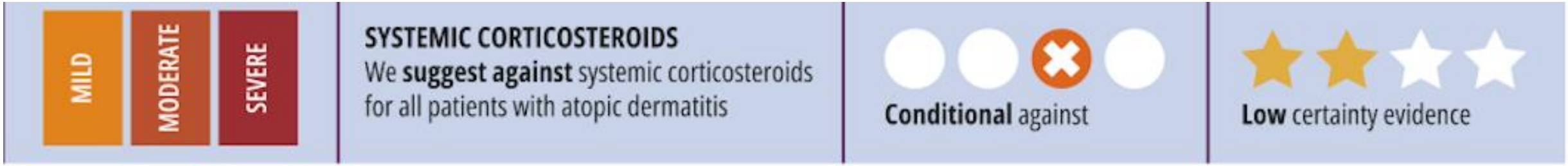
The Patient journey: Treatment options



*Not approved in the United States for treatment of AD

1. Sidbury, R., Davis, D. M., Cohen, D. E., Cordoro, K. M., Berger, T. G., Bergman, J. N., Chamlin, S. L., Cooper, K. D., Feldman, S. R., Hanifin, J. M., Krol, A., Margolis, D. J., Paller, A. S., Schwarzenberger, K., Silverman, R. A., Simpson, E. L., Tom, W. L., Williams, H. C., Elmets, C. A., Block, J.A., Harrod, C.G., Eichenfield, Bego L. F. (2014). Guidelines of care for the management of atopic dermatitis. *Journal of the American Academy of Dermatology*, *71*(2), 327–349.
2. Boguniewicz, M., Fonacier, L., Guttman-Yassky, E., Ong, P. Y., Silverberg, J., & Farrar, J. R. (2018). Atopic dermatitis yardstick: Practical recommendations for an evolving therapeutic landscape. *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology*, *120*(1), 10–22.e2.
3. U.S. Food and Drug Administration. (2021). *DUPIXENT® (dupilumab) Injection, for Subcutaneous Use*. Accessdata FDA. Retrieved June 7, 2022, from https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761055s020lbl.pdf

JTF + AAD Guidelines

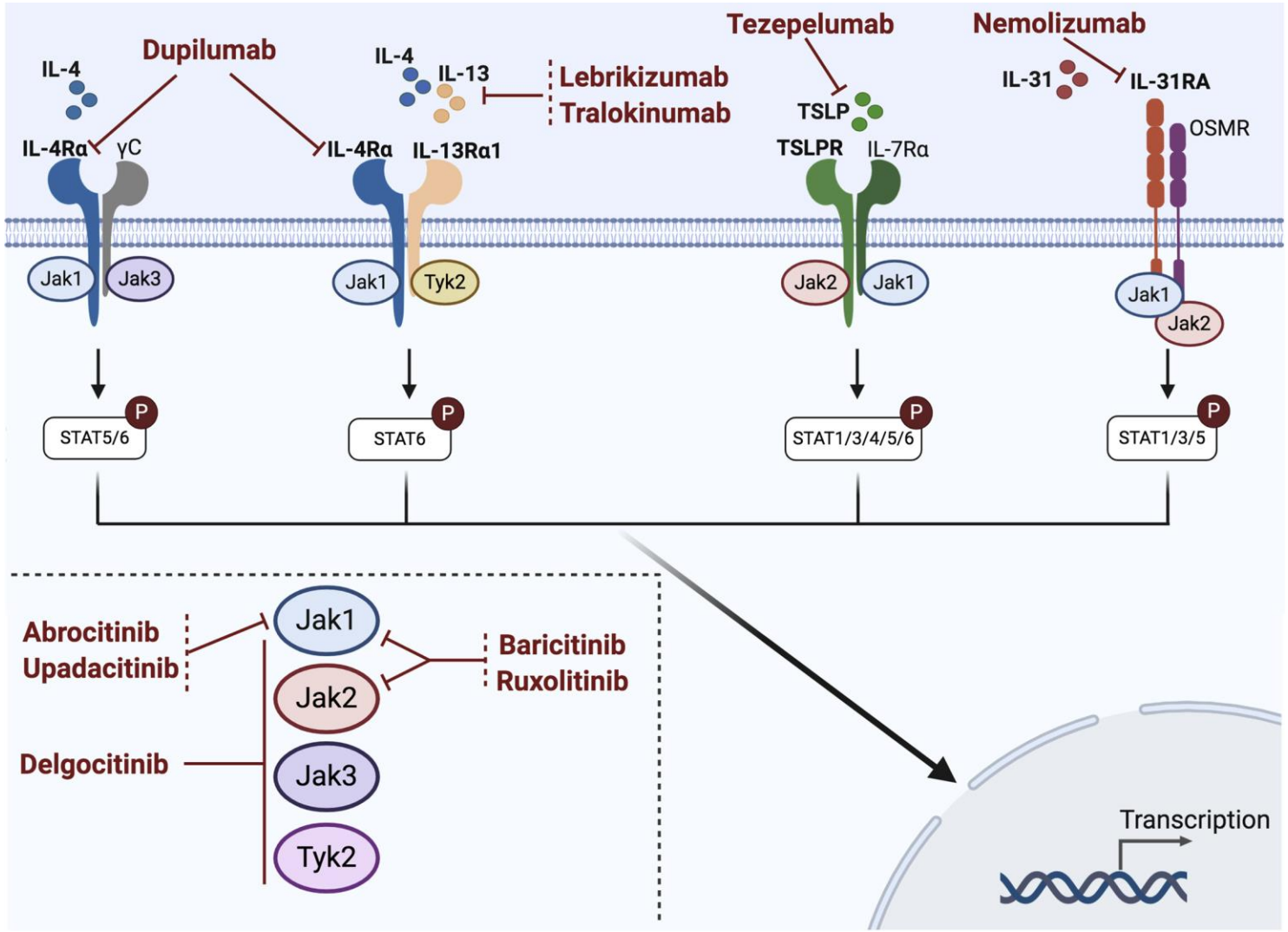


Immuno-suppressants					
5.1	Systemic corticosteroids (eg, prednisone)	On-label	For adults with AD, we conditionally recommend against systemic corticosteroids. Remarks: Their use should be reserved exclusively for acute, severe exacerbations and as a short-term bridge therapy to other systemic, corticosteroid-sparing therapy.	Conditional	Low

Chu DK, Schneider L, Asiniwasis RN, Boguniewicz M, De Benedetto A, Ellison K, Frazier WT, Greenhawt M, Huynh J, Kim E, LeBovidge J. Atopic dermatitis (eczema) guidelines: 2023 American Academy of Allergy, Asthma and Immunology/American College of Allergy, Asthma and Immunology Joint Task Force on Practice Parameters GRADE–and Institute of Medicine–based recommendations. Annals of Allergy, Asthma & Immunology. 2023 Dec 18.

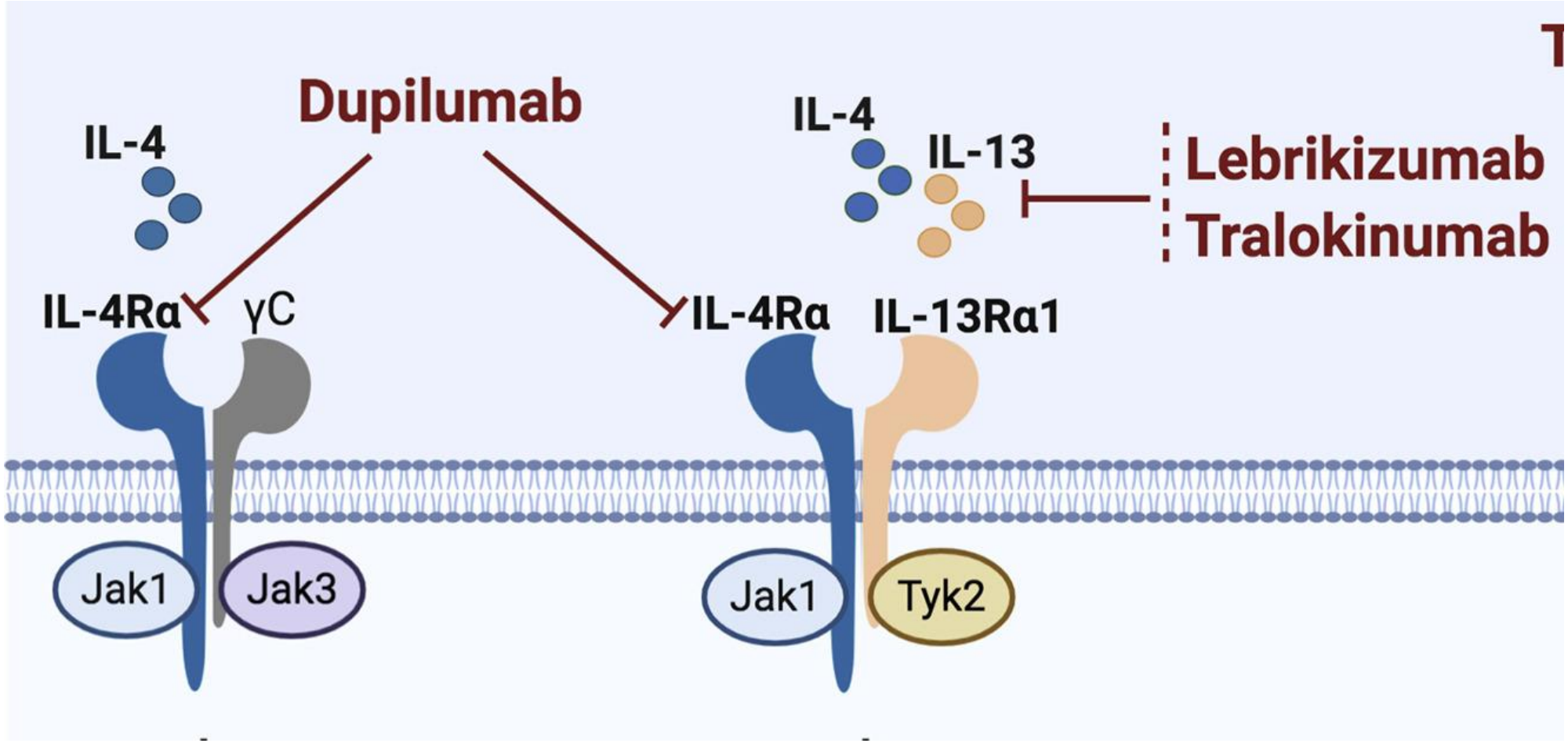
Davis DM, Drucker AM, Alikhan A, Bercovitch L, Cohen DE, Darr JM, Eichenfield LF, Frazer-Green L, Paller AS, Schwarzenberger K, Silverberg JI. Guidelines of care for the management of atopic dermatitis in adults with phototherapy and systemic therapies. Journal of the American Academy of Dermatology. 2024 Feb 1;90(2):e43-56.

Multiple Targets



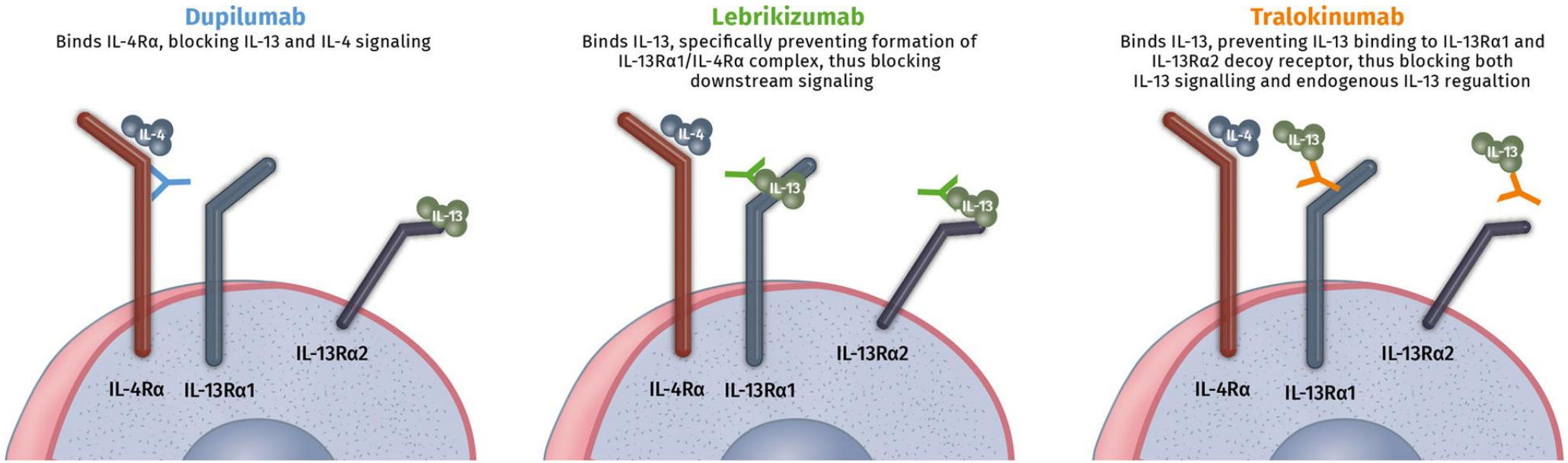
Abreu D and Kim BS. Innate Immune Regulation of Dermatitis. Immunology and Allergy Clinics of North America. 2021. DOI: https://doi.org/10.1016/j.iac.2021.04.011

Multiple Targets



Abreu D and Kim BS. Innate Immune Regulation of Dermatitis. Immunology and Allergy Clinics of North America. 2021. DOI: https://doi.org/10.1016/j.iac.2021.04.011

Not Identical



Lebrikizumab does not prevent binding to Ra2 → no increased levels of IL-13

Tralokinumab prevents the binding to Ra2 → thus increased total IL-13 levels

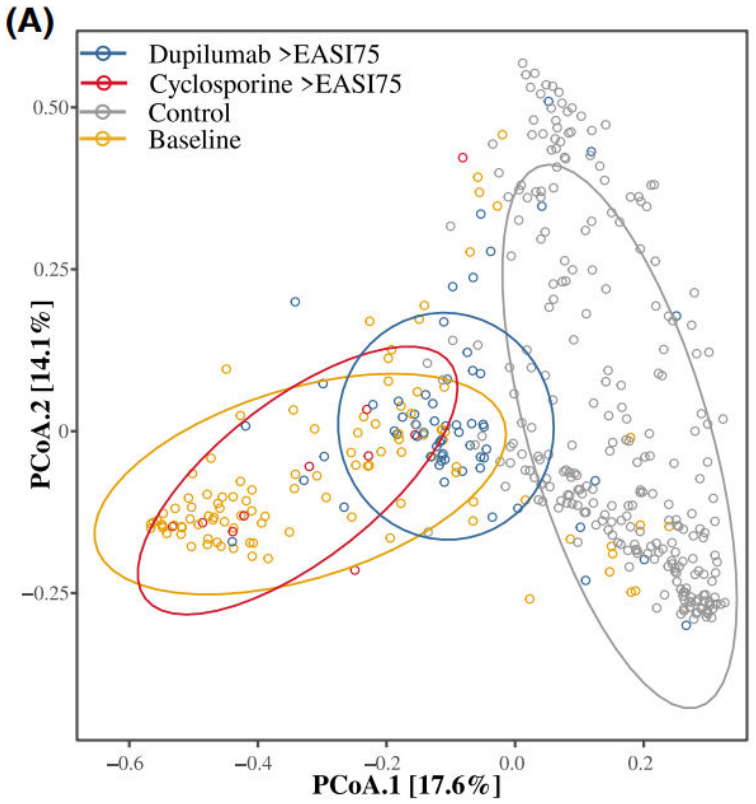
What does this mean?

