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The Ronald O. Perelman Department of Dermatology
NYU Grossman School of Medicine

# COSMETIC IMPROVEMENT OF PSORIASIS & ATOPIC DERMATITIS

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# Disclosures, Conflicts of Interest

None



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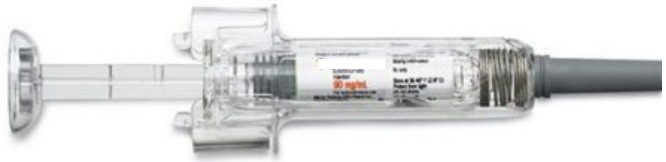



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# Cosmetic Before and After






https://www.botoxcosmetic.com/before-and-after

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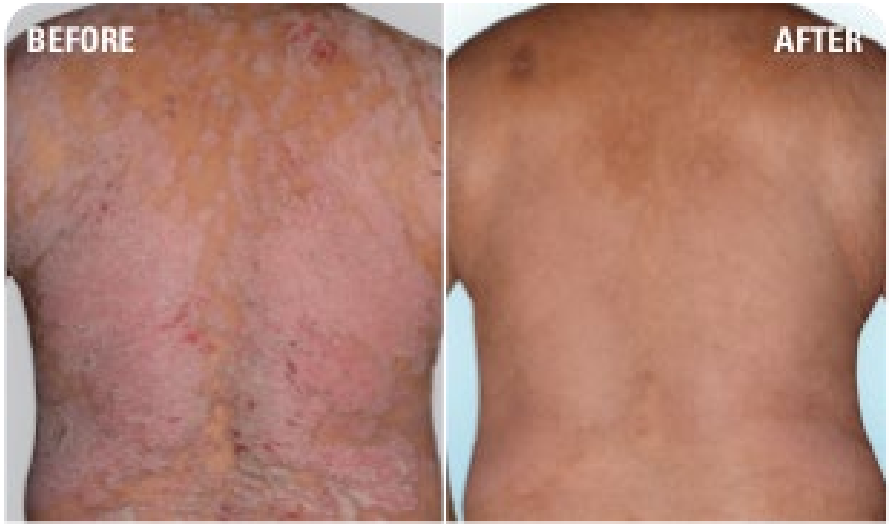
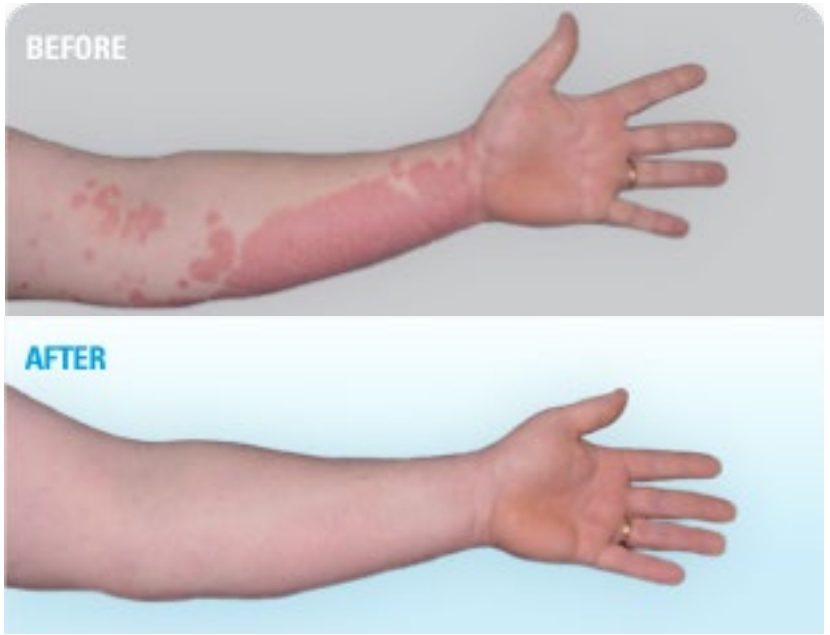
# Psoriasis “Before and After”




https://www.skyrizi.com/psoriasis/psoriasis-treatment/before-and-after-pictures



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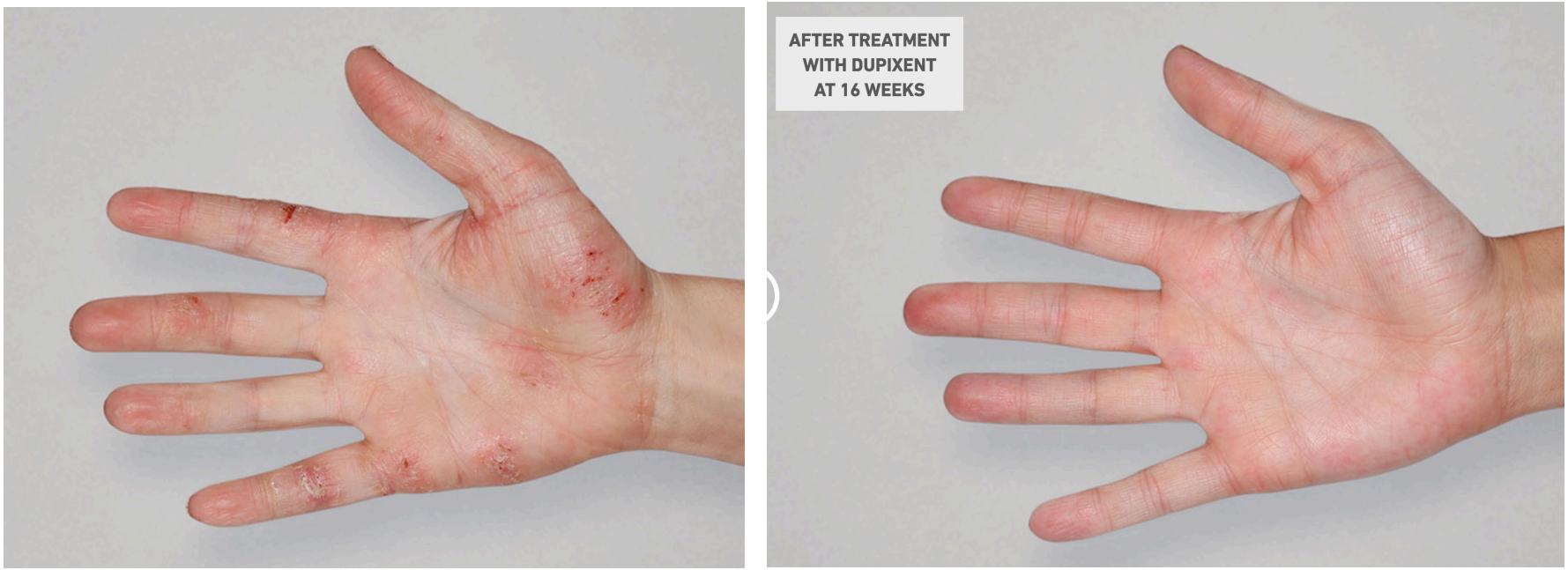
# Atopic Dermatitis “Before and After”




https://www.dupixent.com/atopicdermatitis/about-dupixent/results-in-adults



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# Patients with Clear Skin More Likely to Pursue Cosmetic Procedures

## Patients want clear skin

Survey Study: Psoriasis patients with moderate to severe disease who attain greater than 75% or greater improvement more likely to get cosmetic procedures

→ Credit improved QoL as reason for undergoing cosmetic procedure



Walters ME, Lee DJ, Yamauchi PS. Increased trend of cosmetic procedures in patients with psoriasis who attain 75% or greater improvement. J Drugs Dermatol. 2020;19(8):698-701.

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# Cosmetic Considerations of Psoriasis & Atopic Dermatitis

Chronic diseases, **commonly affecting visible and/or sensitive anatomic sites** including face, scalp, hands, genitals

**Negatively impacts QoL and self-esteem**

Significant burden of **itch and skin discomfort**

Topical therapies often not cosmetically acceptable to patients

Delicate skin area particularly susceptible to steroid atrophy, steroid-induced acne, and other cutaneous side effects

# PSORIASIS

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# Psoriasis Topical/External Treatments

Topicals

- Corticosteroids
- Vitamin D analogues
- Keratolytics (salicylic acid, urea)
- Retinoids
- Coal tar
- **Calcineurin inhibitors**
- **PDE-4 Inhibitors (crisaborole)**
- **Combination therapies**

ILTAC

Phototherapy (nbUVB / Excimer / PUVA)



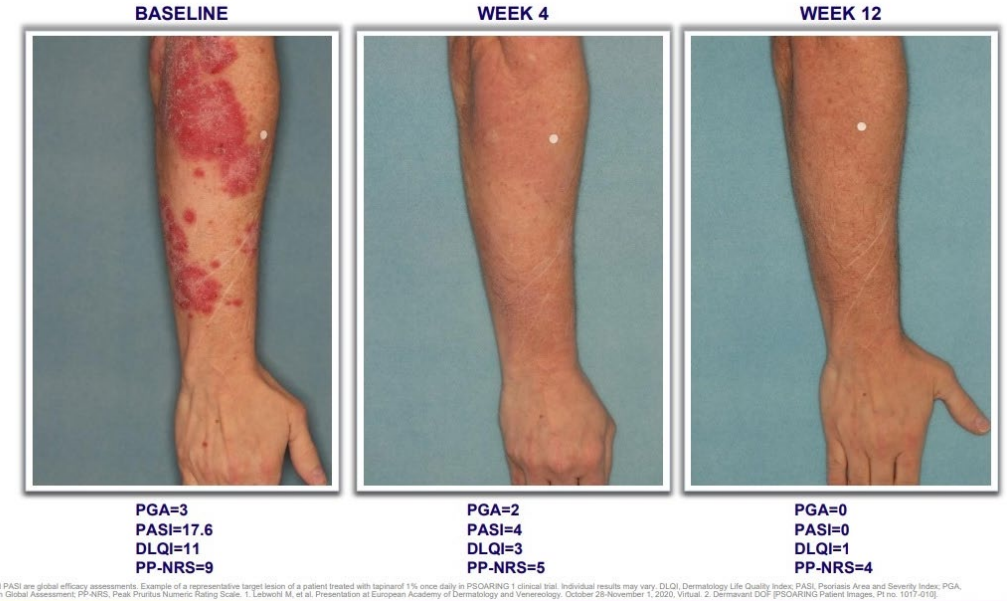
https://dermnetnz.org/topics/coal-tar

# Tapinarof 1% Cream

First novel topical psoriasis treatment developed in decades

Once daily, non-steroidal, aryl hydrocarbon receptor (AHR) agonist

Reduces inflammation/oxidative stress and plaque formation via IL-17A and IL-17F inhibition




PGA and PASI are global efficacy assessments. Example of a representative target lesion of a patient treated with tapinarof 1% once daily in PSOARING 1 clinical trial. Individual results may vary. DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; PP-NRS, Peak Pruritus Numeric Rating Scale. 1. Lebwohl M, et al. Presentation at European Academy of Dermatology and Venereology. October 28-November 1, 2020, Virtual. 2. Dermavant DOF [PSOARING Patient Images, Pt no. 1017-010].

Dermavent PSOARING Patient Images, 2022



Lebwohl MG, Stein Gold L, Strober B, et al. Phase 3 trials of tapinarof cream for plaque psoriasis. N Engl J Med. 2021;3,85(24):2219-2229.
Strober B, Stein Gold L, Bissonnette R, et al. One-year safety and efficacy of tapinarof cream for the treatment of plaque psoriasis: Results from the PSOARING 3 trial. J Am Acad Dermatol. 2022;87(4):800-806.

