

A photograph of an artist's workspace. In the center, a silver tin can holds several paintbrushes of various sizes and colors. To the left, a palette is visible with various colors of paint. The background is a blurred painting with warm tones of red, orange, and yellow. The overall scene is artistic and creative.

Targeted Topicals

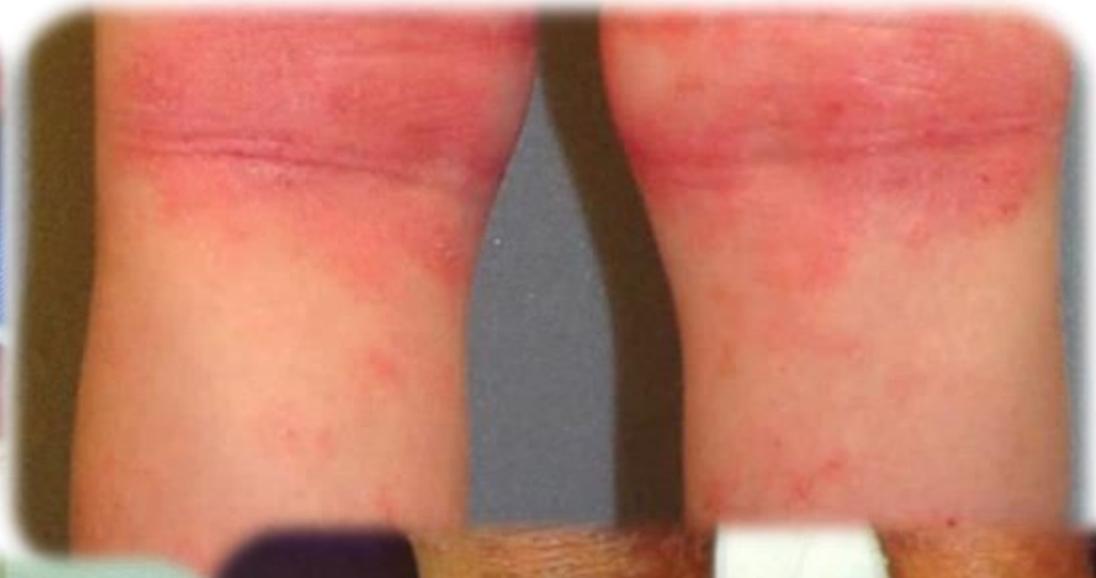
Peter Lio, MD, FAAD

DISCLOSURE

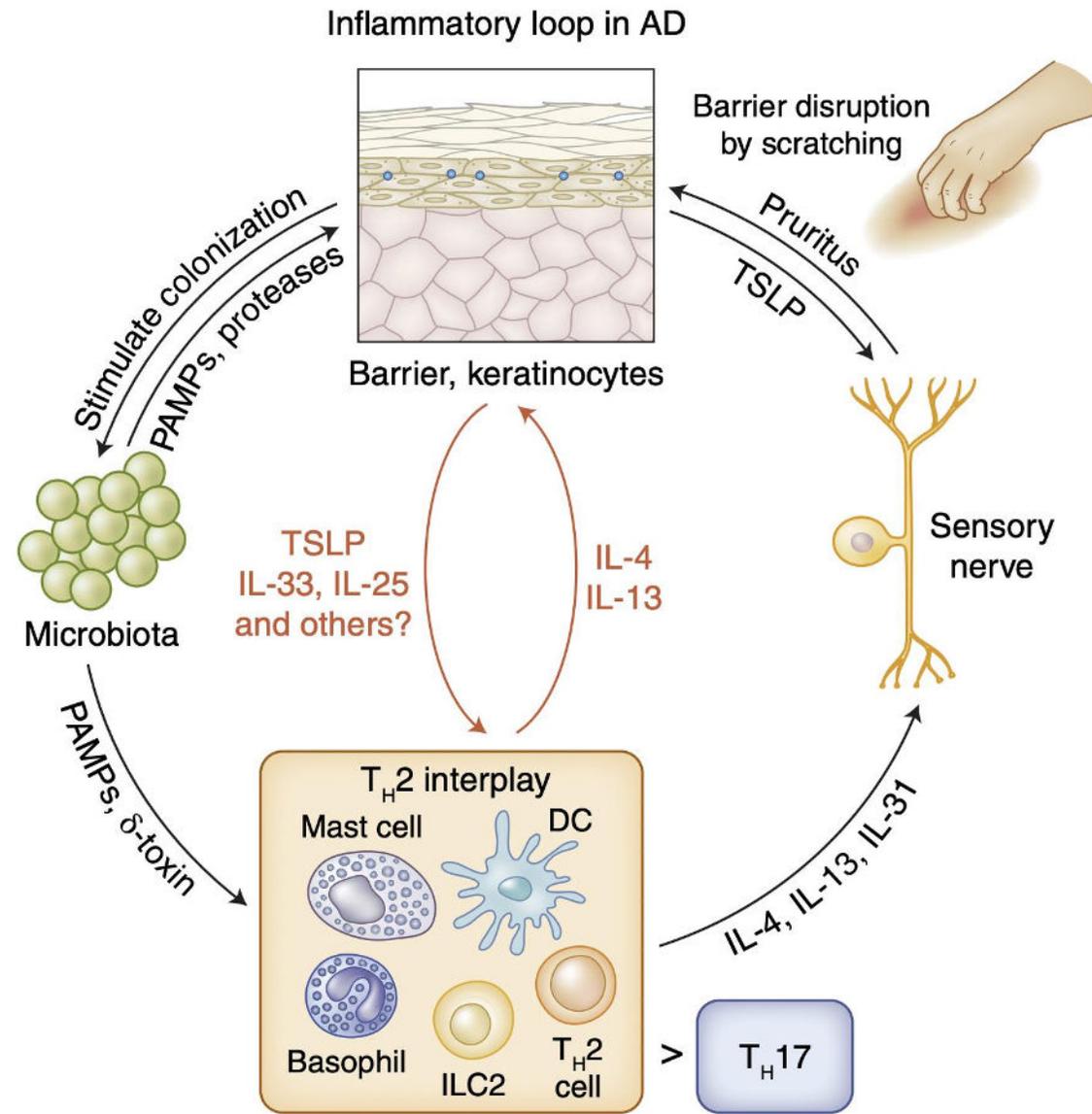
- Peter Lio, MD, FAAD

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, Microcos, 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



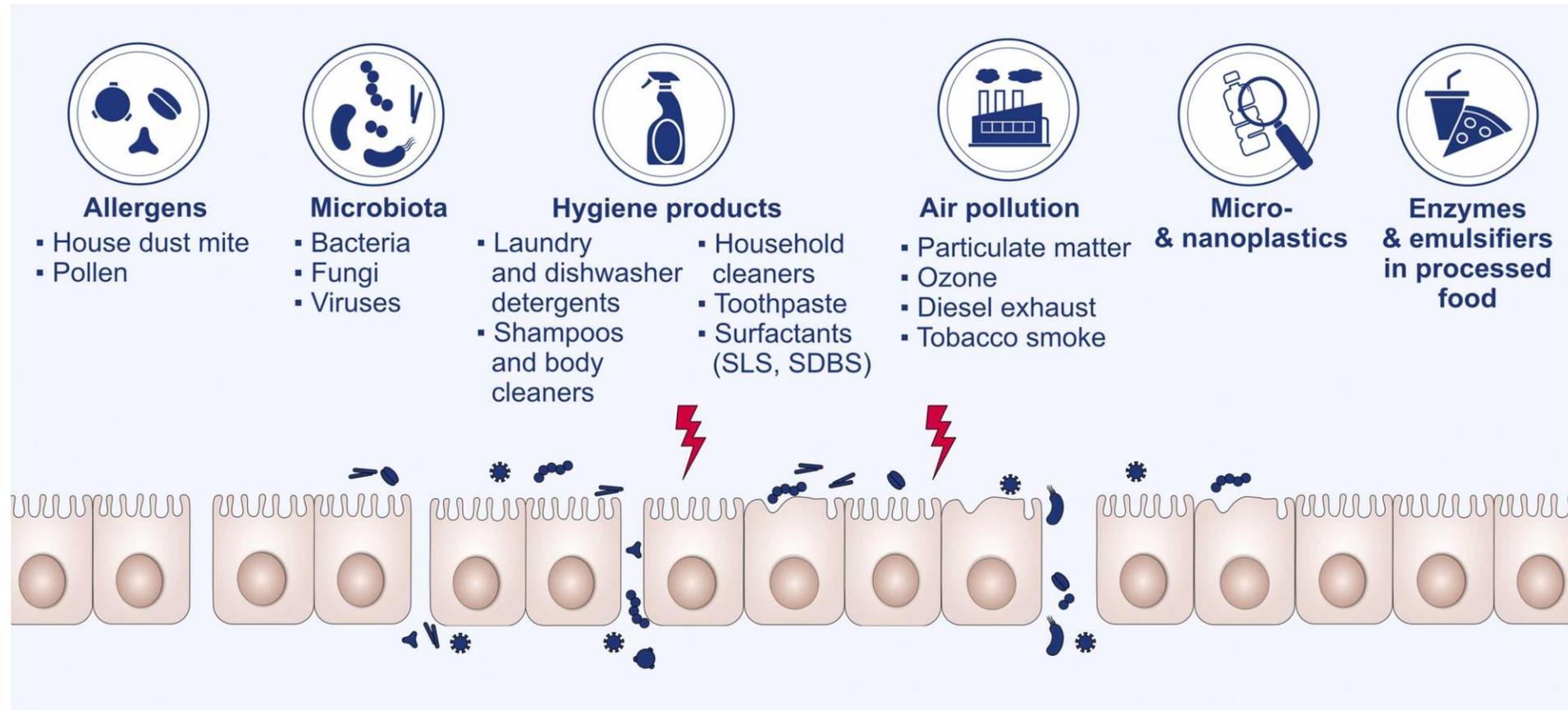
Loop



Barrier is KING!