We don't know!

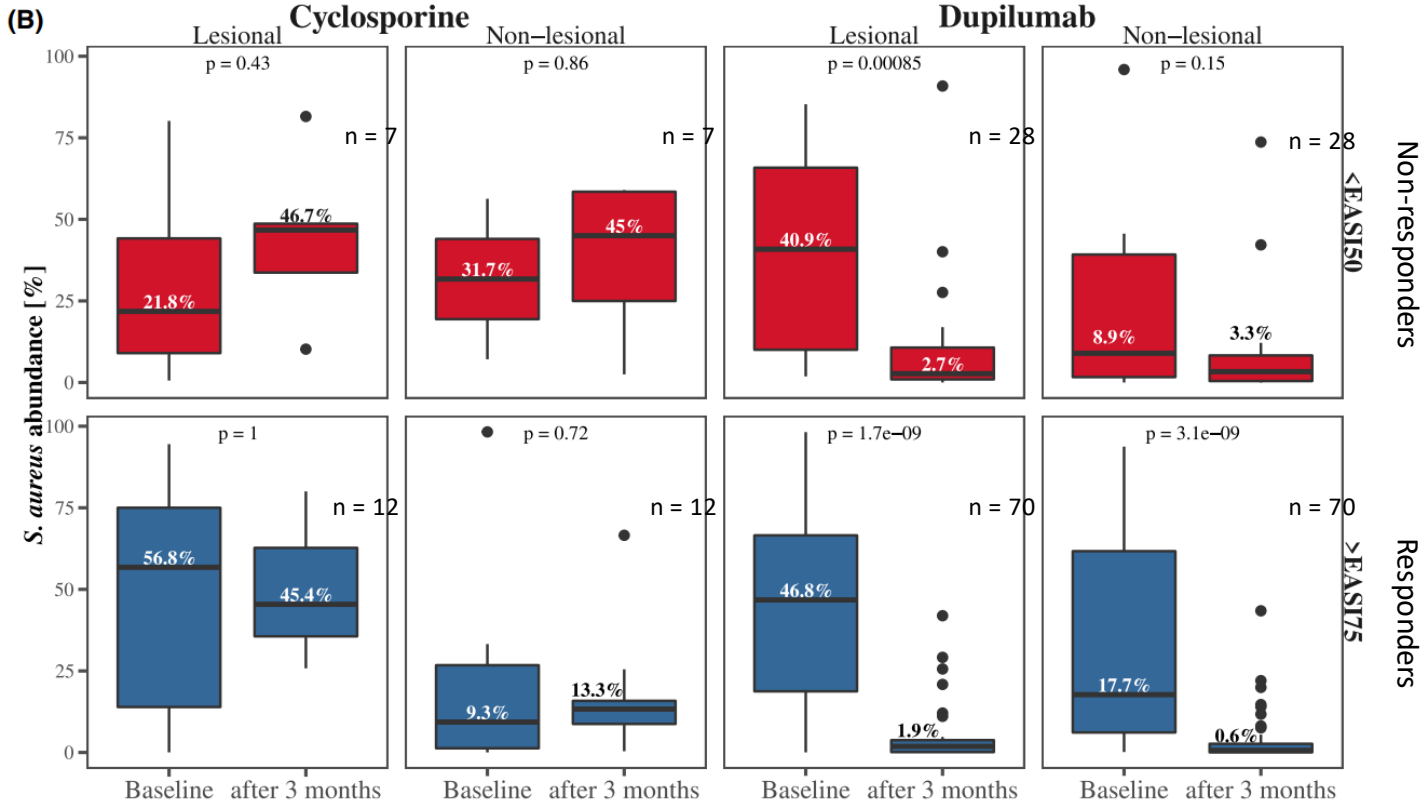
Experimental Dermatology, Volume: 28, Issue: 7, Pages: 756-768, First published: 02 March 2019, DOI: (10.1111/exd.13911)

Dupilumab Shifts the Microbiome Toward a Healthy Skin Flora in Adult Patients With Moderate-to-Severe AD

Dupilumab treatment shifted the microbial signature toward that of controls



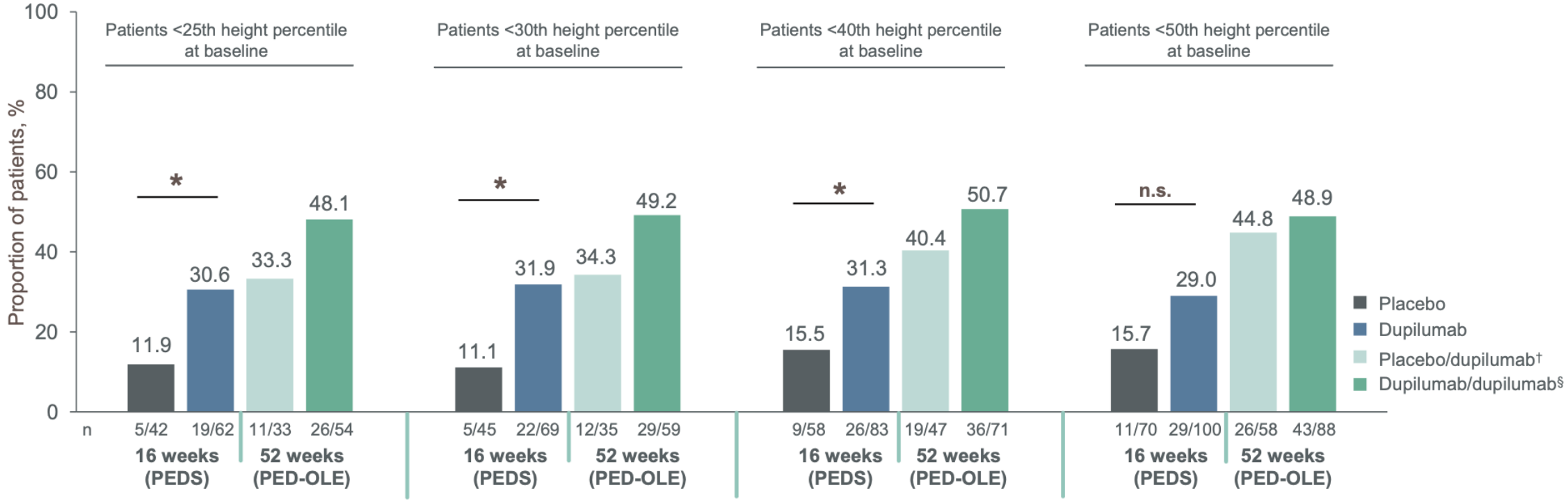
Dupilumab treatment significantly decreased S. aureus levels in lesional and non-lesional skin, and in responders and non-responders



Hartmann J, et al. Allergy. 2023.doi: 10.1111/all.15742.

Dupilumab-treated children below expected height at baseline had improved vertical growth

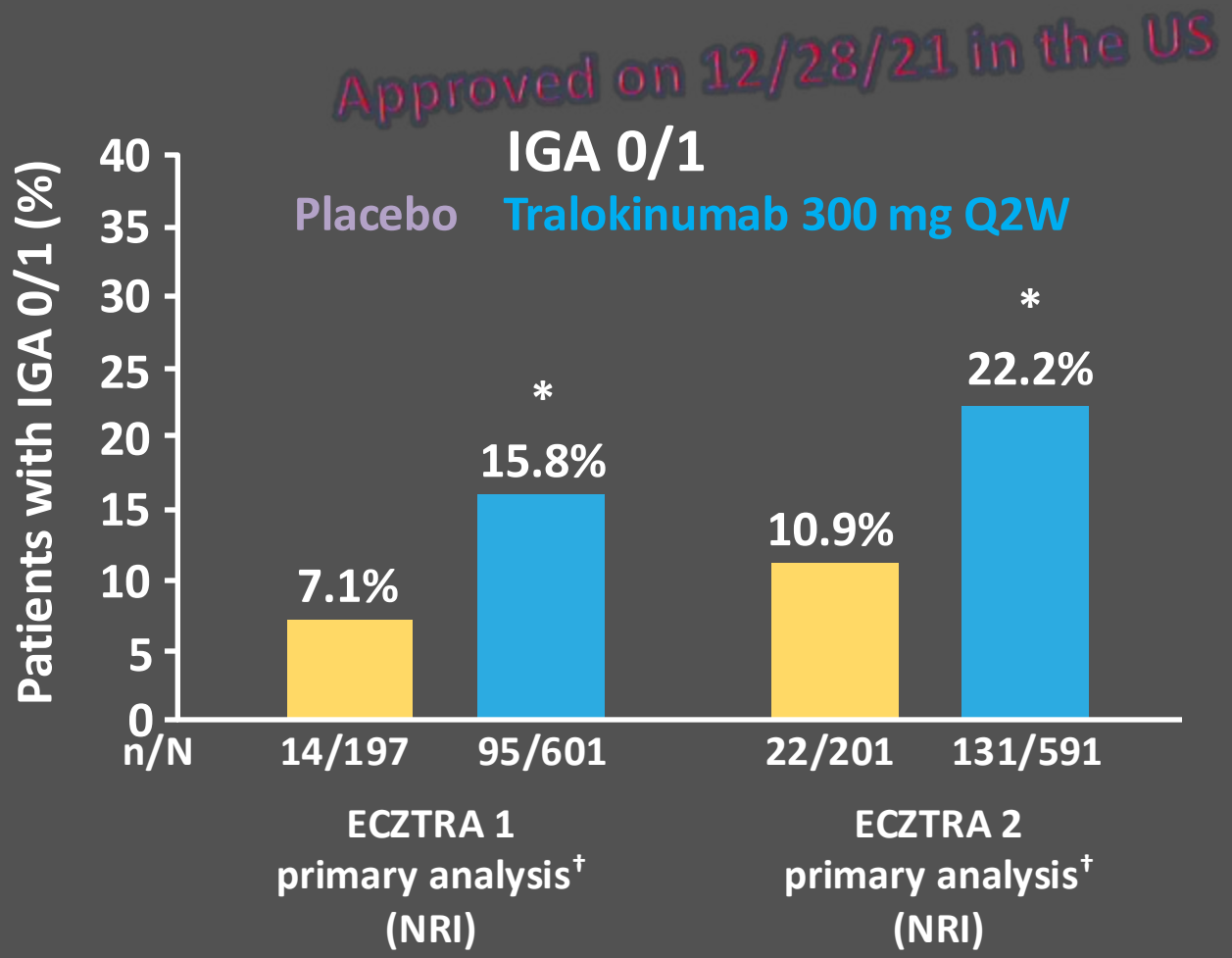
- LIBERTY-AD PEDS/LIBERTY-AD-PED-OLE POST-HOC ANALYSIS
- N = 304 children aged 6 to 11 years with severe AD



1. Irvine A, et al. Poster presented at the 33rd Annual Congress of the European Academy of Dermatology and Venerology (EADV); Amsterdam, Netherlands; September 25-28, 2024. 2. Irvine A, et al. Poster presented at the 83rd Annual Meeting of the American Academy of Dermatology (AAD); Orlando, FL, USA; March 7-11, 2025.

Tralokinumab (Anti–IL-13): IGA 0/1 at Week 16

- Blocks IL-13
- Q2W Dosing
- Common AE: conjunctivitis
- Improved efficacy beyond week 16 with Q4W dosing possible for some patients



****P*< .01 vs placebo. †Use of rescue medication considered as nonresponse; missing data imputed as nonresponse.**

NRI = non-responder imputation.

- 1. Simpson E, et al. AAD virtual meeting experience (VMX). 2020 (https://jofskin.org/index.php/skin/article/view/1066/pdf).
- 2. Weidinger S, et al. AAD VMX. 2020 (https://jofskin.org/index.php/skin/article/view/ 1079/pdf). Accessed 10/27/2021.

