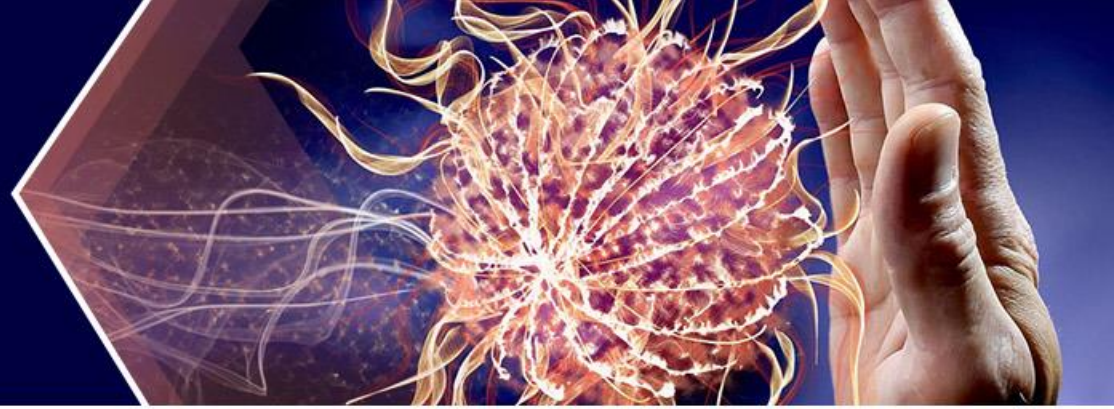
Atopic Dermatitis
A 2025 Update

Dana V. Wallace, MD

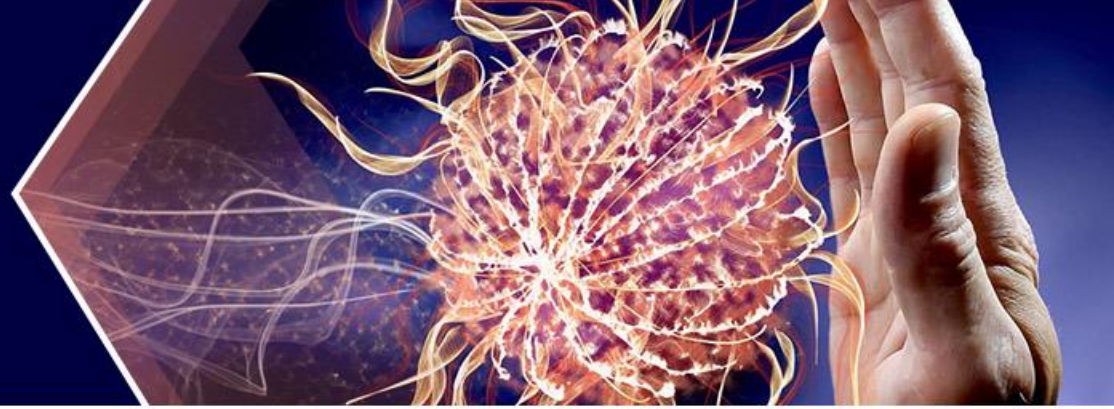
Learning Objectives



At the conclusion of this activity, participants should be able to:

- Describe signaling pathways and their clinical implications in the pathophysiology of atopic dermatitis
- Outline an approach to the use of advanced therapies for atopic dermatitis not adequately responsive to topical corticosteroids and calcineurin inhibitors
- Develop a treatment plan for Ginnie and similar patients in the allergist’s office

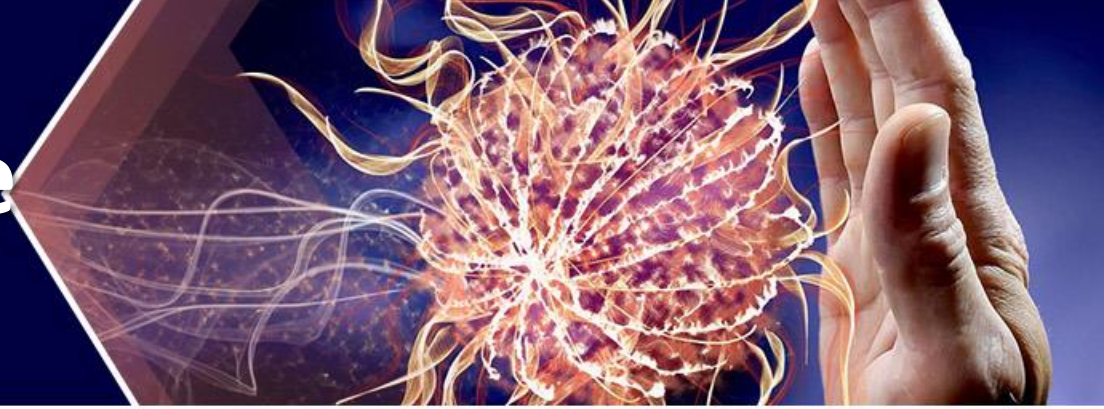
Epidemiology of AD



- 45% begin within the first 6 mo[3]
- **Up to 85% begin before 5 yr[1] (L.P. onset 6 yr., within margin of error)**
- Affects 15-30% of children in westernized countries
  - **African American (AA) children are 1.7x** more likely to develop AD vs. European Americans (EA) even after adjusting for socioeconomic factors[1]
  - AA (vs. EA) are 3x more likely to have a dermatology office visit at which AD is diagnosed[2]
- Up to 65% have spontaneous remission before adolescence but may reappear in early adulthood up to 20 % of the time[4]
- **Affects 2-10% of adults[3]**

1. Shaw, TE. J Invest. Dermatol.2011;131(67) 2. Janumpally, S.R. Arch. Dermatol.2002;138(634)
3. Bieber T. NEJM 2008;358(14):1483-94 4. Bieber T. Allergy 2012; 67: 1475–1482

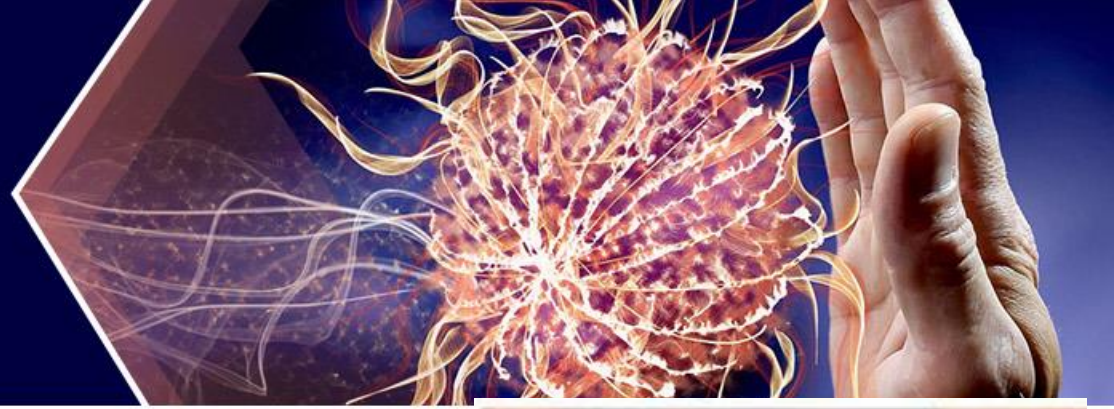
Genetics & Family phenotype

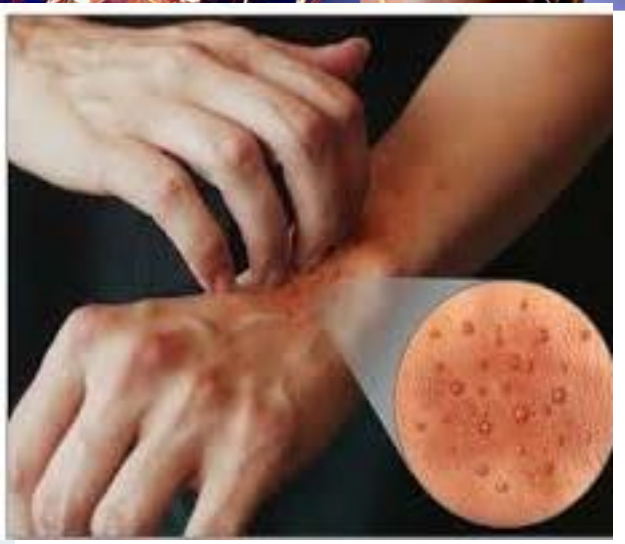


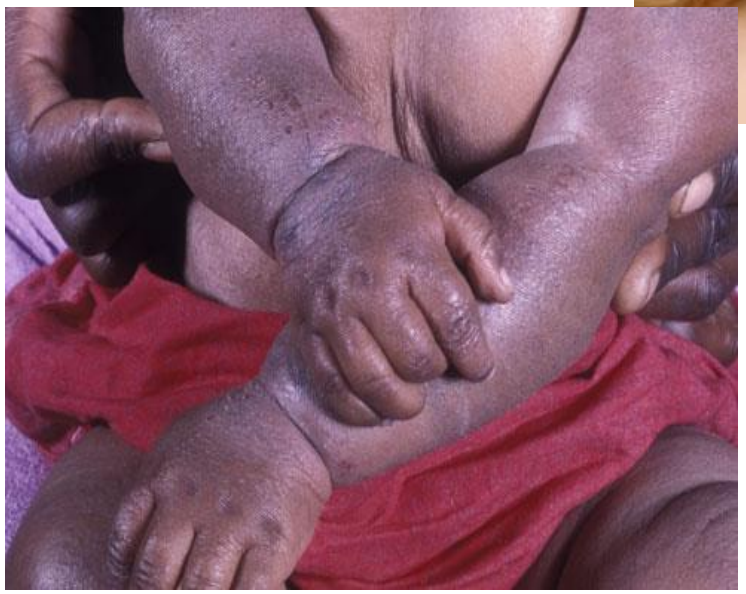
- For atopic dermatitis **monozygotic twins have a 77%** concordance rate vs. 15 % for dizygotic twins
- Incidence rate of AD is **doubled if one parent** as AD and **tripled if both parents** have AD
- Parental hx of **AR and asthma** seem to be **minor** factors in the development of AD, suggesting **AD-specific genes**

Bieber T. Ann Dermatol. 2010. May.22(2). 125-137

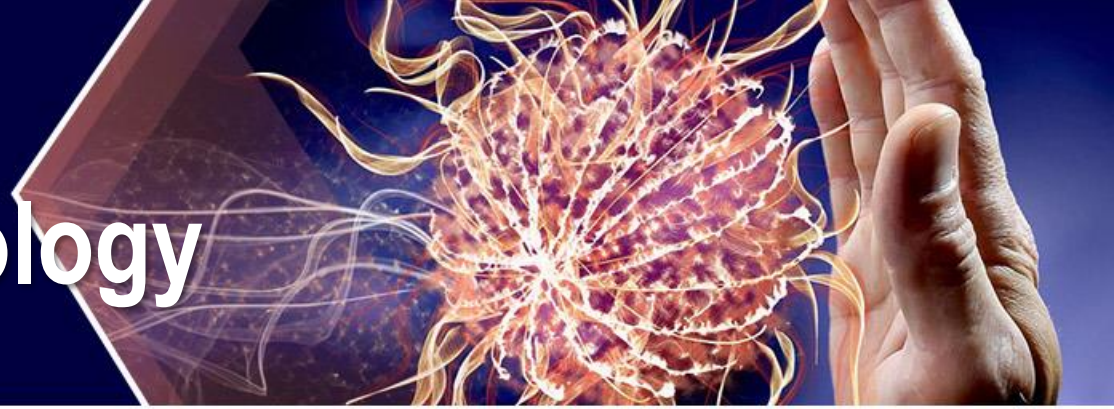
Atopic Dermatitis Always has Itch!







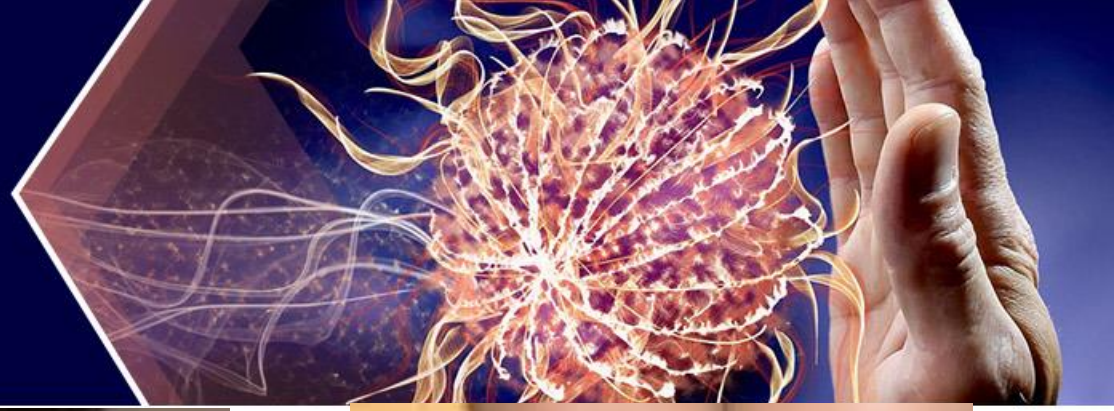
American Academy of Dermatology

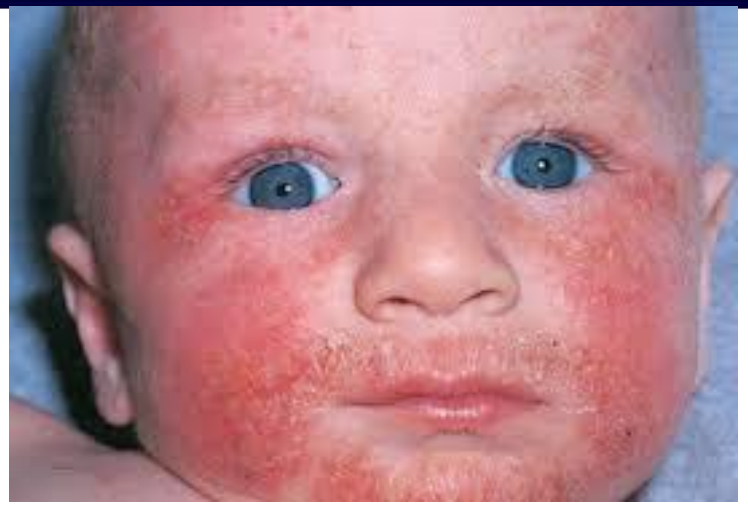


Essential features Must be present	•Pruritus •Eczema (acute, subacute, chronic) • Chronic or relapsing history • Typical morphology and age-specific patterns • Facial, neck, and extensor involvement in infants and children • Current or previous flexural lesions at any age • Sparing of the groin and axillary regions
Important features Seen in most cases, adding support to the diagnosis	•Early age of onset •Atopy • Personal and/or family history • Raised IgE levels •Xerosis (dry skin)

Guidelines of care for the management of eczema. Section 1. Diagnosis and assessment of eczema. American Academy of Dermatology. J Am Acad Dermatol 10.1016/j.jaeczema.2013.10.010

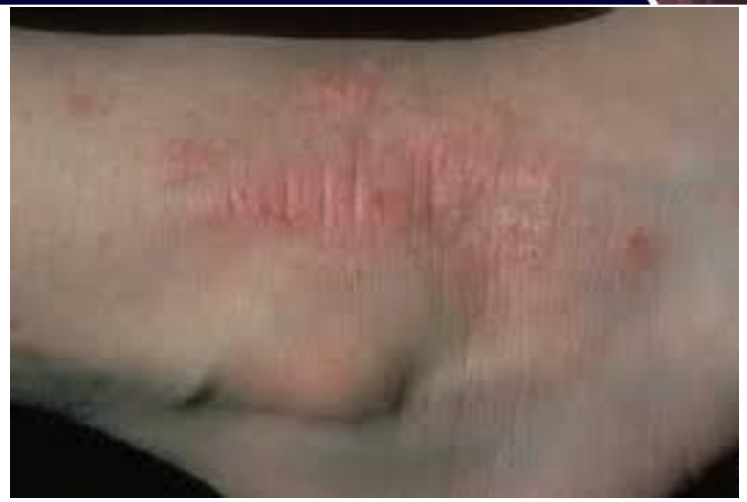
Stages of Eczema





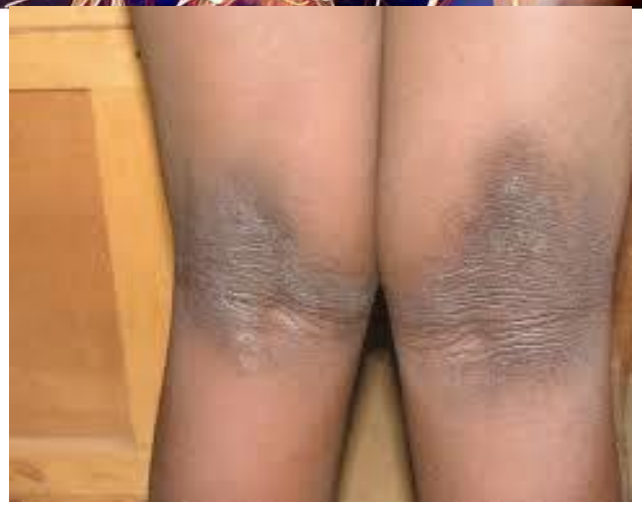
ACUTE

- Erythema
- Oedema
- Vesiculation
- Exudation



SUBACUTE

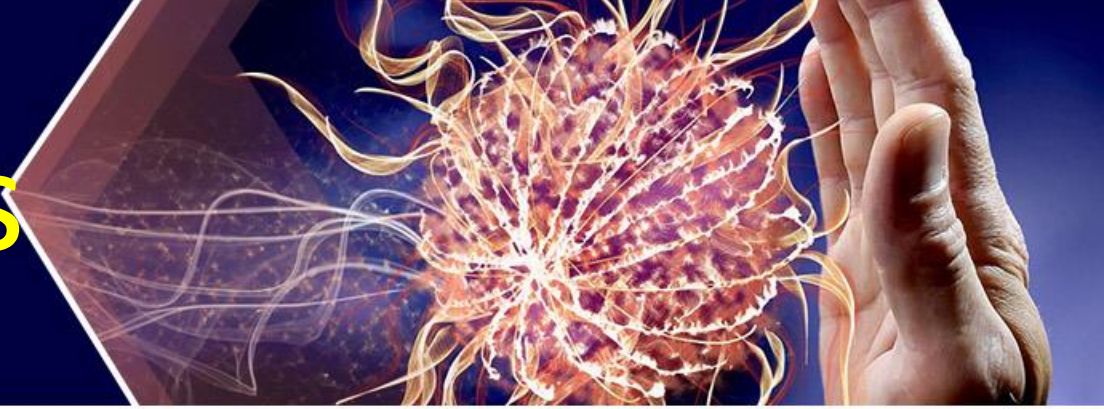
- Slightly elevated
- May be red, brown or purplish in colour
- Scaling and crusting



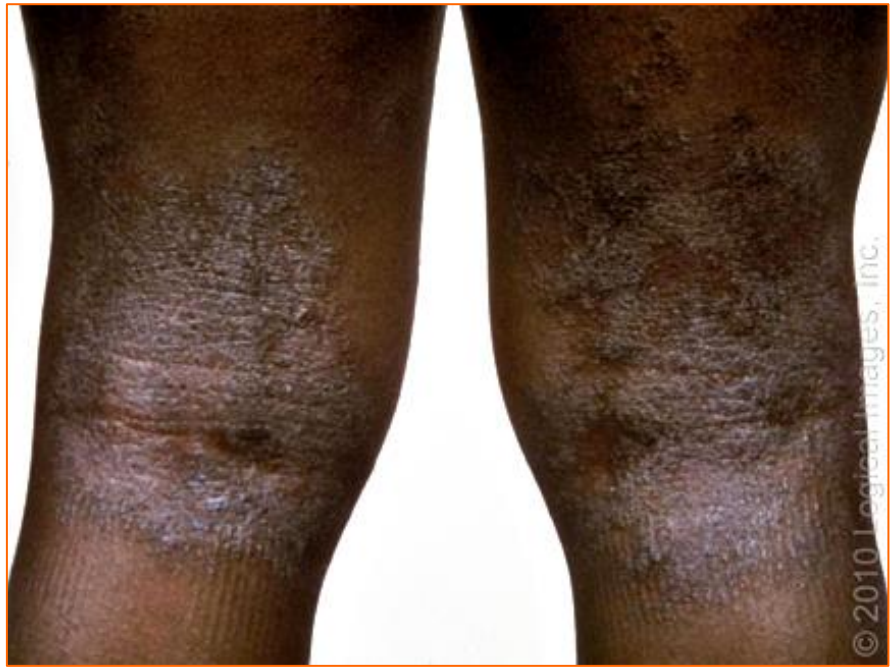
CHRONIC

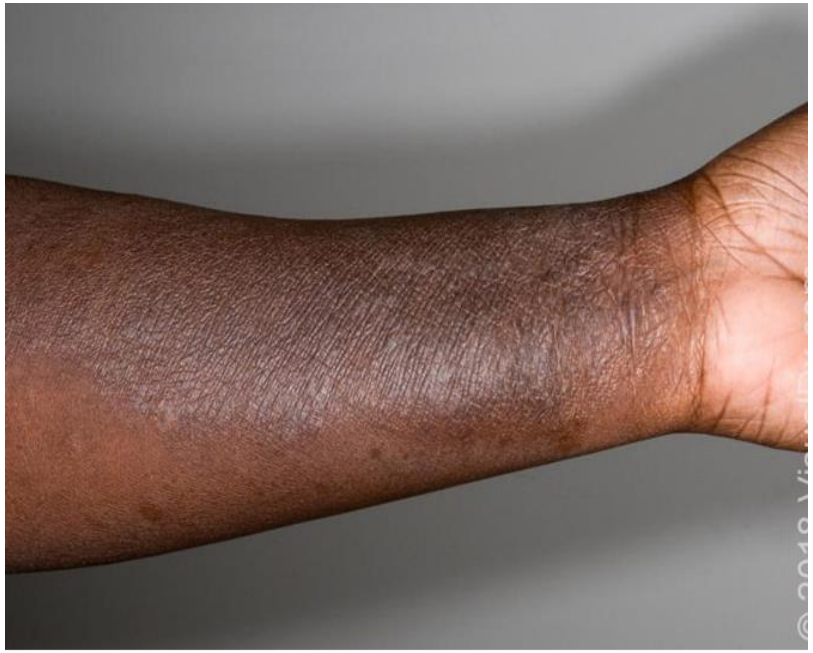
- Hyperpigmentation
- Thick and leathery skin (lichenification)

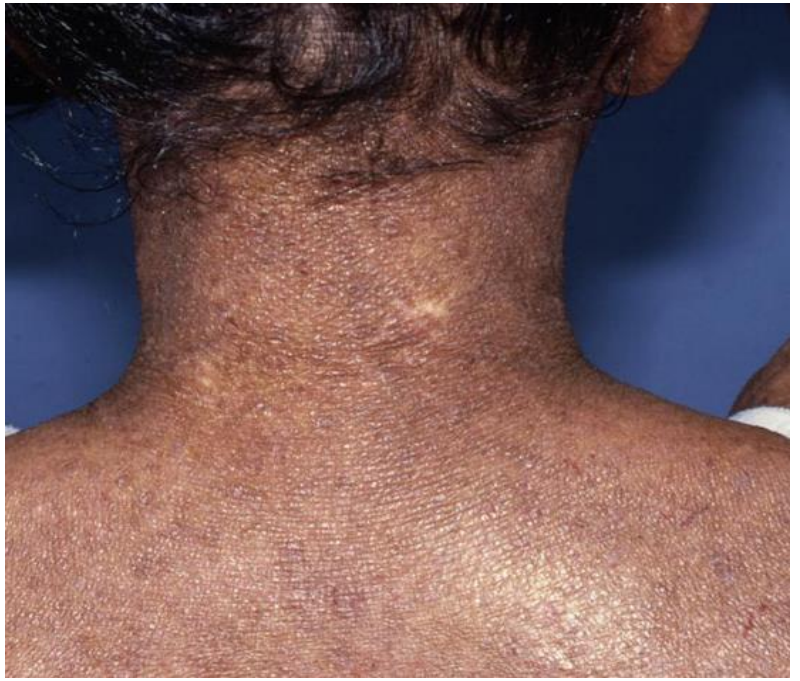
Physical exam findings



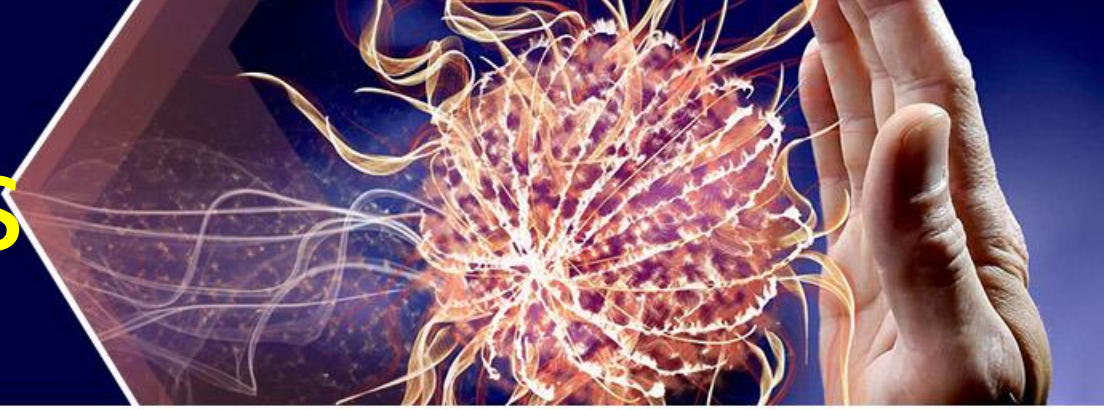
Lichenification with hyper- and hypopigmentation



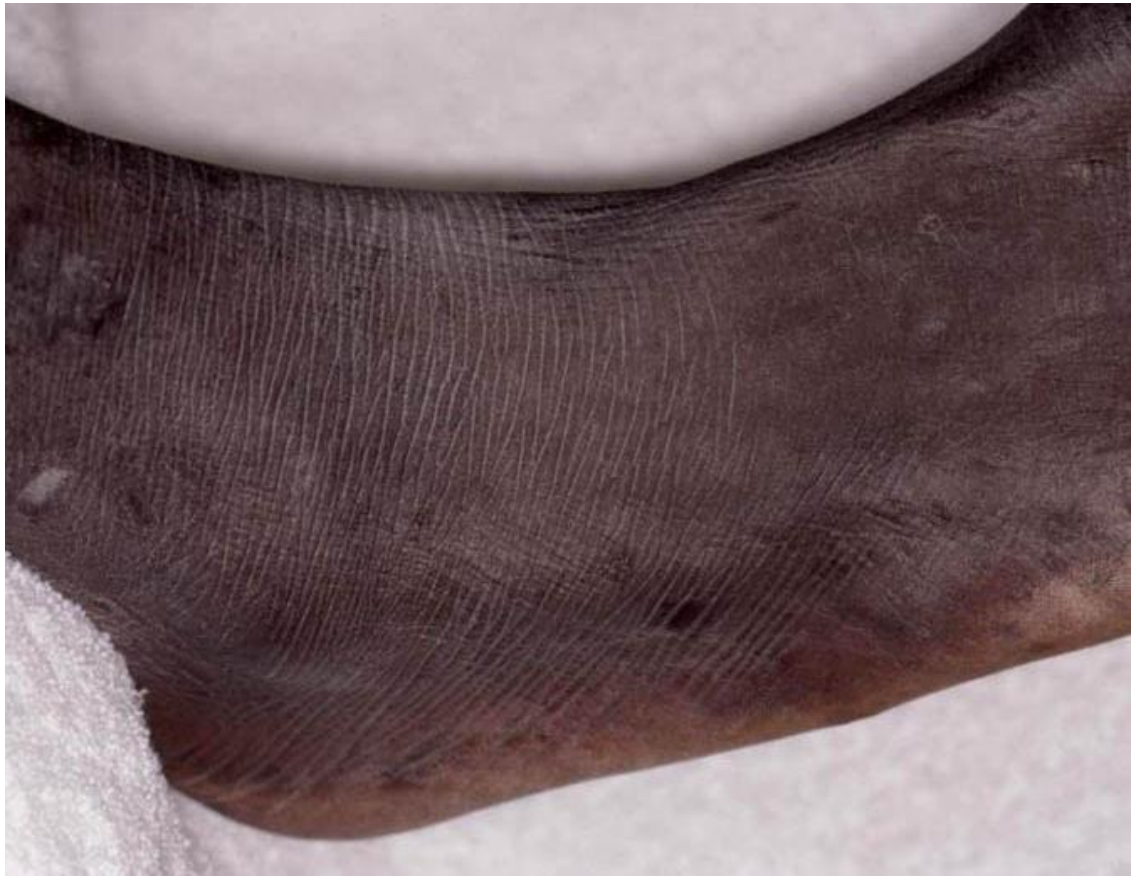




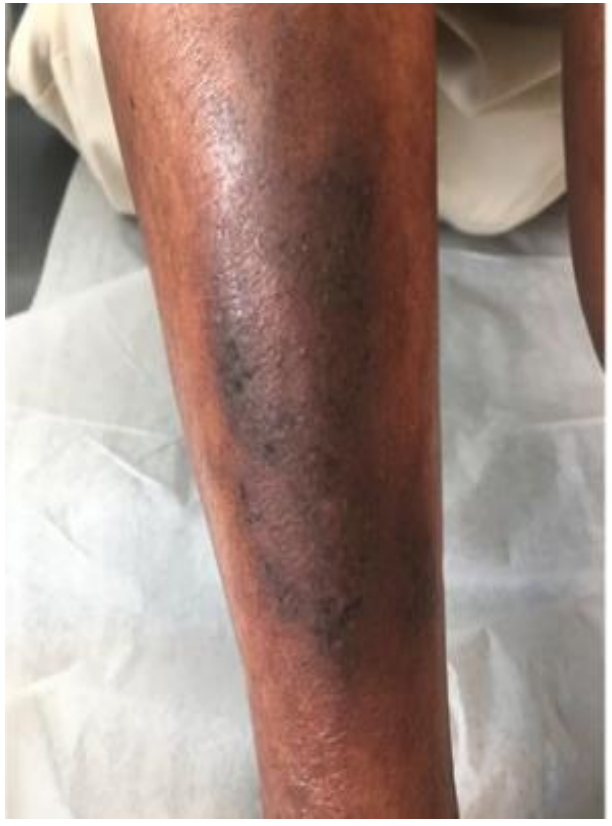
Physical exam findings

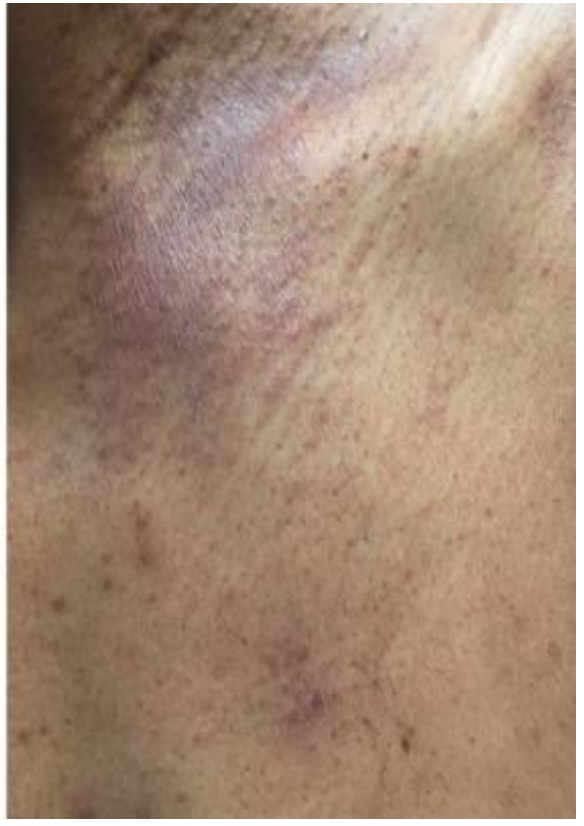


Severe Xerosis and “ashen” skin

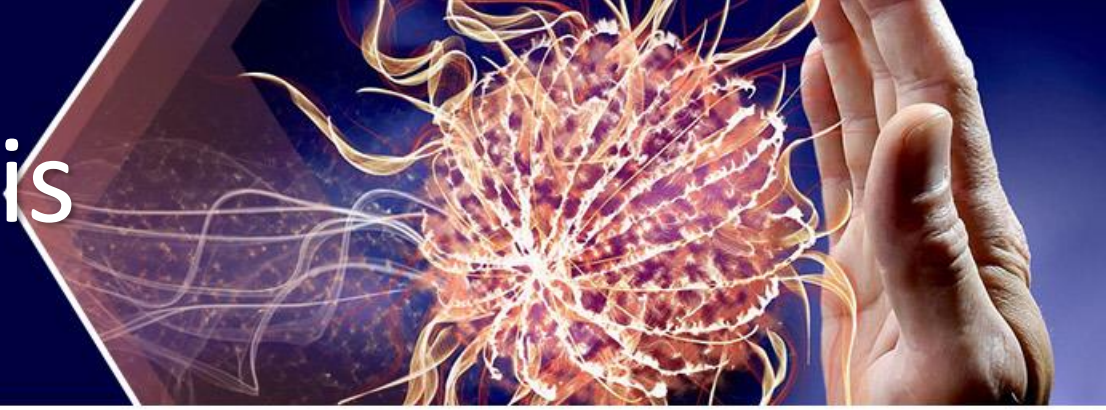


Violaceous discoloration



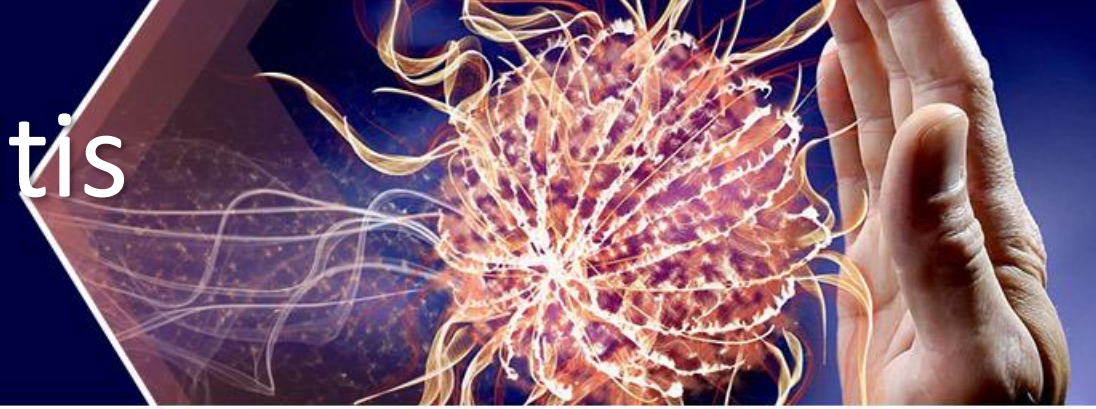


Infantile Atopic Dermatitis

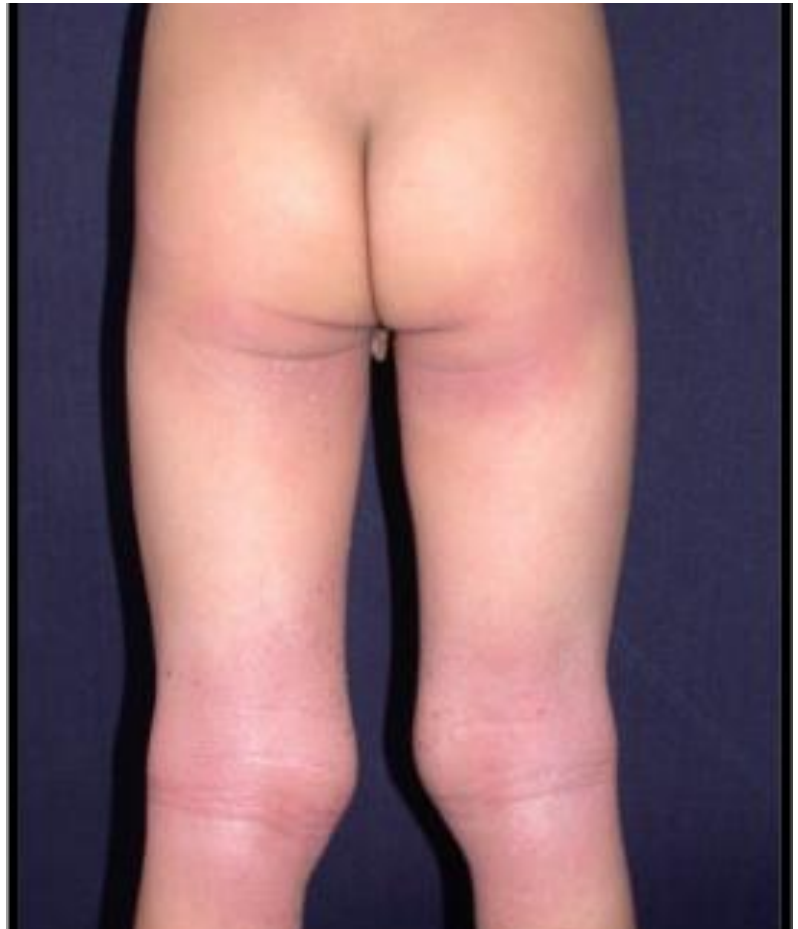


- **Involvement of face and trunk**
- **Typically involves cheeks and chin and spares the area around the nose and eyes**
- **Usually ‘acute’ appearance**
- **Excoriation may be prominent**
- **Knees may become involved with crawling**

