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Optimizing Management of Pediatric Atopic Dermatitis: Integrating Advanced Targeted Topicals into Patient-Centered Care

Peter Lio, MD, FAAD

Clinical Assistant Professor of Dermatology

Northwestern University Feinberg School of Medicine

Founding Director of the Chicago Integrative Eczema Center

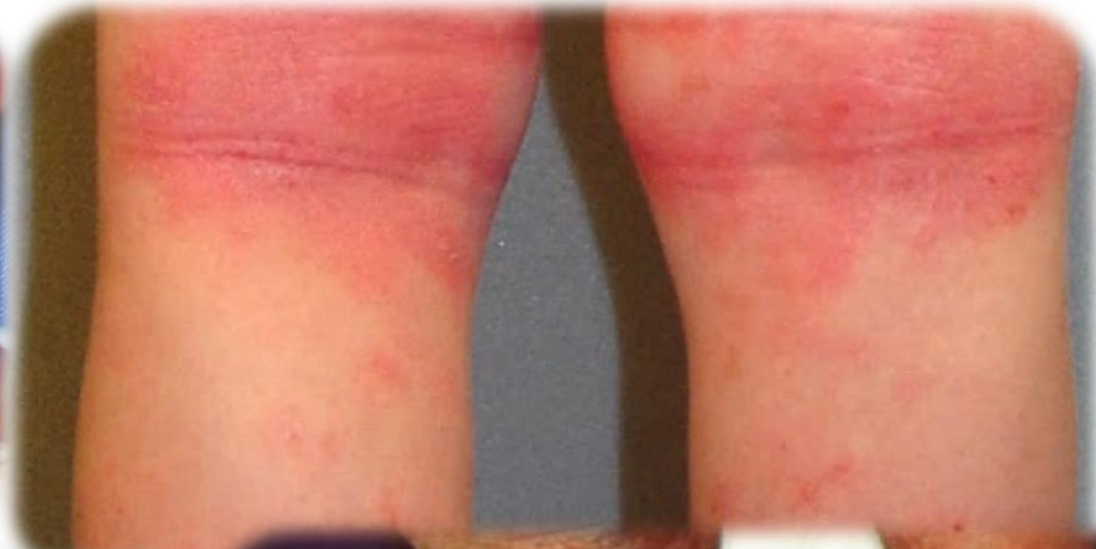
Disclosures

- **Peter Lio, MD, FAAD:** Speaker's bureau – 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 (pending); stock options – Codex Labs, Concerto Biosci, LearnSkin/Learn Health, Medable, Modernizing Medicine, Suneco Technologies, Yobee Care, Verdant Scientific

Learning Objectives

- Apply current guideline-directed and evidence-based strategies to improve the recognition, diagnosis, and assessment of pediatric AD across diverse patient populations
- Evaluate the safety, efficacy, indications, and appropriate clinical use of newer nonsteroidal topical therapies for pediatric AD
- Employ individualized, patient-centered management for pediatric AD that incorporates shared decision-making with patients/caregivers and addresses diverse skin types and patient populations

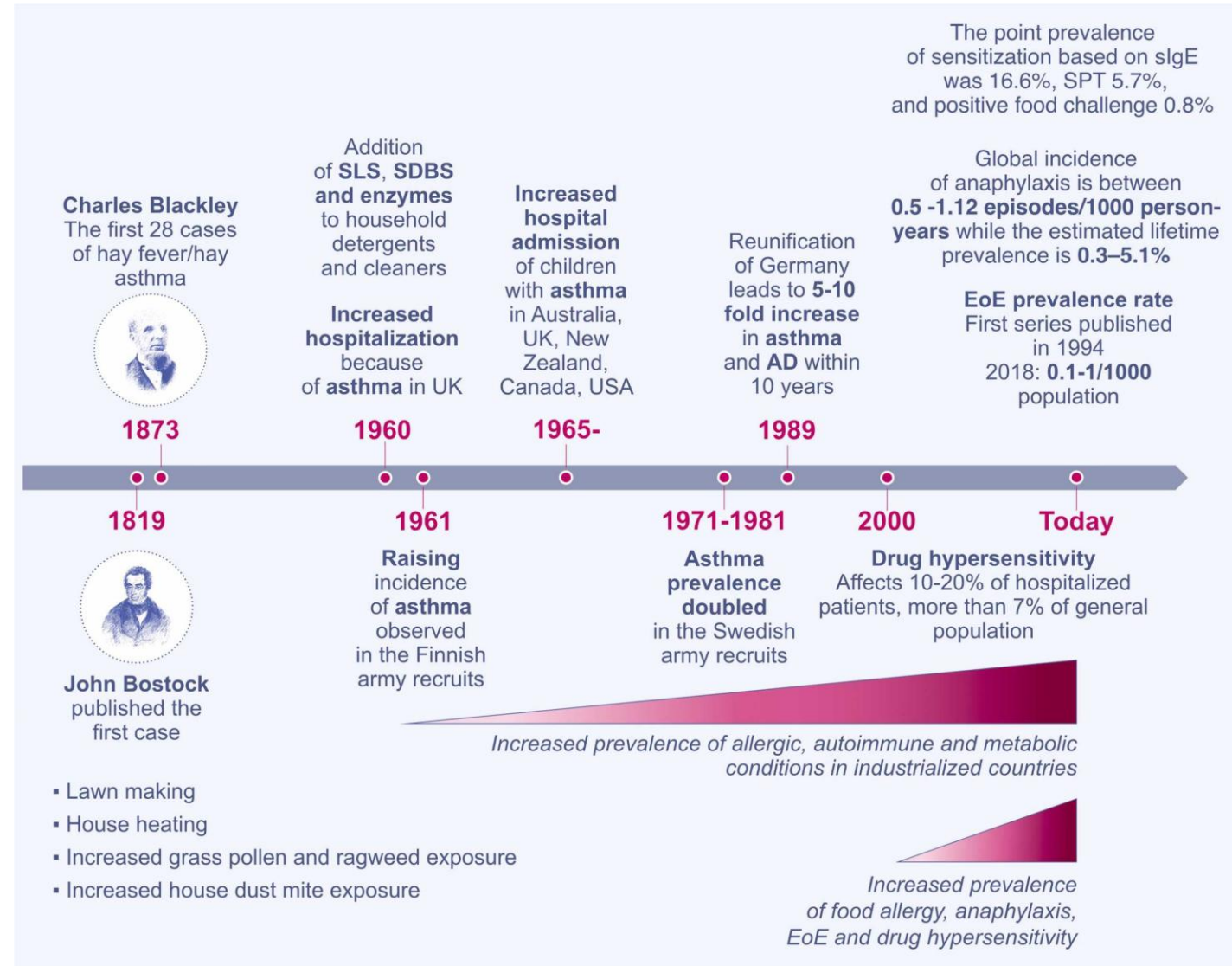
A Heterogeneous Disease



Prevalence of AD

- Children
 - 10% to 12% prevalence in the US
 - Higher rates in Black children (15.9%) compared with White children (9.7%)
 - Black children 6 times more likely to have persistent AD compared with White children
- Adults
 - 7% of adults in the US have AD
 - Black adults have lower rates of AD (5.1%) compared with White adults (6.2%)

The Rise of Allergy



AAD 2014 Guidelines: Diagnostic Criteria

Essential Features	Important Features	Associated Features
Must be present in AD diagnosis	Adds support to diagnosis, observed in most patients	Suggestive of AD but too non-specific to be used for diagnosis
• Pruritus • Eczema – Chronic or relapsing pattern – Typical morphology and age-specific patterns ○ Facial, neck, and extensor involvement in infants and children ○ Current or previous flexural lesions in any age group ○ Sparing of the groin and axillary regions	• Early age of onset • Atopy • Personal and/or family history • IgE reactivity • Xerosis	• Atypical vascular responses – eg. Facial pallor, white dermographism, delayed blanch response • Keratosis pilaris/pityriasis alba/hyperlinear palms/ichthyosis • Ocular/periorbital changes • Other regional finding – Perioral changes/periauricular lesions • Perifollicular accentuation/lichenification/prurigo lesions



NB: In darker skin tones, erythema may appear violaceous, gray, brown, or less conspicuous; attention to morphology, pruritus, texture, and pigmentary change can help avoid under-recognition of AD

Atopic Dermatitis Spectrum

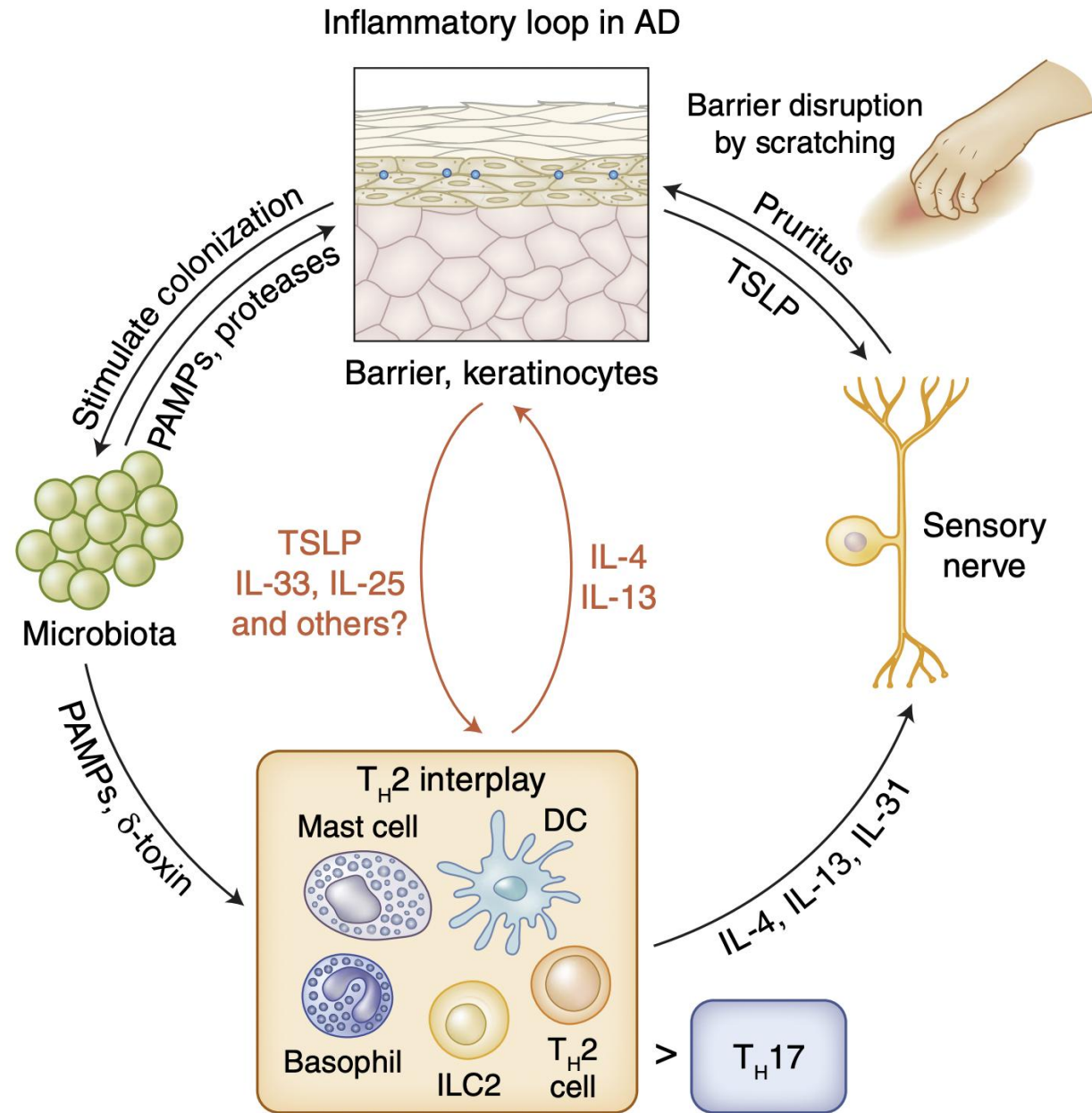
- Conditions included in AD spectrum^a
 - Chronic hand eczema (excluding contact dermatitis)
 - Nummular eczema
 - Follicular eczema
 - Lichenoid eczema
 - Dyshidrosis
 - Prurigo nodularis
 - Lichen simplex chronicus
 - Nipple eczema
 - Asteatotic eczema
 - Gestational eczema
 - Eczema of older adults or atopic dermatitis of the elderly (excluding mycosis fungoides)
 - Eyelid dermatitis (excluding contact dermatitis)

^aList is not comprehensive and may include other conditions.
Butler DC, et al. *J Dermatolog Treat.* 2022;33(4):2397-2399.