Lebrikizumab Monotherapy in Adults With Moderate-to-Severe AD

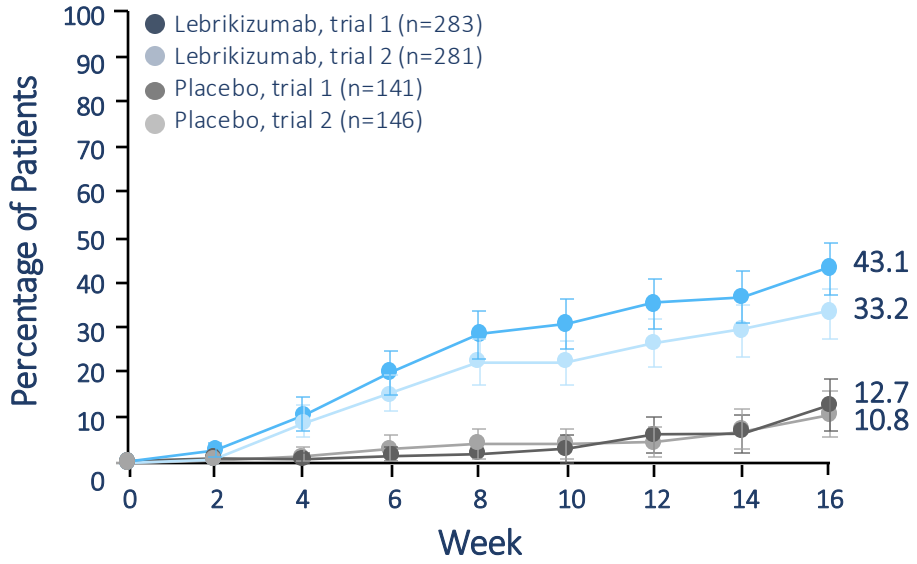
Approved on 9/13/2024 in the US

2 identically designed phase 3 trials[1]

- Total of 851 patients randomized 2:1 to lebrikizumab 250 mg[a] or placebo SC every 2 weeks
- Age ≥12 years (≥40 kg); EASI ≥16; IGA score ≥3; ≥10% BSA; inadequate response or intolerance to topical therapies

IGA response rates at week 16

(score 0 or 1 with an improvement of ≥2 points from baseline)



Notable adverse events (AEs)

Most common AE with lebrikizumab and higher than placebo: **conjunctivitis**

- 7.4% vs 2.8% in trial 1
- 7.5% vs 2.1% in trial 2
- Mostly mild or moderate in severity

More common with placebo than lebrikizumab

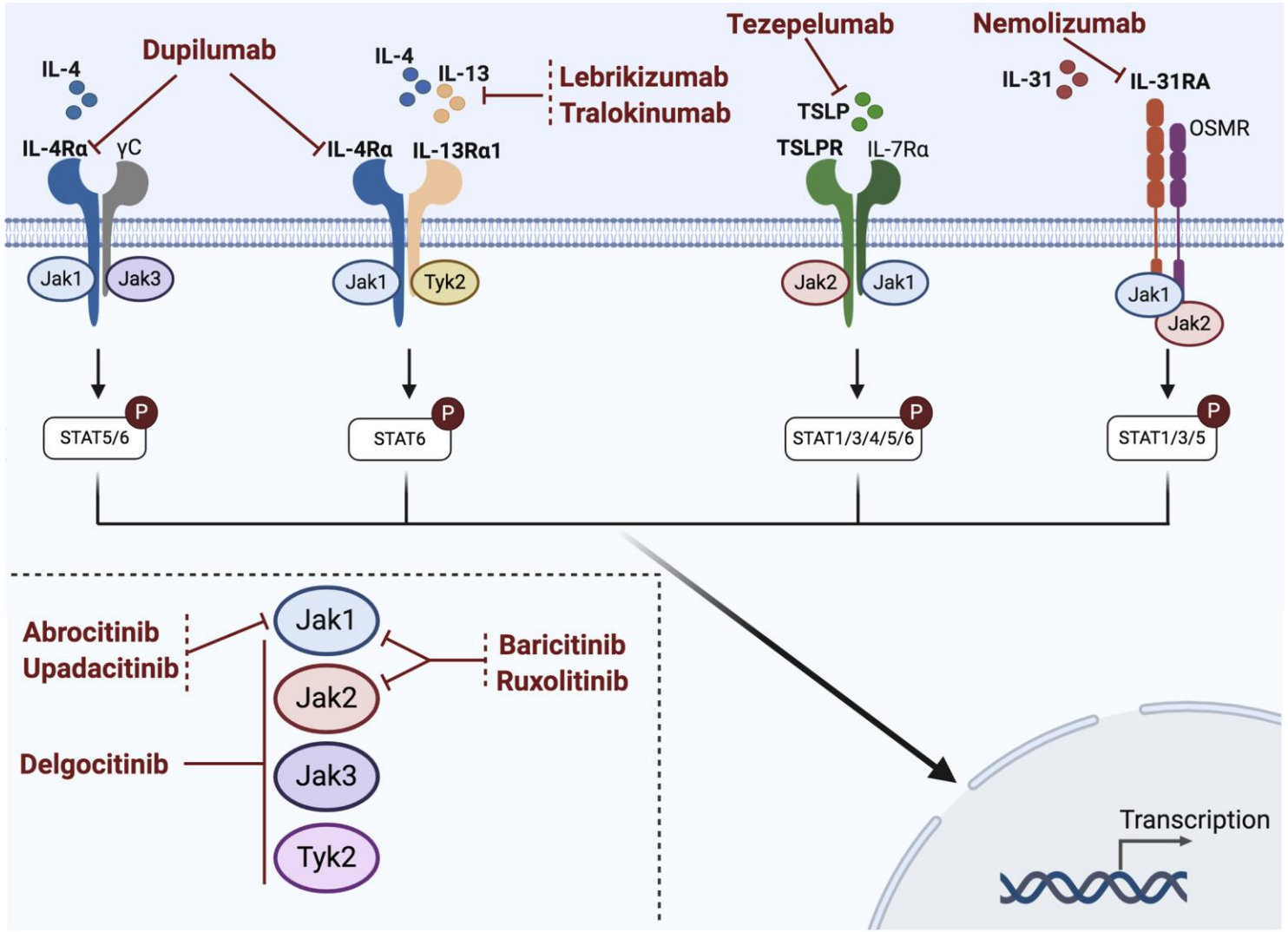
- AD exacerbation
- Skin infections

Similar response rates observed in phase 3 trial of lebrikizumab in combination with TCS[2]

[a]After initial 500 mg loading dose.

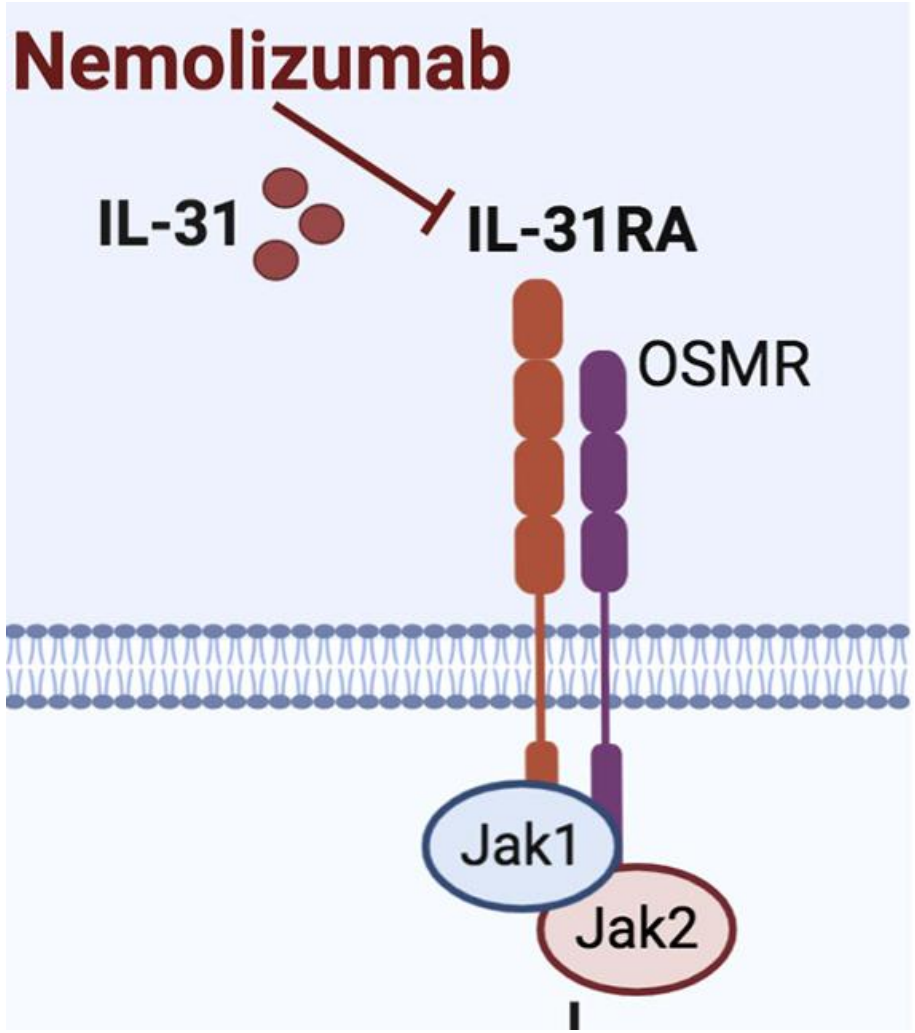
1. Silverberg JI et al. *N Engl J Med*. 2023;388:1080-1091; 2. Simpson EL et al. *JAMA Dermatol.* 2023;159:182-191.

Multiple Targets



Abreu D and Kim BS. Innate Immune Regulation of Dermatitis. Immunology and Allergy Clinics of North America. 2021. DOI: https://doi.org/10.1016/j.iac.2021.04.011

Multiple Targets

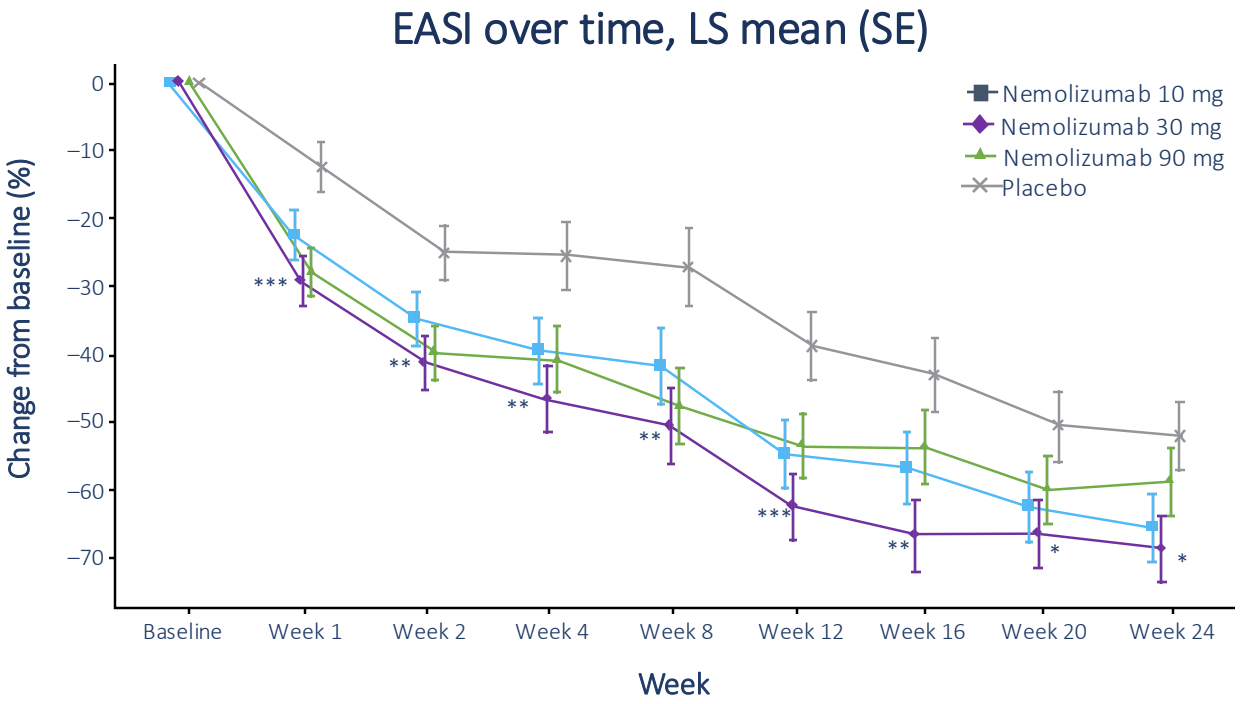


Abreu D and Kim BS. Innate Immune Regulation of Dermatitis. Immunology and Allergy Clinics of North America. 2021. DOI: https://doi.org/10.1016/j.iac.2021.04.011

Nemolizumab With TCS in Adults With Moderate-to-Severe AD and Severe Pruritus

Phase 2b study

- 226 patients randomized to placebo or to 1 of 3 different doses of nemolizumab SC Q4W plus TCS
- Age ≥18 years; IGA score ≥3; EASI ≥12; BSA: ≥10%; severe AD-associated pruritus uncontrolled by topical treatments

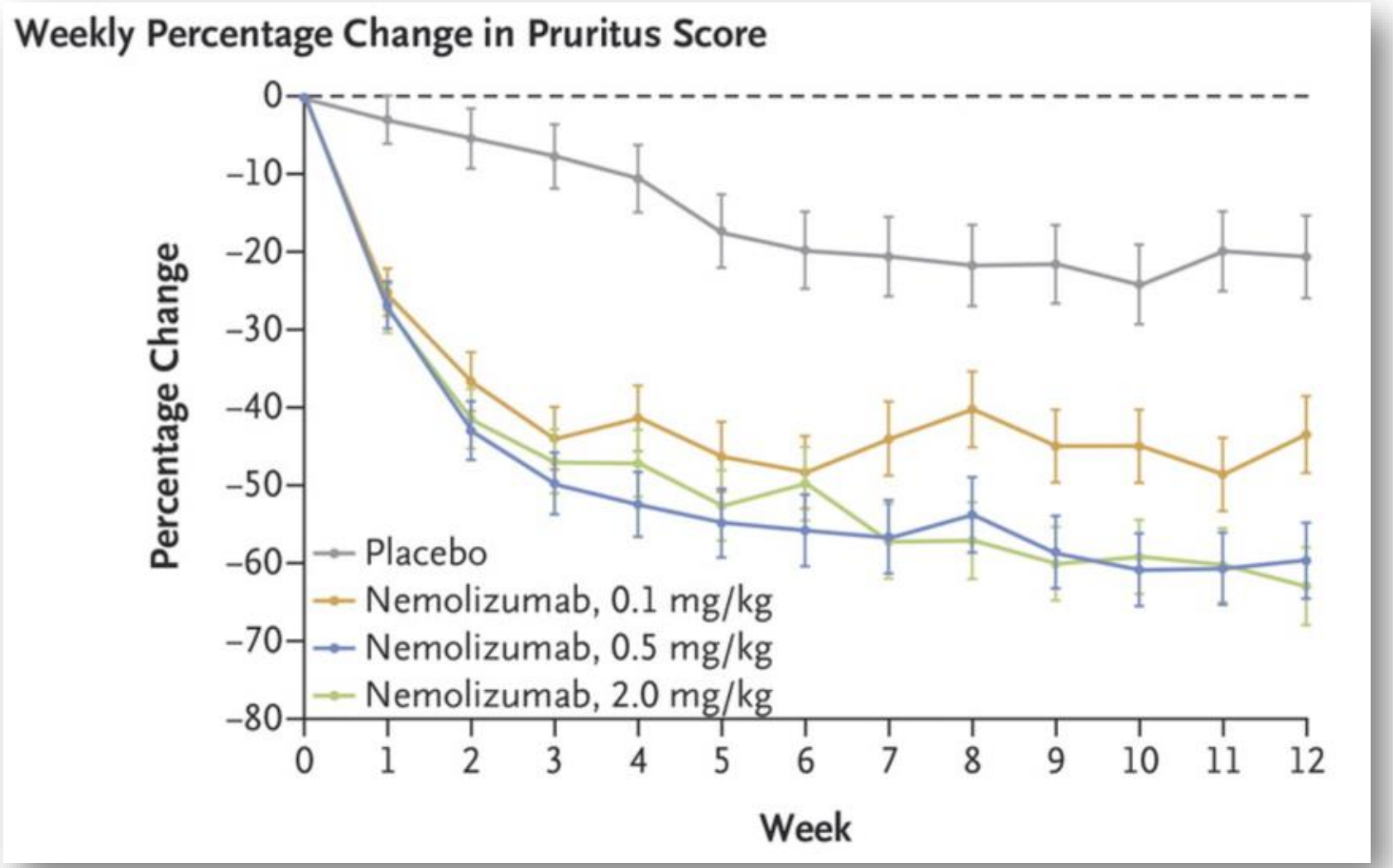


- Rapid decrease in pruritus scores, with statistically significant differences from placebo starting as early as week 1
- Most common AEs: nasopharyngitis and upper respiratory tract infection
- TEAEs of interest:
  - Dose-dependent increased incidence of asthma exacerbation; 1 severe event in 90-mg group

[a]After initial loading dose; *$P \leq 0.05$; **$P \leq 0.01$; ***$P \leq 0.001$; vs placebo.