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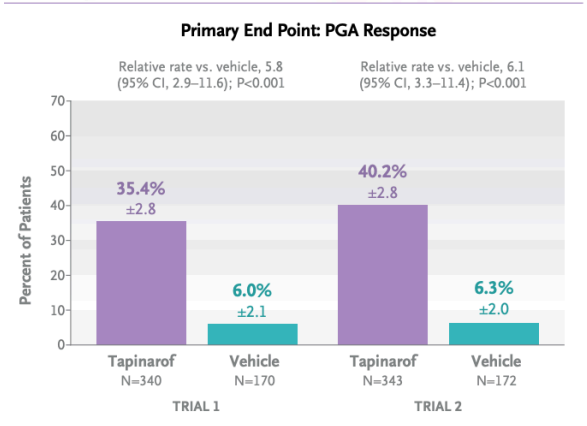
# Tapinarof 1% Cream

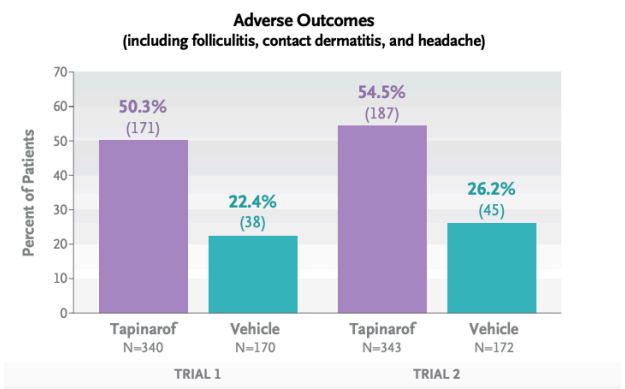
## PSOARING Trials (12 weeks)

35% of tapinarof patients reached primary end points (clear or almost clear, reduction in plaque severity scale), compared to ~6% of control group

Remittive Effect: After discontinuation of treatment, patients' skin remained clear or almost clear for a median of 4 months

Side Effects: Folliculitis, contact dermatitis, headache, nasopharyngitis, URI





Lebwohl MG, Stein Gold L, Strober B, et al. Phase 3 trials of tapinarof cream for plaque psoriasis. N Engl J Med. 2021;3,85(24):2219-2229.
Strober B, Stein Gold L, Bissonnette R, et al. One-year safety and efficacy of tapinarof cream for the treatment of plaque psoriasis: Results from the PSOARING 3 trial. J Am Acad Dermatol. 2022;87(4):800-806.

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# Roflumilast 0.3% Cream

Once daily non-steroidal topical phosphodiesterase-4 (PDE4) inhibitor

Higher affinity for PDE4 than crisaborole

Vehicle cream has high water content containing diethylene glycol monoethyl ether, enhancing emollient effects and penetration in the skin

Approved for adults and children >12yo



Lebwohl MG, Papp KA, Stein Gold L, et al. Trial of roflumilast cream for chronic plaque psoriasis. N Engl J Med. 2020;383(3):229-239.
Lebwohl MG, Kircik LH, Moore AY, et al. Effect of roflumilast cream vs vehicle cream on chronic plaque psoriasis: the dermis-1 and dermis-2 randomized clinical trials. JAMA. 2022;328(11):1073-1084.

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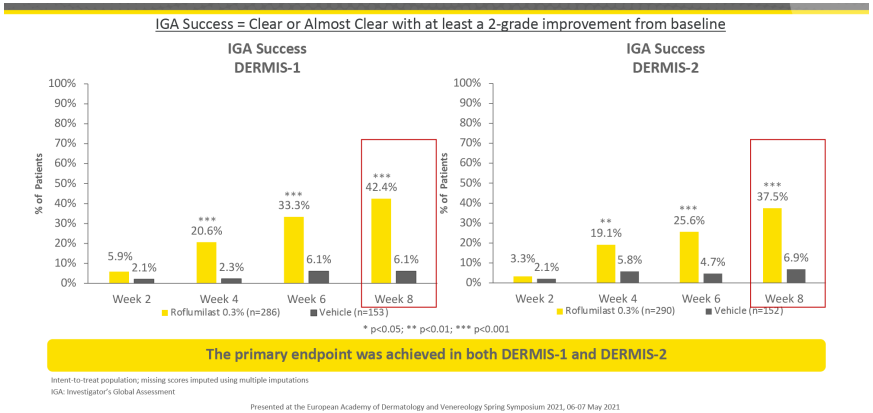
# Roflumilast 0.3% Cream

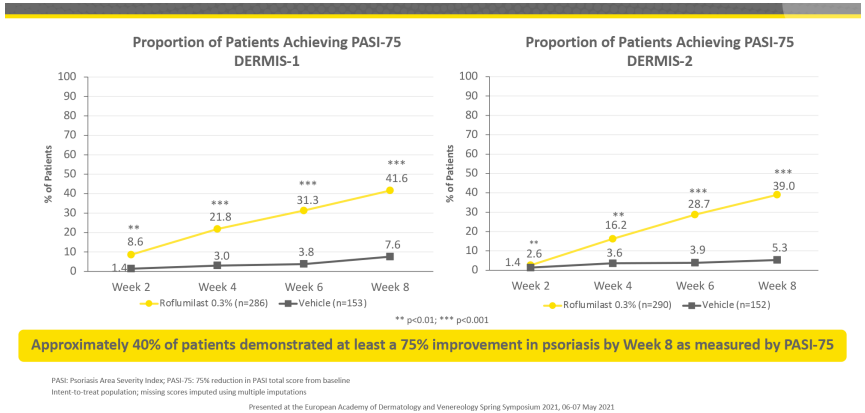
## DERMIS-1 and DERMIS-2 Trials

By 8 weeks…

- ~40% of patients met primary end-points:
  - Clear/almost clear
  - 75% improvement in psoriasis (PASI-75)

Effectiveness was independent of baseline psoriasis severity






Lebwohl MG, Kircik LH, Moore AY, et al. Effect of roflumilast cream vs vehicle cream on chronic plaque psoriasis: the dermis-1 and dermis-2 randomized clinical trials. JAMA. 2022;328(11):1073-1084.

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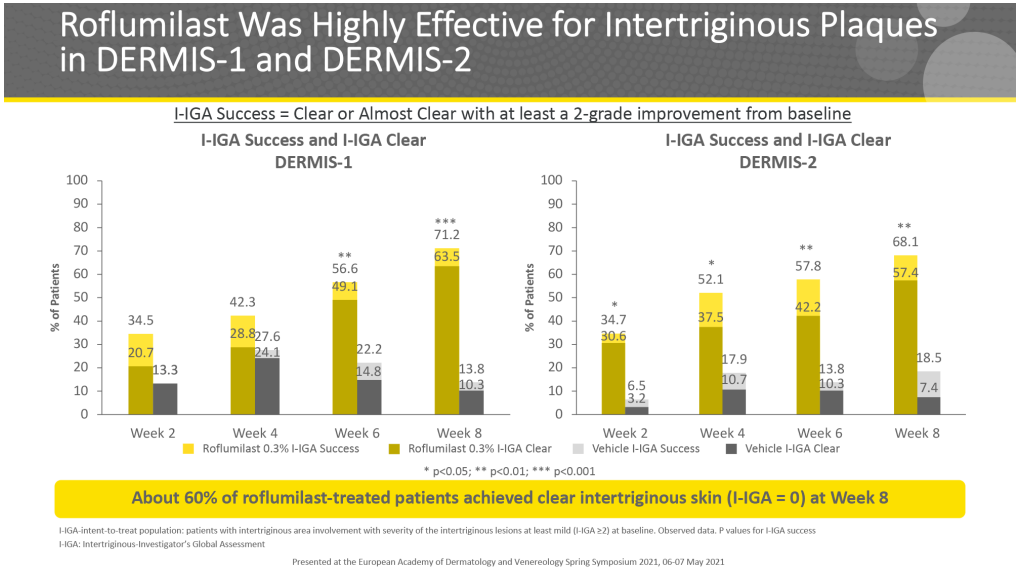
# Roflumilast 0.3% Cream

**Safe and effective for sensitive anatomic sites**, including intertriginous plaques

Robust **reduction in itch occurs early** and consistently improves through week 8

Side effects: Diarrhea (3.1%), headache (2.4%), insomnia (1.4%), nausea (1.2%), application site pain (1%), URI (1%)






Lebwohl MG, Kircik LH, Moore AY, et al. Effect of roflumilast cream vs vehicle cream on chronic plaque psoriasis: the dermis-1 and dermis-2 randomized clinical trials. JAMA. 2022;328(11):1073-1084.

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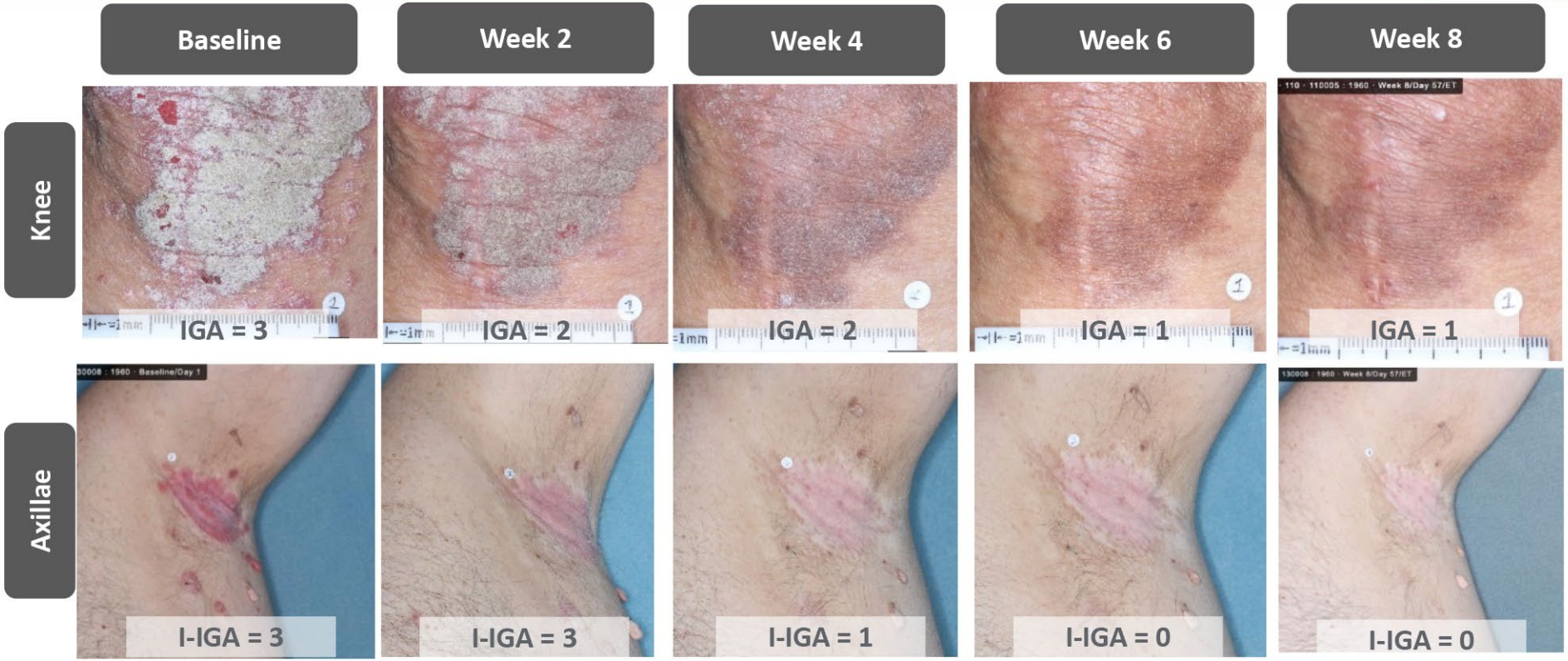
# Patient Examples Illustrating Efficacy of Roflumilast Cream 0.3% From DERMIS-1 & DERMIS-2




IGA: Investigator's Global Assessment; I-IGA: intertriginous-IGA

Presented at the European Academy of Dermatology and Venereology Spring Symposium 2021, 06-07 May 2021

# Systemic Treatments for Psoriasis

Traditional systemic agents
- Methotrexate
- Acitretin
- Cyclosporine

TNF-Alpha Inhibitors
- Infliximab
- Adalimumab
- Etanercept
- Certolizumab pegol

IL-17 Inhibitors
- Secukinumab
- Ixekizumab
- Brodalumab

IL-12/IL-23
- Ustekinumab

IL-23 Inhibitors
- Guselkumab
- Tildrakizumab
- Risankizumab

Other
- Apremilast (small molecule inhibitor of PDE4)
- Deucravacitinib (oral TYK2 Kinase Inhibitor)

