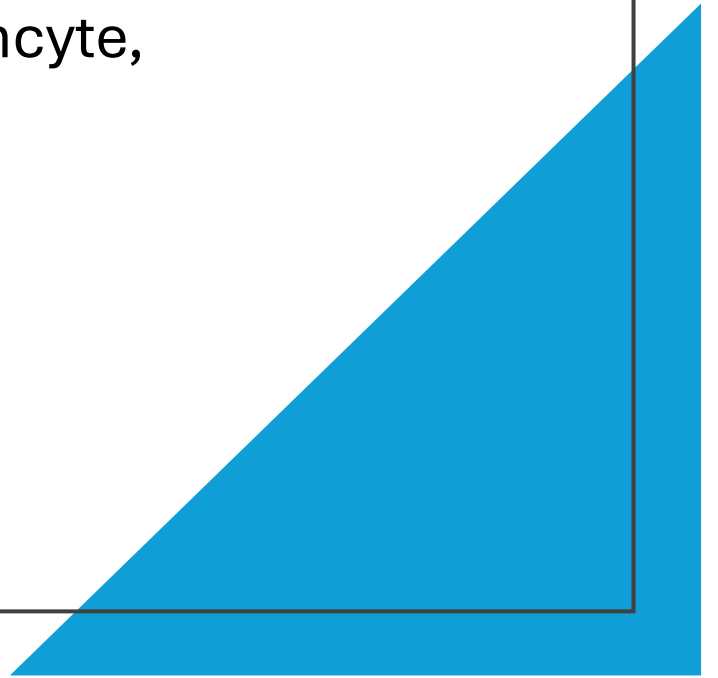


Changing Paradigm in the Management of Atopic Dermatitis

- JiaDe Yu, MD MS
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- Virginia Commonwealth University School of Medicine
 - Richmond, VA

Disclosures

- JY has served as a consultant/speaker/investigator for the following: AminoChain, Astria, Arcutis, Hypothesis, Incyte, Johnson&Johnson, LEO Pharma, Priorvant, Sanofi/Regeneron, Soteri Skin.



Agenda

01

Update our understanding of atopic dermatitis pathogenesis

02

Discuss new data on existing treatments of atopic dermatitis

03

Allude to exciting new therapies in atopic dermatitis

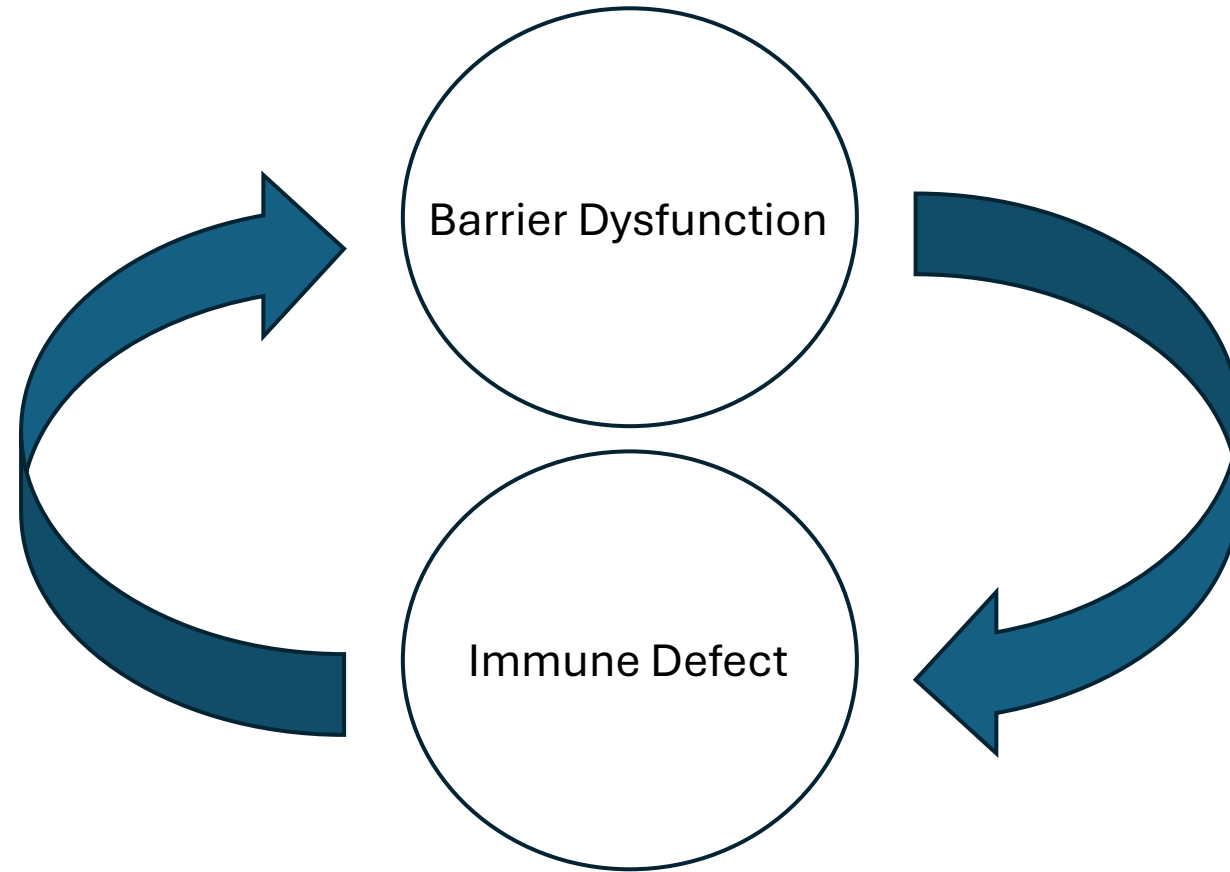
Two complementary theories

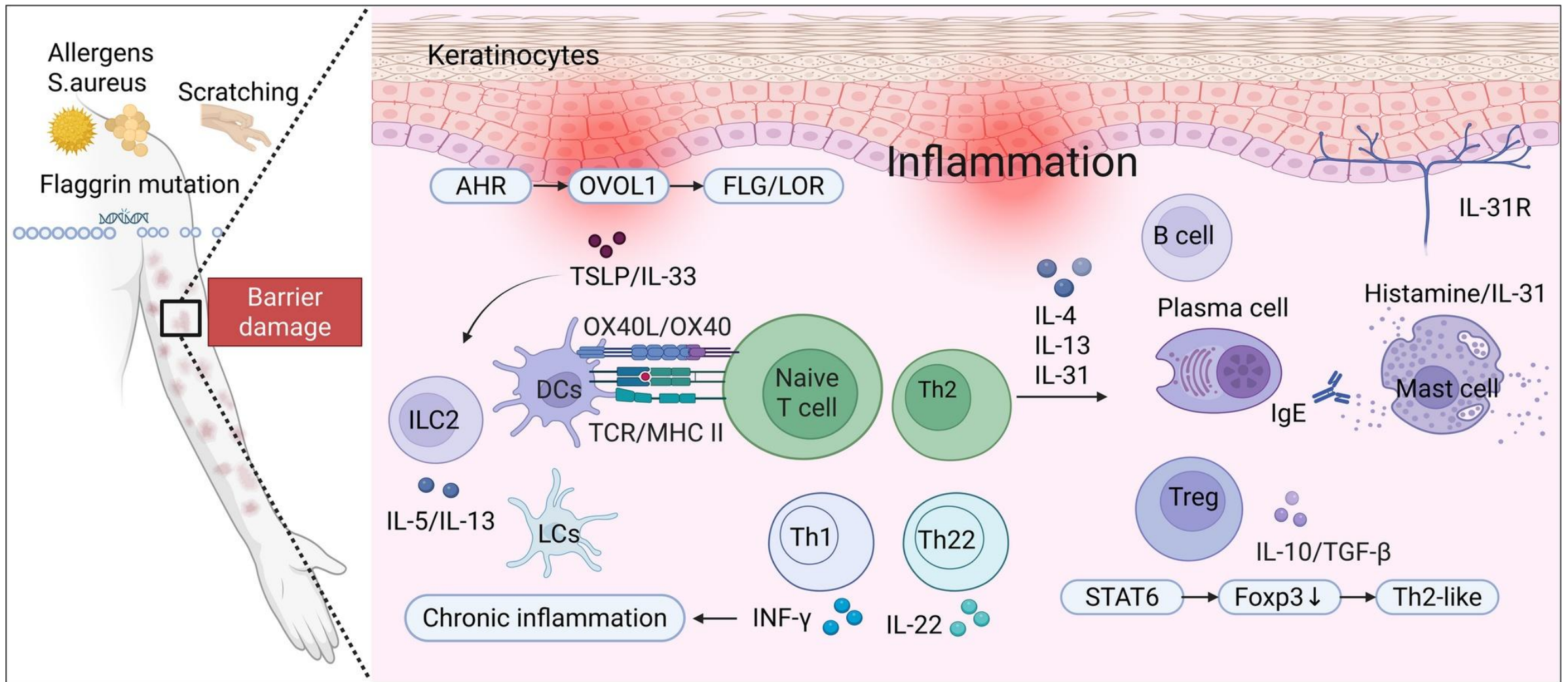
- **1) Outside-In Hypothesis**

- **Primary barrier defect** → allergen penetration → secondary immune activation → itch and scratch
 - Filaggrin deficiency (10-50% of people), abnormal ceramides and lipids, abnormal tight junctions (claudins)
 - Elevated skin pH → activation of proteases → alarmin activation → barrier disruption