Silverberg JI et al. *J Allergy Clin Immunol.* 2020;145:173-182.

Nemolizumab



Anti-Interleukin-31 Receptor A Antibody for Atopic Dermatitis. Ruzicka T, Hanifin JM, Furue M, Pulka G, Mlynarczyk I, Wollenberg A, Galus R, Etoh T, Mihara R, Yoshida H, Stewart J, Kabashima K; XCIMA Study Group. N Engl J Med. 2017 Mar 2;376(9):826-835.

Nemolizumab (anti-IL-31)

TABLE III. TEAEs occurring in 5% or greater by system organ class and preferred term, all causes (safety population)

		Nemolizumab			
	Placebo (n = 56)	10 mg (n = 55)	30 mg (n = 57)	90 mg (n = 57)	All (n = 169)
≥1 TEAE	43 (76.8%)	47 (85.5%)	47 (82.5%)	48 (84.2%)	142 (84%)
Infection and infestation	23 (41.4%)	34 (61.8%)	34 (59.6%)	34 (59.6)	102 (60.4%)
Nasopharyngitis	12 (21.4%)	18 (32.7%)	14 (24.6%)	13 (22.8%)	45 (26.6%)
URTI	1 (1.8%)	4 (7.3%)	6 (10.5%)	4 (7%)	14 (8.3%)
Gastroenteritis	0	0	3 (5.3%)	4 (7%)	7 (4.1%)
Sinusitis	0	3 (5.5%)	3 (5.3%)	1 (1.8%)	7 (4.1%)
Oral herpes	1 (1.8%)	2 (3.6%)	1 (1.8%)	3 (5.3%)	6 (3.6%)
UTI	3 (5.4%)	3 (5.5%)	1 (1.8%)	2 (3.5%)	6 (3.6%)
Rhinitis	3 (5.4%)	0	3 (5.3%)	1 (1.8%)	4 (2.4%)
Herpes infection	5 (8.9%)	4 (7.3%)	3 (5.3%)	5 (8.7%)	12 (7.1%)
Skin and subcutaneous tissue disorders	20 (35.7%)	18 (32.7%)	23 (40.4%)	23 (40.4%)	64 (37.9%)
Atopic dermatitis	18 (32.1%)	12 (21.8%)	14 (24.6%)	16 (28.1%)	42 (24.9%)
Dry skin	0	0	3 (5.3%)	0	3 (1.8%)
Respiratory, thoracic, and mediastinal disorders	7 (12.5%)	6 (10.9%)	13 (22.8%)	12 (21.1%)	31 (18.3%)
Asthma event	1 (1.8%)	2 (3.6%)	7 (12.3%)	10 (17.5%)	19 (11.2%)
Cough	2 (3.6%)	1 (1.8%)	3 (5.3%)	2 (3.5%)	6 (3.6%)

UTI, Urinary tract infection; *URTI*, upper respiratory tract infection.

Silverberg JI et al. Phase 2B randomized study of nemolizumab in adults with moderate-to-severe atopic dermatitis and severe pruritus. Journal of Allergy and Clinical Immunology. 2020 Jan 1;145(1):173-82.

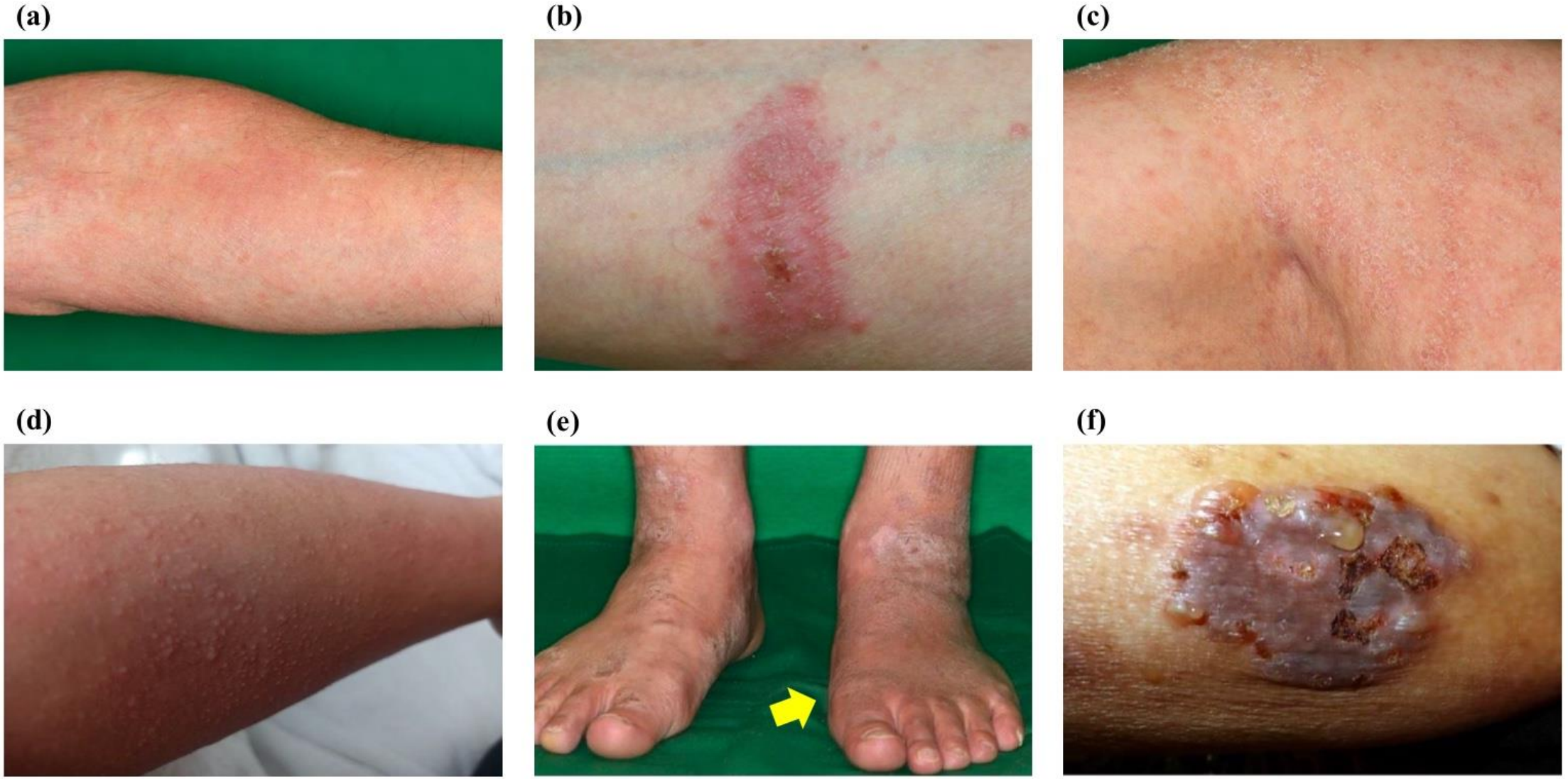


FIGURE 1 | Representative clinical images of six distinct categories of cutaneous manifestations, as defined in this study: (a) erythema; (b) coin-shaped red plaque with exudate; (c) dry skin/scaly lesions; (d) diffuse papules; (e) edema; and (f) vesicle.

Sasaki W, Saito R, Suzuki K, Watanabe D, Minami-Hori M, Kamada H, Amano H, Uchiyama A, Motegi SI, Kamura M, Sugita K. Clinical Characteristics and Risk Factors for Cutaneous Manifestations Associated With Nemolizumab in Atopic Dermatitis: A Multicenter Retrospective Study in Japan. The Journal of Dermatology. 2025 Jul 25.

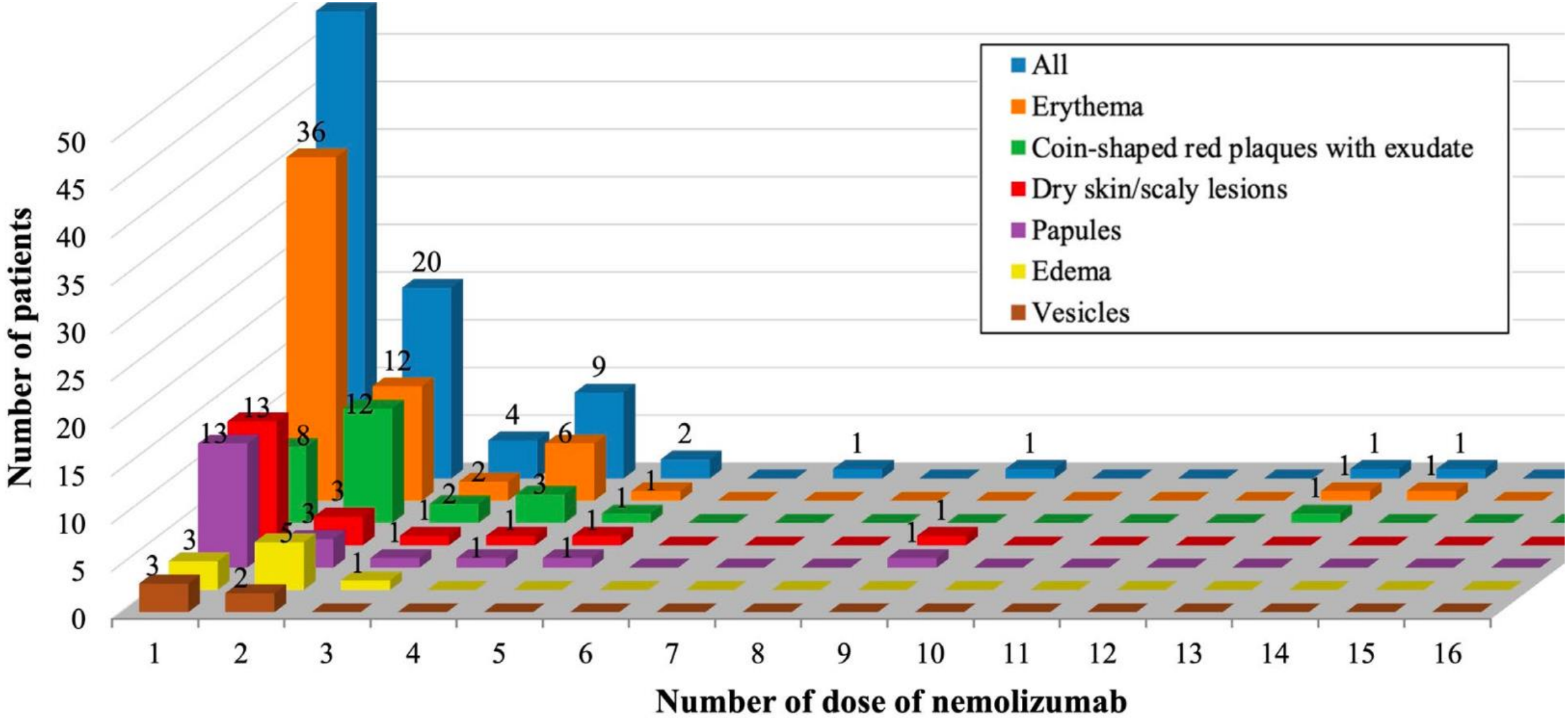
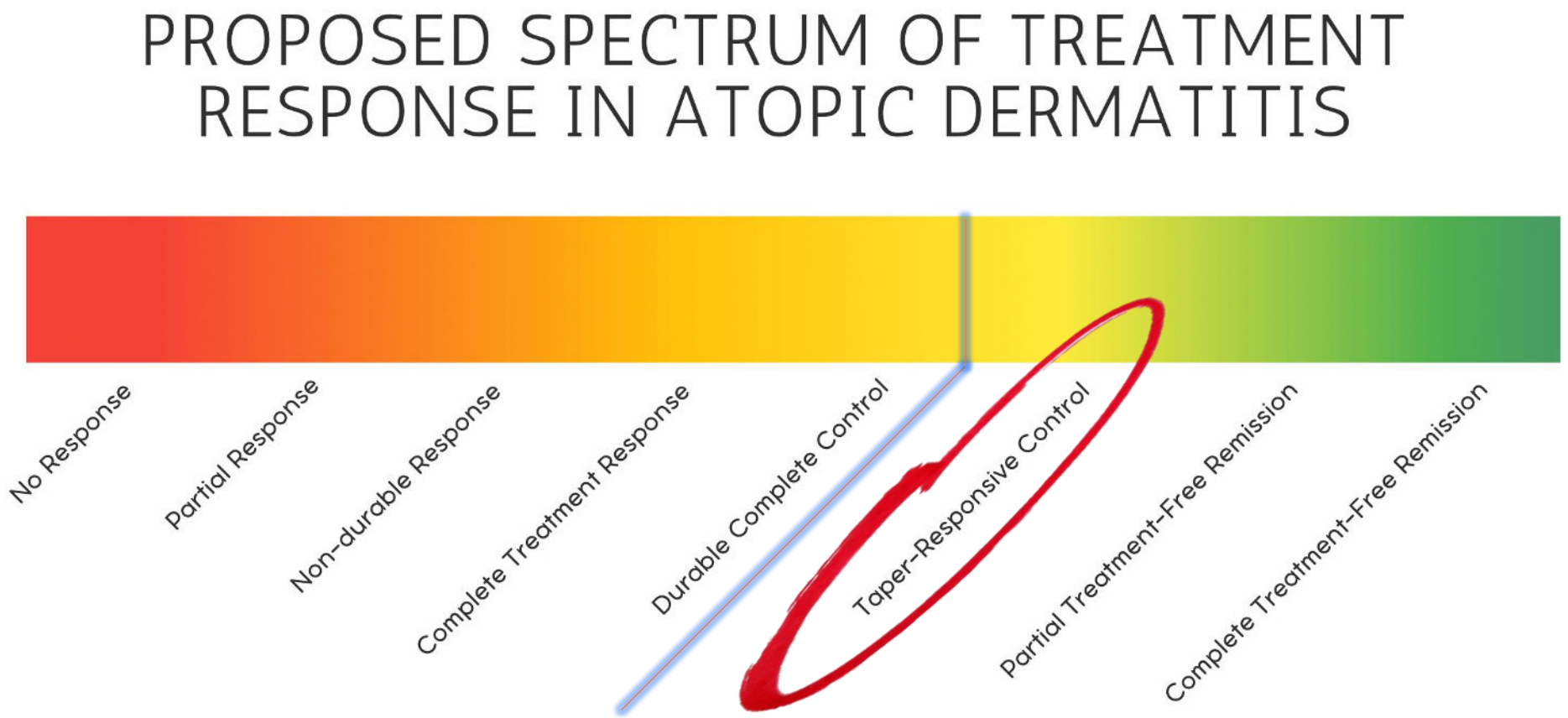