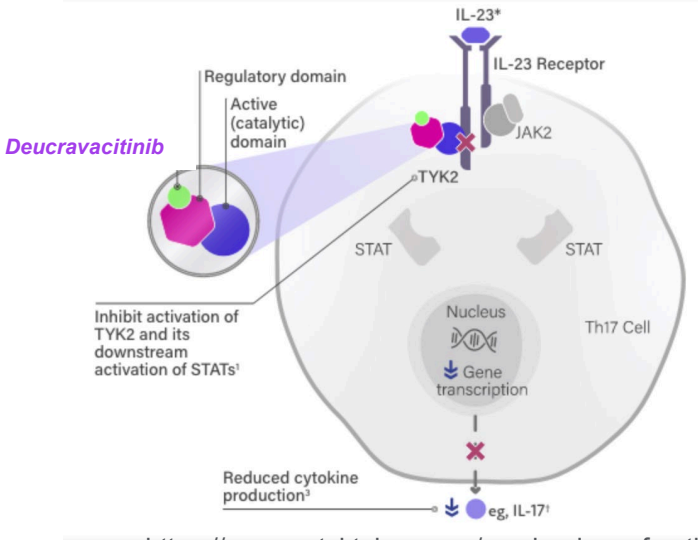
# Deucravacitinib

Selective TYK2 Kinase inhibitor

Once daily oral pill – no dose titration

**POETYK PSO-2 Trial, at week 16**:

**Deucravacitinib PASI-75 → 53%**
Apremilast PASI-75 → 39.8%
Placebo PASI-75 → 9.4%




https://www.sotyktuhcp.com/mechanism-of-action

**Side effects** (52-week data): folliculitis, acne, URI, nasopharyngitis, herpes virus reactivation

No significant laboratory abnormalities other that slight elevation in CPK
No systemic fungal infections, tuberculosis, or opportunistic infections observed (TB test still recommended)



Strober B, Thaçi D, Sofen H, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: Efficacy and safety results from the 52-week, randomized, double-blinded, phase 3 Program fOr Evaluation of TYK2 inhibitor psoriasis second trial. J Am Acad Dermatol. 2023;88(1):40-51.

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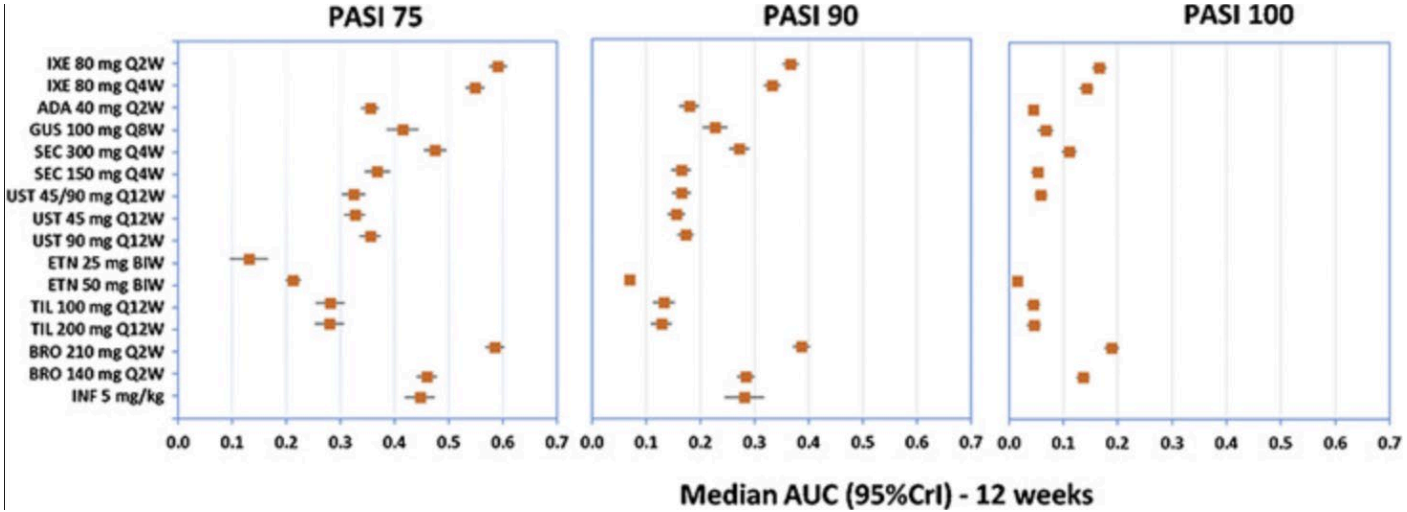
# Network Meta-Analysis (JAAD 2020)




Warren RB, Gooderham M, Burge R, et al. Comparison of cumulative clinical benefits of biologics for the treatment of psoriasis over 16 weeks: Results from a network meta-analysis. J Am Acad Dermatol. 2020;82(5):1138-1149.



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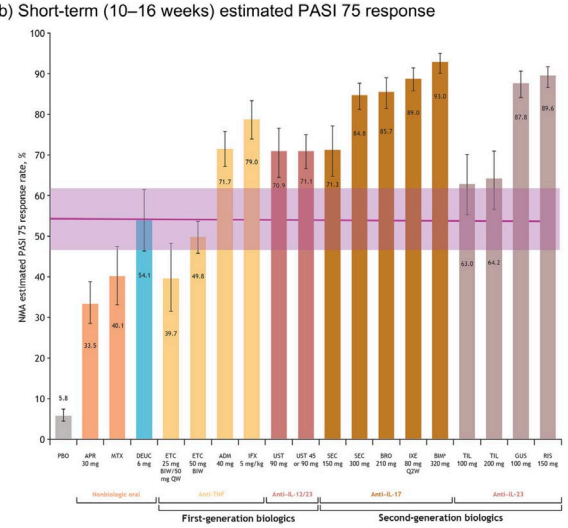
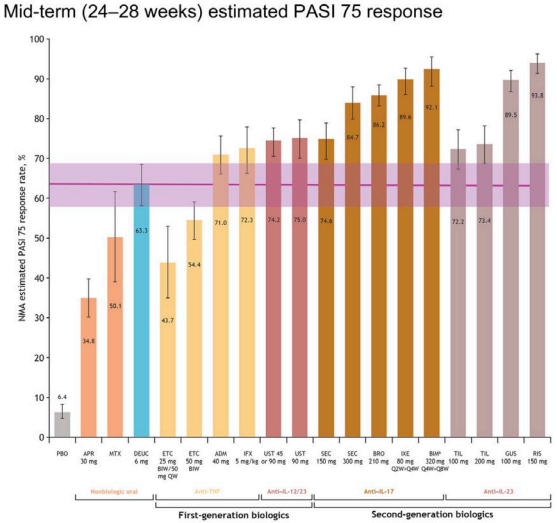
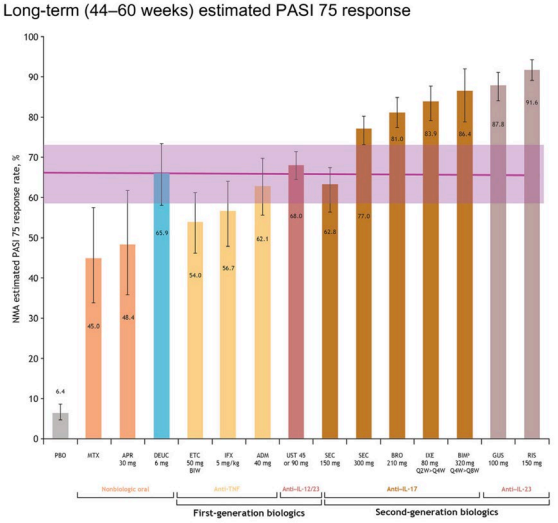
# Network Meta-Analysis






Armstrong AW, Warren RB, Zhong Y, et al. Short-, mid-, and long-term efficacy of deucravacitinib versus biologics and nonbiologics for plaque psoriasis: a network meta-analysis. Dermatol Ther (Heidelb). Published online October 6, 2023.

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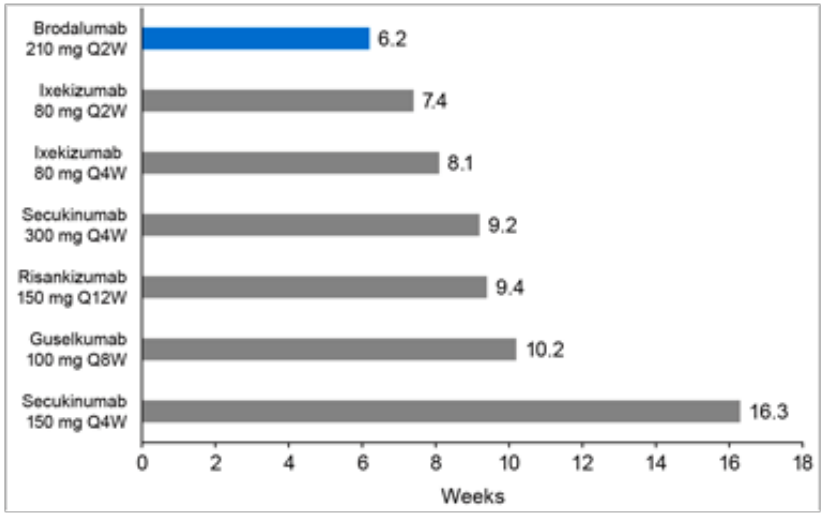
# Onset of Action

**FIGURE 3.** Mean time for 50% of patients receiving IL-17 or IL-23 antagonists in clinical studies to achieve PASI 90. Loading doses (not shown) vary depending on biologic. Data for tildrakizumab were not available for this measure.[17] IL, interleukin; PASI 90, psoriasis area and severity index 90% improvement from baseline; Q2W, every 2 weeks; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks.






Fried R, Lebwohl M, Bettencourt M, Koo J, Jacobson A. Onset of plaque psoriasis treatment responses with anti-il-17/il-23 biologic therapies. J Drugs Dermatol. 2022;21(8):854-860.

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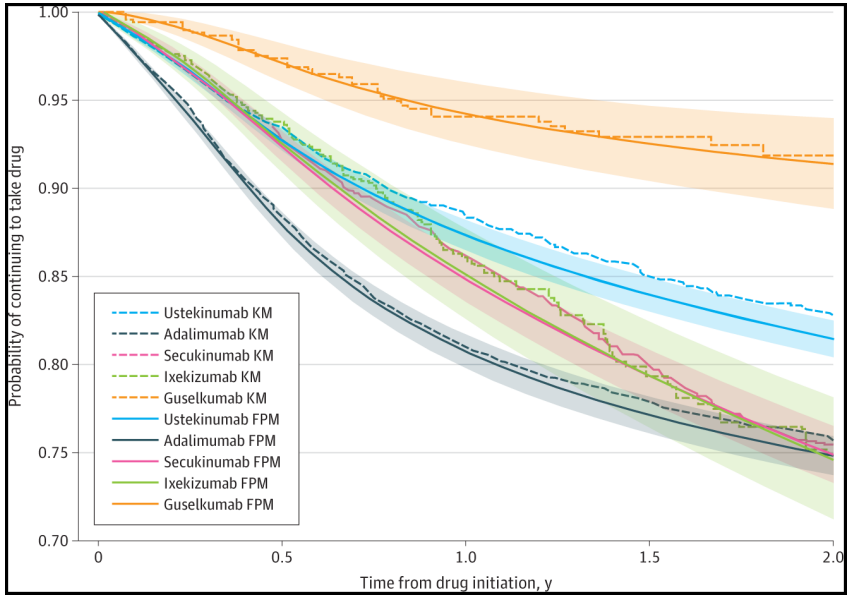
# Drug Survival + Safety

Guselkumab (IL-23i) had highest drug survival for **treatment persistence** a/w efficacy (when compared to ustekinumab, ixekizumab, secukinumab, adalimumab)

Guselkumab had 2nd highest drug survival for **safety** compared to other biologics, after ustekinumab

Increasing “real world evidence” supports IL-23 their efficacy and safety




Overlaid Kaplan-Meier **Survival Curves for Discontinuation Associated With Ineffectiveness** for All Biologic Cohorts During 2 Years


Yiu ZZN, Becher G, Kirby B, et al. Drug survival associated with effectiveness and safety of treatment with guselkumab, ixekizumab, secukinumab, ustekinumab, and adalimumab in patients with psoriasis. JAMA Dermatol. Published online July 6, 2022.