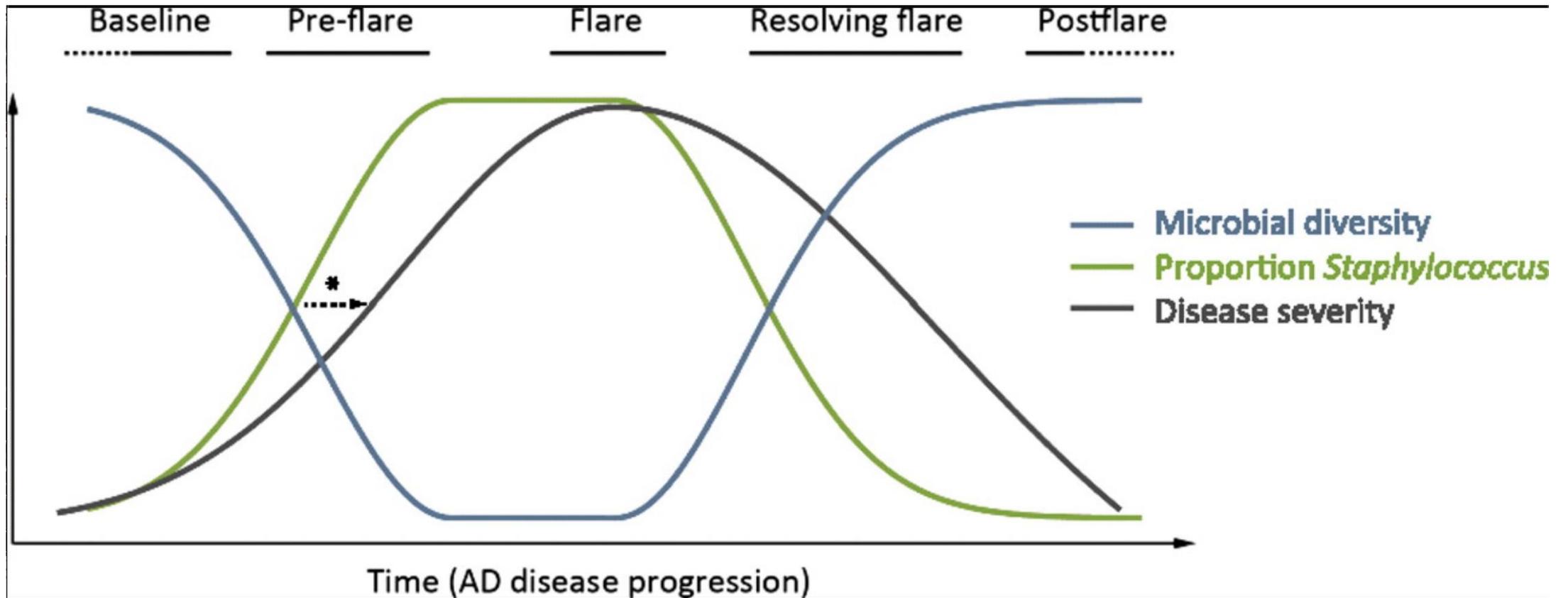
Epithelial Barrier Hypothesis

- 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



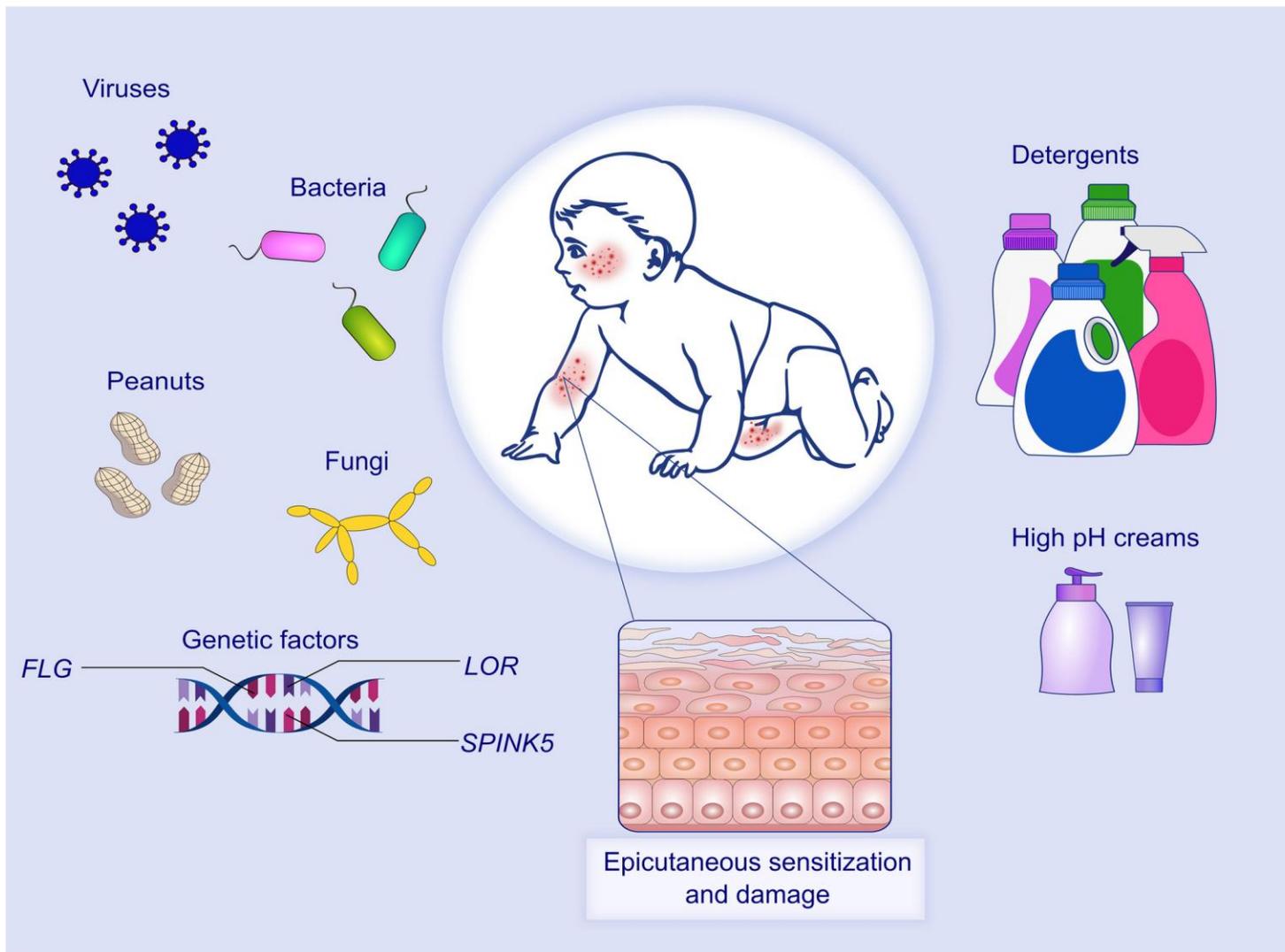
- Kong HH, et al. *Genome Res.* 2012;22(5):850-9.

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

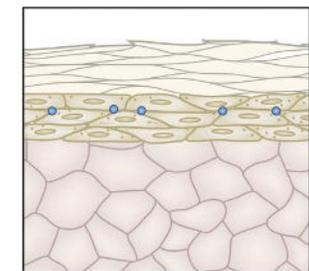
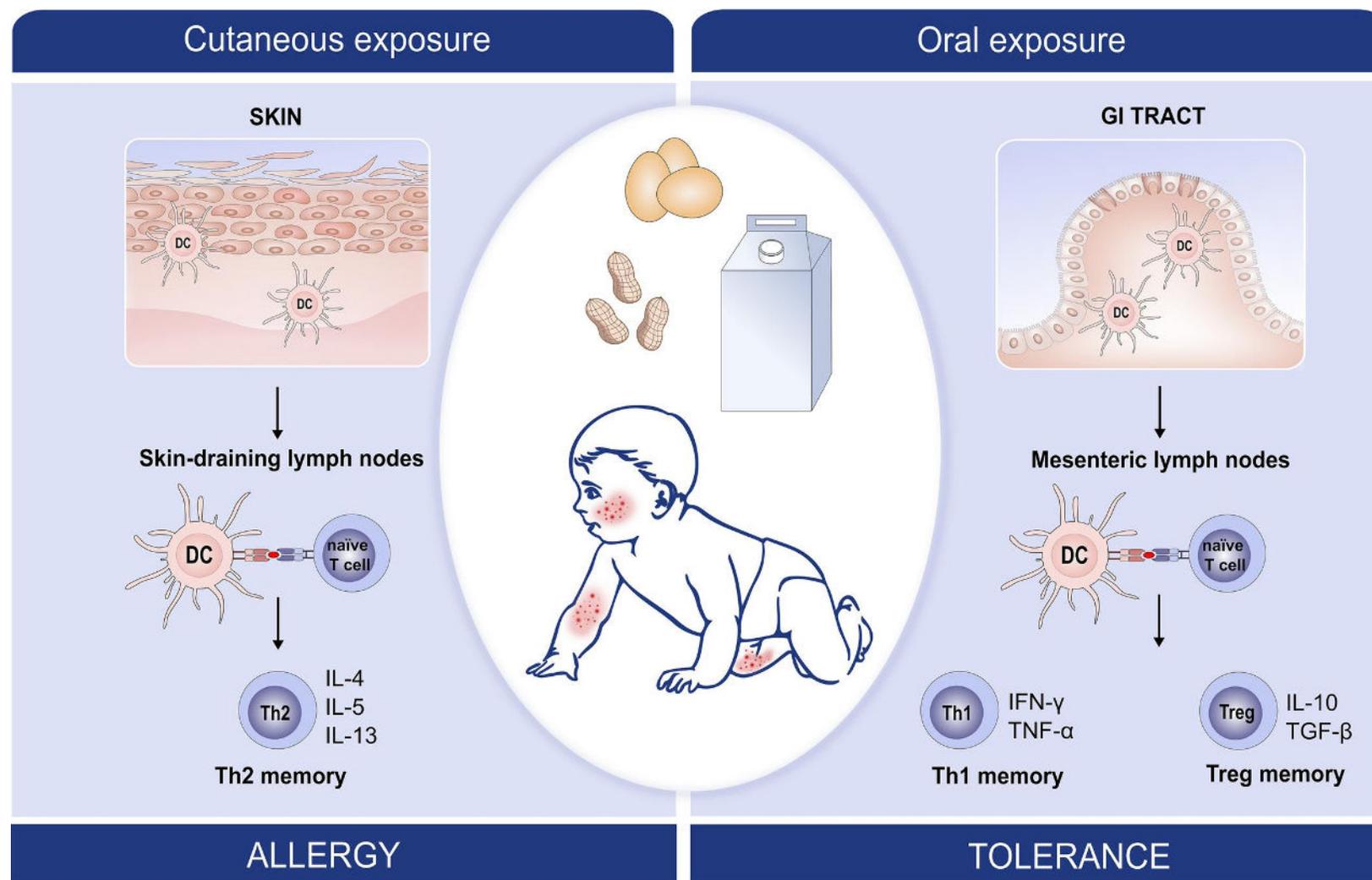
<i>S. aureus</i> proteins	Possible role in AD
Clumping factor B	Adhesion to corneocytes in stratum corneum via loricrin or other ligands
Fibronectin-binding proteins	Adhesion to fibronectin that is present at high levels in the upper strata of epidermis and stratum corneum of AD skin
Protein A	Proinflammatory. 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 <i>S. aureus</i> colonization. Similar role in AD?

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

Environmental and genetic factors leading to epicutaneous damage



Epicutaneous Sensitization



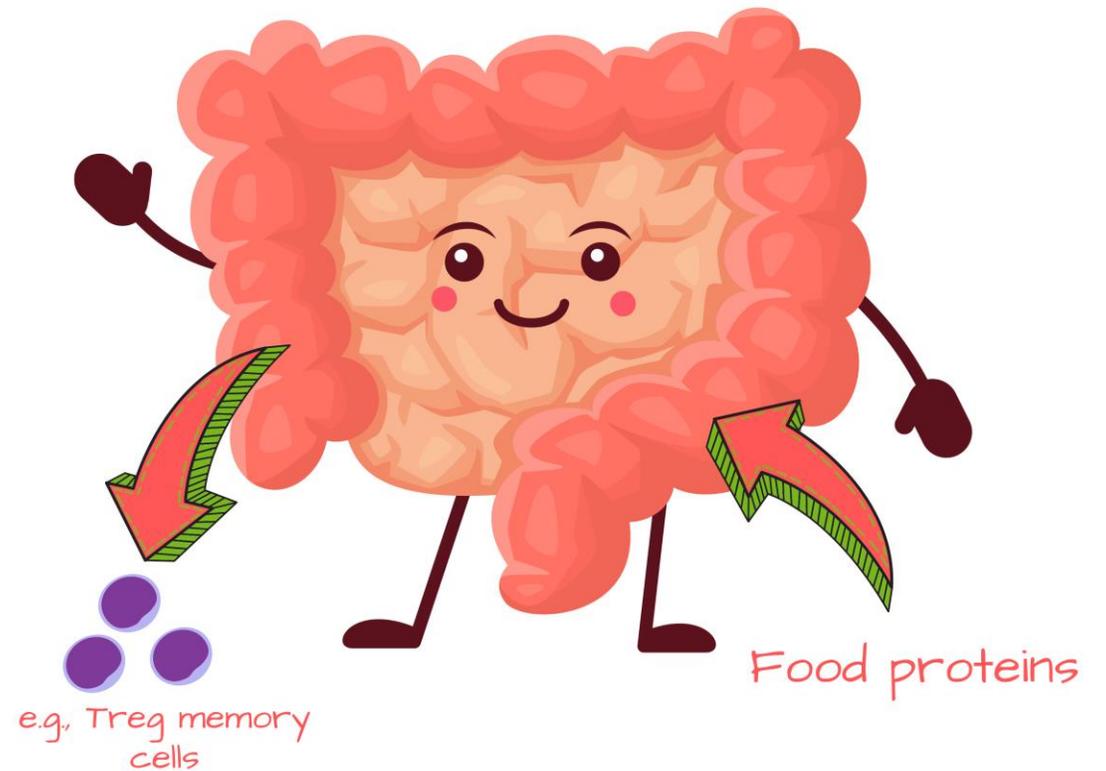
Barrier, keratinocytes

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

Through the skin,
allergies begin.

