MODERATE-TO-SEVERE ATOPIC DERMATITIS:

Addressing Healthcare Disparities in URBAN COMMUNITIES

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This activity is provided by Med Learning Group.
This activity is co-provided by Ultimate Medical Academy/Complete Conference Management (CCM).
This activity is supported by an educational grant from Sanofi Genzyme and Regeneron Pharmaceuticals.

I. Atopic Dermatitis in Urban Communities

a. Epidemiology and burden of AD in urban communities

b. Identifying social and economic determinants of health care disparities

c. Challenges in the management of AD in urban communities

d. Recognizing the mental health and quality-of-life issues associated with AD

II. Assessment and diagnosis of AD

a. Clinical presentation of AD in skin of color

b. Current guideline recommendations for the management of AD in pediatric and adult patients

c. Proactive vs reactive care of AD

d. Assessing disease severity

III. Clinical Trial Data on Systemic Agents for the Management of AD

a. Mechanism of action of approved and investigational agents

b. Efficacy and safety of available and emerging systemic therapies

i. Dupilumab
ii. Tralokinumab
iii. Abrocitinib
iv. Upadacitinib
v. Emerging interleukin inhibitors
vi. Emerging JAK inhibitors

c. Considerations for immunosuppressant and immunomodulator use for AD during COVID-19

IV. Long-term management of AD

a. Optimizing treatment regimens for long-term management of AD

b. Recognizing patients who require specialist care or referrals

V. Case Studies

VI. Conclusions

VII. Questions and Answers

Moderate-to-Severe Atopic Dermatitis: Addressing Healthcare Disparities in Urban Communities

FACULTY

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PROGRAM OVERVIEW

This enduring virtual activity targets healthcare gaps related to the treatment and management of AD in urban communities, impacting outcomes through identifying determinants that impact health in urban communities, implementing strategies in disease severity assessment across varying skin tones, and guideline-based care.

- By addressing these gaps, you can assess whether your approach to AD management through utilization of current treatment guidelines, individualization of care through the "step-up care" approach and strategies for disease severity assessment – could be modified to help close these gaps.

- Expert discussion will guide you in analyzing and identifying challenges to AD management in the urban landscape, and how to navigate proactive vs reactive control.

- You will also be immersed in dynamic animations utilizing a whiteboard platform to memorably highlight key points related to patient-specific factors that contribute to the burden of AD, and essential goals, current and emerging approaches to AD management.

TARGET AUDIENCE

This activity is intended for dermatologists, pediatric dermatologists, primary care physicians, pediatricians, acute care physicians, and other healthcare professionals involved in the management of patients with atopic dermatitis.

LEARNING OBJECTIVES

Upon the completion of this program, attendees should be able to:

- Examine the social and economic determinants of health in urban communities that impact quality of life and health outcomes
- Implement strategies to assess disease severity and health-related quality of life in patients with AD
- Apply treatment guidelines and clinical trial data for the assessment and treatment of AD in underserved populations to ensure optimal outcomes

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Purpose: This program would be beneficial for nurses involved in the care of patients with atopic dermatitis.
CNE Credits: 1.5 ANCC Contact Hours.

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Vivian Shi, MD, FAAD	Discloses that she is on the board of directors of the Hidradenitis Suppurativa Foundation and advisor for the National Eczema Association. She is an advisory board member for AbbVie, Aristea Therapeutics, Boehringer Ingelheim, Burt's Bees, cQuell/Altus Lab, Dermira, Eli Lilly, GpSkin, Incyte, LEO Pharma, Menlo Therapeutics,

	MYOR, Novartis, Pfizer, Polyfins Technology, Regeneron, Sanofi Genzyme, Skin Actives Scientific and SUN Pharma. She is a speaker for AbbVie and Sanofi Genzyme/Regeneron. She has served as an investigator for AbbVie, Burt's Bees, Galderma, Kiniksa, LEO Pharma, Novartis, Regeneron, Skin Actives Scientific and Target-PharmaSolutions. She has received research funding from Pfizer and Skin Actives Scientific. Dr. Shi is a stock shareholder of Learn Health.

CME Content Review

The content of this activity was independently peer reviewed.

The reviewer of this activity has nothing to disclose.

CNE Content Review

The content of this activity was peer reviewed by a nurse reviewer.

Douglas Cox, MSN, MHA, RN
Ultimate Medical Academy/CCM – Lead Nurse Planner

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2. Participate in the web-based enduring activity.
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The THRIVE Initiative— Moderate-to-Severe Atopic Dermatitis: Addressing Healthcare Disparities in Urban Communities

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  - In addition, Dr. Lio has a patent pending for a Theraplex product with royalties paid, is an investor in LearnSkin, and is a board member and Scientific Advisory Committee member of the National Eczema Association.

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Disclosures (continued)

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Learning Objectives

- Examine the social and economic determinants of health in urban communities that impact quality of life and health outcomes
- Implement strategies to assess disease severity and health-related quality of life in patients with atopic dermatitis (AD)
- Apply treatment guidelines and clinical trial data for the assessment and treatment of AD in underserved populations to ensure optimal outcomes

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Burden of Atopic Dermatitis (AD)

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A brief animation exploring patient factors that contribute to the burden of atopic dermatitis

English

Spanish

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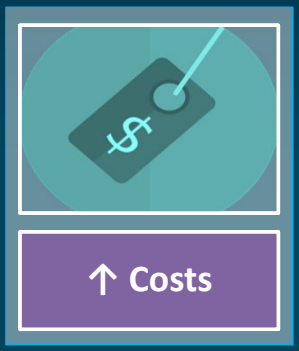
Impact of AD

↑ US prevalence

- Child/adolescent: 10–25%
- Adults: >7%
  - *85% present by 5 years*
  - *Adult onset in 2–8%*



↑ Costs

~$5.3 billion/year (2015 USD)

Impact on quality of life

Greater impact on QoL than type 1 diabetes

AD = atopic dermatitis; QoL = quality of life; US = United States; USD = US dollars.

Silverberg JI. *Ann Allergy Asthma Immunol.* 2019;123:144-151. Silverberg JI, et al. *Ann Allergy Asthma Immunol.* 2018;121:340-347. Drucker AM, et al. *J Invest Dermatol.* 2017;137:26-30. Arkwright PD, et al. *J Allergy Clin Immunol Pract.* 2013;1:142-151. Abuabara K, et al. *Ann Intern Med.* 2019;170:354-356.

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Epidemiology of AD in Urban Communities

AD prevalence and persistence are found to be ***highest*** in **urban areas** in children who are **female or black**

Children with persistent AD living in urban areas are ***more likely*** to have poor quality-of-life measures and asthma

19.3%

In US children, AD prevalence was ***higher*** in **African Americans (19.3%)** compared with children of European American ancestry (16.1%)

There are several theories to explain this discrepancy, including differing rates of key mutations associated with AD and urban pollution

McKenzie C, Silverberg JI. *Ann Allergy Asthma Immunol.* 2019;123:173-178.e1. Brunner PM, Guttman-Yassky E. *Ann Allergy Asthma Immunol.* 2019;122:449-455. Hendricks AJ, et al. *Br J Dermatol.* 2020;183:16-23.

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Special Issues in Skin of Color

Skin of color or richly-pigmented skin is *complex* and encompasses a wide variety of different groups

- 2008 study: need for better dermatology training
- AD disproportionately affects African Americans
- Few studies of differences in skin-disease epidemiology in skin of color
- Healthcare discrepancies include:
  - Delayed treatment courses
  - Increased morbidity and mortality
- Lack of peer-reviewed literature of skin disease in darker skin types

Taylor SC. *J Am Acad Dermatol*. 2002;46(2 suppl):S41-62. Nijhawan RI, et al. *J Am Acad Dermatol*. 2008;59:615-618. Brunner PM, Guttman-Yassky E. *Ann Allergy Asthma Immunol*. 2019122(5):449-455. Alexis AF, et al. *Cutis*. 2007;80:387-394. Jones VA, et al. *J Am Acad Dermatol*. 2021;85:773-775. Montgomery SNB, Elbuluk N. *J Am Acad Dermatol*. 2021;85:241-242.

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The Burden of AD

***Key factors* are itch, pain, sleep, and QoL**

- Self esteem
- Symptoms (itch, pain)
- Work productivity
- Sleep
- Comorbidities (asthma, infection)
- Mental-health impact (depression, anxiety)
- Flares/ unpredictability

Full impact of AD cannot be estimated based on skin signs alone

Silverberg JI. *Ann Allergy Asthma Immunol*. 2019;123:144-151. Kjellstrom T, et al. *J Urban Health*. 2007;84(3 suppl):1-6. Saha S, Feldman JM. *medRxiv*. 2020 (www.medrxiv.org/content/10.1101/2020.12.07.20241018v1.full.pdf). World Health Organization (WHO). *Hidden cities: unmasking and overcoming health inequities in urban settings*. 2010 (www.who.int/publications/i/item/9789241548038). Kiebert G, et al. *Int J Dermatol*. 2002;41:151-158. URLs accessed 11/27/2021.