Blauvelt A, Lebwohl M, Langley RG, et al. Malignancy rates through 5 years of follow-up in patients with moderate-to-severe psoriasis treated with guselkumab: Pooled results from the VOYAGE 1 and VOYAGE 2 trials. J Am Acad Dermatol. 2023;89(2):274-282.

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# Risankizumab: Long-term Safety & Efficacy

Open label extension study (LIMMitless)

- → Long-term continuous risankizumab treatment for up to 5 years was well tolerated and demonstrated high and durable efficacy.

- → At week 256
  - → 85.1%/52.3% of patients achieved PASI 90/100, respectively
  - → 85.8% achieved sPGA 0/1, and 76.4% achieved DLQI 0/1

- → Rates of adverse events were low



Papp KA, Blauvelt A, Puig L, et al. Long-term safety and efficacy of risankizumab for the treatment of moderate-to-severe plaque psoriasis: Interim analysis of the LIMMitless open-label extension trial up to 5 years of follow-up. J Am Acad Dermatol. Published online August 6, 2023:S0190-9622(23)02416-7.

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# Psoriasis: Treatment Pipeline

Bimekizumab

Blocks interleukin (IL)-17A and IL-17F (two IL-17 isoforms)

→ safe but increased rate of oral candidiasis (approx. 15%, likely related to IL-17F blockade)

More oral TYK-2 Inhibitors

Oral biologics (5-10 year lookout)

"Robotic pills" with "digestible needles"

High dose induction knockout therapy ("hit hard early")

# ATOPIC DERMATITIS

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# Atopic Dermatitis

Affects approx. 10-20% of children and 5-10% of adults

Associated with low self-esteem, significant pruritus, QOL burden

Often involves visible anatomic sites (face, neck, hands)

Often co-exists with contact dermatitis

**Topical/External Treatment Options:**

- Topicals
  - Corticosteroids
  - Calcineurin inhibitors
  - PDE-4 Inhibitors (crisaborole)
  - JAK inhibitors
- Phototherapy (nbUVB / Excimer / PUVA)

# Topical JAK Inhibitors

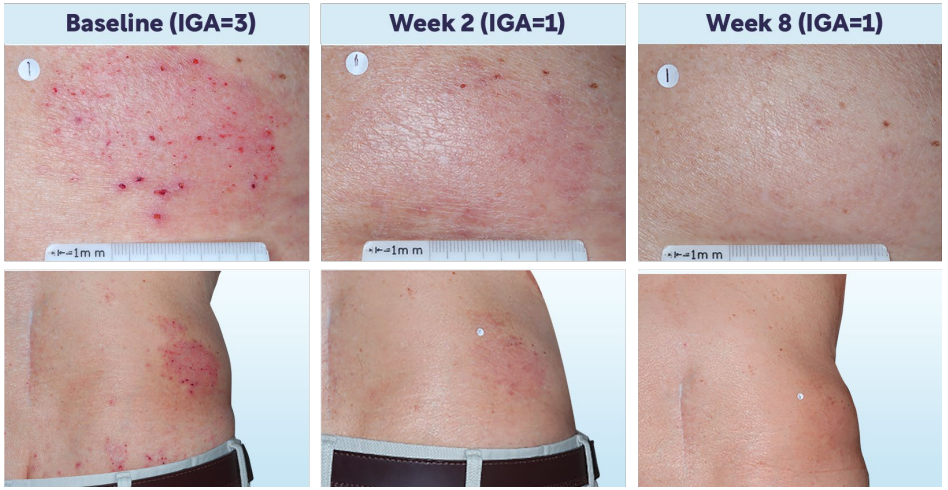
## Ruxolitinib 1.5% cream

Twice daily topical janus kinase inhibitor (JAK1/2) approved for >**12yo**

Rapid reduction in pruritus (**within 12 hours**)

- Hypothesized to block IL-31, IL-4, and IL-13 cytokines expressed on nerve endings responsible for itch sensation

Outperforms triamcinolone 0.1% cream in head-to-head trials




https://www.opzelurahcp.com/atopic-dermatitis/before-and-after


Papp K, Szepietowski JC, Kircik L, et al. Efficacy and safety of ruxolitinib cream for the treatment of atopic dermatitis: Results from 2 phase 3, randomized, double-blind studies. J Am Acad Dermatol. 2021;85(4):863-872.

Blauvelt A, Szepietowski JC, Papp K, et al. Itch-free state in patients with atopic dermatitis treated with ruxolitinib cream: pooled analysis from two randomized phase 3 studies. J Am Acad Dermatol. Published online September 13, 2022:S0190-9622(22)02688-3.

Kim BS, Howell MD, Sun K, et al. Treatment of atopic dermatitis with ruxolitinib cream (JAK1/JAK2 inhibitor) or triamcinolone cream. J Allergy Clin Immunol. 2020;145(2):572-582.

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# Topical JAK Inhibitors

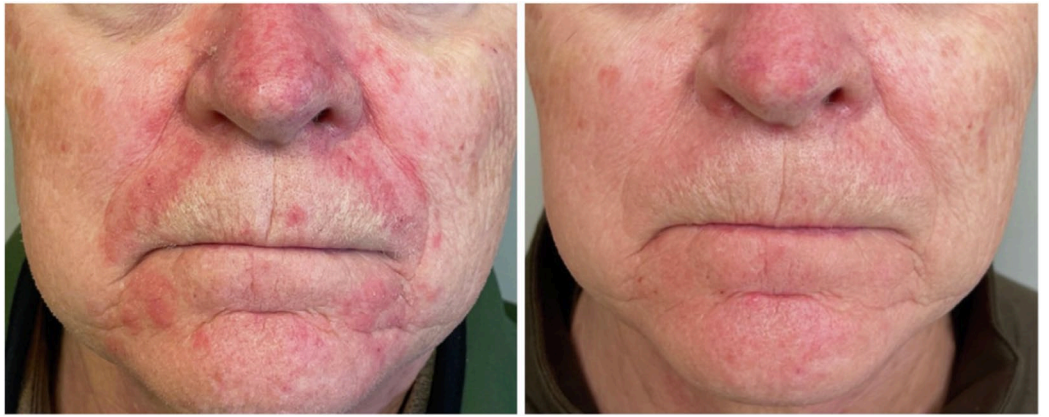
**Ruxolitinib 1.5% cream**

Safe to use in sensitive anatomic sites

Many potential clinical indications

Side Effects: **folliculitis**, nasopharyngitis, diarrhea, bronchitis, ear infection, tonsillitis, rhinorrhea

**Coming soon**: Delgocitinib (pan-JAK)



**Refractory seborrheic dermatitis after 2 weeks of topical ruxolitinib 1.5% cream BID**

Pope E, Kowalski E, Tausk F. Topical ruxolitinib in the treatment of refractory facial seborrheic dermatitis. JAAD Case Rep. 2022;24:59-60.



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# Topical JAK Inhibitors: Safety

**Considerations/Limitations:**

- Black Box Warning
- Indicated for short term non-continuous use, <20% BSA
- Not recommended for concurrent use with systemic immunosuppressants/biologics

Longterm safety data on ruxolitinib is reassuring

Patients who used cream continuously x 8 weeks followed by PRN use → No new safety signals

In “maximal use” studies patients had peak ruxolitinib serum concentrations lower that what is seen after oral ruxolitinib 15mg bid except 2 patients with high baseline BSA (45% and 90%)

Bissonnette et al, Am J Clin Dermatol 23(3): 355, 2022
Stefanko NS, Quan VL, Chovatiya R. Efficacy, safety, and treatment patterns of ruxolitinib 1.5% cream in adult atopic dermatitis: A single center retrospective study. J Am Acad Dermatol. 2023;89(2):415-417.
Leung DYM, Paller AS, Zaenglein AL, et al. Safety, pharmacokinetics, and efficacy of ruxolitinib cream in children and adolescents with atopic dermatitis. *Ann Allergy Asthma Immunol.* 2023;130(4):500-507.e3.
Papp K, Szepietowski JC, Kircik L, et al. Long-term safety and disease control with ruxolitinib cream in atopic dermatitis: Results from two phase 3 studies. J Am Acad Dermatol. 2023;88(5):1008-1016.



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# Systemic Treatments for Atopic Dermatitis

Traditional systemic agents
- Methotrexate
- Cyclosporine
- Mycophenolate mofeitil
- Azathioprine
- Prednisone

Interleukin 4/13 Inhibitors
- Dupilumab

Interleukin 13 Inhibitors
- Tralokinumab
- *?Lebrikizumab*

JAK Inhibitors
- Upadacitinib (Oral JAK1 inhibitor)
- Abrocitinib (Oral JAK1 inhibitor)

# Dupilumab: Updates

Approved to treat AD in patients 6 months and older

**Documented rapid efficacy in erythrodermic atopic dermatitis**

New FDA-approved indication for prurigo nodularis (age 18+ years)

Phase 3 trials investigating use in chronic spontaneous urticaria, bullous pemphigoid

Paller AS, Silverberg JI, Cork MJ, et al. Efficacy and safety of dupilumab in patients with erythrodermic atopic dermatitis: a post hoc analysis of 6 randomized clinical trials. JAMA Dermatol. 2023;159(3):255-266.
Paller AS, Simpson EL, Siegfried EC, et al. Dupilumab in children aged 6 months to younger than 6 years with uncontrolled atopic dermatitis: a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2022;400(10356):908-919.

# Dupilumab: Updates

Reassuring long term efficacy and safety data

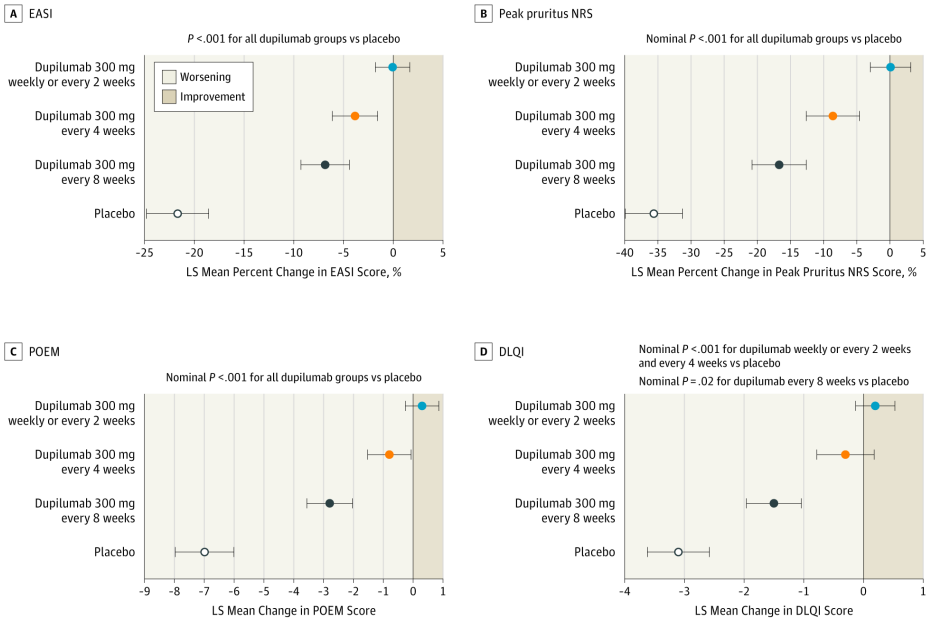
**LIBERTY AD SOLO-CONTINUE**:

Open label extension study to 36 weeks to assess maintenance of efficacy at different dose regimens

→ Continued response rate most consistently maintained with weekly or q2 week dosing

→ Diminution of response with longer dose intervals

→ **No new safety concerns**






Worm M, Simpson EL, Thaçi D, et al. Efficacy and safety of multiple dupilumab dose regimens after initial successful treatment in patients with atopic dermatitis: a randomized clinical trial. JAMA Dermatol. 2020;156(2):131-143.