DDx of Eczematous Dermatoses

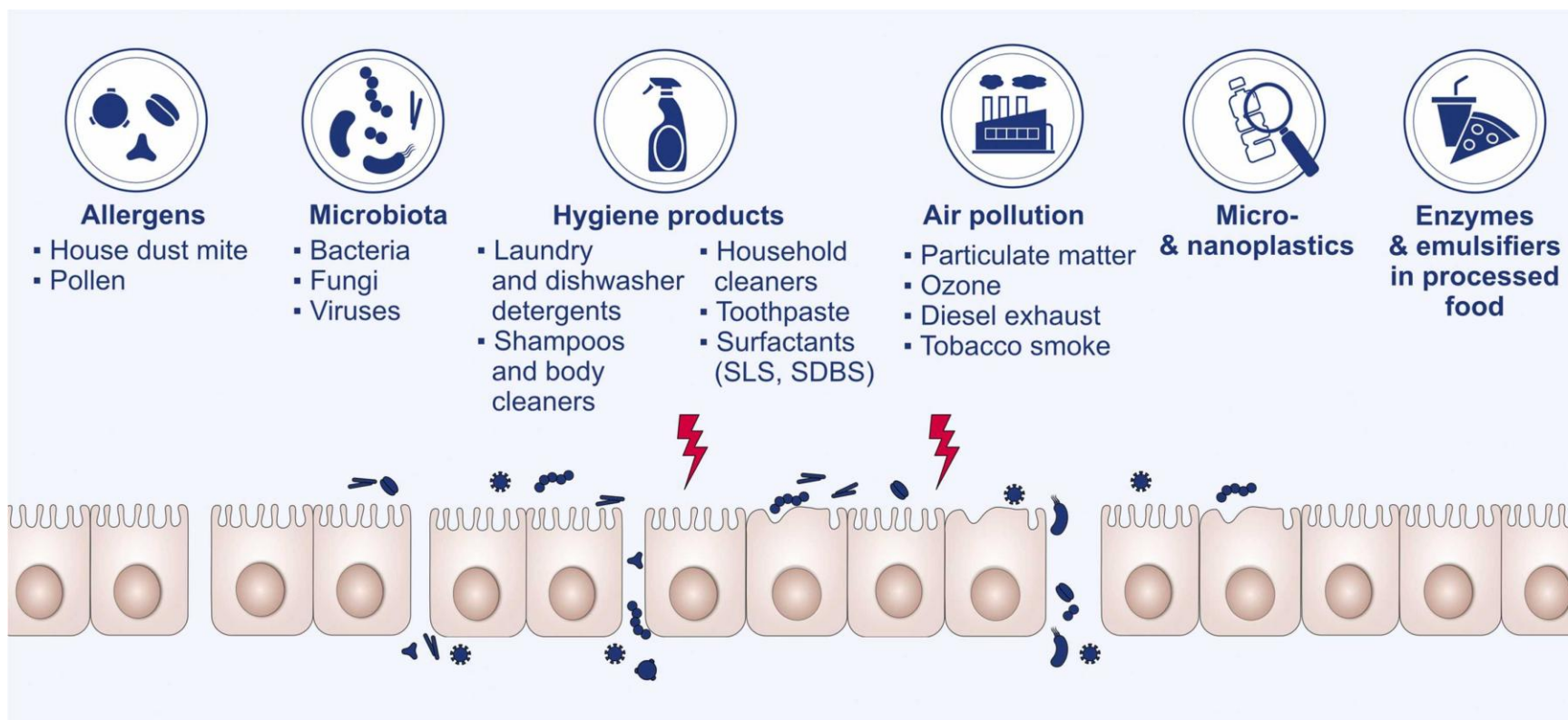
- Scabies
- Seborrheic dermatitis
- Contact dermatitis (irritant or allergic)
- Ichthyoses
- Cutaneous T-cell lymphoma
- Psoriasis
- Photosensitivity dermatoses
- Immune deficiency diseases
- Erythroderma of other causes

Loop



Epithelial Barrier Hypothesis

- Industrialization, urbanization, and Westernized lifestyles have a devastating impact on the epithelial barriers of the skin, airways, and gut mucosa as proposed by the epithelial barrier theory



Staph

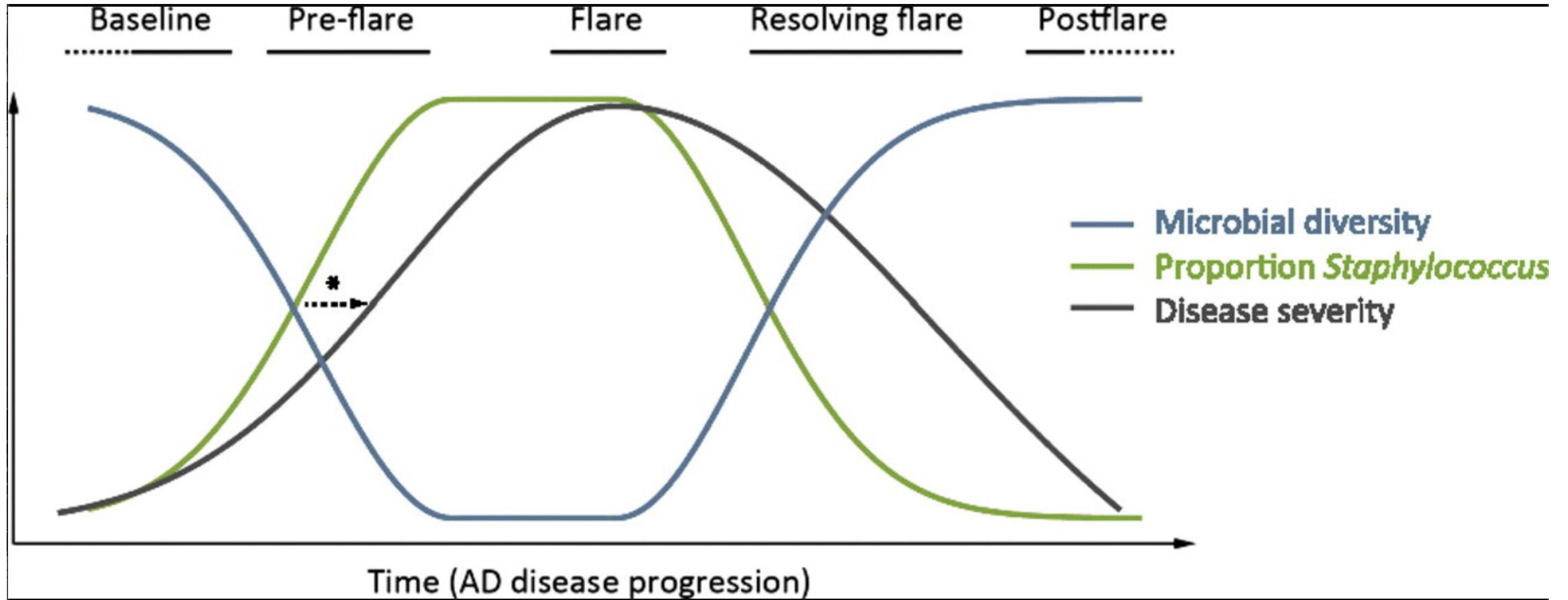


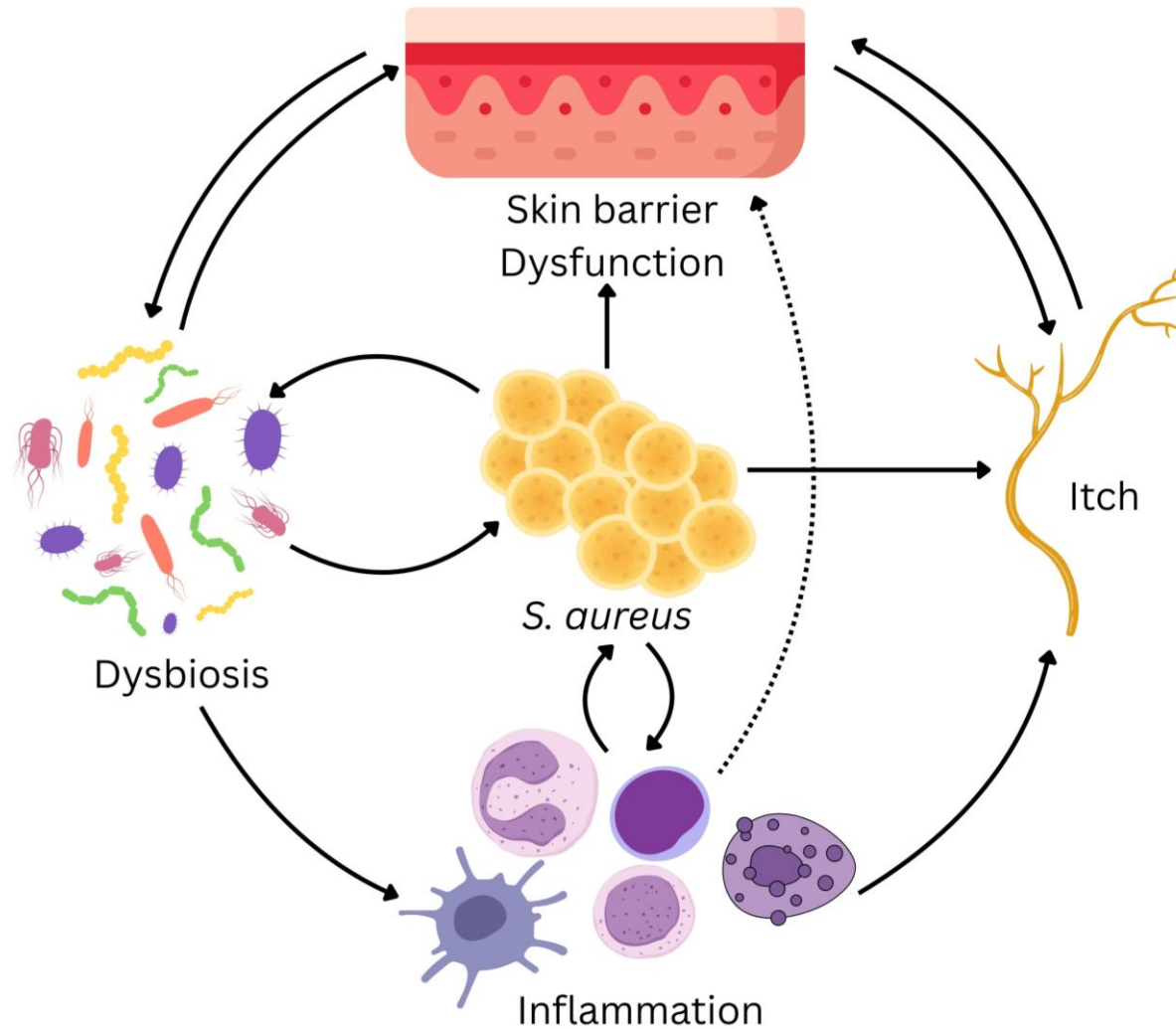
Table 1. *Staphylococcus aureus* Proteins That Contribute to Atopic Dermatitis

<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?

TSST = toxic shock syndrome toxin.

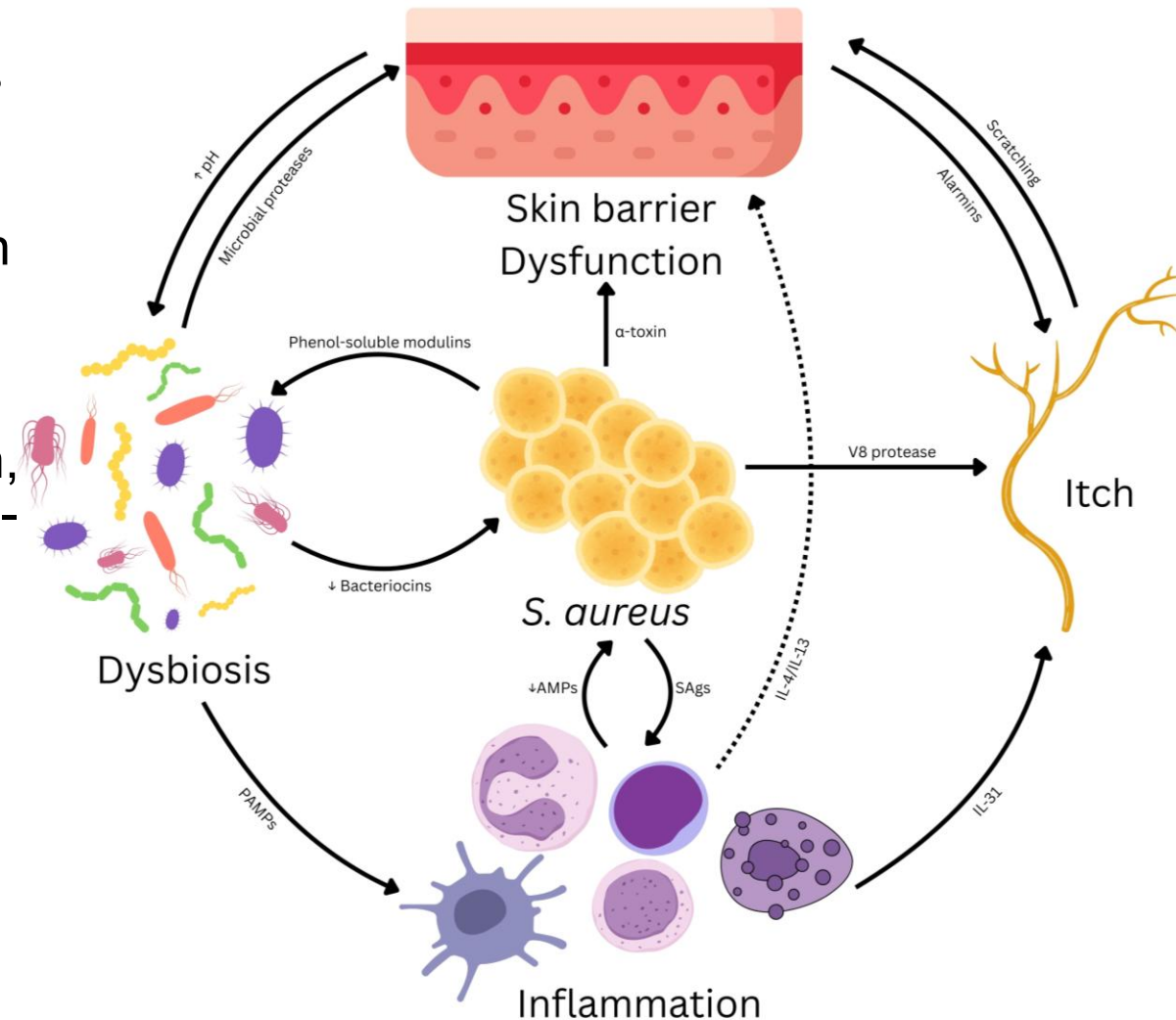
Geoghegan JA, et al. *Trends Microbiol.* 2018;26(6):484-497.