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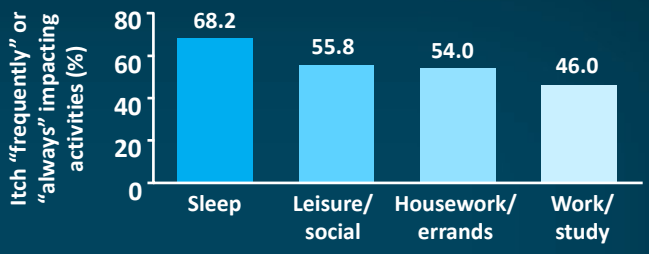
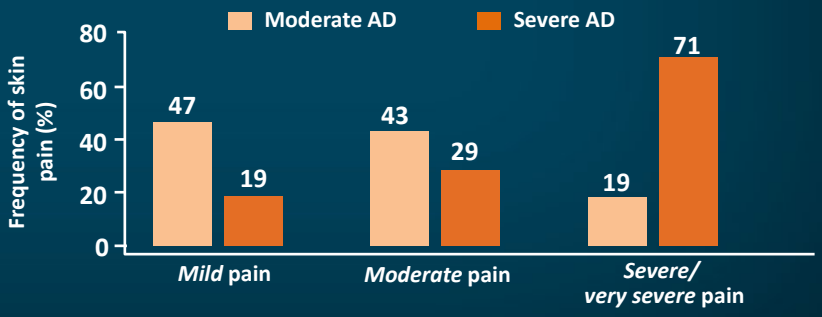
Impact of Itch and Pain in Moderate-to-Severe AD

Itch impact on sleep and activities



Skin pain is often overlooked in AD

Stinging, burning, tingling, pinprick, and crawling sensations affect ≥10% of patients



Simpson EL, et al. *J Am Acad Dermatol.* 2016;74:491-498. Vakharia PP, et al. *Ann Allergy Asthma Immunol.* 2017;119:548-552.e3.

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Impact of Socioeconomic Factors on AD Management

Socioeconomic differences are associated with *large disparities* in health status

- ***Association persists*** throughout life and across many measures of health
- Although effects are largest for those living in poverty, ***gradients of disparity*** are seen across the socioeconomic spectrum
- AD has a ***greater impact*** on quality-of-life for ***patients with skin of color*** than Caucasian patients

Challenges to AD Management

- Poor access to specialist care
- Lack of healthcare provider experience in diagnosing/treating skin of color
- Language barriers and cultural differences
- Financial issues for those living in poverty
- Variability in health literacy levels
- Environmental triggers can vary by home or neighborhood
  (eg, pollution, dust, mold, cockroaches, dust mites, and heat)

Fiscella K, Williams DR. *Acad Med.* 2004;79:1139-1147. Wan J, et al. *JAMA Dermatol.* 2019;155:973-975. American College of Allergy, Asthma & Immunology (ACAAI) and the Asthma & Allergy Network (AAN). Eczema in skin of color: Social and economic factors. (https://eczemainskinofcolor.org/social-and-economic-factors/). Accessed 11/27/21.

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Diagnosis and Presentation Considerations

Vivian Shi, MD, FAAD

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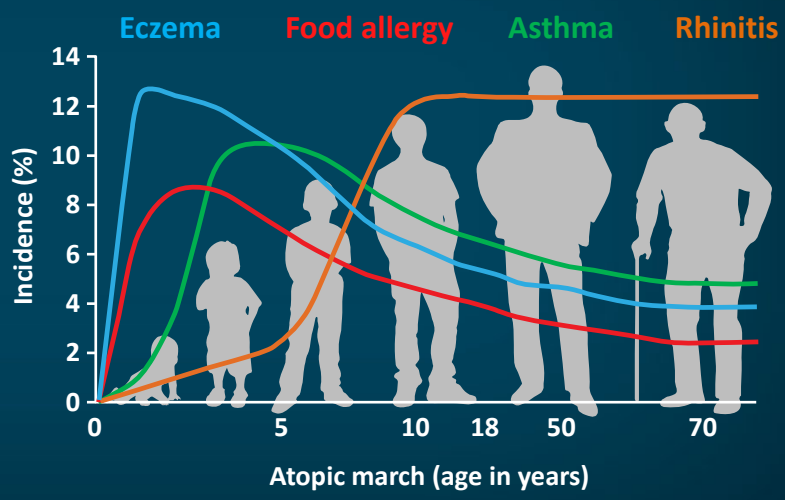
Features of Atopic Dermatitis (AD)

AD is a chronic, pruritic, inflammatory skin disease that is typified by:

- Childhood onset and familial occurrence
- Eczematous change
  - *Erythema, induration, papulation, excoriation, or lichenification*
- Characteristic distribution
- Intermittent flares
- Associated skin conditions *(minor diagnostic criteria)*
- Skin infections
- Associated comorbidities



Siegfried EC, Hebert AA. *J Clin Med.* 2015;4:884-917. Ring J, et al. *J Eur Acad Dermatol Venereol.* 2012;26:1045-1060. Czarnowicki T, et al. *J Allergy Clin Immunol.* 2017;139:1723-1734.

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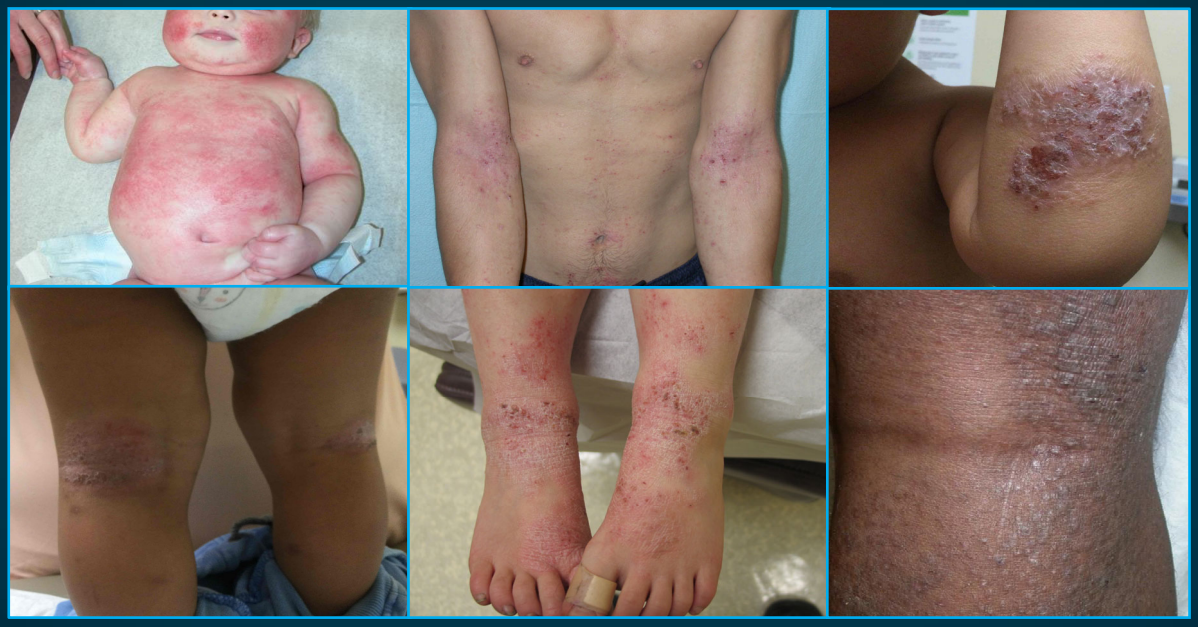
AD Is Heterogenous in Presentation



Photos provided by Dr. Eric L Simpson

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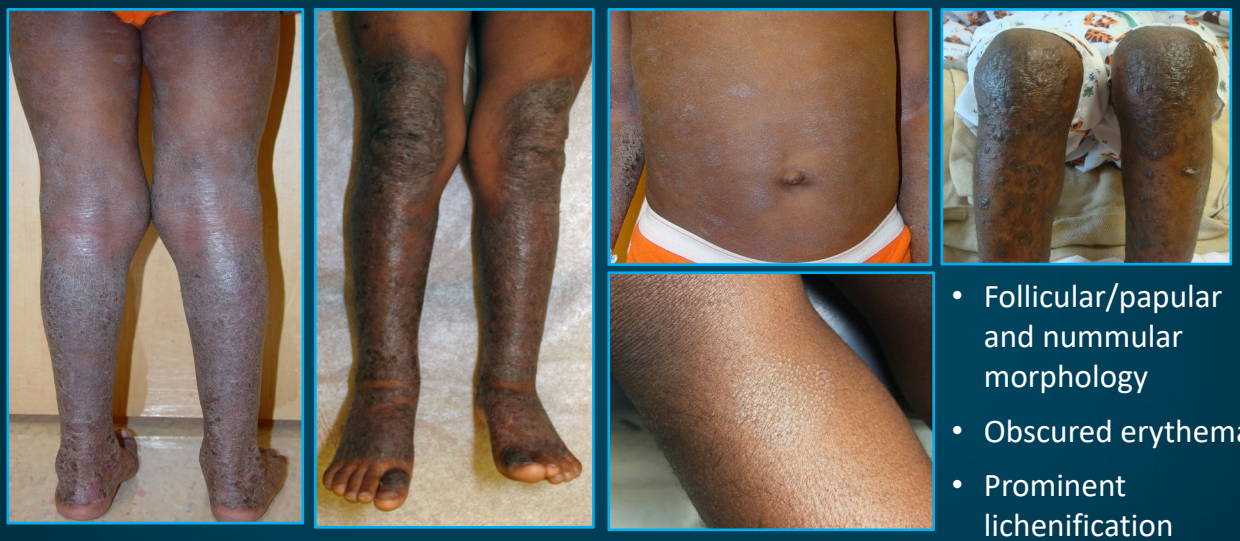
More Common Features in Skin of Color



- Follicular/papular and nummular morphology
- Obscured erythema
- Prominent lichenification
- Dyspigmentation

Boguniewicz M, et al. *J Allergy Clin Immunol Pract.* 2017;5:1519-1531. Poladian K, et al. *Cutis.* 2019;104:164-168. Siegfried EC, Hebert AA. *J Clin Med.* 2015;4:884-917. Kathuria P, Kundu RV. *Skin of Color Society.* 2022. https://skinofcolorsociety.org/patient-dermatology-education/eczema/. Accessed 1/21/22. Images courtesy of Dr. Peter Lio.