FIGURE 2 | Timing of the initial appearance of cutaneous manifestations following nemolizumab treatment. The vertical axis re number of cases, and the horizontal axis indicates the number of nemolizumab doses administered. Blue bars represent the total num tions, and each eruption type is color-coded: orange for erythema, green for coin-shaped red plaques with exudates, red for dry skin/s purple for papules, yellow for edema, and brown for vesicles. No new eruptions were observed beyond the 16th dose.

•Sasaki W, Saito R, Suzuki K, Watanabe D, Minami-Hori M, Kamada H, Amano H, Uchiyama A, Motegi SI, Kamura M, Sugita K. Clinical Characteristics and Risk Factors for Cutaneous Manifestations Associated With Nemolizumab in Atopic Dermatitis: A Multicenter Retrospective Study in Japan. The Journal of Dermatology. 2025 Jul 25.

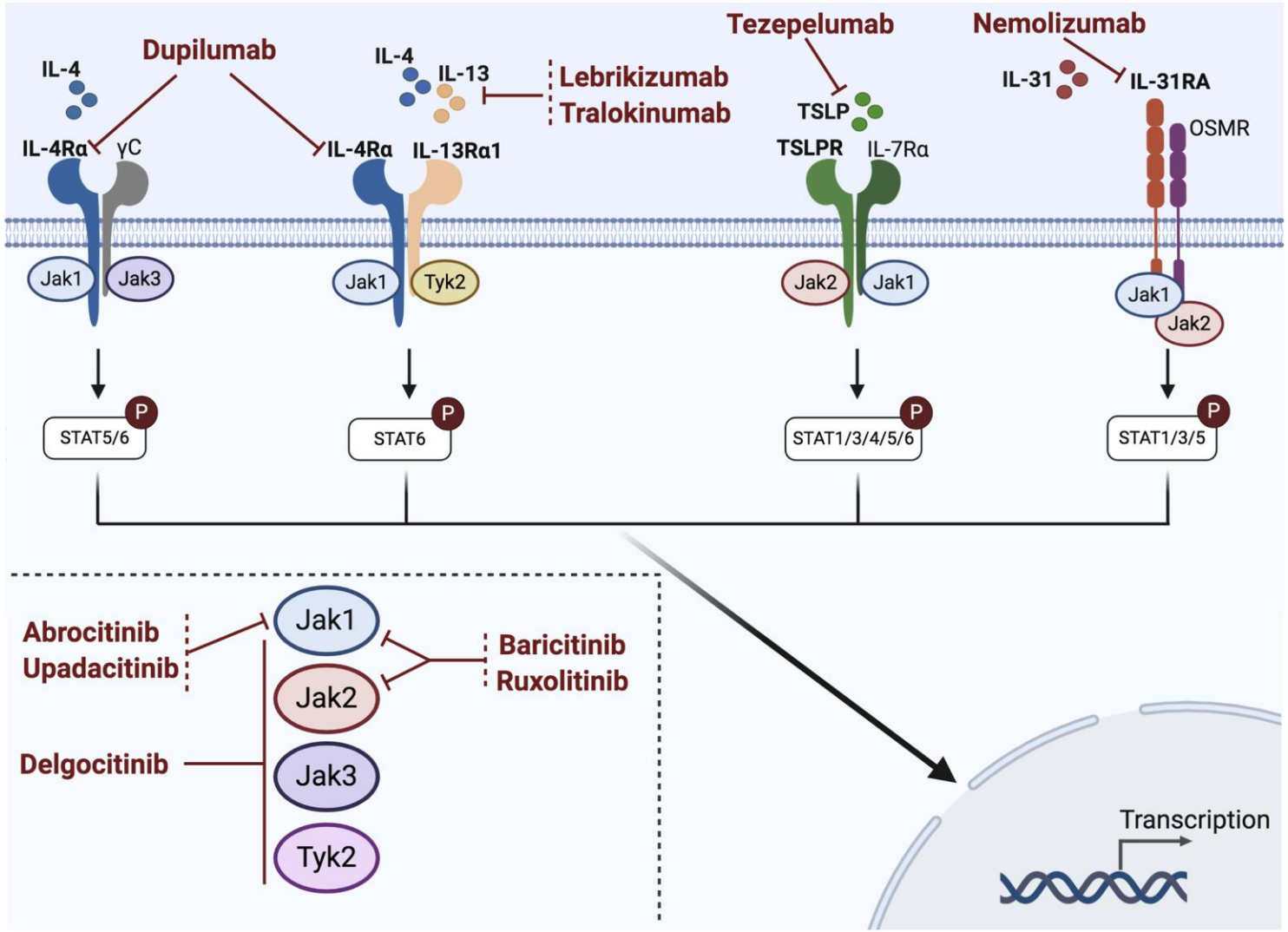
Tralokinumab, Lebrikizumab, and Nemolizumab *all* have decreased dosing built into the approved dosing schedules

- Tralo + Lebri: q2 weeks until week 16 → q4 weeks
- Nemo: q4 weeks until week 16 → q8 weeks



Original figure courtesy of Peter Lio, MD, FAAD

Multiple Targets



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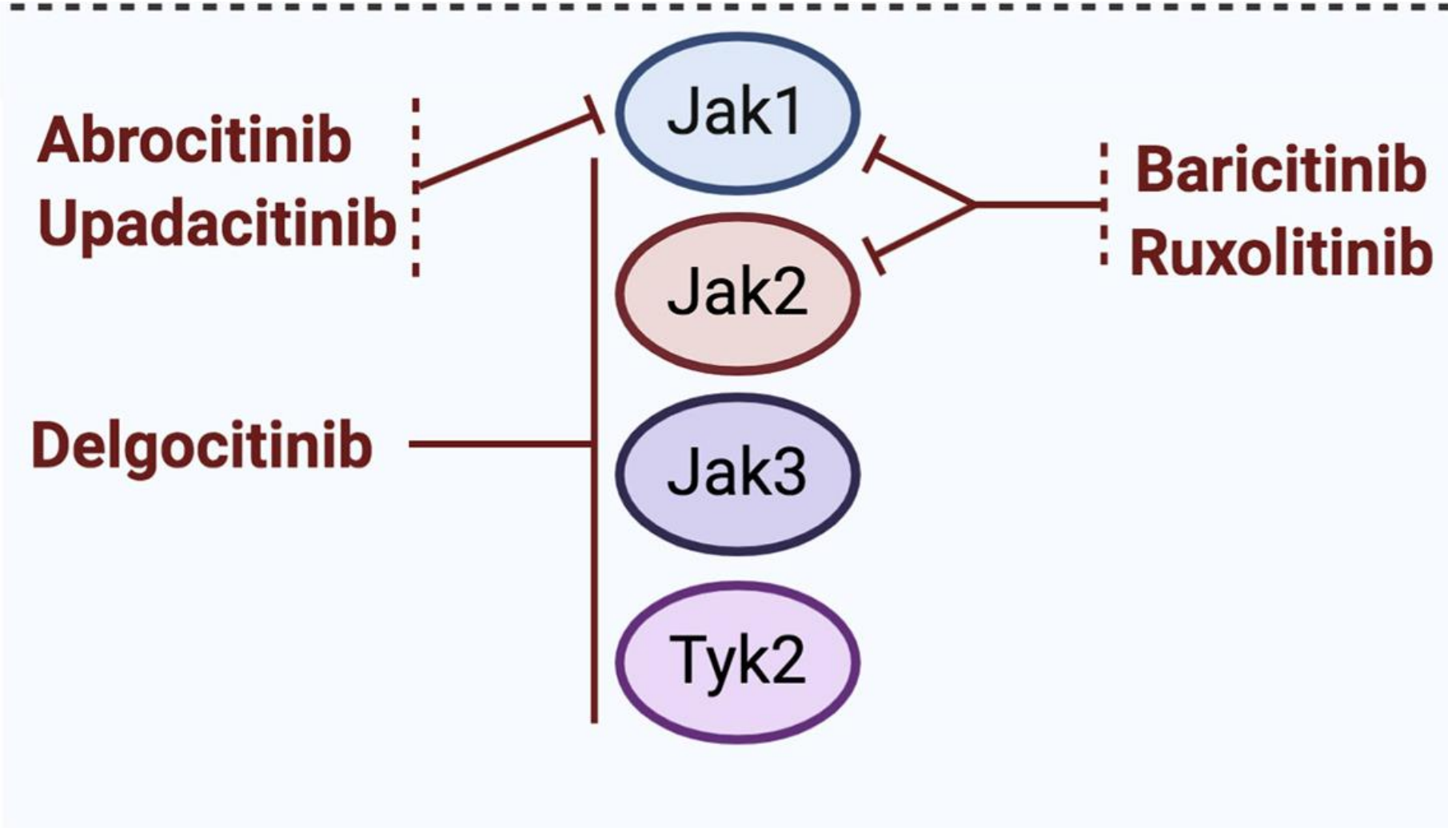


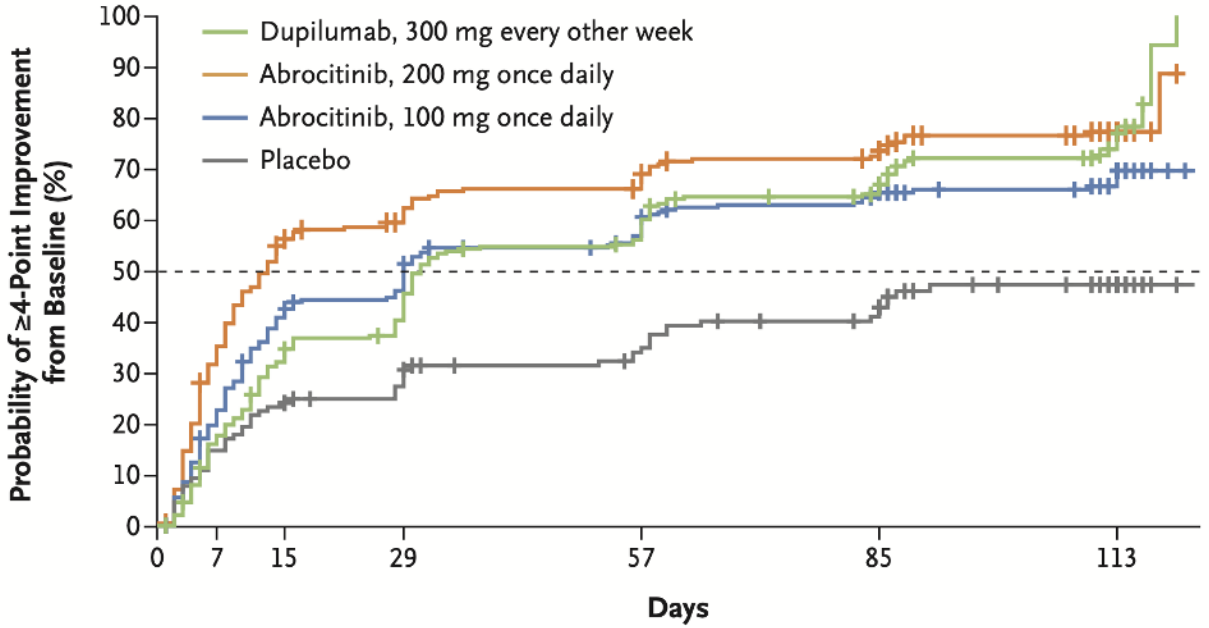
Abreu D and Kim BS. Innate Immune Regulation of Dermatitis. Immunology and Allergy Clinics of North America. 2021. DOI: https://doi.org/10.1016/j.iac.2021.04.011