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# Extending Dupilumab Dosing Intervals

Prospective observational study of 18 moderate to severe AD patients

- Dupixent q2 weeks → **tapered to every 3 or 4 weeks based on clinical judgement**
  - All maintained >EASI-80 after extending intervals of dupilumab
  - 22% of patients revered to every other week dosing due to worsening disease

IL-4Rα expression remained undetectable in q4 week patients

- During treatment with dupilumab q6 week, IL-4Rα expression became fully or partly detectable again
  - Interval of ~40 days may represent “tipping point” where dupilumab is no longer fully saturating IL-4Rα on circulating lymphocytes



Valente C, Farinha P, Duarte B. Extending dupilumab dosing intervals in atopic dermatitis: A prospective observational study in a South European tertiary hospital. J Eur Acad Dermatol Venereol. Published online September 20, 2023.
Dekkers C, der Wal MM van, El Amrani M, et al. Biological tipping point in patients with atopic dermatitis treated with different dosing intervals of dupilumab. J Invest Dermatol. 2023;143(9):1822-1825.e3.

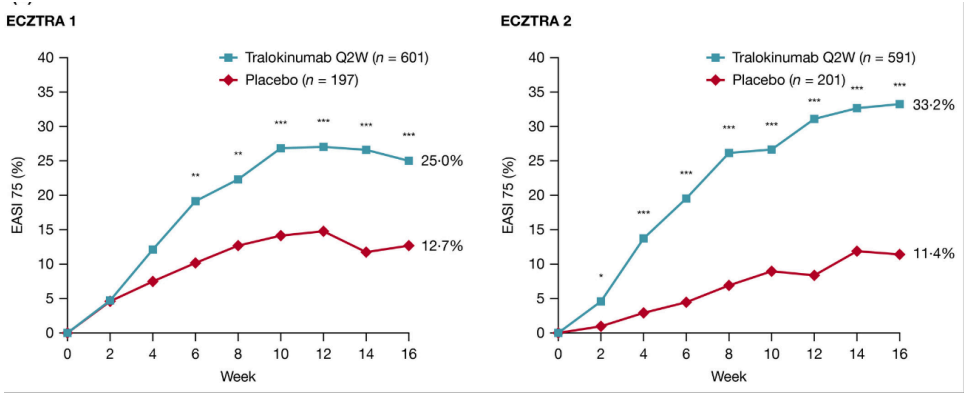
# Tralokinumab

Selective IL-13 Inhibitor for adults >18yo; SubQ Injection

**ECZTRA Trials:**

**Tralokinumab monotherapy vs placebo x 16 wks**

- **Trial 1**: 25-% reached EASI-75 (vs 13% placebo)
- **Trial 2**: 33% reached EASI-75 (vs 10% placebo)





Wollenberg A, Blauvelt A, Guttman-Yassky E, et al. Tralokinumab for moderate-to-severe atopic dermatitis: results from two 52-week, randomized, double-blind, multicentre, placebo-controlled phase III trials (ECZTRA 1 and ECZTRA 2). Br J Dermatol. 2021;184(3):437-449.

Simpson EL, Merola JF, Silverberg JI, et al. Safety of tralokinumab in adult patients with moderate-to-severe atopic dermatitis: pooled analysis of five randomized, double-blind, placebo-controlled phase 2 and phase 3 trials. Br J Dermatol. Published online September 9, 2022.

Gutermuth J, Pink AE, Worm M, Soldbro L, Bjerregård Øland C, Weidinger S. Tralokinumab plus topical corticosteroids in adults with severe atopic dermatitis and inadequate response to or intolerance of ciclosporin A: a placebo-controlled, randomized, phase III clinical trial (ECZTRA 7). Br J Dermatol. 2022;186(3):440-452.

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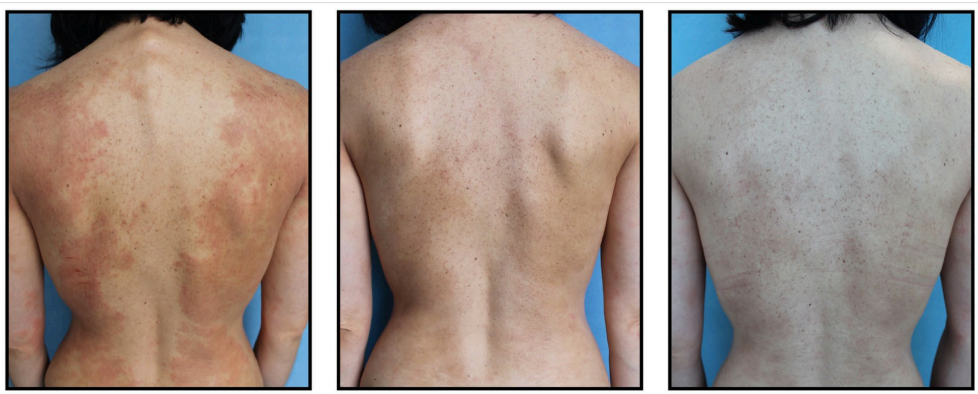
# Tralokinumab

## ECZTRA Trial 3:

**Tralokinumab + TCS *vs* placebo + TCS x 16 wks**

- 56% reached EASI-75 (vs 37% on placebo)
- Statistically significant improvement in NRS itch score and DLQI across all trials
- Side effect profile: Similar to dupilumab



Week 0
IGA score of 4
EASI score of 31.9
Worst daily pruritus NRS score of 8

Week 8
IGA score of 1
EASI score of 4.3
Worst daily pruritus NRS score of 3

Week 16
IGA score of 2
EASI score of 3.6
Worst daily pruritus NRS score of 3

Wollenberg A, Blauvelt A, Guttman-Yassky E, et al. Tralokinumab for moderate-to-severe atopic dermatitis: results from two 52-week, randomized, double-blind, multicentre, placebo-controlled phase III trials (ECZTRA 1 and ECZTRA 2). Br J Dermatol. 2021;184(3):437-449.
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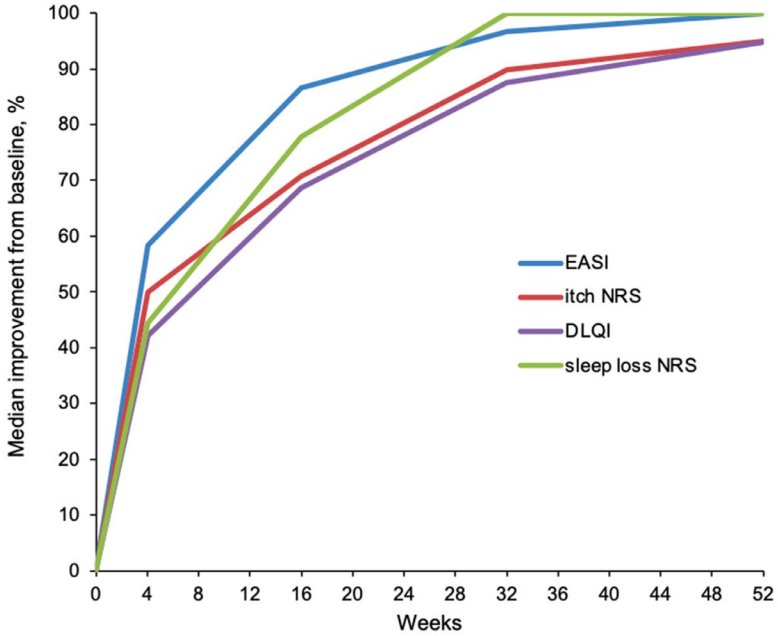
# Tralokinumab: Drug Survival

At week 52, 95.4% of patients (21/22) reached EASI-90




Division Na Pezzolo E, Schena D, Gambardella A, et al. Survival, efficacy and safety of tralokinumab after 32 and 52 weeks of treatment for moderate-to-severe atopic dermatitis in adults: A multicentre real-world study. J Eur Acad Dermatol Venereol. Published online July 22, 2023.

Simpson EL, Guttman-Yassky E, Eichenfield LF, et al. Tralokinumab therapy for moderate-to-severe atopic dermatitis: Clinical outcomes with targeted IL-13 inhibition. Allergy. Published online July 16, 2023.



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# Tralokinumab: Updates

Reports of success in patients with

- Dupixent associated psoriasiform dermatitis
- “Dupixent resistant” atopic dermatitis
- Dupixent related conjunctivitis

# Lebrikizumab *(?coming soon?)*

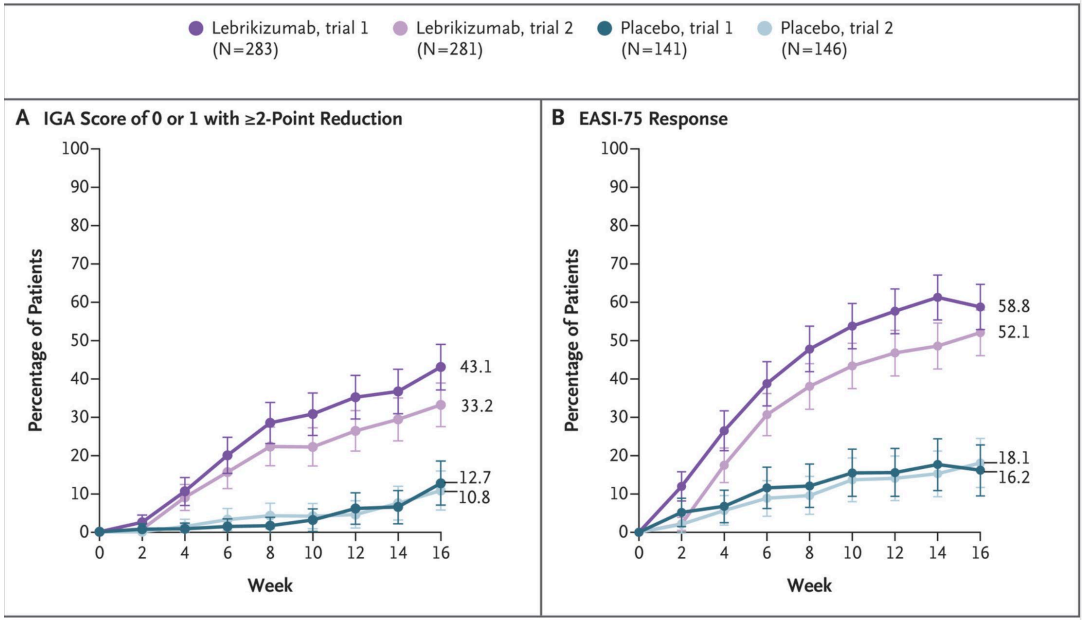
High-affinity IgG4 monoclonal antibody targeting interleukin-13

SubQ Injection, >12 year or older

**ADvocate 1+2 Trials:**

**Lebrikizumab monotherapy vs placebo**
**x 16 wks**

**Trial 1**: 58.8-% reached EASI-75 (vs 16.2% placebo)
**Trial 2**: 52.1% reached EASI-75 (vs 18.1% placebo)






Silverberg JI, Guttman-Yassky E, Thaçi D, et al. Two phase 3 trials of lebrikizumab for moderate-to-severe atopic dermatitis. N Engl J Med. 2023;388(12):1080-1091.