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Diagnostic Considerations in AD

Key Diagnostic Features of AD

Essential features of AD	Skin distribution patterns	Important features *(most cases)*
• **Intense pruritus** • Chronic disease with typical age-related skin distribution	• Facial, neck, & extensor involvement *(infants & children)* • Flexural lesions *(any age group)* • Sparing of the groin & axilla	• Early age of onset • Atopy *(history, immediate skin test reactivity, serum IgE)* • Xerosis

Suspect Another Diagnosis When…

Absence of key AD features	*Poor response* to topical anti-inflammatories	Other features are present
• **Lack of pruritus** • Atypical skin distribution	Make sure to evaluate for secondary infection in a non-responder	• Systemic infection • Failure to thrive • Absence of family history

Modified from Eichenfield LF, et al. *J Am Acad Dermatol.* 2014;70:338-351. Correale CE, et al. *Am Fam Physician.* 1999;60:1191-1198. Maliyar KB, et al. *Adv Skin Wound Care.* 2018;31:538-550.

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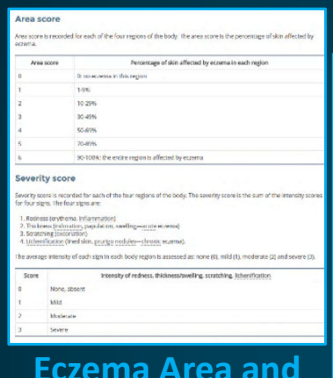
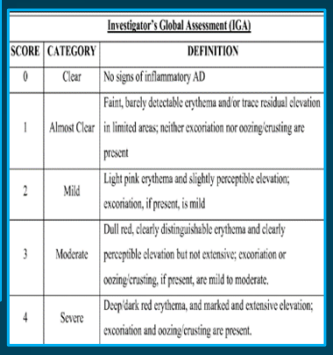
Clinical Assessment Tools



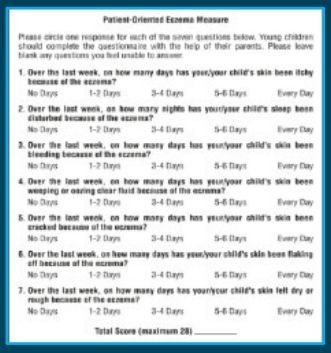
Eczema Area and Severity Index (EASI)[1]



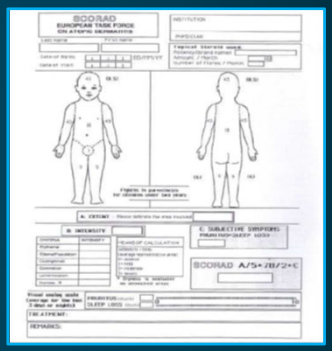
Investigator's Global Assessment (IGA)

SCORE	CATEGORY	DEFINITION
0	Clear	No signs of inflammatory AD
1	Almost Clear	Faint, barely detectable erythema and/or trace residual elevation in limited areas; neither excoriation nor oozing/crusting are present
2	Mild	Light pink erythema and slightly perceptible elevation; excoriation, if present, is mild
3	Moderate	Dull red, clearly distinguishable erythema and clearly perceptible elevation but not extensive; excoriation or oozing/crusting, if present, are mild to moderate.
4	Severe	Deep/dark red erythema, and marked and extensive elevation; excoriation and oozing/crusting are present.

Investigator Global Assessment (IGA)[2]



Patient-Oriented Eczema Measure (POEM)[3]



SCORing Atopic Dermatitis (SCORAD)[4]

1. Hanifin JM, et al. *Exp Dermatol.* 2001;10:11-18. 2. Futamura M, et al. *J Am Acad Dermatol.* 2016;74:288-294. 3. Charman CR, et al. *Arch Dermatol.* 2004;140:1513-1519. 4. European Task Force on AD. *Dermatology.* 1993;186:23-31.

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AD Severity Assessment: IGA vs POEM Scoring

Validated IGA Scale for AD (vIGA-AD)

- Scored *using descriptors* that best describe overall appearance of lesion
- All characteristics under morphological description ***do not*** need to be present

Score	Morphological description
0 **Clear**	No inflammatory signs of AD ± Post-inflammatory hyper- or hypopigmentation
1 **Almost clear**	***Barely perceptible*** erythema or induration/papulation and/or minimal lichenification *No oozing or crusting*
2 **Mild**	***Slight but definite*** erythema (pink), induration/ papulation, and/or lichenification *No oozing or crusting*
3 **Moderate**	***Clearly perceptible*** erythema (dull red), induration/ papulation, and/or lichenification ± *Oozing and crusting*
4 **Severe**	**Widespread disease.** ***Marked*** erythema (deep or bright red), induration/papulation, and/or lichenification ± *Oozing or crusting*

Patient-Oriented Eczema Measure (POEM)

Subjective scoring based on symptoms

1. Over the last week, on how many days has your/your child's skin been itchy because of the 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/your child's sleep been disturbed because of the 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/your child's skin been bleeding because of the 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/your child's skin been weeping or oozing clear fluid because of the 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/your child's skin been cracked because of the 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/your child's skin been flaking off because of the 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/your child's skin felt dry or rough because of the eczema?

No days | 1–2 days | 3–4 days | 5–6 days | Every day

Modified from Simpson E, et al. *J Am Acad Dermatol*. 2020;83:839-846. Charman CR, et al. *Br J Dermatol*. 2013;169:1326-1332.

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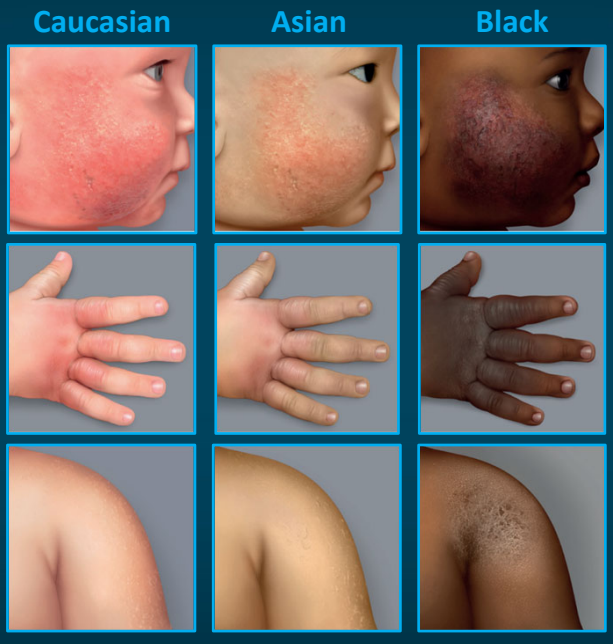
Disease Severity Assessment in Differing Skin Tones



Eczema Foundation. PO-SCORAD (www.fondation-dermatite-atopique.org/en/healthcare-professionals-space/po-scored). Accessed 11/27/2021. PO-SCORAD. (https://www.poscorad.com/#/poscorad/uk). Accessed 12/1/21.

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A brief animation discussing current and emerging approaches to AD management

English

Spanish

21

Algorithm for "Step-Up Care"

	MILD	MODERATE *Continue basic maintenance*	SEVERE *Continue basic maintenance*
Maintenance	***Basic maintenance:*** **Skin care** Short, daily warm bath/shower Moisturizer use (liberal/frequent) **Trigger avoidance** Common irritants, allergens (if proven) **Consider comorbidities**	**Maintenance TCS** • Medium potency, 2–3x/wk ("proactive") to recurrent areas • Low potency several times weekly to sensitive areas **Maintenance TCI or crisaborole** • TCI—2–3x/wk to BID ("proactive") • Crisaborole 2%—several times weekly **Consider adding bleach baths** 2–7x/wk – based on severity & crusting tendency at excoriation sites	**Phototherapy** **Dupilumab, Tralokinumab; JAKi's for refractory disease** **Systemic immunosuppressants** • Cyclosporine A* • Methotrexate* • Mycophenolate mofetil* • Azathioprine* • Corticosteroids **Consider acute care to gain control** • Wet wraps • Short-term hospitalization **Referral to AD specialist**
Flare	**TCS** *(low-to-medium potency)* • BID x 2 wks → QD x 1 wk → few days beyond clearance • Consider crisaborole 2% or TCI	**TCS** *(medium-high-potency)* • BID x 2 wks → QD x 1 wk → 2x/wk to "hot spots" • Low potency (sensitive areas) *or* consider crisaborole 2%	**TCS** *(medium-to-high potency)* • BID x 3–7 days beyond clearance • Low potency (sensitive areas) ***or*** consider crisaborole 2% • Unresolved >7 days

Next steps: Nonadherence; Infection; Misdiagnosis; Contact allergy to medications; Referral

BID = twice daily; TCS = topical corticosteroid; TCI = topical calcineurin inhibitor; FDA = US Food and Drug Administration.