S. aureus-Driven Amplification Loops



S. aureus-Driven Amplification Loops

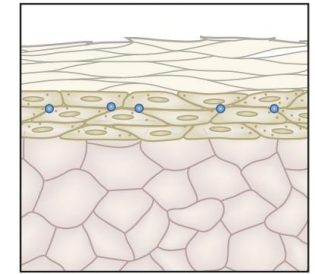
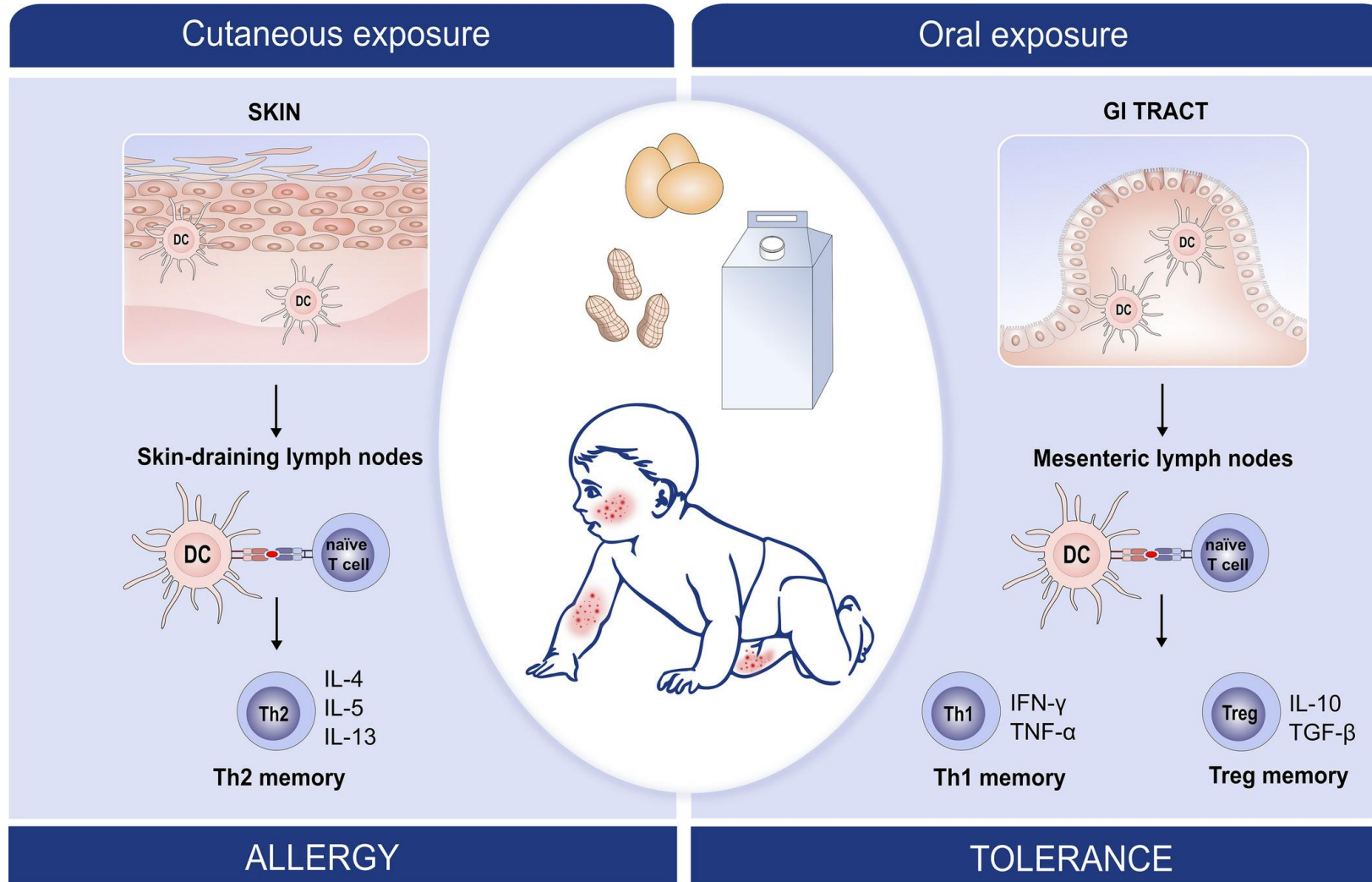
- Arrows indicate proposed directional influences among skin barrier dysfunction, dysbiosis, *S. aureus*, inflammation, and itch
- Example mediators are shown adjacent to each connection (illustrative, not exhaustive): *S. aureus* virulence factors (eg. α -toxin; V8 protease; phenol-soluble modulins; superantigens) can promote barrier dysfunction, itch, and inflammation; type 2 cytokines (IL-4/IL-13) can worsen barrier dysfunction and reduce antimicrobial defenses (vAMPs), facilitating *S. aureus* persistence; itch and scratching further exacerbate barrier disruption; and microbial products (PAMPs) may contribute to inflammation



AMP = antimicrobial peptide; PAMP = pathogen-associated molecular patterns; PSM = phenol-soluble modulin; SAg = superantigen.

Chen H, et al. *Toxins (Basel)*. 2022;14(7):464.

Epicutaneous Sensitization



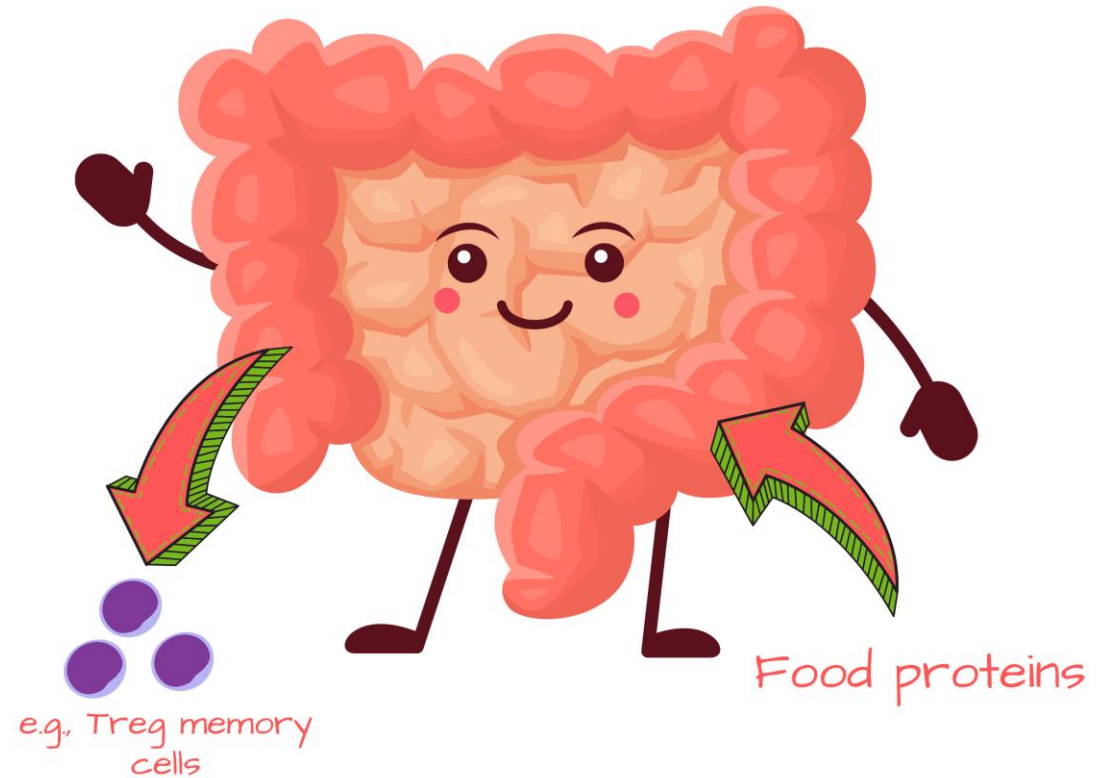
Barrier, keratinocytes

Through the skin,
allergies begin.



Allergens, irritants, pathogens

Through the diet,
allergies stay quiet.