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# Oral JAK Inhibitors

Two FDA-Approved options

**Upadacitinib**: Measure Up 1 and 2 Monotherapy Trials (16 weeks):

69.6% and 60.1% of patients (15mg dose) achieved EASI-75

79.7% and 72.9% of patients (30mg dose) achieved EASI-75

*Placebo EASI-75 16.3% (Measure Up 1) and 12.3% (Measure Up 2)*

**Abrocitinib**: JADA MONO-1 and -2 Monotherapy Trials (16 weeks):

40% and 44.5% of patients (100mg dose) achieved EASI-75

63% and 61% of patients (200mg dose) achieved EASI-75

*Placebo EASI-75 12% (MONO-1) and 10.4% (MONO-2)*



Guttman-Yassky E, Teixeira HD, Simpson EL et al. Once-daily upadacitinib versus placebo in adolescents and adults with moderate-to-severe atopic dermatitis (Measure Up 1 and Measure Up 2): results from two replicate double-blind, randomised controlled phase 3 trials. Lancet. 2021 Jun 5;397(10290):2151-2168.
Simpson EL, Sinclair R, Forman S et al. Efficacy and safety of abrocitinib in adults and adolescents with moderate-to-severe atopic dermatitis (JADE MONO-1): a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial. Lancet. 2020 Jul 25;396(10246):255-266.

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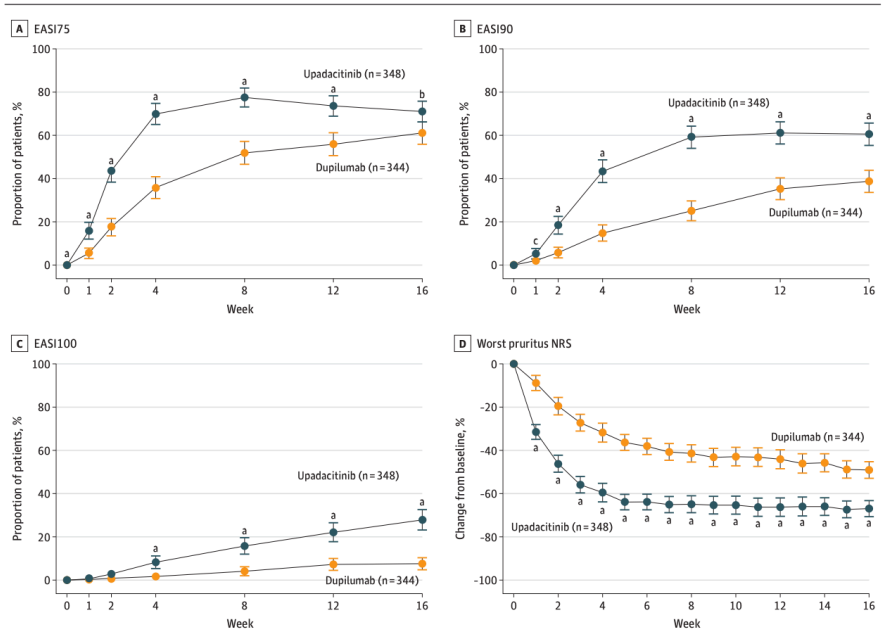
# Upadacitinib vs Dupilumab for AD






Blauvelt A, Teixeira HD, Simpson EL, et al. Efficacy and safety of upadacitinib vs dupilumab in adults with moderate-to-severe atopic dermatitis: a randomized clinical trial. JAMA Dermatol. 2021;157(9):1047-1055.

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# Oral JAK Inhibitors

## Considerations/Limitations:

- Side effect profile: URI, acne, HA, HSV, zoster, increased CPK, nausea, abdominal pain, muscle aches, influenza like illness, among others
- Black box warning

Document thorough risk/benefit discussion

Consider avoiding in patients >50 years with at least one risk factor for MACE

Vaccination should be up to date including for herpes zoster

Monitoring labs and visits required

Screen for TB, Hep B/C, +/- HIV

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

***See full prescribing information for complete boxed warning.***

- **Increased risk of serious bacterial, fungal, viral, and opportunistic infections leading to hospitalization or death, including tuberculosis (TB). Interrupt treatment with RINVOQ if serious infection occurs until the infection is controlled. Test for latent TB before and during therapy; treat latent TB prior to use. Monitor all patients for active TB during treatment, even patients with initial negative, latent TB test. (5.1)**
- **Higher rate of all-cause mortality, including sudden cardiovascular death with another Janus kinase (JAK) inhibitor vs. tumor necrosis factor (TNF) blockers in rheumatoid arthritis (RA) patients. (5.2)**
- **Malignancies have occurred in patients treated with RINVOQ. Higher rate of lymphomas and lung cancers with another JAK inhibitor vs. TNF blockers in RA patients. (5.3)**
- **Higher rate of MACE (defined as cardiovascular death, myocardial infarction, and stroke) with another JAK inhibitor vs. TNF blockers in RA patients. (5.4)**
- **Thrombosis has occurred in patients treated with RINVOQ. Increased incidence of pulmonary embolism, venous and arterial thrombosis with another JAK inhibitor vs. TNF blockers. (5.5)**

https://www.rxabbvie.com/pdf/rinvoq_pi.pdf



Guttman-Yassky E, Teixeira HD, Simpson EL et al. Once-daily upadacitinib versus placebo in adolescents and adults with moderate-to-severe atopic dermatitis (Measure Up 1 and Measure Up 2): results from two replicate double-blind, randomised controlled phase 3 trials. Lancet. 2021 Jun 5;397(10290):2151-2168.
Simpson EL, Sinclair R, Forman S et al. Efficacy and safety of abrocitinib in adults and adolescents with moderate-to-severe atopic dermatitis (JADE MONO-1): a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial. Lancet. 2020 Jul 25;396(10246):255-266.
Guttman-Yassky E, Thyssen JP, Silverberg JI, et al. Safety of upadacitinib in moderate-to-severe atopic dermatitis: An integrated analysis of phase 3 studies. J Allergy Clin Immunol. Published online October 1, 2022:S0091-6749(22)01327-6.

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# Oral JAK Inhibitors: Newer Safety Evidence for Upadacitinib

Open label extension trials demonstrate persistent efficacy, without new safety concerns through 40 weeks

Reassuring safety data in adolescents (age 12-17) through 16 weeks

Treatment withdrawal –> return of AD and pruritus, though able to be salvaged with upadacitinib 30mg re-initiation

Blauvelt A, Ladizinski B, Prajapati VH, et al. Efficacy and safety of switching from dupilumab to upadacitinib versus continuous upadacitinib in moderate-to-severe atopic dermatitis: Results from an open-label extension of the phase 3, randomized, controlled trial (Heads up). J Am Acad Dermatol. 2023;89(3):478-485.
Paller AS, Ladizinski B, Mendes-Bastos P, et al. Efficacy and safety of upadacitinib treatment in adolescents with moderate-to-severe atopic dermatitis: analysis of the measure up 1, measure up 2, and ad up randomized clinical trials. JAMA Dermatol. 2023;159(5):526-535.



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# CDC Advisory Committee on Immunization Practices (ACIP)

**Table 1. Current Vaccination Recommendations for Psoriasis and Atopic Dermatitis Patients on Biologic Therapy**

| Vaccine | Biologic | | | | | Comments |
|---|---|---|---|---|---|---|
| | TNFα | IL-12/23 | IL-23 | IL-17 | IL-4/IL-13 | |
| Pneumococcal | ✓[a] | ✓ | ✓ | ✓ | ✓ | Should be administered to all patients age ≥19 on biologics |
| Inactivated Influenza | ✓ | ✓ | ✓ | ✓ | ✓ | Should be administered annually to all patients on biologics |
| Recombinant Zoster | ✓ | ✓ | ✓ | ✓ | ✓ | Should be administered (2-doses) to all patients age ≥19 on biologics[c] |
| Other inactivated | ✓ | ✓ | ✓ | ✓ | ✓ | Includes *Haemophilius influenzae* type b, hepatitis A and B, human papillomavirus (HPV), tetanus and diphtheria toxoids and acellular pertussis (TDAP) |
| Live-attenuated | X[b] | X | X | X | X | Includes mumps, measles, rubella (MMR), oral poliomyelitis, oral typhoid fever, yellow fever, and varicella zoster |
| COVID-19 | ✓ | ✓ | ✓ | ✓ | ✓ | Approved for 3-dose Pfizer-BioNTech BNT162b2 and Moderna mRNA-1273 vaccines or 1st-dose Johnson & Johnson's Janssen JNJ-78436735 + 2nd dose mRNA COVID-19 vaccine |
| COVID-19 Booster | ✓ | ✓ | ✓ | ✓ | ✓ | Should administer additional booster of Pfizer-BioNTech or Moderna at least 3 months after 3rd dose or 2 months after 2nd dose for those who received the Johnson & Johnson's Janssen JNJ-78436735 vaccine. |

[a]✓ = Indicated for administration. [b]X = Not indicated for administration while concurrently on therapy. If indicated, can be administered 14-30 days prior to initiation of therapy or at least 3 months after cessation of therapy. [c]Based on most recent ACIP recommendations. National Psoriasis Foundation guidelines from 2019 recommend recombinant zoster vaccination for all psoriasis patients >50 and those <50 on biologic therapy only in combination with other systemic treatment.



Fan R, Cohen JM. Vaccination recommendations for psoriasis and atopic dermatitis patients on biologic therapy: a practical guide. Yale J Biol Med. 2022;95(2):249-255.

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# JAKi and Herpes Zoster

In upadacitinib trials, zoster incidence ranges from 4-6%

In 2-year upadacitinib data, zoster reactivation is:

6% at the 15mg dose

12% at the 30mg dose

Real life data is lacking

Recommendations: Vaccinate patients >18 years of age, ideally before treatment



Ortoncelli M, Mastorino L, Gelato F, et al. Herpes zoster infection in atopic patients undergoing upadacitinib: practical suggestions on vaccination and management. Dermatitis. Published online July 11, 2023.

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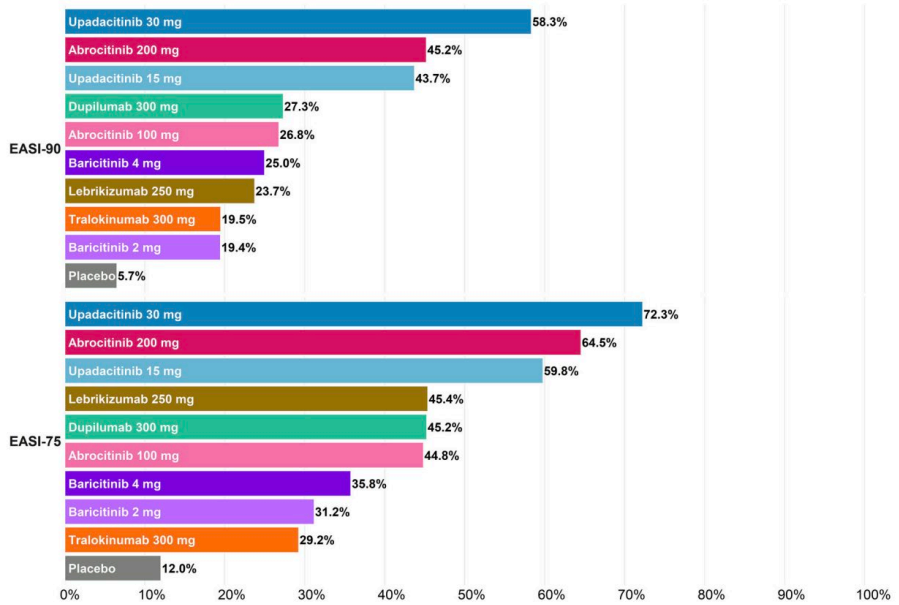
# Comparative Treatment Effectiveness at Week 12-16






Silverberg JI, Hong HCH, Calimlim BM, et al. Comparative efficacy of targeted systemic therapies for moderate-to-severe atopic dermatitis without topical corticosteroids: an updated network meta-analysis. Dermatol Ther (Heidelb). 2023;13(10):2247-2264.