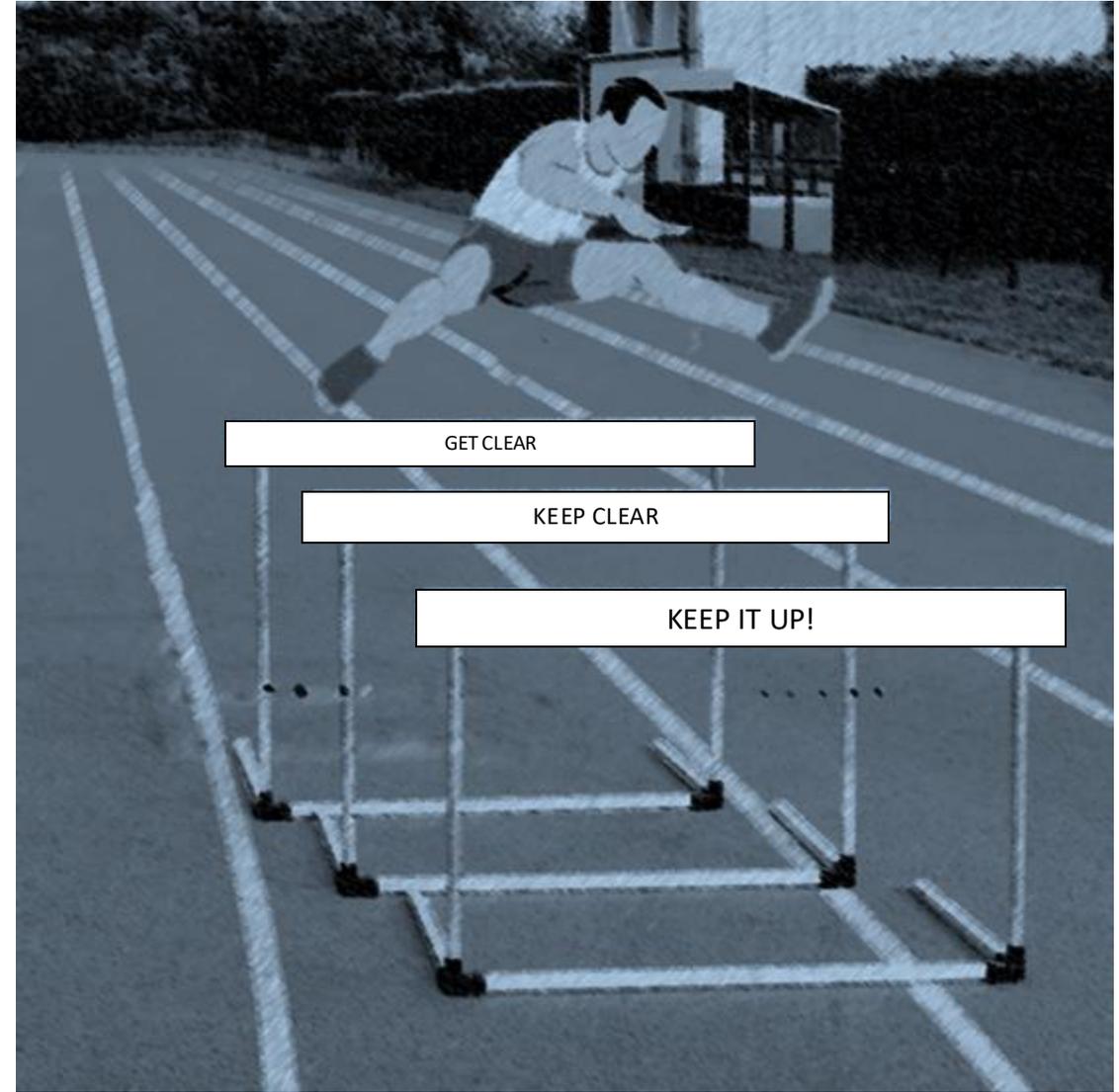


Through the diet,
allergies stay quiet.

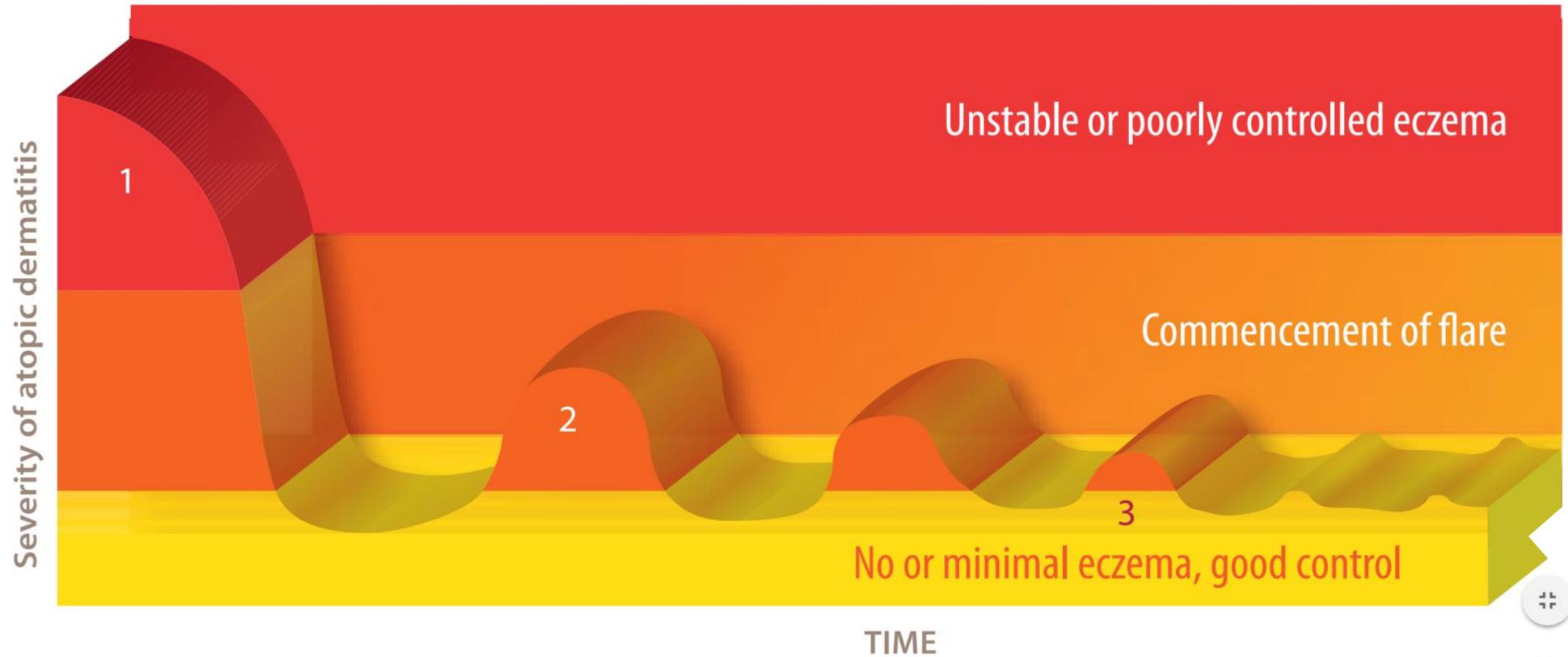


GOALS

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

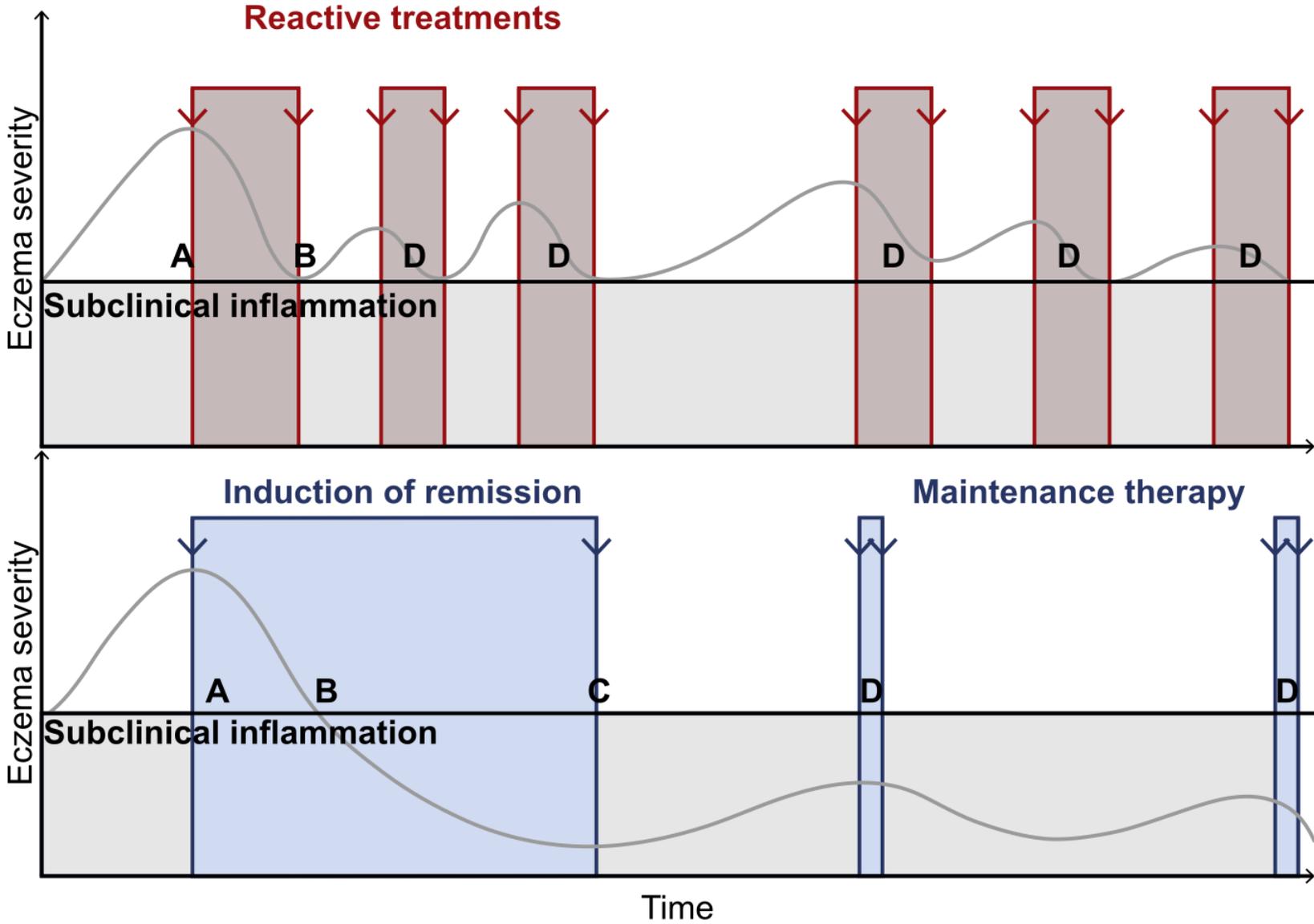


Treatment Goal



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

JTF Guidelines



AAAAI/ACAAI JTF Atopic Dermatitis Guideline Panel; Chu DK, Schneider L, Asinowas 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.anaai.2023.11.009. Epub ahead of print. PMID: 38108679.