Modified by LF Eichenfield from Boguniewicz M, et al. *Ann Allergy Asthma Immunol*. 2018;120:10-22.e2.

**Indicates not FDA-approved for AD treatment.*

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Flares: Maintenance and Management

Preventing *or* **increasing time intervals** between flares is a *critical goal of management*[1]

Act *quickly* and ***aggressively*** when treating flares[1]

Types of approaches *(with continued basic management)*[1–4]	
Reactive	**Proactive**
TCI or TCS applied *at first signs/symptoms* of flare	**TCS 2–3 times/week *or* TCI 2–3 times/week**

Antiseptic/antibiotic therapy

- ***Topical***: dilute bleach bath (minimally twice-weekly; severe flares may require daily baths)[5]
- ***Systemic***: ***S aureus* most common pathogen**; MSSA >> MRSA[6-8]
  - Oral cephalosporin; amoxicillin/clavulanate

MRSA = methicillin-resistant *Staphylococcus aureus;* MSSA = methicillin-sensitive *Staphylococcus aureus*.

1. Wollenberg A, et al. *J Eur Acad Dermatol Venereol.* 2016;30:729-747. 2. Sidbury R, et al. *J Am Acad Dermatol.* 2014;71:1218-1233. 3. Eichenfield LF, et al. *Pediatrics.* 2015;136:554-565. 4. Schmitt J, et al. *Br J Dermatol.* 2011;164:415-428. 5. Maliyar KB, et al. *Adv Skin Wound Care.* 2018;31:538-550. 6. Suh L, et al. *Pediatr Dermatol.* 2008;25:528-534. 7. Kim J, et al. *Allergy Asthma Immunol Res.* 2019;11:593-603. 8. Nieburhr M, et al. *Exp Dermatol.* 2008;17:953-957.

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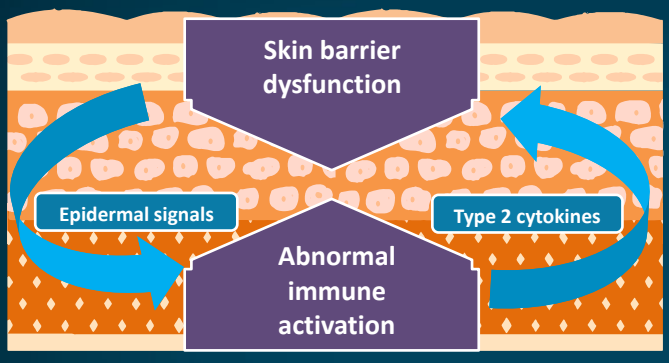
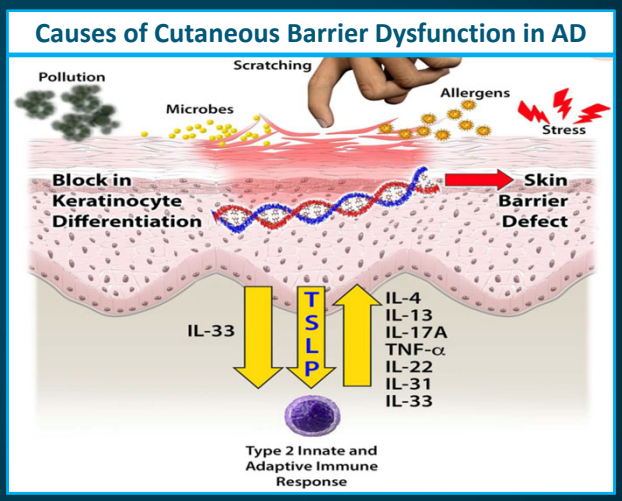
AD Pathogenesis



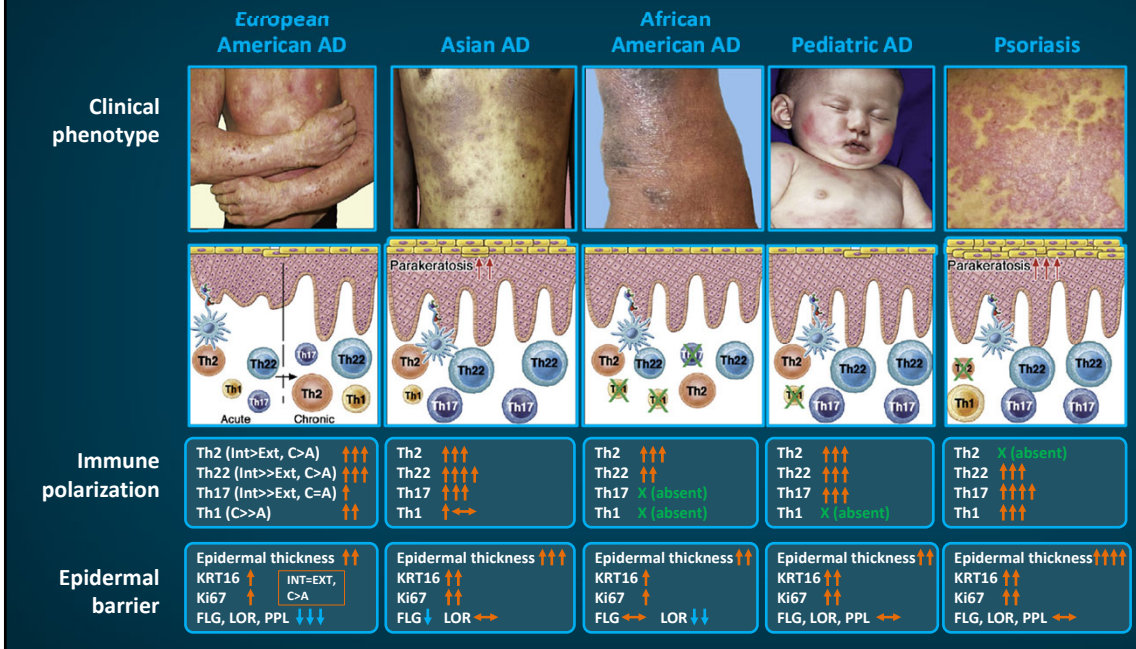


IL = interleukin; TSLP = thymic stromal lymphopoietin; TNF = tumor necrosis factor.

Bin L, Leung DY. *Allergy Asthma Clin Immunol.* 2016;12:52. Adapted from Boguniewicz M, Leung DYM. *Immunol Rev.* 2011;242:233-246. Leung DYM, et al. *J Allergy Clin Immunol.* 2020;145:1485-1497.

24

Phenotypic and Endotypic Variations Across AD Skin Types



Th = T helper (cell); Int = intrinsic; Ext = extrinsic; A = acute; C = chronic; KRT16 = keratin 16; FLG = filaggrin; LOR = loricrin; PPL = periplakin.

Czarnowicki T, et al. *J Allergy Clin Immunol*. 2019;143:1-11.

25

Case Study 1

- **CC:** *3-year-old with a history of atopic dermatitis with recurrent skin infections*
  - She is constantly scratching and has had several infected areas requiring oral antibiotics
  - She has been on oral prednisolone several times, which helps for a bit, but symptoms come back with a vengeance
- **HPI**
  - Eczema patches developed on her cheeks in first few months of life; by age 2 she had widespread disease (including arms, legs, abdomen, and hands)
  - Multiple staph infections in the last few years, each requiring oral antibiotics
  - Seasonal flares of eczema (especially winter), some requiring oral prednisolone
  - She has difficulty staying asleep due to scratching
  - Behavioral problems at daycare are noted as well

CC = chief complaint; HPI = history of present illness.

Image courtesy of Dr. Peter Lio.

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Case Study 1: Current Therapy

- Mometasone ointment BID to affected areas
- Wet-wrap therapy with mometasone at night (most nights of the week)
- Dilute bleach baths 3x per week
- Hydroxyzine 1–2 teaspoons po qhs
- Cetirizine po qAM
- Various moisturizers
- No current antibiotics

po = per os (by mouth); qhs = at bedtime; qAM = every morning.

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Case Study 1: Question 1

What severity of atopic dermatitis does this patient exhibit?

A. Mild AD
B. Moderate AD
C. Severe AD
D. This is not atopic dermatitis

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Case Study 1: Question 2

What testing would you consider in assessing management strategies for her condition?

A. Contact allergy testing
B. Food allergy testing
C. Lesion culture
D. All of the above
E. None of the above

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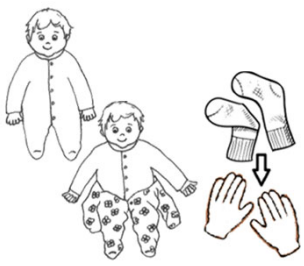
Wet Wraps

1. **Take one pair of onesies, pajamas, gloves, and/or socks and soak it in warm water.**

2. **Wring out the onesies, pajamas, gloves, or socks until they are only slightly damp.**

3. **Put damp onesies, pajamas, gloves, or socks on child. Then put dry onesies, pajamas, gloves, or socks on top of damp layer.**



4. **Make sure the room is warm enough before you go to sleep.**

How to apply wet wraps (http://chicagoeczema.com/resource/wet-wrap-therapy/). Accessed 11/27/2021.