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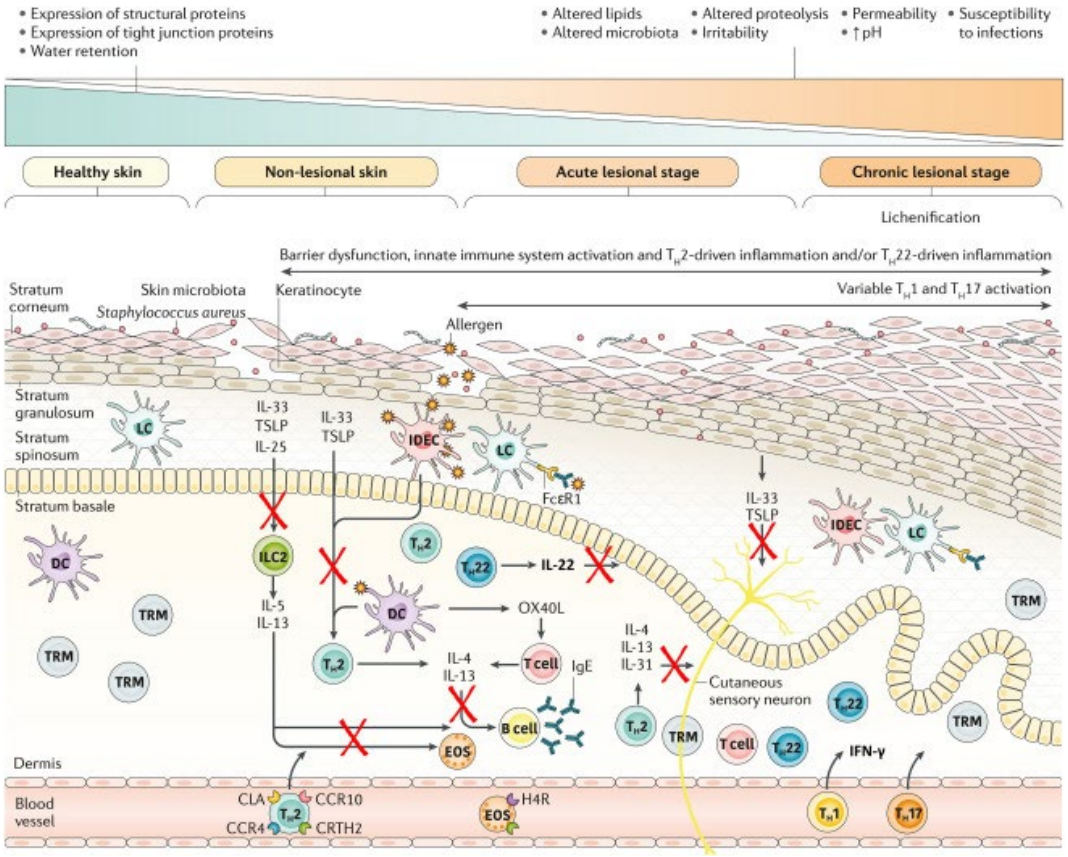




Guttman-Yassky E, Irvine AD, Brunner PM, et al. The role of Janus kinase signaling in the pathology of atopic dermatitis. J Allergy Clin Immunol. Published online August 1, 2023:S0091-6749(23)00970-3.

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# ALLERGIC CONTACT DERMATITIS

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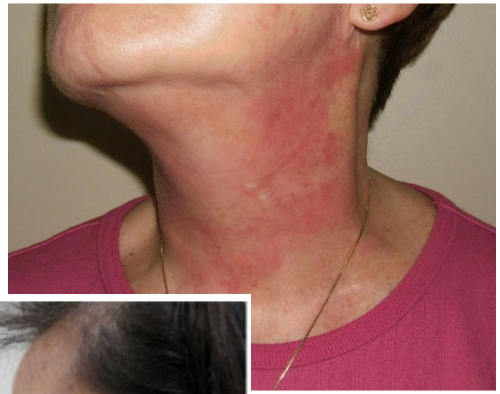
# Contact Dermatitis in the Atopic Patient

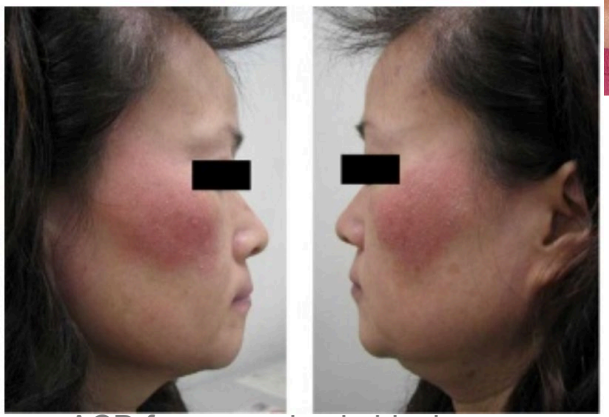
Atopic patients have a similar rate or ACD to non-AD patients, and <u>may even have a higher risk of ACD</u>

This is likely due to:

- Skin barrier disruption
- Overlapping immune pathophysiology
- Chronic application of topical emollients & medications



ACD from perfume



ACD from carmine in blush

Milam EC, Jacob SE, Cohen DE. Contact dermatitis in the patient with atopic dermatitis. J Allergy Clin Immunol Pract. 2019;7(1):18-26.
Silverberg JI, Hou A, Warshaw EM, et al. Prevalence and trend of allergen sensitization in adults and children with atopic dermatitis referred for patch testing, north american contact dermatitis group data, 2001-2016. *J Allergy Clin Immunol Pract*. Published online March 27, 2021.
Zirwas MJ. Contact dermatitis to cosmetics. Clin Rev Allergy Immunol. 2019;56(1):119-128.
Suzuki K, Hirokawa K, Yagami A, Matsunaga K. Allergic contact dermatitis from carmine in cosmetic blush. Dermatitis. 2011;22(6):348-349.



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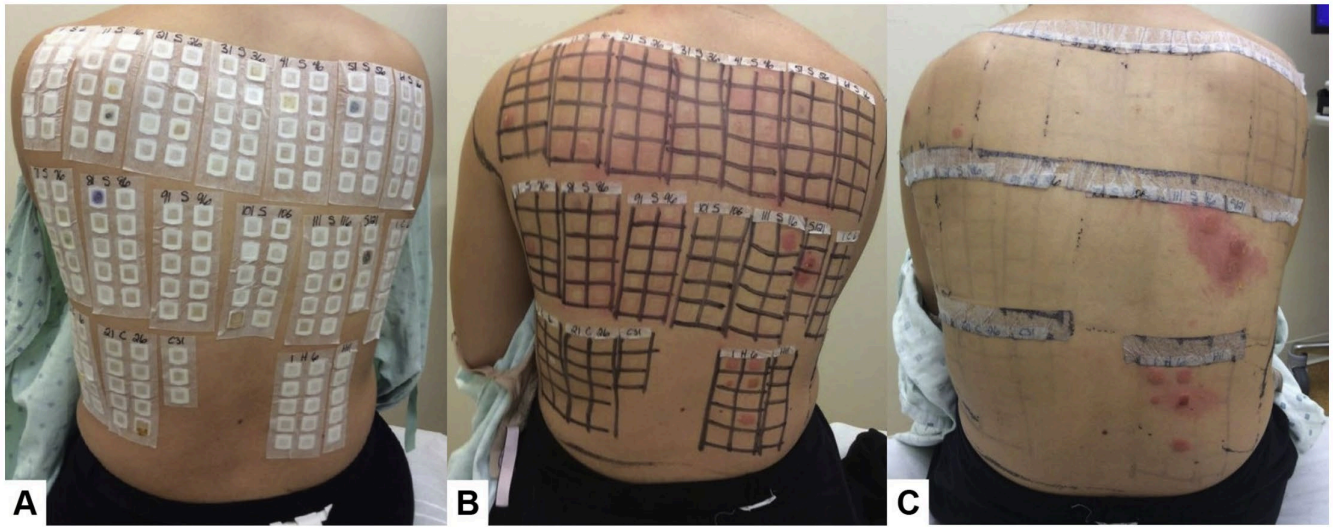
# Patch Testing






Milam EC, Jacob SE, Cohen DE. Contact dermatitis in the patient with atopic dermatitis. J Allergy Clin Immunol Pract. 2019;7(1):18-26.
Thyssen JP, Schuttelaar MLA, Alfonso JH, et al. Guidelines for diagnosis, prevention, and treatment of hand eczema. Contact Dermatitis. 2022;86(5):357-378.
Diepgen TL, Andersen KE, Chosidow O, et al. Guidelines for diagnosis, prevention and treatment of hand eczema--short version. J Dtsch Dermatol Ges. 2015;13(1):77-85.

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# Top 20 Patch Testing Allergens in North America (2019-2020)

| Rank | Allergen | Category |
|---|---|---|
| #1 | Nickel sulfate hexahydrate | Metal |
| #2 | Methylisothiazolinone (MI) | Preservative |
| #3 | Fragrance Mix I | Fragrance |
| #4 | Hydroperoxides of linalool | Fragrance |
| #5 | Benzisothiazolinone (BIT) | Preservative |
| #6 | Methylchloroisothiazolinone/ Methylisothiazolinone (MCI/MI) | Preservative |
| #7 | Propolis | Resin |
| #8 | *Myroxylon pereirae* (Balsam of Peru) | Fragrance |
| #9 | Cobalt chloride hexahydrate | Metal |
| #10 | Formaldehyde 2% | Preservative |

| Rank | Allergen | Category |
|---|---|---|
| #11 | Neomycin | Medicament |
| #12 | Gold sodium thiosulfate | Metal |
| #13 | p-phenylenediamine (PPD) | Dye |
| #14 | Fragrance Mix II | Fragrance |
| #15 | Bacitracin | Medicament |
| #16 | Quaternium-15 | Preservative |
| #17 | Thiuram Mix | Rubber etc |
| #18 | Lanolin | Wool alcohol |
| #19 | Propylene Glycol 100% | Preservative |
| #20 | Hydroxyperoxides of limonene | Fragrance |



DeKoven JG, Warshaw EM, Reeder MJ, et al. North american contact dermatitis group patch test results: 2019-2020. Dermatitis. 2023;34(2):90-104.

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# T.R.U.E. Test (36 Allergens) versus NACDG-70

| Rank | Allergen | Category |
|---|---|---|
| #1 | Nickel sulfate hexahydrate | Metal |
| #2 | Methylisothiazolinone (MI) | Preservative |
| #3 | Fragrance Mix I | Fragrance |
| #4 | Hydroperoxides of linalool | Fragrance |
| #5 | Benzisothiazolinone (BIT) | Preservative |
| #6 | Methylchloroisothiazolinone/ Methylisothiazolinone (MCI/MI) | Preservative |
| #7 | Propolis | Resin |
| #8 | *Myroxylon pereirae* (Balsam of Peru) | Fragrance |
| #9 | Cobalt chloride hexahydrate | Metal |
| #10 | Formaldehyde 2% | Preservative |

| Rank | Allergen | Category |
|---|---|---|
| #11 | Neomycin | Medicament |
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| #13 | p-phenylenediamine (PPD) | Dye |
| #14 | Fragrance Mix II | Fragrance |
| #15 | Bacitracin | Medicament |
| #16 | Quaternium-15 | Preservative |
| #17 | Thiuram Mix | Rubber etc |
| #18 | Lanolin | Wool alcohol |
| #19 | Propylene Glycol 100% | Preservative |
| #20 | Hydroxyperoxides of limonene | Fragrance |

**The T.R.U.E test *will not identify***
**8 of the top 20 allergens**



DeKoven JG, Warshaw EM, Reeder MJ, et al. North american contact dermatitis group patch test results: 2019-2020. Dermatitis. 2023;34(2):90-104.