ECZEMA ACTION PLAN TEMPLATE

When Flaring

AM

- Apply steroid ointment to eczema areas
- Apply moisturizer liberally

PM

- Gentle bathing
- Apply steroid ointment to eczema areas
- Apply moisturizer liberally
- Apply damp layer of gauze or clothing*
- Apply dry layer of clothing

***Do this for several days (up to 1 week)
then move to “When Better” plan***

When Better

AM

- Apply non-steroidal to any remaining eczema areas or trouble spots
- Apply moisturizer liberally

PM

- Gentle bathing
- Apply non-steroidal to any remaining eczema areas or trouble spots
- Apply moisturizer liberally

*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: _____

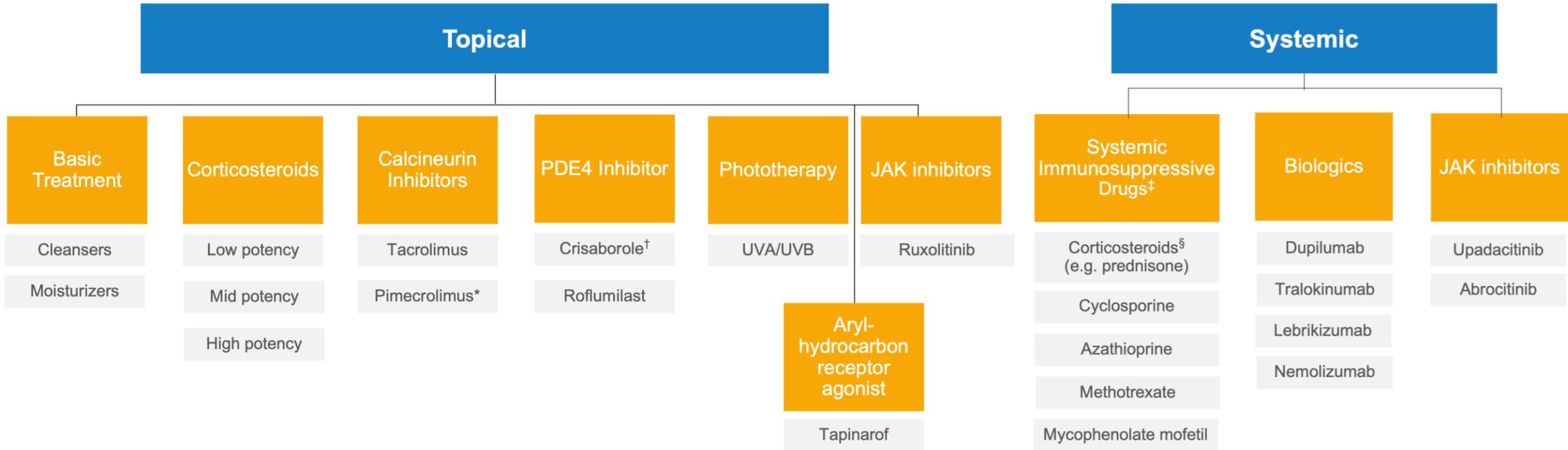
MOISTURIZER: _____

<p>1 Take one pair of onesies, pajamas, gloves, and/or socks and soak it in warm water.</p> 	<p>2 Wring out the onesies, pajamas, gloves, or socks until they are only slightly damp.</p> 
<p>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.</p> 	<p>4 Make sure the room is warm enough before you go to sleep.</p> 

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.

Treatment Landscape in 2025



Topical

Basic Treatment

Cleansers

Moisturizers

Corticosteroids

Low potency

Mid potency

High potency

Calcineurin Inhibitors

Tacrolimus

Pimecrolimus*

PDE4 Inhibitor

Crisaborole[†]

Roflumilast

Phototherapy

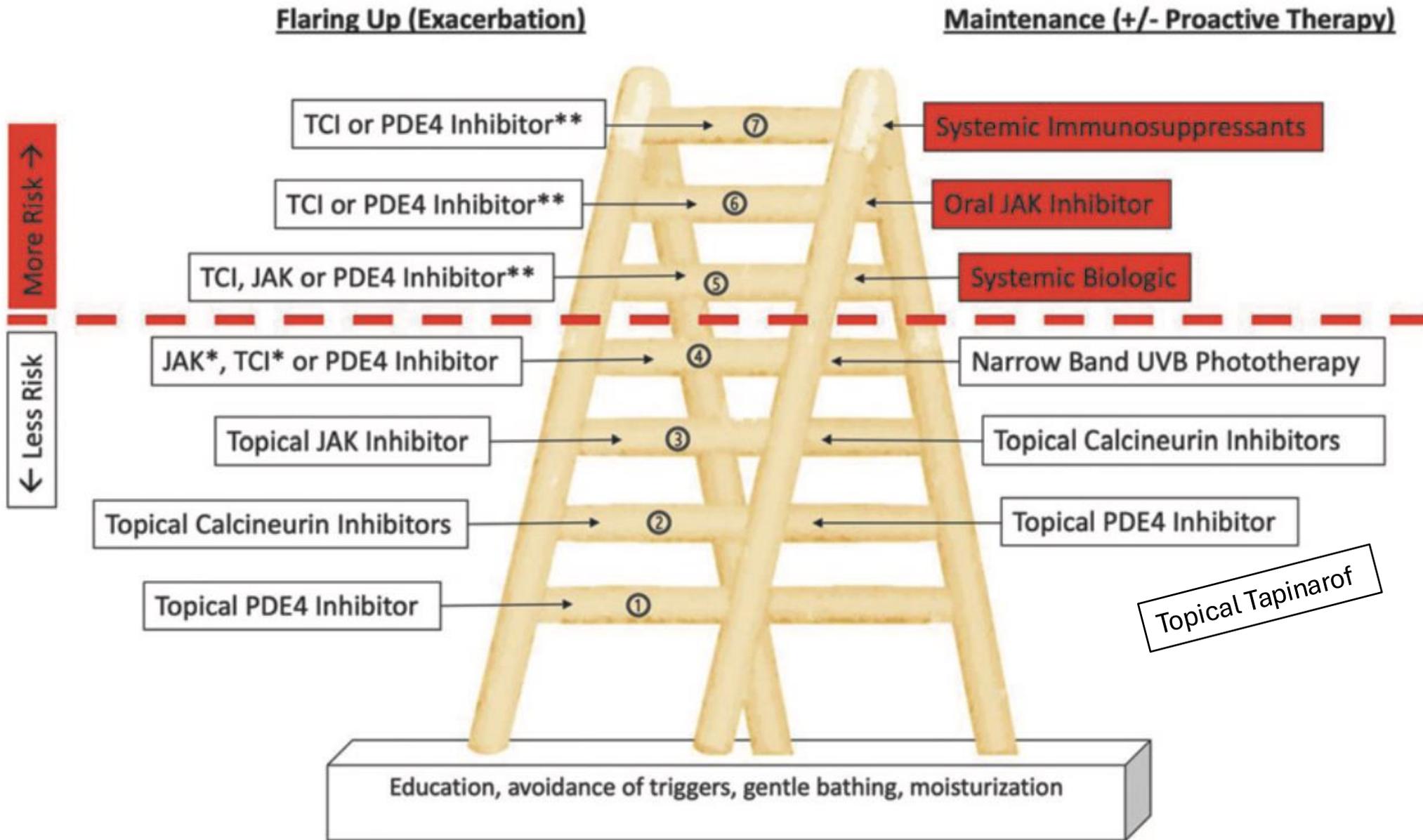
UVA/UVB

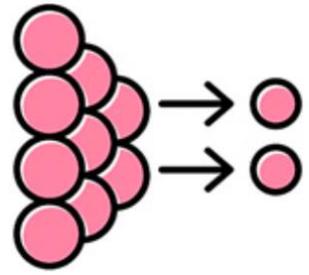
JAK inhibitors

Ruxolitinib

Aryl- hydrocarbon receptor agonist

Tapinarof





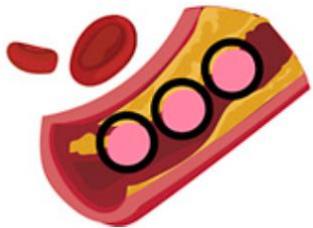
Liberation: Diffusion-Based Release



Penetration: passage through the stratum corneum



Permeation: diffusion in the corium and partly subcutaneous tissue



Absorption: absorption of the active agent by the lymph and blood vessels

Ahuja K, An M, Lio P. A brief review of vehicles for topical therapies. *Skin Pharmacology and Physiology*. 2025 Feb 12;37(4-6):104-8.



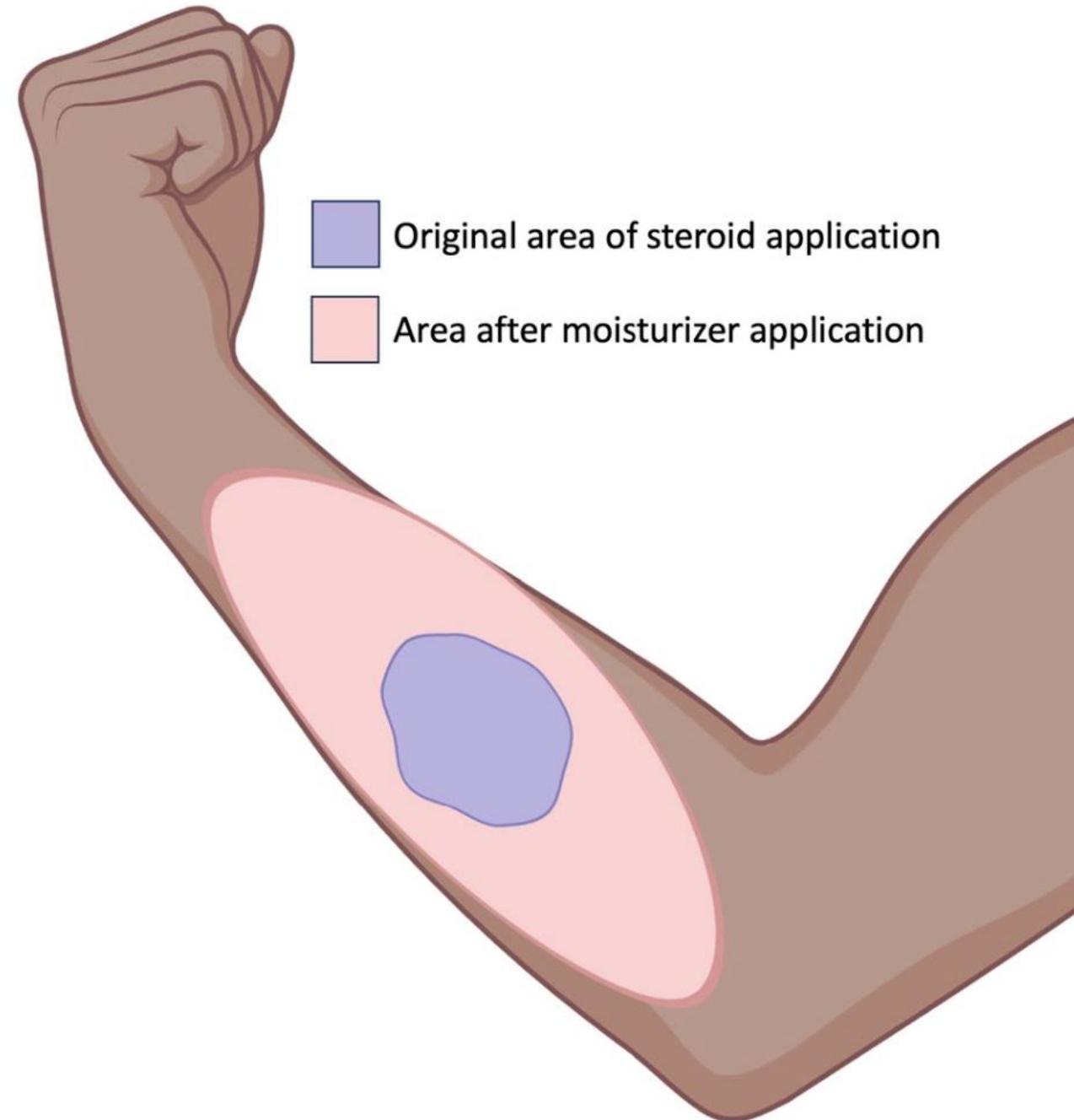
Fig. 1. Schematic of topical agents. The figure depicts the classification of topical agents based on chemical properties.