- **2) Inside-Out Hypothesis**

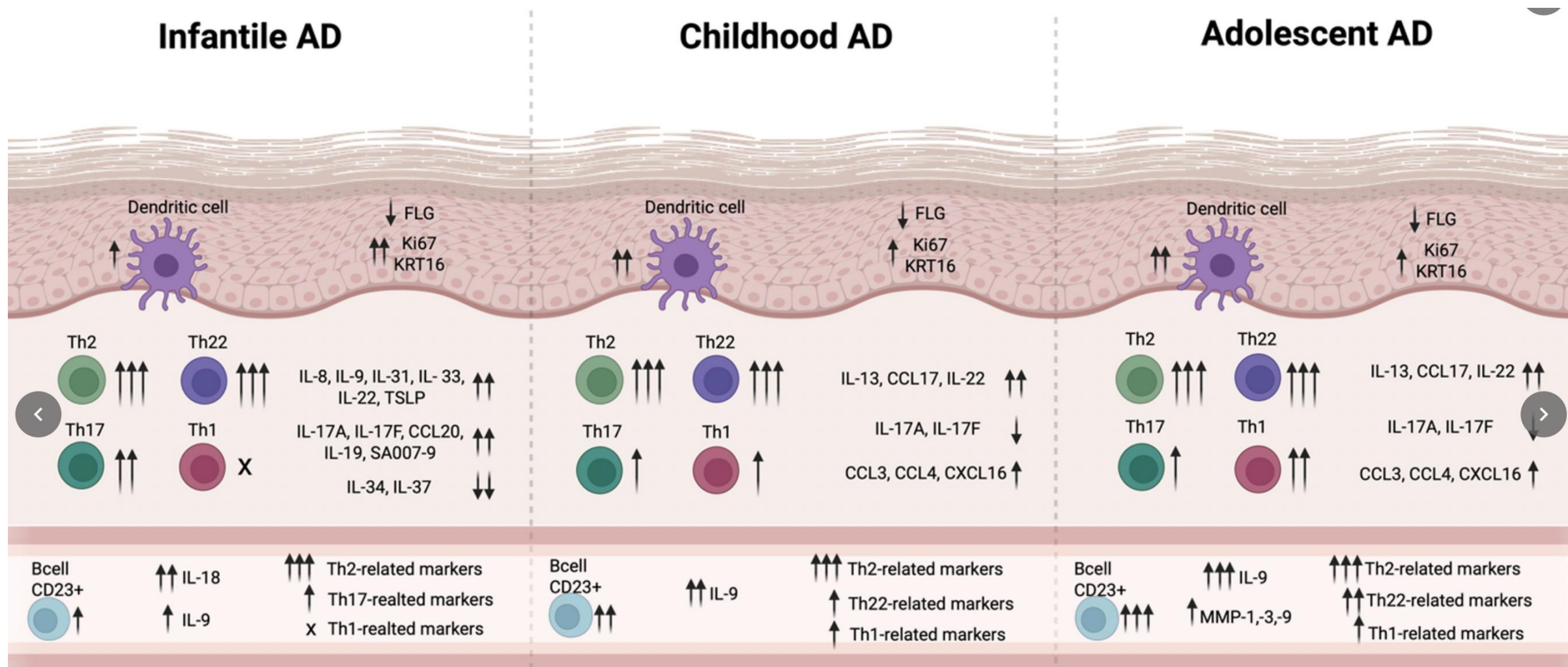
- **Primary immune defect** → secondary barrier defect and dysbiosis
→ itch and scratch
 - Th2 polarization → overexpression of IL4/13, IL5, IL31
 - IL-4/13 → downregulation of filaggrin, loricrin, involucrin,
 - IL-31 → itch
 - High IgE in 80% of patients with AD
 - Th17 predominates in Asians





Immunologic Markers Vary Across Ages

Age group	Dominant molecular features
Infants (<6 mo onset)	Th2/Th22 with the highest Th17 activation and innate-immunity markers; Th1 absent; elevated IL-33, IL-1RL1/IL-33R, IL-9 (linked to allergic/food sensitization); robust barrier gene downregulation despite short disease duration
Children	Th2/Th22 dominant; Th17 diminishes; slight emergence of Th1 (early chronicity)
Adolescents	Sustained Th2/Th22; increasing Th1 and tissue-remodeling markers (MMPs), approaching but below adult levels
Adults	Th2/Th22 plus unique, significant Th1 polarization (IFN- γ , CXCL9/10/11); only adults show significant filaggrin reduction; second Th17 peak
Elderly (≥ 60 yr)	Reduced canonical Th2 markers, elevated pro-inflammatory/innate cytokines (IL-18, IL-6) driving Th1/Th17; shift from naïve to effector/cytotoxic T cells

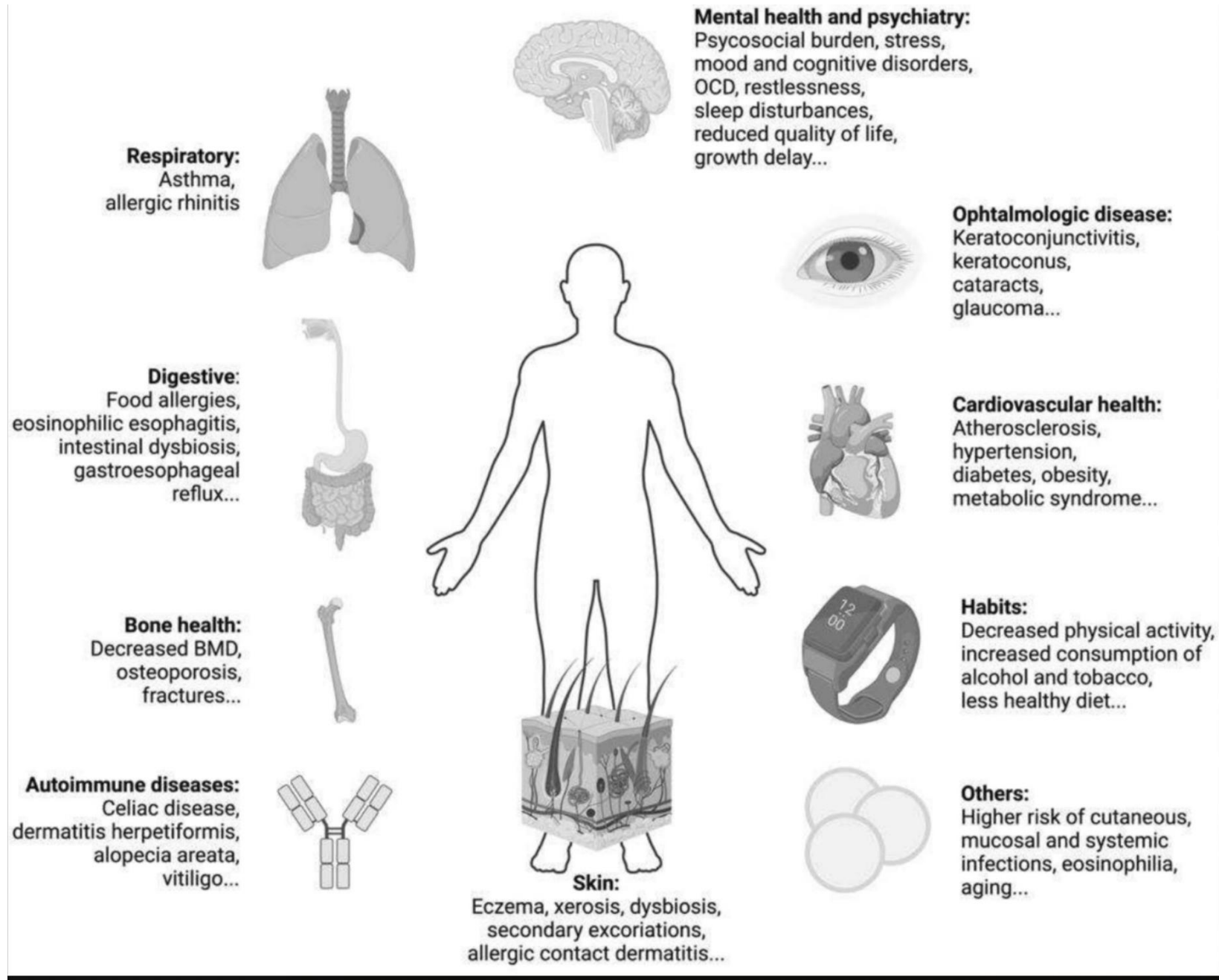




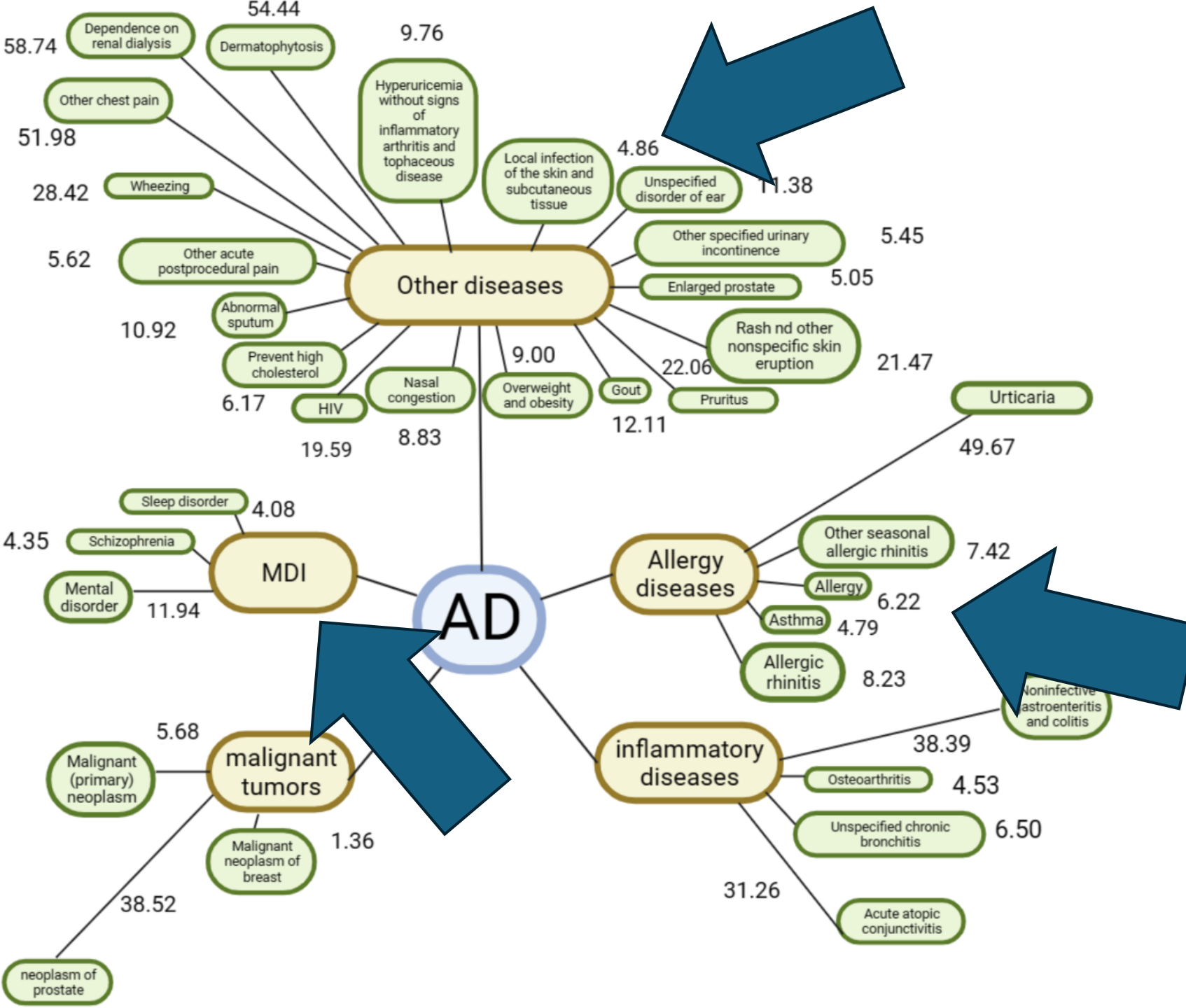
Immunologic Markers Vary by Race

Age group	Dominant molecular features
European / White	Th2-dominant with Th1 involvement, less Th17; strong FLG-driven barrier defect; thinner epidermis
Asian (East/South)	Blended Th2 plus prominent Th17/Th22 activation (psoriasiform features, scaling, lichenification); most pronounced lipid-gene downregulation
African / Black	Strong Th2/Th22 skewing with robust IgE; attenuated/absent Th1 and Th17
Hispanic	Mixed phenotype resembling both White and Black AD; broad systemic inflammation on proteomics