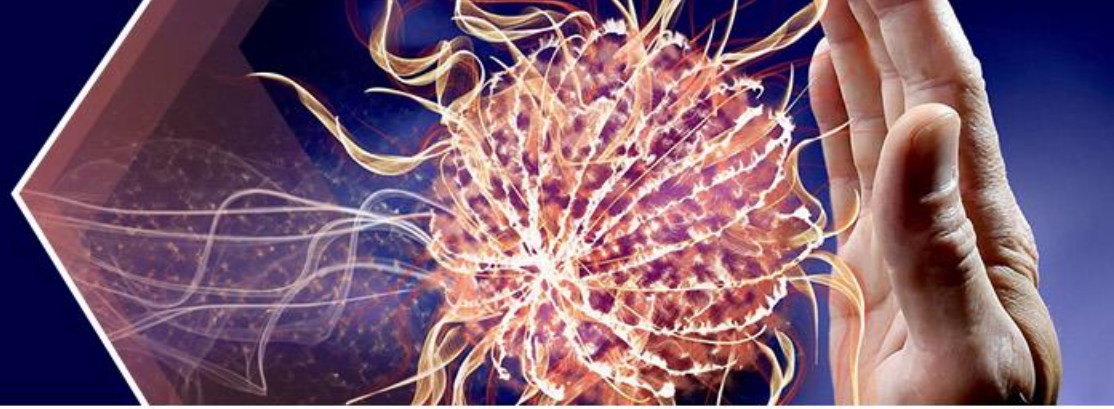
Childhood Atopic Dermatitis



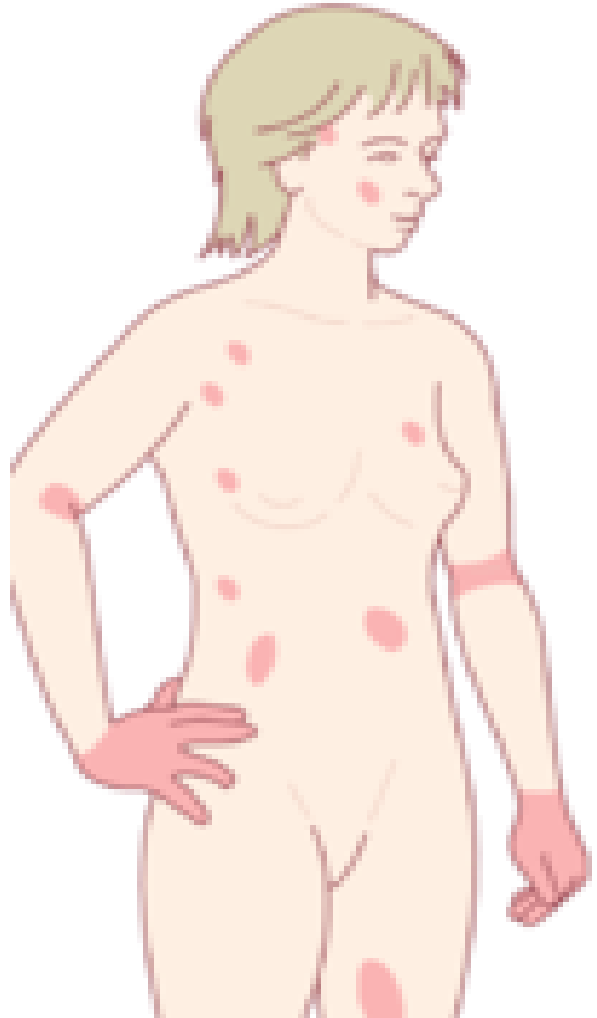
- **Involvement of the flexures, neck, hands and wrists**
- **Acute, sub-acute and chronic lesions**
- **May have discoid or nummular lesions**



Adolescent & Adult AD

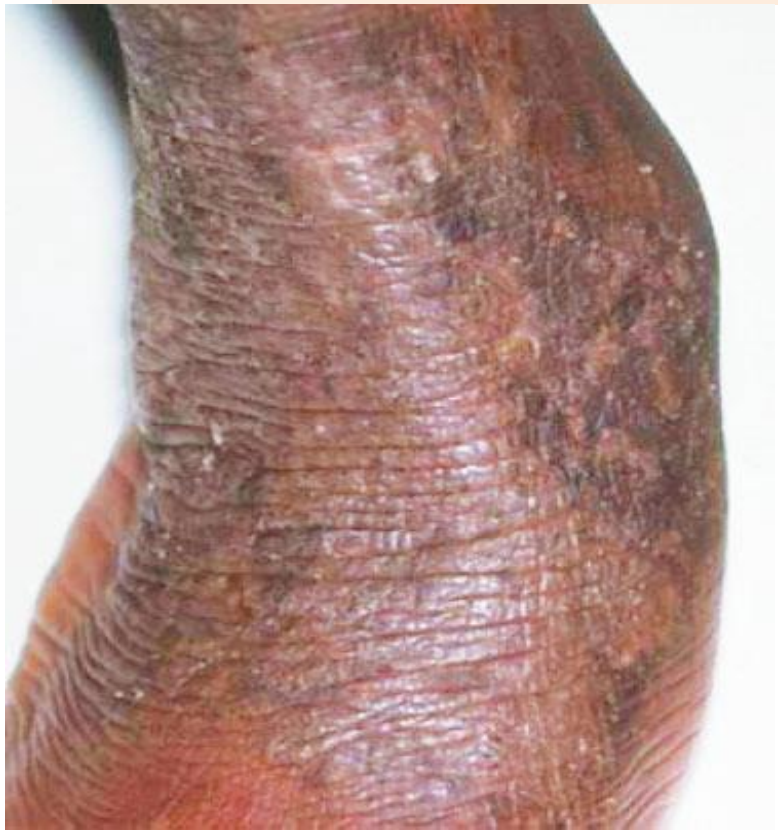


- Flexural areas
- Forehead, periorbital, and perioral dermatitis
- Hand and feet eczema
  - Hyperlinerality, fissures, crusting
- Neck with lichenified plaques
- Dry skin severe problem
- Overall **more isolated** but also **more lichenification & plaques** than childhood



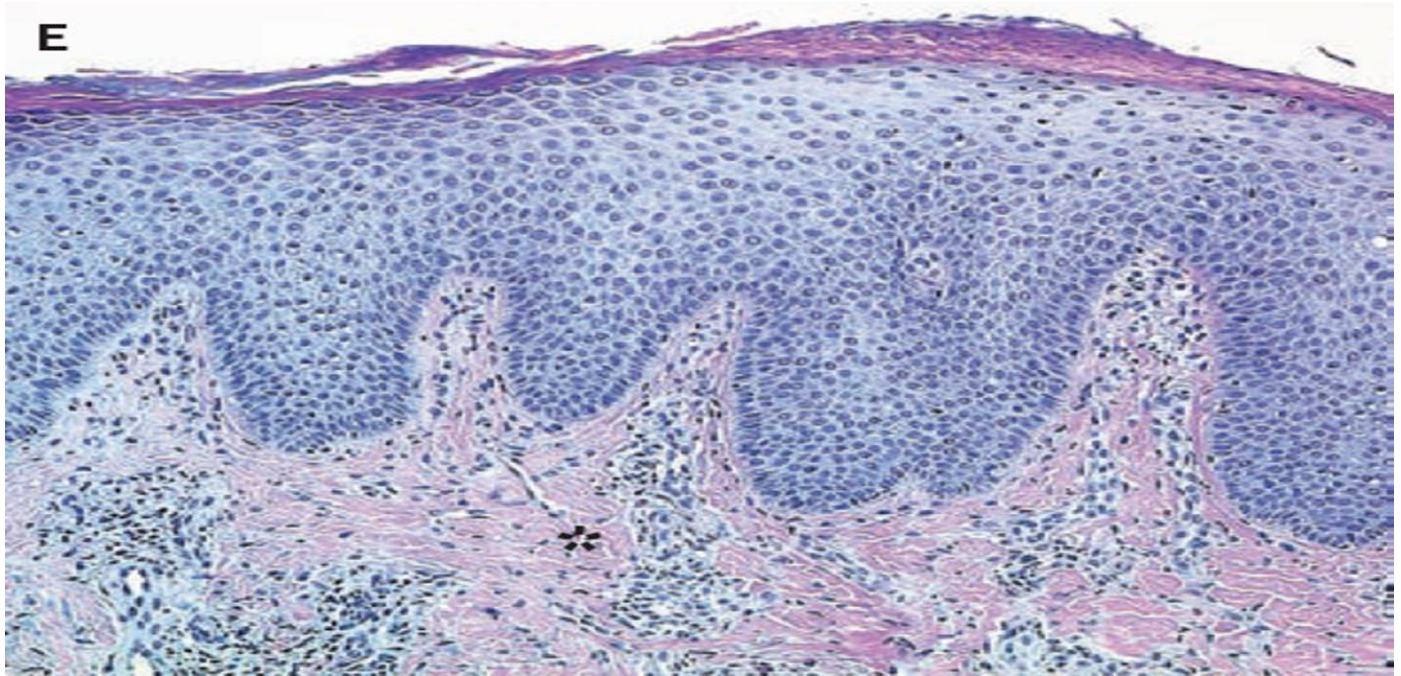
Chronic ATOPIC DERMATITIS

- Thickened plaques with increased lichenification



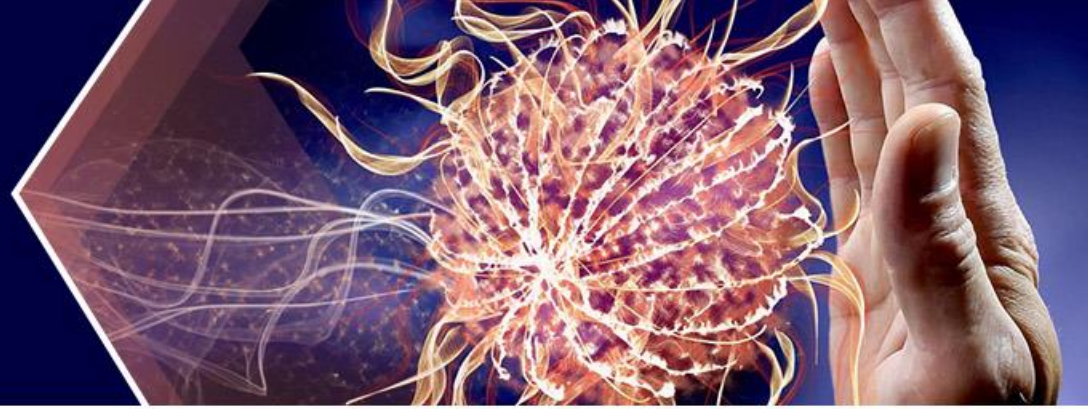
Adv Immunol.2009;102;135-226

- Pathology : marked epidermal **hyperplasia**, **hyperkeratosis, acanthosis**
- **Macrophage-**dominated mononuclear **cell infiltrate in dermis**, and perivascular accumulation of lymphocytes in smaller numbers than seen in acute AD
- Increased **eosinophils** in tissue and blood



Validated Instruments for AD

Used in most of the recent RCTs



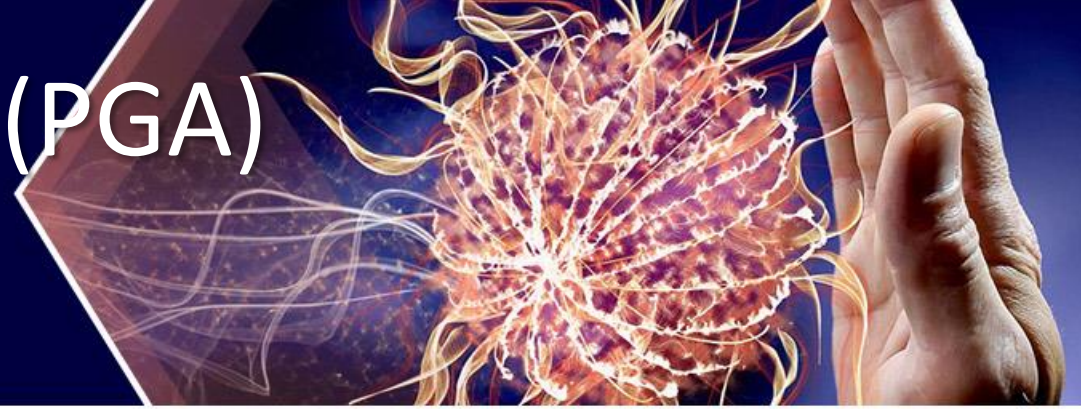
- Scoring of Atopic Dermatitis (SCORAD): Max of 103
  - (A/5 +7B/2+C; A=extent (0-100); B=intensity (0-18); C=subjective (0-20)
  - Moderate 25-50 or recurrent dz.; Severe >50 or persistent dz
- Eczema Area and Severity Index (EASI): Max* of 72
  - Moderate 21.1-50; Severe 50.1-72[1]
- EASI-75: 75% improvement compared to baseline
- Physician's Global Assessment (PGA): Max of 4, controlled= 0/1
- Dermatology Life Quality Index (DLQI): Max of 30
- Six Area Six Signs AD (SASSAD) Max is 108
- Peak Pruritus-Numerical Rating Scale (PP-NRS): Max 10, ≥ 2–4-point change=clinically meaningful

Ginnie is 33 (moderate)

Ginnie scores an 8

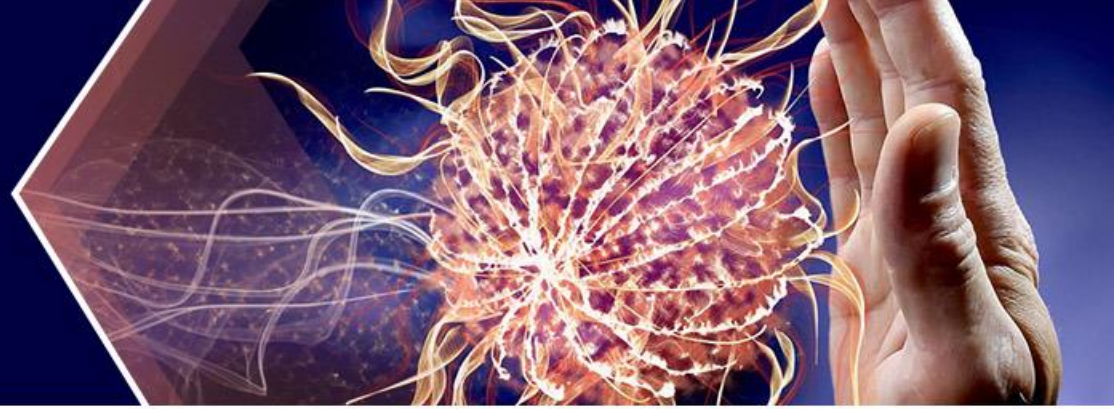
1. Wollenberg, A. 2018. J. Eur Acad Dermatol Venereol 32(5):657-682

Physician's Global Assessment (PGA)



Score	Morphological Description
0 – Clear	No inflammatory signs of atopic dermatitis (no erythema, no induration/papulation, no lichenification, no oozing/crusting). Post-inflammatory hyperpigmentation and/or hypopigmentation may be present.
1 – Almost clear	Barely perceptible erythema, barely perceptible induration/papulation, and/or minimal lichenification. No oozing or crusting.
2 – Mild	Slight but definite erythema (pink), slight but definite induration/papulation, and/or slight but definite lichenification. No oozing or crusting.
3 – Moderate	Clearly perceptible erythema (dull red), clearly perceptible induration/papulation, and/or clearly perceptible lichenification. Oozing and crusting may be present.
4 – Severe	Marked erythema (deep or bright red), marked induration/papulation, and/or marked lichenification. Disease is widespread in extent. Oozing or crusting may be present.

Eczema Area and Severity Index (EASI): Overview



📝 **EASI Assessment Components:**

- Evaluates 4 body regions: Head/Neck, Trunk, Upper Limbs, Lower Limbs
- Rates severity of 4 signs: Erythema, Edema/Papulation, Excoriation, Lichenification
- Scores each sign from 0 (none) to 3 (severe)
- Estimates % area affected per region (0–6 scale)

📊 **Total Score Range:**

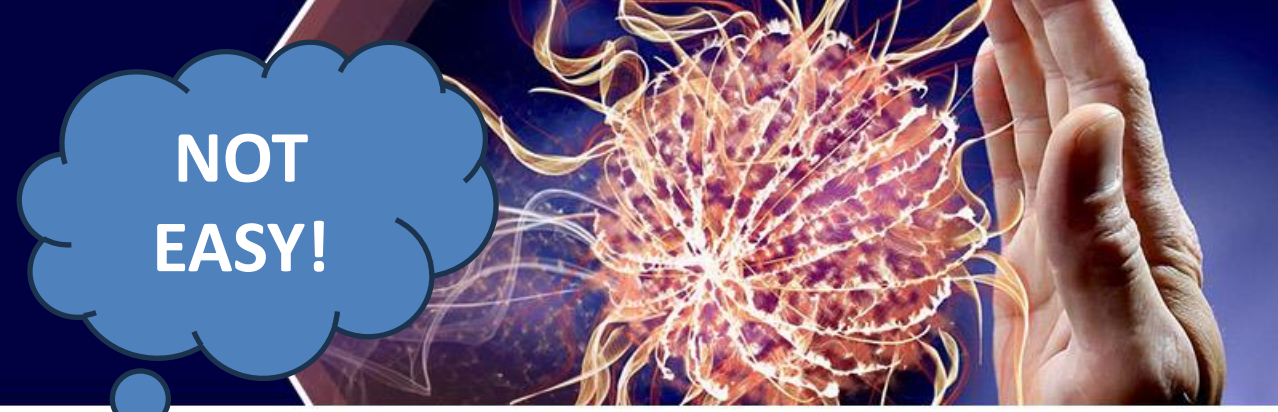
- EASI score: 0 to 72
- Higher scores = greater severity

Severity Grading

Mild: 1-7
Moderate: 7.1-21
Severe: 21.1-50
Very Severe: >50

1. Hanifin JM et al., Exp Dermatol. 2001;10(1):11–8. 2. Chopra R et al., Dermatol Clin. 2017;35(3):275–283.

EASI Score Calculation
Ginnie (Total 33=Severe)



🧮 Formula per Region:

EASI = Area Score × Sum of Signs × Region Weight

🧮 Region Weighting in Total EASI Score:

- Head/Neck = 10% (×0.1)
- Upper Limbs = 20% (×0.2)
- Trunk = 30% (×0.3)
- Lower Limbs = 40% (×0.4)

📊 EASI Area Score Conversion (Per Region):

- 0% = 0
- <10% = 1
- 10–29% = 2
- 30–49% = 3
- 50–69% = 4
- 70–89% = 5
- 90–100% = 6

🔷 **Head/Neck: 50% affected → Area Score = 4**
Signs = 2+2+2+2 = 8
Weight = 0.1 (for head/neck)
4 × 8 × 0.1 = 3.2

🔷 **Upper Limbs: 75% affected → Area Score = 5**
Signs = 3+2+2+2 = 9,
Weight = 0.2 (upper limbs)
5 × 9 × 0.2 = 9.0

🔷 **Trunk: 40% affected → Area Score = 4**
Signs = 3+3+2+2 = 10,
Weight = 0.3 (trunk)
4 × 10 × 0.3 = 12.0

🔷 **Lower Limbs: 25% affected → Area Score= 3**
Signs = 2+2+2+2 = 8,
Weight = 0.4 (lower limbs)
3 × 8 × 0.4 = 9.6

✅ **Total EASI = 3.2 + 9.0 + 12.0 + 9.6 = 33 (SEVERE)**

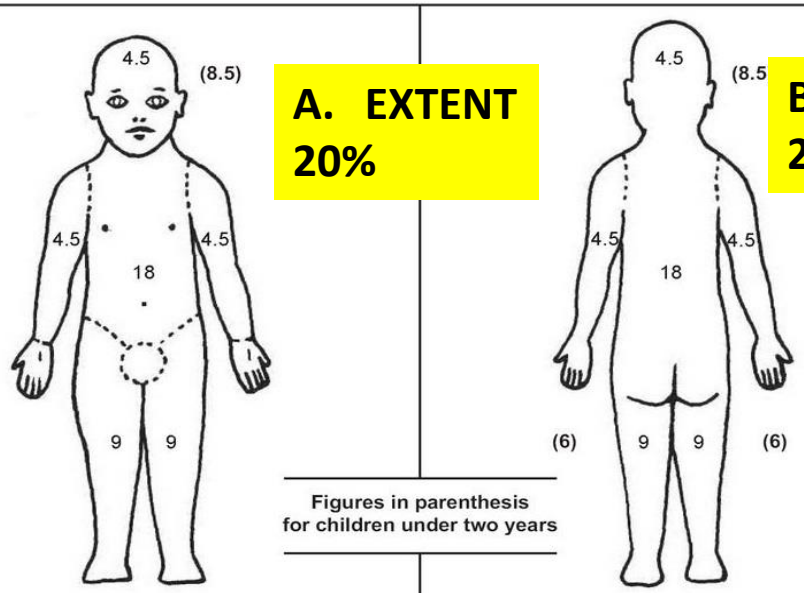
SCORAD INDEX

EUROPEAN TASK FORCE ON ATOPIC DERMATITIS

Last Name | First Name: Ginnie

Date of Birth: DD/MM/YY

Date of Visit:



Figures in parenthesis for children under two years

A. EXTENT 20%

B. EXTENT 20%

A: EXTENT Please indicate the area involved	40
B: INTENSITY	10
C: SUBJECTIVE SYMPTOMS PRURITUS + SLEEP LOSS	15

A/5 + 7B/2 + C

40/5 + 7(10)/2 + 15=58

2. INTENSITY SYMPTOMS

CRITERIA	INTENSITY
Erythema	
Oedema/Papulation	
Oozing/crust	
Excoriation	
Lichenification	
Dryness*	

* Dryness is evaluated on uninvolved areas

MEANS OF CALCULATION

INTENSITY ITEMS
(average representative area)
0= absence
1= mild
2= moderate
3= severe

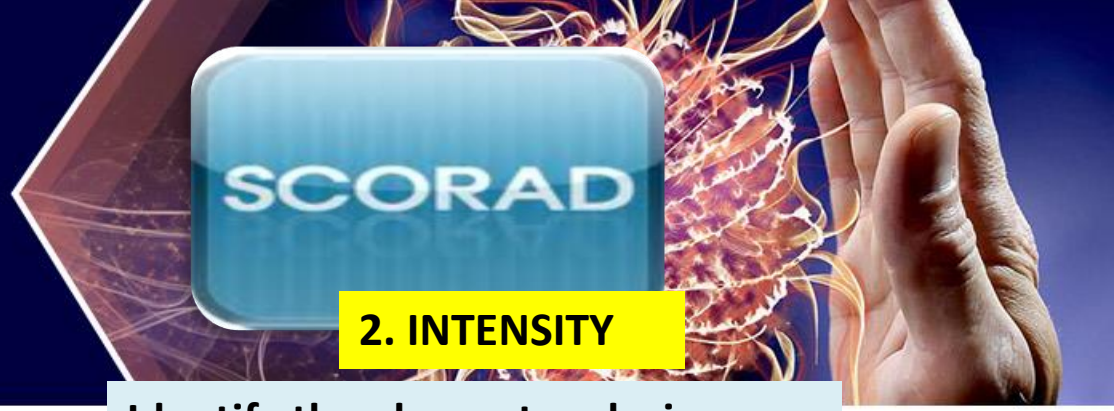
3. SUBJECTIVE SYMPTOMS

Visual analog scale (average for the last 3 days or nights)

PRURITUS (0 to 10) 8

0 10

SLEEP LOSS (0 to 10) 7



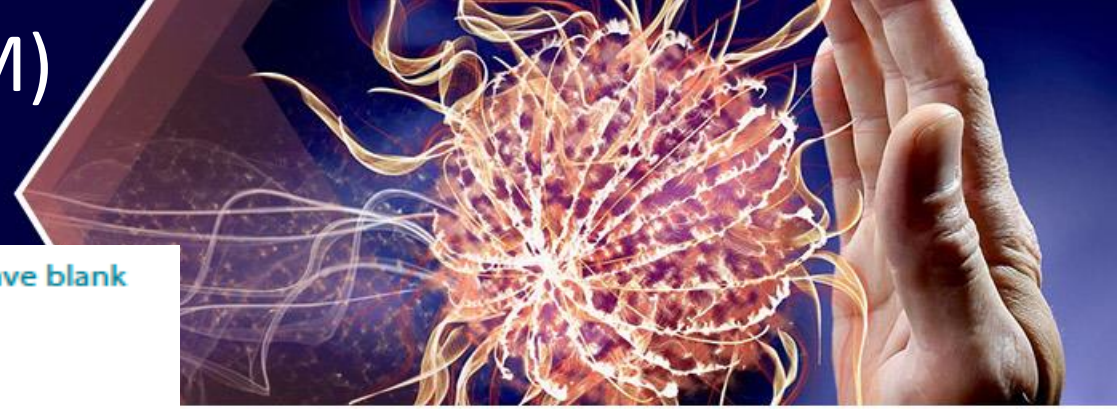
2. INTENSITY

Identify the elementary lesions:

1. **Erythema (0-3)** 3
2. **Edema (0-3)** 0
3. **Oozing/crusting (0-3)** 0
4. **Excoriation (0-3)** 3
5. **Lichenification** (0-3) 2
6. **Dryness (0-3)** 2

Eczema grading	Mild	Moderate	Severe
SCORAD index	< 25	25–50	> 50
Objective SCORAD	< 15	15–40	> 40
TIS	< 3	3–6	≥ 6

Patient Oriented Eczema Measure (POEM)



Please circle one response for each of the seven questions below about your eczema. Please leave blank any questions you feel unable to answer.

1. Over the last week, on how many days has your skin been itchy because of your eczema?

No days 1-2 days 3-4 days 5-6 days Every day

2. Over the last week, on how many nights has your sleep been disturbed because of your eczema?

No days 1-2 days 3-4 days 5-6 days Every day

3. Over the last week, on how many days has your skin been bleeding because of your eczema?

No days 1-2 days 3-4 days 5-6 days Every day

4. Over the last week, on how many days has your skin been weeping or oozing clear fluid because of you eczema?

No days 1-2 days 3-4 days 5-6 days Every day

5. Over the last week, on how many days has your skin been cracked because of your eczema?

No days 1-2 days 3-4 days 5-6 days Every day

6. Over the last week, on how many days has your skin been flaking off because of your eczema?

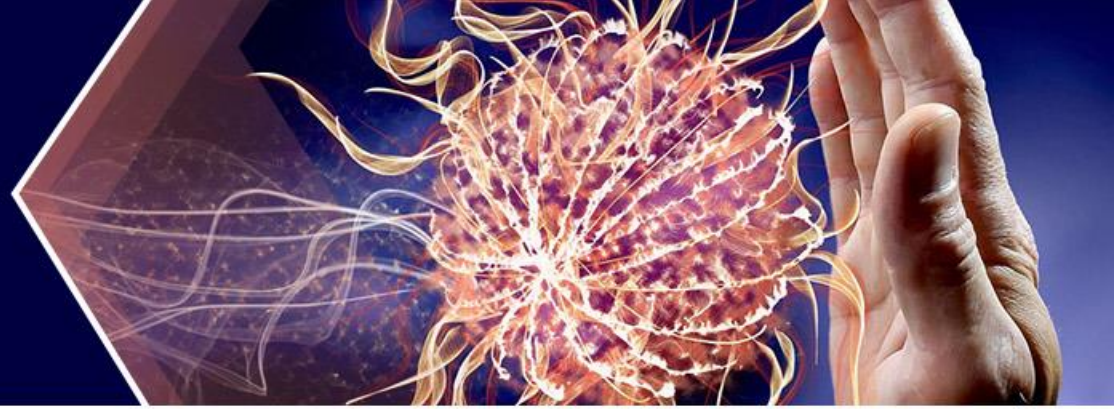
No days 1-2 days 3-4 days 5-6 days Every day

7. Over the last week, on how many days has your skin felt dry or rough because of your eczema?

No days 1-2 days 3-4 days 5-6 days Every day

- 0 to 2 = Clear or almost clear
- 3 to 7 = Mild eczema
- 8 to 16 = Moderate eczema **
- 17 to 24 = Severe eczema
- 25 to 28 = Very severe eczema

Atopic Dermatitis Control Test



📝 **ADCT Questionnaire (Past Week):**

1. Overall severity of AD symptoms
2. Frequency of intense itching episodes
3. Degree of bother from AD
4. Impact on sleep
5. Effect on daily activities
6. Influence on mood or emotions

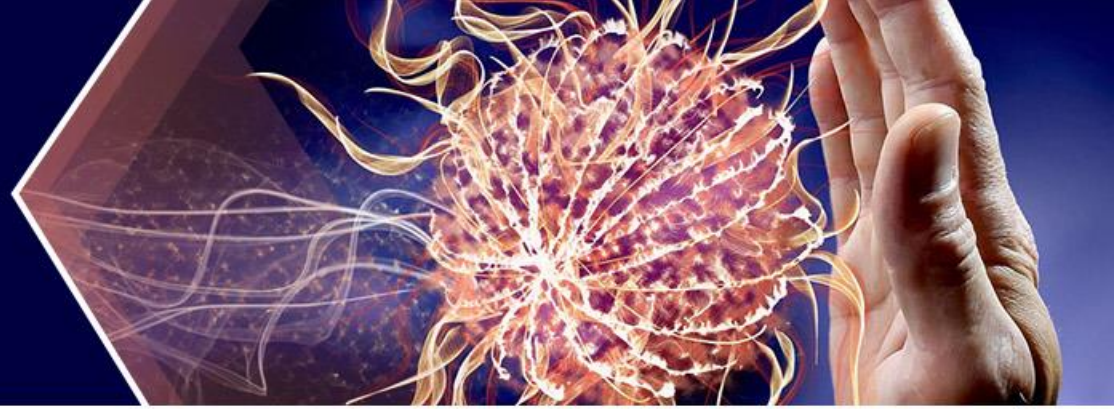
Ginnie scores 19

📊 **Scoring System:**

- Each item scored 0 (none) to 4 (very severe)
- Total score range: 0–24
- AD Controlled: Total < 7
- AD Uncontrolled: Total ≥ 7
- Change ≥5 points = clinically meaningful

1. Pariser DM et al. Curr Med Res Opin. 2020;36(3):367–376. 2. Simpson EL et al. BMC Dermatol. 2019;19(1):15.

Pathophysiology of AD

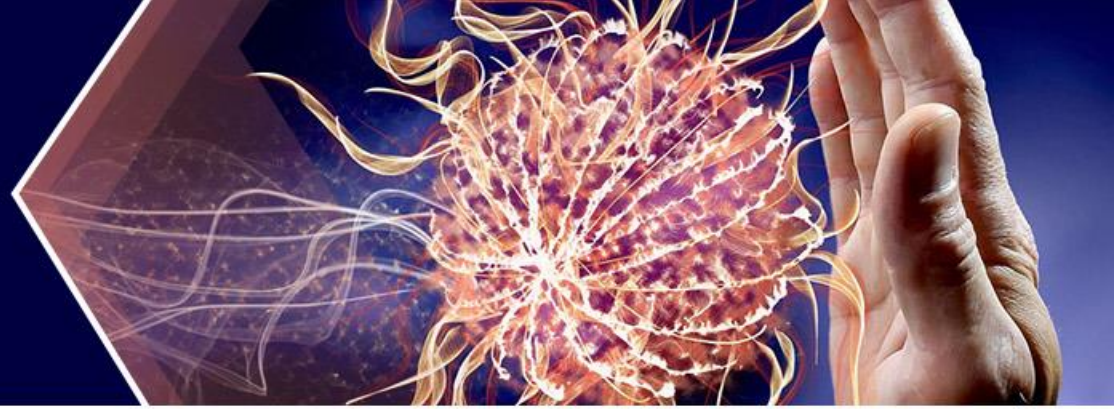


1. **Genetics:** 31 loci associated (e.g.,1q21.3, 5q35.1, 11q35.5, EMSY, LRRC32)
2. **Epithelial barrier dysfunction**
   - Filaggrin null mutation most common single gene defect
   - Lipid abnormalities, reduced fatty acid elongates due to T2 activation
   - Imbalance of stratum corneum protease and antiproteases

1. NJEM 2008;358:1483-94 2. Czarnowicki, T. JACI. 2019l 143:1

Filaggrin (FLG) Null mutation

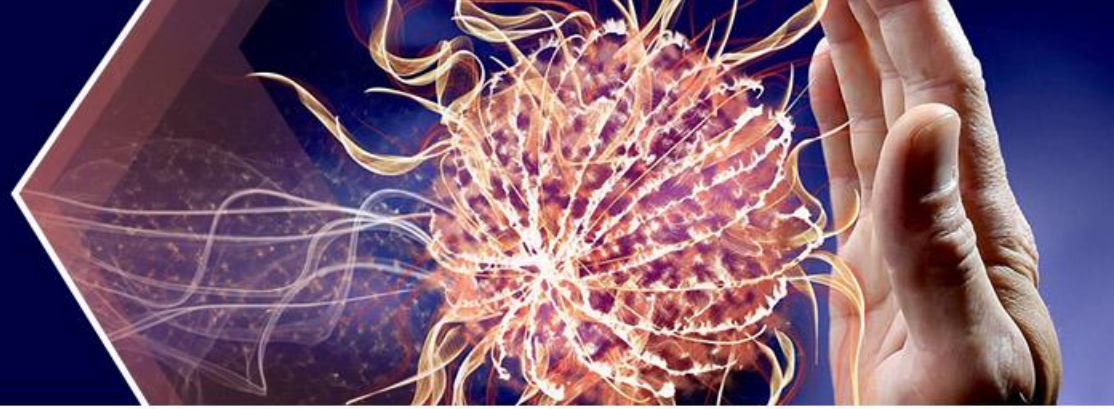
L.P. has low risk



- FLG loss-of-function variants on chromosome 1q23.3 are the most common single gene defect, varies by geographic areas and ethnic origin
- US white children 31.5%
  - US African American children 15.3%
  - African: <1%
- SCORAD scores are usually higher, more widespread dermatitis
- Palmar hyperlinearity (NPV 86%) and/or keratosis pilaris common (NPV 79.3)

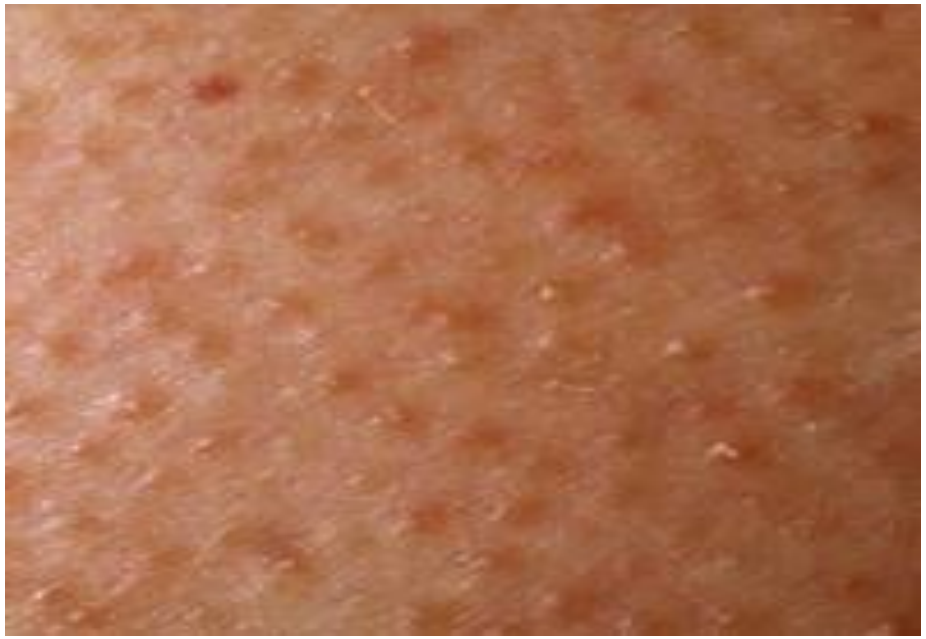
Carson CG, Rasmussen MA, Thyssen JP, Menné T, Bisgaard H (2012) Clinical Presentation of Atopic Dermatitis by Filaggrin Gene Mutation Status during the First 7 Years of Life in a Prospective Cohort Study. PLoS ONE 7(11): e48678. doi:10.1371/journal.pone.0048678
http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0048678