Fig. 2. Major steps in active transport of a drug. The figure depicts the four major steps involved in active transport of an agent from penetration into skin to systemic absorption.

ORDER OF TOPICALS

Undesirable spreading. When a topical steroid is focally applied, even after waiting 30 min, the subsequent application of a lipophilic moisturizer can spread the drug far beyond the intended area.

Ahuja K, Lio PA. Topical steroids or emollients: does order matter?. Archives of Dermatological Research. 2024 Mar 15;316(4):104.



ORDER OF TOPICALS

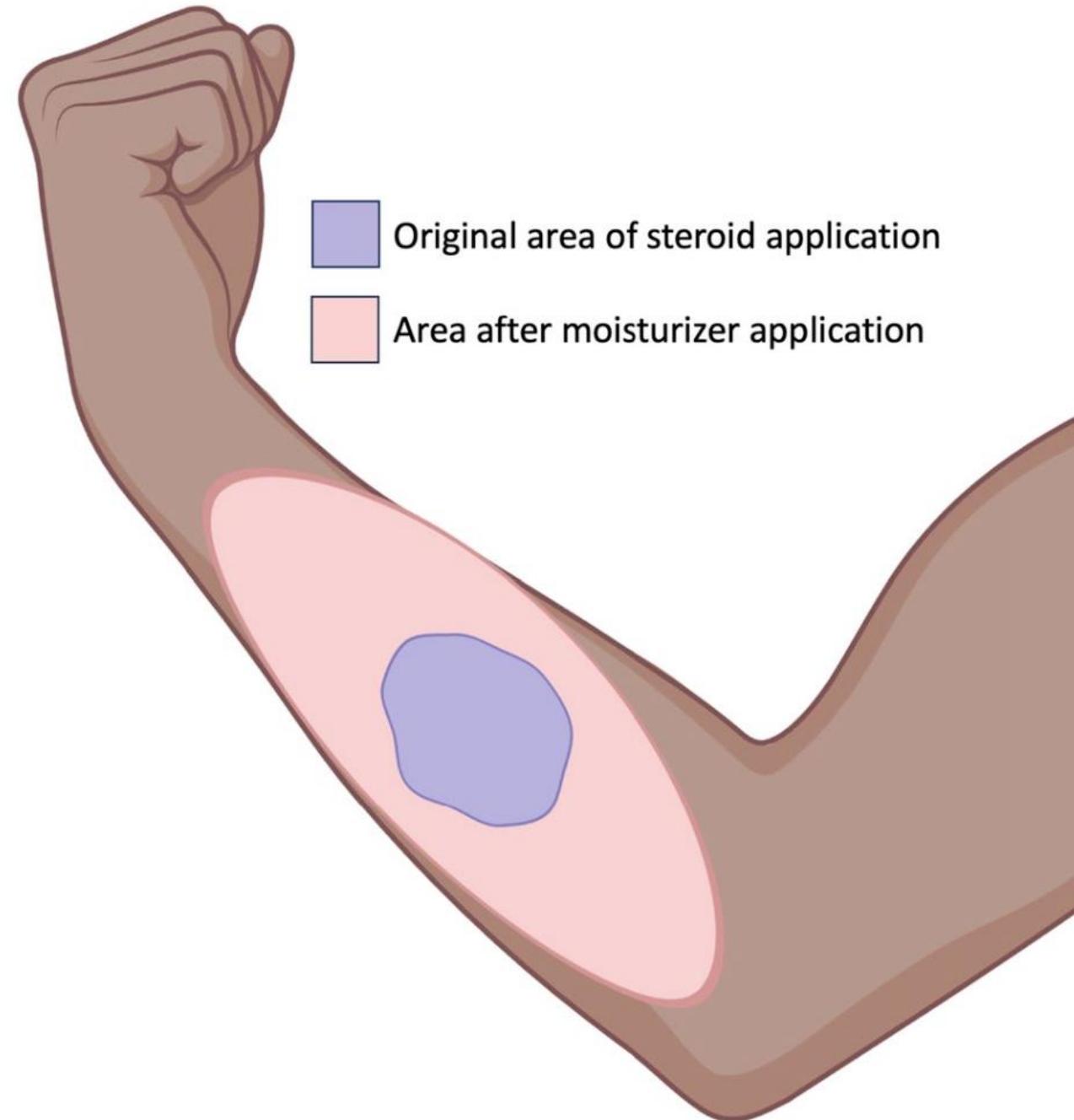
“...Highly credible sources as well as current randomized controlled trial practices, sway towards topical corticosteroids being applied first.

However, compelling arguments exist for applying moisturizer first:

- Minimizing unwanted distribution of medications
- Helping alleviate stinging and burning of SSAs.

Additional research assessing varying sequences of application and time intervals with different medications and moisturizers is needed to understand this issue fully.”

Ahuja K, Lio PA. Topical steroids or emollients: does order matter?.
Archives of Dermatological Research. 2024 Mar 15;316(4):104.



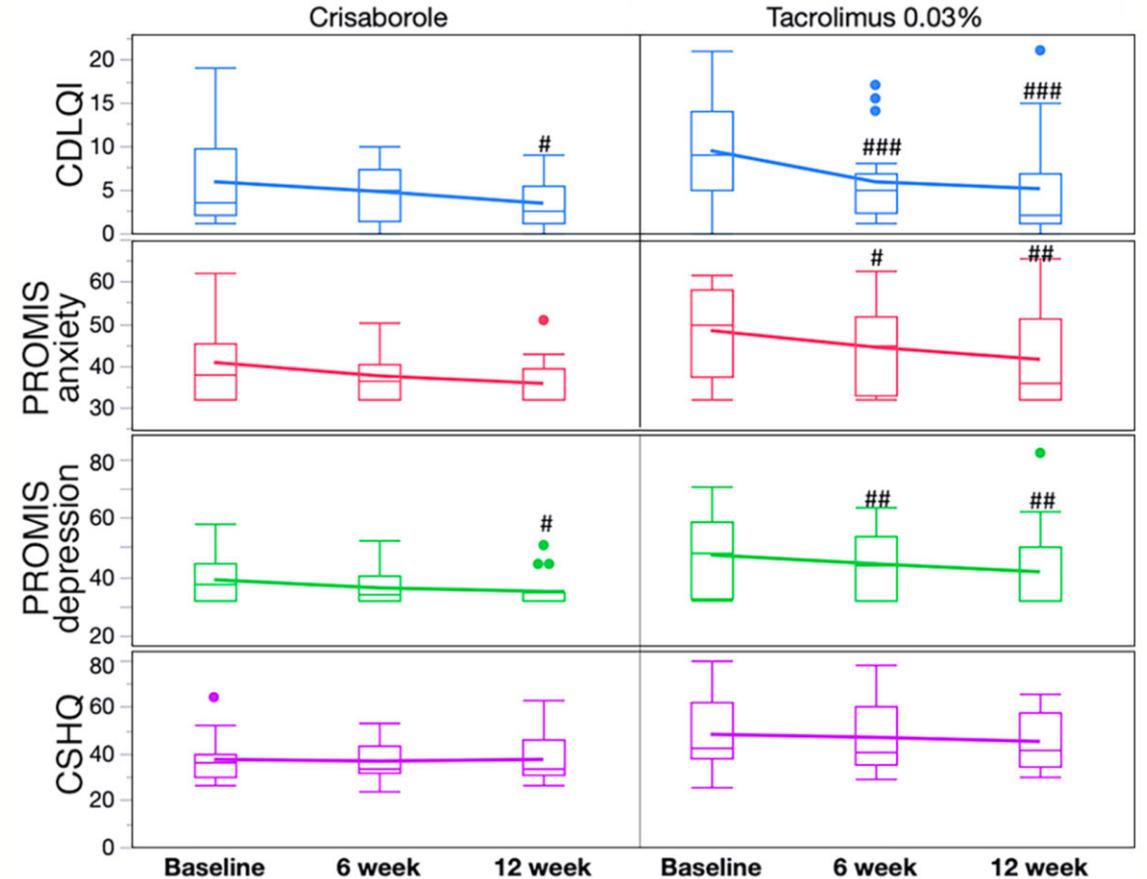
Tacrolimus vs. Crisaborole

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

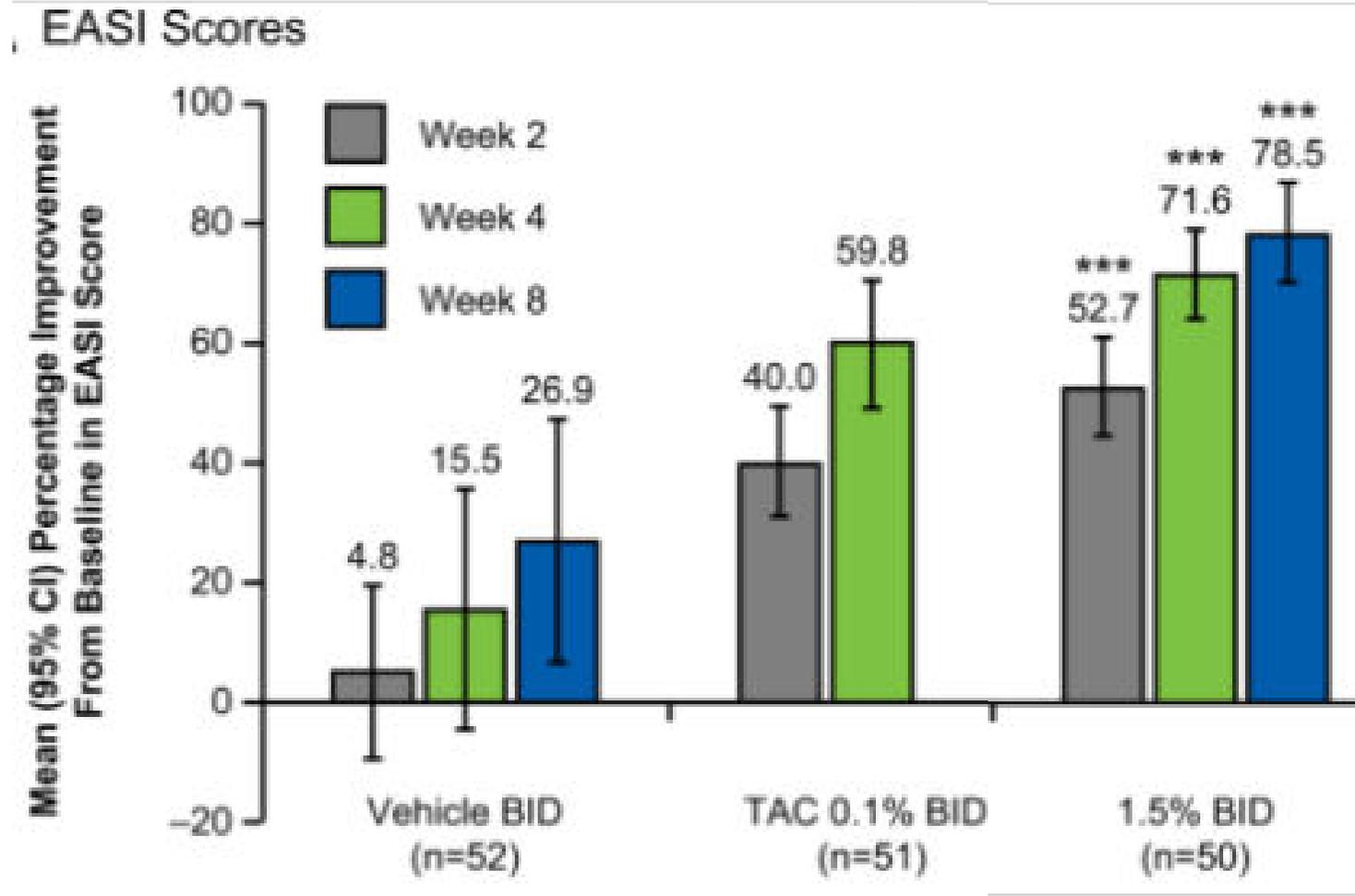
“Our results suggest that TAC may be the better overall treatment for mild AD based on patient and caregiver perspectives.”