Atopic Dermatitis is a SYSTEMIC Disease



Prados-Carmona A, Husein-ElAhmed H, Navarro-Triviño FJ, Ruiz-Villaverde R. Atopic Dermatitis beyond Eczema: A Review on its Systemic Impact through Pruritus and Associated Comorbidities. Clin Rev Allergy Immunol. 2025 Jul 16;68(1):66. doi: 10.1007/s12016-025-09075-w. PMID: 40668306.

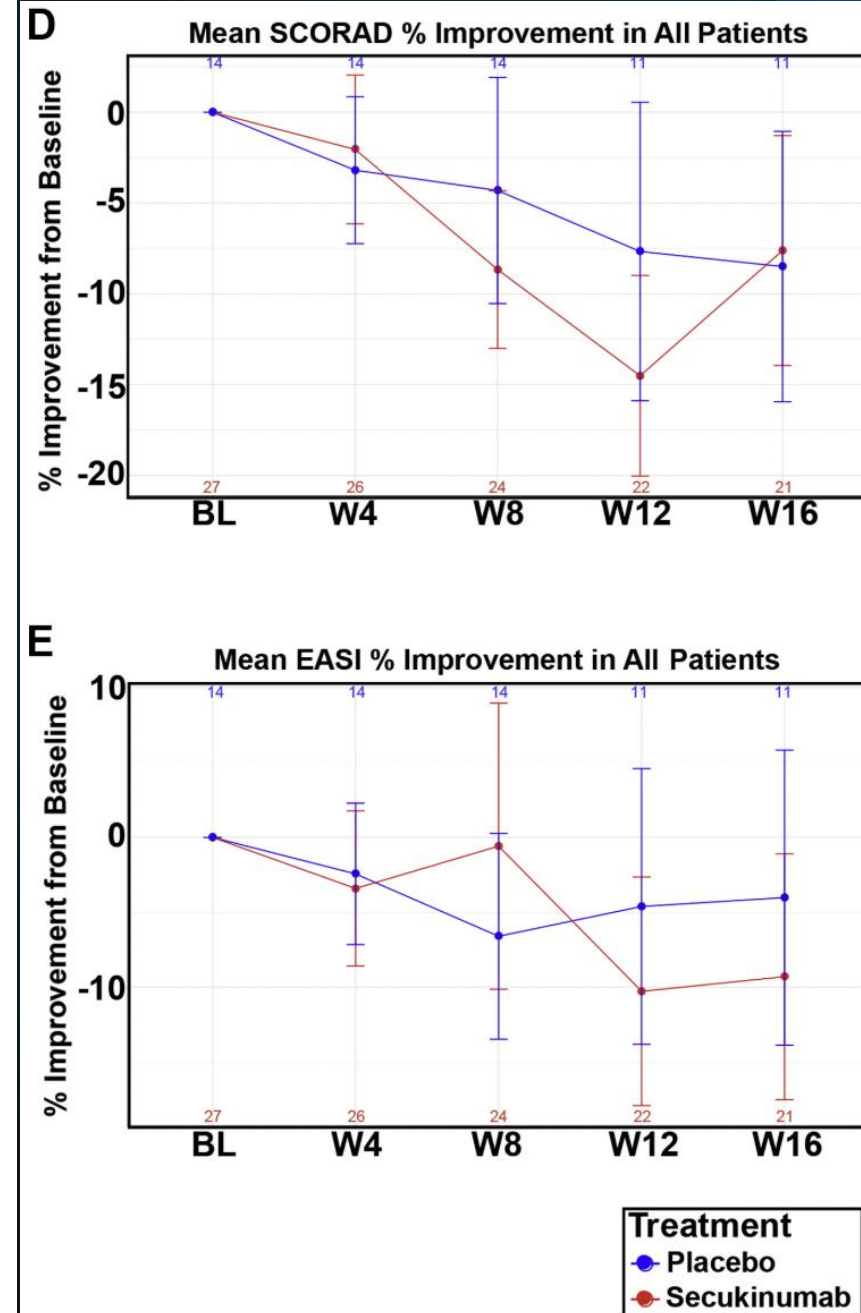


Liu, Y., Chen, X., Su, Z. *et al.* Identification of atopic dermatitis-associated diseases based on the National health and nutrition examination survey (NHANES) 2013–2018. *Sci Rep* **15**, 13778 (2025).
<https://doi.org/10.1038/s41598-025-98551-6>

Has differing molecular markers
informed treatment?

No.

Ungar B, Pavel AB, Li R, Kimmel G, Nia J, Hashim P, Kim HJ, Chima M, Vekaria AS, Estrada Y, Xu H, Peng X, Singer GK, Baum D, Mansouri Y, Taliercio M, Guttman-Yassky E. **Phase 2 randomized, double-blind study of IL-17 targeting with secukinumab in atopic dermatitis.** J Allergy Clin Immunol. 2021 Jan;147(1):394-397. doi: 10.1016/j.jaci.2020.04.055. Epub 2020 May 16. PMID: 32428528.





Updated Data for Existing AD Treatments



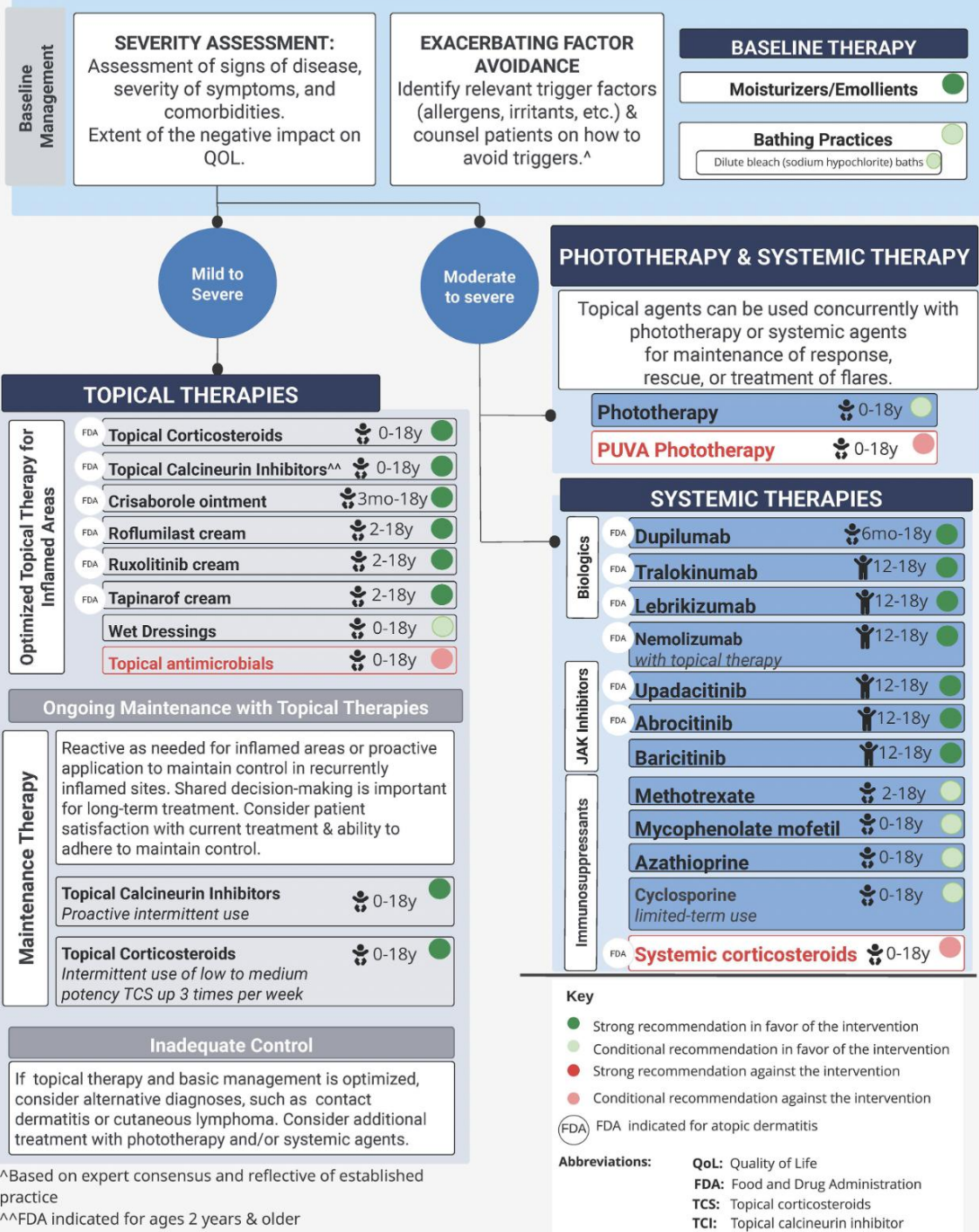
TOPICAL THERAPIES

Optimized Topical Therapy for Inflamed Areas

FDA	Topical Corticosteroids	0-18y	●
FDA	Topical Calcineurin Inhibitors ^{^^}	0-18y	●
FDA	Crisaborole ointment	3mo-18y	●
FDA	Roflumilast cream	2-18y	●
FDA	Ruxolitinib cream	2-18y	●
FDA	Tapinarof cream	2-18y	●
	Wet Dressings	0-18y	●
	Topical antimicrobials	0-18y	●