Phenotypes in FLG-null mutations

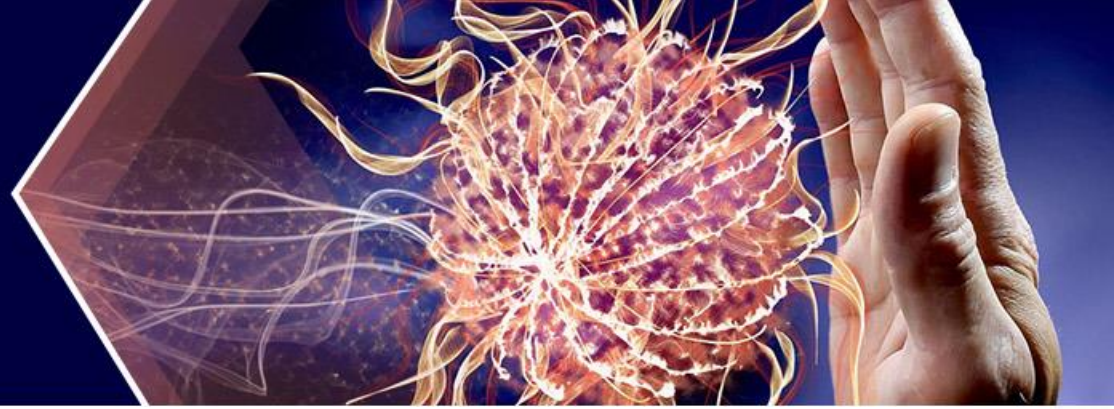


PALMER HYPERLINEARITY

KERATOSIS PILARIS



Filaggrin (FLG) Null mutation



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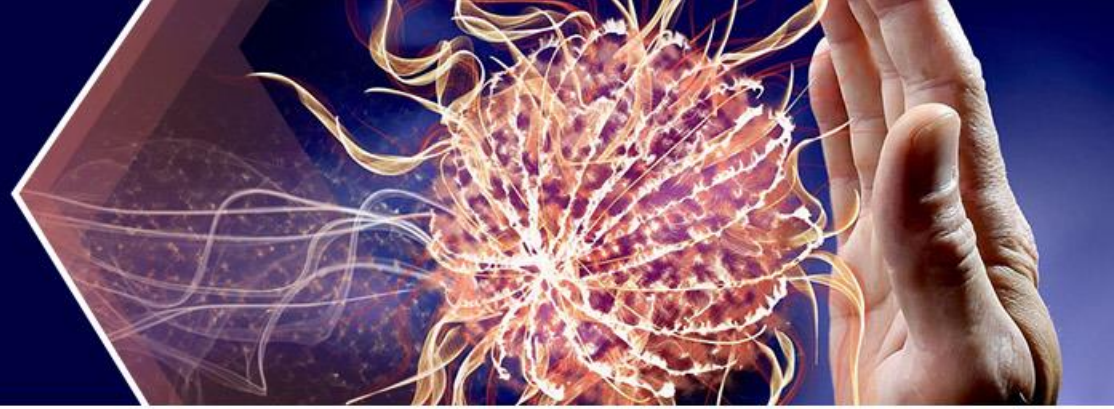
  - US white children 31.5%
  - US African American children 15.3%
  - African: <1%
- SCORAD scores are usually higher, more widespread dermatitis
- Palmar hyperlinearity (NPV 86%) and/or keratosis pilaris common (NPV 79.3)
- Earlier onset of AD
- Persistence into adulthood; hand/foot eczema
- Higher risk for asthma, AR, and food allergy, higher # of contact allergens
- BUT, in all patients, filaggrin expression decreased by Type 2 inflammation

Carson CG, Rasmussen MA, Thyssen JP, Menné T, Bisgaard H (2012) Clinical Presentation of Atopic Dermatitis by Filaggrin Gene Mutation Status during the First 7 Years of Life in a Prospective Cohort Study. PLoS ONE 7(11): e48678. doi:10.1371/journal.pone.0048678 http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0048678

Pathophysiology of AD



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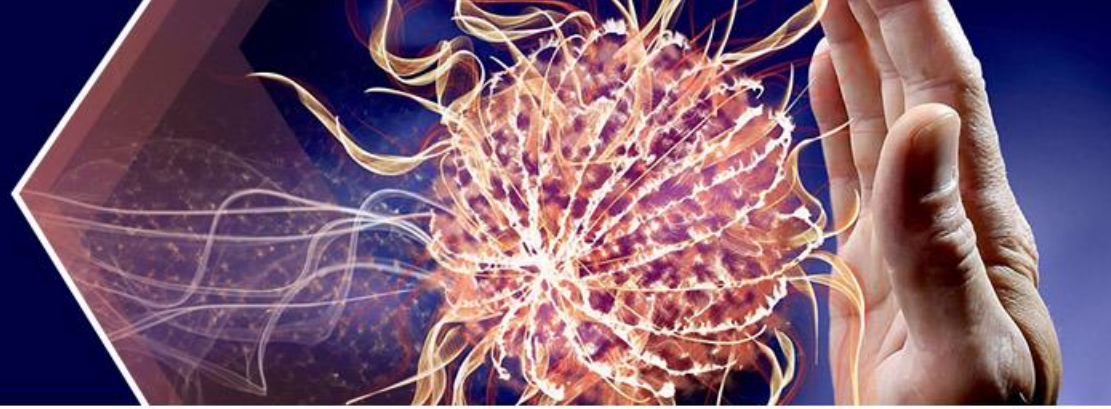
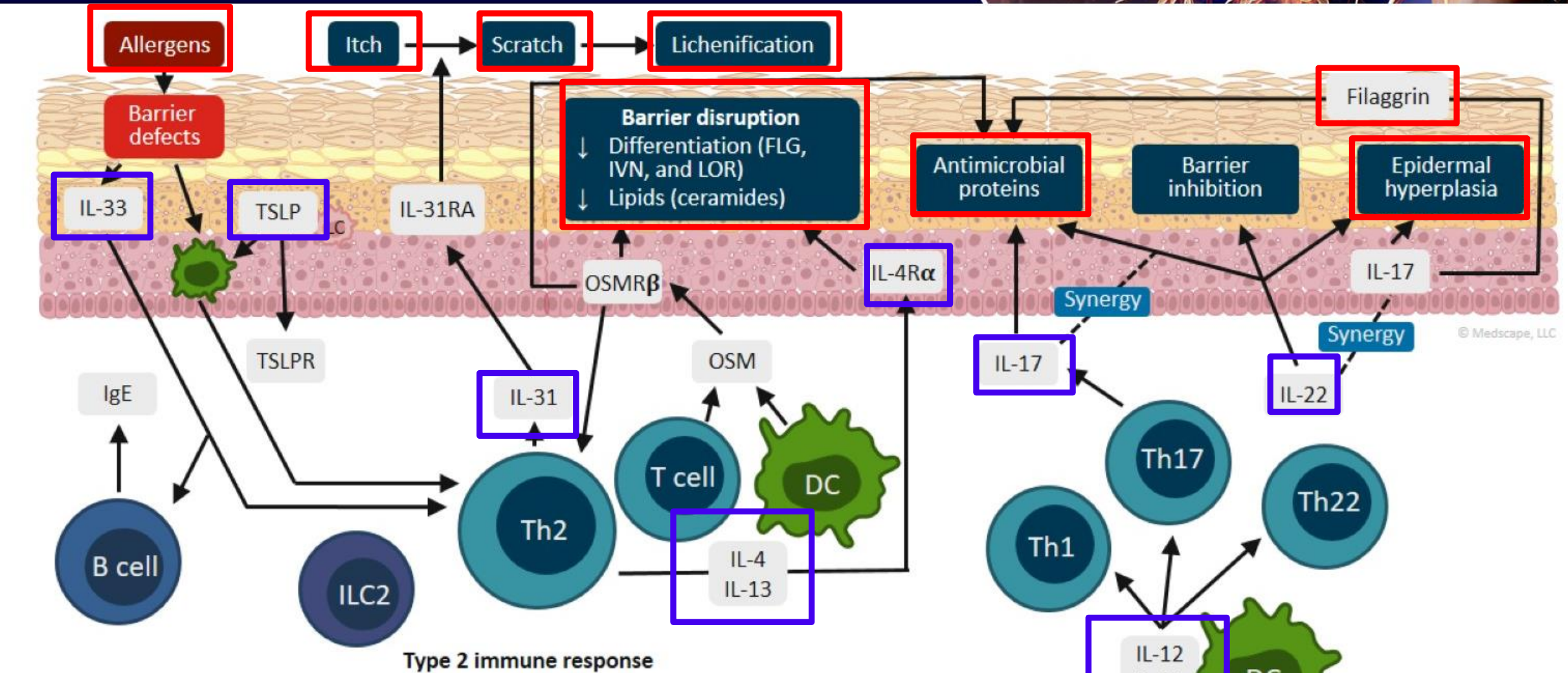
2. **Epithelial barrier dysfunction**
   - Filaggrin null mutation most common single gene defect
   - Lipid abnormalities, reduced fatty acid elongates due to T2 activation
   - Imbalance of stratum corneum protease and antiproteases
3. **Alterations of cutaneous microbiome**
   - Loss of microbial diversity & *Staph aureus & Staph epidermidis* overgrowth
4. **Neuroimmune interactions**
   - Peripheral C-nerve fibers + keratinocytes+Th2 contribute to chronic itch
5. **Immune dysregulation & inflammation: type 2 inflammation**
   - African American ↑ Th2, Th22, ~~Th17,Th1~~

1. NJEM 2008;358:1483-94 2. Czarnowicki, T. JACI. 2019l 143:1

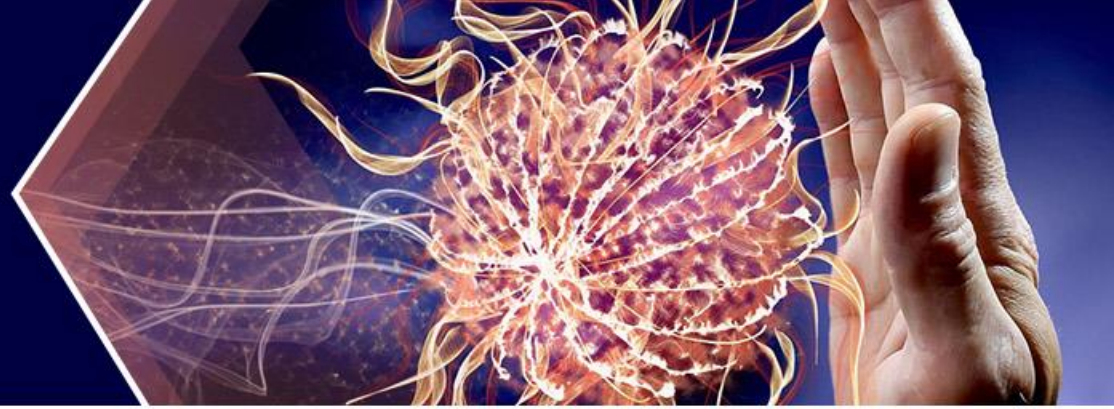
Greater Understanding of AD



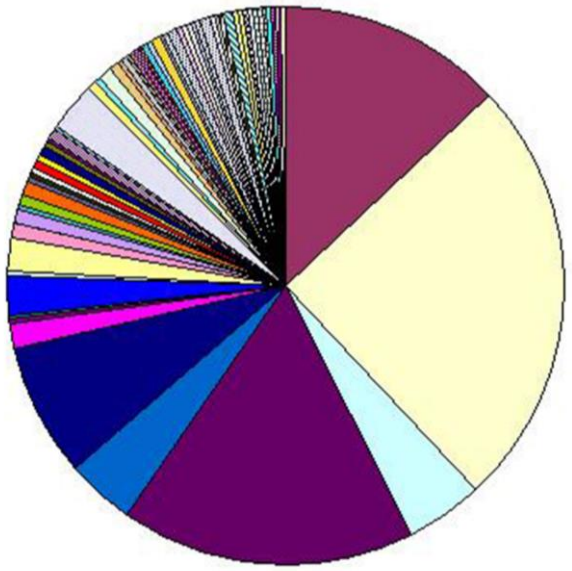


Type 2 immune response

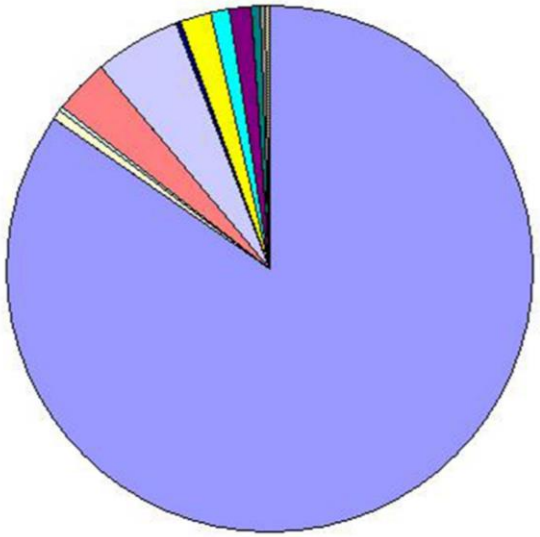
Microbial Diversity

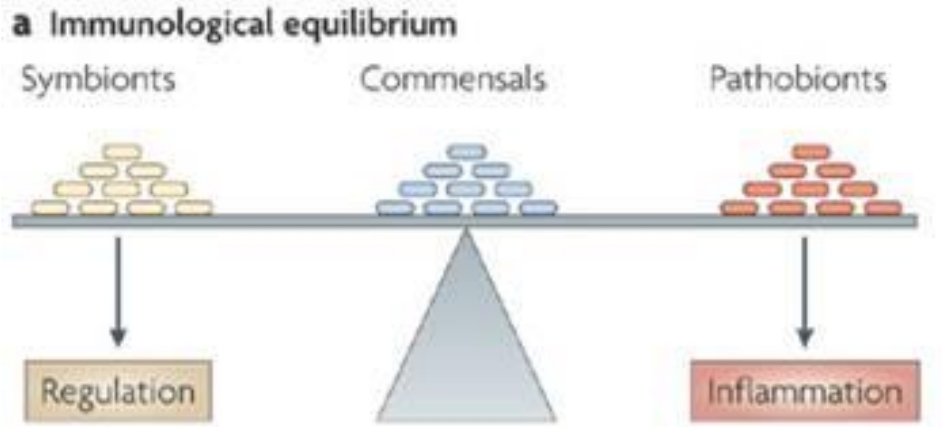


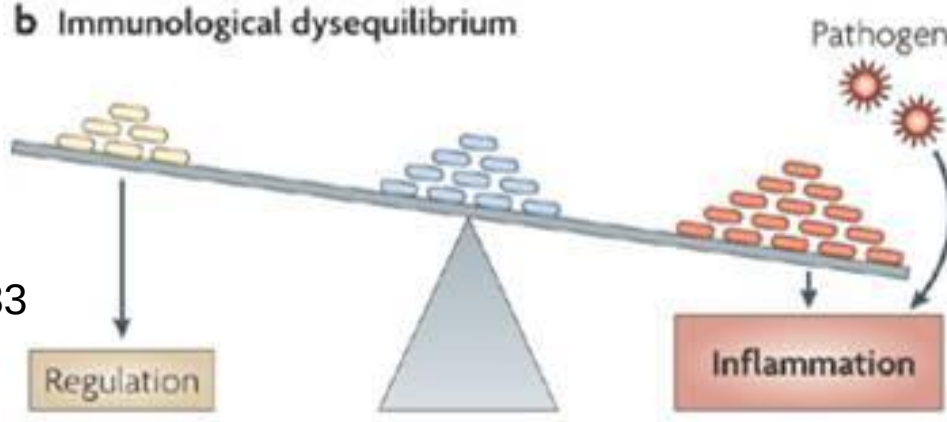
NORMAL



ATOPIC DERMATITIS

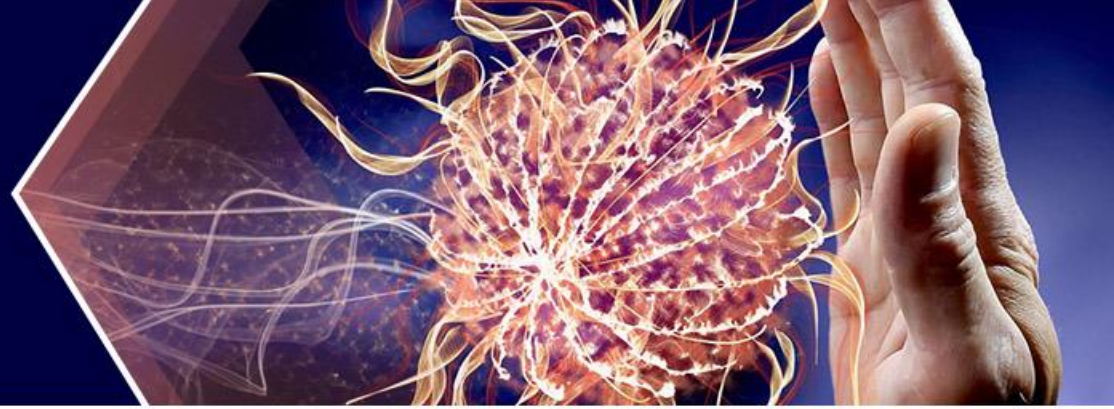






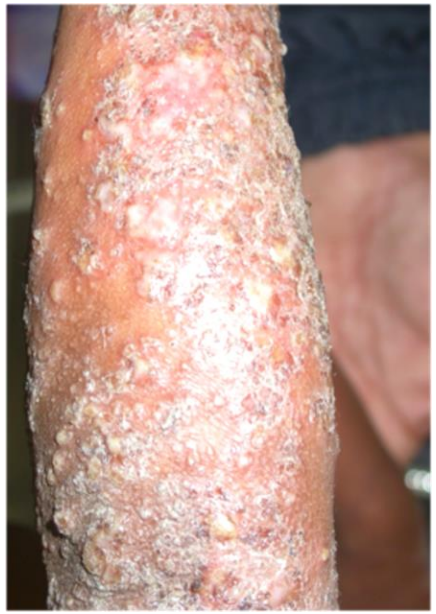
Salava et al. Role of the skin microbiome in atopic dermatitis. CTA 2014; 4, 33

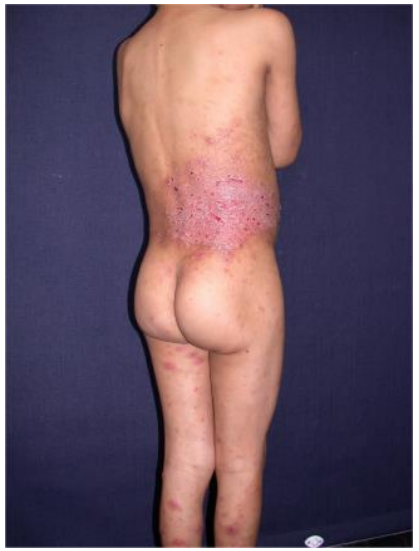
Infections are common



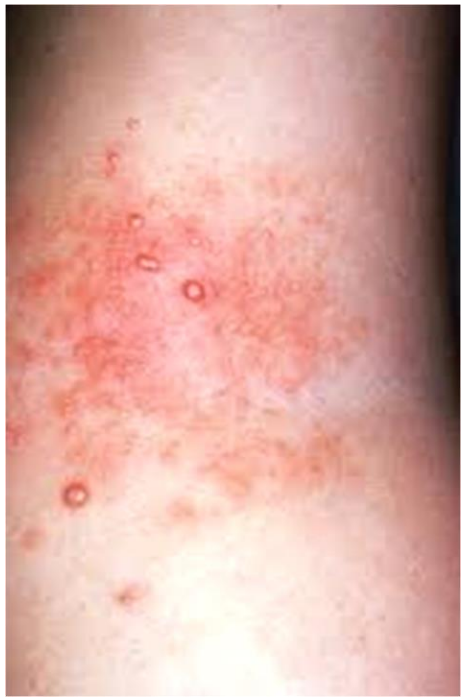
1. Staphylococcus Aureus
2. Candida
3. Herpes Herpeticum
4. Molluscum Contagiosum
5. Less common:
   - Scabies
   - Malassezia

#1





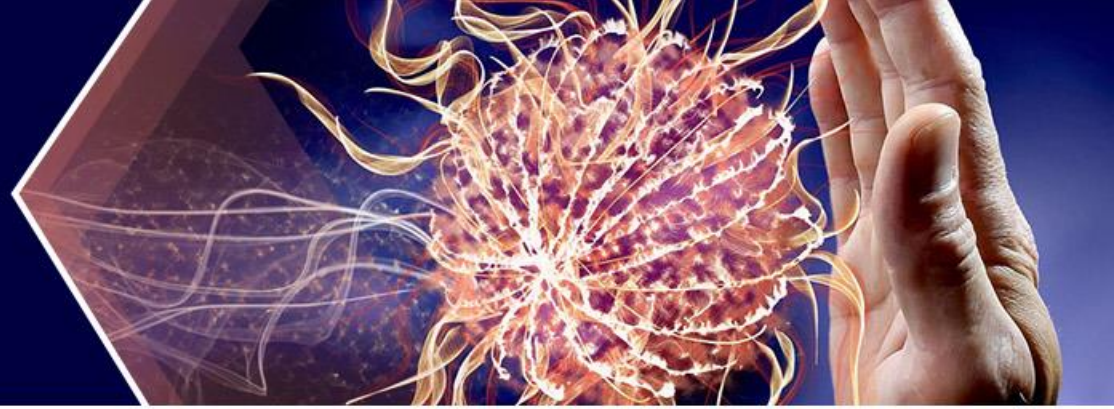
3



4

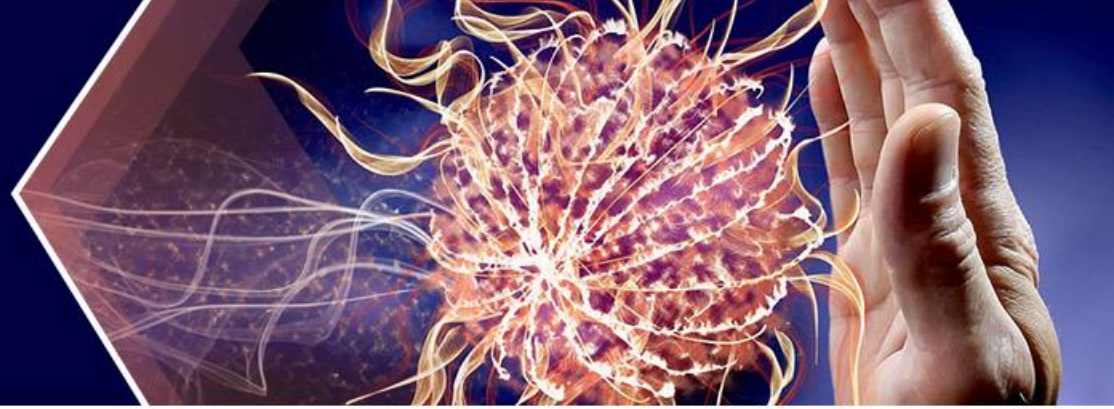
Wollenberg et al. ETFAD/EADV Eczema task force 2020 position paper on diagnosis and treatment of atopic dermatitis in adults and children Journal of the European Academy of Dermatology and Venereol. 2020;34(12):2712-2744

Clinical Features of Atopic Dermatitis



CAUSE	PHENOTYPIC CONSEQUENCE
Defective skin barrier	Ichthyosis, xerosis, palmar hyperlinearity
Irritants / allergens	Pruritus, erythema, chronic variable course
Secondary infection	Oozing, weeping, pain
Scratching	Excoriation, edema, lichenification, flaking

Comorbidities of AD
In addition to atopy

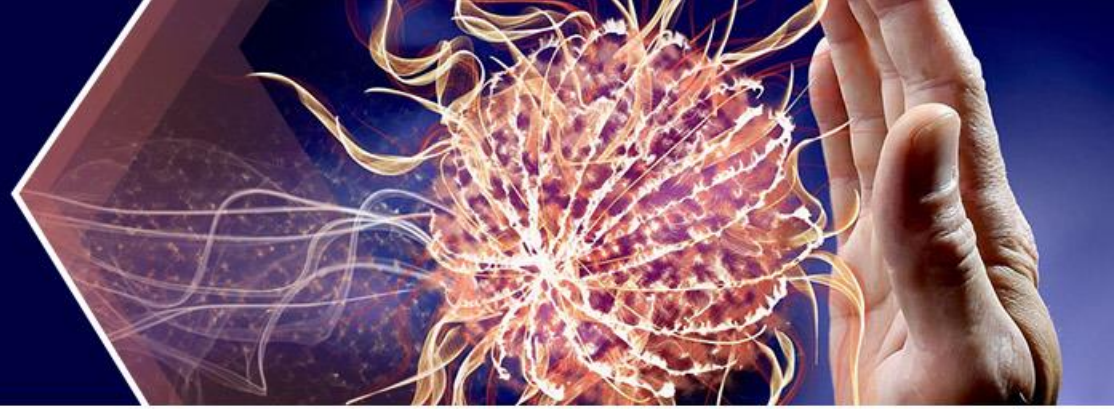


38.2%	**Atopy (allergic rhinitis, asthma, and/or eczema)**
25.5%	Depression or anxiety
24.5%	Hyperlipidemia
21.9%	Hypertension
17.3%	Gastroesophageal reflux disease
14.6%	Thyroid disease
11.1%	Diabetes mellitus
6.3%	Psoriasis and psoriatic arthritis
4.3%	Systemic lupus erythematosus
3.9%	Rheumatoid arthritis
2.0%	Inflammatory bowel disease

GWAS studies: IL-13, CTLA4, IL-2RA, IL-2/IL-21, ULBP3/ULBP6, PRDX5, STX17, and IKZF4/ERBB3 identified in the 1st North American study

Huang KP et al. JAMA Dermatol 2013
Jagielska D et al. J Invest Dermatol. 2012 Sep;132(9):2192-7.

Depression and obesity in AD
Ginnie has BMI of 32.5



- Meta-analysis of 37 observational studies showed depression 2x higher in AD patients (OR 1.71).[1]
  - Subset analysis (14 studies) showed 2x higher suicidal ideation (OR 1.97)[1]
- Meta-analysis of 15 observational studies showed increased suicidal ideation (OR 1.44) and attempts (OR 1.36) in AD patients[2]
- Meta-analysis of 30 observational studies showed increased BMI/obesity associated with risk of AD (OR 1.47)[3]

1. Patel KR. J Am Acad Dermatol 2019; 80:402. 2. Sandhu JK. JAMA Dermatol 2019; 155:178. 3 Zhang A. J Am Acad Dermatol 2015; 72:606.

PHQ-9 depression questionnaire

Name:	Date:			
Over the last 2 weeks, how often have you been bothered by any of the following problems?	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
Little interest or pleasure in doing things	0	1	2	3
Feeling down, depressed, or hopeless	0	1	2	3
Trouble falling or staying asleep, or sleeping too much	0	1	2	3
Feeling tired or having little energy	0	1	2	3
Poor appetite or overeating	0	1	2	3
Feeling bad about yourself, or that you are a failure, or that you have let yourself or your family down	0	1	2	3
Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
Moving or speaking so slowly that other people could have noticed? Or the opposite, being so fidgety or restless that you have been moving around a lot more than usual.	0	1	2	3
Thoughts that you would be better off dead, or of hurting yourself in some way	0	1	2	3
Total ___ =	___	+ ___	+ ___	+ ___

SCORE 0-27

PHQ-9 score ≥10: Likely major depression

Depression score ranges:

5 to 9: mild

10 to 14: moderate

15 to 19: moderately severe

≥20: severe

2023 JTFPP PP Atopic Dermatitis

ATOPIC DERMATITIS

AAAAI/ACAAI JTFPP 2023 guidelines

Clinicians managing all severities of atopic dermatitis should, before issuing any new therapy, address:

1. **Diagnosis** — Ensure correct diagnosis and identify any complicating diagnoses
2. **Education** — Inform about the disease, skin care, and action plan
3. **Triggers** — Address trigger avoidance
4. **Adherence** — Ensure proper medication use/adherence
5. **Moisturizer** — Encourage use of a bland moisturizer at least once a day

A joint guideline made by:

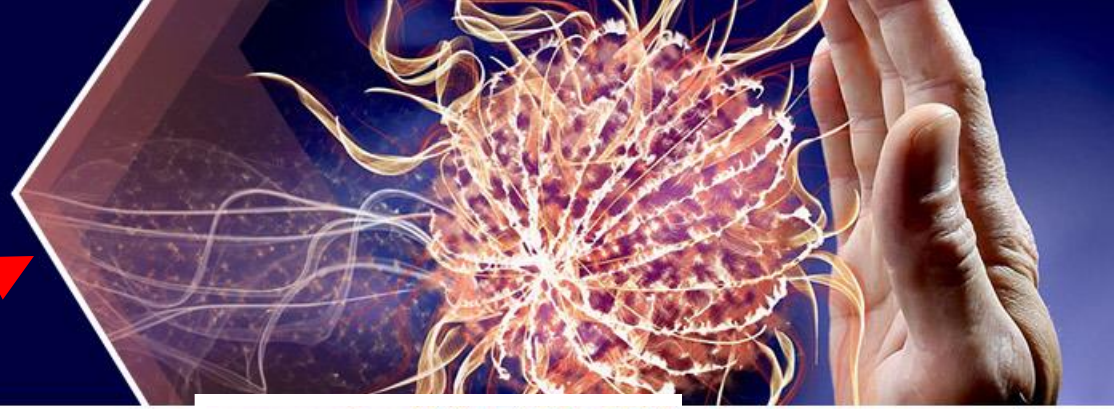
- Patients and caregivers
- Clinical experts: Allergists and dermatologists
- Methodologists
- Allied health: Psychologists, nurses, pharmacists
- Front-line clinicians: Family medicine, pediatricians, internal medicine

FURTHER INFORMATION
Read the full guideline for conditions to consider, practical issues, remarks, and rationales
https://www.allergyparameters.org/
Ann Allergy Asthma Immunol 2023

INTERVENTION Treatment or category of treatments considered	SEVERITY Severity of dermatitis that this recommendation applies to	RECOMMENDATION Text summary of recommendation	STRENGTH The strength of the recommendation	CERTAINTY GRADE rating for the certainty of evidence
TOPICAL TREATMENTS				
If refractory to moisturizers	MILD, MODERATE, SEVERE	**PRESCRIPTION MOISTURIZERS** We **suggest against** using prescription moisturizers rather than a fragrance-free over-the-counter moisturizer	**Conditional** against	**Low** certainty evidence
If refractory to moisturizers	MILD, MODERATE, SEVERE	**TOPICAL CORTICOSTEROIDS** We **recommend** adding a topical corticosteroid Age 3mo+	**Strong** in favor	**High** certainty evidence
If refractory to moisturizers	MILD, MODERATE, SEVERE	**TOPICAL CALCINEURIN INHIBITORS** We **recommend** adding a topical calcineurin inhibitor Age 3mo+	**Strong** in favor	**High** certainty evidence
If refractory to moisturizers	MILD, MODERATE	**TOPICAL PDE4 INHIBITORS** We **suggest** adding crisaborole Age 3mo+	**Conditional** in favor	**Moderate** certainty evidence
If refractory to moisturizers	MILD, MODERATE	**TOPICAL JAK INHIBITORS** We **suggest against** adding topical ruxolitinib Age 12yo+	**Conditional** against	**Low** certainty evidence
If refractory to moisturizers	MILD, MODERATE, SEVERE	**APPLICATION FREQUENCY** We **suggest** applying mid to high potency topical medicines once per day over twice per day	**Conditional** in favor	**Low** certainty evidence
localized lesions refractory to mid to high potency topical treatment	MODERATE, SEVERE	**OCCLUSIVE APPLICATION** (WET WRAPS) We **suggest** a time and body surface area-limited trial of occlusive low to mid potency topical steroid	**Conditional** in favor	**Very low** certainty evidence
	MILD, MODERATE, SEVERE	**TOPICAL ANTIMICROBIALS** We **suggest against** adding topical antimicrobials to topical anti-inflammatories in patients with no clear signs of infection	**Conditional** against	**Very low** certainty evidence
	MILD, MODERATE, SEVERE	**MAINTENANCE OF REMISSION** We **recommend** use of proactive therapy to areas that flare with a topical calcineurin inhibitor or mid potency topical steroid	**Strong** in favor	**Moderate** certainty evidence
Chu et al Network meta-analysis; Devasenapathy & Chu meta-analysis				
BLEACH BATHS	MODERATE, SEVERE	We **suggest** adding dilute bleach bathing	**Conditional** in favor	**Moderate** certainty evidence

Annals of Allergy, Asthma & Immunology 2024 132(3):274-312.e3. DOI: (10.1016/j.anai.2023.11.009)

Treatment Strategy for Atopic Dermatitis



Severe

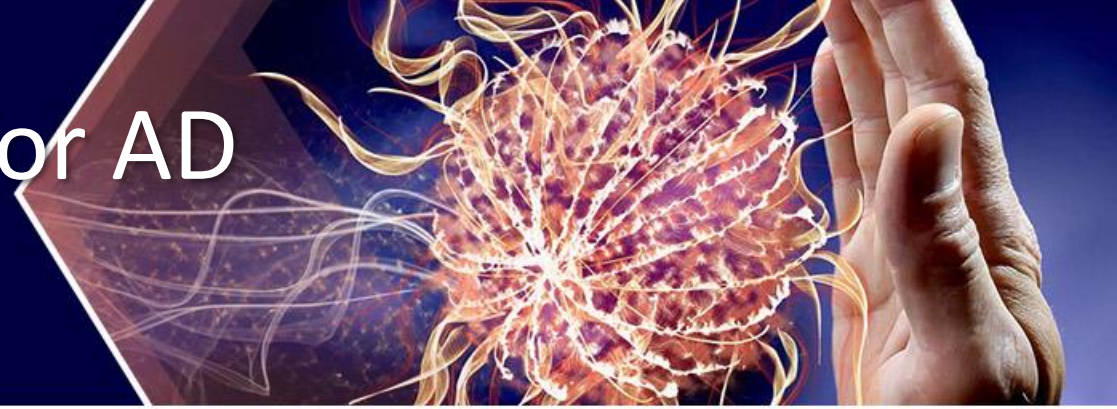
Moderate to severe

Mild-Moderate

Dry Skin & all stages

Hydration of Skin- Emollient
Identify and avoid triggers: contact allergens, aeroallergens, irritants, microorganisms, food

Dust and Cockroach Avoidance for AD Limited evidence of benefit



- **Dust Mites: Environmental reduction in sensitized AD patients has not been beneficial in controlling disease(2015 Cochrane Systematic review)[1-2]**
- **Cockroach Allergen Avoidance: Experimental models support a role in AD pathogenesis, but clinical evidence is limited.[3-4]**
- **Environmental control measures (e.g., pest management, cleaning) may be considered to reduce exposure to both**

1.Bumbacea, RS. Experimental and Therapeutic mediine.2020 20(4):3554. 2. Nankervis, H. Cochrane Database Syst Rev. 2015.:CD008426.
3. Lee M-F. 35 al. (2023) Indoor aeroallergens from American cockroaches and mites initiate atopic march via cutaneous contact in a murine model. ONE 18(7): e0289138. https://doi.org/10.1371/journal.pone.0289138. 4. Luo et al. 2022 JCI Insight. 7 (5) https://doi.org/10.1172/jci.insight.152559

Emollients

Start with the Basics: Emollients

$10.72/ oz

$0.91 oz

$0.80 oz

- Vanicream Moisturizing Cream ($0.85/oz)
- Cephaphil ($0.80/oz)
- CeraVe ($0.91/oz)
- Vaseline is most cost effective and chemical free ($0.64/oz)
- No scientific evidence that one emollient is more efficacious tha another.