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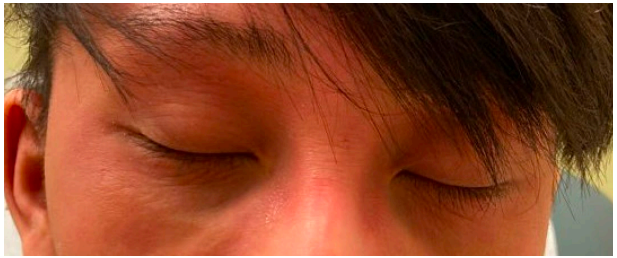
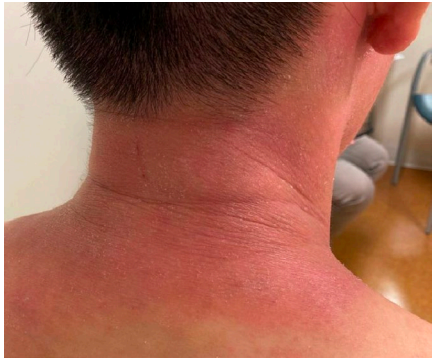
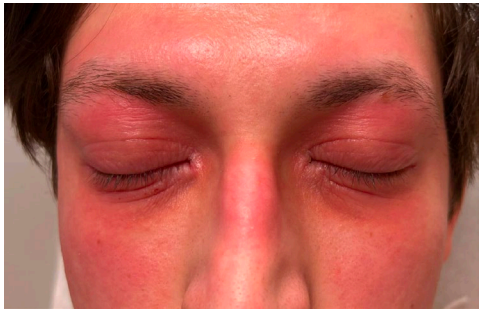
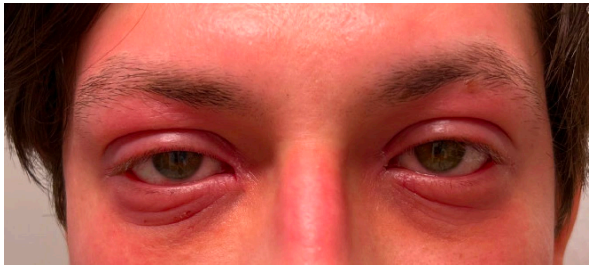
# Chronic Atopic Dermatitis with Exacerbation











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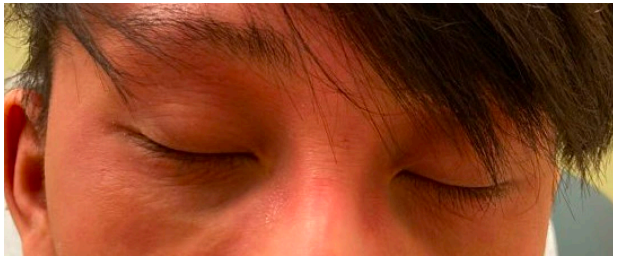
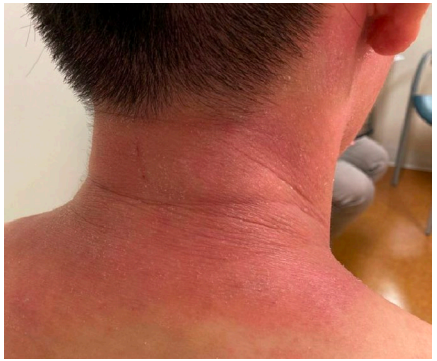
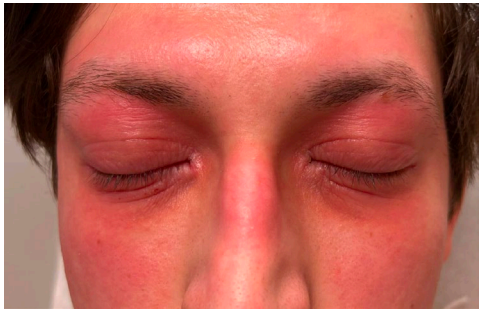
# Chronic Atopic Dermatitis with Exacerbation

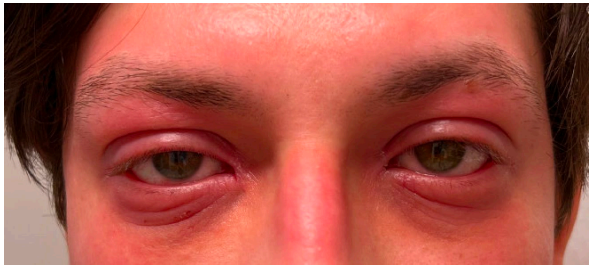




**Patch Testing Positives:**

**Propylene Glycol 30 % + 100%**
**Butylene Glycol**
**Lauryl polyglucose**
**Decyl Glucoside**





**Propylene Glycol 30 % + 100%**
**Butylene Glycol**



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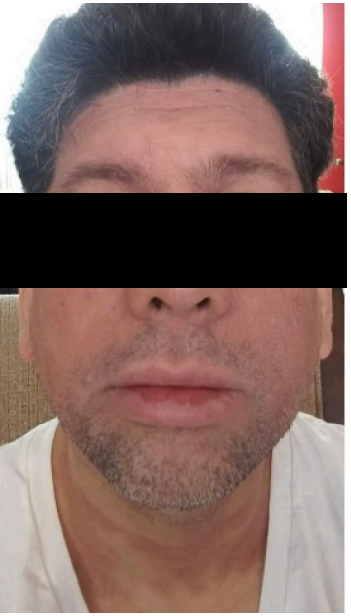
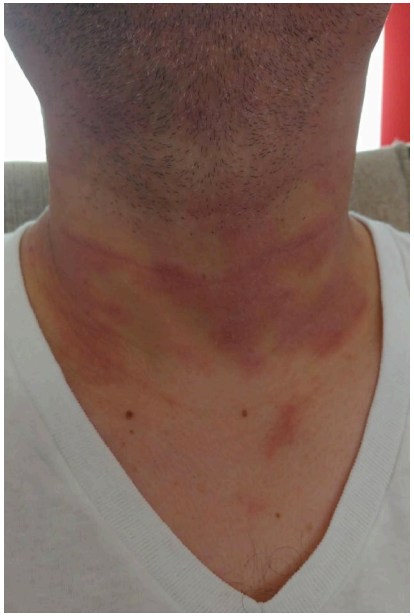
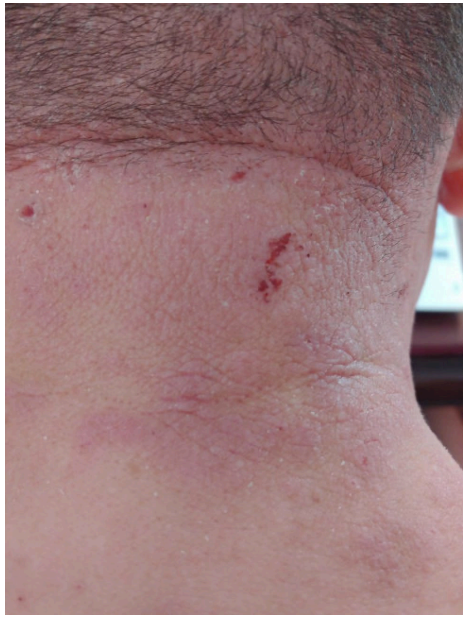
# Chronic Atopic Dermatitis with Flare







Patch testing revealed:

**1+ Fragrance Mix I**
**1+ Hydroxyperoxide of Limonene**
**1+ Propylene Glycol (30 and 100%)**



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**Lauryl glucoside**
**Coco-glucoside**


**Propylene Glycol**


**Propylene Glycol**


**Propylene Glycol**



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# Propylene Glycol

Prevalent in <u>many</u> personal care products + medicaments

- 37% of the 4674 products logged in the 2016 ACDS CAMP database have PG

Propylene glycol is most common allergen in topical corticosteroid vehicles

- Present in ~64% of topical corticosteroids


58 Milam EC, Cohen DE. Contact dermatitis: emerging trends. Dermatol Clin. 2019;37(1):21-28.
Coloe J, Zirwas MJ. Allergens in corticosteroid vehicles. *Dermatitis*. 2008;19(1):38-42.

# Allergen of the Year: Sodium Metabisulfite

Aka sodium disulfite, sodium pyrosulfite (≠ sulfates)

Antioxidants and preservatives in personal care products, pharmaceutials, foods/beverages to extend shelf life

Can cause Type I hypersensitivity reactions (anaphylaxis, urticaria, gastrointestinal symptoms, and bronchoconstriction), and nonimmunologic adverse reactions

TABLE 3. Nonoccupational and Occupational Sources of Sulfites (Table view)

| *Nonoccupational* | *Occupational* |
|---|---|
| • Personal care products | • Food and drink (preservation, sterilization, and sugar refining) |
| Shampoo | • Brewing, wine making (sterilization during fermentation) |
| Hair colors and bleaches | • Photography (developers and fixers) |
| Hair waving/straightening agents | • Textile industry (color stripper) |
| Hairspray | • Leather (tanning, solubilizing agent for tannins, reducing chrome liquors) |
| Skin lighteners | • Mineral extraction (ore flotation aid) |
| Tanning lotions | • Effluent treatment (to reduce chromium salts) |
| Antiaging products | • Chemical manufacture (sulfosuccinates and sodium formaldehyde bisulfite) |
| Facial cleansers | • Rubber manufacture (latex anticoagulant) |
| Body washes | • Health care (contact with medications and gloves) Parenteral solutions (prevent oxidation of adrenaline) |
| Bath oils/salts | • Wood, pulp, and paper industries (soften wood material) |
| Eye creams | • Glass industry (facilitates melting process) |
| Make-up (foundation, blush, bronzers, highlighters) | • Glove manufacturing (anticoagulant and preservative) |
| Sunscreens | • Personal care product production (preservative) |
| Perfume | • Pharmaceutical manufacturing (preservative) |
| Deodorants | |
| • Swimming pool water | |
| • Medications | |
| Topical antifungals | |
| Topical corticosteroids | |
| Local anesthetics | |
| Ophthalmics | |
| Nasal solutions | |
| Intravenous solutions | |
| • Gloves | |

*Adapted from Ralph et al[9] and García-Gavín et al.[6]*



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# Allergen of the Year: Sodium Metabisulfite

High dietary sulfite consumption has been linked to systemic contact dermatitis

In1986 FDA regulation banned sulfite use in fresh fruits and vegetables, and packaged foods containing 10 ppm or more of sulfites are required to disclose this on labels

TABLE 5. SULFITE CONTENT OF FOOD AND BEVERAGES (Table view)

| *High (>100 ppm)* | *Moderate to High (50–99.9 ppm)* | *Low to Moderate (10.1–49.9 ppm)* | *Low (<10 ppm)* |
|---|---|---|---|
| • Dried fruit (excluding dark raisins and prunes)<br>• Bottled lemon juice (nonfrozen)<br>• Bottled lime juice (nonfrozen)<br>• Wine<br>• Molasses<br>• Sauerkraut juice<br>• Grape juice (white, white sparkling, pink sparkling, and red sparkling)<br>• Pickled cocktail onions | • Dried potatoes<br>• Wine vinegars<br>• Gravies/sauces<br>• Fruit toppings<br>• Maraschino cherries | • Pectin<br>• Shrimp (fresh)<br>• Corn syrup<br>• Sauerkraut (without juice)<br>• Pickled peppers<br>• Pickles/relishes<br>• Corn starch<br>• Hominy<br>• Frozen potatoes<br>• Maple syrup<br>• Imported jam/jelly<br>• Fresh mushrooms<br>• Imported sausage/meat<br>• Cordial alcohols<br>• Dehydrated vegetables<br>• Corn bread/muffin mix<br>• Canned/jarred clams<br>• Clam chowder<br>• Avocado dip/guacamole<br>• Imported fruit juices<br>• Imported soft drinks<br>• Cider<br>• Cider vinegar | • Crackers<br>• Malt vinegar<br>• Sugar (especially beet sugar)<br>• Gelatin<br>• Canned potatoes<br>• Coconut<br>• Fresh fruit salad<br>• Dry soup mix<br>• Pizza dough (frozen)<br>• Pie dough (frozen)<br>• Grapes<br>• Domestic jams/jellies<br>• Soft drinks<br>• Instant tea<br>• Beer cookies |


*Metcalfe et al* [61]



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# Conclusions

Managing inflammatory dermatoses and minimizing risk of PIH is paramount for cosmesis. Patients want clear skin.

Novel and promising topical and systemic therapeutics are newly available, with more on the horizon.

Contact dermatitis is a common cause of inflamed skin, particularly among atopics.

Several top 40 allergens can be found in cosmetics and personal care products. Patch testing is the gold standard of identifying causes of contact dermatitis.

# THANK YOU


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