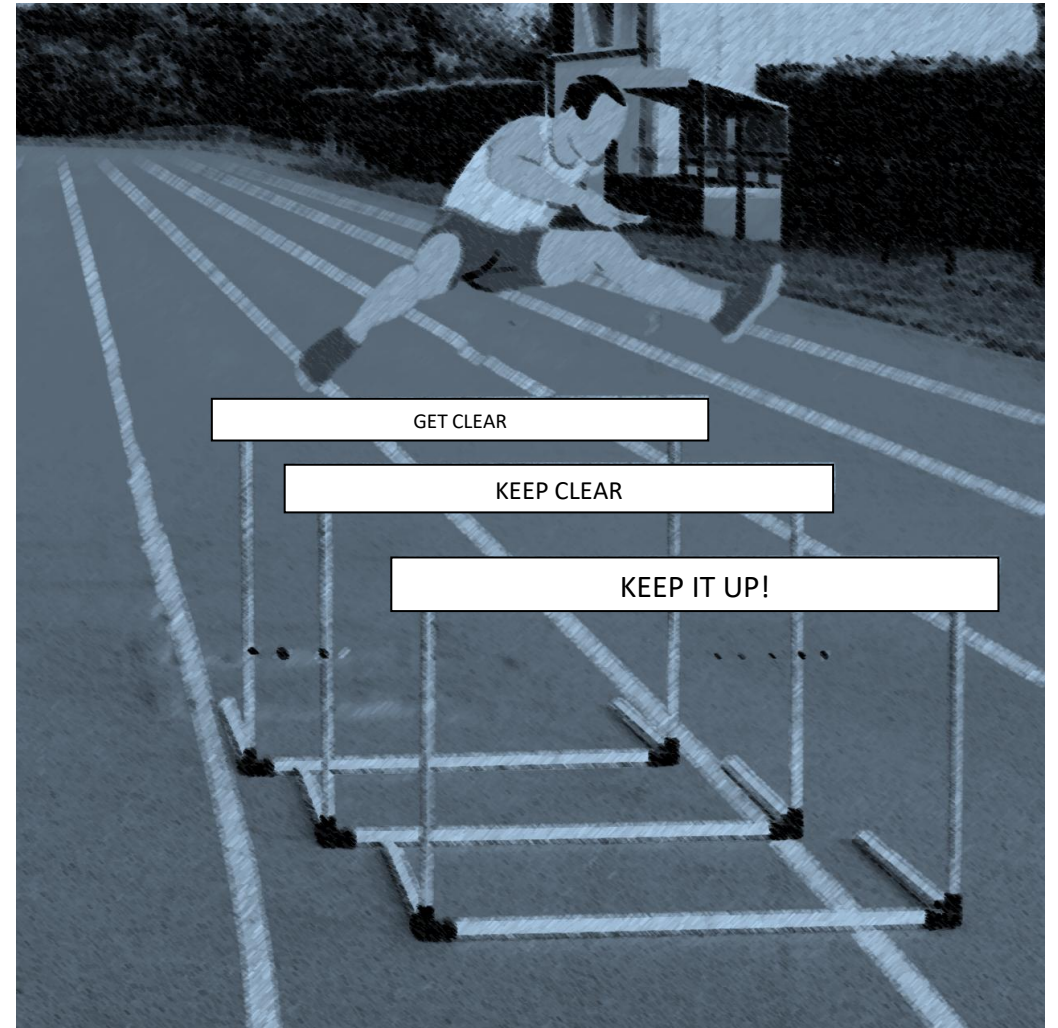


e.g., Treg memory
cells

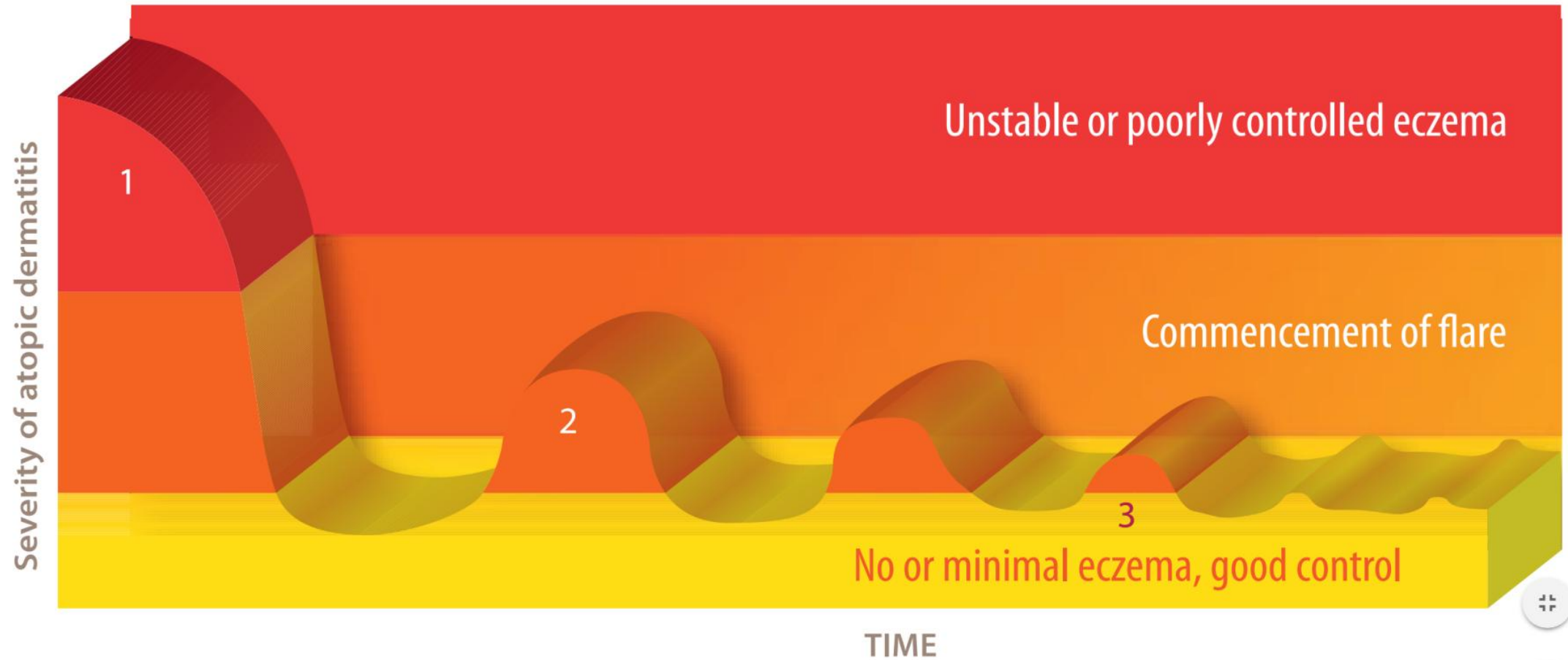
Food proteins

Goals

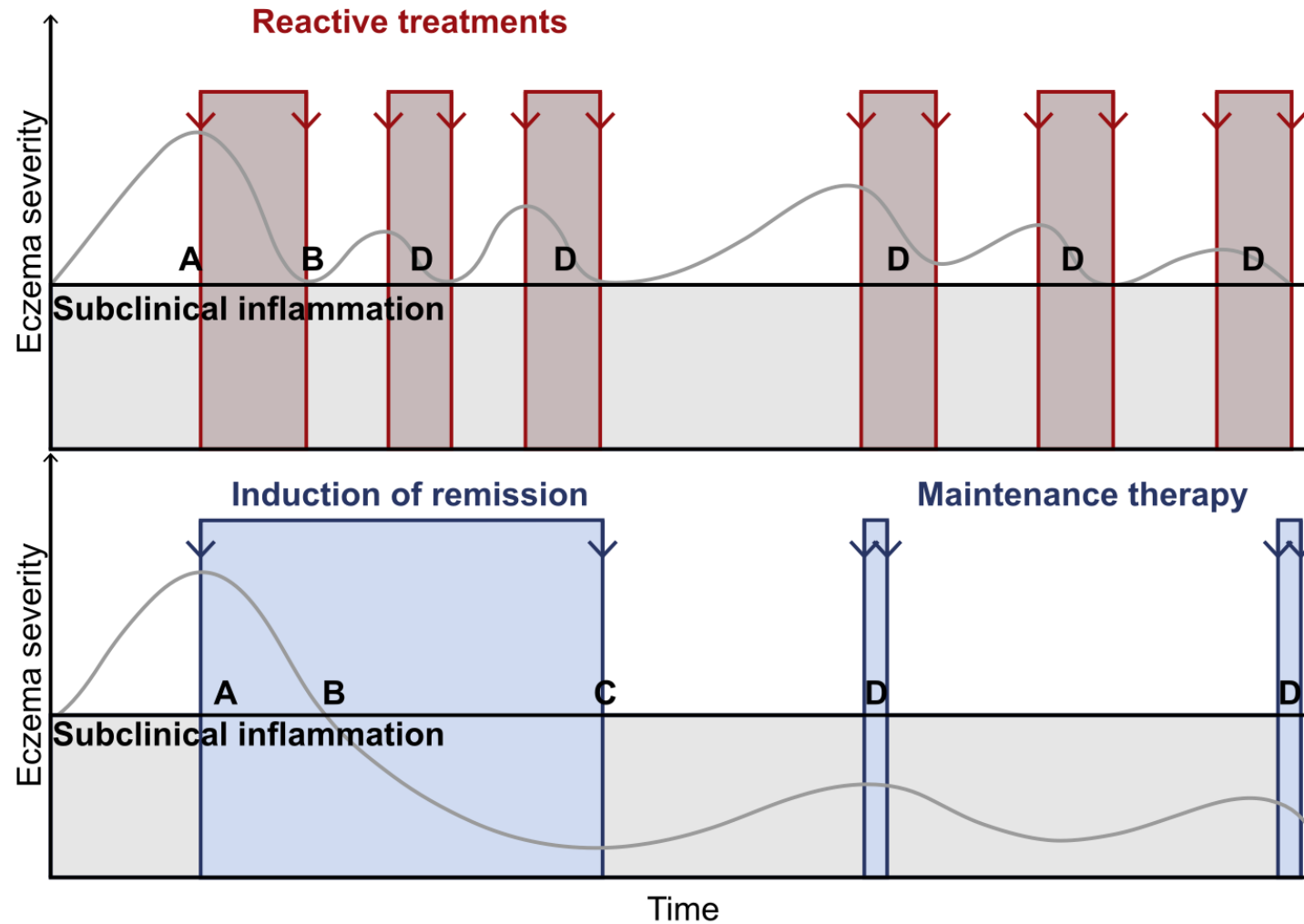
1. Get clear
2. Keep clear – safely
3. Keep it up



Treatment Goal

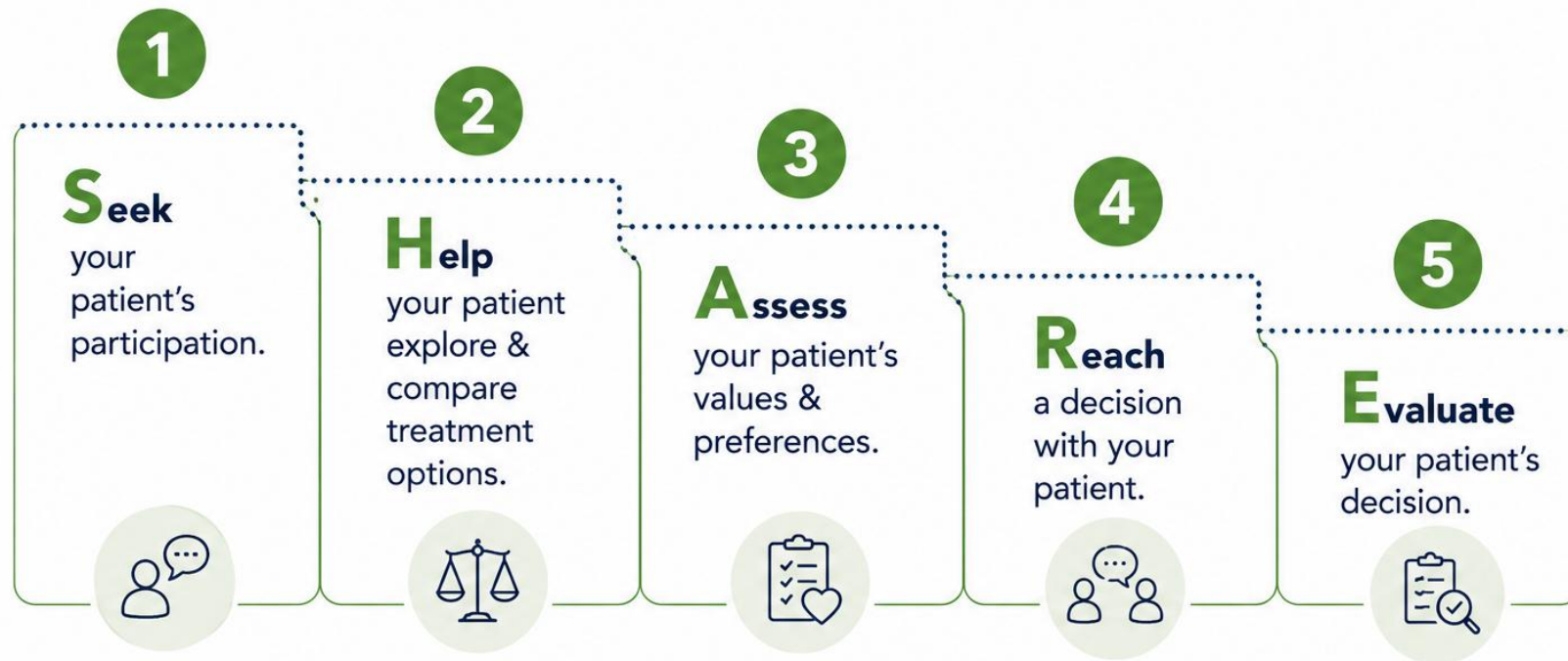


Joint Task Force Guidelines



The **SHARE** Approach

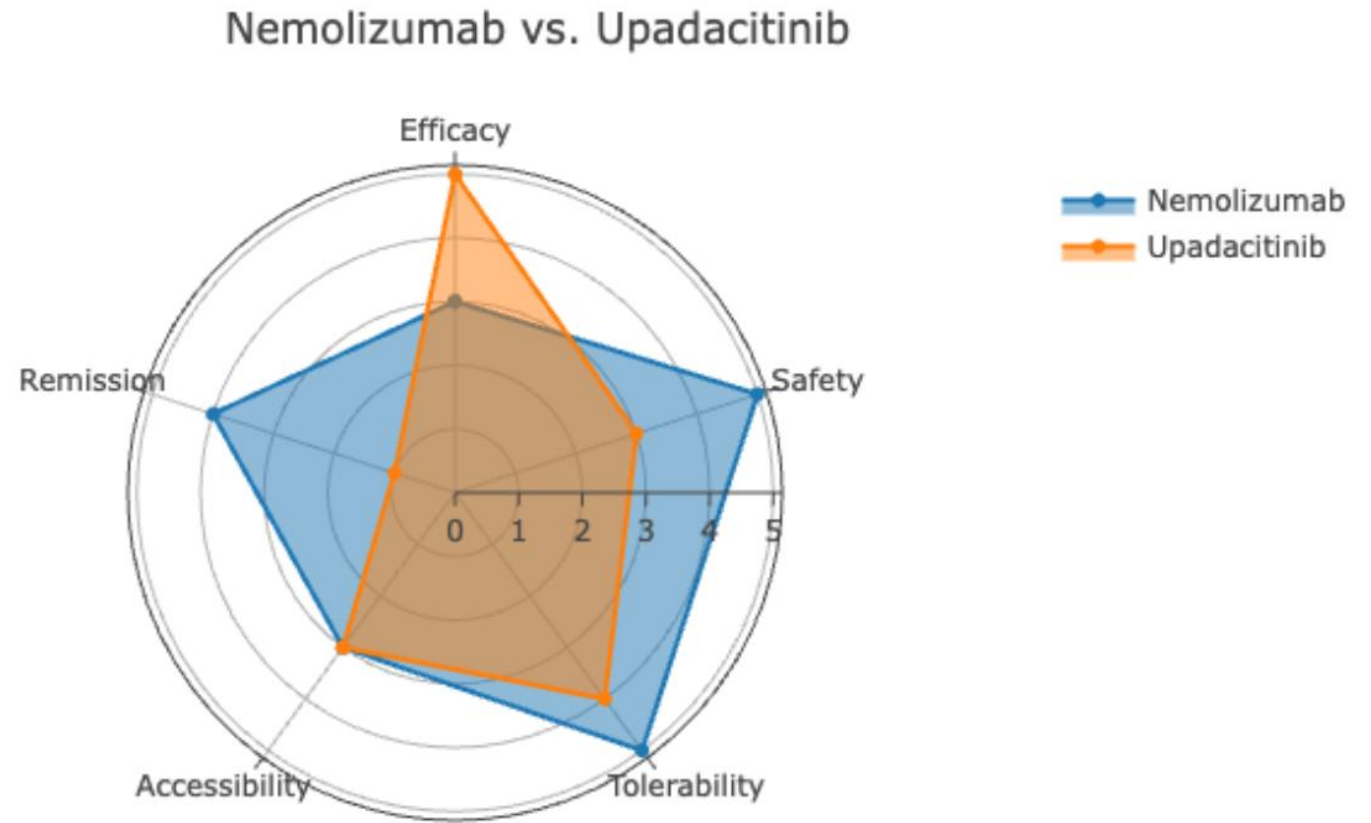
5 Essential Steps of Shared Decision Making



Shared decision making supports patient-centered care by aligning treatment choices with clinical evidence, patient values, and individual circumstances.

Shared Decision Making: Updated **ESTAR**

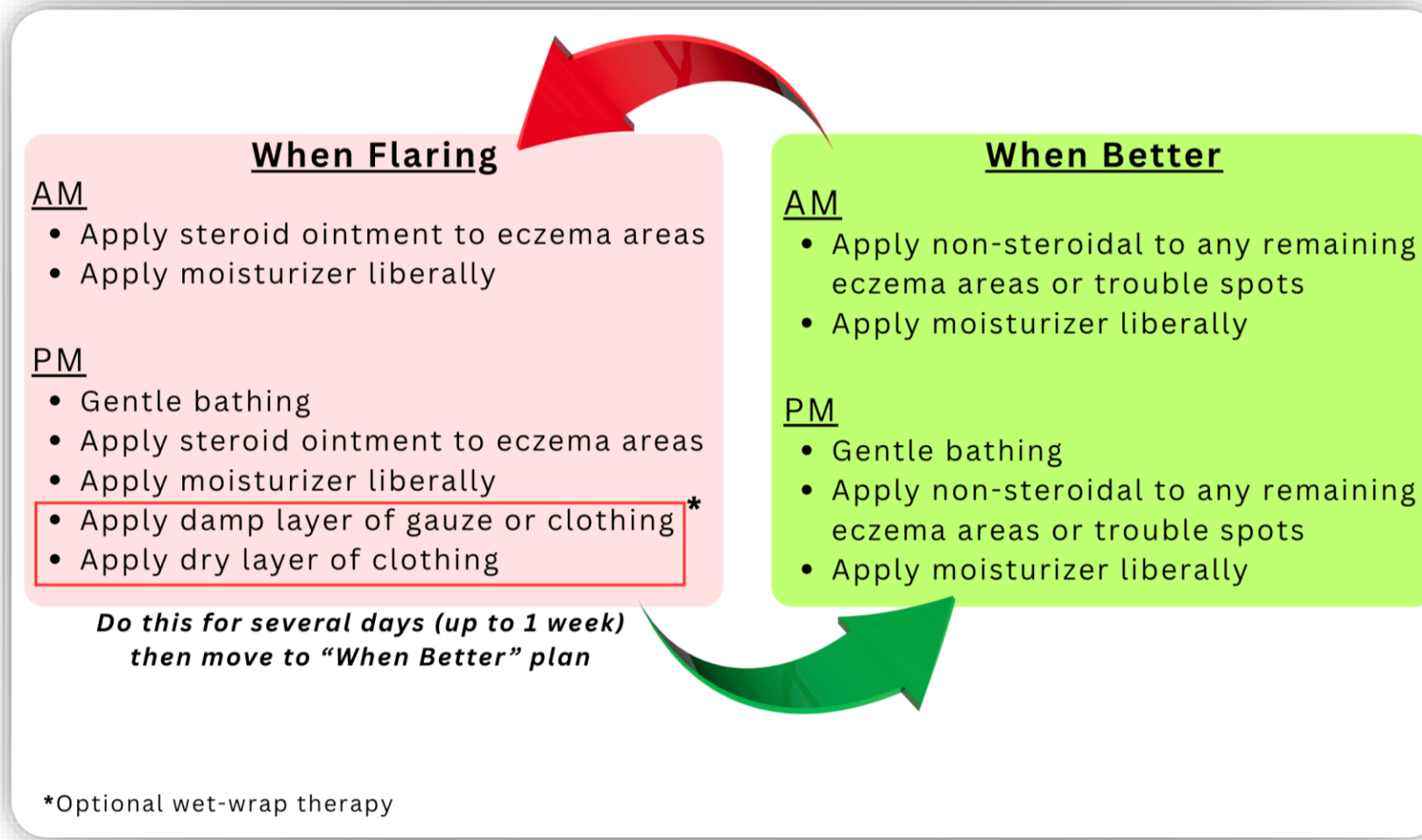
- **Efficacy**
- **Safety**
- **Tolerability**
- **Accessibility**
- **Remittive potential**



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.