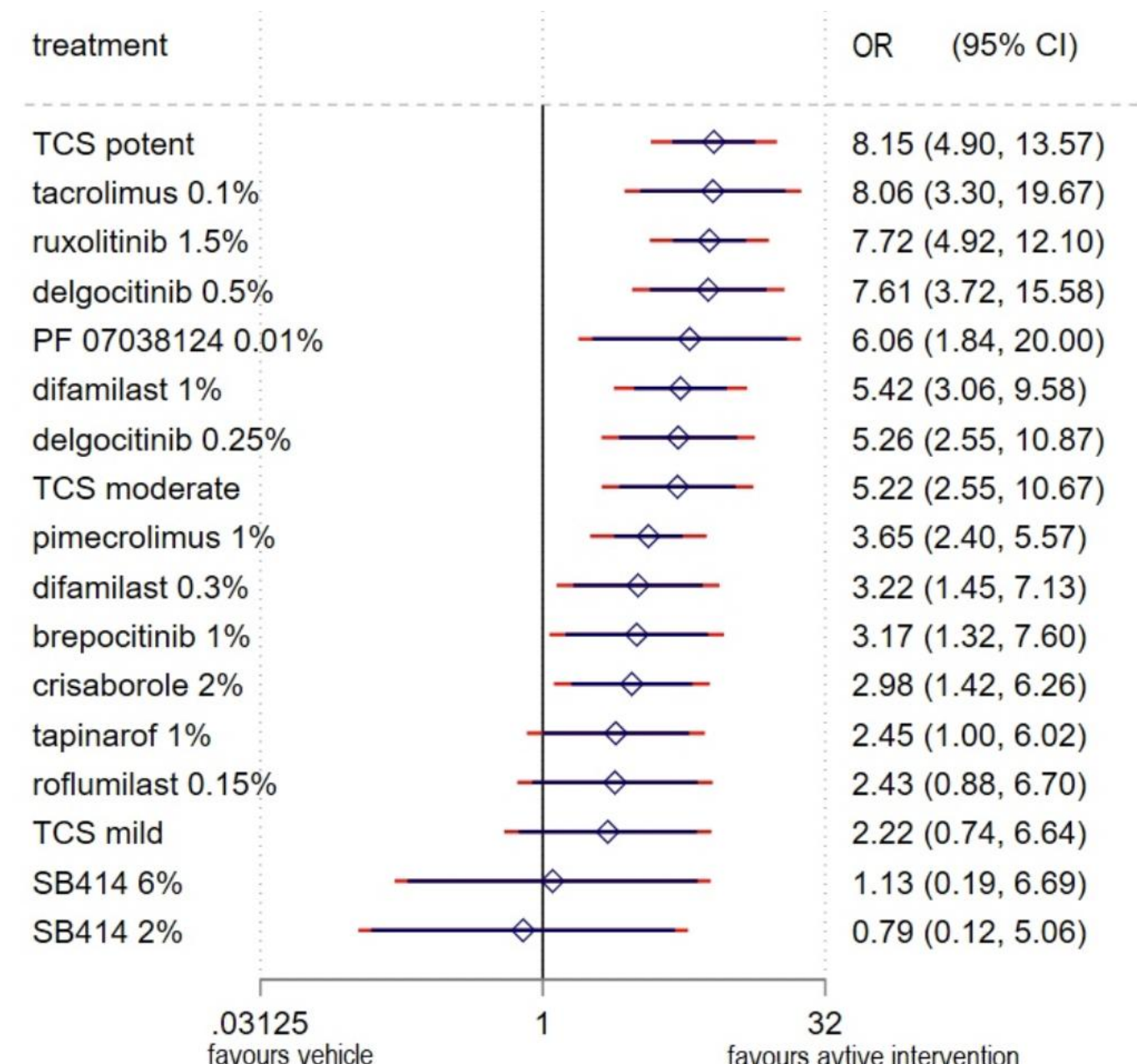
Ongoing Maintenance with Topical Therapies