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.

Child QoL, Anxiety, Depression, Sleep Habits Over 12 Weeks
arm_label



Treatment of AD With Ruxolitinib Cream or Triamcinolone Cream



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](#)

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 $\geq 1\%$) are nasopharyngitis, diarrhea, bronchitis, ear infection, eosinophil count increased, urticaria, folliculitis, tonsillitis, and rhinorrhea. (6)

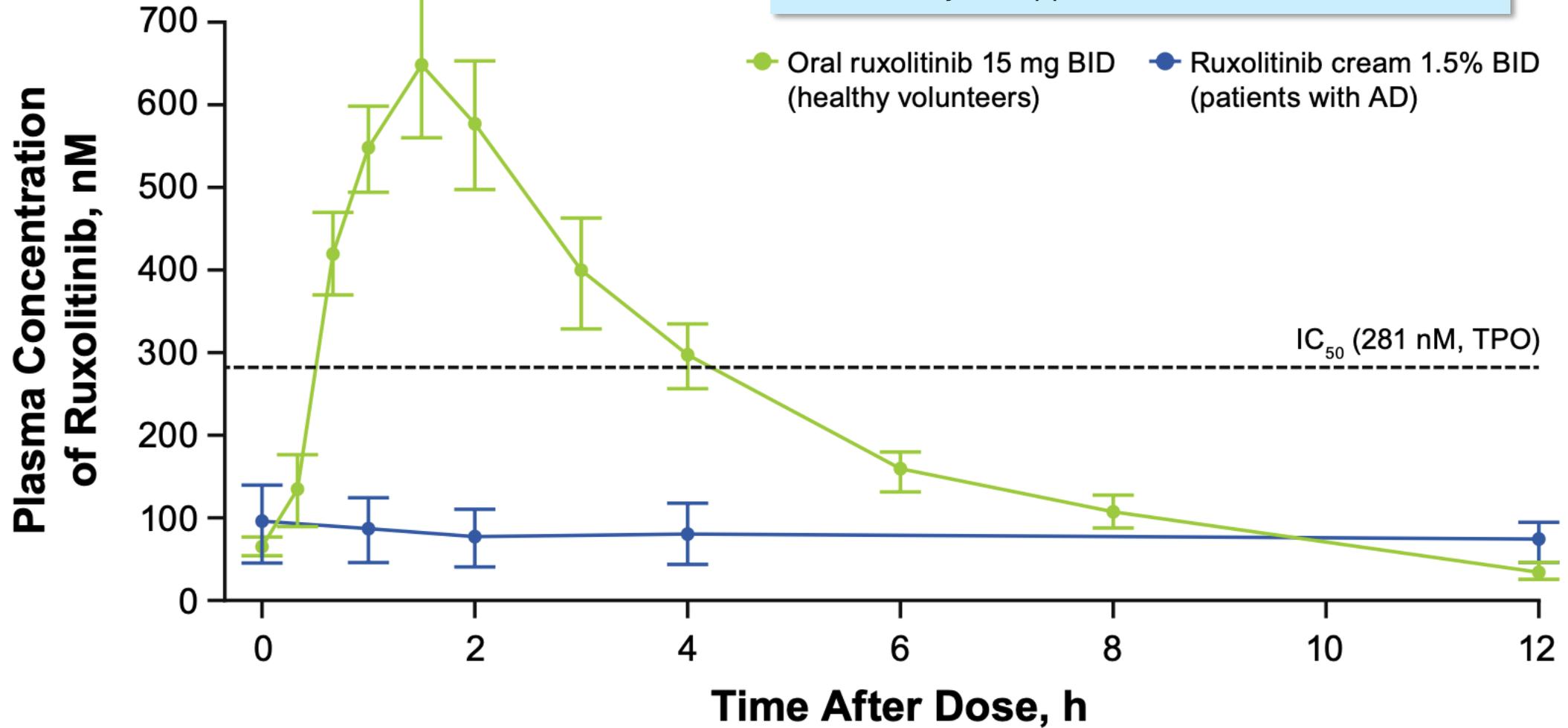
WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE), AND THROMBOSIS

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)**

Ruxolitinib

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



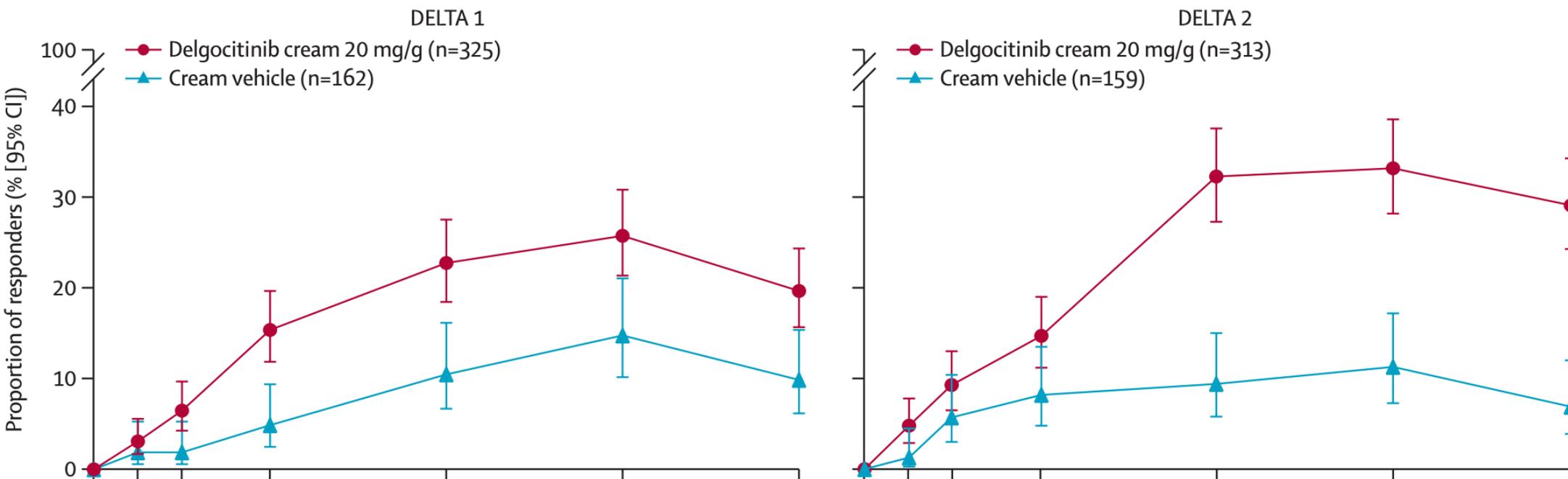
IC_{50} half-maximal inhibitory concentration, TPO thrombopoietin

Delgocitinib

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

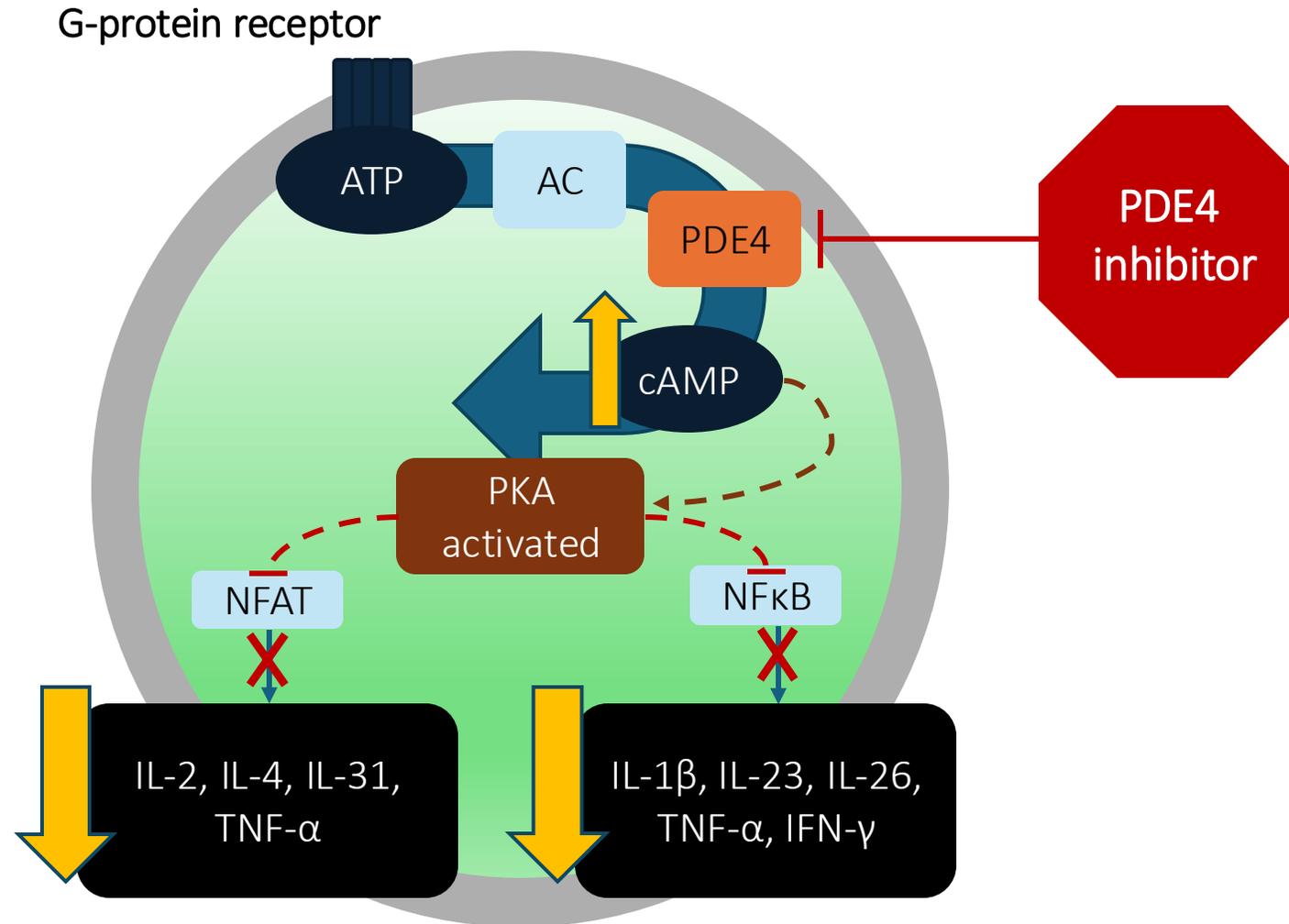
Chronic hand eczema subtype†	
Atopic hand eczema	217 (45%)
Allergic contact dermatitis	84 (17%)
Hyperkeratotic eczema	77 (16%)
Irritant contact dermatitis	75 (15%)
Vesicular hand eczema (pompholyx)	34 (7%)