Emollients

Start with the Basics: Emollients

$10.72/ oz

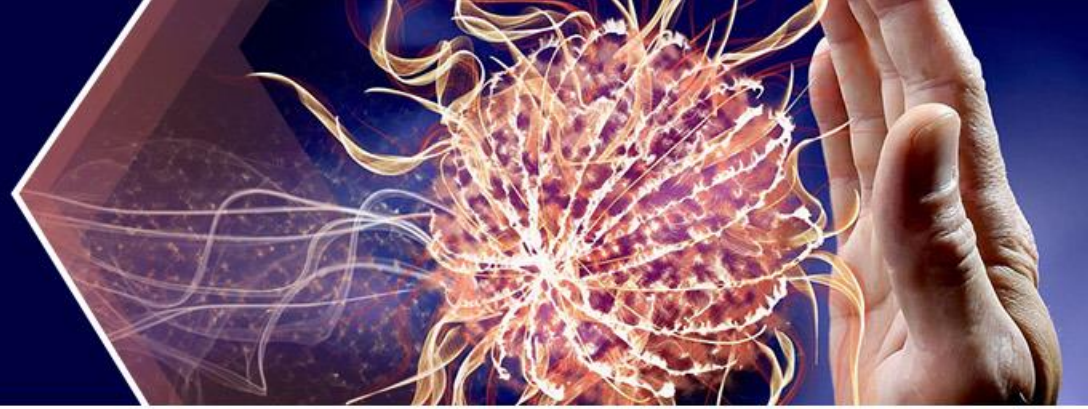
$0.91 oz

$0.80 oz

- Vanicream Moisturizing Cream ($0.85/oz)
- [illegible] ($0.80/oz)
- [illegible] and chemical free ($0.64/oz)
- No scientific evidence that one emollient is more efficacious tha another.

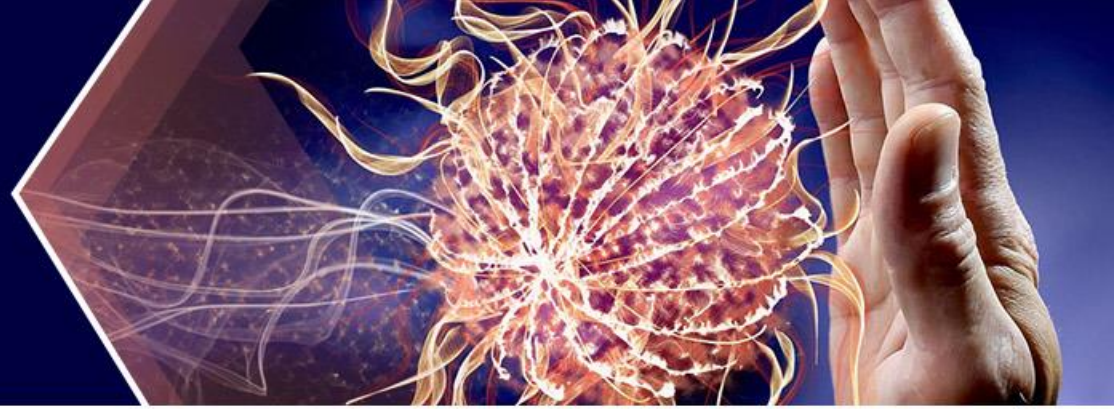
SEVERITY	RECOMMENDATION	STRENGTH	CERTAINTY
Severity of dermatitis that this recommendation applies to	Text summary of recommendation	The strength of the recommendation	GRADE rating for the certainty of evidence
MILD MODERATE SEVERE	**PRESCRIPTION MOISTURIZERS** We **suggest against** using prescription moisturizers rather than a fragrance-free over-the-counter moisturizer	**Conditional** against	**Low** certainty evidence

Emollients



- Oil based emollients are effective for restoring skin barrier function in AD.
- Creams and lotions may be less effective than ointments due to the lower proportion of oil
- Use a spatula or a pump action container
- Use regularly at least twice daily (preferably more) as a preve strategy, even if the skin is clear.
- In severe AD, use as often as possible, preferably 6-8 times a day or more!
- Use at least 30 g/day or 1 kg/month for an adult,

Steps to Soak and Seal



The soak and seal method is recommended to combat dry skin and reduce flares. To get the full benefit, soak and seal often and follow the steps in order.

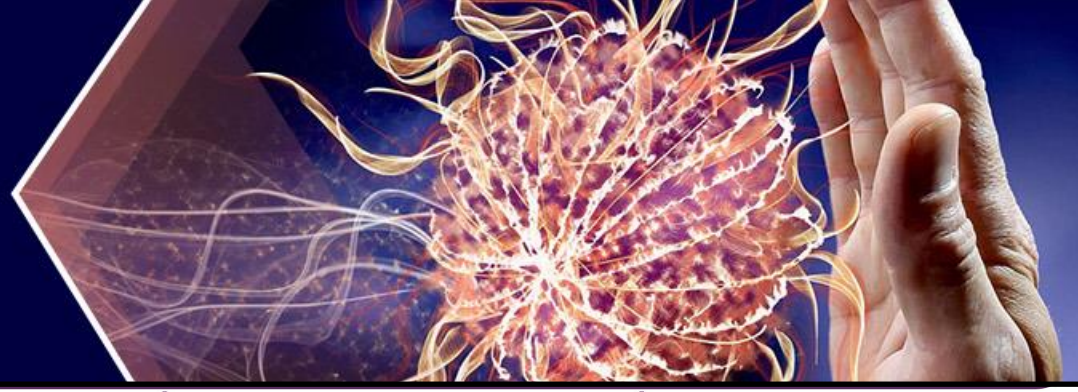
1 Bathtub
Warm water

2 Blot dry

3 RX Meds
Steroids,
Calcineurin inhibitors

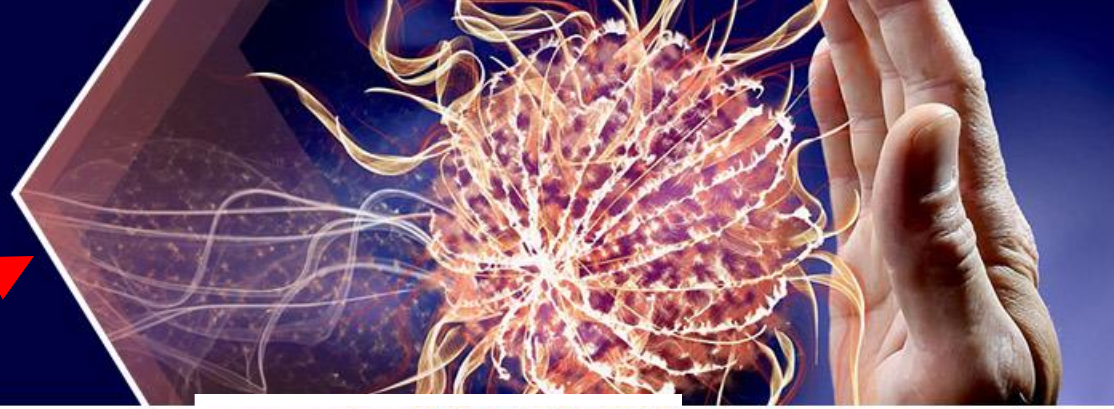
4 Emollients

Steps to Soak and Seal



INTERVENTION Treatment or category of treatments considered	SEVERITY Severity of dermatitis that this recommendation applies to	RECOMMENDATION Text summary of recommendation	STRENGTH The strength of the recommendation	CERTAINTY GRADE rating for the certainty of evidence
BLEACH BATHS  Bakaa et al 2022. Systematic review	MODERATE, SEVERE	We **suggest** adding dilute bleach bathing	**Conditional** in favor	**Low** certainty evidence
	MILD	We **suggest against** adding dilute bleach bathing	**Conditional** against	**Low** certainty evidence

Treatment Strategy for Atopic Dermatitis



Mild-Moderate

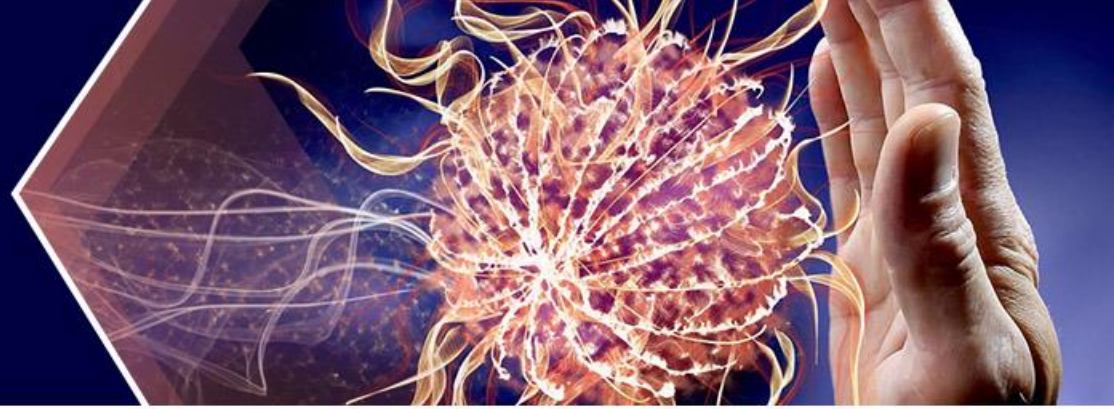
Acute: Midpotent /Superpotent Steroids (acute: qd to bid);
Chronic: Low-med potent steroids qod OR 2 consecutive days/wk. to previous areas

Topical Corticosteroids
Topical Calcineurin Inhibitors
PDE4; Antibiotics if needed
Topical JAK Inhibitors (Ruxolitinib)

Dry Skin & all stages

Hydration of Skin- Emollient
Identify and avoid triggers: contact allergens, aeroallergens, irritants, microorganisms, food

Topical Treatments for Mild-Moderate Disease



Corticosteroids: First line treatment but can cause skin atrophy & thinning

Non Steroidal

cAMP, cyclic adenosine monophosphate; PDE4, phosphodiesterase 4.

Boguniewicz M, et al. *Ann Allergy Asthma Immunol*. 2018:120:10-22; Paller AS, et al. *J Allergy Clin Immunol*. 2017;140:633-643.

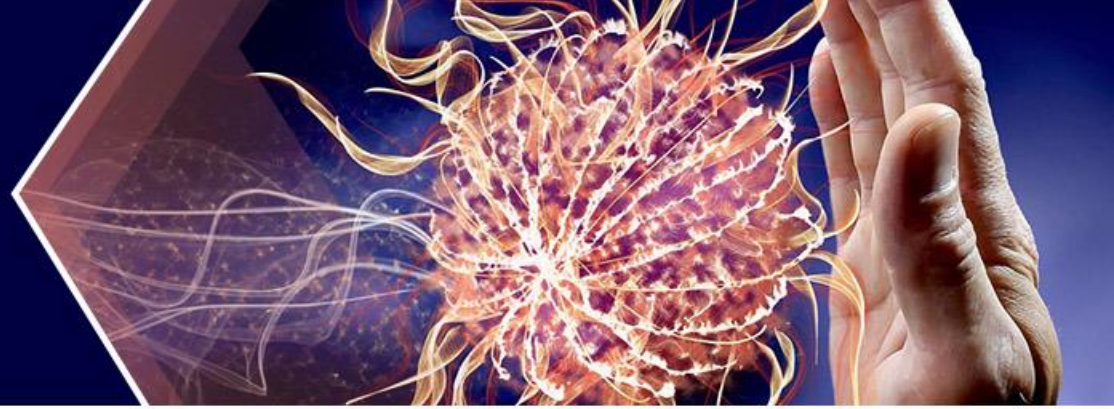
Topical Steroids Potency Table

Ginnie is using Class 2 & a 3-4 agent

Class	Drug	Vehicle	Strength (%)
Superpotent (1)	Augmented betamethasone dipropionate	O	0.05
	Clobetasol propionate	C F O	0.05
	Diflorasone diacetate	O	0.05
	Halobetasol propionate	C O	0.05
Potent (2)	Amcinonide	C L O	0.1
	Augmented betamethasone dipropionate	C	0.05
	Betamethasone dipropionate	C F O S	0.05
	Desoximetasone	C O	0.25
	Desoximetasone	G	0.05
	Diflorasone diacetate	C	0.05
	Fluocinonide	C G O S	0.05
	Halcinonide	C O	0.1
	Mometasone furoate	O	0.1
	Triamcinolone acetonide	C O	0.5
Mid-Strength (3 – 4)	Betamethasone valerate	C F L O	0.1
	Clocortolone pivalate	C	0.1
	Desoximetasone	C	0.05
	Fluocinolone acetonide	C O	0.025
	Flurandrenolide	C O	0.05
	Fluticasone propionate	C	0.05
	Fluticasone propionate	O	0.005
	Mometasone furoate	C	0.1
	Triamcinolone acetonide	C O	0.1
Lower Mid-Strength (5)	Hydrocortisone butyrate	C O S	0.1
	Hydrocortisone probutate	C	0.1
	Hydrocortisone valerate	C O	0.2
	Prednicarbate	C	0.1
Mild (6)	Alclometasone dipropionate	C O	0.05
	Desonide	C G F O	0.05
	Fluocinolone acetonide	C S	0.01

- Topical steroids come in a range of strengths from mild to very potent.
- They come in different vehicles like ointments, creams and lotions.
- Ointments may be better for very dry areas.
- Creams might be better for wetter areas.
- Lotions might be better for hairy areas.

Topical Treatments for Mild-Moderate Disease



Corticosteroids: First line treatment but can cause skin atrophy & thinning

Non Steroidal

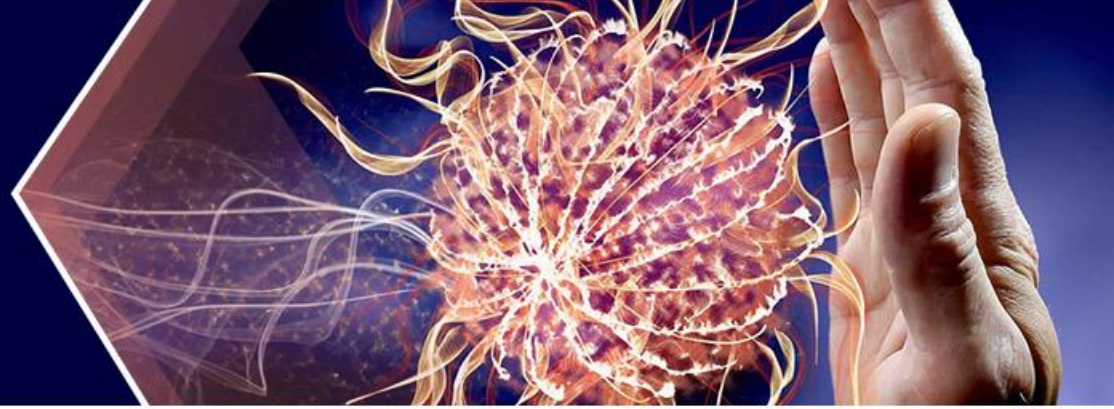
Calcineurin Inhibitors

- Tacrolimus & Pimecrolimus
- Especially useful in areas prone to atrophy: eyelid, perioral, genital, axilla, inguinal

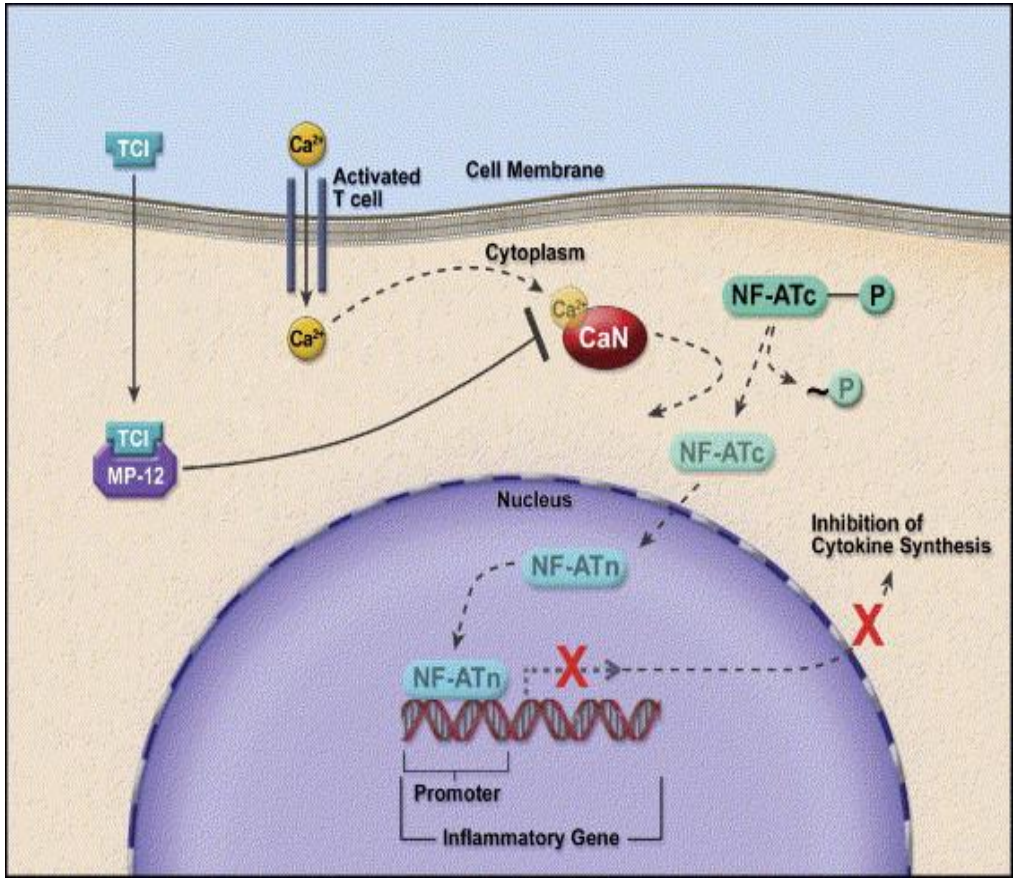
cAMP, cyclic adenosine monophosphate; PDE4, phosphodiesterase 4.

Boguniewicz M, et al. *Ann Allergy Asthma Immunol*. 2018:120:10-22; Paller AS, et al. *J Allergy Clin Immunol*. 2017;140:633-643.

Topical Calcineurin Inhibitors

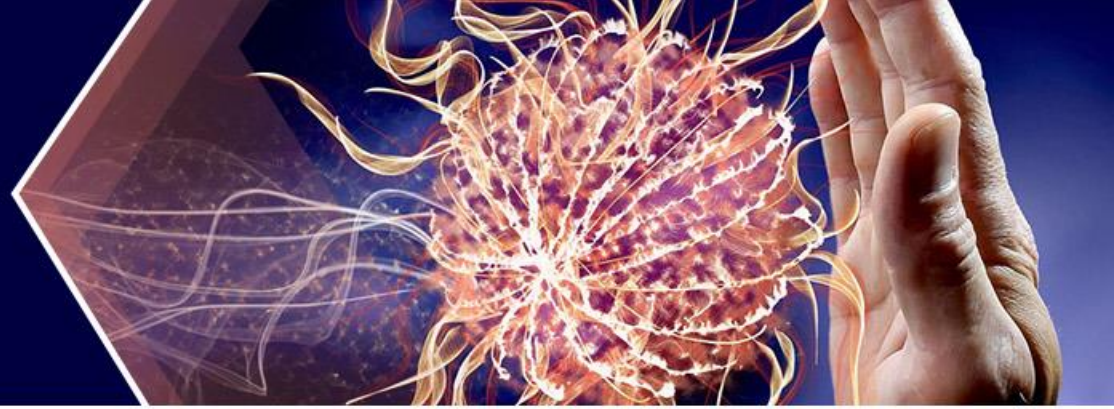


- Inhibit T-cell activation & production of pro-inflammatory cytokines
- Anti-inflammatory potency:
  0.1% & 0.03% Tacrolimus ~ intermediate strength Corticosteroid (Group 4-5)
  0.1%Tacrolimus potency >1% Pimecrolimus
- Tacrolimus preferred over Pimecrolimus
- May cause transient “burning”
- Uses (no skin atrophy)
  - Mild flares
  - In-between flares to prevent symptoms and possibly reduce the need for topical steroids



Norris DA. Mechanisms of action of topical therapies and the rationale for combination therapy. J Am Acad Dermatol. 2005;53(1 Suppl 1):S17-25

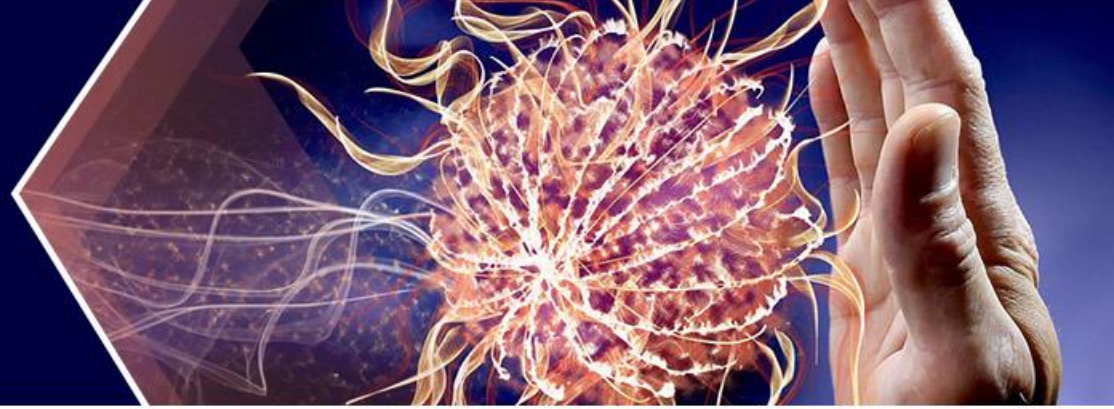
Cancer risk for TCI's



- **Comprehensive Meta-Analysis (2023)**[1]
  A systematic review and meta-analysis encompassing over 3.4 million patients across 110 studies found no significant increase in overall cancer risk associated with TCI use. The study concluded that TCIs are safe for treating AD in both children and adults.
- A 2021 meta-analysis reported a relative risk of 1.03 (95% CI: 0.92–1.16) for overall cancer (including lymphoma), indicating no significant association.[2]
- While current data are reassuring, clinicians should continue to monitor patients for any adverse effects and stay updated with ongoing research.

1. Devasenapathy N, et al. Lancet Child Adolesc Health. 2023;7(1):13–25.
2. Lam M, et al. JAMA Dermatol. 2021;157(5):549–558.

Topical Treatments for Mild-Moderate Disease



Corticosteroids: First line treatment but can cause skin atrophy & thinning

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- Especially useful in areas prone to atrophy: eyelid, perioral, genital, axilla, inguinal

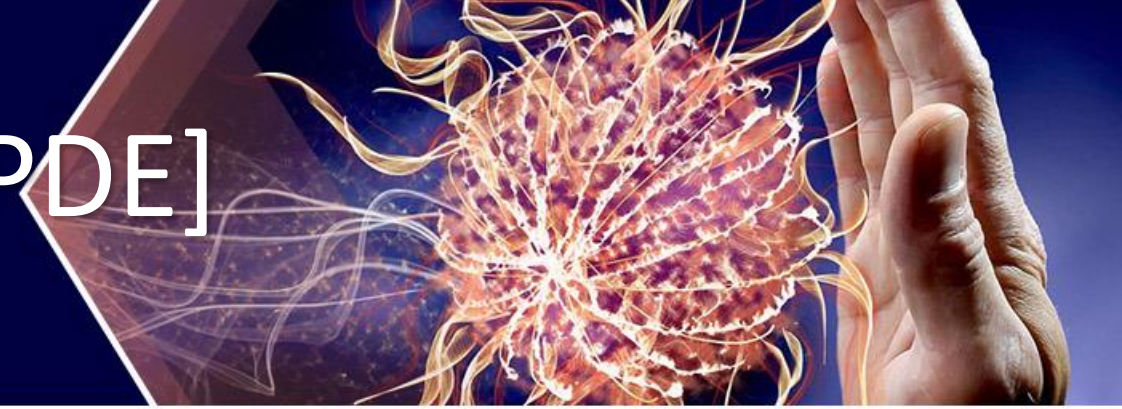
PDE4 Inhibitor

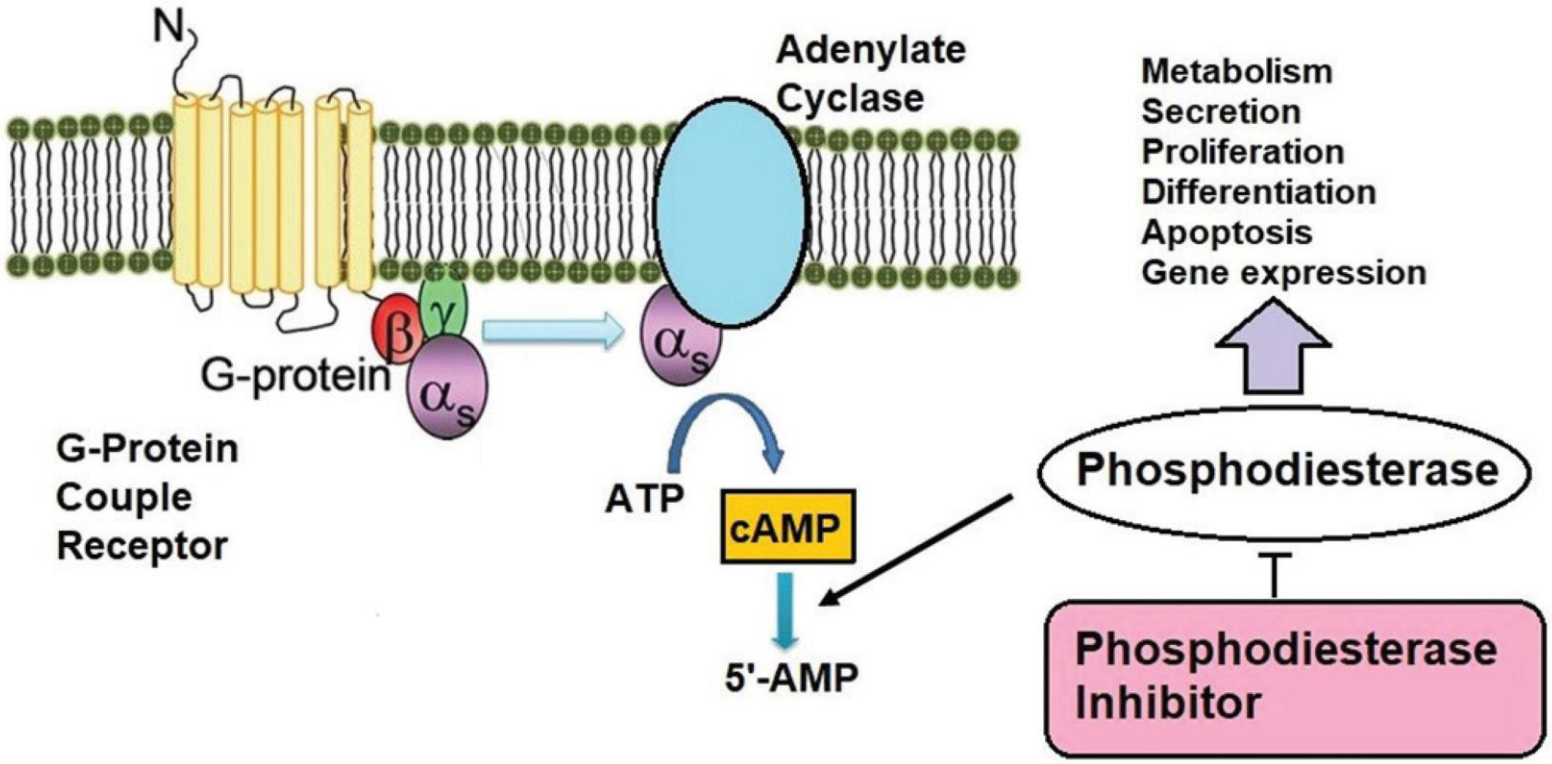
- Crisaborole
- Inhibits cAMP levels
- PDE4 directly regulates pruritus
- Favorable safety profile

cAMP, cyclic adenosine monophosphate; PDE4, phosphodiesterase 4.

Boguniewicz M, et al. *Ann Allergy Asthma Immunol*. 2018:120:10-22; Paller AS, et al. *J Allergy Clin Immunol*. 2017;140:633-643.

Anti-phosphodiesterase [PDE]





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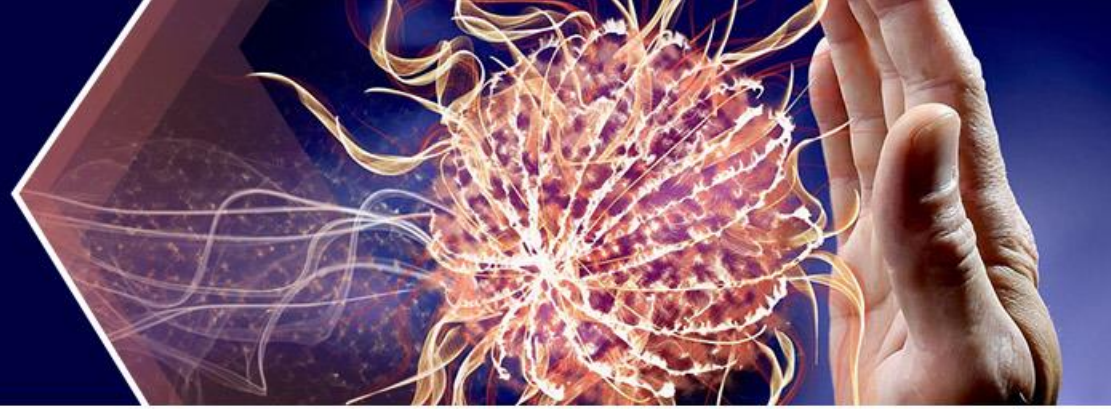
Brunner, E Guttman-Yassky, D Leung. The immunology of atopic dermatitis and its reversibility with broad-spectrum and targeted therapies. J Allergy Clin Immunol 2017;139:S65-76

Topical Treatments for Mild-Moderate Disease



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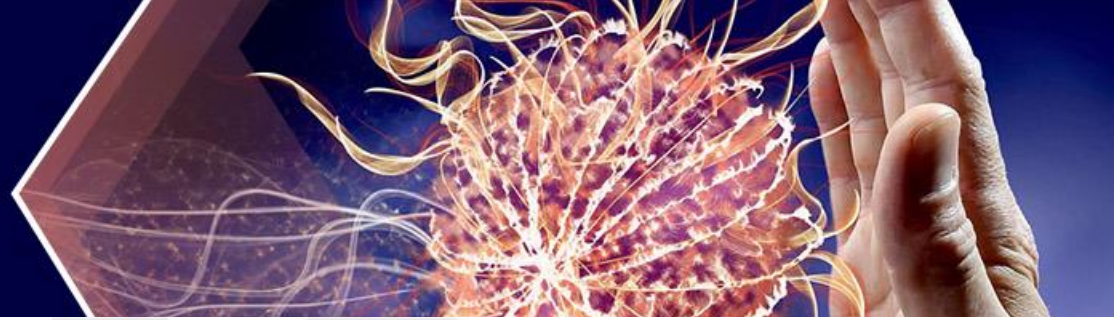
JAK Inhibitor: Ruxolitinib

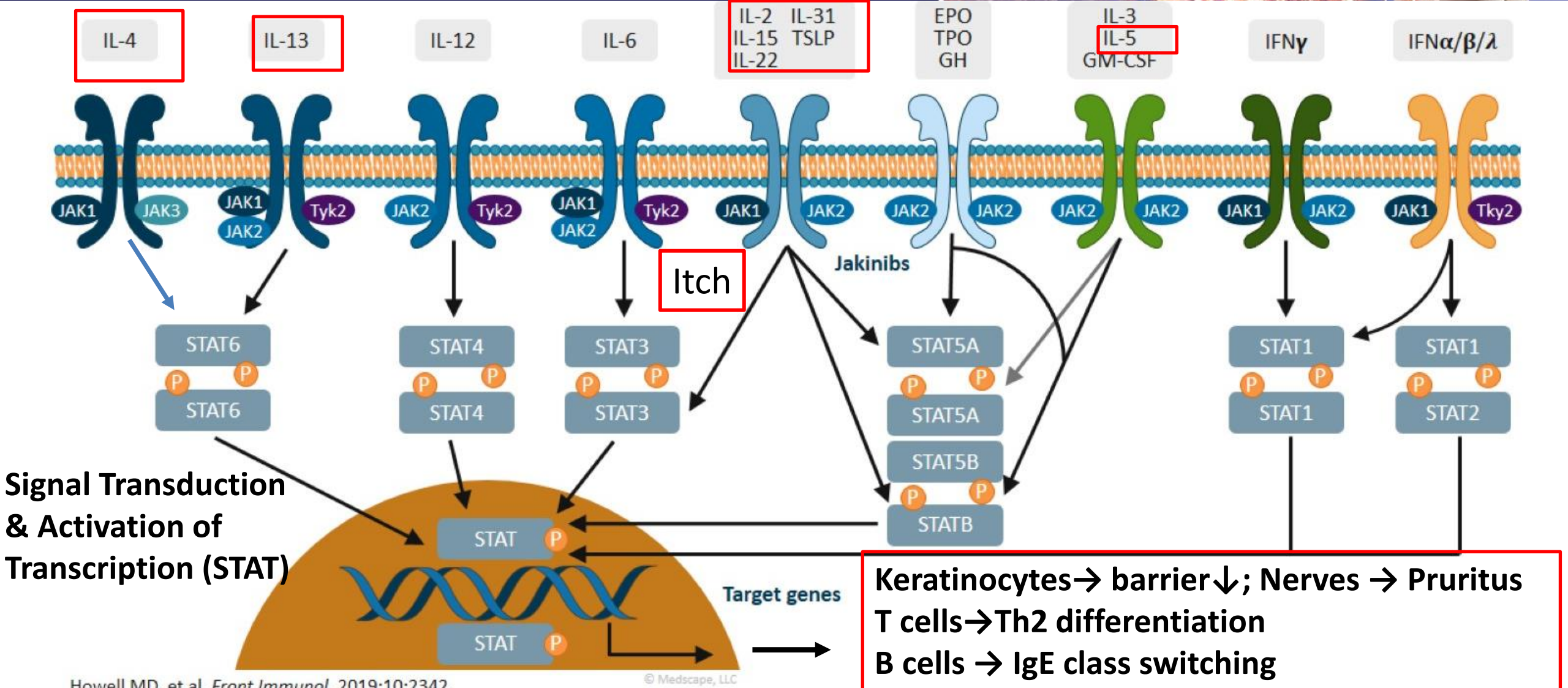
- Blocks intracellular signaling pathway on which many proinflammatory cytokines elicit their pathophysiologic functions

cAMP, cyclic adenosine monophosphate; PDE4, phosphodiesterase 4.

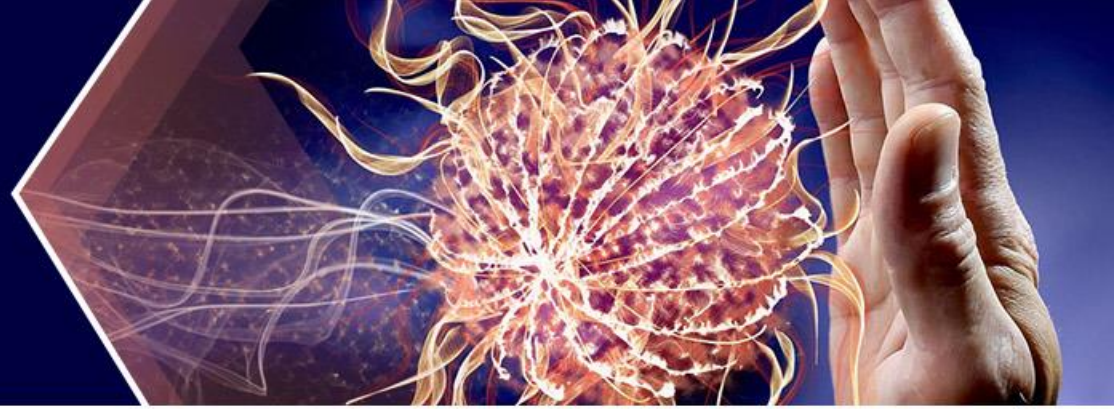
Boguniewicz M, et al. *Ann Allergy Asthma Immunol*. 2018:120:10-22; Paller AS, et al. *J Allergy Clin Immunol*. 2017;140:633-643.