An M, Lio P. *J Clin Aesthet Dermatol*. 2025;18(11):16-20.

Eczema Action Plan Template



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: _____

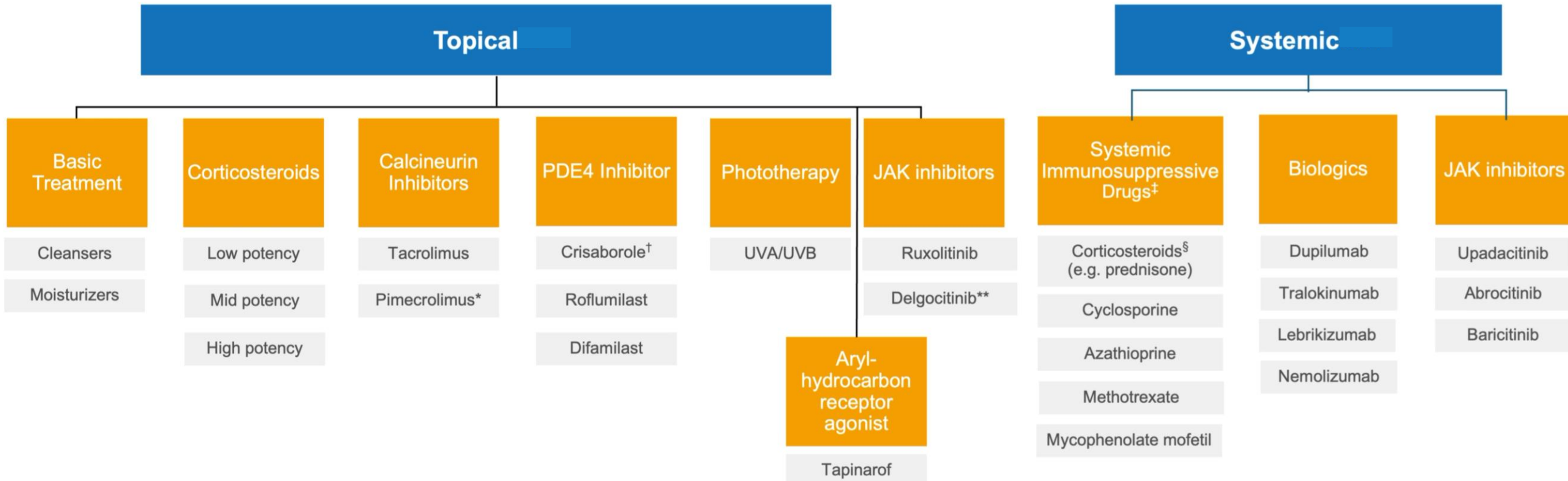
MOISTURIZER: _____

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.

Treatment Landscape

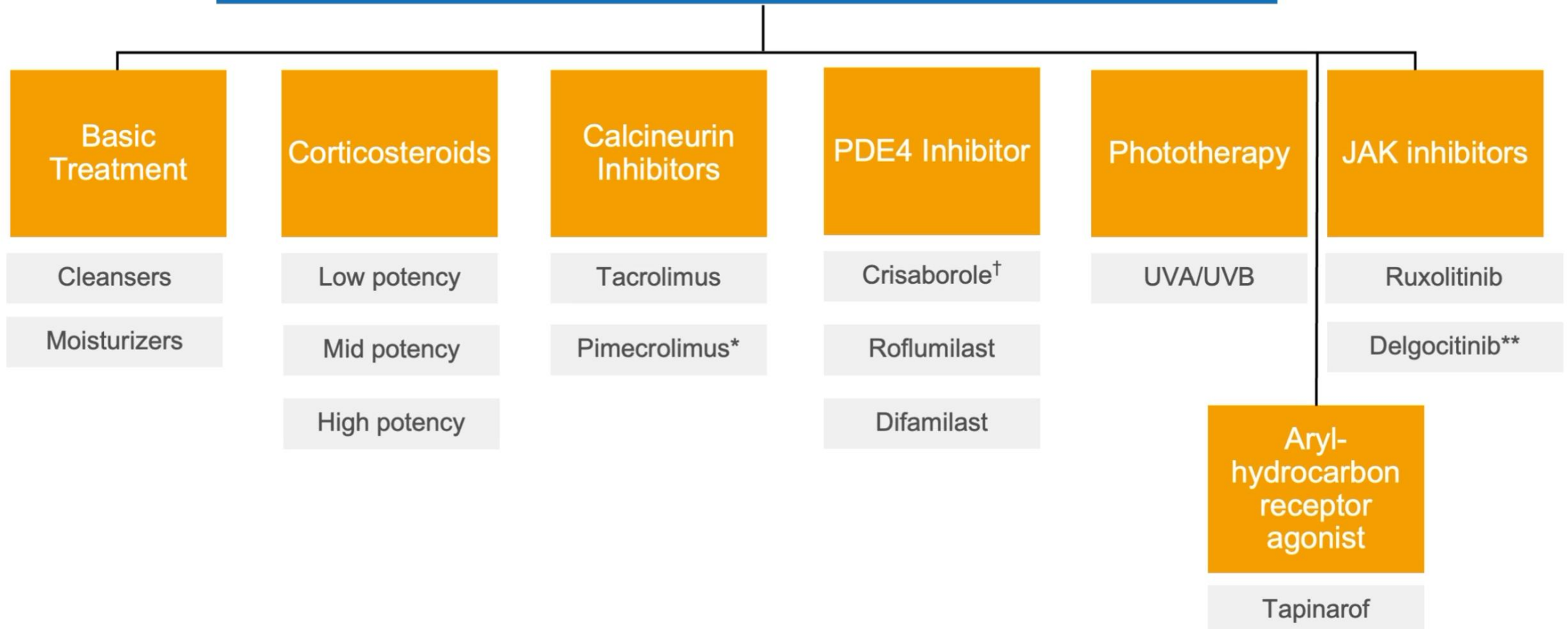


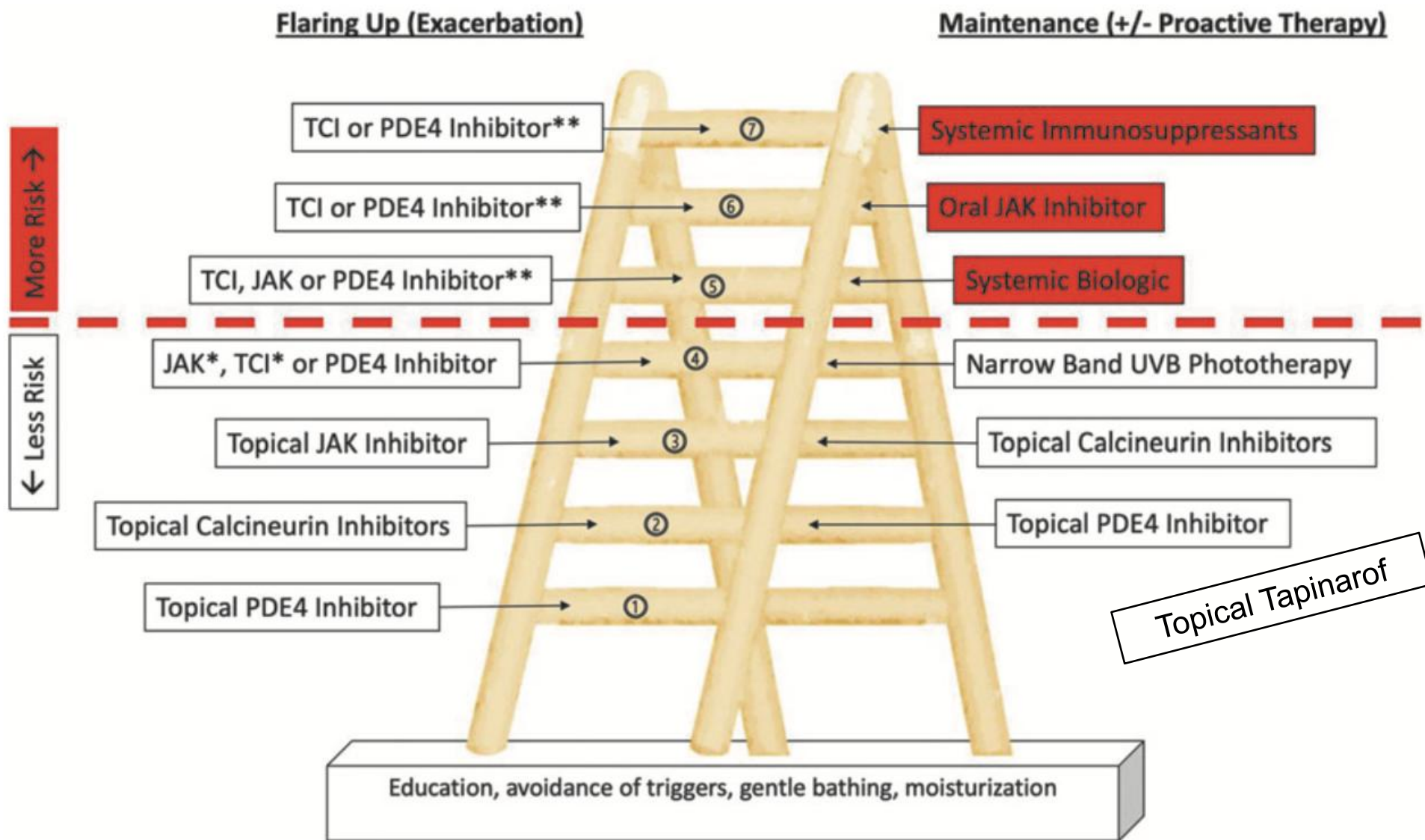
*Pimecrolimus is recommended by EADV and AAD, but not by JDA; **Delgocitinib is approved for chronic hand eczema only; [†]In 2016, the FDA approved crisaborole for the topical treatment of mild-to-moderate AD in patients aged ≥3 months; [‡]Cyclosporine is the only approved systemic immunosuppressive drug for AD (approved in most European countries and Japan). Off-label use of cyclosporine is recommended by AAD. Off-label use of azathioprine, methotrexate, and mycophenolate mofetil is recommended by AAD and EADV. ^{\$}Treatment guidelines recommend oral/injectable corticosteroids for the short-term treatment of acute flare in patients with severe AD.

FDA = Food and Drug Administration; PDE4 = phosphodiesterase 4; UV = ultraviolet; JAK = Janus kinase; EADV = European Academy of Dermatology and Venereology; JAD = Japanese Dermatological Association.

Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;71:116-132. Ring J, et al. *J Eur Acad Dermatol Venereol*. 2012;26:1045-1060. Saeki H, et al. *J Dermatol*. 2016;43:1117-1145. Sidbury R, et al. *J Am Acad Dermatol*. 2014;71:327-349. Ring J, et al. *J Eur Acad Dermatol Venereol*. 2012;26:1176-1193. Bieber T, Straeter B. *Allergy*. 2015;70:6-11. Gooderham M, et al. *J Cutan Med Surg*. 2017;21(1):31-39. FDA. Accessed August 12, 2026. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm533371.htm>.