IGA 0 or 1

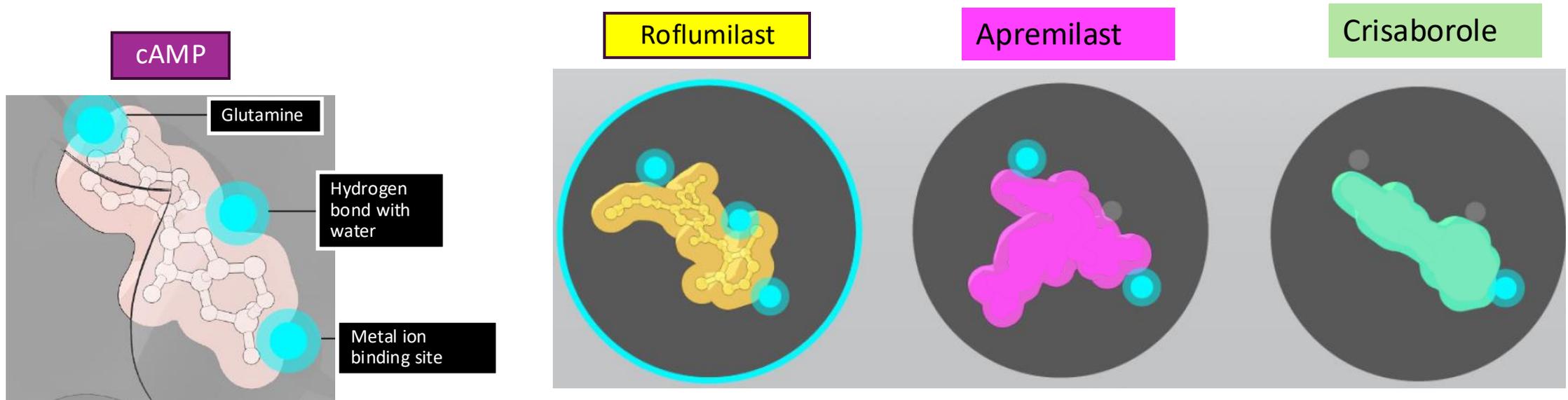


Bissonnette R, Warren RB, Pinter A, Agner T, Gooderham M, Schuttelaar ML, Crépy MN, Stingeni L, Serra-Baldrich E, Baranowski K, Korn S. Efficacy and safety of delgocitinib cream in adults with moderate to severe chronic hand eczema (DELTA 1 and DELTA 2): results from multicentre, randomised, controlled,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

PDE4 Inhibition Reduces Production of Proinflammatory Mediators in AD



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.

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

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%)

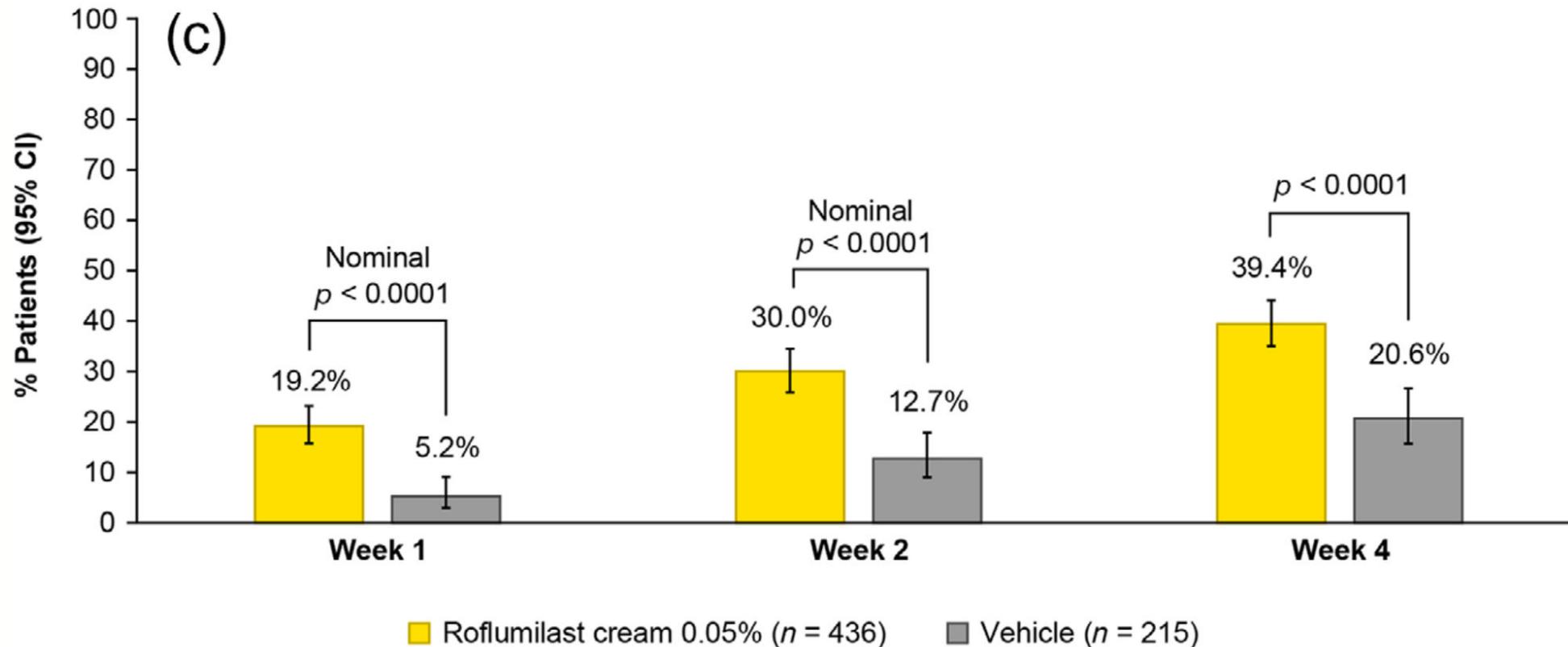
- Stinging or burning: 1.6% with roflumilast vs 2.0% with vehicle after first application

Prescribing information. Arcutis Biotherapeutics, Inc; 2024.

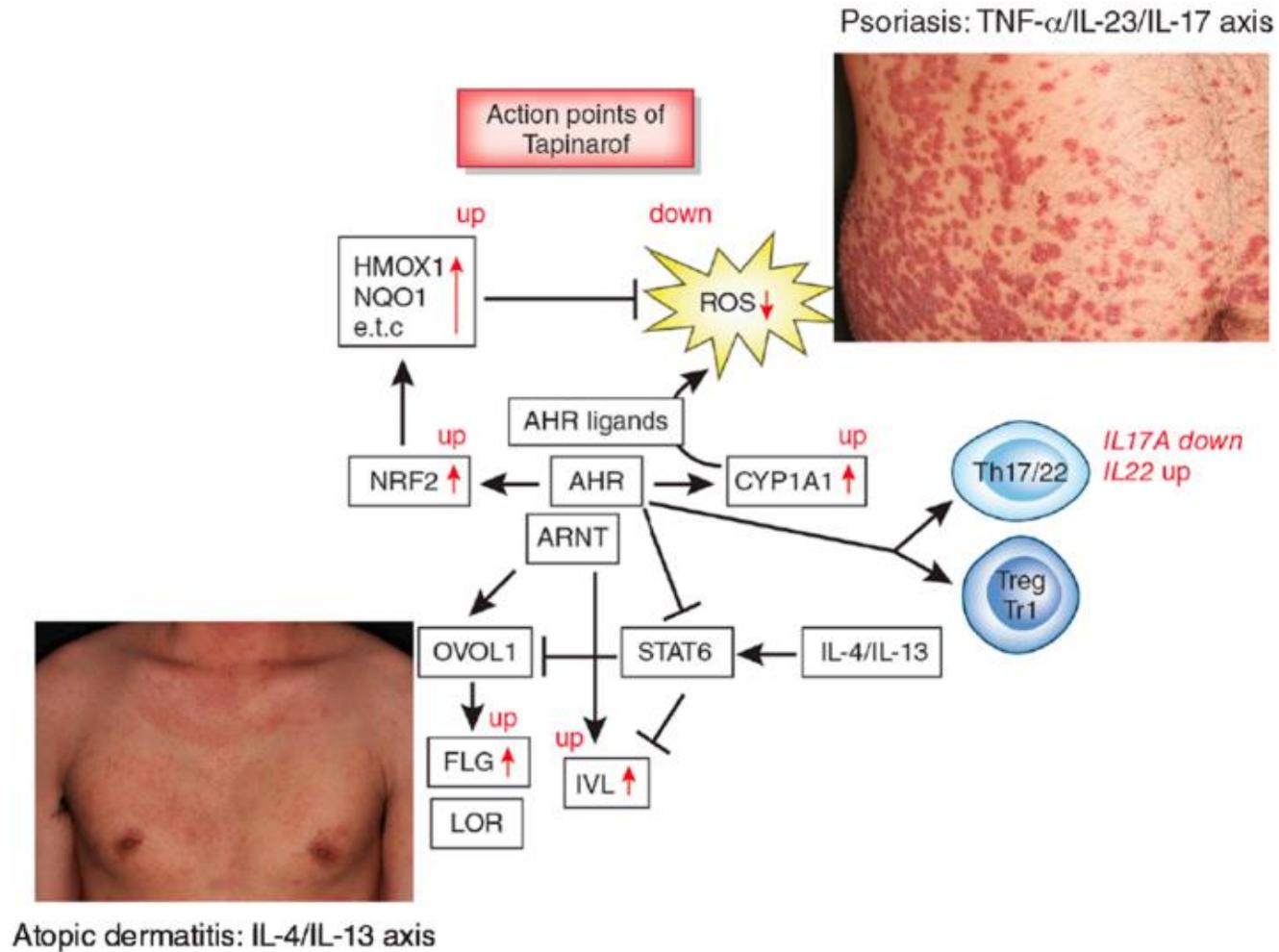
Bunick CG, et al. Poster presented at: Fall Clinical Dermatology Conference Meeting; October 19-22, 2023; Las Vegas, NV

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

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



Therapeutic Aryl Hydrocarbon Receptor Modulation in AD With Tapinarof Cream



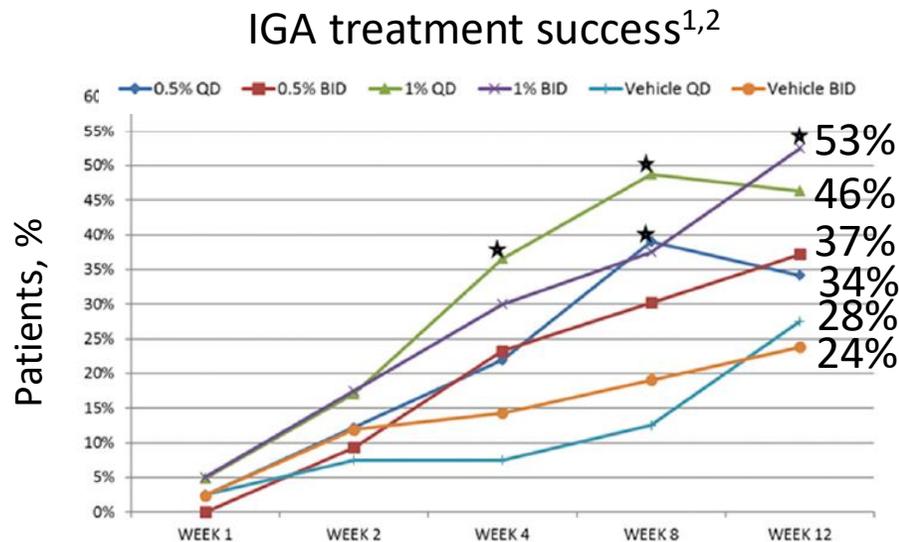
Approved by FDA for the treatment of plaque psoriasis in adults May 2022 and for adults and children down to age 2 years with AD in Dec 2024 (tapinarof 1% cream once daily)

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)



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

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.