JAK-STAT in Cytokine Signaling
Master downstream regulator



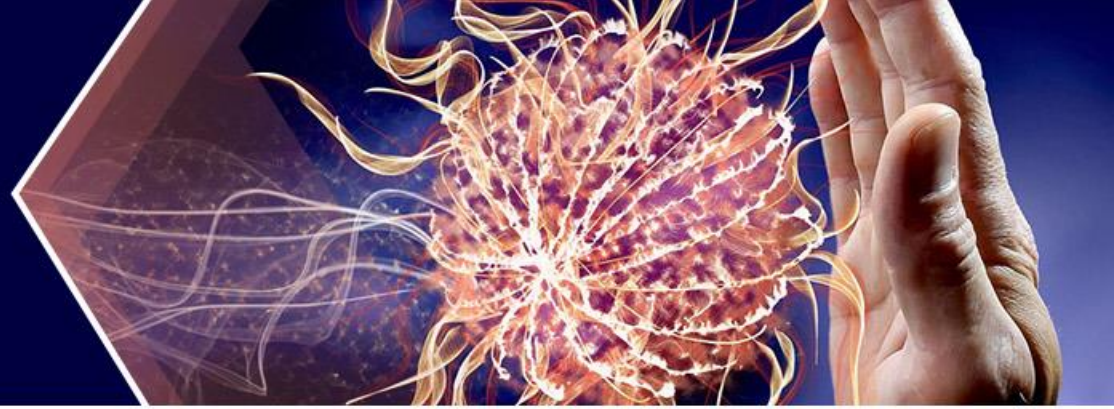


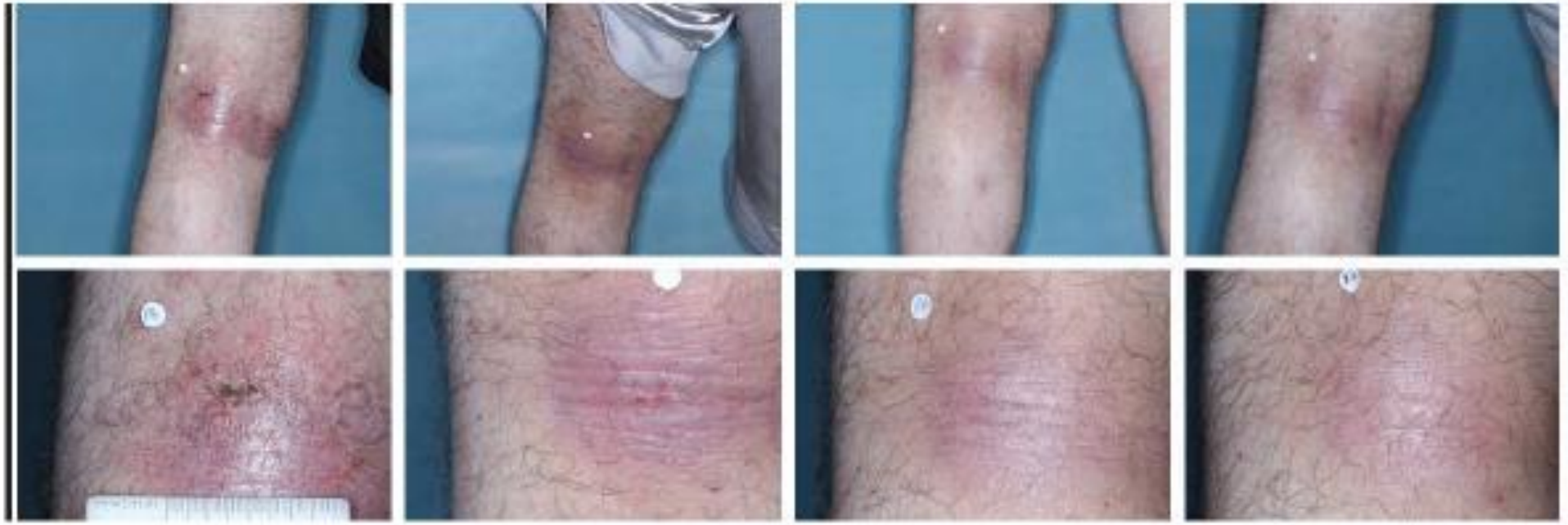
Topical JAK Inhibitor



- Ruxolitinib 1.6 % cream
- Blocks JAK 1/2
- Blocks intracellular signaling pathway on which many proinflammatory cytokines elicit their pathophysiologic functions
- Approved for mild to moderate Atopic dermatitis
- Use on ≤20% body surface area
- Use intermittently
- Thrombocytopenia, anemia, neutropenia reported
- CBC monitoring as “clinically indicated”

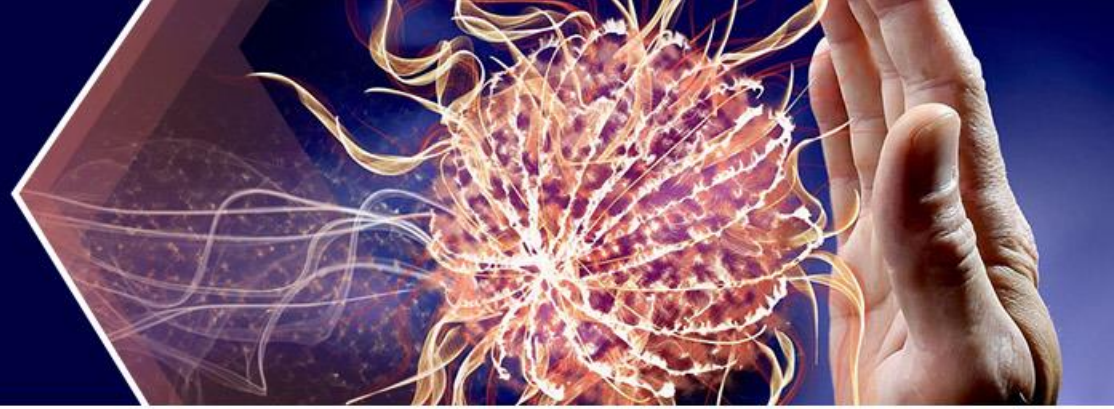
Ruxolitinib 1.5% cream



	Baseline	Week 2	Week 4	Week 8
Patient 2 1.5% RUX				

Ruxolitinib 1.5% Cream Black Box Warning

* {Side effects reported with topical agents



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

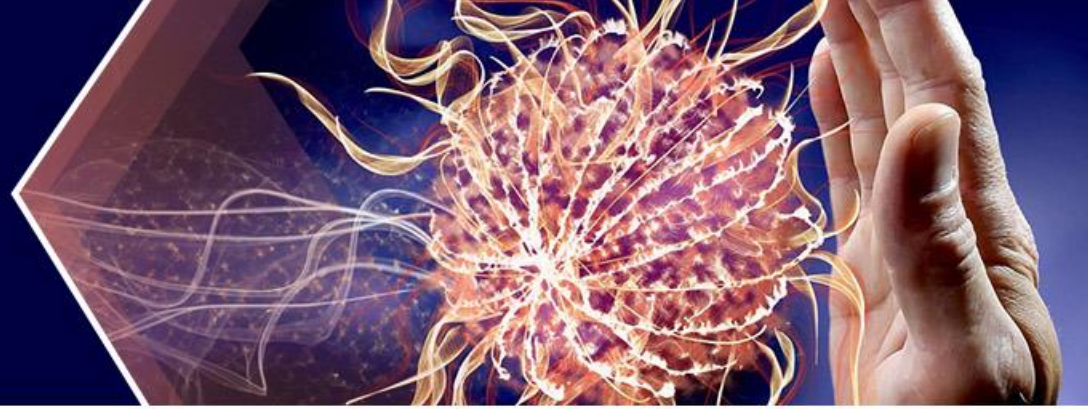
See full prescribing Information for complete boxed warning.

- 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 rates 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 condition. (5.6)

MACE=Major adverse cardiovascular events

- Serious infections:
  - None reported with topical cream in AD patients
- Mortality:
  - None reported in AD patients
- Malignancy:
  - Lymphoma, etc. Oral Tx inflammatory conditions
  - * Non-melanoma skin C/A in topical Tx (vitiligo & ? AD in 2 cases)
- MACE:
  - None reported in AD patients
- Thrombosis
  - No reported cases in topical use in AD patients
- Post-marking surveillance data is very encouraging for these side effects from topical administration

Topical Treatments for Mild-Moderate Disease
JTFPP 2023 Recommendations



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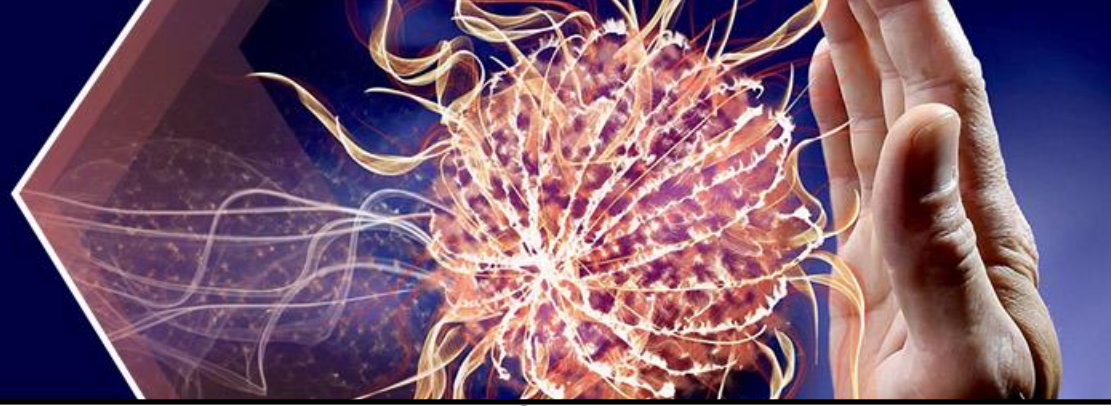
Topical Treatments for Mild-Moderate Disease
JTFPP 2023 Recommendations

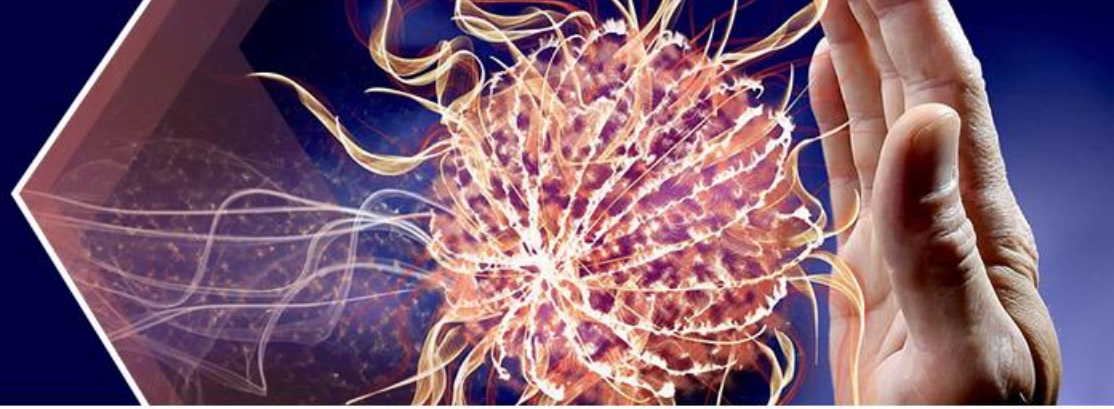


SEVERITY Severity of dermatitis that this recommendation applies to	RECOMMENDATION Text summary of recommendation	STRENGTH The strength of the recommendation	CERTAINTY GRADE rating for the certainty of evidence
MILD, MODERATE, SEVERE	**TOPICAL CORTICOSTEROIDS** We **recommend** adding a topical corticosteroid Age 3mo+	**Strong** in favor	**High** certainty evidence
MILD, MODERATE, SEVERE	**TOPICAL CALCINEURIN INHIBITORS** We **recommend** adding a topical calcineurin inhibitor Age 3mo+	**Strong** in favor	**High** certainty evidence
MILD, MODERATE	**TOPICAL PDE4 INHIBITORS** We **suggest** adding crisaborole Age 3mo+	**Conditional** in favor	**Moderate** certainty evidence
MILD, MODERATE	**TOPICAL JAK INHIBITORS** We **suggest against** adding topical ruxolitinib Age 12yo+	**Conditional** against	**Low** certainty evidence

cAMP, cyclic adenosine monophosphate; PDE4, phosphodiesterase 4.

Boguniewicz M, et al. *Ann Allergy Asthma Immunol*. 2018:120:10-22; Paller AS, et al. *J Allergy Clin Immunol*. 2017;140:633-643.

Chronic Atopic dermatitis: Anti-inflammatory topical treatment



Moderate/Severe AD: Adults & Adolescents

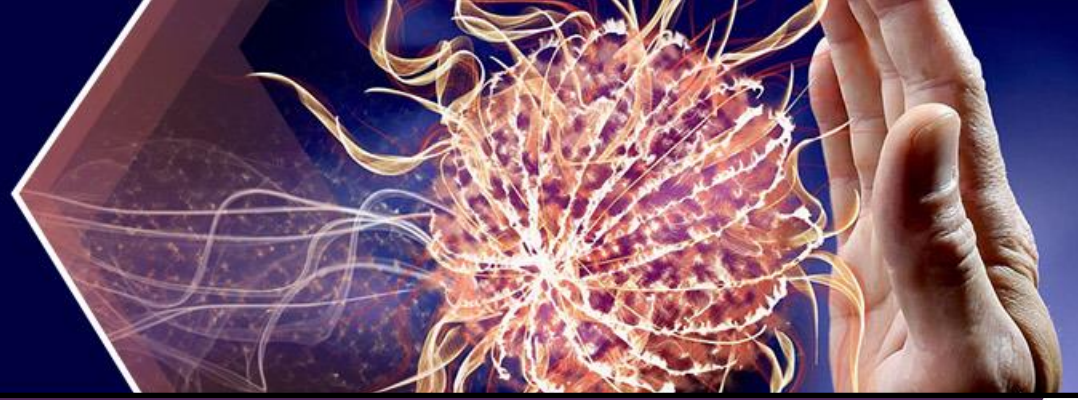
- Topical anti-inflammatory agent to previously affected areas for 2 consecutive days/week
  - Medium/high potency TCS to thick skin
  - Low/medium potency TCS or TCI to thin skin
  - Apply TCS **1-2x/day** and **TCI bid**
- Meta-analysis suggest TCS more effective and less adverse effects vs. TCI

Moderate/Severe AD: Children

- Topical corticosteroids(TCS) low potency to previously affected areas for 2 consecutive days/week
  - Apply **once daily** on days it is used

Weston, WL. Treatment of atopic dermatitis. UpToDate accessed 5.22.21

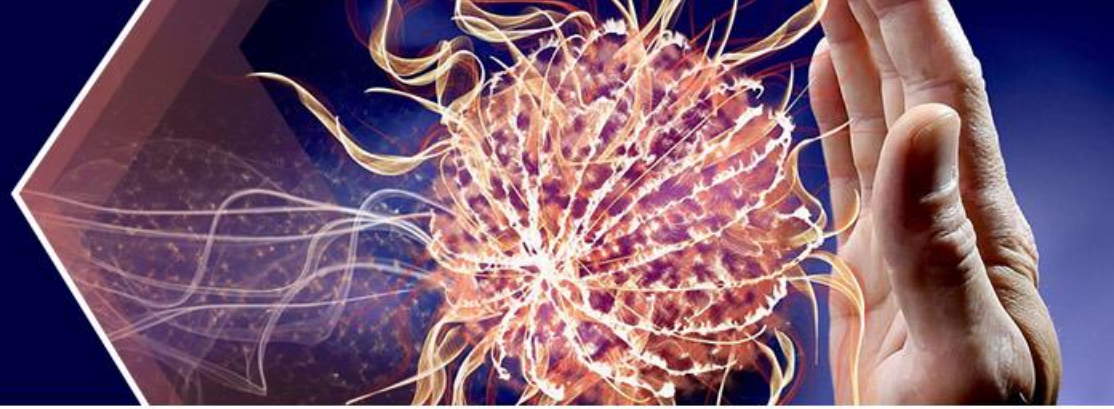
Chronic Atopic dermatitis
JTFPP 2023 Recommendations



SEVERITY	RECOMMENDATION	STRENGTH	CERTAINTY
Severity of dermatitis that this recommendation applies to	Text summary of recommendation	The strength of the recommendation	GRADE rating for the certainty of evidence
MILD, MODERATE, SEVERE	**MAINTENANCE OF REMISSION** We **recommend** use of proactive therapy to areas that flare with a topical calcineurin inhibitor or mid potency topical steroid	**Strong** in favor	**Moderate** certainty evidence

Weston, WL. Treatment of atopic dermatitis. UpToDate accessed 5.22.21

2023 JTFPP Suggest Against



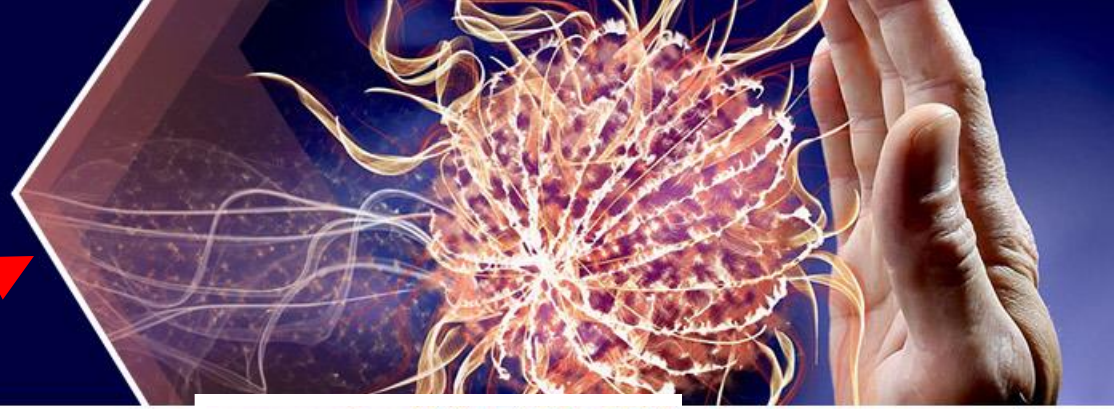
ATOPIC DERMATITIS

AAAAI/ACAAI JTFPP 2023 Guidelines

INTERVENTION	SEVERITY	RECOMMENDATION	STRENGTH	CERTAINTY
ELIMINATION DIETS  Oykhman et al Systematic review	MILD MODERATE SEVERE	We **suggest against** the use of elimination diets	**Conditional** against	**Low** certainty evidence

SEVERITY Severity of dermatitis that this recommendation applies to	RECOMMENDATION Text summary of recommendation	STRENGTH The strength of the recommendation	CERTAINTY GRADE rating for the certainty of evidence
MILD MODERATE SEVERE	**TOPICAL ANTIMICROBIALS** We **suggest against** adding topical antimicrobials to topical anti-inflammatories in patients with no clear signs of infection	**Conditional** against	**Very low** certainty evidence

Treatment Strategy for Atopic Dermatitis



Severe

Moderate to severe

Wet wraps
Allergen Immunotherapy
Biologics (Dupilumab, Tralokinumab)
UV Therapy
Small molecules (Oral JAK inhibitors & other agents)

Mild-Moderate

Topical Corticosteroids
Topical Calcineurin Inhibitors
PDE4; Antibiotics if needed
Topical JAK Inhibitors (Ruxolitinib)

Dry Skin & all stages

Hydration of Skin- Emollient
Identify and avoid triggers: contact allergens, aeroallergens, irritants, microorganisms, food

2023 JTFPP PP Atopic Dermatitis

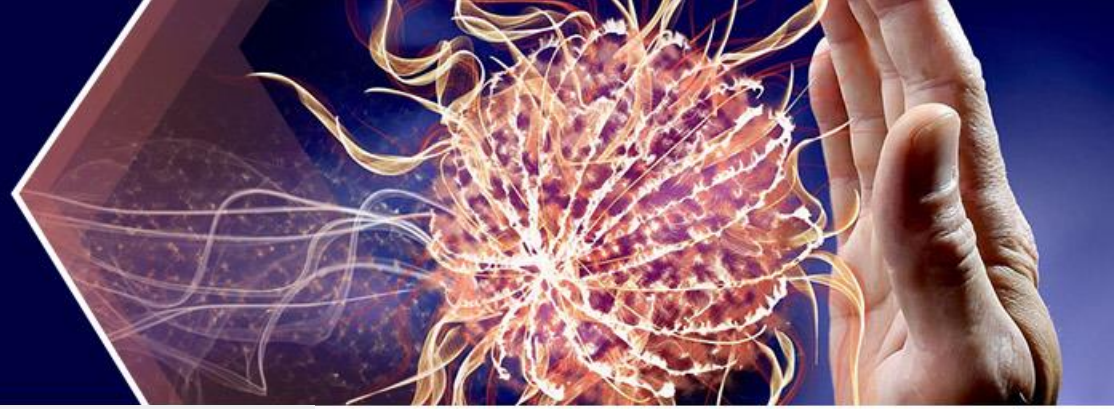
ATOPIC DERMATITIS

AAAAI/ACAAI JTFPP 2023 Guidelines

INTERVENTION	SEVERITY	RECOMMENDATION	STRENGTH	CERTAINTY
ELIMINATION DIETS Oykhman et al Systematic review	MILD, MODERATE, SEVERE	We **suggest against** the use of elimination diets	**Conditional** against	**Low** certainty evidence
ALLERGEN IMMUNOTHERAPY Sublingual; Subcutaneous; Best evidence for dust mite allergy Yepes-Nuñez & Chu et al Systematic review	MODERATE, SEVERE	We **suggest** adding allergen immunotherapy If refractory, intolerant, or unable to use mid potency topical treatments	**Conditional** in favor	**Moderate** certainty evidence
	MILD	We **suggest against** adding allergen immunotherapy See conditions to consider, e.g. comorbidities, values and preferences	**Conditional** against	**Moderate** certainty evidence
SYSTEMIC TREATMENTS Consider if refractory, intolerant, or unable to use mid to high potency topical treatment	MODERATE, SEVERE	BIOLOGICS / MONOCLONAL ANTIBODIES **DUPILUMAB** We **recommend** adding dupilumab Age 6mo+	**Strong** in favor	**High** certainty evidence
	MODERATE, SEVERE	BIOLOGICS / MONOCLONAL ANTIBODIES **TRALOKINUMAB** We **recommend** adding tralokinumab Age 12yo+	**Strong** in favor	**High** certainty evidence
	MODERATE, SEVERE	**UVB TREATMENT** We **suggest** adding clinic-based narrow band UVB treatment	**Conditional** in favor	**Low** certainty evidence
Consider if refractory, intolerant, or unable to use mid to high potency topical treatment and systemic treatment inclusive of a biologic recommended above See conditions to consider, e.g. comorbidities, risk factors, values and preferences, and exceptional circumstances	MODERATE, SEVERE	SMALL MOLECULE IMMUNOSUPPRESSANTS **ABROCITINIB, BARICITINIB, OR UPADACITINIB** We **suggest** adding one of these three JAK inhibitors Age varies: 12 or 18 yo+ Suggested daily doses: Abrocitinib 100–200 mg; Baricitinib 2–4 mg; Upadacitinib 15–30 mg	**Conditional** in favor	**Low** certainty evidence
	MODERATE, SEVERE	SMALL MOLECULE IMMUNOSUPPRESSANTS **BARICITINIB 1 mg DAILY** We **recommend against** adding baricitinib 1 mg daily	**Strong** against	**Low** certainty evidence
	MODERATE, SEVERE	SMALL MOLECULE IMMUNOSUPPRESSANTS **AZATHIOPRINE** We **suggest against** adding azathioprine	**Conditional** against	**Low** certainty evidence
	MODERATE, SEVERE	SMALL MOLECULE IMMUNOSUPPRESSANTS **CYCLOSPORINE** We **suggest** adding cyclosporine Shared-decision making should determine whether to start therapy at high dose (5mg/kg) or low dose (3 mg/kg)	**Conditional** in favor	**Low** certainty evidence
	MODERATE, SEVERE	SMALL MOLECULE IMMUNOSUPPRESSANTS **METHOTREXATE** We **suggest against** adding methotrexate	**Conditional** against	**Low** certainty evidence
	MODERATE, SEVERE	SMALL MOLECULE IMMUNOSUPPRESSANTS **MYCOPHENOLATE** We **suggest against** adding mycophenolate	**Conditional** against	**Low** certainty evidence
	MILD, MODERATE, SEVERE	**SYSTEMIC CORTICOSTEROIDS** We **suggest against** systemic corticosteroids for all patients with atopic dermatitis	**Conditional** against	**Low** certainty evidence

Annals of Allergy, Asthma & Immunology
ELSEVIER

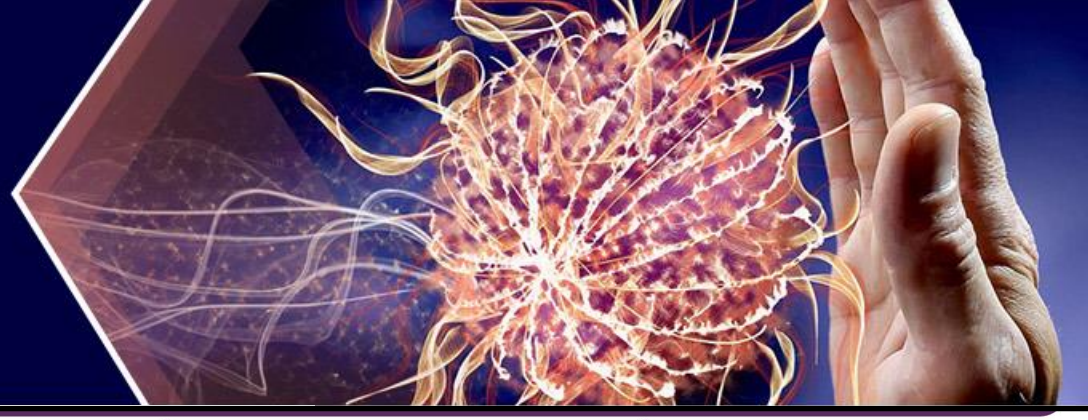
Wet Wraps



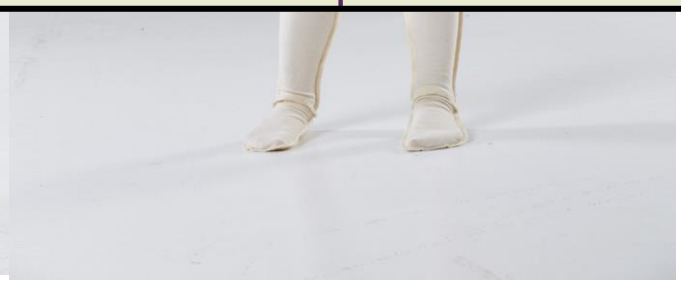
- Reduce the itch
- Cooling and soothing
- Moisturize the skin
- Protect the skin
- Promote sleep

Wet Wraps

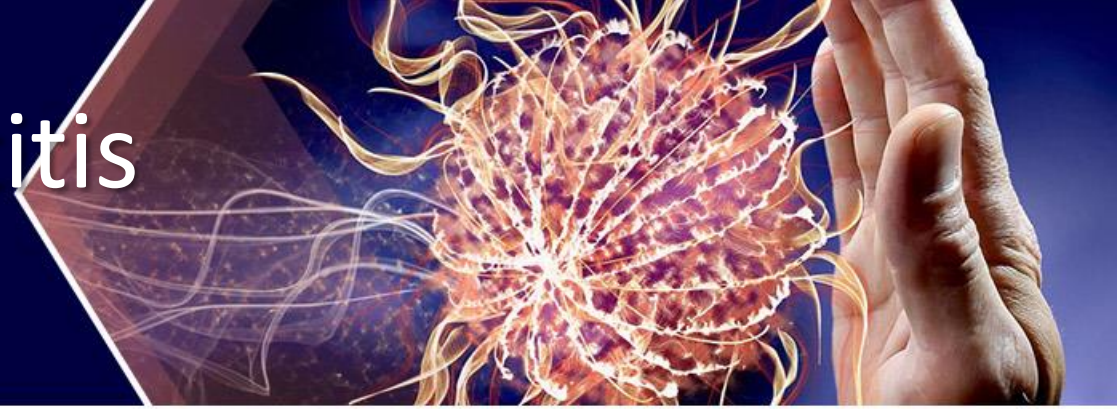
JTFPP 2023 Recommendations



INTERVENTION Treatment or category of treatments considered	SEVERITY Severity of dermatitis that this recommendation applies to	RECOMMENDATION Text summary of recommendation	STRENGTH The strength of the recommendation	CERTAINTY GRADE rating for the certainty of evidence
localized lesions refractory to mid to high potency topical treatment	MODERATE, SEVERE	**OCCLUSIVE APPLICATION** (WET WRAPS) We **suggest** a time and body surface area-limited trial of occlusive low to mid potency topical steroid	**Conditional** in favor	**Very low** certainty evidence



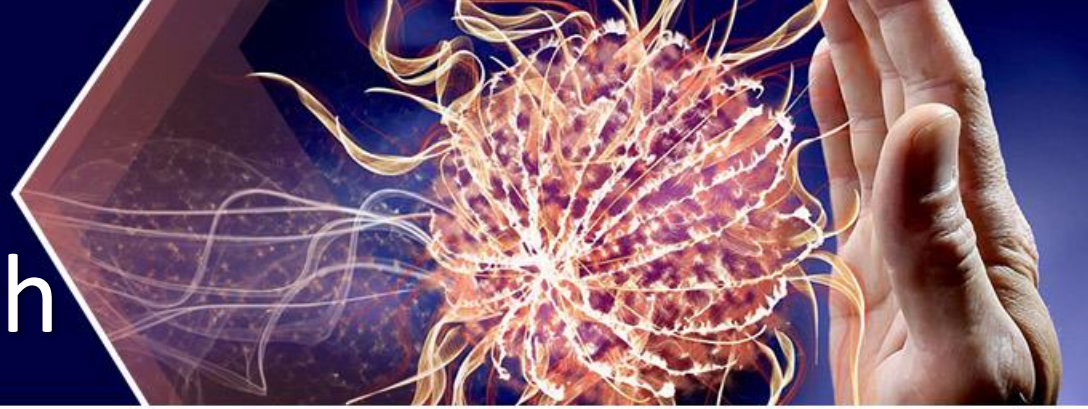
SCIT & SLIT for Atopic Dermatitis Especially Dust Mite



- A 2023 systematic review & meta-analysis
  - 23 randomized controlled trials with 1,957 participants (most HDM)
  - SCIT and SLIT likely lead to significant improvements in AD severity and QoL
  - 50% reduction in SCORAD) scores in 40% of pts. receiving AIT vs. 26% in control groups (Risk Ratio [RR]: 1.53; 95% Confidence Interval [CI]: 1.31–1.78).
  - 56% of pts. Had a ≥4-point improvement in the Dermatology Life Quality Index (DLQI) vs. 39% in controls (RR: 1.44; 95% CI: 1.03–2.01).
  - Adverse events higher in SCIT (66%) vs. 41% controls; SLIT (13%) vs. 8% controls.
  - Effect on sleep disturbance and exacerbations was uncertain

Yepes-Nuñez JJ, et al. J Allergy Clin Immunol. 2023;151(1):147–158.

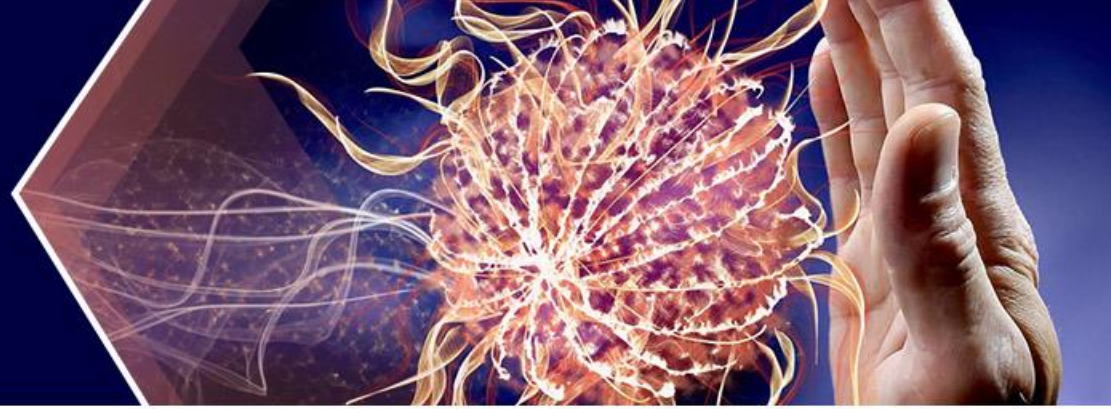
SCIT & SCIT for AR, Asthma Dust Mites, Grass, & Cockroach

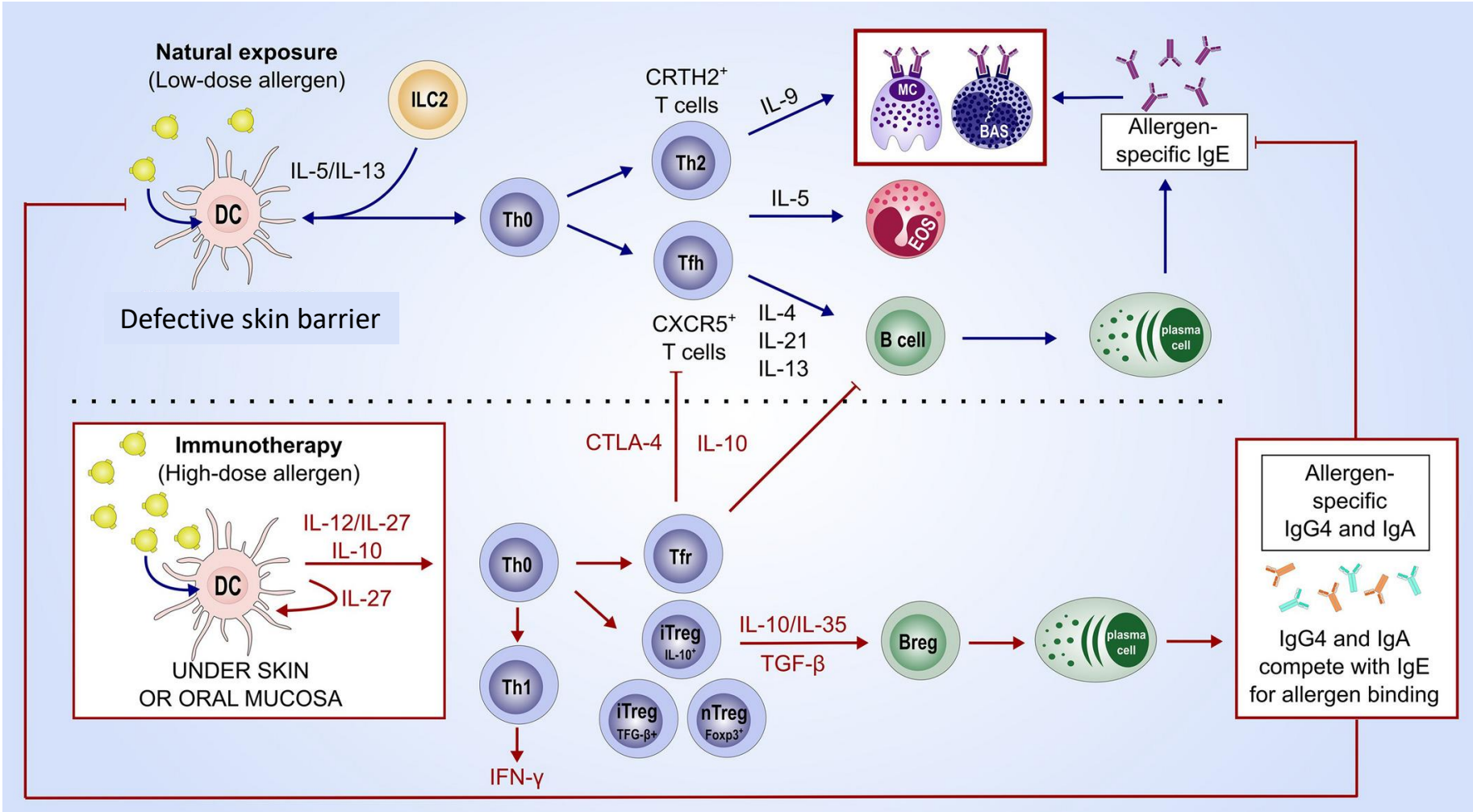


- **Efficacy of SCIT & SLIT for Dust mite and Grass for AR and asthma is well established**
- **Efficacy for SCIT/SLIT for cockroach is not as well established**
  - **Small older SCIT studies suggested benefit for asthma[1-2]**
  - **2024 study found 1 yr SCIT failed to alter Nasal Allergen Challenge TNSS and nasal transcriptome responses to cockroach allergen challenge despite systemic effects on allergen-specific skin tests, induction of sIgG4 serum down-modulation of allergen-stimulated T-cell responses.[3]**
  - **2024 RCT with SCIT in urban children with asthma sensitized to cockroach allergens; improved IgG_4, no symptom change[4]**
  - **Cockroach SLIT pilot; modest immune response, limited symptom benefit[5]**

1. Kang B, et al. J Allergy Clin Immunol. 1979;63(2):80–86. 2. Srivastava D,. Et al. Eur J Clin Invest. 2011;41(8):879–888. 3. Zoratti, E. J Allergy Clin Immunol 2024 Sep;154(3):735-744.e10. 4. Gergen et al J Allergy Clin Immunol. 2024;153(6):1650–1660. 5. Calatroni et al. Allergy Clin Immunol. 2014;133(3):837–845.