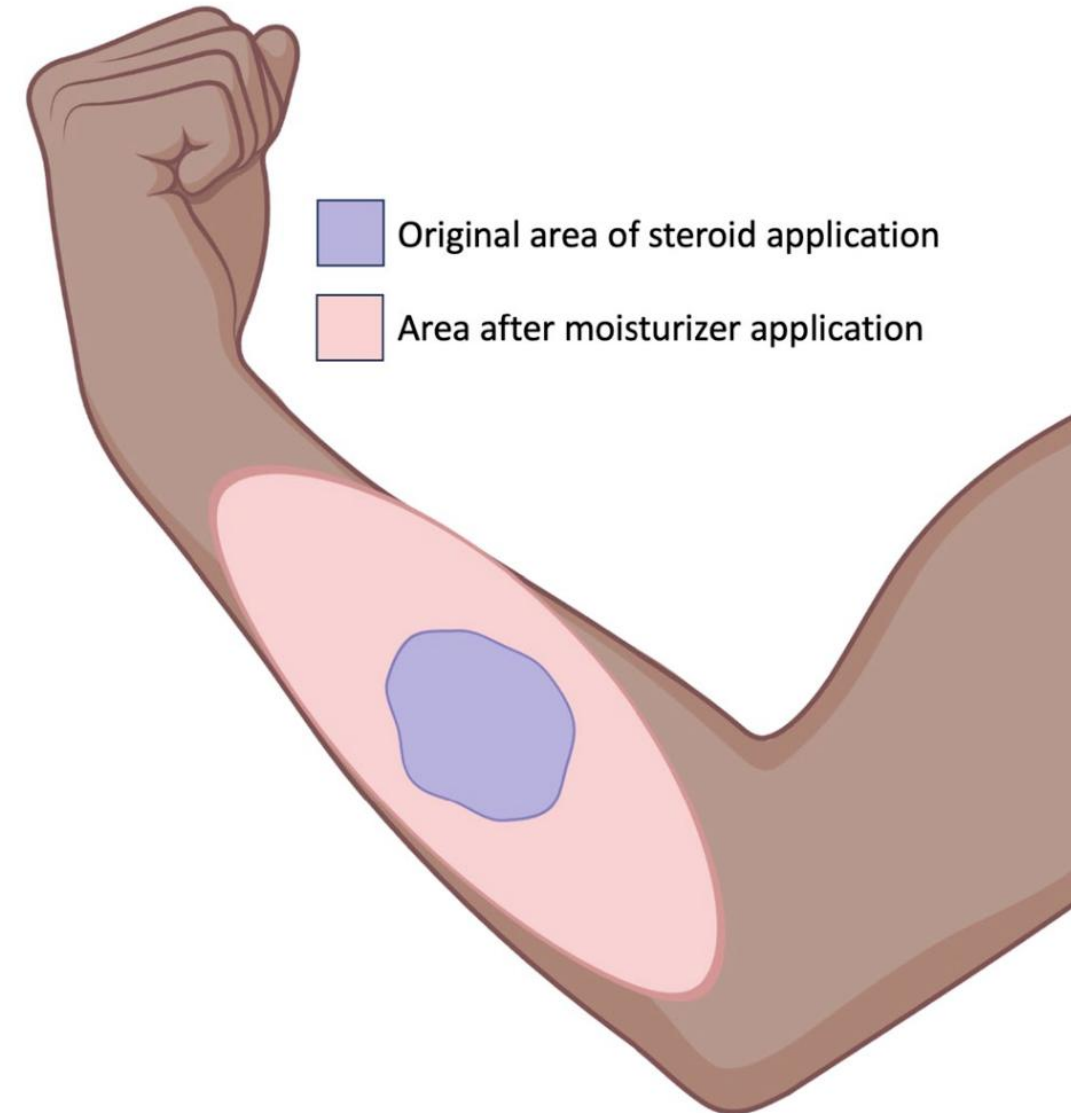
Topical





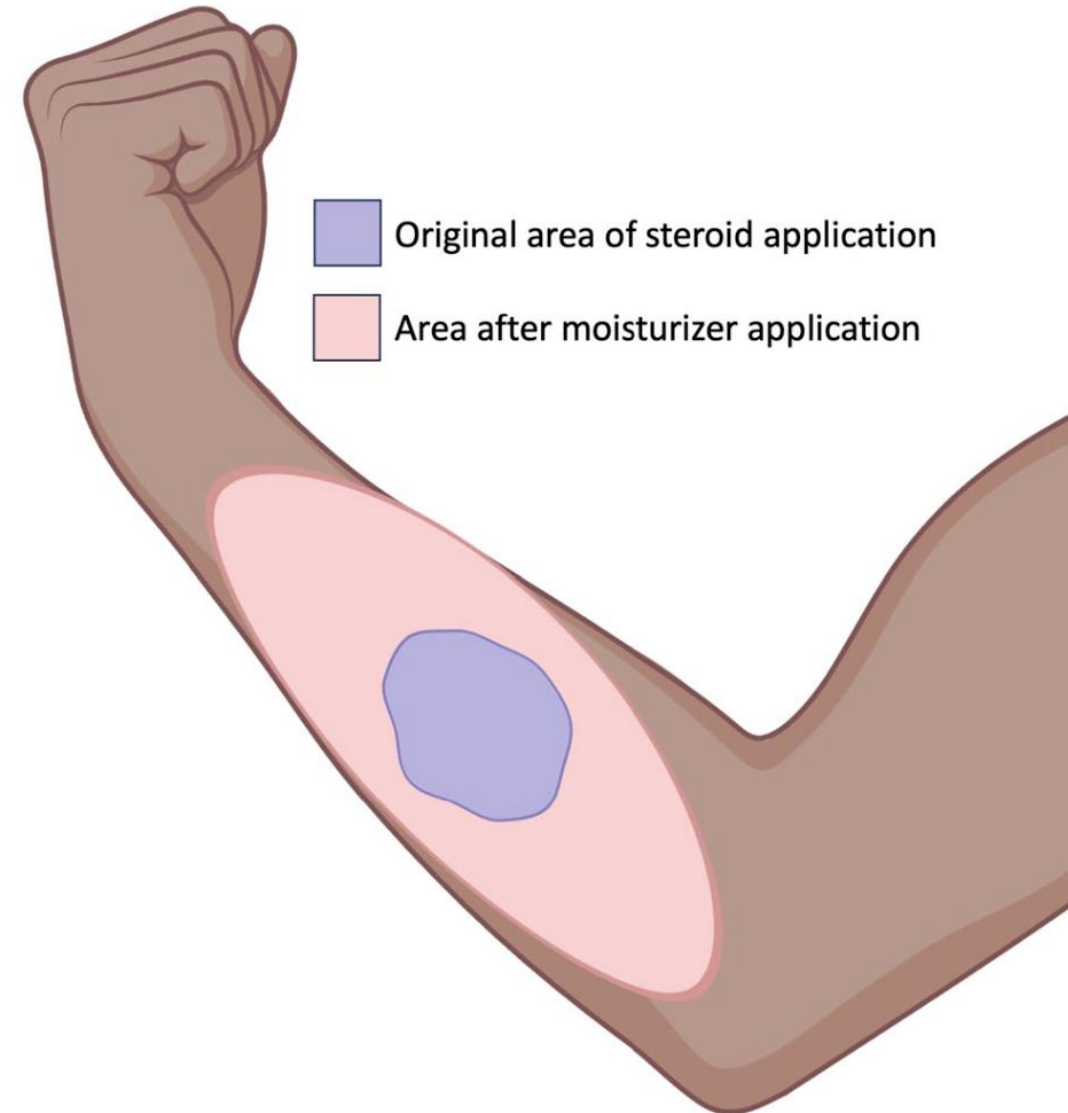
Order of Topicals

- 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



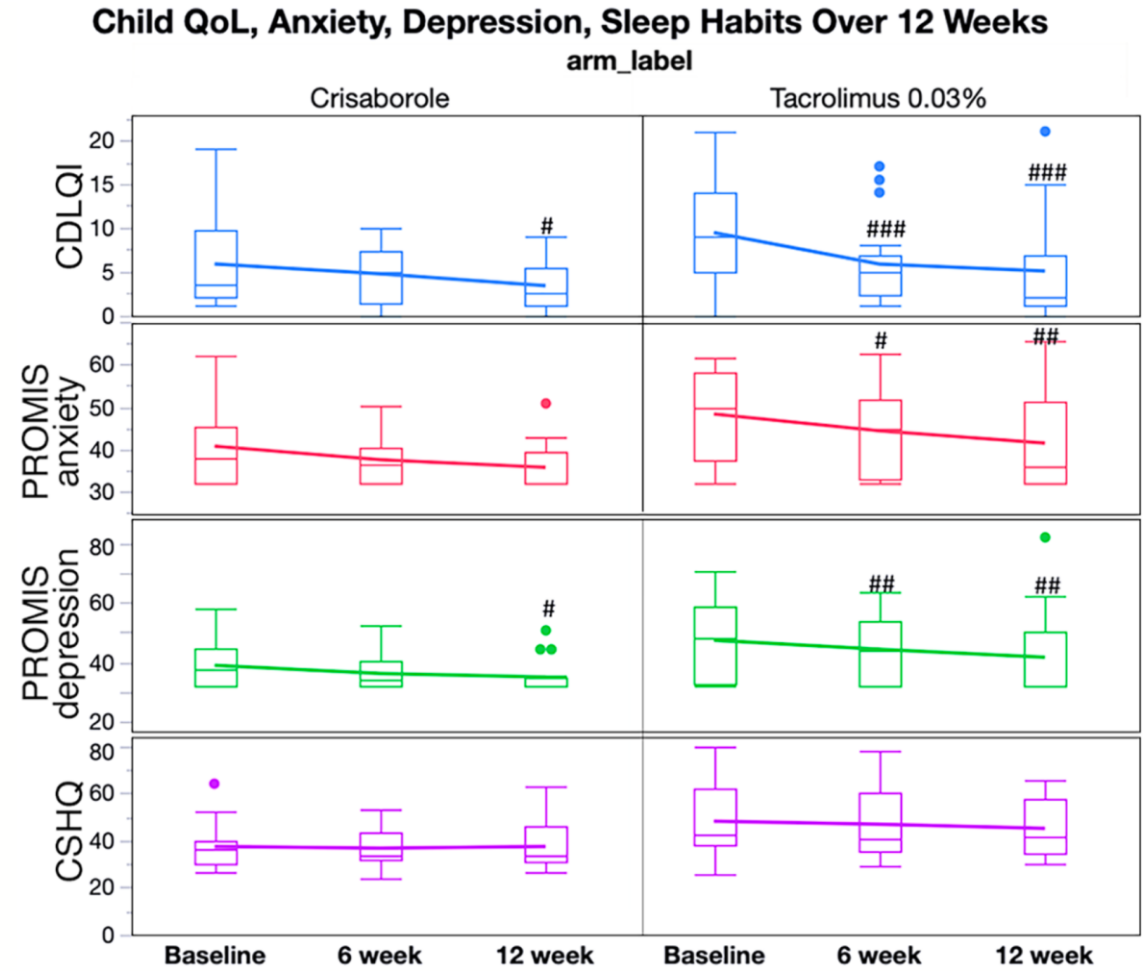
Order of Topicals

- "...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"

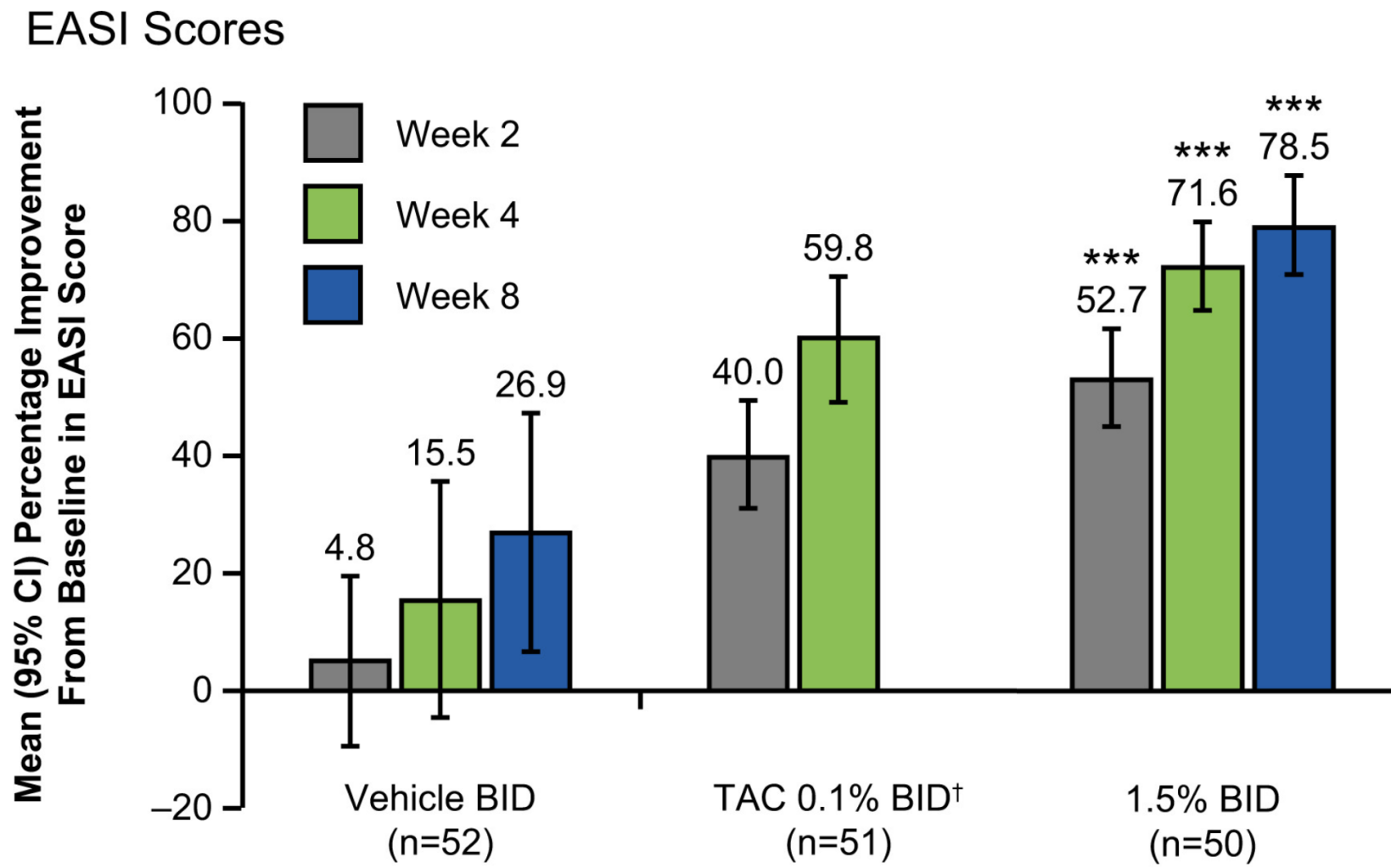


Tacrolimus vs Crisaborole

- 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”



Treatment of AD with Ruxolitinib Cream or Triamcinolone Cream



EASI = Eczema Area and Severity Index.
Kim BS, et al. *J Allergy Clin Immunol.* 2020;145(2):572-582.

Ruxolitinib Safety

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.