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Interval Q&A

Peter Lio, MD and Vivian Shi, MD, FAAD

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Topical Therapies

Peter Lio, MD

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Newer Topical Therapies

Crisaborole

Approved for mild-to-moderate AD

- Adults
- Pediatric patients aged ≥3 months

Ruxolitinib

Approved for *topical short-term* and *non-continuous chronic treatment* of mild-to-moderate AD

- In non-immunocompromised patients
- ≥12 years of age whose disease is not adequately controlled with topical prescription therapies

Black box warning (JAKi class)
Serious infections, mortality, malignancies, MACE, and thrombosis
Application no greater than 20% BSA
60 grams/week dosage limit

JAKi = janus kinase inhibitor; MACE = major adverse cardiovascular events; BSA = body surface area.

Crisaborole (Eucrisa®) prescribing information (PI) 2020 (http://labeling.pfizer.com/ShowLabeling.aspx?id=5331). Ruxolitinib (Opzelura™) PI 2021 (www.opzelura.com/prescribing-information.pdf). URLs accessed 1/16/2022.

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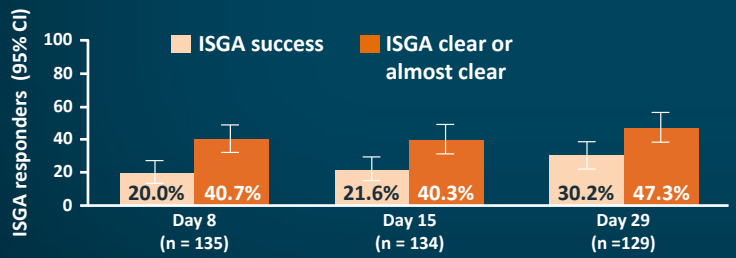
CrisADe CARE 1 Study: Crisaborole

- Phase 4, open-label study of crisaborole in 137 infants aged 3 to <24 months with mild-to-moderate AD
- Clear or almost clear skin with ≥2-grade improvement on ISGA achieved by 30.2% of patients at day 29



TEAEs reported for ≥2.5% of patients		
Overall TEAEs, n (%)	All-Cause	Treatment-Related
Pyrexia	13 (9.5)	0
URTI	10 (7.3)	1 (0.7)
Diarrhea	10 (7.3)	0
Atopic dermatitis	9 (6.6)	0
Dermatitis, diaper	9 (6.6)	0
Cough	7 (5.1)	0
Otis media	6 (4.4)	1 (0.7)
Eczema	5 (3.6)	2 (1.5)
Application-site pain	5 (3.6)	5 (3.6)
Conjunctivitis	5 (3.6)	0
Rhinorrhea	5 (3.6)	0
Contact dermatitis	4 (2.9)	1 (0.7)
Erythema	4 (2.9)	4 (2.9)
Rash	4 (2.9)	0
Application-site discomfort	4 (2.9)	4 (2.9)
Application-site erythema	4 (2.9)	3 (2.2)
Ear infection	4 (2.9)	0
Nasopharyngitis	4 (2.9)	0
Teething	4 (2.9)	0

ISGA = Investigator's Static Global Assessment; CI = confidence interval; TEAE = treatment-emergent adverse event; URTI = upper respiratory tract infection.

Schlessinger J, et al. *Am J Clin Dermatol*. 2020;21:275-284.

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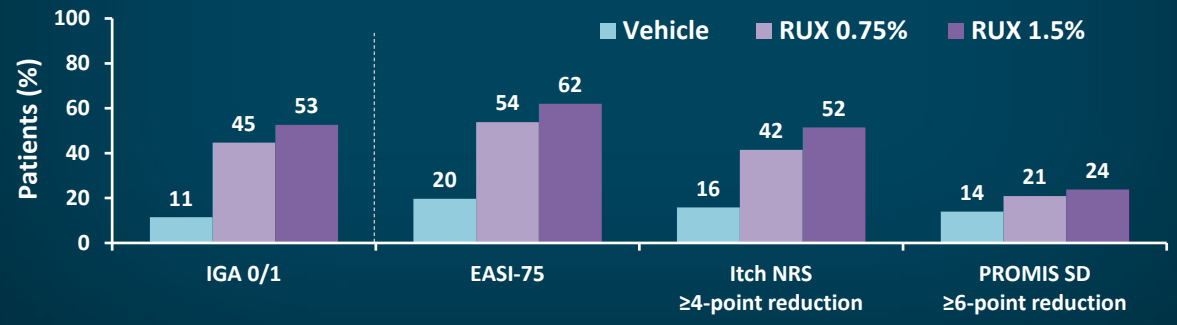
Topical JAK Inhibitor: Ruxolitinib

- Well tolerated with minimal application-site reactions in 2 phase 3 studies
- No treatment-related AEs (and all TEAEs mild-to-moderate)
- Itch reduction within 1st day of use

Efficacy outcomes at week 8



AE = adverse event; RUX = ruxolitinib; JAK = Janus kinase; NRS = numerical rating scale; PROMIS SD = Patient-Reported Outcomes Measurement Information System Sleep Disturbance.

Papp K, et al. *J Am Acad Dermatol*. 2021;85:863-872. Ruxolitinib (Opzelura™) PI 2021 (www.opzelura.com/prescribing-information.pdf). Accessed 1/16/2022.

35

When to Use Systemic Therapy

International Eczema Council Expert Panel Recommendations

Use systemic therapy…

IF

aggressive topical therapy is not achieving adequate control of the disease

AND

WHEN

- Adequate education delivered
- Infection addressed
- Large impact on QoL
- Diagnosis ***reconsidered***, eg, cutaneous T-cell lymphoma or allergic contact dermatitis
- Phototherapy considered

Simpson EL, et al. *J Am Acad Dermatol*. 2017;77:623-633.

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Systemic Therapies

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Systemic Treatment Options

- **Dupilumab** *(blocking IL-4 & IL-13),* **Tralokinumab** *(blocking IL-13)*
- **Abrocitinib, Upadacitinib**
- **Phototherapy**
- **Cyclosporine***
- **Methotrexate***
- **Mycophenolate mofetil***
- **Azathioprine***

Dupilumab is the *only FDA-approved biologic therapy* for AD in patients aged ≥6 years

FDA = US Food and Drug Administration.

**Not FDA-approved for the treatment of AD.*

Sidbury R, et al. *J Am Acad Dermatol.* 2014;71:327-349. Boguniewicz M, et al. *Ann Allergy Asthma Immunol.* 2018;120:10-22.e2. Dupilumab (Dupixent®) PI 2021 (www.regeneron.com/downloads/dupixent_fpi.pdf). Tralikinumab (Adbry™) PI 2021 (www.leo-pharma.us/Files/Billeder/US%20Website%20Product%20PIs/AdbryPI.pdf). *Dermatology Times.* FDA approves Ttalokinumab-ldrm for AD (www.dermatologytimes.com/view/fda-approves-tralokinumab-idrm-for-ad). URLs accessed 1/16/2022.. Reuters. US FDA approves drugs from AbbVie, Pfizer to treat eczema. https://www.reuters.com/business/healthcare-pharmaceuticals/fda-approves-expanded-use-abbvies-arthritis-drug-treat-eczema-2022-01-14/. Accessed 1/18/21.

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Discontinuation Rate of Immunosuppressives

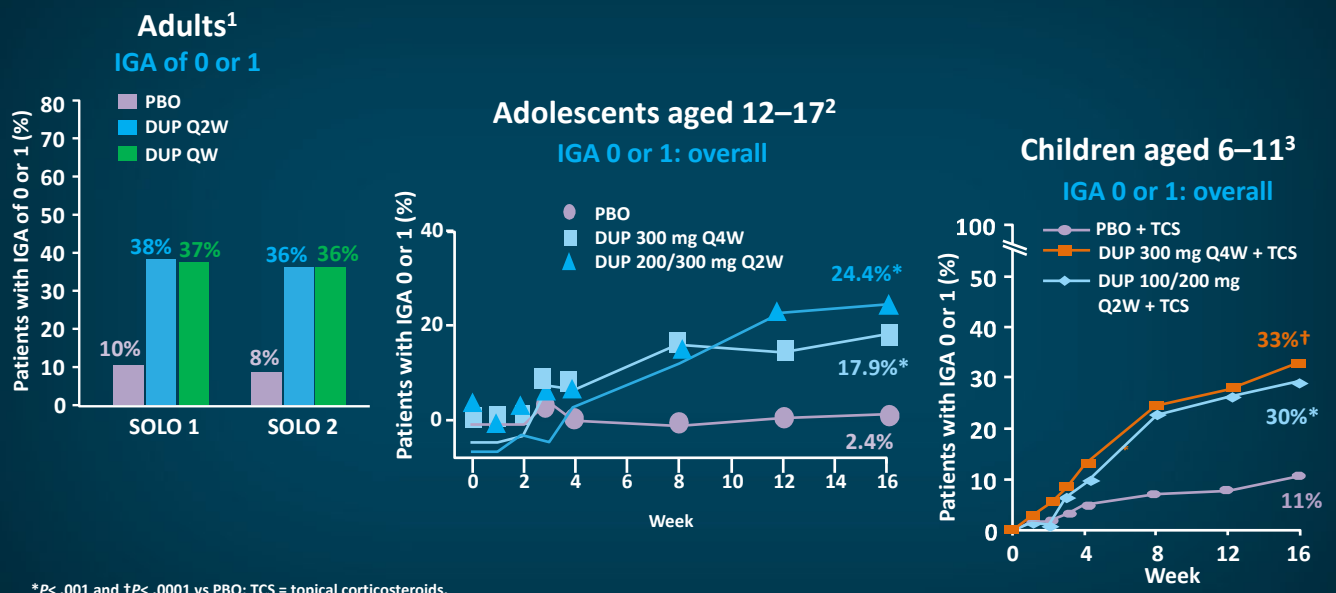
	CsA (N = 356) (at 6-year follow-up)[1]	AZA (N = 94) (at 3-year follow-up)[2]	MTX (N = 89) (at 2-year follow-up)[3]	EC-MPS (N = 84) (at 3-year follow-up)[2]
Adverse event	22%	36%	25%	14%
Inefficacy	16%	19%	15%	38%
Controlled AD	26%	11%	6%	11%
Other reasons	11%	6%	7%	4%

CsA = cyclosporine A; AZA = azathioprine; MTX = methotrexate; EC-MPS = enteric-coated mycophenolate sodium.