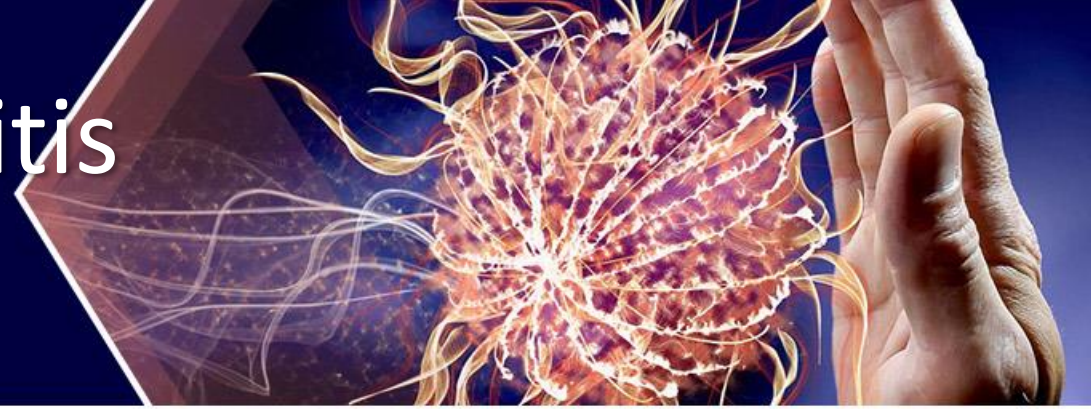
Allergen immunotherapy for Atopic Dermatitis





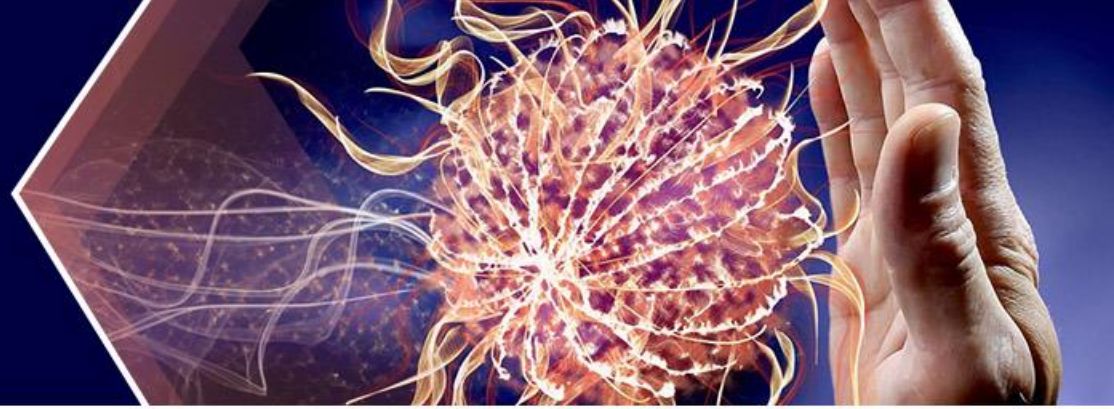
SCIT & SLIT for Atopic Dermatitis

JTFPP 2023 Recommendations



INTERVENTION Treatment or category of treatments considered	SEVERITY Severity of dermatitis that this recommendation applies to	RECOMMENDATION Text summary of recommendation	STRENGTH The strength of the recommendation	CERTAINTY GRADE rating for the certainty of evidence
ALLERGEN IMMUNOTHERAPY  Yepes-Nuñez & Chu et al Systematic review	MODERATE, SEVERE	We **suggest** adding allergen immunotherapy If refractory, intolerant, or unable to use mid potency topical treatments	**Conditional** in favor	**Moderate** certainty evidence
	MILD	We **suggest against** adding allergen immunotherapy See conditions to consider, e.g. comorbidities, values and preferences	**Conditional** against	**Moderate** certainty evidence

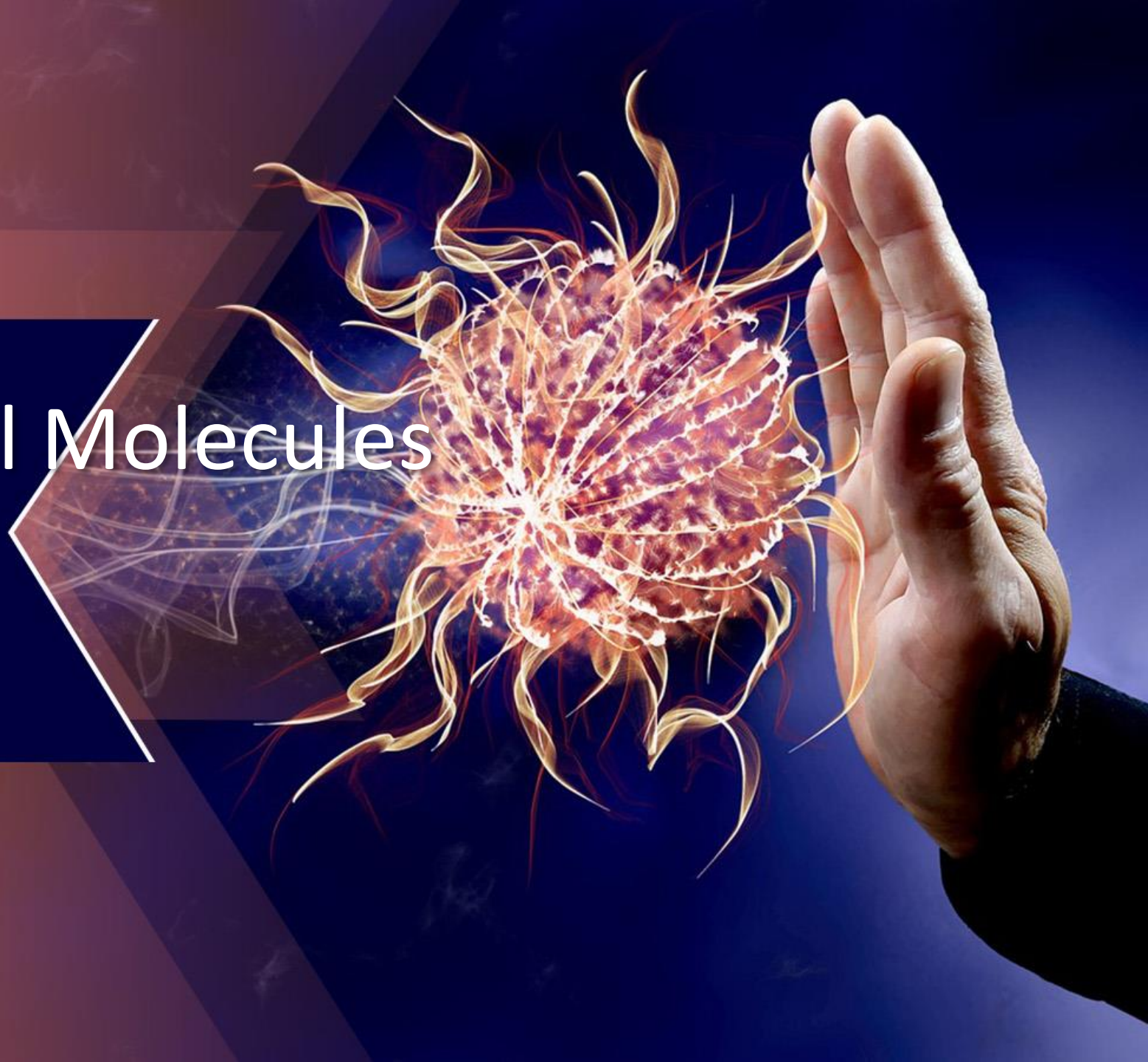
Dupilumab vs. AIT vs. Dupilumab + AIT



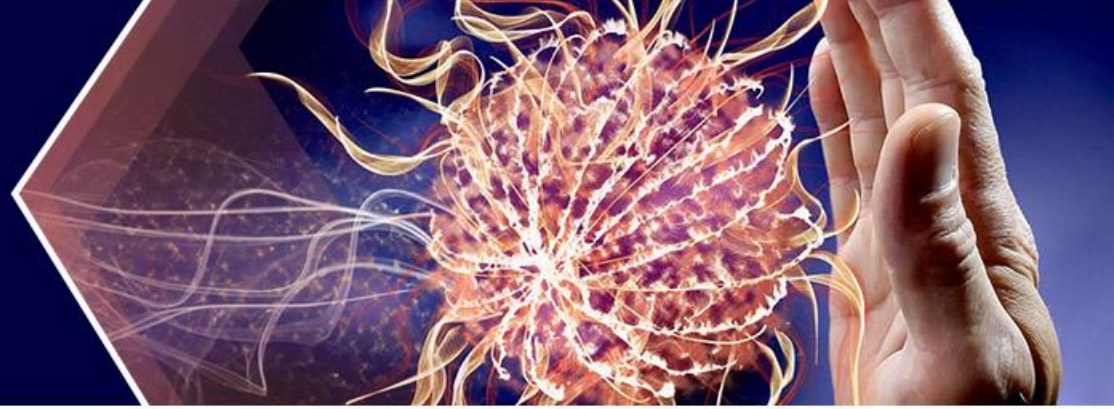
- 2025 study investigated clinical and immunological effects after 6 mo.:
  - AIT only n=39 ; dupilumab n=19; AIT + dupilumab group n=19
  - SCORAD scores significantly improved in all groups after 6 months
- HDM-s IgE and total IgE:
  - AIT: Stable
  - Dupilumab and combination groups: decreased AIT alone led to increased levels of HDM-specific IgG_4 antibodies, indicating enhanced allergen tolerance.
  - IgG(4) against Der p1 and Der p23 increased in the AIT group & combined treatment group.
  - CCL17 decreased in the dupilumab group and Th1/Th2 and Th17/Th2 ratios increased after dupilumab treatment.
- Combination group had all of the above immunological changes but no significant greater improvement in clinical symptoms

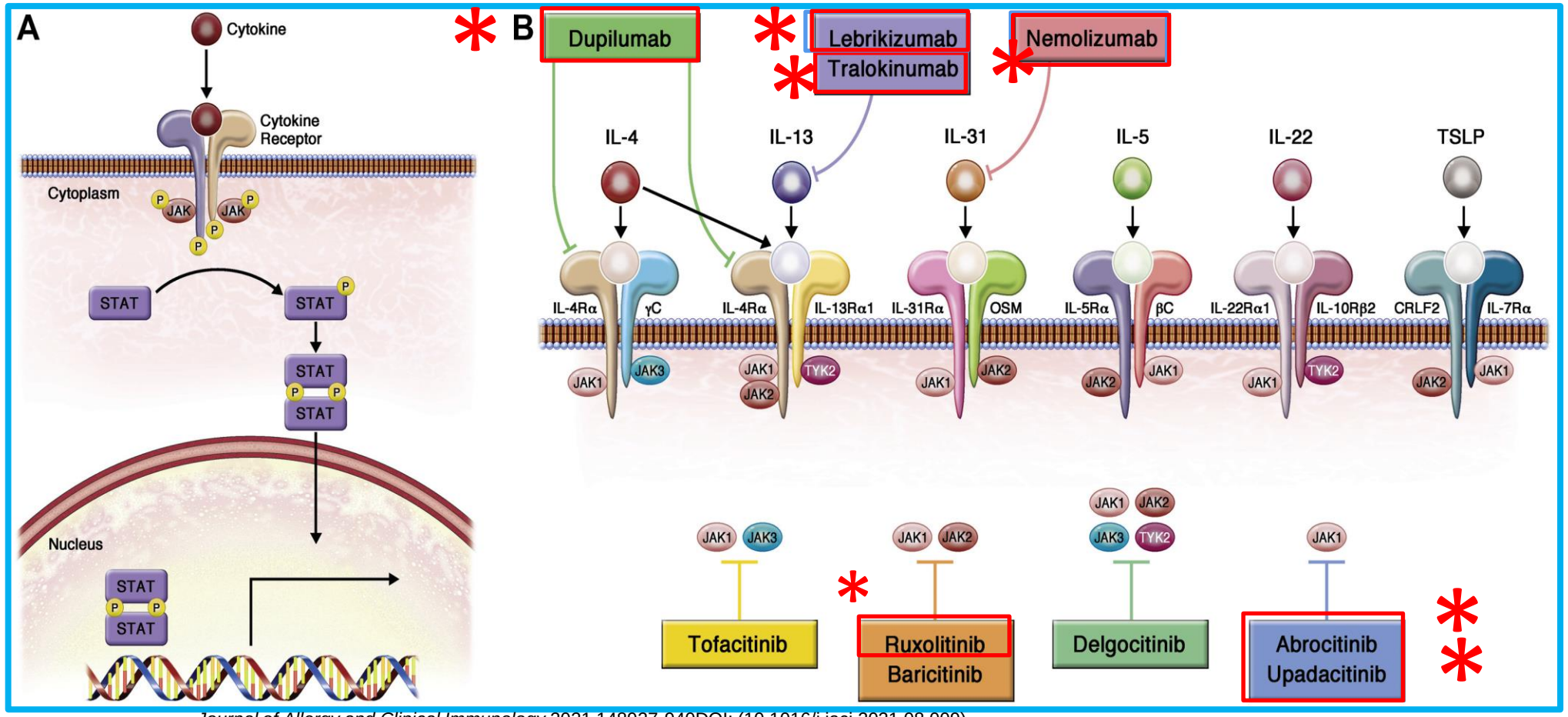
Liu, J. et al. World Allergy Organ J. 2025. Issue 3 Pages 101043

Biologics & Small Molecules FDA approved



Biologics & Small Molecules
FDA approved agents *





Journal of Allergy and Clinical Immunology 2021 148927-940DOI: (10.1016/j.jaci.2021.08.009)

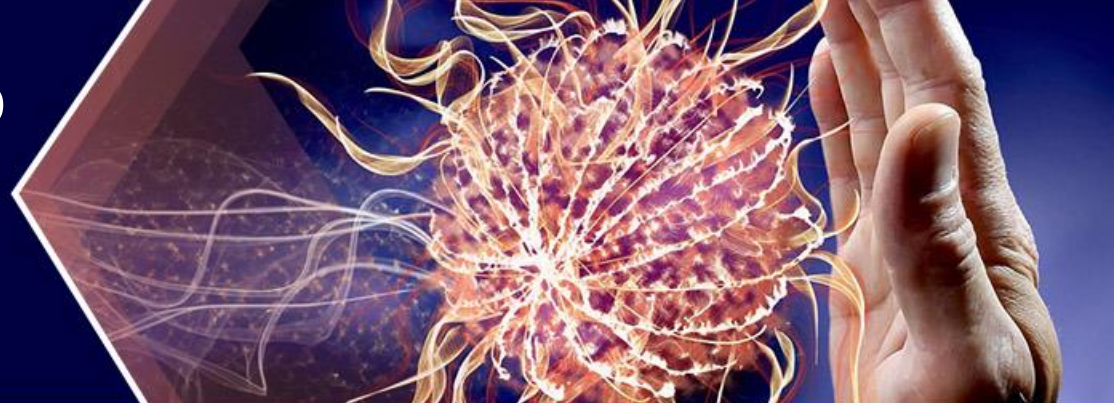
FDA-Approved Advanced Treatments for Atopic Dermatitis: Biologics

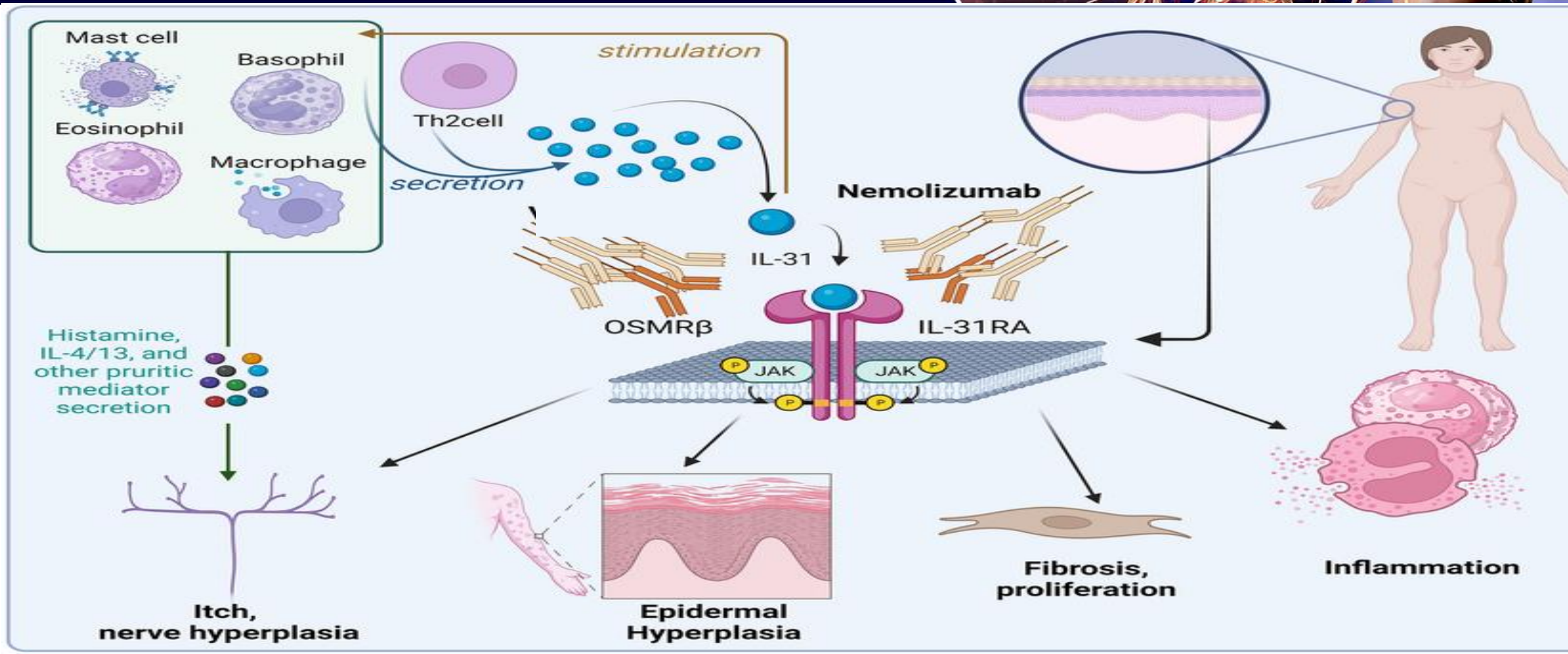
Drug (Brand)	Mechanism of Action	FDA Approval (AD)	Approved Age	Estimated Monthly cost	Dosing Frequency	Type
Dupilumab (Dupixent®)	Anti-IL-4Rα (blocks IL-4 & IL-13)	Mar 2017	≥6 mo..	$3000	600 mg loading, then 300 mg Q2W Q4W option	Biologic
Tralokinumab (Adbry®)	Anti-IL-13	Dec 2021	≥12 yr.	$3000	600 mg loading, then 300 mg Q2W (No 4W option) Slower onset of actin	Biologic
Lebrikizumab (Ebglyss®)	Anti-IL-13	Oct 2023	≥12 yr.	$3000	500 mg loading, then 250 mg Q2W Q 4W option	Biologic
Nemolizumab (Nemluvio®)	Anti-IL-31RA	Sep 2024	≥12 yr.	$3000	60 mg loading, then 30 mg Q4W	Biologic

The newest biologics: Lebrikizumab vs. Nemolizumab

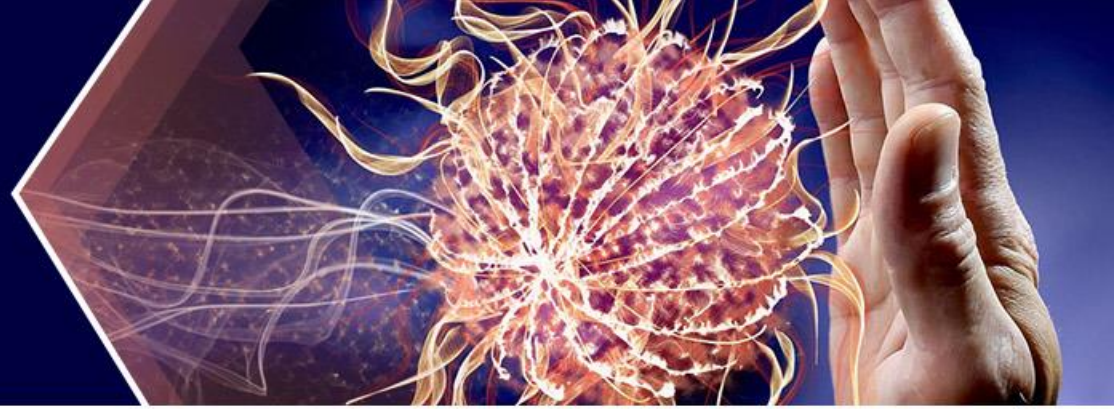
Feature	Lebrikizumab	Nemolizumab
Receptor Blockade	Inhibits IL-13 from binding to IL-13 receptor α1 (IL-13Rα1)	Blocks signaling at the IL-31RA on sensory nerves and immune cells
Primary Pathway Affected	Type 2 inflammatory signaling	Pruritus (itch) signaling and inflammation
Biological Effect	Reduces inflammation, epidermal thickening, eosinophilia, and barrier damage	Reduces chronic itch, sensory nerve activation, and improves sleep quality
Clinical Focus	Anti-inflammatory and skin barrier restoration	Anti-pruritic effect with additional anti-inflammatory benefits
Therapeutic Implication	Useful in patients with inflamed, thickened skin and systemic involvement	Particularly effective for patients with severe itch and sleep disturbances
Onset of action	1-2 wk., meaningful by wk. 4, peak wk. 16 (same as dupilumab)	1 week for itch reduction

Mechanism of Action of Nemolizumab



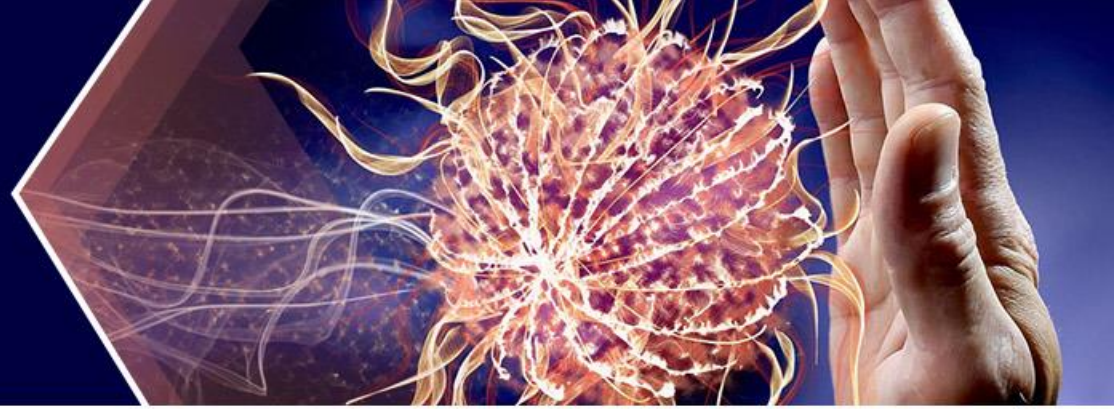


Nemolizumab Phase 3 Trials: ARCADIA 1 & 2



Endpoint	ARCADIA 1 (Nemolizumab vs Placebo)	ARCADIA 2 (Nemolizumab vs Placebo)
IGA 0/1 (Week 16)	36% vs 25%	38% vs 26%
EASI-75 (Week 16)	44% vs 29%	42% vs 30%
≥4-pt Itch Reduction	48.6% vs 20.5%	48.1% vs 20.6%
≥4-pt Sleep Improvement	38% vs 20%	34% vs 16%
Onset of Itch Relief	Week 1	Week 1

Comparative Effectiveness of FDA-Approved Biologics for Atopic Dermatitis



🧪 Overall Effectiveness (Week 16 Efficacy):

- **Dupilumab**: EASI-75 ~43–52%; IGA 0/1 ~38–40%; rapid onset; effective in both adults and children ≥6 months.
- **Tralokinumab**: EASI-75 ~27–33%; IGA 0/1 ~16–22%; typically requires combination with topical steroids.
- **Lebrikizumab**: EASI-75 ~58–70%; IGA 0/1 ~33%; comparable to dupilumab in head-to-head meta-analyses.
- **Nemolizumab**: EASI-75 ~42–44%; IGA 0/1 ~36–38%; standout efficacy in itch relief (NRS-4 ≥4 pt reduction ~48%).

🧠 Role of Nemolizumab in AD Management:

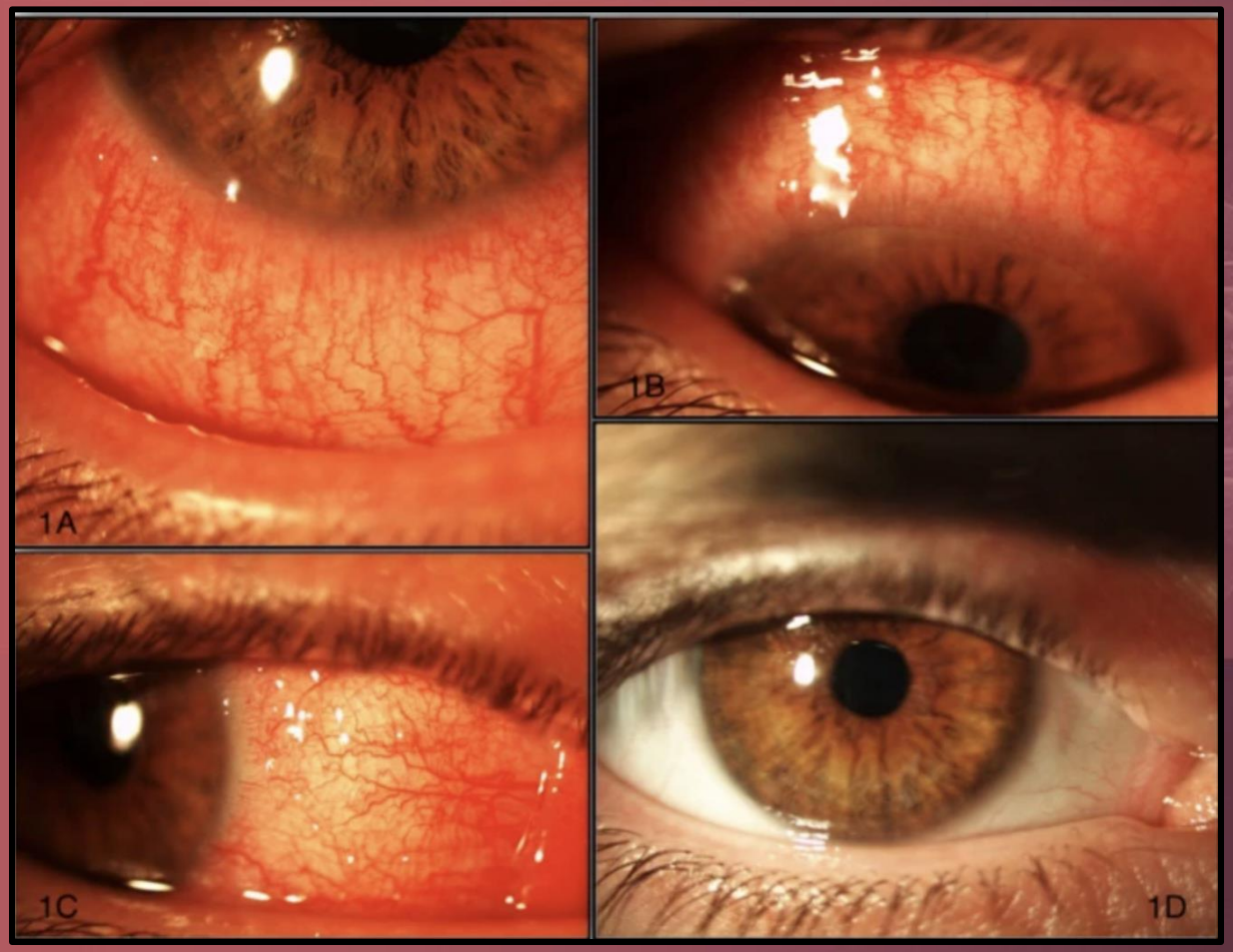
- Ideal for **itch-dominant** or recalcitrant itch phenotypes.
- Provides **rapid antipruritic effect** (as early as Week 1); could be used intermittently or for seasonal flares.
- May be used **in combination with topical agents** where inflammation is moderate but itch is severe.
- Offers a **non-immunosuppressive mechanism**, beneficial for patients at higher infection risk or preferring safer long-term profiles.

📚 **Source: ARCADIA 1 & 2 Trials (Blauvelt et al., Lancet 2024); LIBERTY AD, ECZTRA, ADvocate Trials.**

Adverse Events by Biologic in Atopic Dermatitis

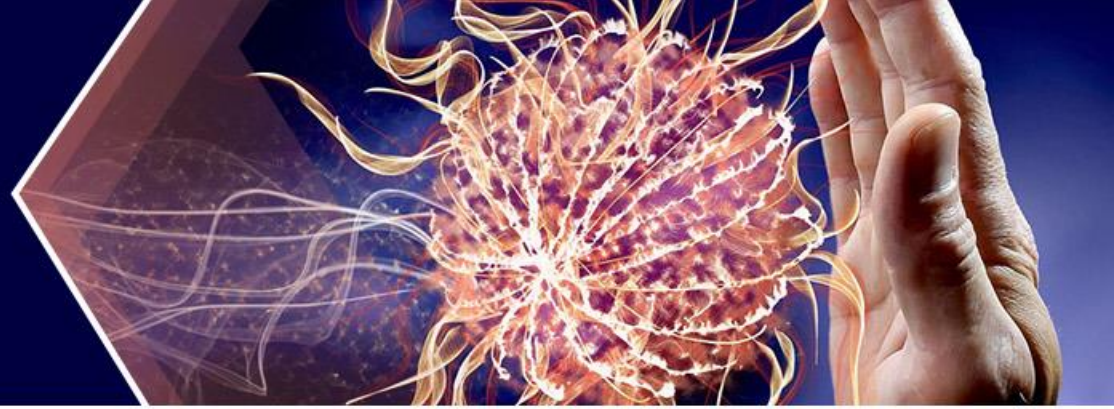
Adverse Event	Lebrikizumab	Dupilumab	Tralokinumab	Nemolizumab
Conjunctivitis	6.3–8.5%, mild-mod	8.6–28% (up to 60%), mild-mod	7.5%, mild	No increase vs placebo
Injection site reactions	2–4%, mild	5–10%, mild	~3%, mild	~10%, mild
Herpes simplex/oral herpes	<2%, mild	2–4%, mild	NR	NR
Eosinophilia	1–2%, transient	2–10%, transient	Up to 3%, non-clinical	NR
Headache	~3%, mild	~4%, mild	NR	~6%, transient
URTIs	3–5%	5–10%	5–8%	NR
Arthralgia	NR	Rare	NR	~3%, mild
Possible asthma worsening or new onset	NR	NR	NR	Rare early trials; not substantiated later trials
Facial rash	Very rare	Red face syndrome	Very rare	NR
CPK elevation	NR	NR	NR	Reported

Acute presentation of dupilumab-associated conjunctivitis



Resolution with steroid eye gtt.

Ocular Surface Disease with IL-4/IL-13 Biologics in Atopic Dermatitis



🧬 **Mechanism of Ocular Surface Disease (OSD):**

- **IL-4/IL-13 blockade (e.g., Dupilumab, Tralokinumab, Lebrikizumab) reduces goblet cell density and mucin secretion.**
- **Results in tear film instability and ocular surface inflammation.**

⚠️ **Risk Factors:**

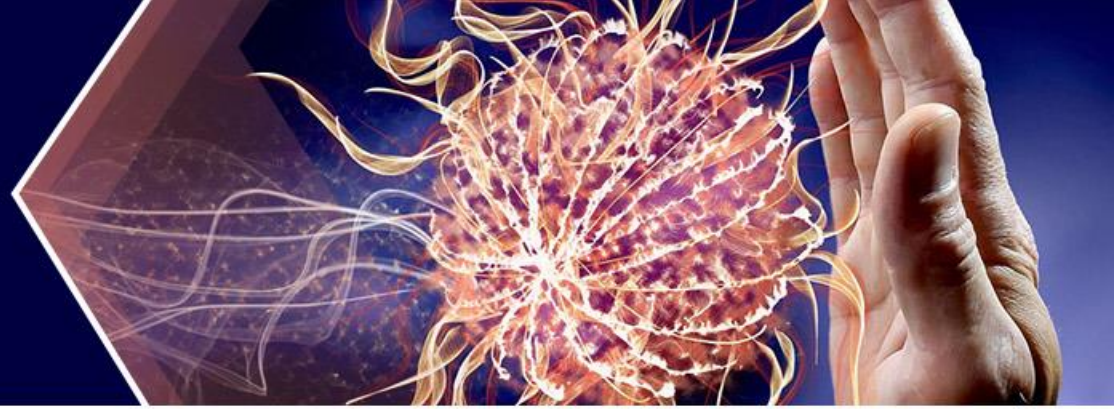
- **History of allergic conjunctivitis or chronic eye irritation**
- **More severe baseline AD**
- **Atopic keratoconjunctivitis (AKC)**

👁️ **Common Presenting Symptoms:**

- **Redness, dryness, tearing, foreign body sensation**
- **Burning, itching, blurred vision**
- **Mean onset 6.75 weeks**

1. Akinlade B et al., Br J Dermatol. 2019;181(3):459–473 2. Faergemann J et al., Acta Derm Venereol. 2024;104:adv00562 3. de Wijs LEM et al., Br J Dermatol. 2021;185(2):261–2704. Bakker DS et al., Am J Clin Dermatol. 2019;20(5):635–642

Management of Biologic-Associated Ocular Surface Disease (OSD)



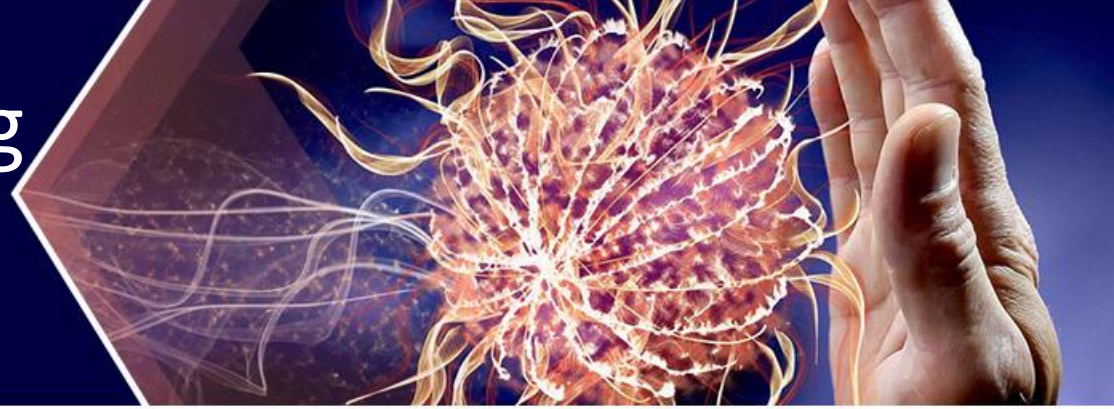
💊 **Recommended Treatment:**
- **Mild: Artificial tears, cold compresses**
- **Moderate: Topical antihistamines or mast cell stabilizers**
- **Severe: Topical corticosteroids (e.g., loteprednol), ciclosporin A drops, tacrolimus ointment**

⏳ **Treatment Duration:**
- **Typically 4–8 weeks for mild to moderate cases**
- **Dupilumab associated OSD may require long-term ocular therapy (>6 months in some cases) with steroids/cyclosporine 0.1% ointment (off-label)**

🩺 **Pre-Screening Before Biologic Initiation:**
- **Recommend baseline ophthalmologic evaluation for patients with history of chronic conjunctivitis or atopic keratoconjunctivitis (or all patients)**

1. Akinlade B et al., Br J Dermatol. 2019;181(3):459–473 2. Faergemann J et al., Acta Derm Venereol. 2024;104:adv00562 3. de Wijs LEM et al., Br J Dermatol. 2021;185(2):261–2704. Bakker DS et al., Am J Clin Dermatol. 2019;20(5):635–642