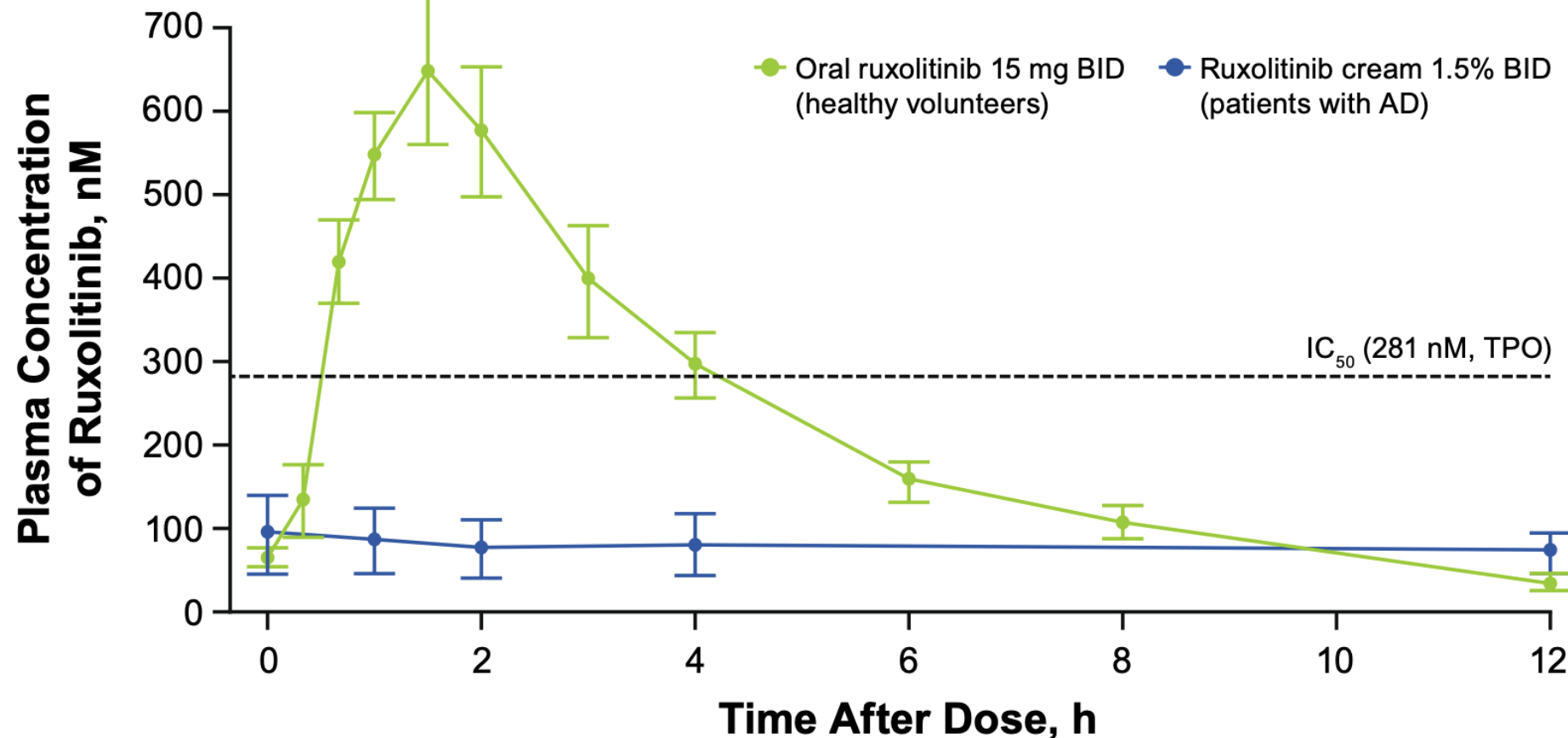
- The most common adverse reactions (incidence $\geq 1\%$) are nasopharyngitis, diarrhea, bronchitis, ear infection, eosinophil count increased, urticaria, folliculitis, tonsillitis, and rhinorrhea. (6)

MACE = major adverse cardiovascular events; CBC = complete blood count.

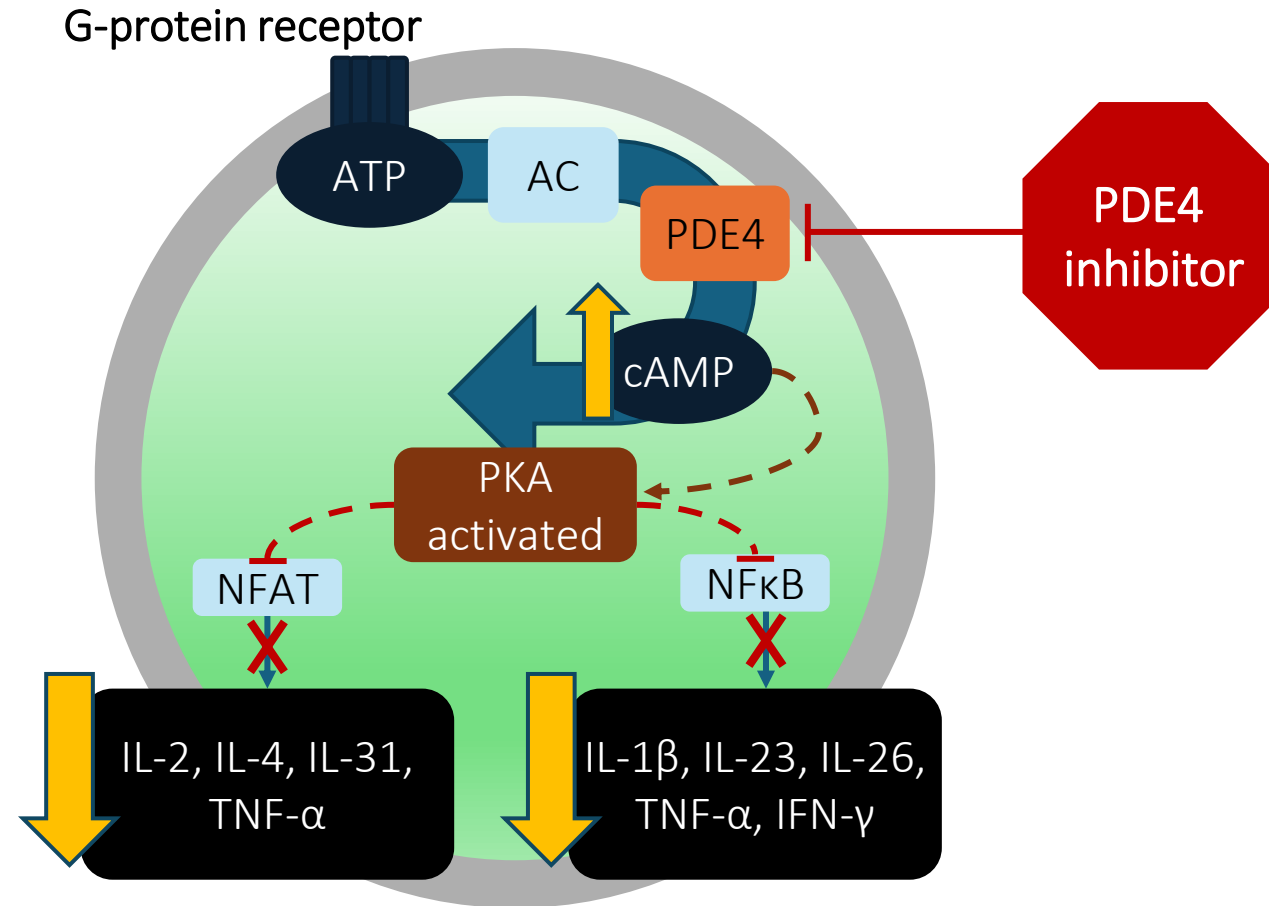
Drugs@FDA: FDA-Approved Drugs. Accessed August 12, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2026/215309s009sdn953lbl.pdf.

Ruxolitinib

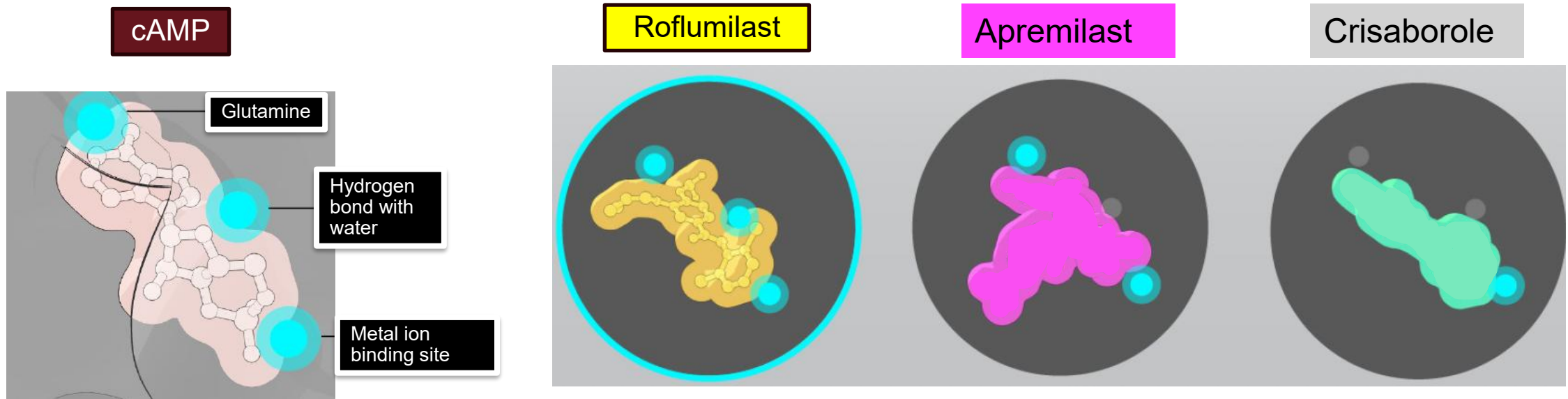
"The mean steady-state plasma concentration of ruxolitinib remained consistently below the half-maximal inhibitory concentration of Janus kinase-mediated myelosuppression."



PDE4 Inhibition Reduces Production of Pro-Inflammatory 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

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

$P < 0.05$ vs vehicle unless otherwise indicated.

BSA = body surface area; TEAE = treatment emergent AE; vIGA-AD = validated Investigator Global Assessment for AD.

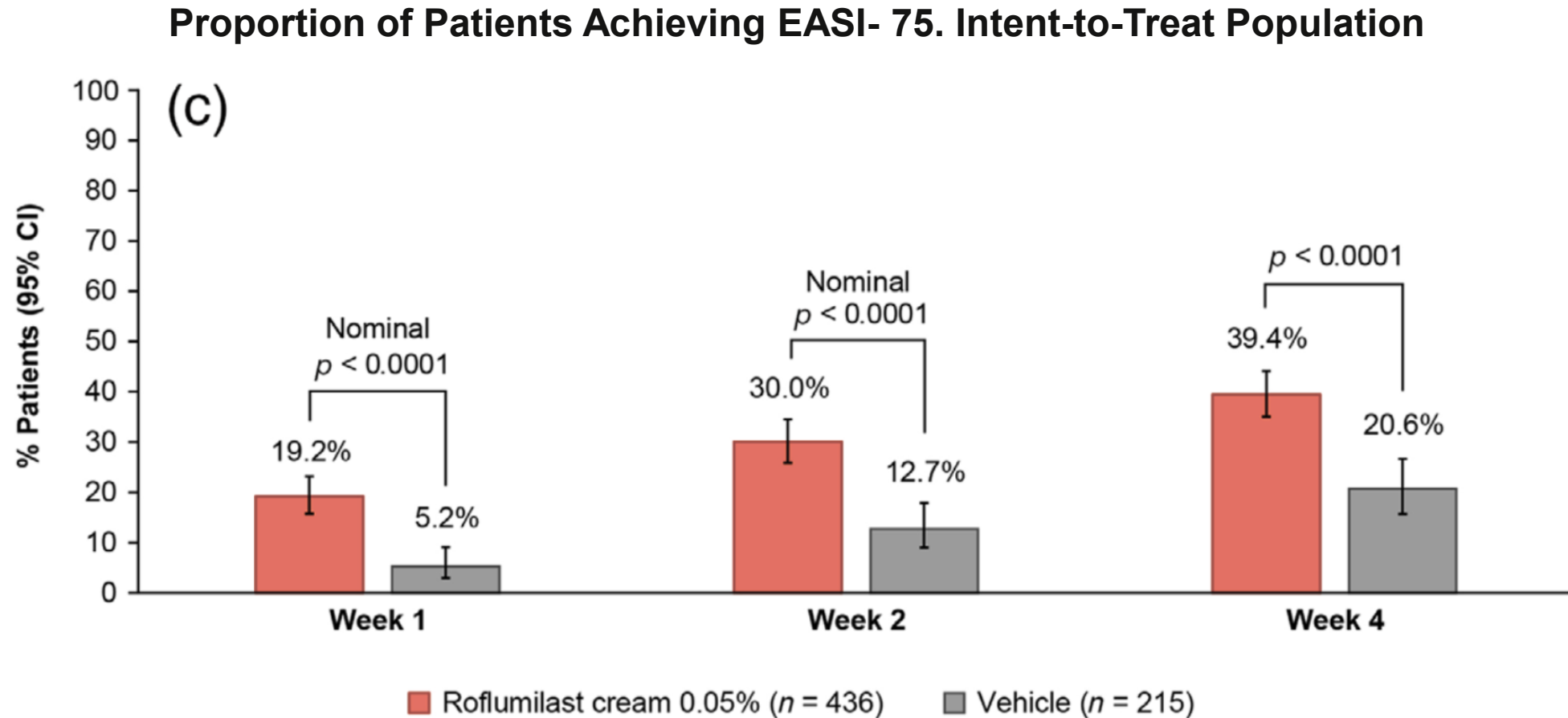
Gooderham MJ, et al. *J of Skin*. 2020;4(6):s93.