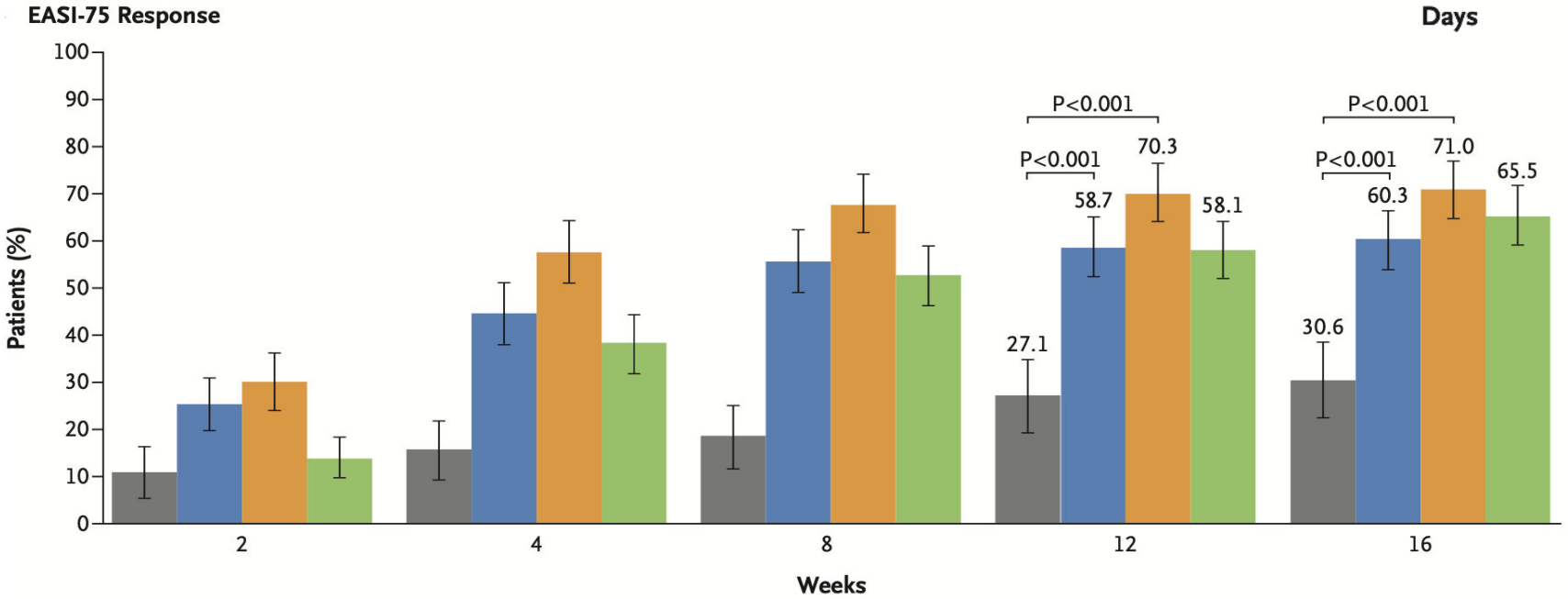
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Abrocitinib versus Placebo or Dupilumab for Atopic Dermatitis

T. Bieber, E.L. Simpson, J.I. Silverberg, D. Thaçi, C. Paul, A.E. Pink, Y. Kataoka, C.-Y. Chu, M. DiBonaventura, R. Rojo, J. Antinew, I. Ionita, R. Sinclair, S. Forman, J. Zdybski, P. Biswas, B. Malhotra, F. Zhang, and H. Valdez, for the JADE COMPARE Investigators*





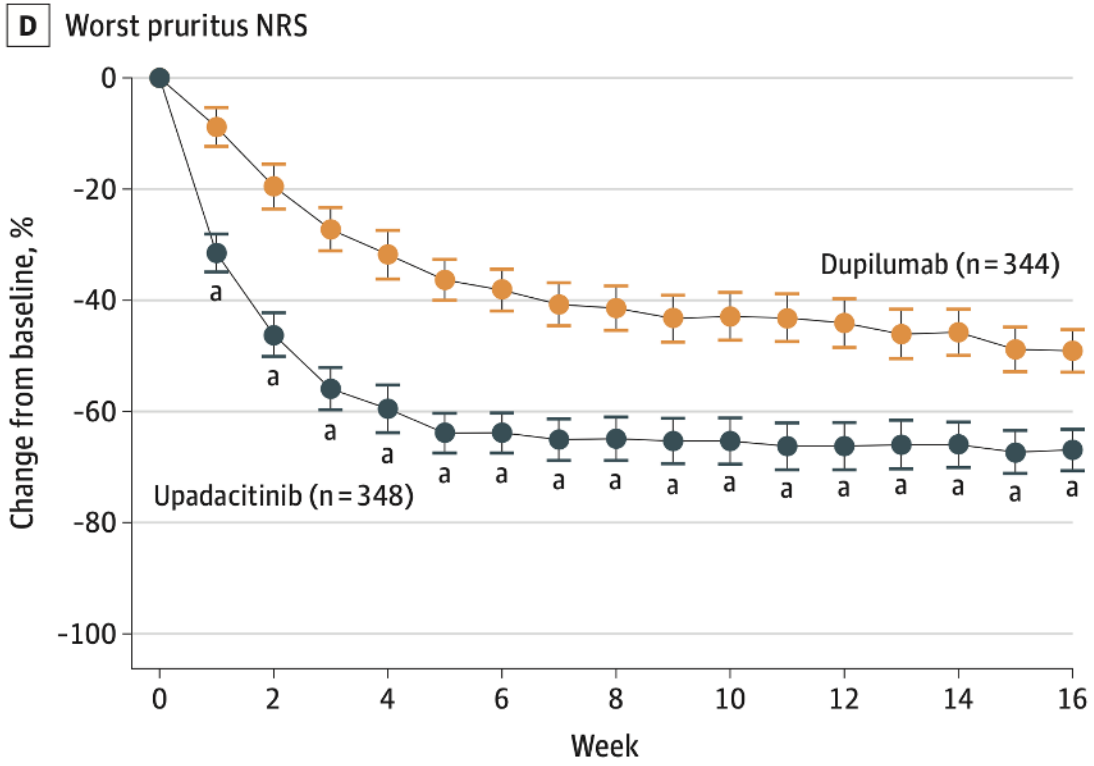
Bieber T, Simpson EL, Silverberg JI, Thaçi D, Paul C, Pink AE, Kataoka Y, Chu CY, DiBonaventura M, Rojo R, Antinew J. Abrocitinib versus placebo or dupilumab for atopic dermatitis. New England Journal of Medicine. 2021 Mar 25;384(12):1101-12.

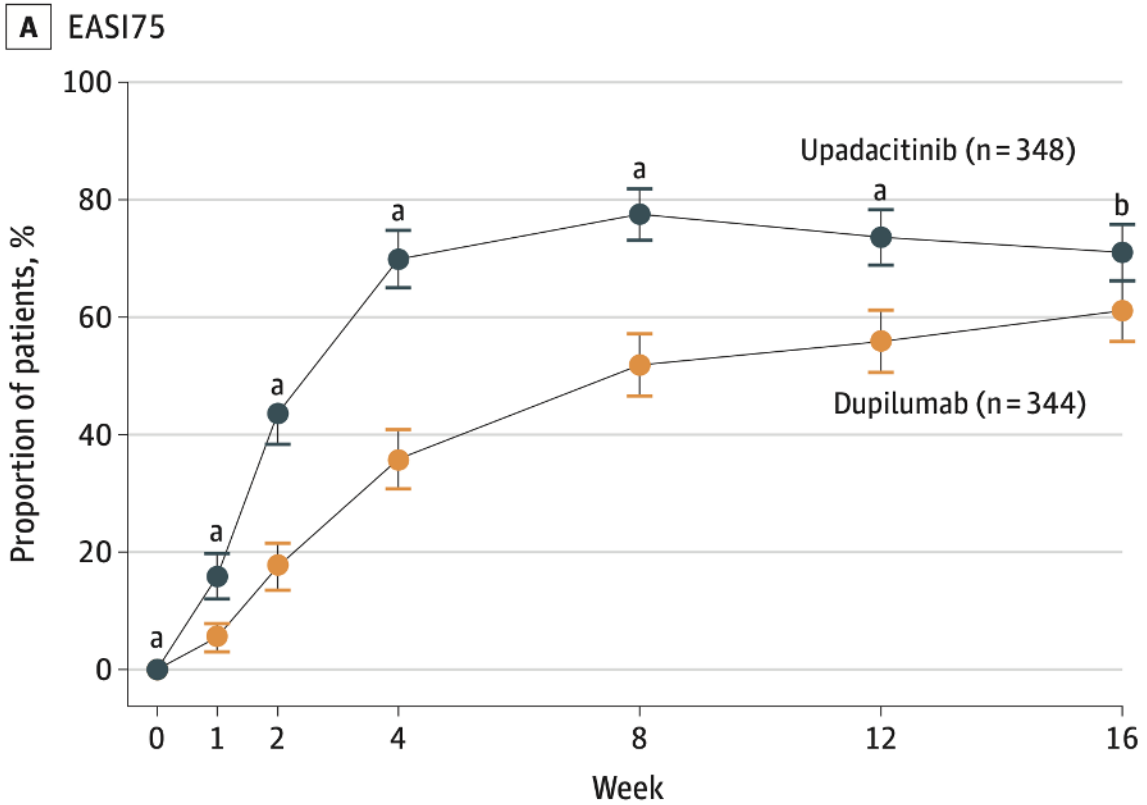
Abrocitinib

Event	Treatment group, No. (%)		
		Abrocitinib	
	Placebo (n = 78)	100 mg (n = 158)	200 mg (n = 155)
Deaths	0	1 (0.6)	0
Serious adverse events of any cause	1 (1.3)	5 (3.2)	2 (1.3)
Most frequently reported TEAEs of any cause (≥3% in any treatment group)			
Nausea	2 (2.6)	12 (7.6)	22 (14.2)
Nasopharyngitis	5 (6.4)	20 (12.7)	12 (7.7)
Headache	2 (2.6)	9 (5.7)	12 (7.7)
Upper respiratory tract infection	3 (3.8)	14 (8.9)	5 (3.2)
Dermatitis atopic	12 (15.4)	9 (5.7)	6 (3.9)
Acne	0	2 (1.3)	9 (5.8)
Vomiting	1 (1.3)	2 (1.3)	8 (5.2)
Upper abdominal pain	0	2 (1.3)	6 (3.9)
Blood creatine phosphokinase increased	2 (2.6)	3 (1.9)	5 (3.2)
Folliculitis	2 (2.6)	0	5 (3.2)
Thrombocytopenia	0	0	5 (3.2)

Silverberg JI, Simpson EL, Thyssen JP, et al. Efficacy and Safety of Abrocitinib in Patients With Moderate-to-Severe Atopic Dermatitis: A Randomized Clinical Trial. JAMA Dermatol. doi:10.1001/jamadermatol.2020.1406

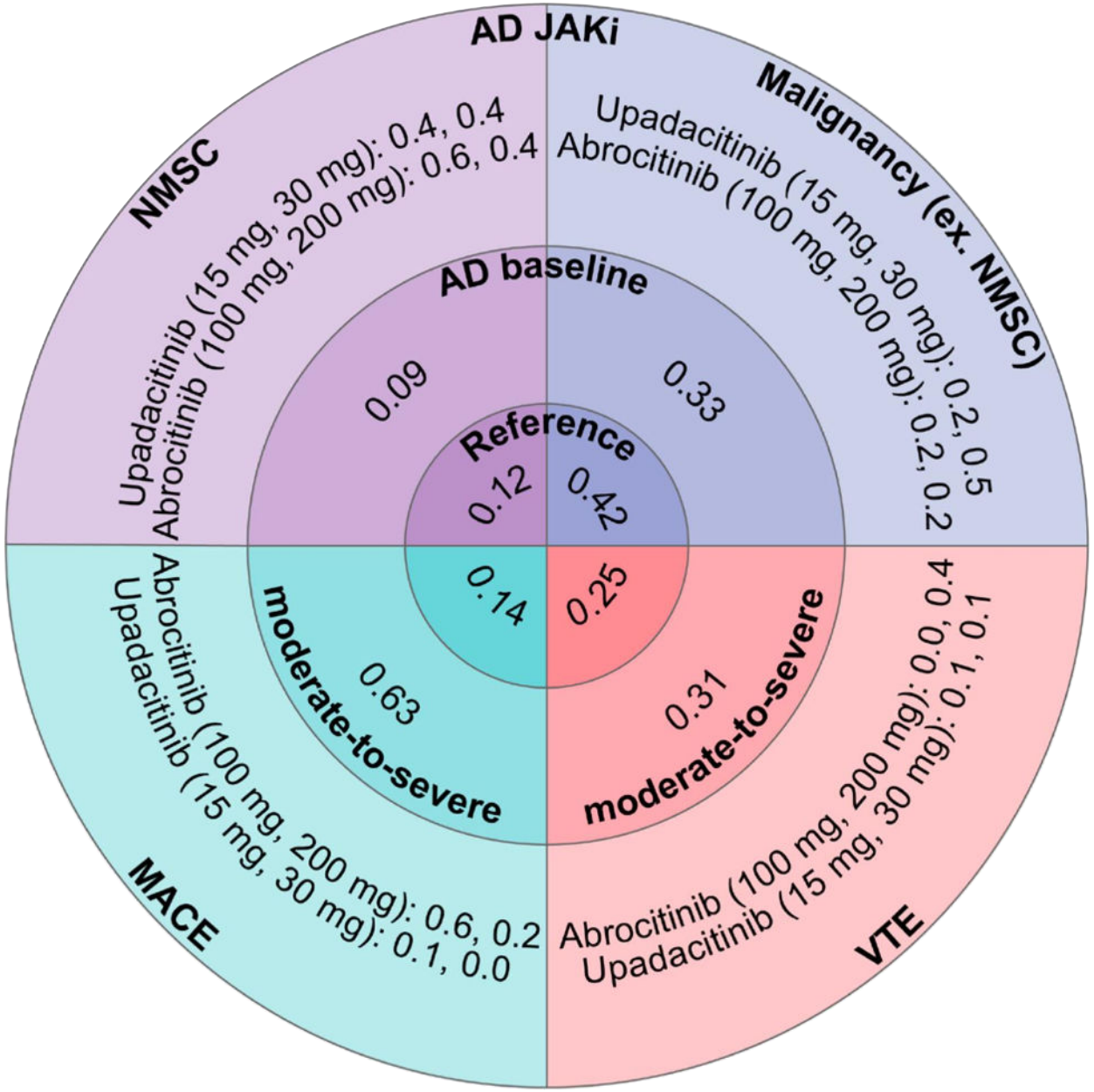
Upadacitinib vs. Dupilumab





Blauvelt A, Teixeira HD, Simpson EL, et al. Efficacy and Safety of Upadacitinib vs Dupilumab in Adults With Moderate-to-Severe Atopic Dermatitis: A Randomized Clinical Trial. JAMA Dermatol. Published online August 04, 2021. doi:10.1001/jamadermatol.2021.3023