Children & adolescents with atopic dermatitis

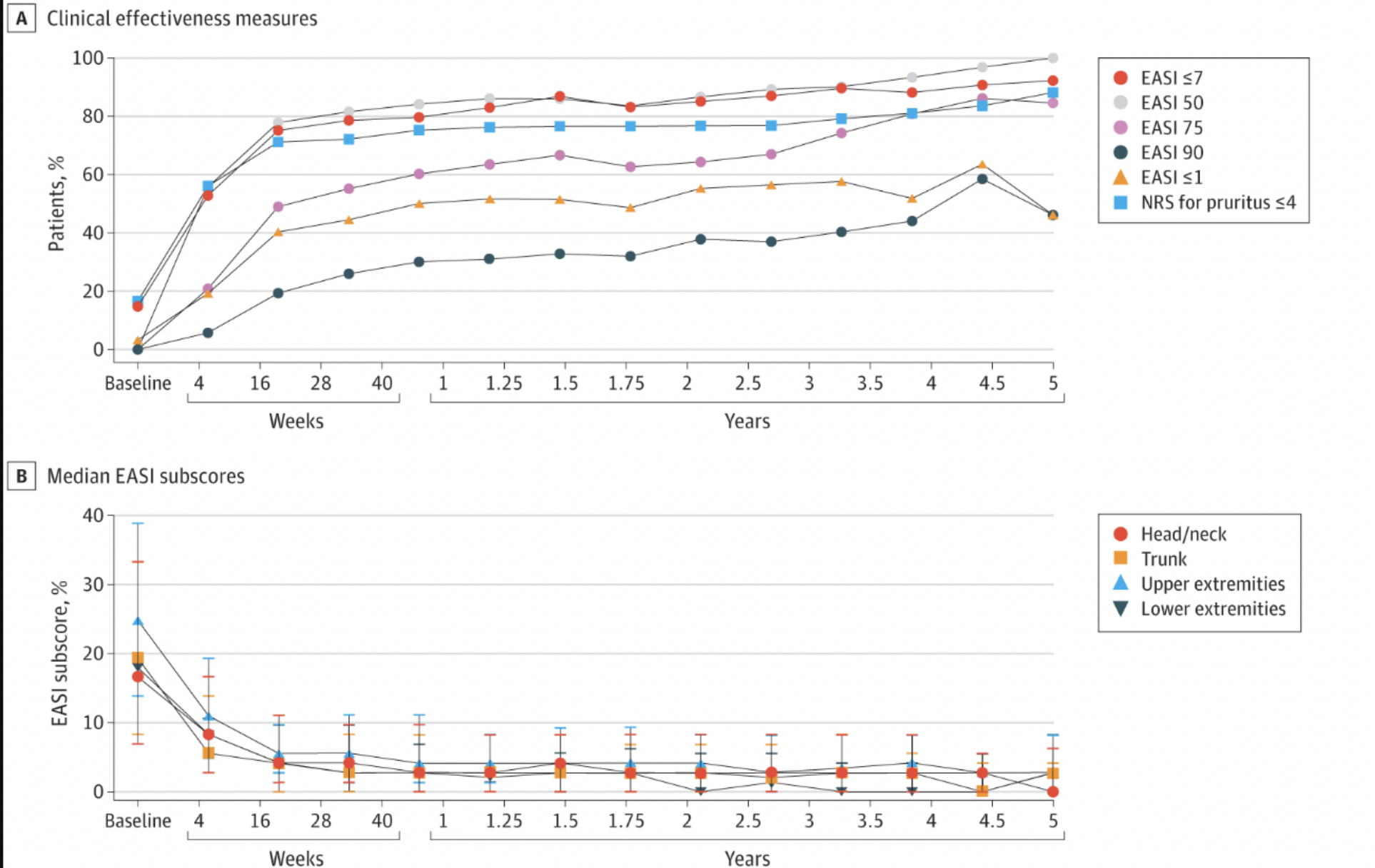


[^]Based on expert consensus and reflective of established practice

^{^^}FDA indicated for ages 2 years & older

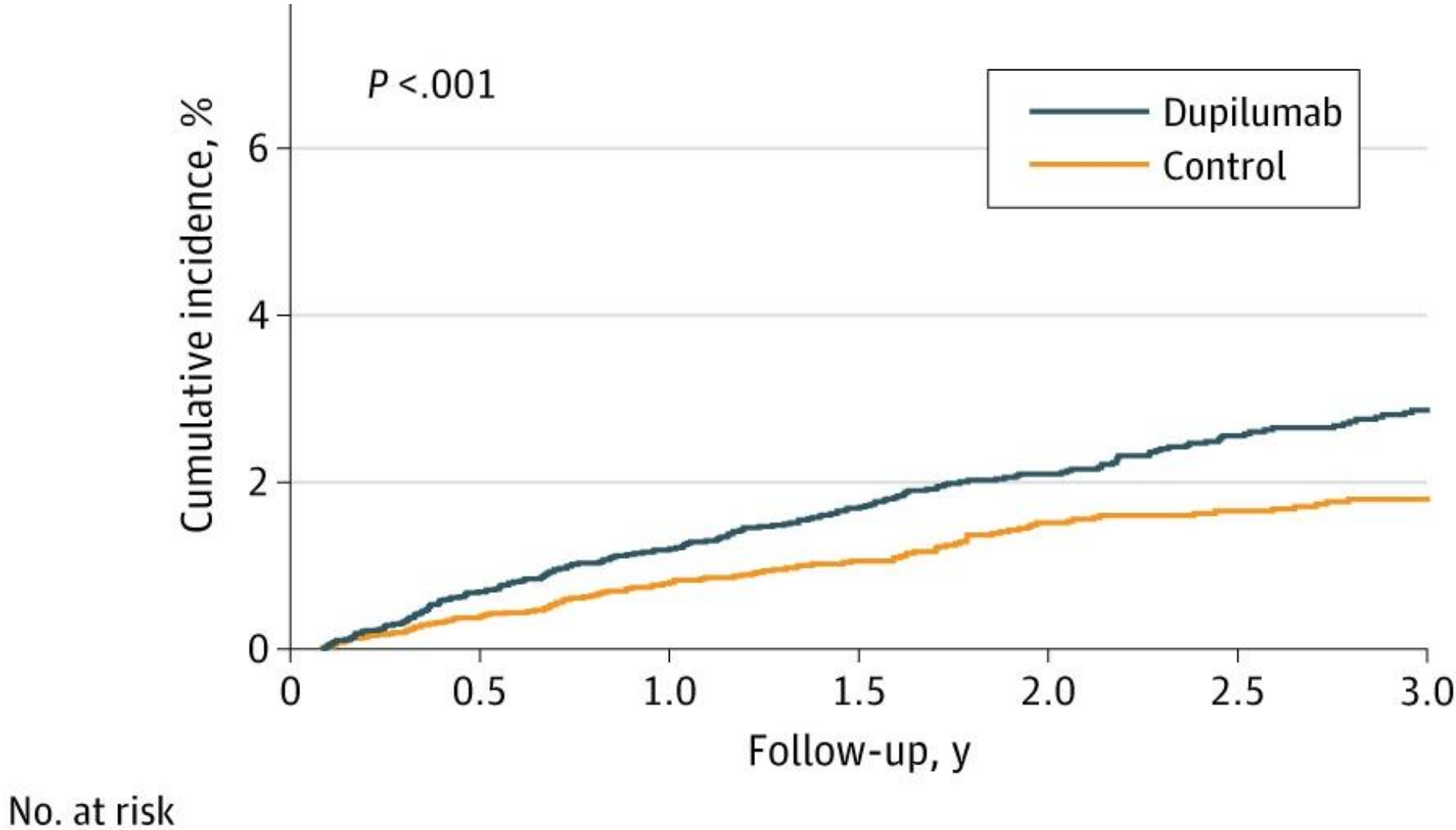


Dupilumab response highly durable after 5 years



Boesjes CM, Kamphuis E, de Graaf M, et al. Long-Term Effectiveness and Reasons for Discontinuation of Dupilumab in Patients With Atopic Dermatitis. JAMA Dermatol. 2024;160(10):1044–1055.

Dupilumab has higher risk of developing paradoxical psoriasis



Dupilumab Improves Growth in Children

Children with atopic dermatitis found to underperform peers in growth

In children < 40%tile in height, 31.3% gained at least 5%tiles by 16 weeks compared to 15.5% of placebo

Bone alkaline phosphatase significantly higher in dupilumab children

Likely due to chronic inflammation, sleep disruption, and topical/systemic corticosteroid use

Dupilumab induced blindness

- Result of severe, untreated eye disease and not likely drug effect
- Out of 210 patients in one study, 1% (3 patients) developed vision threatening complications (scarring)
- Added to the FDA label

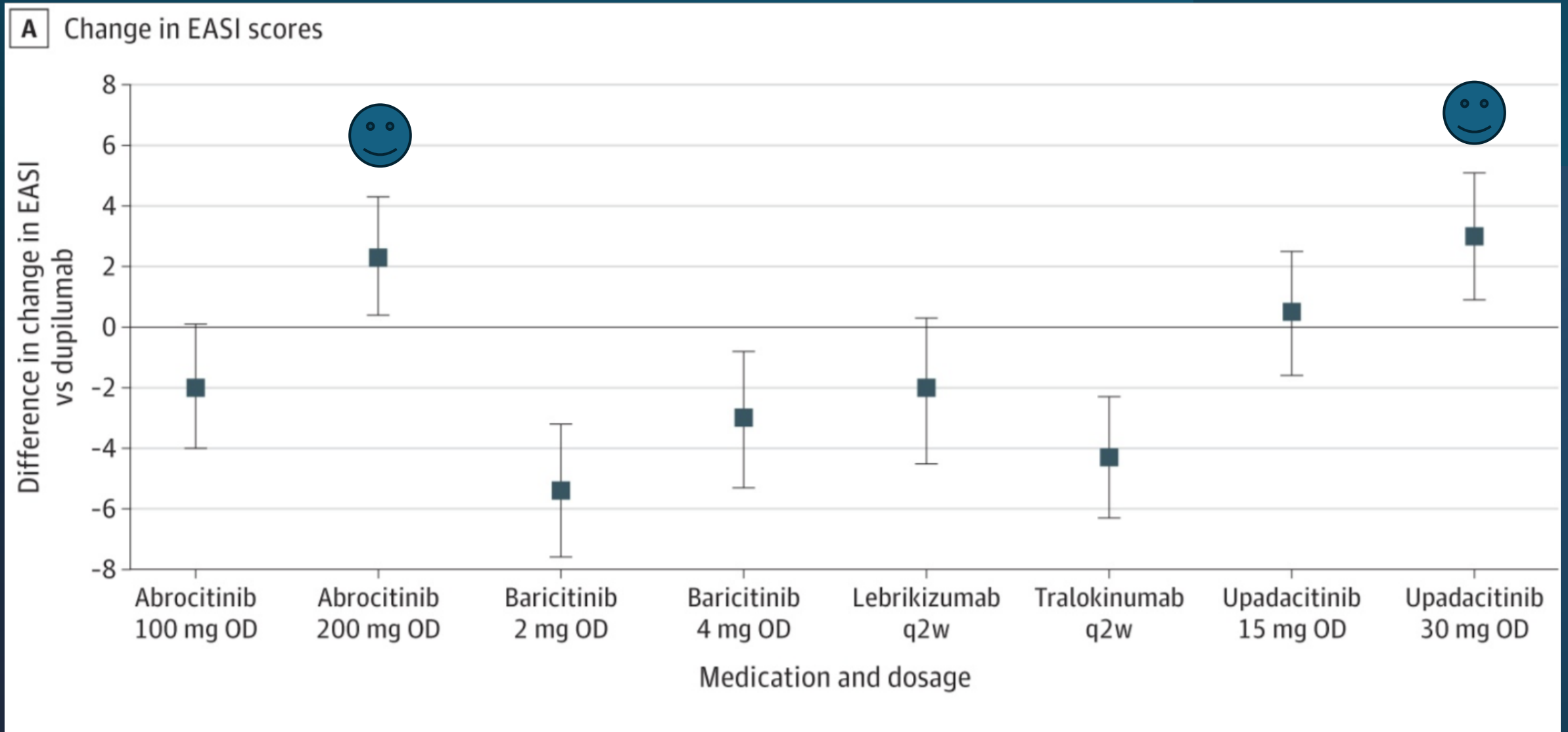
According to the FDA-approved drug label, **dupilumab (Dupixent) can cause temporary or ongoing vision loss, including visual impairment and blindness**, listed under postmarketing ocular disorders as occurring **in association with conjunctivitis, keratitis, or blepharitis.**  FDA

Blindness is therefore not a direct, independent toxicity but the endpoint of severe, inadequately treated ocular surface disease driven by these inflammatory reactions.  FDA

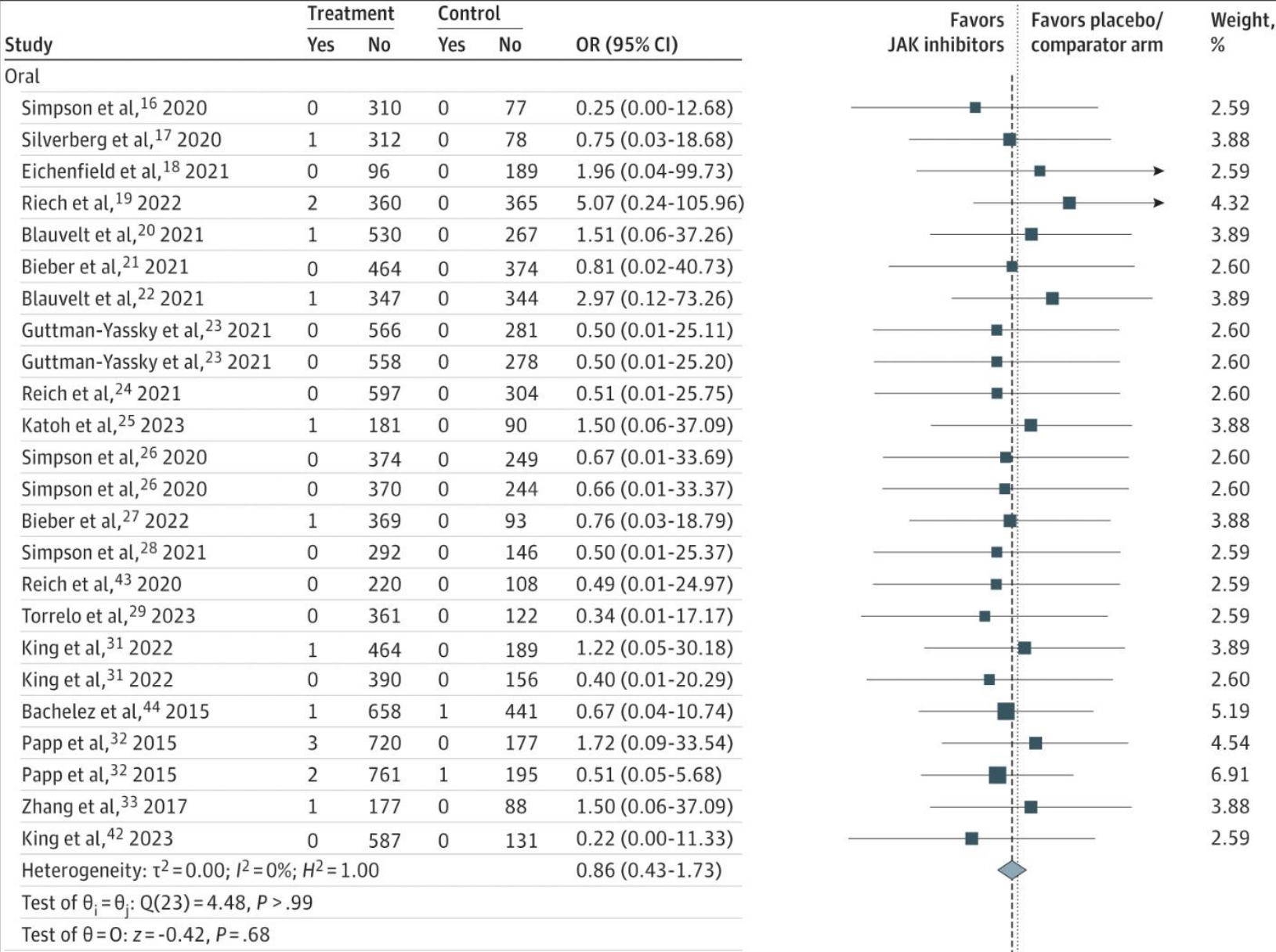
Dupi → Tralo due to conjunctivitis or facial redness?