Shared Decision Making: Updated **ESTAR**

Efficacy

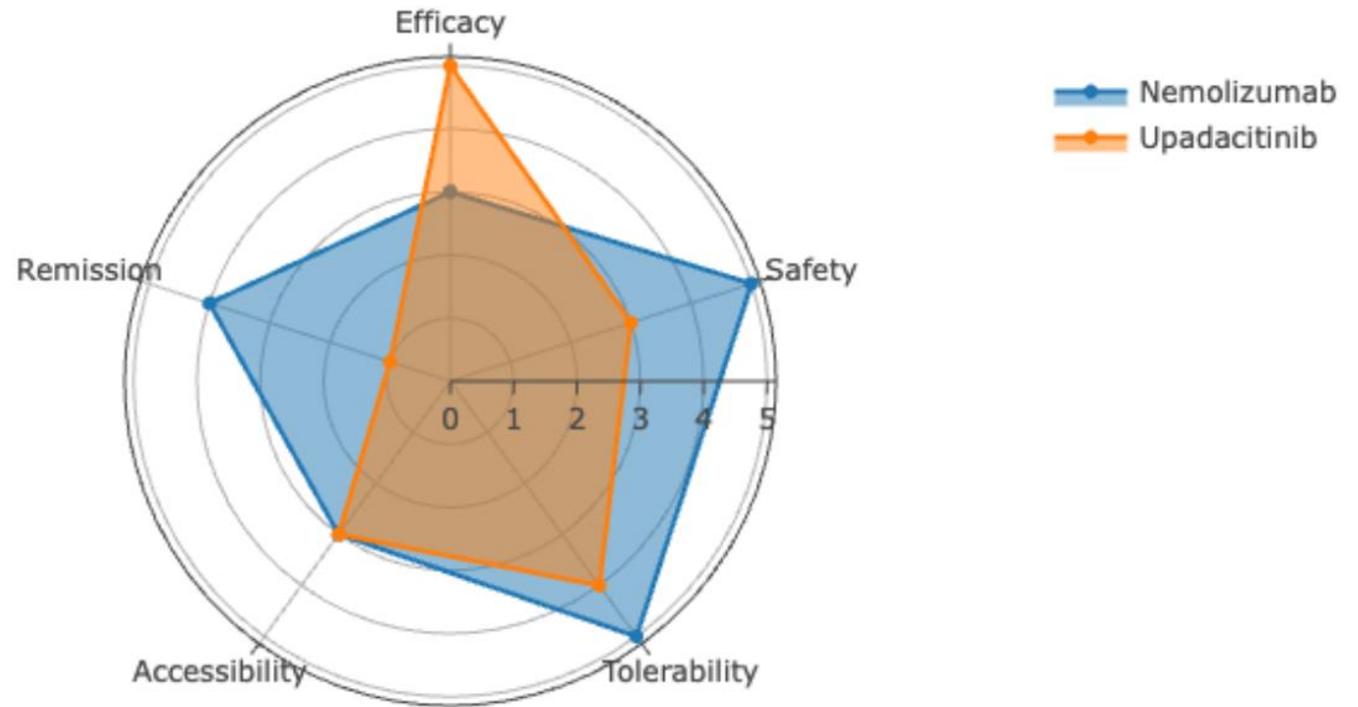
Safety

Tolerability

Accessibility

Remittive potential

Nemolizumab vs. Upadacitinib



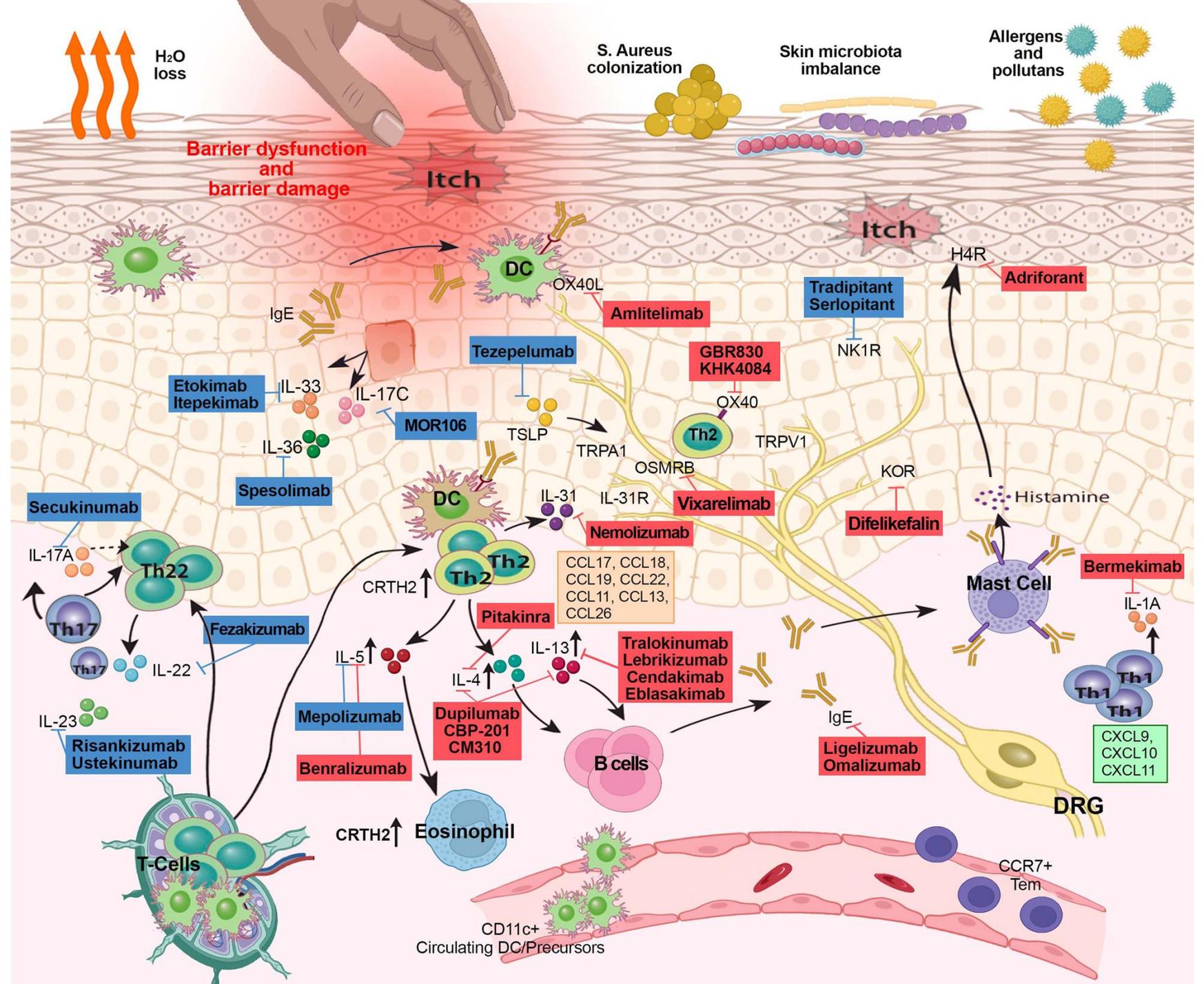
Radar Chart comparing nemolizumab (blue) and upadacitinib (orange).

**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.*

An M, Lio P. Reaching for the Stars in Atopic Dermatitis: Efficacy, Safety, Tolerability, Accessibility, and Remission/Remittive Effects (ESTAR). J Clin Aesthet Dermatol. 2025;18(11):16–20.

<https://jcadonline.com/reaching-for-the-stars-in-atopic-dermatitis-efficacy-safety-tolerability/>

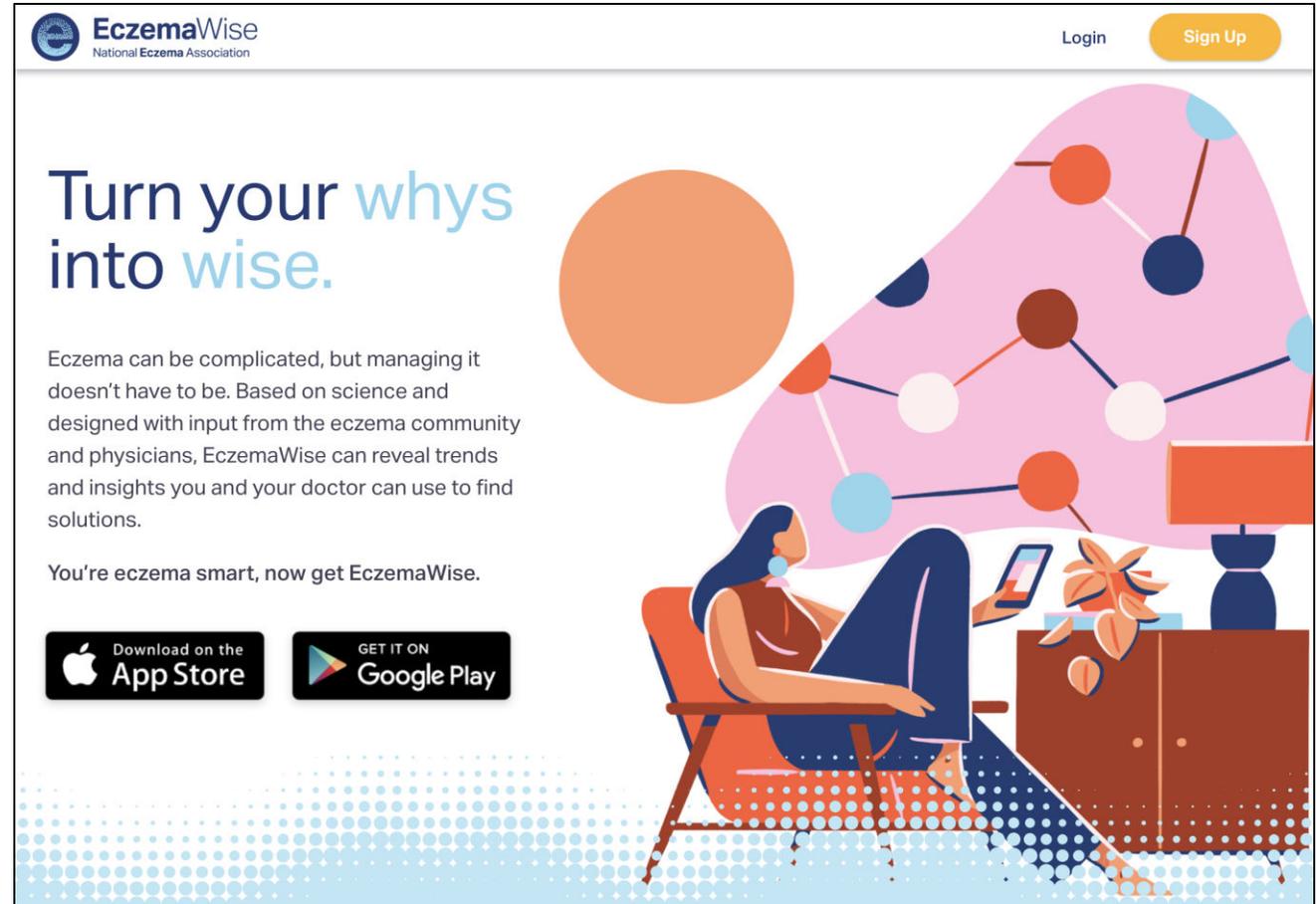
Pipeline . . .



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/>



EczemaWise
National Eczema Association

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Thank you!