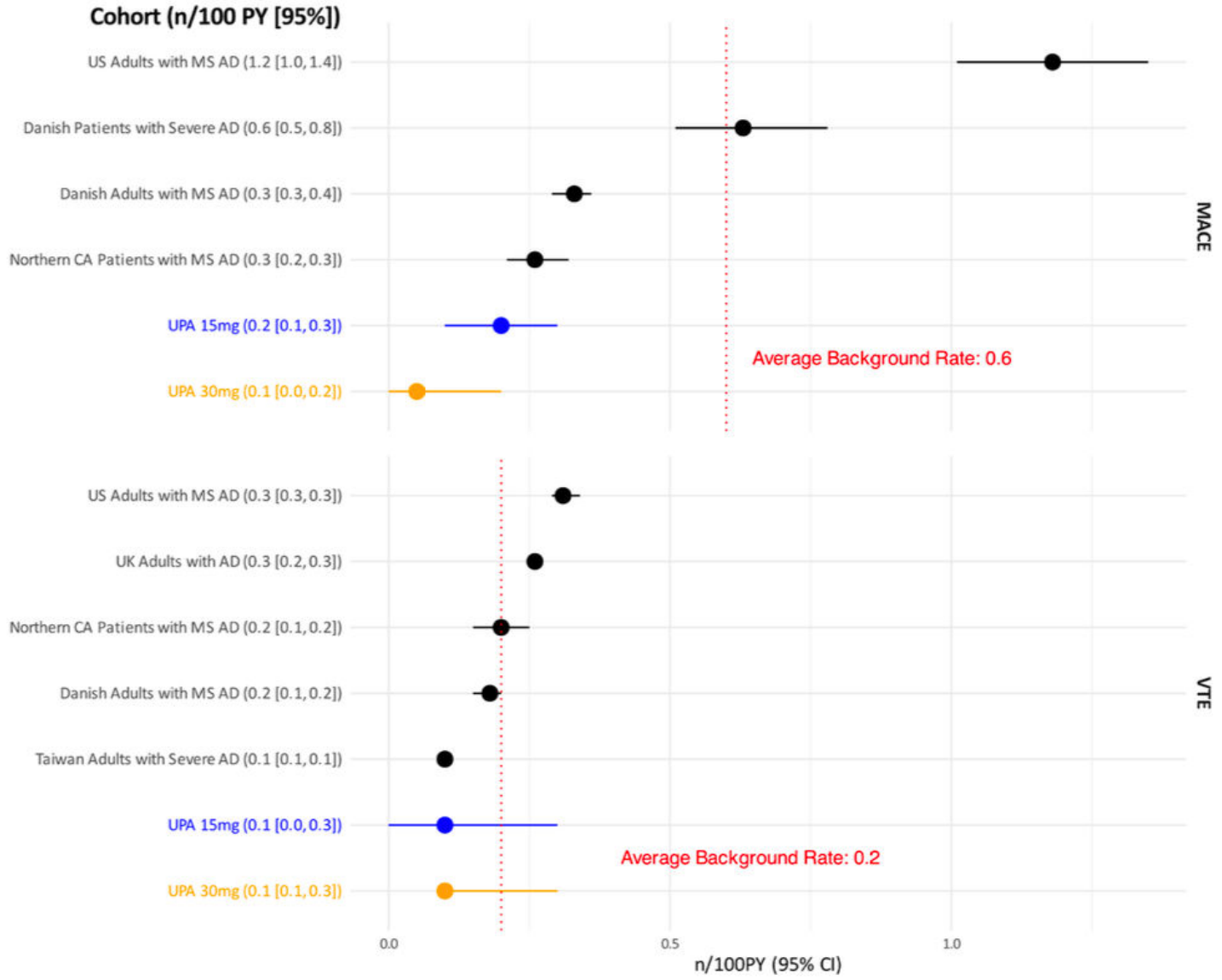
Risks…



Daniele S, Bunick C. JAK Inhibitor Safety Compared to Traditional Systemic Immunosuppressive Therapies. Journal of Drugs in Dermatology: JDD. 2022 Dec 1;21(12):1298-303.

Is Upadacitinib Cardioprotective in Chronic Inflammatory Diseases? A Review of Major Adverse Cardiovascular Events and Venous Thromboembolism in Atopic Dermatitis

Omar Alani ScB,[a] David Wang,[b] Samer Wahood BA,[c] Sabine Obagi BA,[d] Diego Dasilva MD,[e] Matthew J. Zirwas MD,[f] Fabrizio Galimberti MD PhD,[g] Christopher G. Bunick MD PhD[h]



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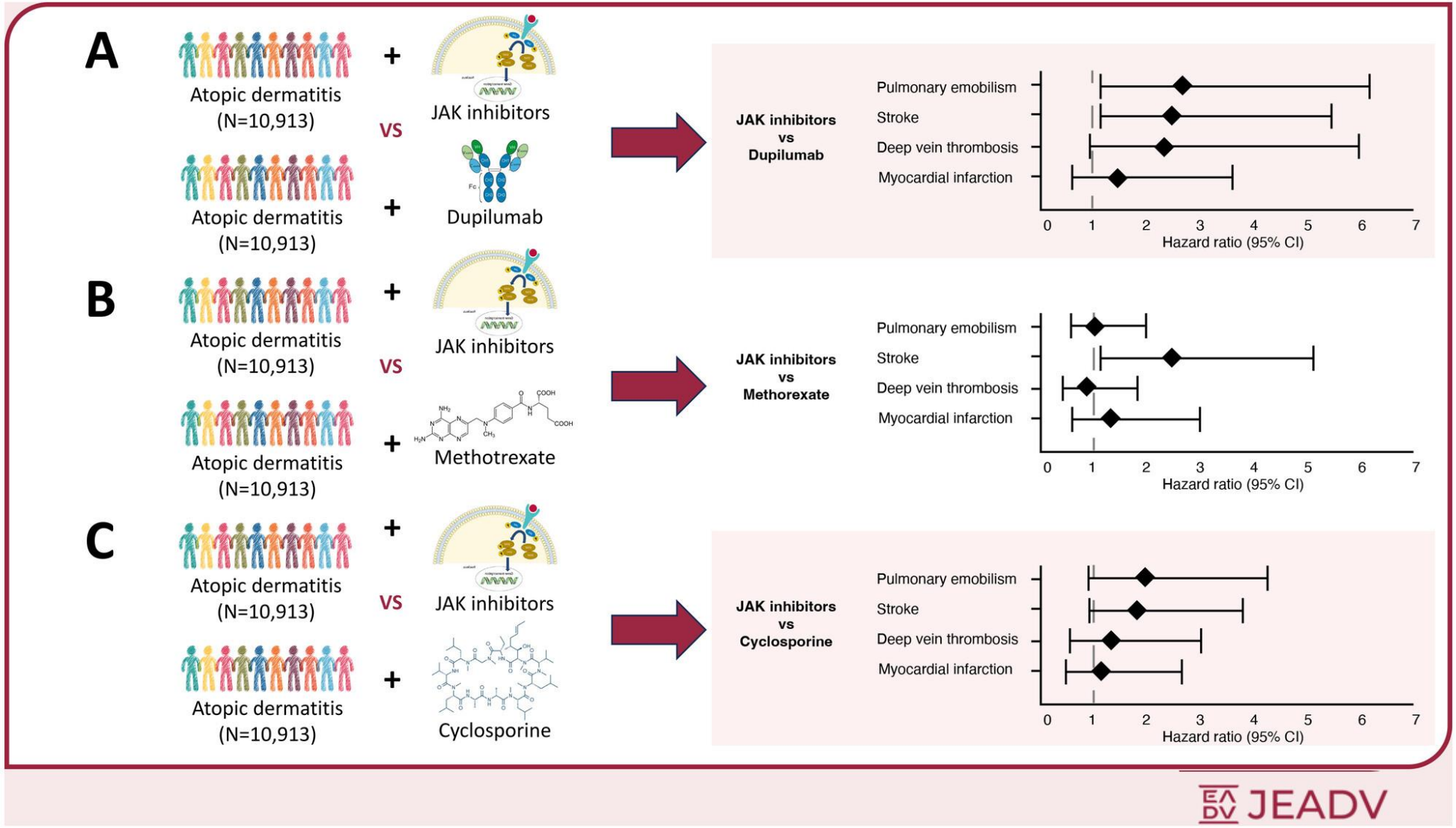
But…

"JAK inhibitor use in patients with AD is associated with a slightly increased risk of PE and DVT compared to dupilumab and methotrexate. These findings underscore the need for careful patient selection and thrombotic risk assessment when prescribing JAK inhibitors."



JEADV

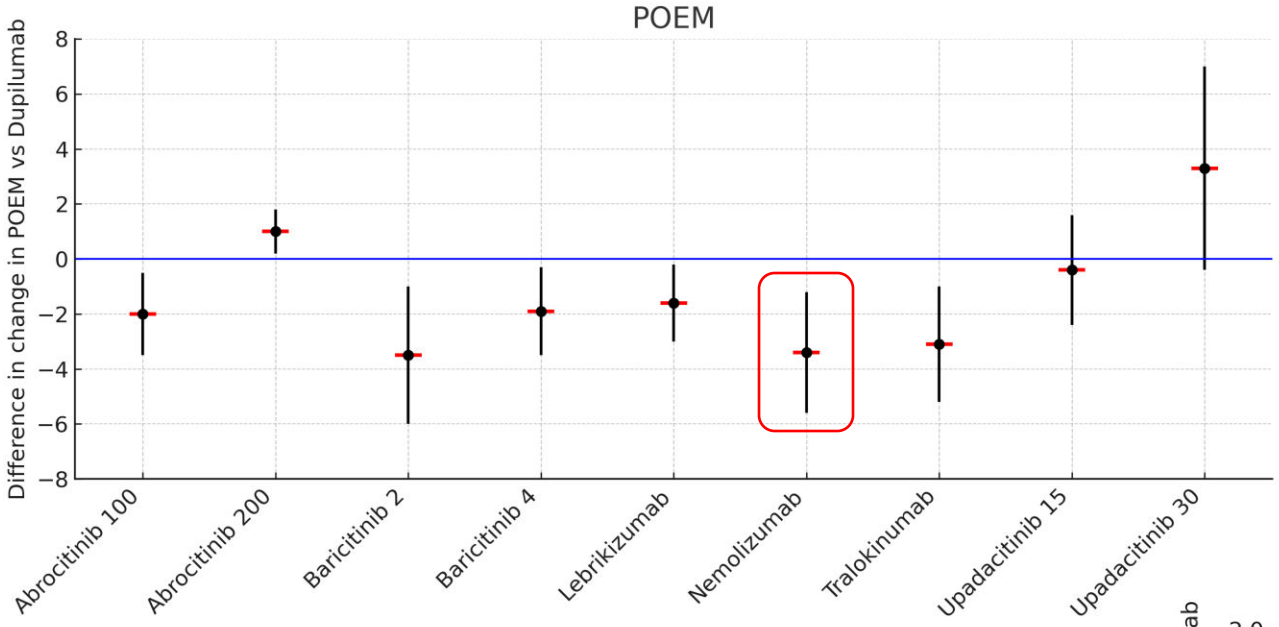
- Kridin K, Kridin S, Mayer E, Sawaed W, Ludwig RJ. Cardiovascular and thromboembolic risks of JAK inhibitors in atopic dermatitis: A global cohort study. Journal of the European Academy of Dermatology and Venereology. 2025 Jul 21.

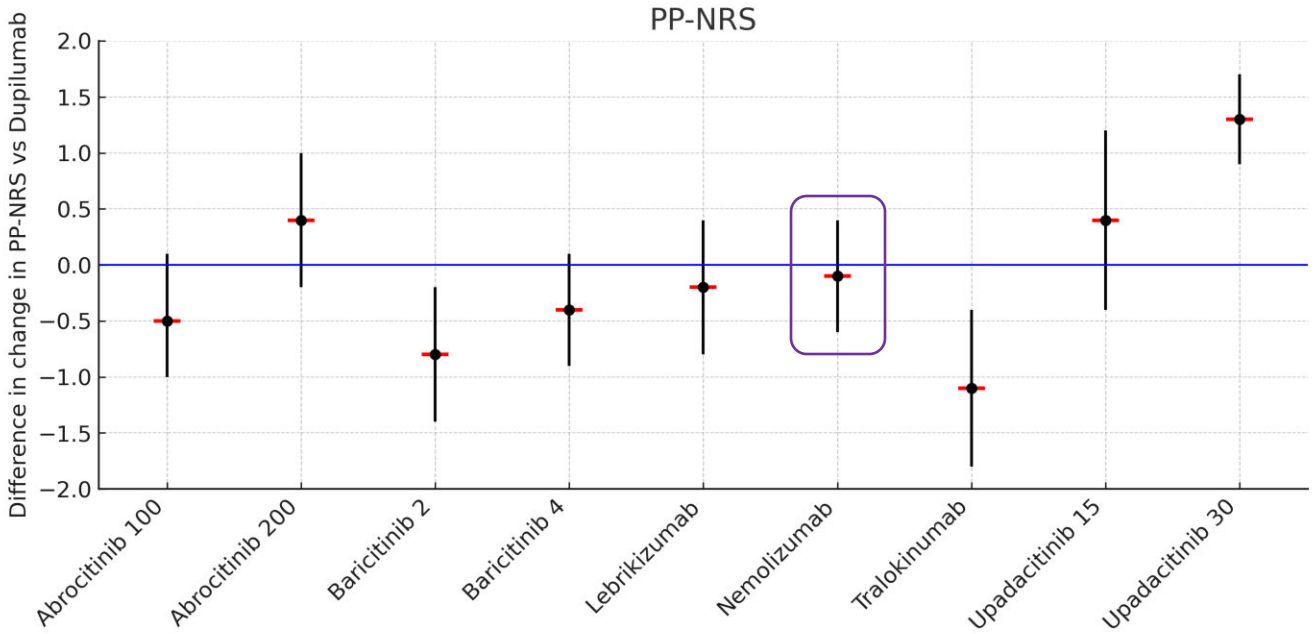
Comparison of Serious Adverse Event Incidence Rates Between Oral JAK Inhibitors Approved for Atopic Dermatitis and Traditional Systemic Immunosuppressive Therapies

Serious adverse events incidence rates (events per 100 patient-years)					
Drug	Malignancy (excluding-NMSC)	NMSC	MACE	VTE	Reference
Upadacitinib (15mg)*[a]	0.2	0.4	0.1	0.1	Simpson, E.L., et al[15]
Upadacitinib (30mg)*[b]	0.5	0.4	0.0	0.1	Simpson, E.L., et al[15]
Abrocitinib (100mg)*[c]	0.2	0.6	0.6	0.0	Simpson, E.L., et al[16]
Abrocitinib (200mg)*[d]	0.2	0.4	0.2	0.4	Simpson, E.L., et al[16]
Methotrexate	0.5	0.3	0.5	0.5	Cohen, S.B., et al[17]
Cyclosporine	0.6[f]	0.5[g]	--	DNF	Paul, C.F., et al[18]
	--	--	2.8[h]		Hong, J.R., et al[19]
Systemic Corticosteroids	4.3[i]	3.9[i]	--	--	Khan, N., et al[20]
	--	--	7.6[j]	--	Wei, L., et al[21]
	--	--	--	0.02[k]	Huerta, C., et al[22]

Daniele S, Bunick C. JAK Inhibitor Safety Compared to Traditional Systemic Immunosuppressive Therapies. Journal of Drugs in Dermatology: JDD. 2022 Dec 1;21(12):1298-303.