Switch		
Tralokinumab	 72,4%	 33,3%
JAKi	 92,2%	 85,2%

High dose JAKi superior to injectable biologics for treatment of atopic dermatitis

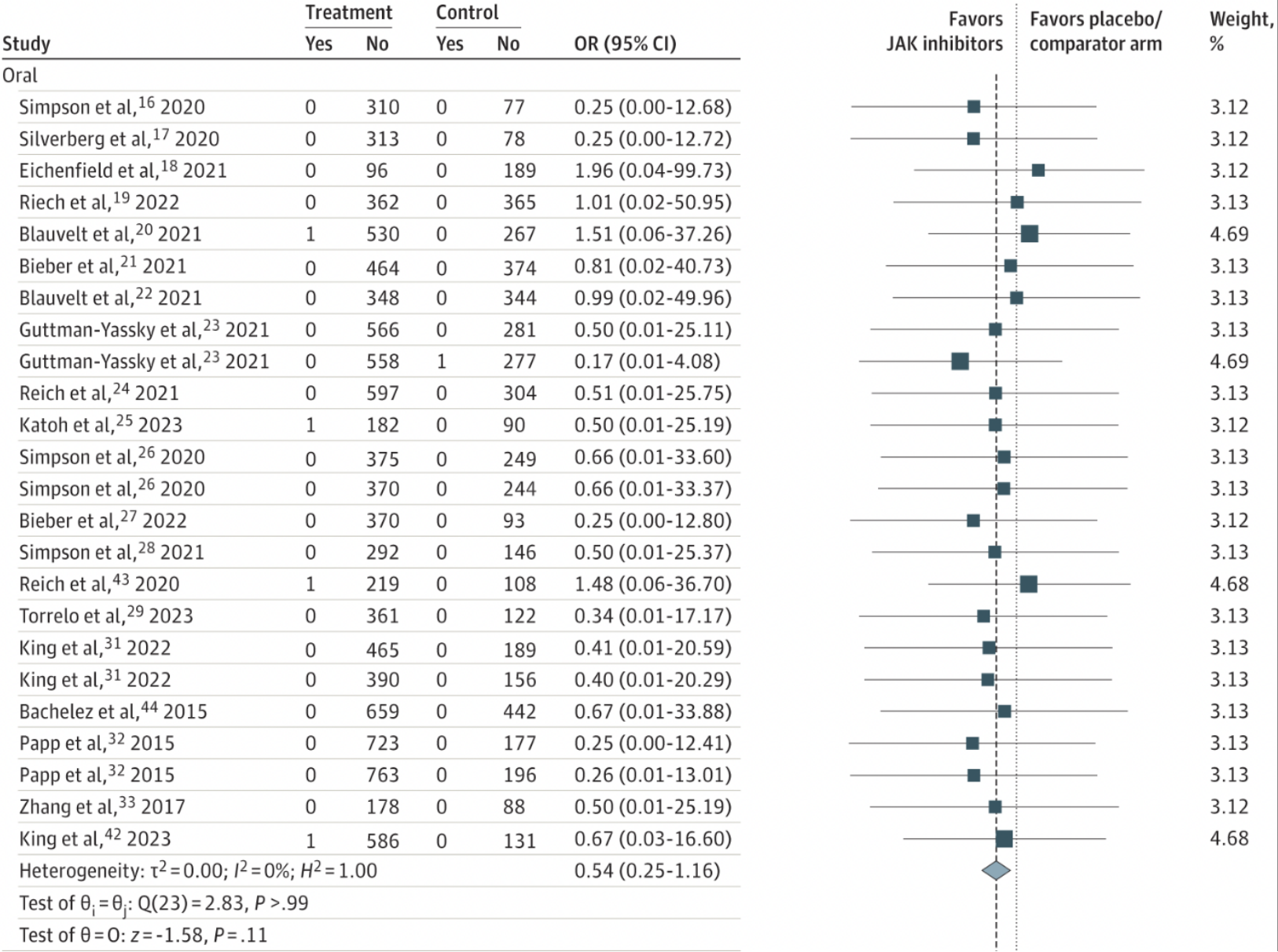


No significant increase in MACE with JAKi



Ingrassia JP, Maqsood MH, Gelfand JM, et al. Cardiovascular and Venous Thromboembolic Risk With JAK Inhibitors in Immune-Mediated Inflammatory Skin Diseases: A Systematic Review and Meta-Analysis. JAMA Dermatol. 2024;160(1):28–36.

No significant increase in VTE with JAKi



Ingrassia JP, Maqsood MH, Gelfand JM, et al. Cardiovascular and Venous Thromboembolic Risk With JAK Inhibitors in Immune-Mediated Inflammatory Skin Diseases: A Systematic Review and Meta-Analysis. JAMA Dermatol. 2024;160(1):28–36.

**Although
Nemolizumab
is less effective
at EASI-75, it's
MUCH faster
for itch relief**

	Nemolizumab (anti-IL-31Rα)	Dupilumab (anti-IL-4Rα)	Lebrikizumab (anti-IL-13)
EASI-75 at wk 16 (+ topicals)	42–44%	64–69%	~70%
IGA 0/1 at wk 16	36–38%	36–40%	~41%
Skin clearance vs dupilumab	Inferior (EASI MD 6.0)	Reference	Similar (slightly lower on binary outcomes)
Itch (PP-NRS) vs dupilumab	Comparable (MD 0.1)	Reference	Comparable
Onset of itch relief	Week 1	Week 2	Week 6



Novel therapies in the pipeline



A doctor in a white lab coat is sitting at a desk, looking towards a patient. He has a concerned expression and his hand is on his chest. The patient, a man in a tan sweater, is gesturing with his hands while asking a question. The background shows a white shelving unit with binders and a small potted plant.

IDK

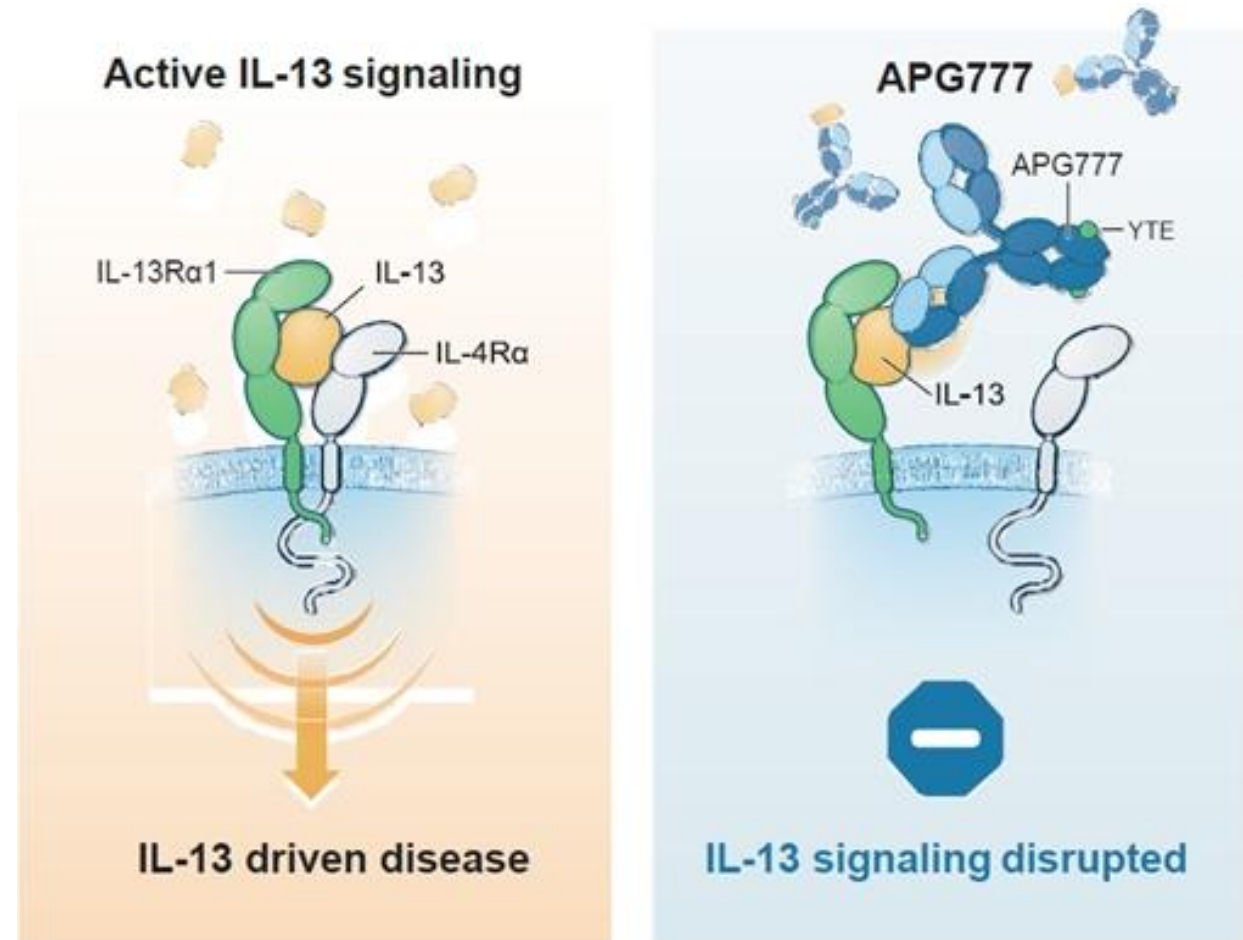
So how long will I be on this drug?