TEAE: (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

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



0.05% Daily for Ages 3 Months to <24 Months

- INTEGUMENT-INFANT enrolled 101 infants
- 34.4% vIGA-AD success at week 4, with 49% reaching vIGA-AD 0/1
- EASI-75 achieved in 58.3% at week 4 vs 34% at week 2
- Caregiver-reported itch improved meaningfully, with 72.7% achieving ≥ 4 -point WSI-NRS improvement at week 4 and DPS-25 improvements observed within 10 minutes of application
- Safety consistent with prior pediatric data: Mostly mild systemic AEs (eg. diarrhea, URTI) and $\geq 97.9\%$ reporting no application-site irritation; one discontinuation and no serious AEs

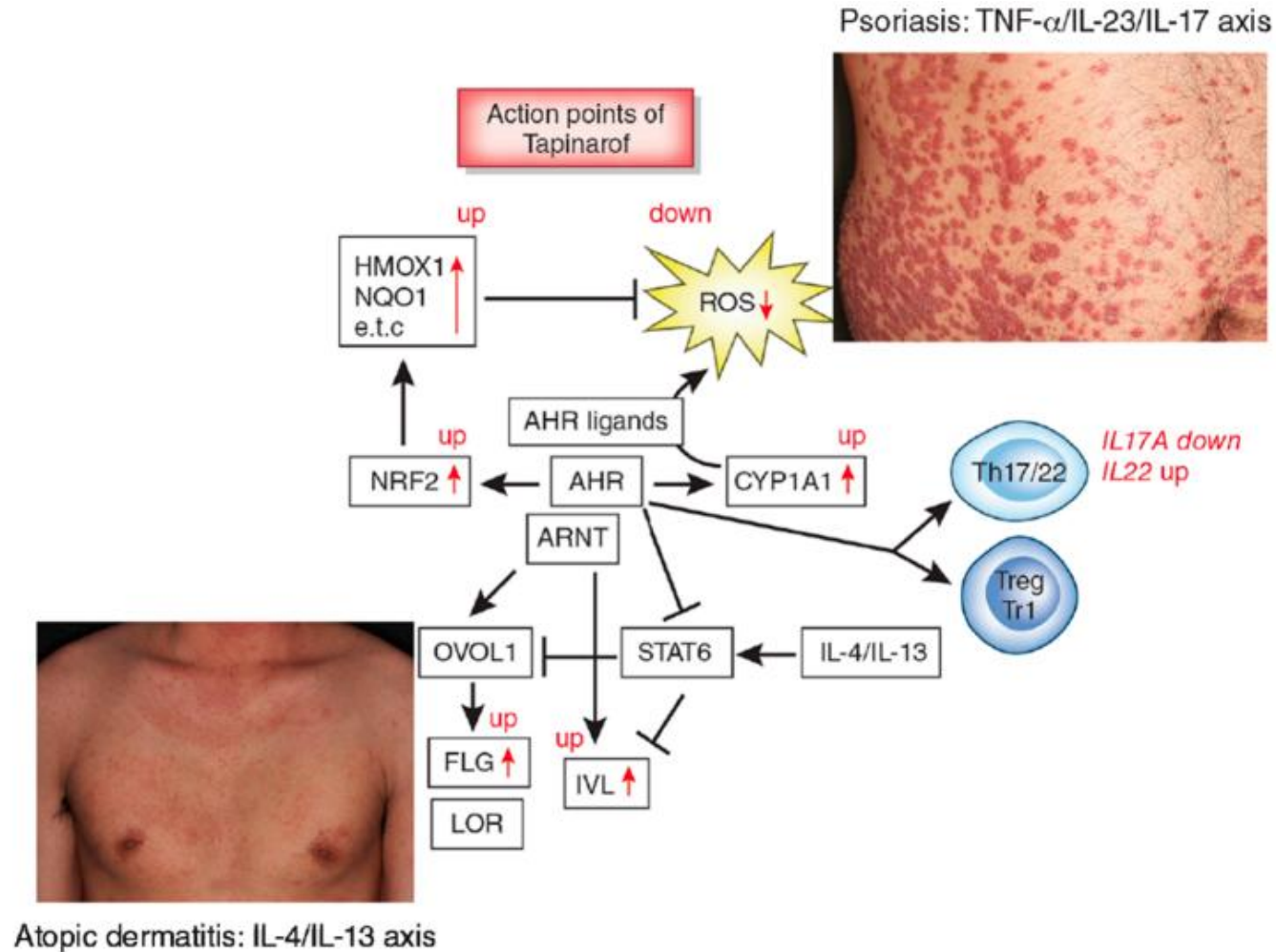


WSI-NRS = Worst Scratch/Itches Numeric Rating Scale; DPS = Dynamic Pruritus Scale; URTI = upper respiratory tract infection.

Eichenfield L. Presented at: 2026 AAD Annual Meeting; March 27-31, 2026; Denver, CO. Bunick CG, et al. *Dermatology Times*. Accessed August 12, 2026.

<https://www.dermatologytimes.com/view/late-breaking-data-roflumilast-cream-0-05-demonstrates-efficacy-and-favorable-tolerability-in-infantile-atopic-dermatitis>.

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 AD

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 vs vehicle QD at week 12)

Primary endpoint

IGA treatment success rate 46% vs 28%

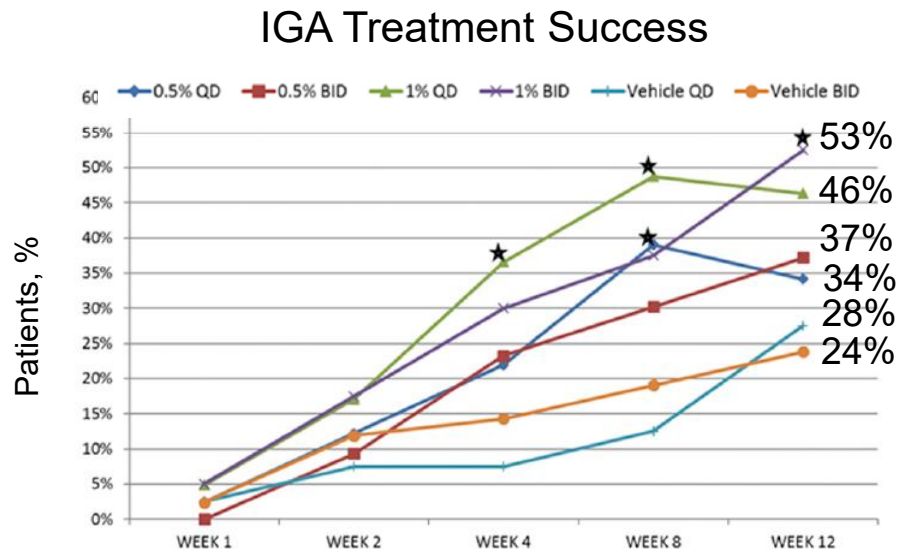
Secondary and post-hoc endpoints

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%*

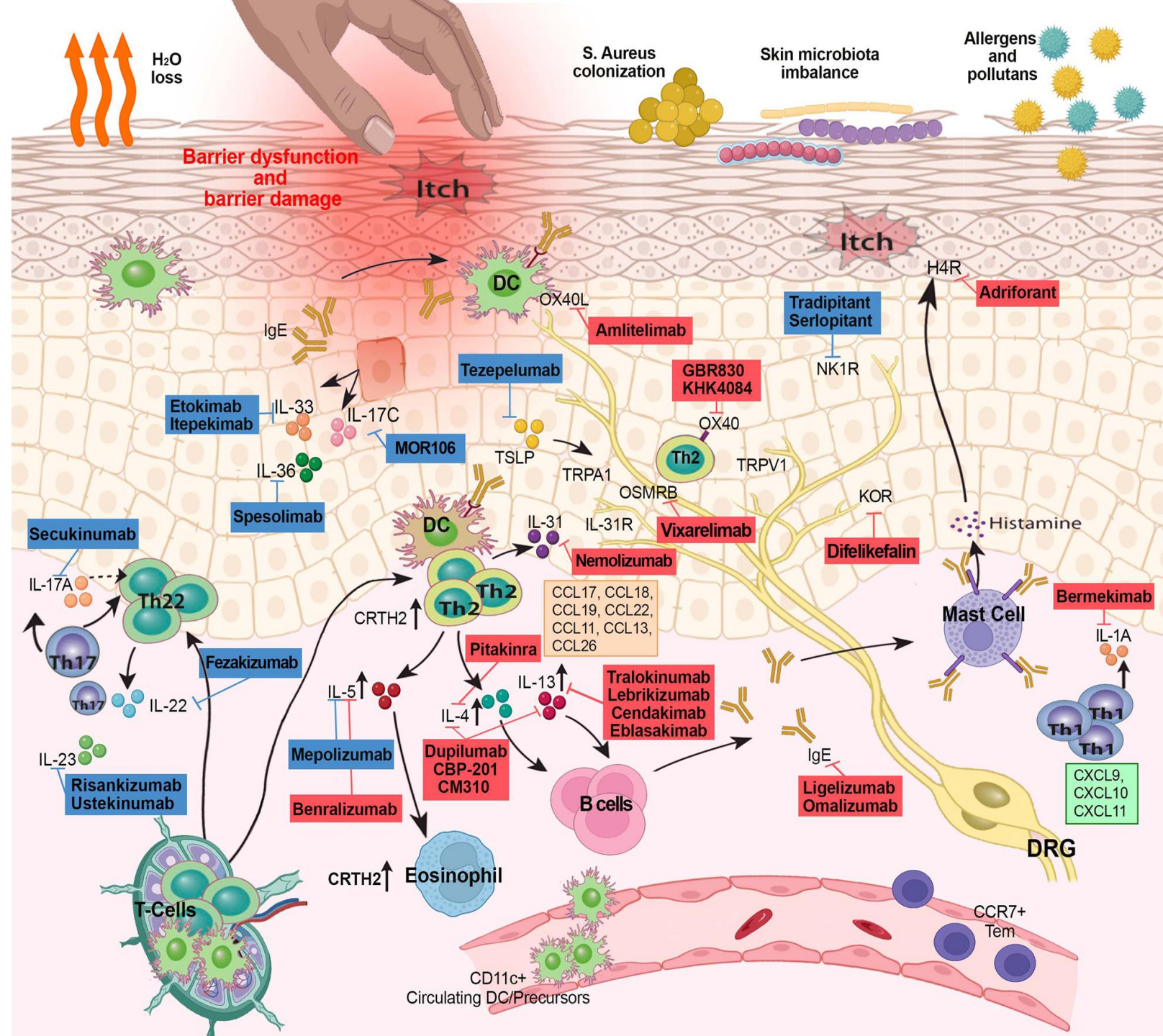


Improvements were maintained for 4 weeks after last application in most patients

Safety and Tolerability of Tapinarof

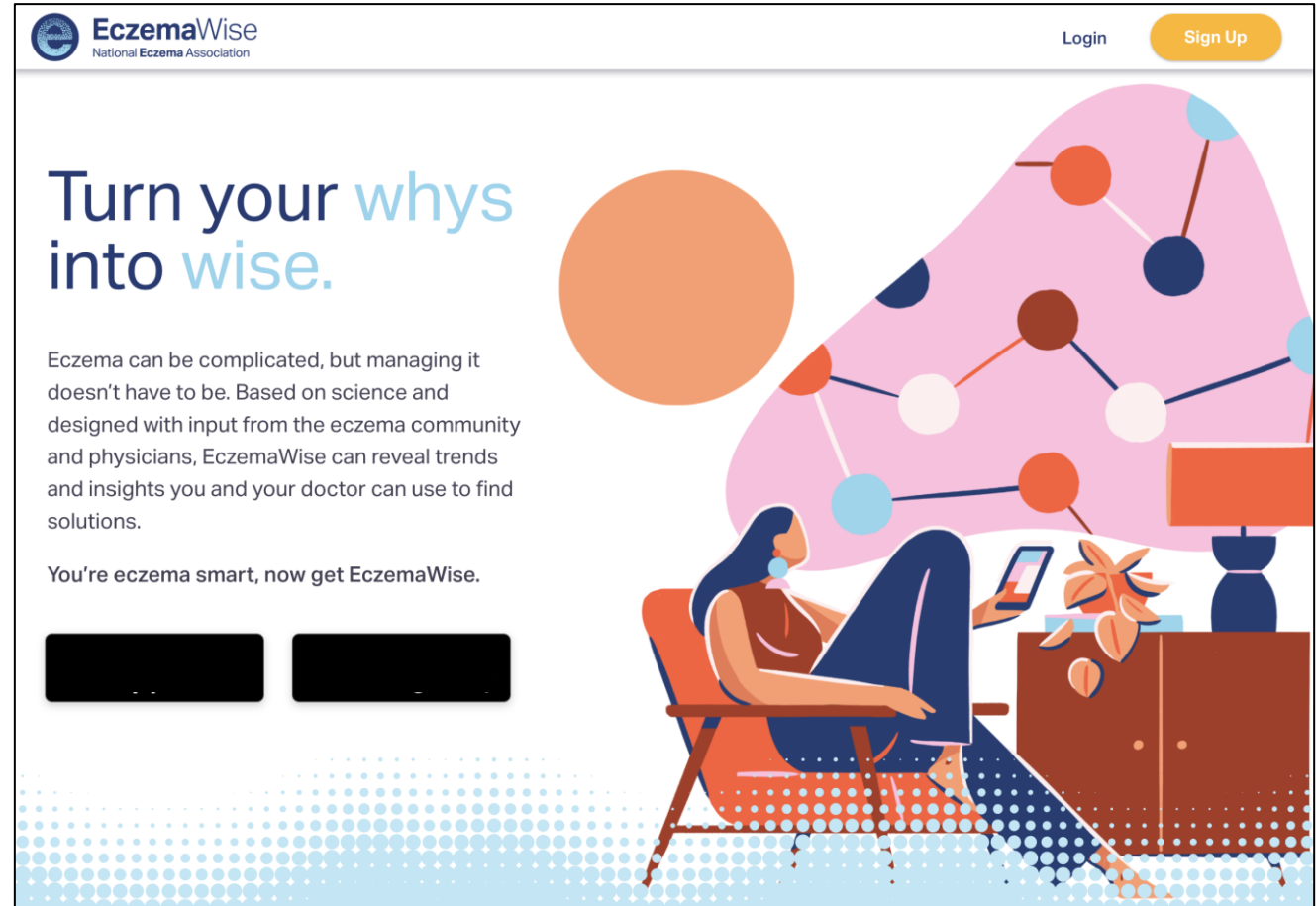
- AEs related to tapinarof treatment
 - Follicular events (~10%)
- No serious treatment-related AEs reported

Pipeline...



AD Patient Education: Apps and Tools

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



Key Learning Points



- Recognize pediatric AD: Pruritic, ill-defined eczematous lesions involving the face, neck, and extensor surfaces are characteristic in infants and young children; presentation may vary across skin tones
- Individualize topical therapy: Treatment selection should incorporate age, disease severity and location, efficacy/safety, treatment burden, and patient/caregiver preferences through shared decision-making
- Expand beyond topical corticosteroids: Newer targeted nonsteroidal therapies provide additional options across pediatric age groups and can help address concerns about long-term corticosteroid use
- Know the newer agents: Roflumilast is a once-daily topical PDE4 inhibitor available in multiple cream strengths across pediatric age groups; both roflumilast and tapinarof have distinct tolerability and safety profiles that should inform treatment selection

Thank you!