Network Meta-Analysis—Updated!



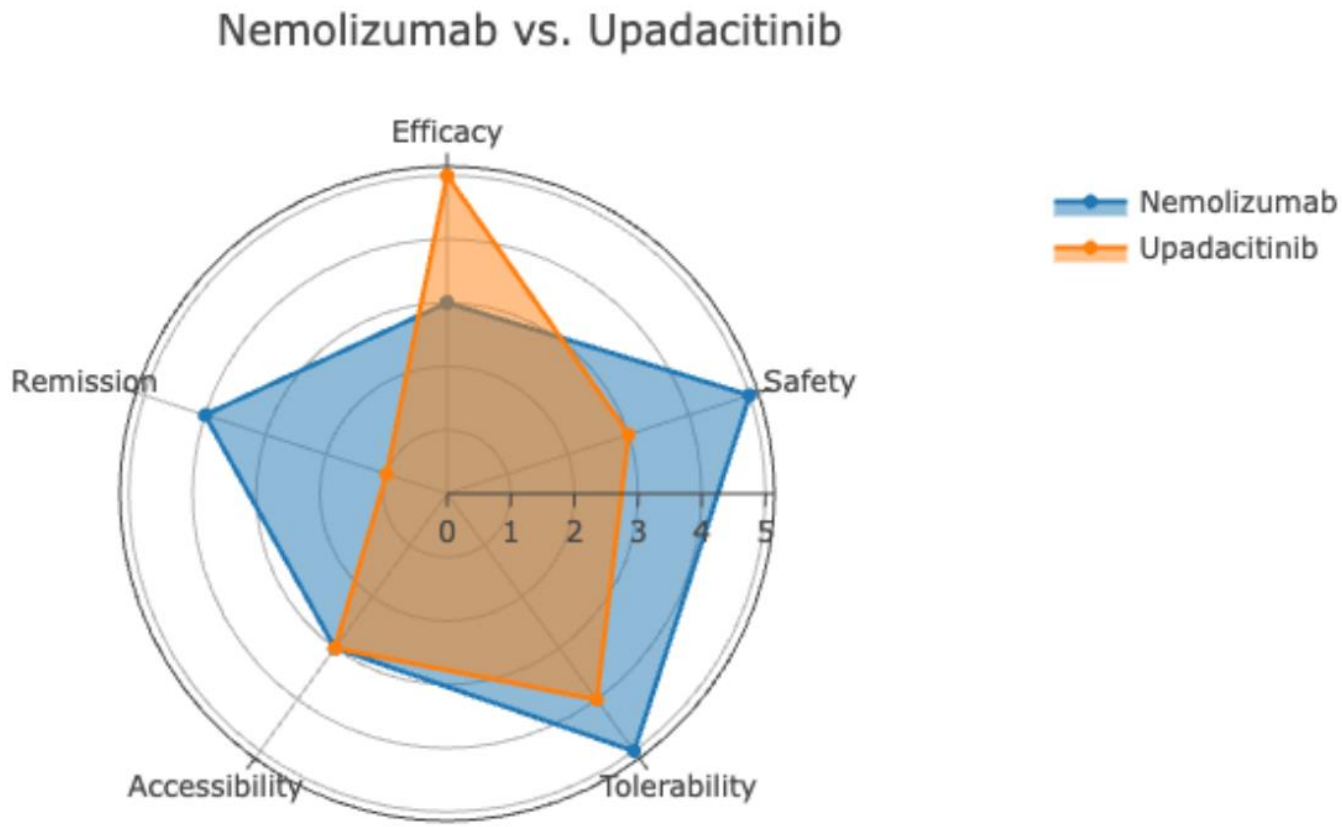


Drucker AM, Walwyn C, Chu C, Yiu ZZ, Rochwerg B, Di Giorgio S, Arents BW, Mohan T, Burton T, Spuls PI, Schmitt J. Living network meta-analysis to compare nemolizumab against other available targeted systemic treatments for atopic dermatitis. The British journal of dermatology. 2025 May 7:ljaf166.

Shared Decision Making: Updated

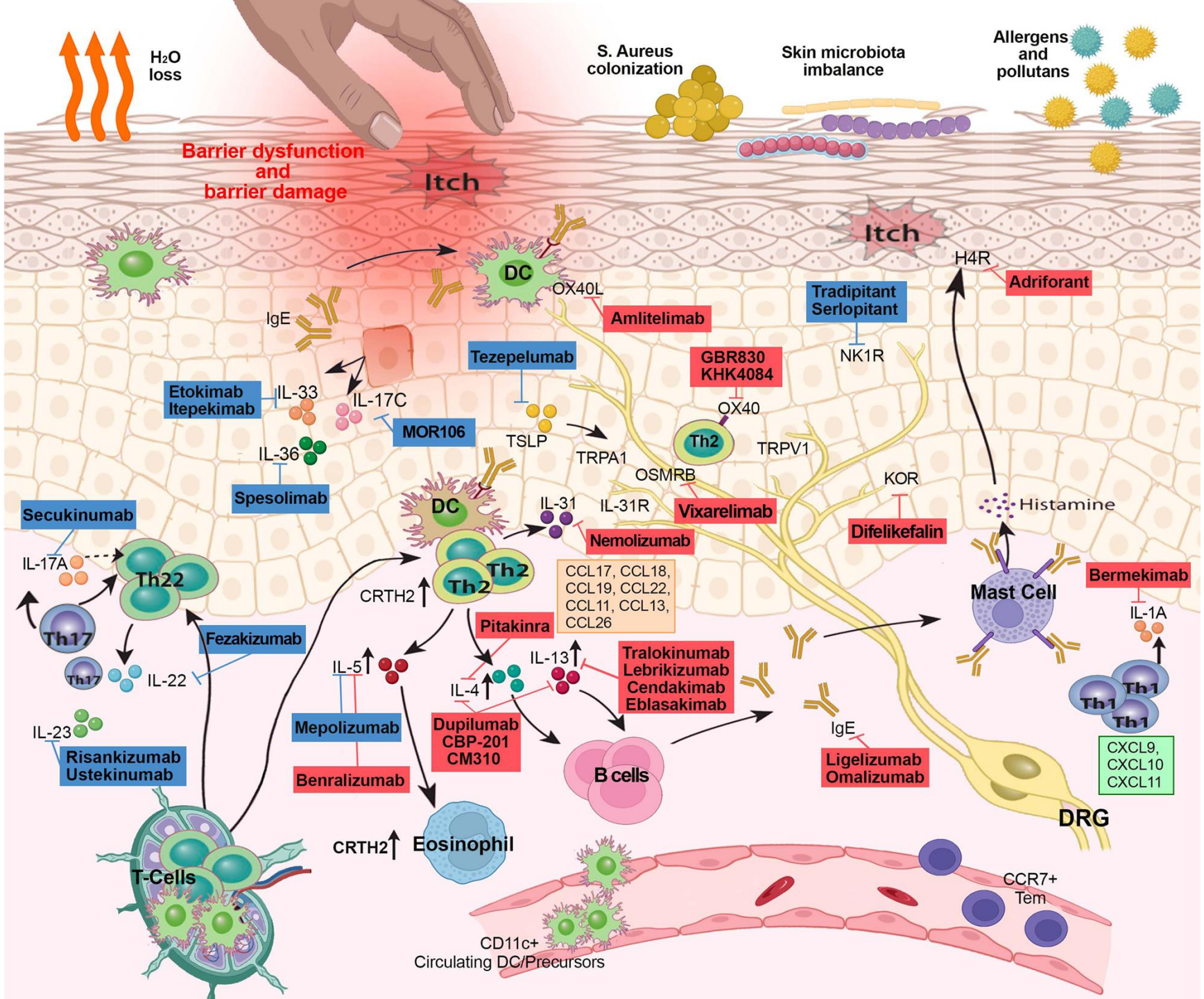
ESTAR

Efficacy
Safety
Tolerability
Accessibility
Remittive potential



Radar Chart comparing nemolizumab (blue) and upadacitinib (orange).
**This example is for illustrative purposes only and is not based on absolute data. Rather, it represents relative aspects of two medications intended to facilitate shared decision-making with the patient and/or family.*

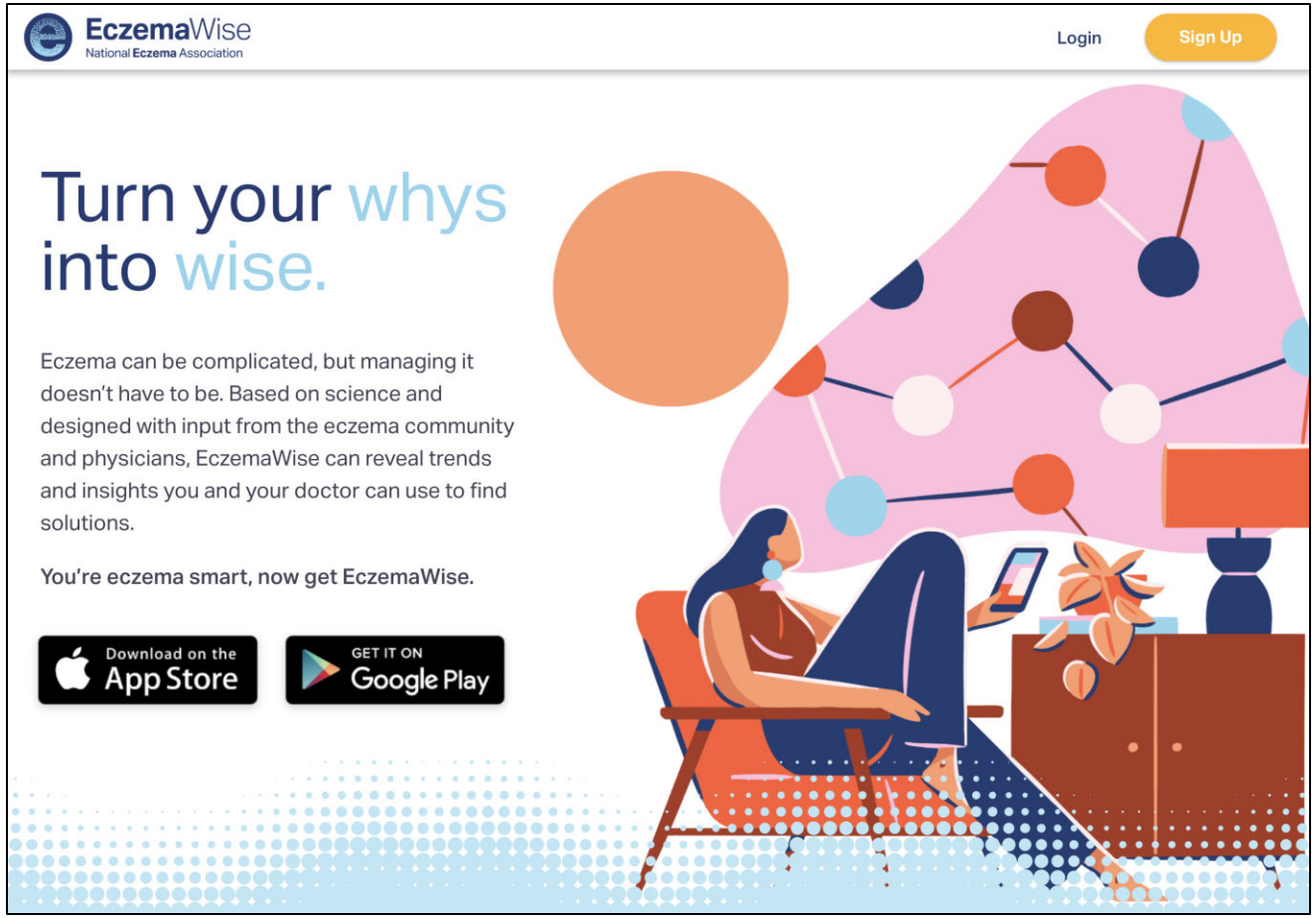
Pipeline . . .



Facheris, P., Jeffery, J., Del Duca, E. et al. The translational revolution in atopic dermatitis: the paradigm shift from pathogenesis to treatment. Cell Mol Immunol 20, 448–474 (2023). https://doi.org/10.1038/s41423-023-00992-4

AD Patient Education: Apps and Tools

EczemaWise by the National Eczema Association
https://www.eczemawise.org/



Thank you!

peterlio@gmail.com