1. van der Schaft J, et al. *Br J Dermatol*. 2015;172:1621-1627. 2. van der Schaft J, et al. *Br J Dermatol*. 2016;175:199-202. 3. Politiek K, et al. *Br J Dermatol*. 2016;174:201-203.

39

Dupilumab: IGA Improvements in 3 Age Cohorts



*P< .001 and †P< .0001 vs PBO; TCS = topical corticosteroids.

PBO = placebo; DUP = dupilumab; Q2W = every 2 weeks; QW = every week.

1. Simpson EL, et al. *N Engl J Med*. 2016;375:2335-2348. 2. Simpson EL, et al. *JAMA Dermatol*. 2020;156:44-56. 3. Paller AS, et al. *J Am Acad Dermatol*. 2020;83:1282-1293.

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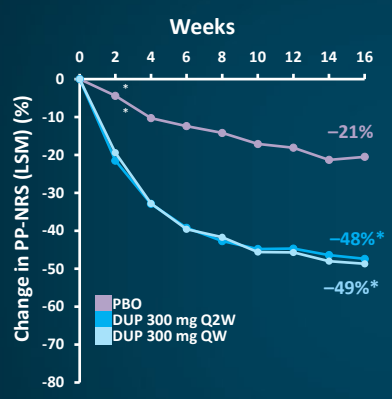
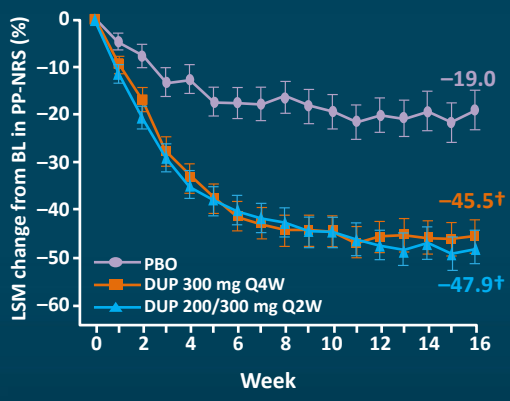
Dupilumab: Impact on Pruritus

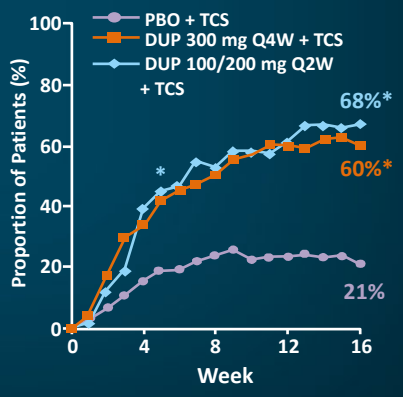
Adults
SOLO 1 and 2



Adolescents aged 12–18
Change in PP-NRS score



Children aged 6–11
Patients with ≥3-point improvement in PP-NRS: overall population



*P< .0001 vs PBO or PBO + TCS; †P< .001 vs PBO.

LSM = least squares mean; PP-NRS = Peak Pruritus Numerical Rating Scale; BL = baseline.

Simpson EL, et al. *N Engl J Med*. 2016;375:2335-2348. Simpson EL, et al. *JAMA Dermatol*. 2020;156:44-56 and supplement. Paller AS, et al. *J Am Acad Dermatol*. 2020;83:1282-1293.

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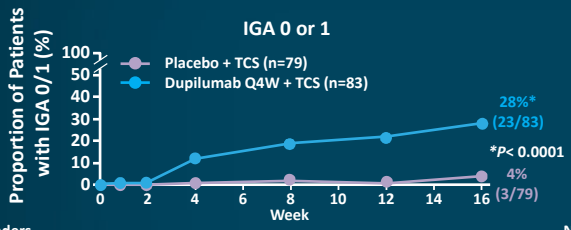
LIBERTY AD PRESCHOOL: Dupilumab + TCS

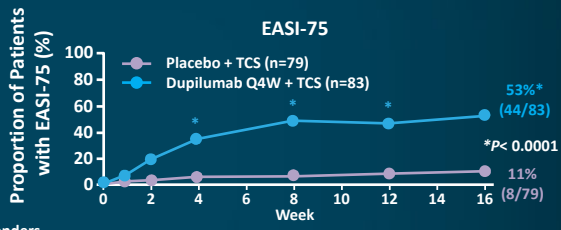
Phase 3, double-blind, placebo-controlled study over 16 weeks
≥6 months to < 6 years with moderate-to-severe AD

Primary endpoint: clear or almost-clear skin



No. of responders							
Placebo + TCS	0	0	0	1	1	1	1
Dupilumab Q4W + TCS	0	1	1	10	16	18	23

Co-primary endpoint: Improvement in overall disease severity



No. of responders							
Placebo + TCS	0	2	2	5	5	7	8
Dupilumab Q4W + TCS	0	6	16	29	41	39	44

- 49% average improvement from baseline itch (vs ~2% placebo, P< .0001)

Dupilumab Q4W + low-potency TCS showed *rapid, significant improvement in signs and symptoms of AD*; safety data was consistent with known profiles in adults and older children.

PBO = placebo; Q4W = every 4 weeks; BL = baseline.

Paller AS, et al. *RAD*. 2021: abstract 690.

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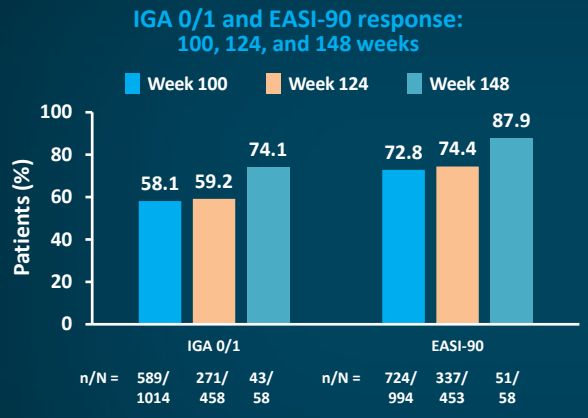
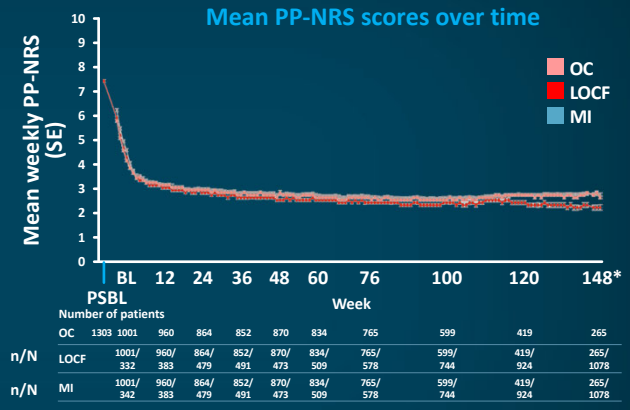
Liberty AD OLE: Dupilumab Long-Term Sustained Clinical Efficacy in Adults Up to 3 Years





Dupilumab 300 mg QW (approved dose Q2W) evaluation in Liberty AD OLE study showed *long-term, sustained efficacy in signs, symptoms, and QoL* for up to 3 years

LOCF = last observation carried forward; MI = multiple imputation; OC = observed cohort; OLE = open-label extension study; PSBL = parent study BL; n/N = number of patients/imputed patients.

Beck LA, et al. *Am J Clin Dermatol*. 2020;21:567-577.