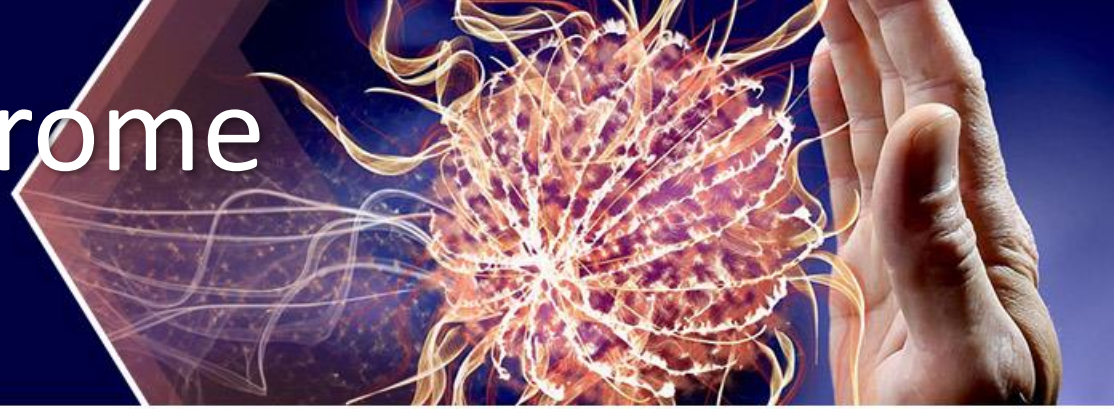
Ocular Surface Disease patients using Biologics for Atopic Dermatitis

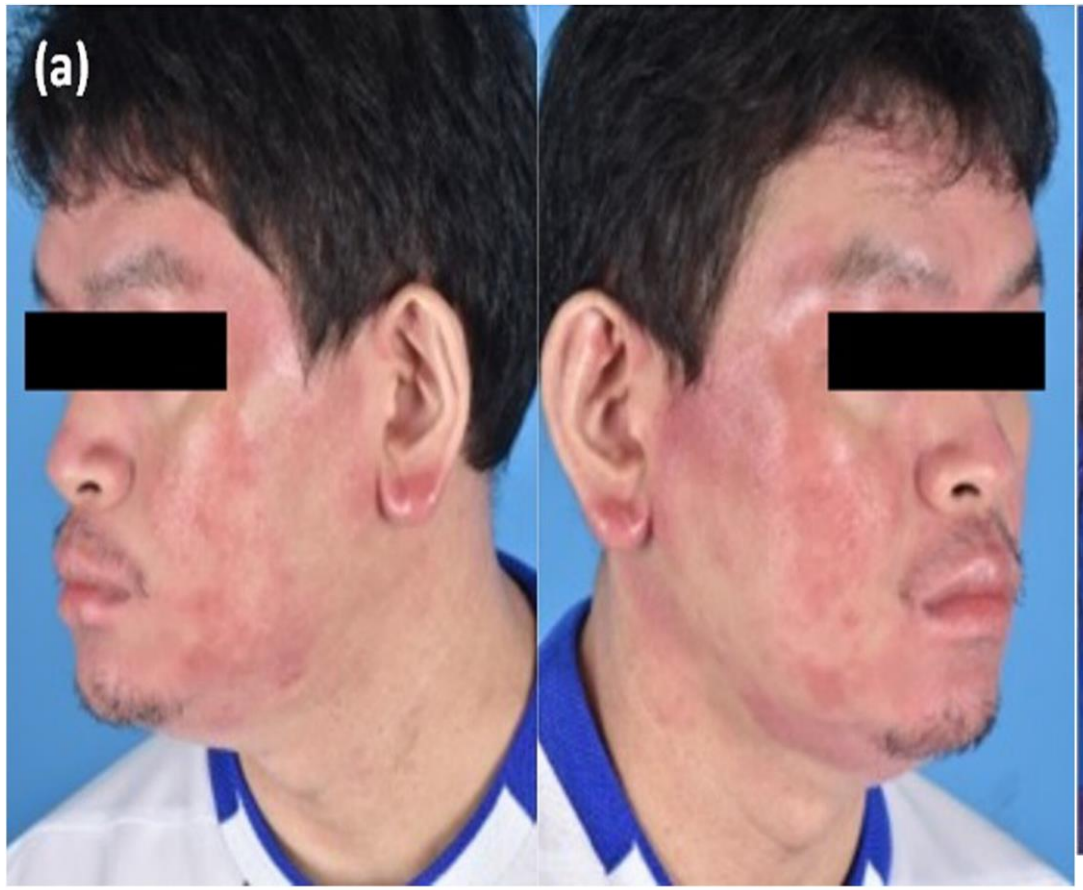


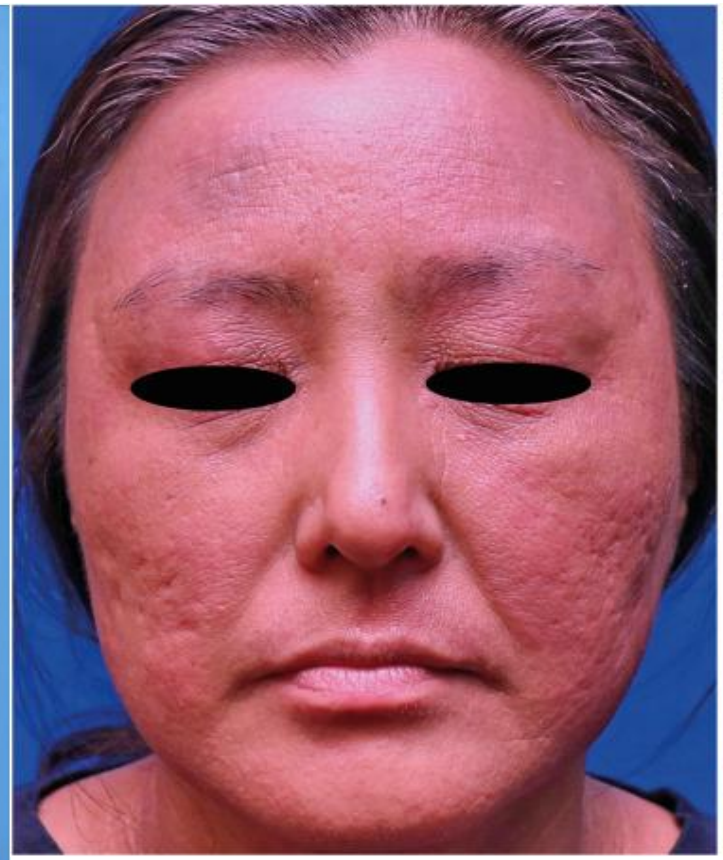
Biologic	Conjunctivitis Incidence	Biologic Discontinuation Rate	% Requiring Steroid Treatment	Source Type
Dupilumab	8.6%–28%[1]	3.8%–20%[2]	Up to 50%[2]	RCTs & Real-world
Tralokinumab	7.5%[3]	5.9%[4]	~40%[4]	RCTs & Real-world
Lebrikizumab	6.3%–8.5%[5]	2.3%[5]	~20%[5]	RCTs
Nemolizumab	No increase vs placebo[6]	NR	NR	RCTs

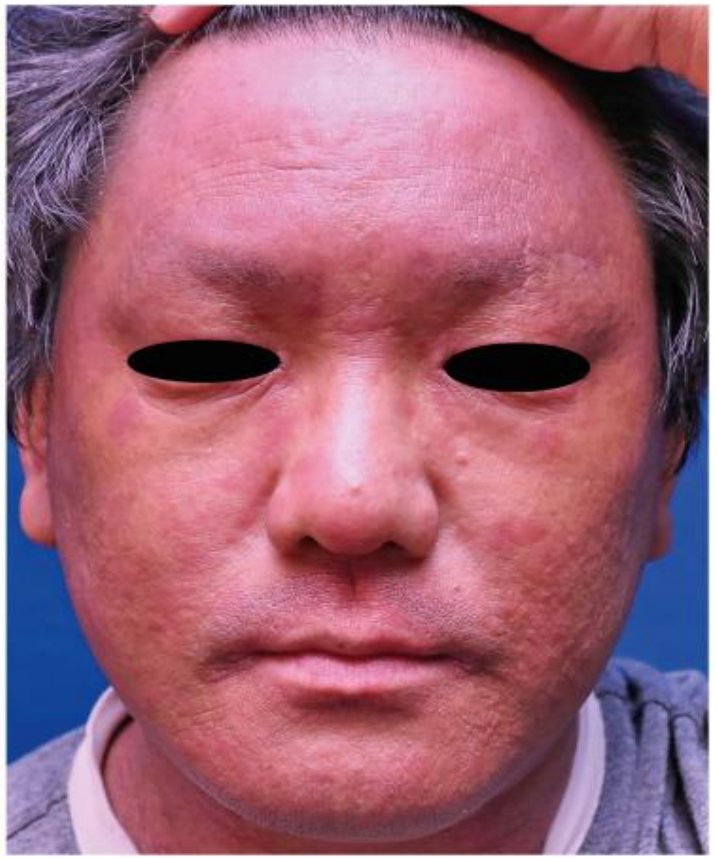
1. Akinlade B et al., Br J Dermatol. 2019;181(3):459–473. 2. Bowe W et al., Clin Exp Dermatol. 2023;48(8):e334–e341. 3. Silverberg JI et al., Br J Dermatol. 2022;186(3):453–463.
4. Faergemann J et al., Acta Derm Venereol. 2024;104:adv00562. 5. Simpson EL et al., Am J Clin Dermatol. 2023;24(3):339–351.6. Blauvelt A et al., Lancet. 2024;403(10429):1214–1226.

Dupilumab Red Face Syndrome

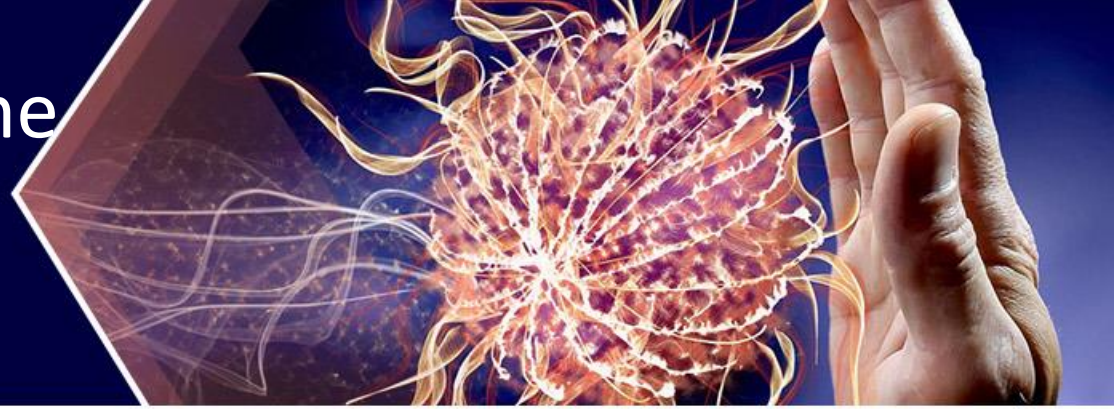








Dupilumab-Associated Red Face Syndrome (DFR): Clinical Overview



📊 Prevalence:

- Reported in ~9% to 10.6% of patients in real-world studies
- One of the most common skin-related adverse events in dupilumab-treated AD patients

-Onset usually 4-8 weeks, range 2-28 wks..

👥 Affected Demographics:

- Most frequently reported in adolescents and adults
- Slight female predominance in some case series

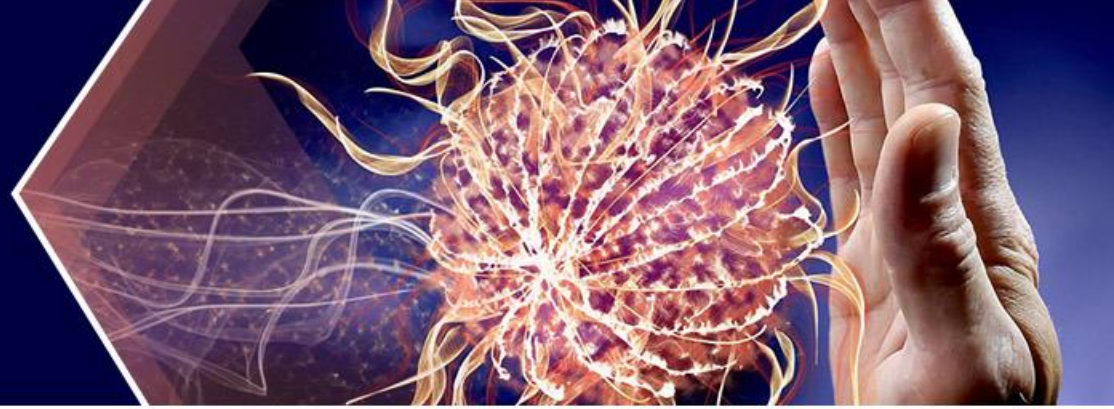
🩺 **Symptoms:** erythema, papules, and itching, scaling, erosive exudation, edema, flushing, telangiectasia, pain, and burning sensations.

⏳ Duration:

- Mild cases resolve within weeks with treatment
- Moderate to severe cases may persist for months without targeted therapy

de Wijs LEM et al., Br J Dermatol. 2021;185(2):261–270. Stingeni L et al., Am J Clin Dermatol. 2021;22(6):803–810. Napolitano M et al., Clin Exp Dermatol. 2023;48(8):e334–e341

Mechanism & Management of Red Face Syndrome



Possible Mechanisms:

- Immune deviation: suppression of IL-4/13 may unmask Th1/Th17-driven inflammation
- Seborrheic dermatitis, rosacea, contact dermatitis, or Malassezia hypersensitivity may be unmasked

Management Strategies:

- Mild: emollients, oral AH, topical corticosteroids or calcineurin inhibitors
- Moderate-severe: consider antifungals, minocycline, patch testing, or adjusting therapy
- Persistent/refractory: possible switch to JAK inhibitors (e.g., upadacitinib)

Discontinuation Rates of patients with red face syndrome:

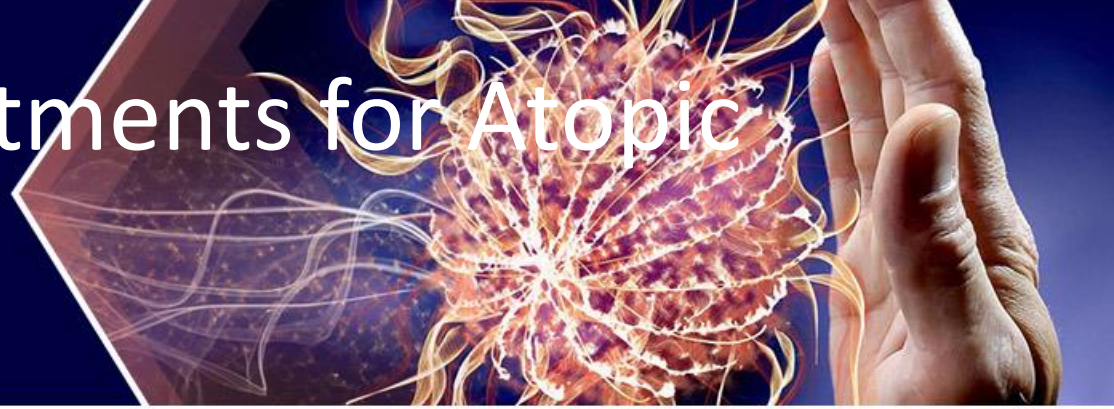
- **~3.8% in pediatric patients; up to 20% in adults**

Other Anti-IL-13 Agents:

- Red face syndrome not commonly reported with tralokinumab or lebrikizumab
- Isolated cases may occur but data are limited

Faergemann J et al., Acta Derm Venereol. 2024;104:adv0056. Bakker DS et al., Am J Clin Dermatol. 2019;20(5):635–642. Dermatitis Journal, 2022 (Patch testing review)

FDA-Approved Advanced Treatments for Atopic Dermatitis: Biologics



Drug (Brand)	Mechanism of Action	FDA Approval (AD)	Approved Age	Estimated Monthly cost	Dosing Frequency	Type
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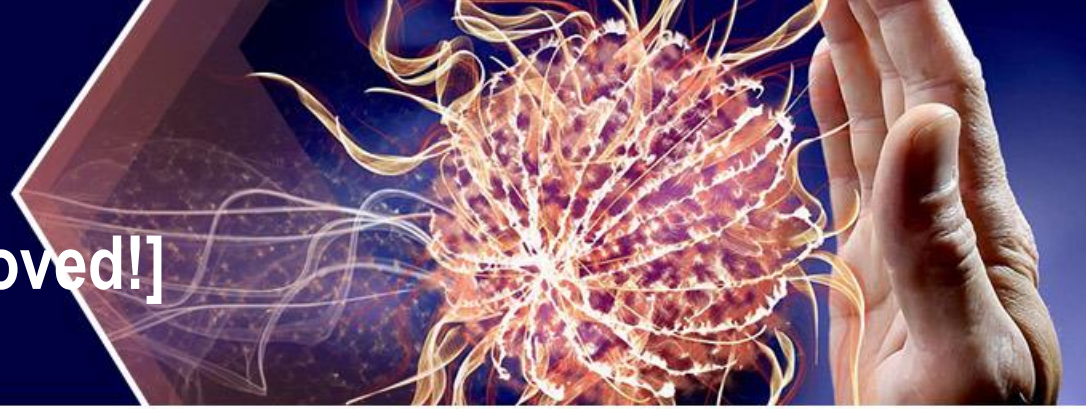
Nemolizumab (Nemluvio®)	Anti-IL-31RA	Sep 2024	≥12 yr.	$3000	60 mg loading, then 30 mg Q4W	Biologic

2023 JTFPP PP Atopic Dermatitis

[Lebrikizumab and Nemolizumab were not approved!]



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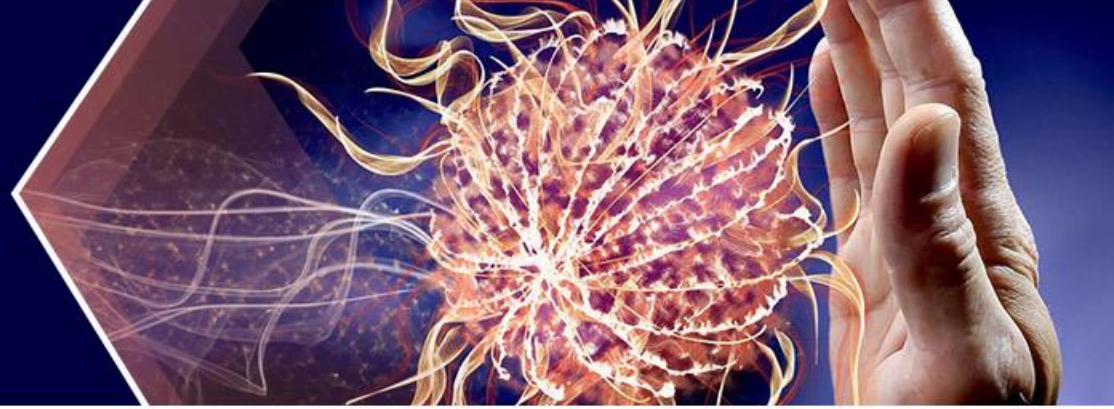
INTERVENTION Treatment or category of treatments considered	SEVERITY Severity of dermatitis that this recommendation applies to	RECOMMENDATION Text summary of recommendation	STRENGTH The strength of the recommendation	CERTAINTY GRADE rating for the certainty of evidence
SYSTEMIC TREATMENTS Consider if refractory, intolerant, or unable to use mid to high potency topical treatment	MODERATE, SEVERE	BIOLOGICS / MONOCLONAL ANTIBODIES **DUPILUMAB** We **recommend** adding dupilumab Age 6mo+	**Strong** in favor	**High** certainty evidence
	MODERATE, SEVERE	**TRALOKINUMAB** We **recommend** adding tralokinumab Age 12yo+	**Strong** in favor	**High** certainty evidence

Phototherapy Chronic Tx

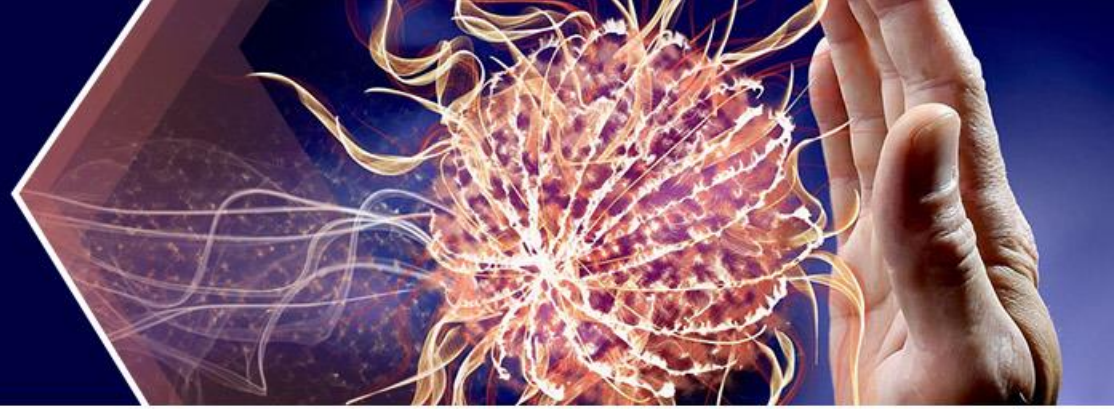
Phototherapy
Mechanism of action



- Suppresses Th2, T22, Th1 pathways, and antigen-presenting function of Langerhans' cells
- Normalizes epidermal hyperplasia and differentiation
- Reduces # of epidermal nerve fibers and axon guidance molecules
- Upregulates FoxP3+ Tregs
- Induces antimicrobial peptides
- Induces apoptosis of infiltrating T cells
- Reduces colonization of *S. Aureus & Malassezia*

. Wollenberg, A. 2018. J. Eur Acad Dermatol Venereol 32(6):850-578 Megna, S.2017. Lancet 367(9513):839-836
Wollenberg, A. 2020. J. Eur Acad Dermatol Venereol 32(12): 2717-2744.

Dosing Guidelines for NB-UVB



According to skin type:			
Skin Type	**Initial UVB dose (mJ/cm^2)**	**UVB Increase After Each Treatment (mJ/cm^2)**	**Maximum dose (mJ/cm^2)**
I	130	15	2000
II	220	25	2000
III	260	40	3000
IV	330	45	3000
V	350	60	5000
VI	400	65	5000

Maintenance therapy for NB-UVB after >95% clearance:		
1×/ wk	NB-UVB for 4 wk	Keep dose same
1×/ 2 wk	NB-UVB for 4 wk	Decrease dose by 25%
1×/ 4 wk	NB-UVB	50% of highest dose

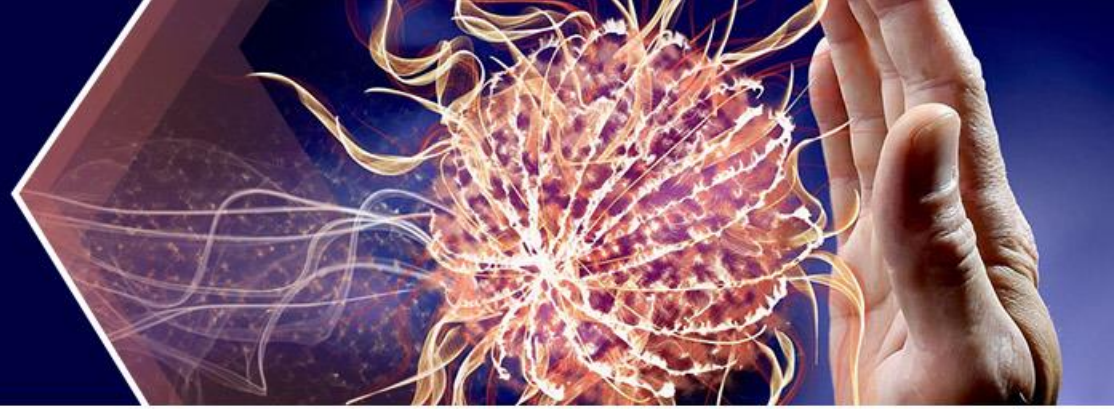
MED, Minimal erythema dose; NB, narrowband; *UV*, ultraviolet.

According to MED:	
Initial UVB	50% of MED
Treatments 1 -20	Increase by 10% of initial MED
Treatment ≥ 21	Increase as ordered by physician

MED=minimum erythema dose

Note: Initial Tx is 3-5x/wk.
Maintenance usually requires 1x/wk. or maintenance

Advantages & Barriers to phototherapy



Advantages

- Relieves pruritus
- Reduces need for TCS
- Can be used for maintenance therapy
- Overall low incidence of adverse Rxns
- No lab monitoring
- No increased melanoma C/A
- Low C/A risk for darker skin type (3-6)
- Home units can be cost effective (compared to biologics, small molecules)
- Not contraindicated in children [-.D]

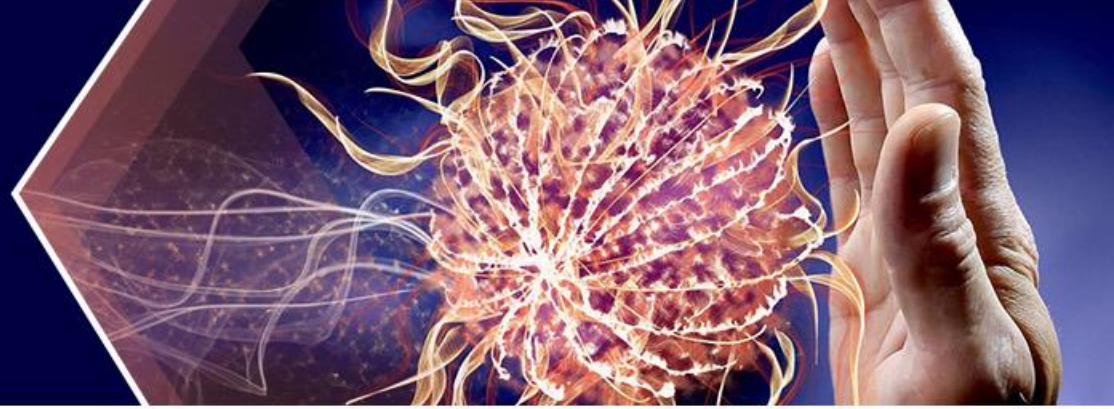
Barriers

- Does not effectively Tx hairy areas and skin folds
- Burning, stinging, actinic damage, photosensitive eruptions, HSV reactivation, facial hypertrichosis, pre-mature skin aging
- Requires eye protection (cataracts)
- Requires physician knowledgeable in phototherapy techniques
- Requires special equipment/room
- Minimal 3x/week at onset
- Pt skin type, skin C/A hx, cost, time, availability, patient preference

.Sidbury R. 2014. J of Am Aca Dermatology 71(2):327-349

Phototherapy

2023 JTFPP PP Atopic Dermatitis

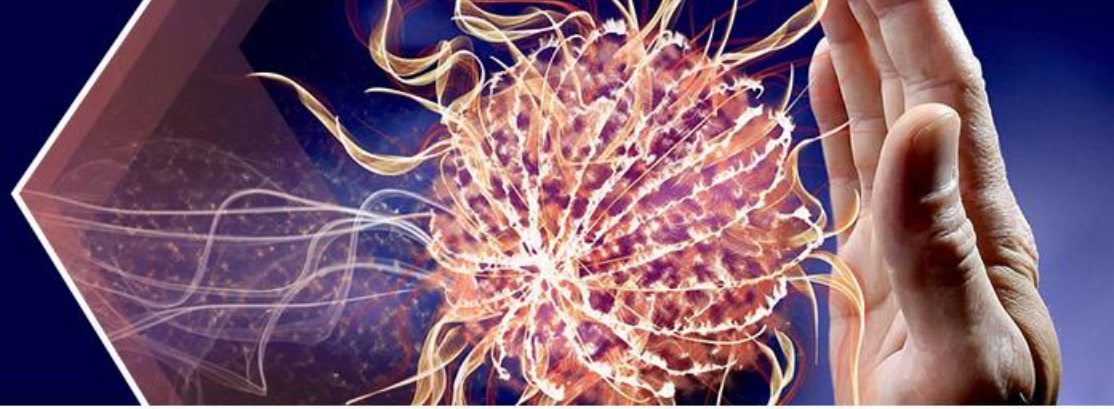


SEVERITY	RECOMMENDATION	STRENGTH	CERTAINTY
Severity of dermatitis that this recommendation applies to	Text summary of recommendation	The strength of the recommendation	GRADE rating for the certainty of evidence
MODERATE SEVERE	**UVB TREATMENT** We **suggest** adding clinic-based narrow band UVB treatment	**Conditional** in favor	**Low** certainty evidence

Consider if refractory, intolerant, or unable to use mid to high potency topical treatment and systemic treatment inclusive of a recommended biological agent

Narrowband UVB (311–313 nm)
In-office only

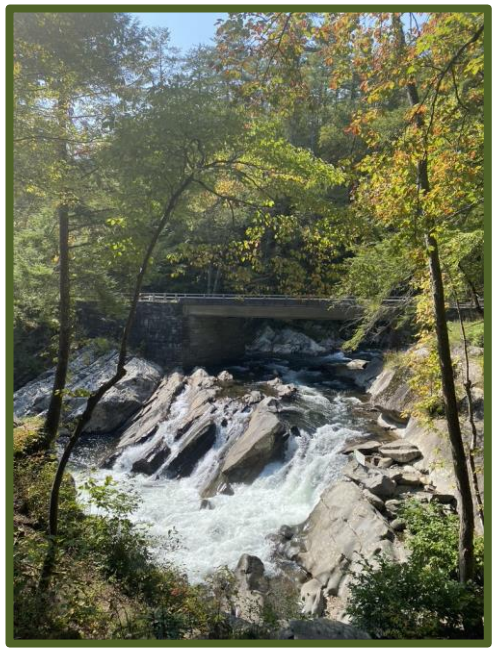
“Vacation Phototherapy”



Palm Beach

OR

Mountains



- 74% pts with mild-moderate AD had complete resolution during summer holidays, another 16 % had improvement.
- Seaside holiday gave complete resolution in 91% vs. 11% with mountain holiday

Patrizi, AF.2009. G Ital Dermatol Venereol **144**(4): 463-466.

Treatment Strategy for Atopic Dermatitis

Severe

Jak Inhibitors
Oral corticosteroid rescue
Cyclosporin; other Immunosuppressants
PUVA
Hospitalization

Moderate to severe

Topical JAK Inhibitors (Ruxolitinib)
Biologics (Dupilumab, Tralokinumab)
UV Therapy; wet wraps
Acute: Midpotent /Superpotent Steroids (acute: qd to bid);
Chronic: Low-med potent steroids qod previous areas

Mild-Moderate

Topical Corticosteroids
Topical Calcineurin Inhibitors
PDE4; Antibiotics if needed

Dry Skin & all stages

Hydration of Skin- Emollient
Identify and avoid triggers: contact allergens, aeroallergens, irritants, microorganisms, food

Oral JAK inhibitors FDA approved

FDA-Approved Advanced Treatments for Atopic Dermatitis

Drug (Brand)	Mechanism of Action	FDA Approval (AD)	Approved Age	Monthly cost	Dosing Frequency	Type
Dupilumab (Dupixent®)	Anti-IL-4Rα (blocks IL-4 & IL-13)	Mar 2017	≥6 mo..	$3000	600 mg loading, then 300 mg Q2W Q4W option	Biologic
Tralokinumab (Adbry®)	Anti-IL-13	Dec 2021	≥12 yr.	$3000	600 mg loading, then 300 mg Q2W (No 4W option) Slower onset of actin	Biologic
Lebrikizumab (Ebglyss®)	Anti-IL-13	Oct 2023	≥12 yr.	$3000	500 mg loading, then 250 mg Q2W Q 4W option	Biologic
Nemolizumab (Nemluvio®)	Anti-IL-31RA	Sep 2024	≥12 yr.	$3000	60 mg loading, then 30 mg Q4W	Biologic
Upadacitinib (Rinvoq®)	JAK1 inhibitor	Jan 2022	≥12 yr.	$5200-$7200	15 mg or 30 mg QD Limit 15 mg ≥65 yr.	Small Molecule
Abrocitinib (Cibinqo®)	JAK1 inhibitor	Jan 2022	≥12 yr.	$5200-$6800	100 mg or 200 mg	Small Molecule
Baricitinib (Olumiant)	JAK1/JAK2 inhibitor	Not FDA-approved for AD	NA	$2800	2 mg or 4	Small Molecule

FDA-Approved Advanced Treatments for Atopic Dermatitis

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Upadacitinib (Rinvoq®)	**JAK1 inhibitor**	**Jan 2022**	**≥12 yr.**	**$5200-$7200**	**15 mg or 30 mg QD Limit 15 mg ≥65 yr.**	**Small Molecule**
Abrocitinib (Cibinqo®)	**JAK1 inhibitor**	**Jan 2022**	**≥12 yr.**	**$5200-$6800**	**100 mg or 200 mg**	**Small Molecule**
Baricitinib (Olumiant)	**JAK1/JAK2 inhibitor**	**Not FDA-approved for AD**	**NA**	**$2800**	**2 mg or 4**	**Small Molecule**

FDA-Approved Oral JAK Inhibitors for Atopic Dermatitis

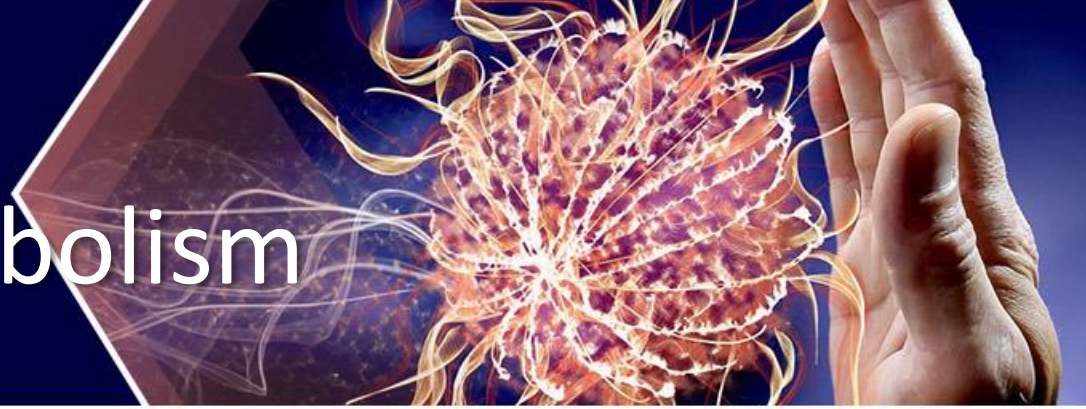
	Abrocitinib	Upadacitinib
Mechanism	JAK1	JAK1
Age Indication	≥ 12 yr.	≥ 12 yr.
Black box warnings	serious infections, mortality, malignancies major adverse cardiovascular events, thrombosis	serious infections, mortality, malignancies, major adverse cardiovascular events, thrombosis
Adverse reactions	Nasopharyngitis Nausea (19%) Headache Herpes simplex(1.2/100 pt yrs) Avoid anti-platelet drugs (ASA 81 mgs OK)	URTI Acne (14%) Headache; Acne (up to 16%) Herpes simplex (2.6/100 pt. yrs) Potential embryo/fetal toxicity
Lab Monitoring	TB, CBC, CMP, Hepatitis, pregnancy**	TB, CBC, CMP, Hepatitis, pregnancy*
Drug-drug interaction	CYP450 (2C19)	CYP450 (3A4)
Immunization	Update prior to starting Tx No live vaccines	Update prior to starting Tx No live vaccines

- Avoid if absolute lymphocyte count < 500 cells/mm^3, absolute neutrophil count < 1000 cells/mm^3, Hb < 8 g/dL.

** above plus platelet Ct <150,000/mm^3

MACE: major adverse cardiovascular events

Oral JAK inhibitors for RA/IMID:
Risk for Venous Thromboembolism



- 7 Meta-analyses (110 articles) of oral JAK inhibitors (tofacitinib, baricitinib, upadacitinib, arbrocitinib, filgotinib, peficitinib, decernotinib, ostamatinib) looking at VTE in RA & other immune-mediated inflammatory disease patients treated vs. placebo did not find any significant difference in risk.
- FDA Adverse Events Reporting System:
  - DVT or PE no increased risk for tofacitinib and ruxolitinib
  - Pulmonary arterial thrombosis risk ratio of 2.46 for tofacitinib.

Mori, S. Clin Rheumatol.2021;40(11):4457-4471

FDA-Approved JAK Inhibitors for Atopic Dermatitis

Consider if refractory, intolerant, or unable to use mid to high potency topical treatment and systemic treatment inclusive of a recommended biological agent.

Consider co-morbidities; risk factors; patient value and preferences; and exceptional circumstances.