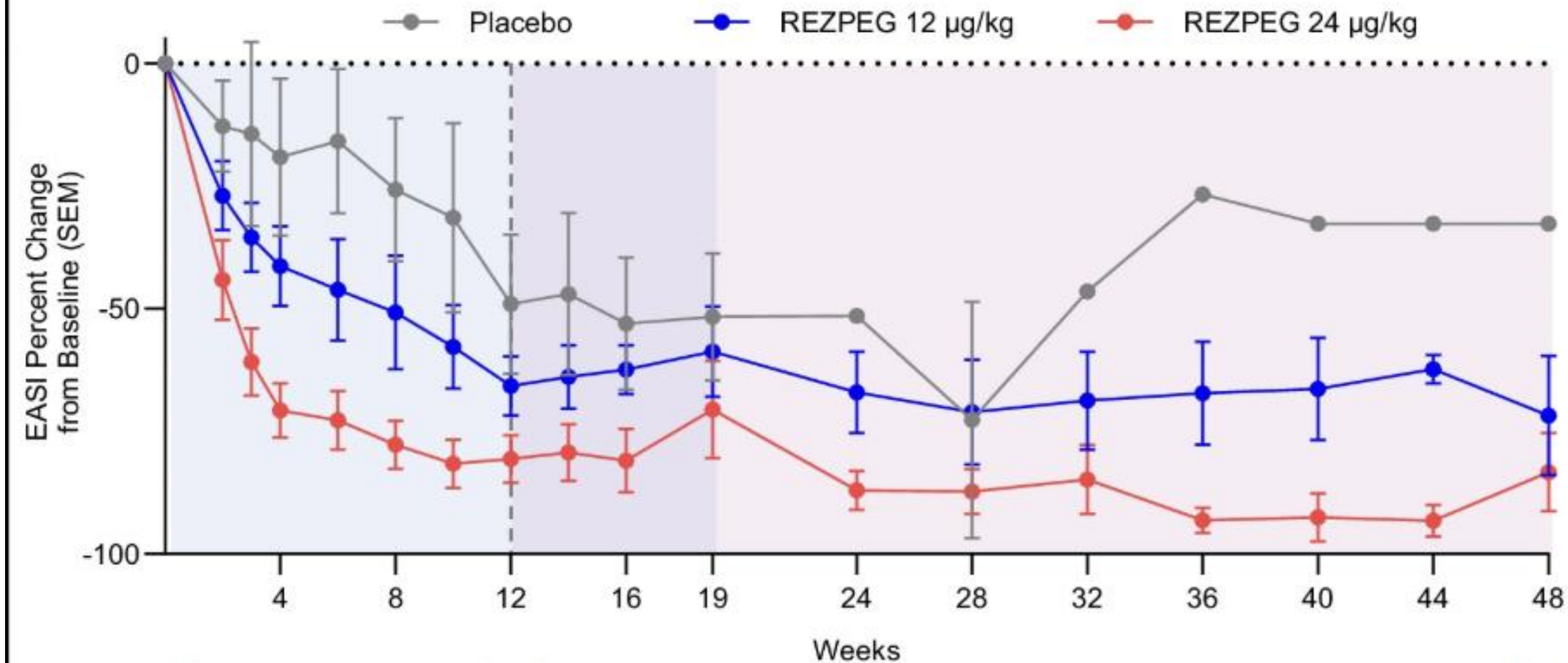
**Long-acting
therapies are
coming!!!!**



Zumilokibart

- Long-acting IL-13 therapy
- YTE modification on the Fc portion of the antibody
- Every 3 to 6 month maintenance dosing
- Comparable efficacy



a



shutterstock.com • 2050672196

**Combination
therapies are
coming!!!!**

Galvokimig

- IL13/IL17A/F inhibitor
- Phase 2A
 - 64.9% achieved EASI-75, 46.6% achieved EASI-90
- Expected data in 2028

Tilrekimig

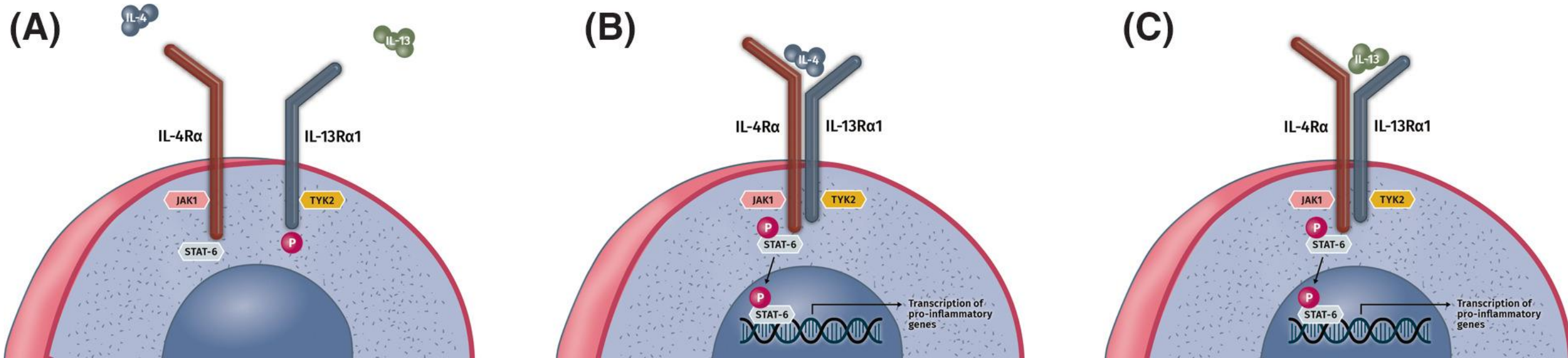
- IL4/IL13/TSLP inhibitor
- Phase 2
 - 51.9% achieved EASI-75
- Monthly dosing

A large billboard on a tall white pillar in a city street. The billboard is white with black text. The background shows a city street with buildings, trees, and a blue sky with clouds.

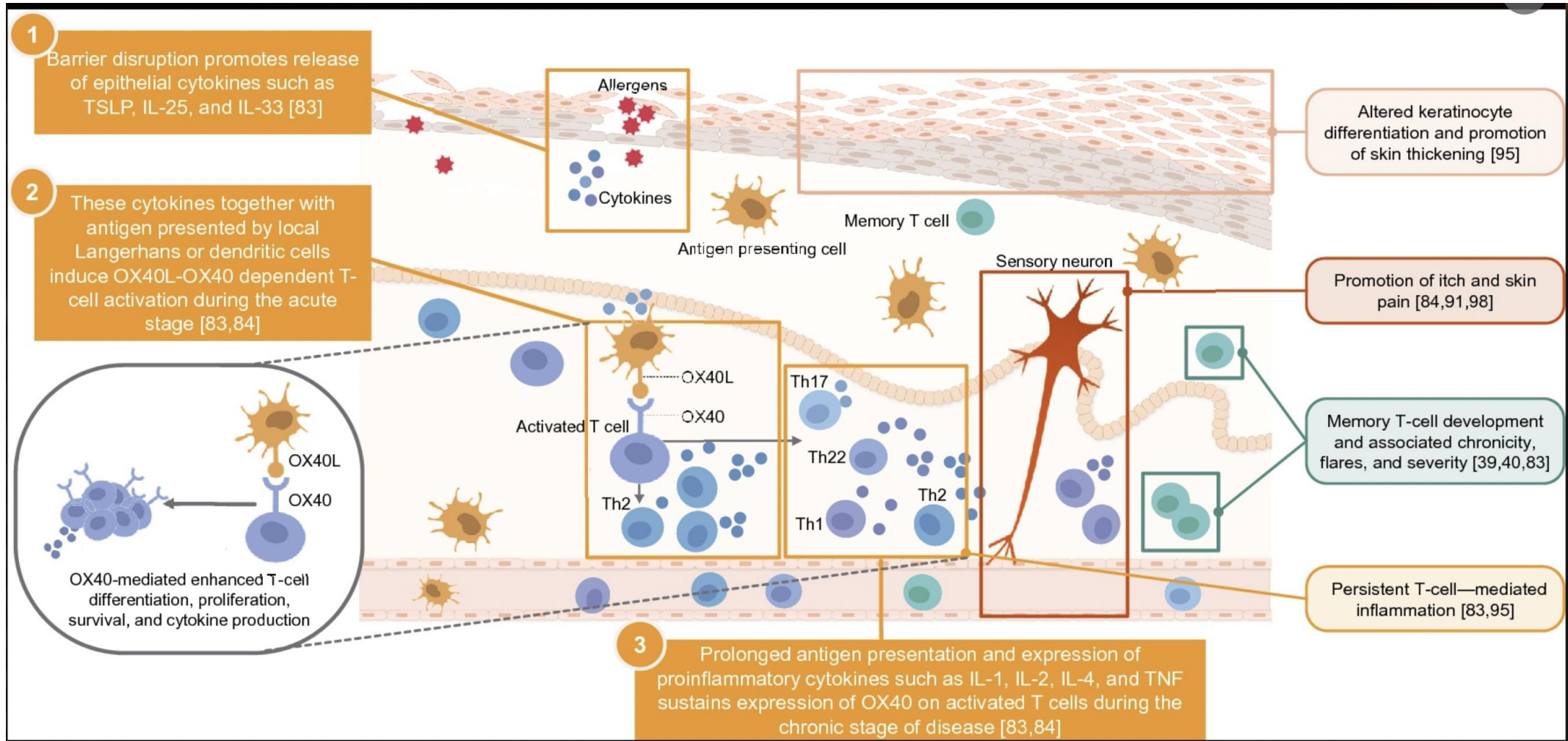
More oral therapies are coming!!