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Liberty AD OLE: Dupilumab
Long-Term Sustained Safety Up to 3 Years

Adverse events	CHRONOS (52 week)				Current study (OLE)	
	Placebo + TCS (n = 315)		300 mg QW + TCS (n = 315)		300 mg QW (n = 2677)	
	Events	nP/100 PY	Events	nP/100 PY	Events	nP/100 PY
TEAEs	1520	325.1	1500	322.43	13,826	173.7
Serious TEAEs	24	5.75	11	3.40	354	5.28
Severe TEAEs	46	10.31	24	5.88	355	5.08
TEAEs leading to discontinuation	29	9.14	10	3.06	116	1.87
Serious TEAEs related to treatment	3	1.06	2	0.68	36	0.61
Death	0	0	1	0.34	2	0.04
Most common TEAEs						
Nasopharyngitis	90	24.93	86	24.16	1543	19.16
Atopic dermatitis	243	74.32	91	20.71	736	9.61
Upper respiratory tract infection	48	12.03	65	15.85	532	7.56
Headache	31	6.98	48	8.97	408	4.54
Conjunctivitis	**29**	**9.24**	**91**	**23.37**	**826**	**11.96**
Injection-site reactions	105	9.39	232	25.46	855	5.58
Herpes viral infections	32	9.17	43	7.72	715	7.21
Skin infections	**NA**	**20.21**	**NA**	**7.87**	**291**	**4.81**
Eczema herpeticum	6	2.13	0	0	14	0.24

nP/100 PY = number of patients per 100 patient-years; TEAE = treatment-emergent adverse event; NA = not available.

Beck LA, et al. *Am J Clin Dermatol*. 2020;21:567-577.

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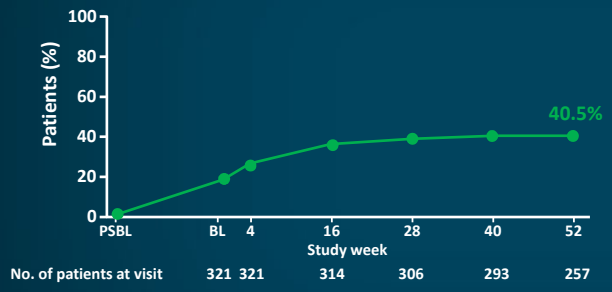
LIBERTY AD PED-OLE: Long-Term Sustained Efficacy with Dupilumab

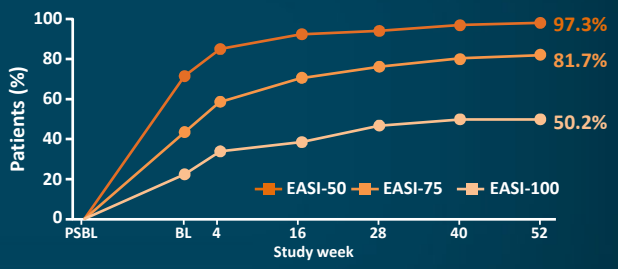
Patients aged ≥6 to <12 years with moderate-to-severe AD over 52-weeks
300 mg Dupi Q4W (with option to up-titrate to Q2W regimen in inadequate response)

Patients achieving IGA score 0/1



No. of patients at visit	321	321	314	306	293	257

Patients achieving EASI-50/75/100 relative to PSBL



No. of patients at visit	321	321	314	306	290	257

Long-term treatment with dupilumab showed *substantial, sustained improvement in signs and symptoms of AD* with improvement in health-related quality of life; safety data were consistent with known profiles

Dupi = dupilumab; EASI-50/75/90 = 50%/755/100% improvement from baseline in EASI.

Paller AS, et al. RAD. 2021: abstract 663.

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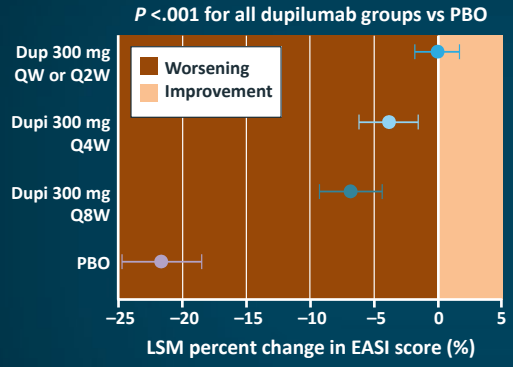
Effect on AD with Dose Reductions of Dupilumab

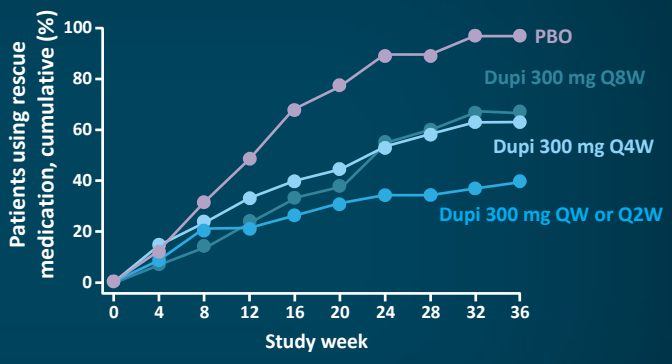
LIBERTY AD SOLO-CONTINUE Study

EASI

P <.001 for all dupilumab groups vs PBO



Rescue medication use



Continued response over time was most consistently maintained with dupilumab dosing weekly or biweekly; longer intervals between administration resulted in diminished response (vs placebo)

Q8W = every 8 weeks; LSM = least squares mean.

Worm M, et al. *JAMA Dermatol.* 2020;156:131-143.

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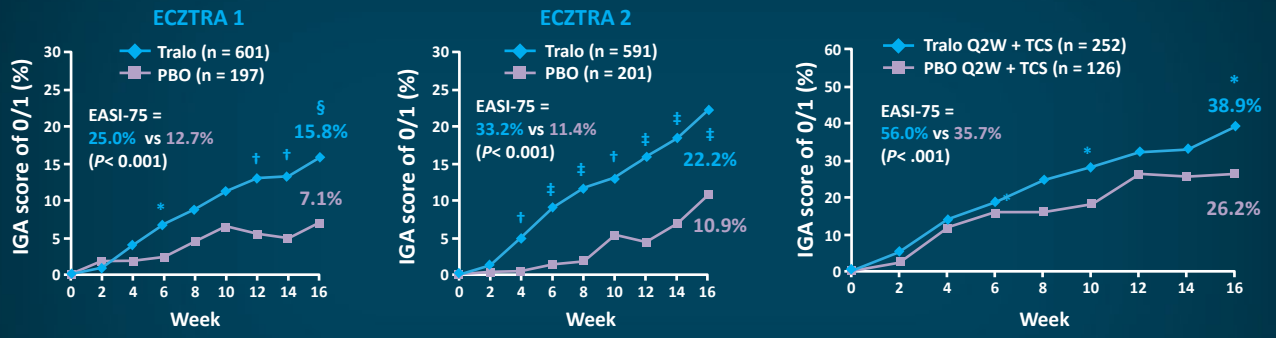
ECZTRA: Tralokinumab Efficacy (Phase 3 Trials)

ECZTRA 1 and 2 (≥18 years of age)
Randomized 3:1 to SC tralokinumab 300 mg Q2W (after 600 mg loading dose at day 0) or PBO

ECZTRA 3 (≥18 years of age)
Tralokinumab 300 mg Q2W + TCS (prn) vs PBO + TCS (prn)



- **ECZTRA 1 and 2 (rerandomization after 16 weeks):** IGA 0/1 *was* ***maintained*** without rescue medication at 52 weeks in 51% (ECZTRA 1) and 59% (ECZTRA 2) with ***continued*** *tralo* Q2W vs transition from Q2W tralo to PBO (47% [*P*= 0.68] and 25% [*P*= .004])
- **ECZTRA 3 (initial responders at 32 weeks):** IGA 0/1 ***was maintained*** without rescue medication in 89.6% of Q2W +TCS and 92.5% achieved EASI 75; Q4W dosing demonstrated slightly lower rates of efficacy (77.6% IGA 0/1 and 90.8% EASI 75)

*P <.05; †P <.01; ‡P <.001; §P= .002 vs PBO.

Tralo = tralokinumab; SC = subcutaneous; prn = as needed.

Wollenberg A, et al. *Br J Dermatol.* 2021;184:437-449. Silverberg JI, et al. *Br J Dermatol.* 2021;184:450-463.

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ECZTRA: Safety Signals

AEs	ECZTRA1		ECZTRA2	
	PBO, n = 196 PYE = 57.13	Tralo Q2W, n = 602 PYE = 177.6	PBO, n = 200 PYE = 57.35	Tralo Q2W, n = 592 PYE = 176.9
Total number of AEs, n	491	1482	408	997
Total number of SAEs, n	11	24	6	10
Patients with AEs, n (%)				
≥1 AE	151 (77.0)	460 (76.4)	132 (66.0)	364 (61.5)
≥1 SAE	8 (4.1)	23 (3.8)	5 (2.5)	10 (1.7)
Leading to permanent discontinuation of IMP	8 (4.1)	20 (3.3)	3 (1.5)	9 (1.5)
Frequent AEs, n (%)				
Atopic dermatitis	75 (38.3)	156 (25.9)	67 (33.5)	98 (16.6)
Viral URTI	41 (20.9)	139 (23.1)	17 (8.5)	49 (8.3)
URTI	2 (1.0)	9 (1.5)	17 (8.5)	59 (10.0)
Conjunctivitis	4 (2.0)	43 (7.1)	3 (1.5)	18 (3.0)
Skin infection	3 (1.5)	6 (1.0)	11 (5.5)	12 (2.0)
Pruritus	10 (5.1)	32 (5.3)	5 (2.5)	12 (2.0)
Headache	10 (5.1)	28 (4.7)	6 (3.0)	16 (2.7)
AEs of special interest, n (%)				
Eye disorders	7 (3.6)	62 (10.3)	6 (3.0)	33 (5.6)
Conjunctivitis	7 (3.6)	60 (10.0)	5 (2.5)	31 (5.2)
Keratoconjunctivitis	0	1 (0.2)	0	2 (0.3)
Keratitis	0	3 (0.5)	1 (0.5)	1 (0.2)
Skin infections requiring systemic treatment, n (%)	4 (2.0)	13 (2.2)	22 (11.0)	21 (3.5)
Eczema herpeticum, n (%)	2 (1.0)	3 (0.5)	5 (2.5)	2 (0.3)
Malignancies diagnosed after randomization, n (%)	0	0	0	1 (0.2)

With exception of conjunctivitis, overall incidence of AEs was similar across treatment groups, with event rates comparable to placebo across ECZTRA 1, 2, and 3 trials, and was well tolerated up to 52 weeks of treatment

SAE = serious AE; IMP = investigational medicinal product; PYE = patient-years of exposure.