INTERVENTION Treatment or category of treatments considered	SEVERITY Severity of dermatitis that this recommendation applies to	RECOMMENDATION Text summary of recommendation	STRENGTH The strength of the recommendation	CERTAINTY GRADE rating for the certainty of evidence
TOPICAL TREATMENTS				
SYSTEMIC IMMUNOSUPPRESSANTS	MODERATE, SEVERE	**ABROCITINIB, ~~BARICITINIB~~, OR UPADACITINIB** We **suggest** adding one of these three JAK inhibitors Age varies: 12 or 18 yo+ Suggested daily doses: Abrocitinib 100-200 mg; ~~Baricitinib 2-4 mg~~; Upadacitinib 15-30 mg	**Conditional** in favor	**Low** certainty evidence
SYSTEMIC IMMUNOSUPPRESSANTS	MODERATE, SEVERE	**BARICITINIB 1 mg DAILY** We **recommend against** adding baricitinib 1 mg daily	**Strong** against	**Low** certainty evidence

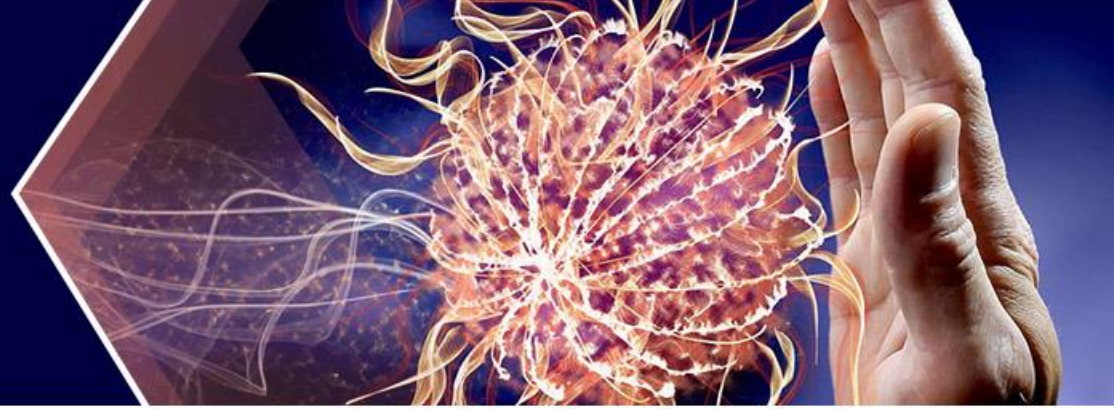
Systematic reviews & Meta-analysis of Systemic Txs of AD

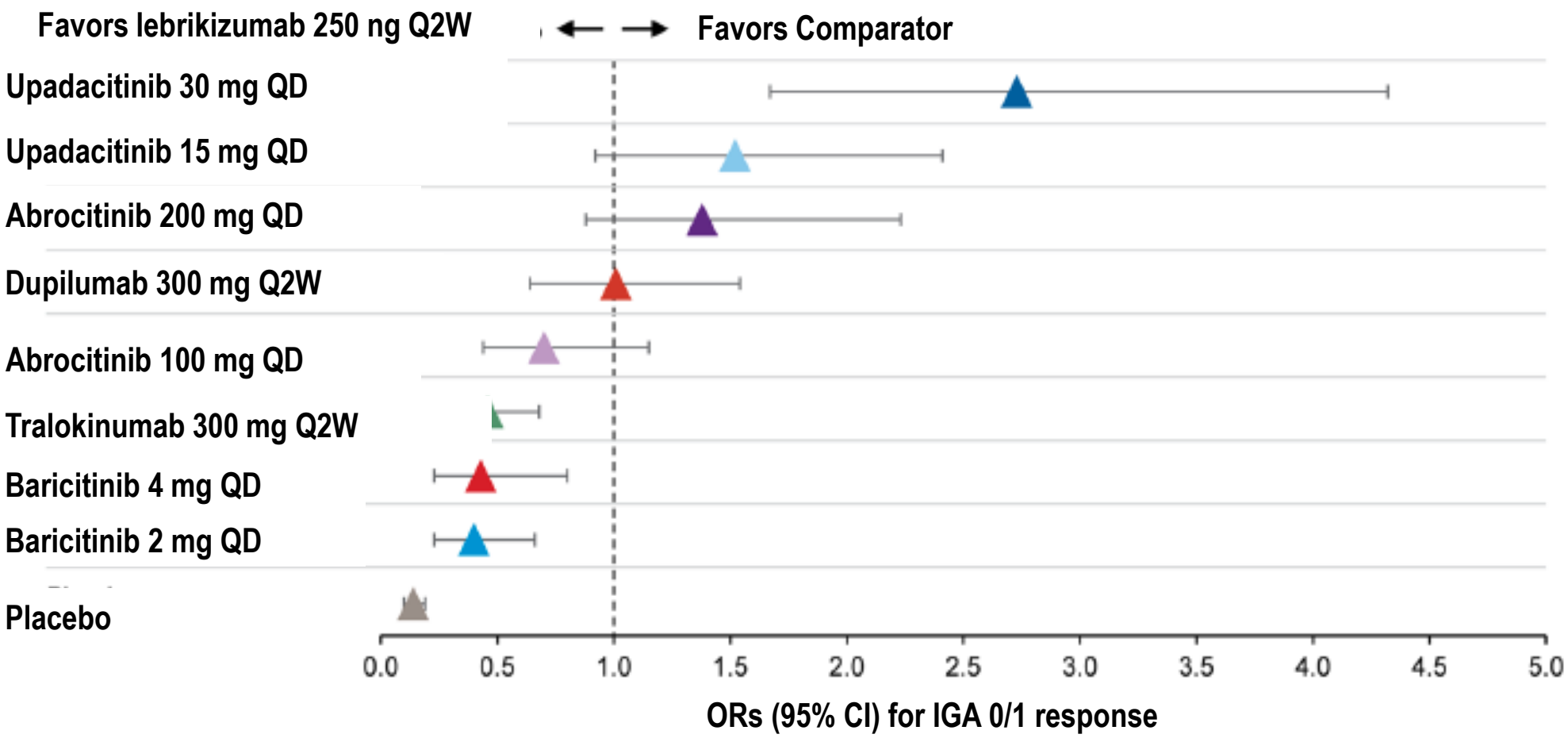
Short-term Efficacy of Systemic Therapies

Therapy)	EASI-75 Response (% patients)	IGA 0/1 Response (% patients)	Notable Itch Improvement
Upadacitinib 30 mg	70.8% (vs 11.3% placebo)	~48–50% (vs ~8% placebo)	Rapid, major itch relief in most pts
Abrocitinib 200 mg	62.9% (vs 11.3% placebo)	~45% (vs ~8–10% placebo)	Rapid itch relief (1–2 wks.)
Upadacitinib 15 mg	58.1% (vs 11.3% placebo)	~40% (vs ~8% placebo)	Rapid itch relief
Dupilumab)	43.5% (vs 11.3% placebo)	~38–40% (vs ~10% placebo)	Significant itch reduction by ~4 weeks
Abrocitinib	43.0% (vs 11.3% placebo)	~32% (vs ~8% placebo)	Marked itch reduction
Baricitinib 4 mg	34.1% (vs 11.3% placebo)	~20% (vs ~5% placebo)	Moderate itch reduction
Tralokinumab	27.8% (vs 11.3% placebo)	~16–22% (vs ~7–11% placebo)	Noticeable itch reduction by ~4 weeks
Baricitinib 2 mg	29.6% (vs 11.3% placebo)	~15% (vs ~5% placebo)	Moderate itch reduction
Nemolizumab)	~43% (vs ~30% placebo)	~36% (vs ~25% placebo)	Early, dramatic itch relief (48% vs 20%)
Placebo	11.3%	~5–11%	—

Silverberg, J. et al. Dermatol Ther (2025) 15:615–633

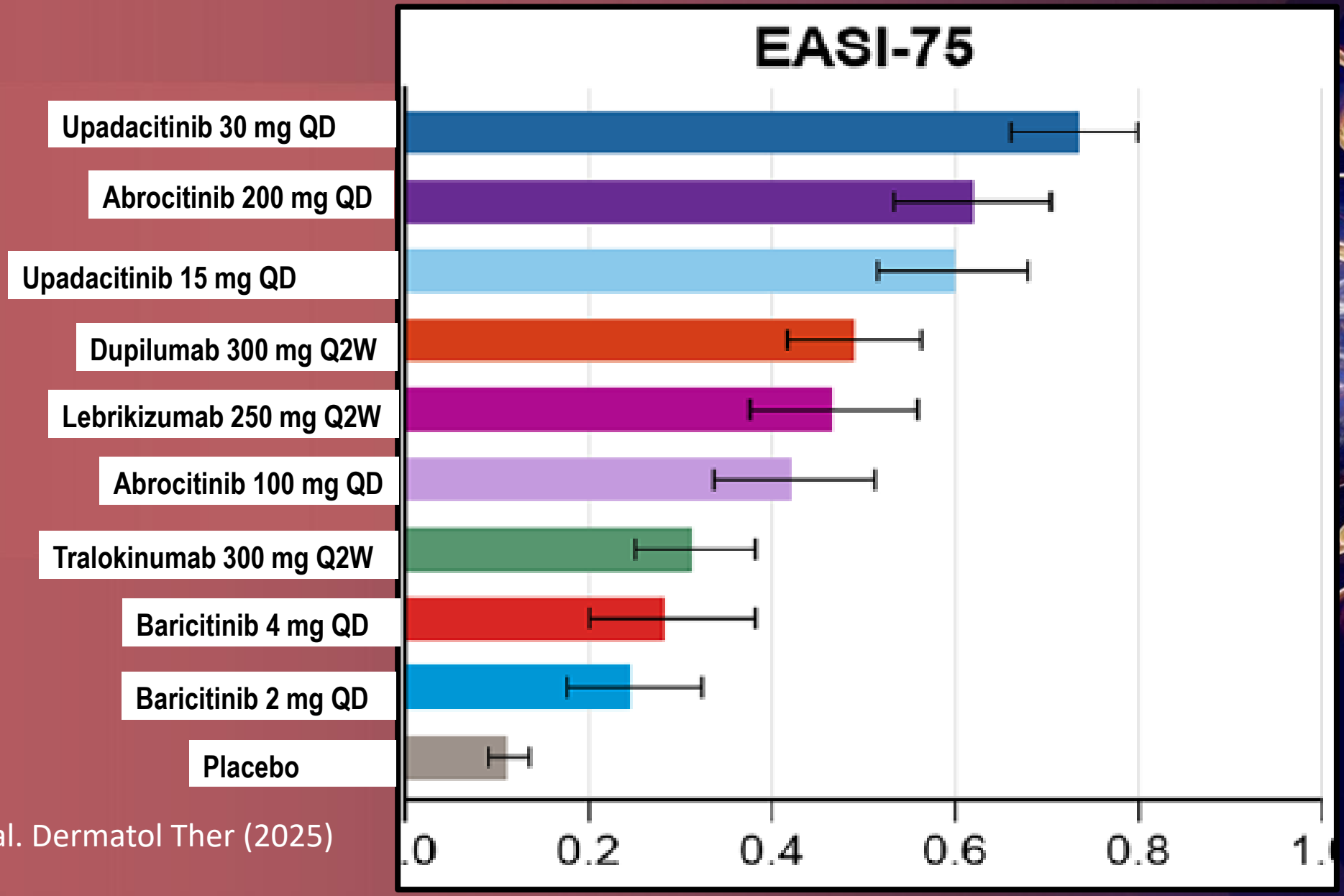
2025 Network Meta-Analysis IGA 0/1 Response Relative to Lebrikizumab





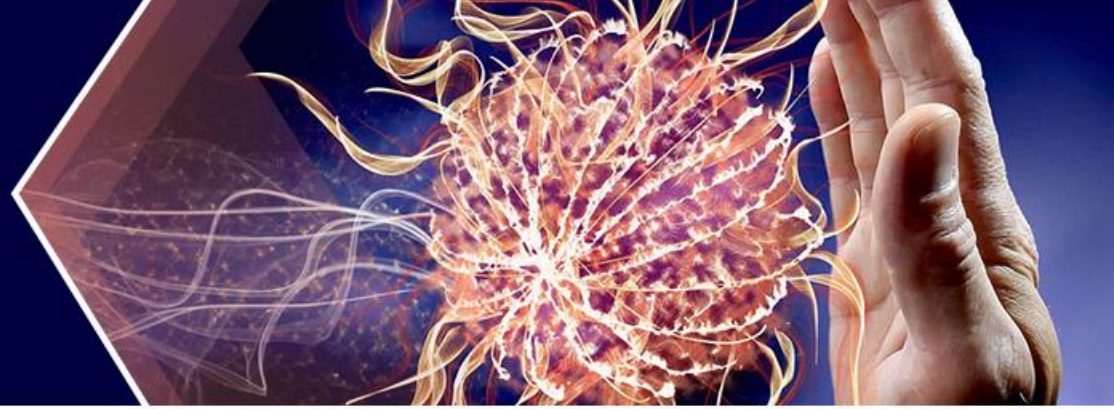
Silverberg, J. et al. Dermatol Ther (2025) 15:615-633

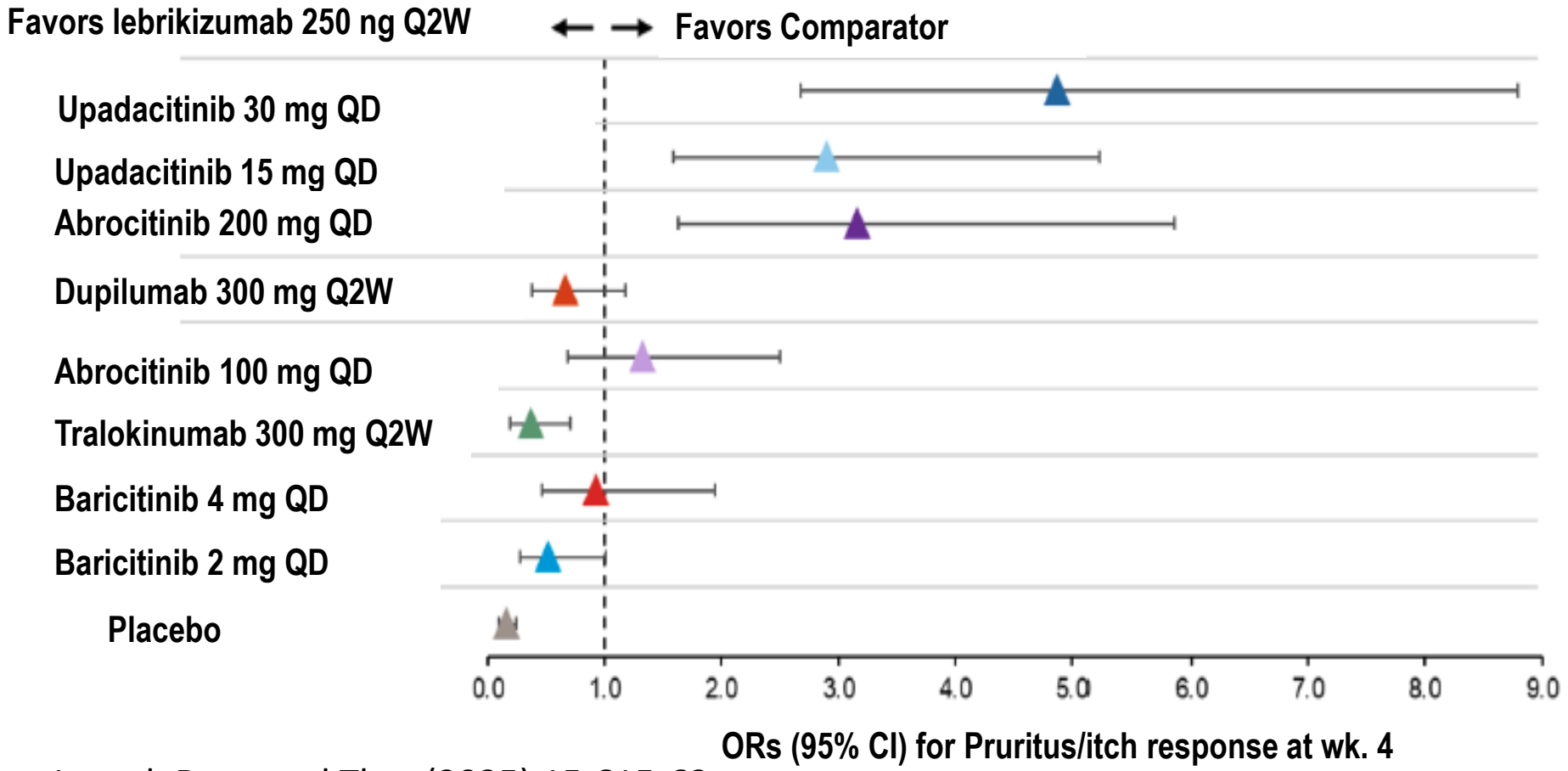
2025 Network Meta-Analysis EASI-75



Silverberg, J. et al. Dermatol Ther (2025) 15:615-633

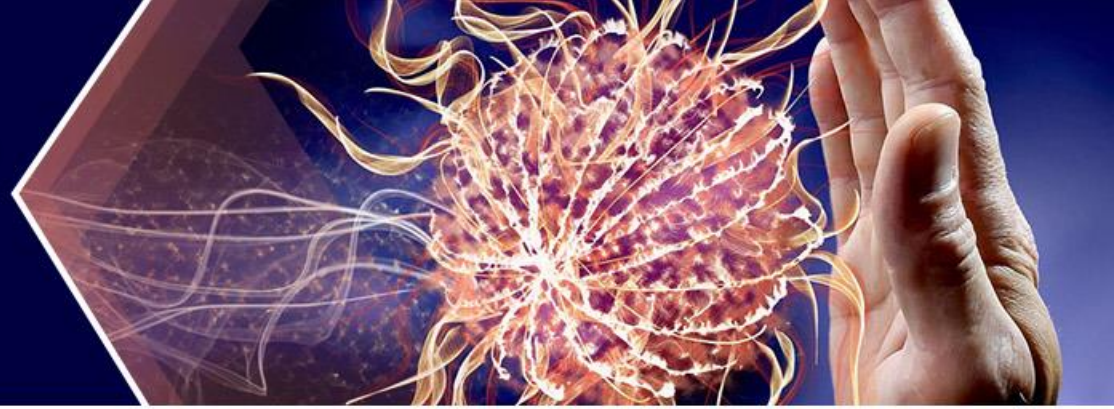
2025 Network Meta-Analysis
Week 4 Pruritus/itch NRS response





Silverberg, J. et al. Dermatol Ther (2025) 15:615-633

Biologics or JAK inhibitors?



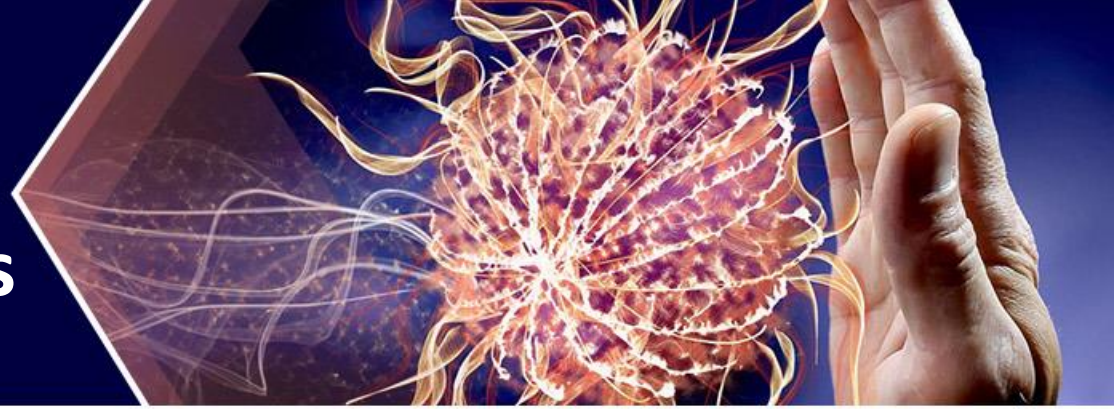
Biologics

- Established safety adults, adolescents, children
- No lab testing monitoring
- Less frequent dosing
- Dupilumab treats co-morbidities of AD
  - Asthma, AR, CRSwNP
  - EoE, CSU
  - Prurigo nodularis

JAK inhibitors

- Oral bioavailability
- Rapid efficacy
- Predictable pharmacokinetics
- No immunogenicity
- Flexible dosing
- Use as induction in acute phase
- Use intermittently or seasonally

Other Available Systemic Therapies



Representative risks with systemic immunosuppressants include[3]

Cyclosporine	Methotrexate	Azathioprine	Mycophenolate mofetil
▪ Boxed warning for malignancies, infection, HTN, and nephrotoxicity/ structural renal damage; need for blood monitoring of CsA[4]	▪ Boxed warning for malignancies, bone marrow suppression, infection, hepatic and renal toxicity, teratogenic, pulmonary fibrosis[5]	▪ Boxed warning for malignancies ▪ Mutagenic potential ▪ Hematologic toxicitites[6]	▪ Boxed warnings for pregnancy, loss/congenital malformations; malignancies, serious infection[7]

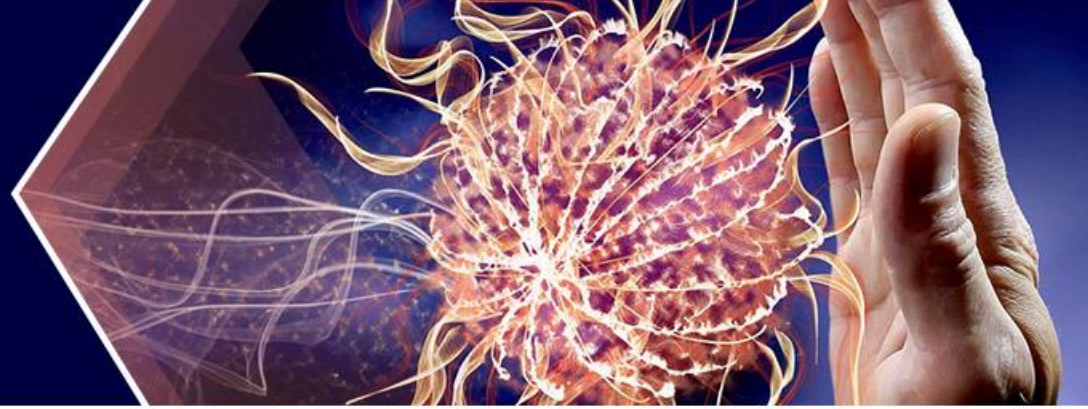
1. Sidbury R et al. *J Am Acad Dermatol*. 2014;71(6):1218–1233. 2. Akhavan A, Rudikoff D. *Semin Cutan Med* Surg. 2008;27:151–155.
3. Lindstrom J. Atopic dermatitis inadequately responsive to topical therapy. http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ DermatologicandOphthalmicDrugsAdvisoryCommittee/UCM439354.pdf. Accessed December 22, 2015. 4. Neoral ® [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2015. 5. Methotrexate [package insert]. Lake Forest, IL, Hospira; 2011. 6. Imuran® [package insert]. San Diego, CA. Pharmaceutics Internal Inc; 2011. 7. CellCept® [package insert]. Nutley, NJ: Roche; 2009

Other Systemic Agents

JTFPP 2023 Recommendations

SEVERITY Severity of dermatitis that this recommendation applies to	RECOMMENDATION Text summary of recommendation	STRENGTH The strength of the recommendation	CERTAINTY GRADE rating for the certainty of evidence
MODERATE, SEVERE	SMALL MOLE **CYCLOSPORINE** We **suggest** adding cyclosporine Shared-decision making should determine whether to start therapy at high dose (5mg/kg) or low dose (3 mg/kg)	**Conditional** in favor	**Low** certainty evidence
MODERATE, SEVERE	**METHOTREXATE** We **suggest against** adding methotrexate	**Conditional** against	**Low** certainty evidence
MODERATE, SEVERE	**MYCOPHENOLATE** We **suggest against** adding mycophenolate	**Conditional** against	**Low** certainty evidence
MILD, MODERATE, SEVERE	**SYSTEMIC CORTICOSTEROIDS** We **suggest against** systemic corticosteroids for all patients with atopic dermatitis	**Conditional** against	**Low** certainty evidence

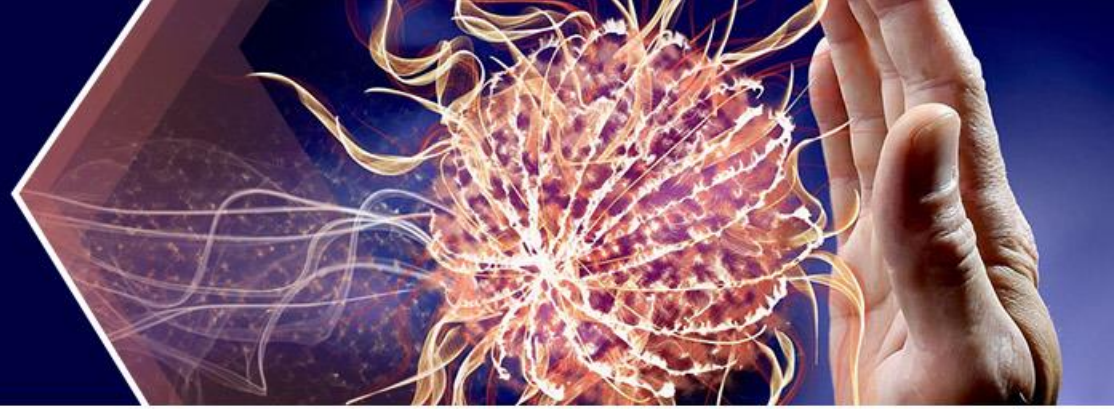
Cyclosporine A (Acute & Chronic AD Tx)



- **Mechanism:** Inhibits calcineurin-dependent signaling-- suppressing IL-2, interferons, and T cell activation[1]
- **Evidence for efficacy:**
  - Meta-analysis of 25 RCT: 55% improvement after 6-8 wks[1]
  - Systematic review of 34 RCT, 50-95% improvement; preferred over prednisone
- **Onset:** 2 wks. (micro-emulsions); significant symptom improvement after 6-8 wks..; relapse <2-6 wks. after d/ced [2]
- **Dose**: Induction 3-5 mg/kg x 4-6 wks.., maintenance 2.5-3 mg/kg divided AM and PM; after therapeutic response, consider step-wise dose reduction[1-2]

1. Werfel,T.2021. J Dtsch Dermatol Ges 19(1): 151-168 2. Wollenberg, A. 2018. J. Eur Acad Dermatol Venereol 32(6):850-578
3. Sidbury R. 2014. J of Am Aca Dermatology 71(2):327-349.

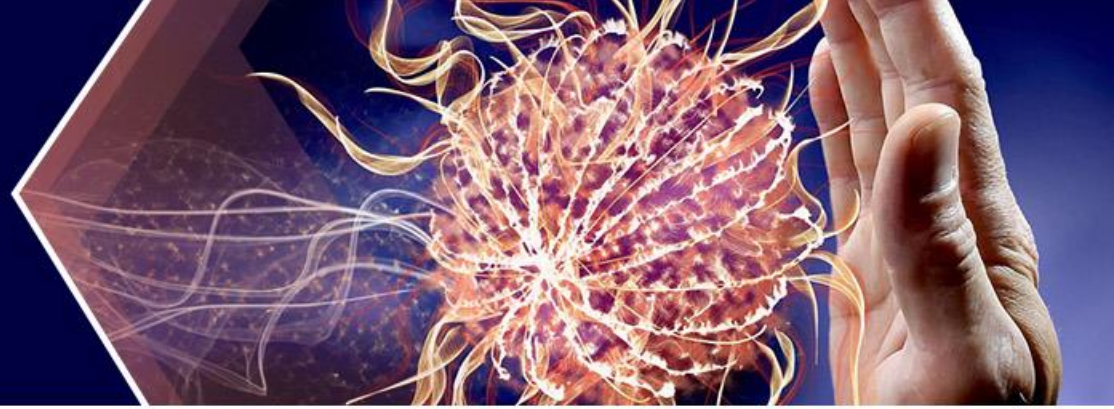
Cyclosporine A efficacy comparisons:



- Cyclosporine > phototherapy in efficacy
- Cyclosporine trends to have > efficacy than chronic prednisolone[2]
- Cyclosporine = methotrexate efficacy in children (SCORAD) but shorter drug survival [2]
- Cyclosporine = mycophenolic acid [1-3] in efficacy ; cyclosporine has quicker onset of action but shorter duration after d/cing[3]
- Cyclosporine< dupilumab in risk/benefit assessment due to side effects of cyclosporine[1]

. 1.Werfel,T.2021. J Dtsch Dermatol Ges 19(1): 151-168 2. Wollenberg, A. 2018. J. Eur Acad Dermatol Venereol 32(6):850-578
3.Haeck, IM. 2011. Am Acad Dermatol **64**(6): 1074-1084

Cyclosporine A



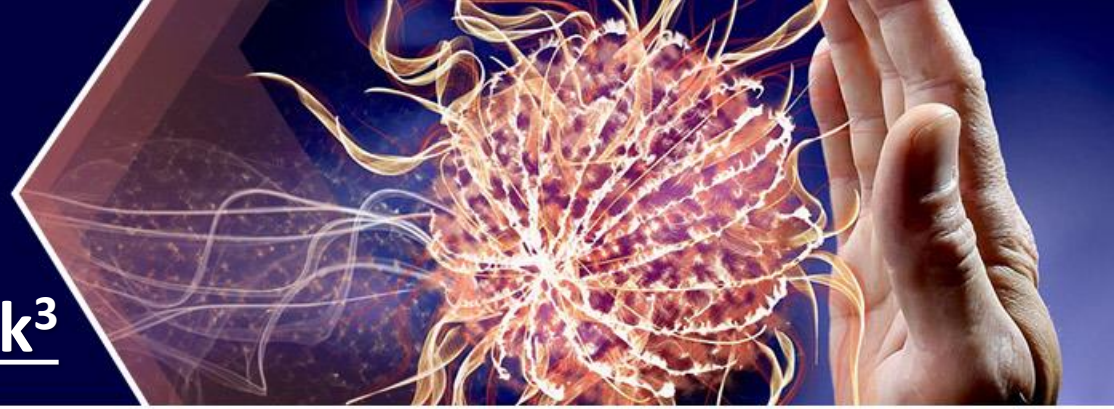
- **Monitoring**[2-3]
  - Baseline: BP, Kidney& liver function, U/A, lipids, CBC, Mg, K, uric acid , TB test, HIV & HCG if indicated
  - Follow-up: BP each visit; Kidney& liver function, U/A, CBC, C, Mg, K, uric acid q 2 wks.. for 2-3 mo.. then monthly; TB test q yr. Trough levels not needed
- **Risks:** increased with higher dose, reduced renal function, and in elderly; avoid live vaccinations; hypertrichosis; gum hyperplasic; serious infections; do not combine with phototherapy & provide UV protection[3-5]
- **Teratogenicity: ?,** Possible use with pregnancy/fathering[3]
- **General safety:** 50% on long-term Tx have serum creatine increase > 30%; treat hypertension; reduce dose if side effects. Drug interactions: e.g., anti-fungals, macrolides, statins, Ca Channel blockers, warfarin.[3,4,6]

1. Schmitt, I. J Eur Acad Dermatol Venereol **21**(5): 606-619. 2. Roekevisch, EP.2014.JACI 133(2)"429-418
3. Sidbury R. 2014. J of Am Aca Dermatology 71(2):327-349. 4.Wollenberg, A. 2018. J. Eur Acad Dermatol Venereol 32(6):850-578.
5.Berger, TG. 2022. UptoDate. 6. Sawangjit, R.P. 2020.Cochrane Database Syst Rev 9:CD013206

Acute flares of AD:

Guideline Recommendations:

US AAD2014[1]; European EG2018[2]; German52k[3]



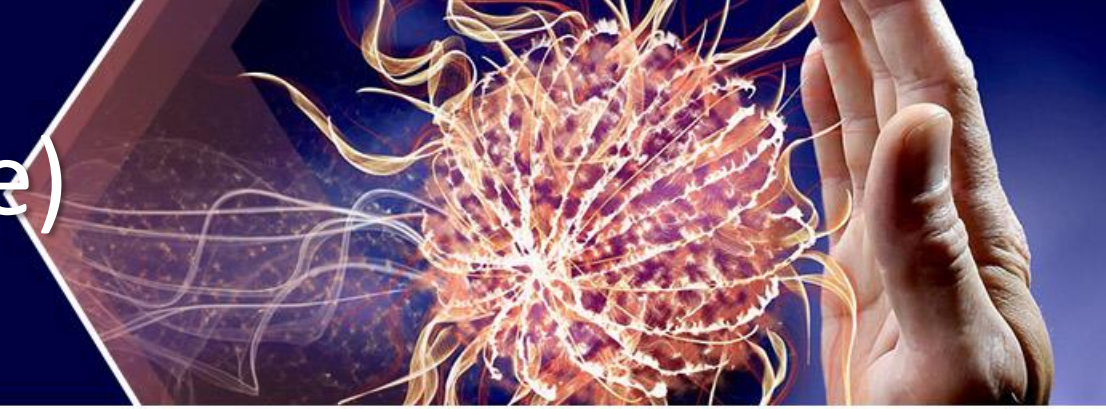
- Rapid onset (1-2 wks.)/bridge to slow-acting systemic immunosuppressants
  - Oral corticosteroids (not FDA approved), risk of rebound
    - Adults-may be considered **([II, C][1]; [-,D][2]; [Strong consensus]**[3]
    - Children-use with caution, exceptional cases ([N/A] [1]; [-,D][2]; [-·D][3]
  - Cyclosporine (FDA approved adults) may consider in children; no immediate rebound; recommended over oral corticosteroids[4]
    - **Adults [I-II, B]** [1]; **[1a, A]** [2]**;[Strong consensus]** [3]
    - Children [1-2, B] [1]; [2b,B] [2]; [Strong consensus] [3]

1. Sidbury R. 2014. J of Am Aca Dermatology 71(2):327-349 2. Wollenberg, A. 2018. J. Eur Acad Dermatol Venereol 32(6):850-578

3. Werfel,T.2021. J Dtsch Dermatol Ges 19(1): 151-168 4.Berger, T.G. 2022. UpToDate. T. Post. UpToDate, Waltham, MA

Traditional Oral immunosuppressant

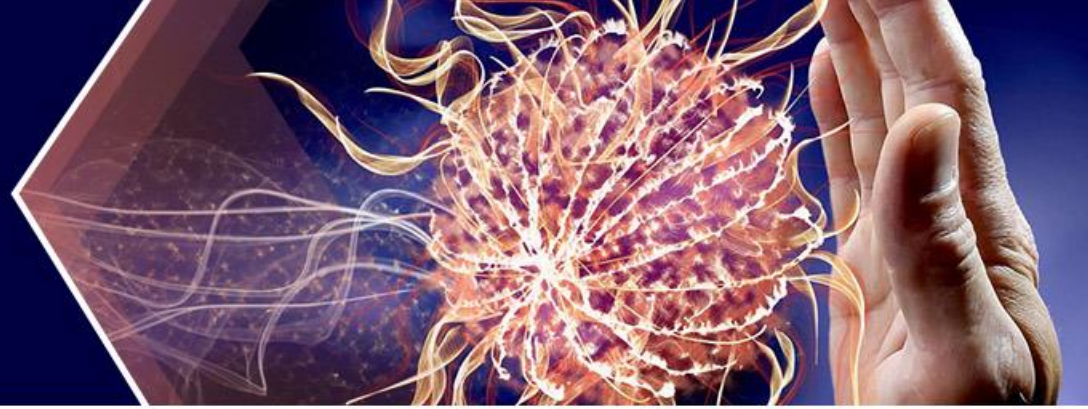
Oral Corticosteroids (acute use)



- **Mechanism:** Broad anti-inflammatory, non-specific suppression of immunological functions
- **Evidence:**
  - 3 small PC, randomized studies (12-20 patients/study); 2-4 week studies showed efficacy vs. placebo[1-3]
  - Efficacy supported by non-controlled observational studies and consensus[4]
- **Onset** 1-2 wks.; relapse < 2 wks.
- **Dose:** $\leq$ 0.5 mg/kg prednisolone equivalent for 1-2 wks.. and taper over 2-4 wks..

1. Heddke, RJ.1984. Br Med J (Clin Res Ed) **289**(6446): 651-654. 2. La Rosa, MI. 1995. Current therapeutic research **56**(7): 720-726.
3. Price ES. 2019.JACI 143(2):AB134 4. Werfel,T.2021. J Dtsch Dermatol Ges 19(1): 151-168

Algorithm for Treatment of Atopic Dermatitis for Ginnie



Emollients + acute & chronic (proactive) use of TCS+ CNI + dust mite & cockroach avoidance + avoidance of cocamide DEA containing products.

SHARED DECISION MAKING

Consider Dust Mite & Grass SCIT or SLIT and ? wet wraps for flares

Comorbidities Consider Ginnie's Asthma, AR

Skin improves but remains uncontrolled

Check im Ginnie has any drug interactions

Trial of Biological Tx

SHARED DECISION MAKING

Oral Small Molecule

Treat for 8-12 wks.. and reassess

Thank you!

drdanawallace@gmail.com