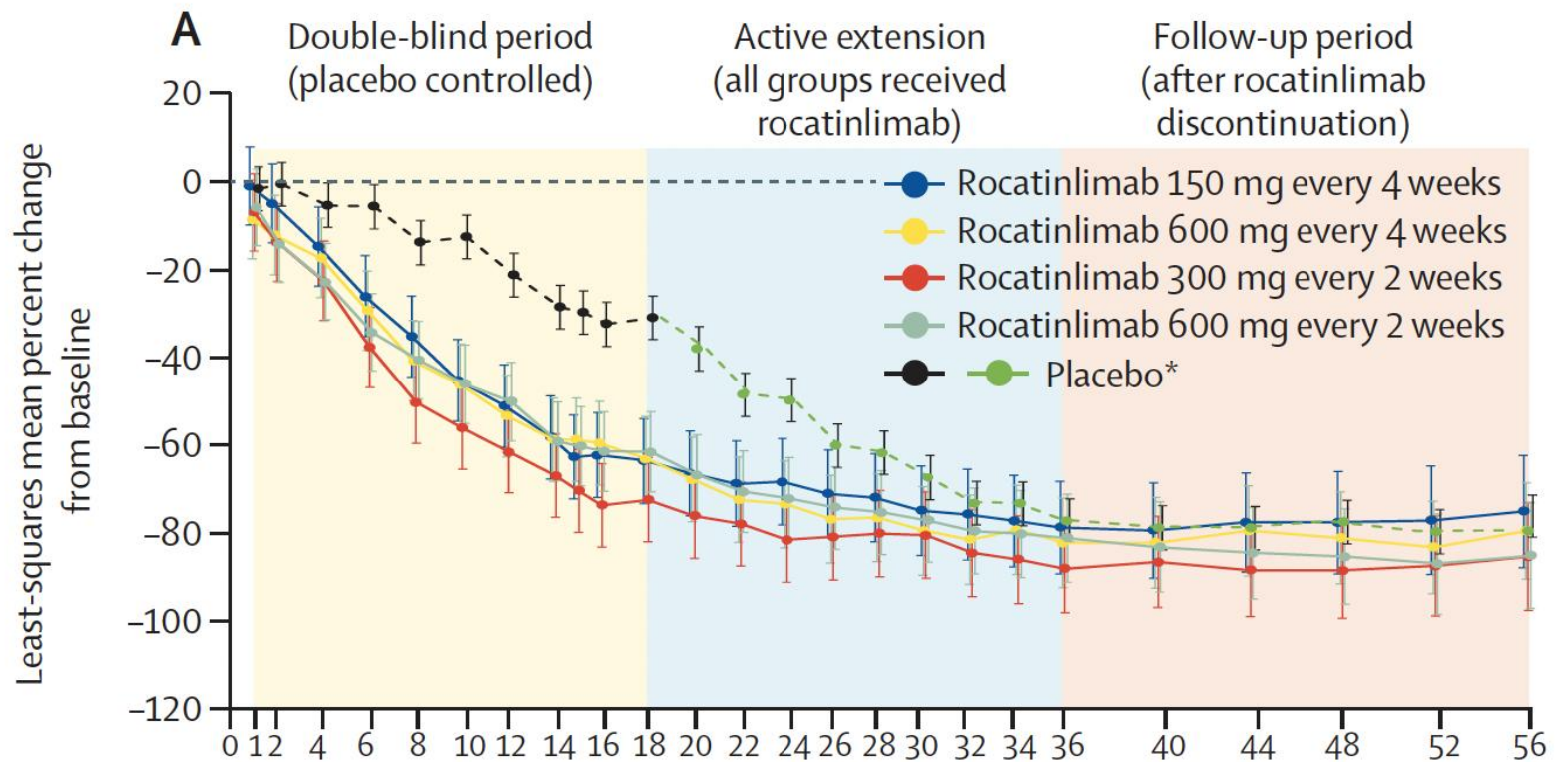
KT-621

- Oral STAT-6 Degradator
- Daily PO medication
- Phase 1 data shows average 63% EASI reduction after 29 days
- Phase 2 ongoing



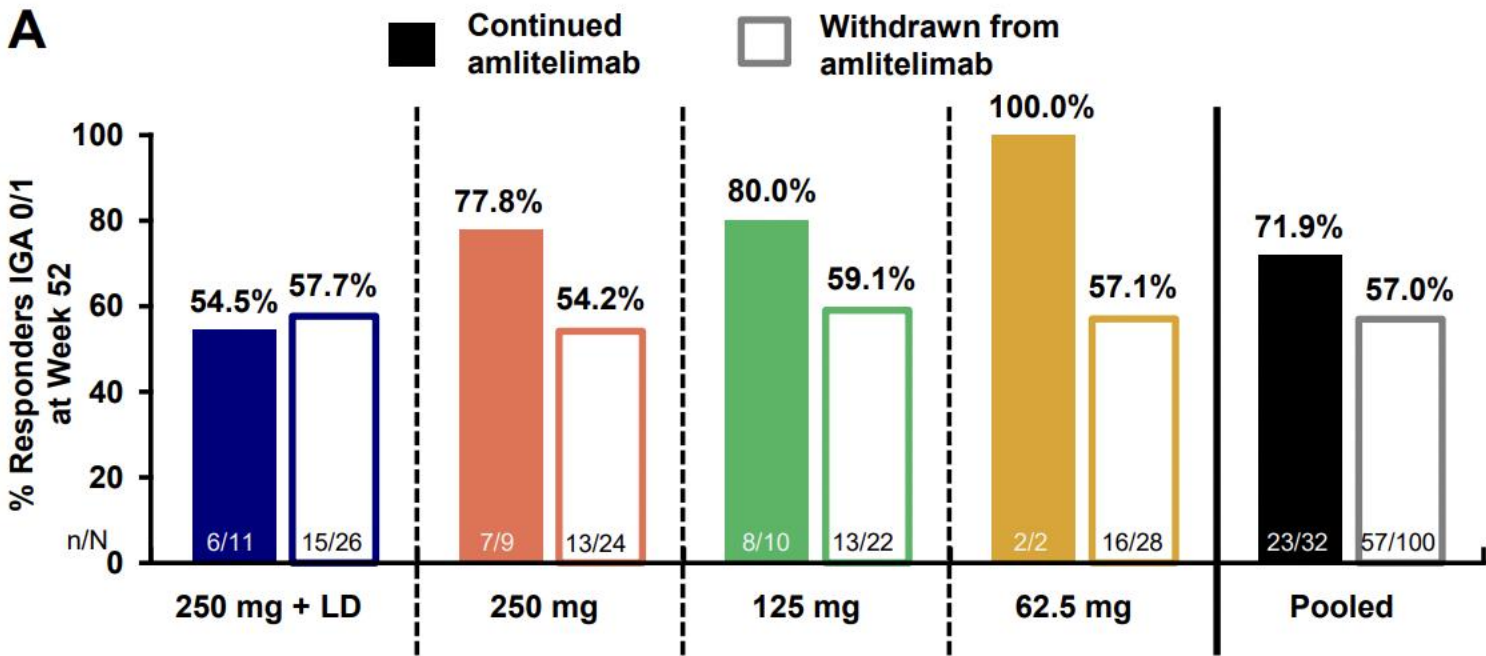
What Happened to OX40L?



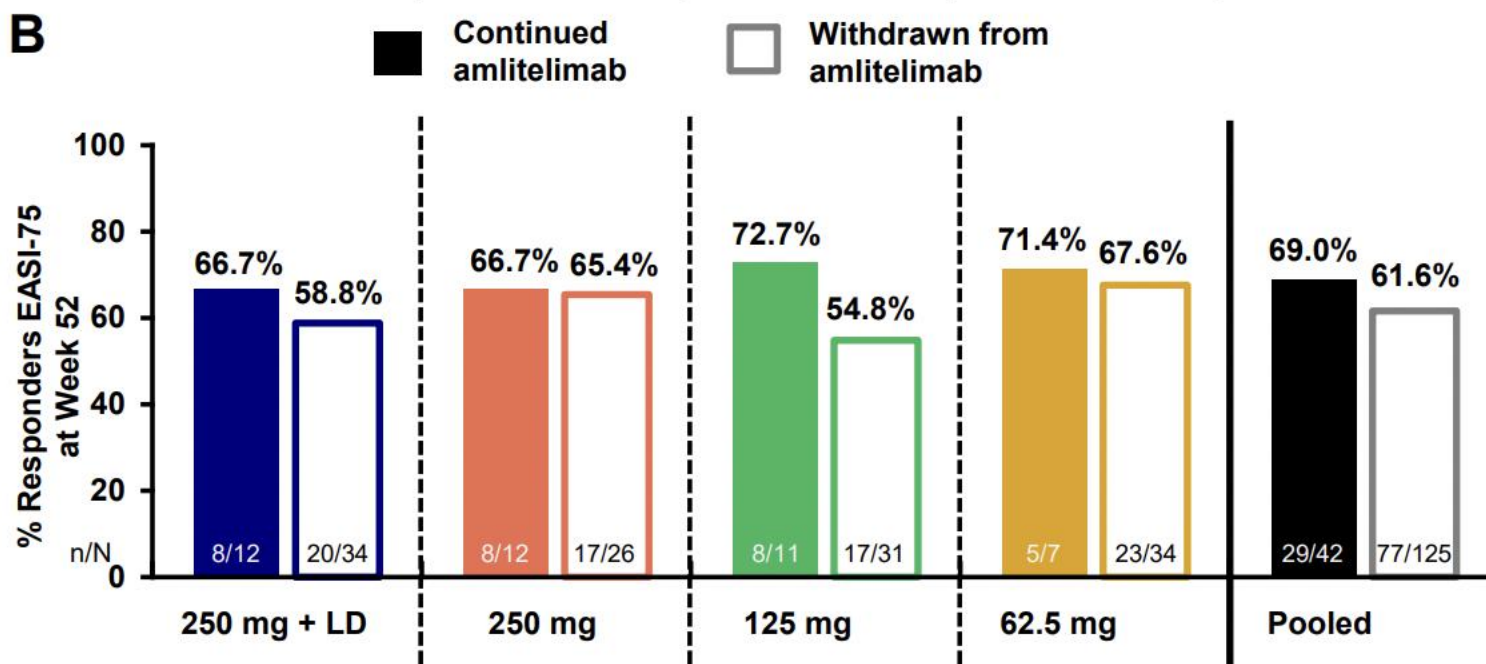


Percentage change				
Rocatinlimab 150 mg every 4 weeks	-62.2	-68.3	-78.7	-75.0
Rocatinlimab 600 mg every 4 weeks	-59.5	-73.4	-82.3	-79.5
Rocatinlimab 300 mg every 2 weeks	-73.6	-81.6	-88.1	-85.4
Rocatinlimab 600 mg every 2 weeks	-61.4	-72.2	-81.1	-85.1
Placebo	-32.3	-49.7	-77.2	-79.6





Amlitelimab was withdrawn at week 24 and patients followed to 52 weeks (open bars)



Most patients preserved their IGA and EASI response

**1 confirmed and 1 suspected case of
Kaposi Sarcoma in Rocatinlimab Trial**

**2 confirmed cases of Kaposi Sarcoma in
Amlitelimab trial**

PERSPECTIVE article

Front. Immunol., 01 June 2026

Sec. Inflammation

Volume 17 - 2026 | <https://doi.org/10.3389/fimmu.2026.1870289>

**Is Kaposi's sarcoma the end of the
OX40/OX40L axis in atopic dermatitis?**

Sanofi abandons eczema drug approval efforts in another blow to OX40 class

While amlitelimab elicited durable responses in AD, Sanofi does not believe the drug is meaningfully differentiated from current eczema treatment offerings.

Annabel Kartal Allen | July 24, 2026

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Kyowa Kirin Ends Late-Stage Rocatinlimab OX40 Development

Author(s) [Maddi Hebebrand, MC, Associate Editor](#)

Fact checked by: [Yasmeen Qahwash](#)

Take Home Messages

- **It's an exciting time to be in atopic dermatitis and a hopeful time to be a patient with atopic dermatitis**
- **Jiade.yu@vcuhealth.org**