Wollenberg A, et al. *Br J Dermatol.* 2021;184:437-449. Silverberg JI, et al. *Br J Dermatol.* 2020;184:450-463.

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JAK Inhibitors

	Abrocitinib			Upadacitinib		
Approval	January 2022			January 2022		
Pivotal studies	JADE MONO-1 and -2, JADE COMPARE			Measure Up 1 and 2 (no TCS), AD Up (+TCS)		
Significant findings	vIGA-AD 0/1 and EASI 75 greatest with 200 mg dosing vs PBO; met primary endpoints			vIGA-AD 0/1 and EASI (75/90/100) greatest with 30 mg dosing vs PBO; met primary endpoints (± TCS)		
	At week 12 (200 mg)	**vIGA-AD 0/1**	**EASI-75**	**At week 16 (30 mg)**	**vIGA-AD 0/1**	**EASI-75**
	MONO-1	44% vs 8%	62% vs 12%	Measure Up 1	62% vs 8%	80% vs 16%
	MONO-2	38% vs 9%	61% vs 10%	Measure Up 2	52% vs 5%	73% vs 13%
	COMPARE	47% vs 14%	68% vs 27%	AD Up	59% vs 11%	77% vs 26%
Age	Adults			≥12 years of age		
Indication	*Refractory*, moderate-to-severe atopic dermatitis whose disease is *not adequately controlled with other systemic drug products*, including biologics, or when use of those therapies is inadvisable					
Safety	**Black box warning—*MACE, malignancy, infection, thrombosis***					
Use considerations	Not recommended for use in combination with other JAK inhibitors, biologic immunomodulators, or with other immunosuppressants					

Pfizer press release (www.pfizer.com/news/press-release/press-release-detail/us-fda-approves-pfizers-cibinqor-abrocitinib-adults). Abrocitinib PI. 2021 (https://cdn.pfizer.com/pfizercom/USPI_Med_Guide_CIBINQO_Abrocitinib_tablet.pdf). AbbVie press release (news.abbvie.com/news/press-releases/us-fda-approves-rinvoq-upadacitinib-to-treat-adults-and-children-12-years-and-older-with-refractory-moderate-to-severe-atopic-dermatitis.htm?view_id=6943). Upadcitinib PI. 2022 (www.rxabbvie.com/pdf/rinvoq_pi.pdf). URLs accessed 1/18/22.

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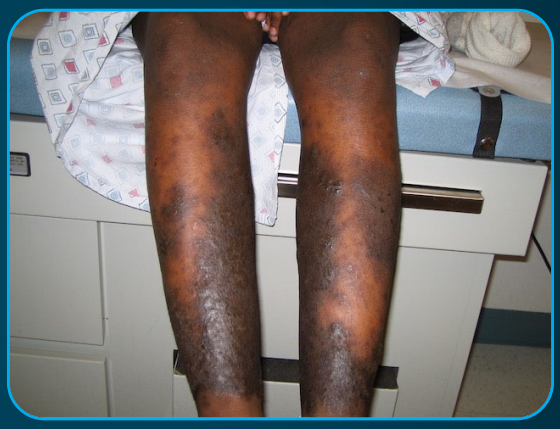
Case Study 2

- **CC:** *15-year-old with very itchy, dry skin affecting extensor surfaces of arms and legs*
  - His father notes that he constantly scratches and is often up in the middle of the night with itching
  - He is exhausted mentally and physically, and is angry that he keeps receiving prescriptions for triamcinolone…



- **HPI**
  - He first developed eczema patches as a baby
  - Although he has had some good periods, lichenified plaques have been constant for the past few years
  - Beyond sleep issues, he is having lots of problems at school

Image courtesy of Dr. Peter Lio.

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Case Study 2: Current Therapy

- Triamcinolone 2–3x per day to the affected areas for many months
- Tacrolimus does not seem to work
- Pimecrolimus does not seem to work
- Crisaborole does not seem to help much but did sting and burn
- He takes 50 mg of hydroxyzine morning and night and has done so for the past 6 months

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Case Study 2: Question 1

Based on this patients' symptoms and treatment history, do you suspect uncontrolled atopic dermatitis?

A) Yes, he has significant itching with widespread lesions
B) No, because he responded poorly to topical agents
C) No, I suspect another disease due to chronicity of symptoms

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Case Study 2: Question 2

- After skin scraping and culture, you confirm no infectious etiology
- The chronicity, intense pruritus, and skin distribution pattern are all hallmark features of AD; his quality-of-life appears significantly impacted
- What course of treatment would you recommend?

A) Crisaborole + cyclosporine

B) Mycophenolate mofetil

C) Low-potency TCS + methotrexate

D) Dupilumab + medium-to-high potency TCS

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Emerging Therapies

Vivian Shi, MD, FAAD

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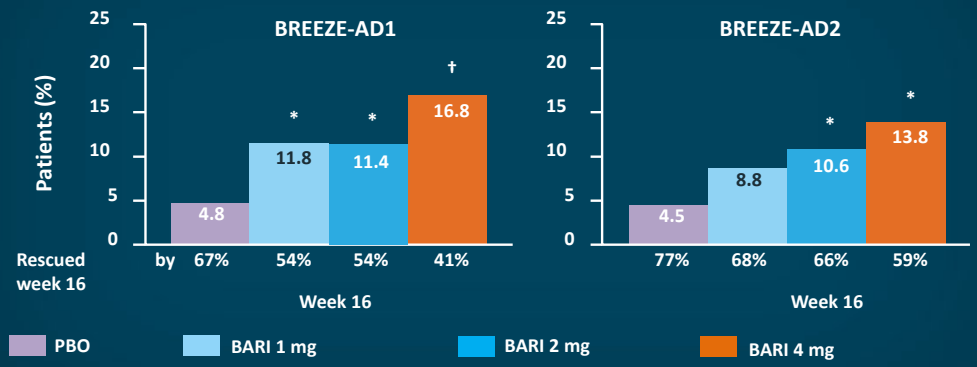
Additional JAK Inhibitors in AD

Proportion of clear/almost clear at week 16 (monotherapy)

Baricitinib (BARI)



*P <.05; †P <.001vs PBO.

Simpson EL, et al. *Br J Dermatol*. 2020;183:242-255 and supplement.

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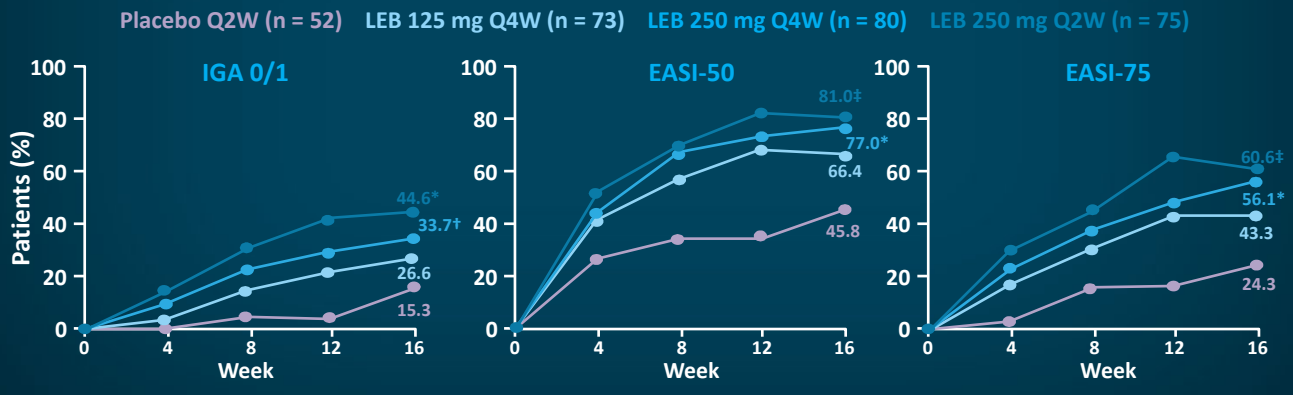
Emerging Agent: Lebrikizumab (anti-IL-13)

- Phase 2b, randomized, monotherapy trial in 280 adults with moderate-to-severe AD, inadequately controlled with TCS
- At week 16, significantly more patients achieved EASI-50/75/90 with lebrikizumab (LEB) 250 mg Q2W or Q4W than with placebo



*P< .01; †P< .05; ‡P< .001, all vs placebo.

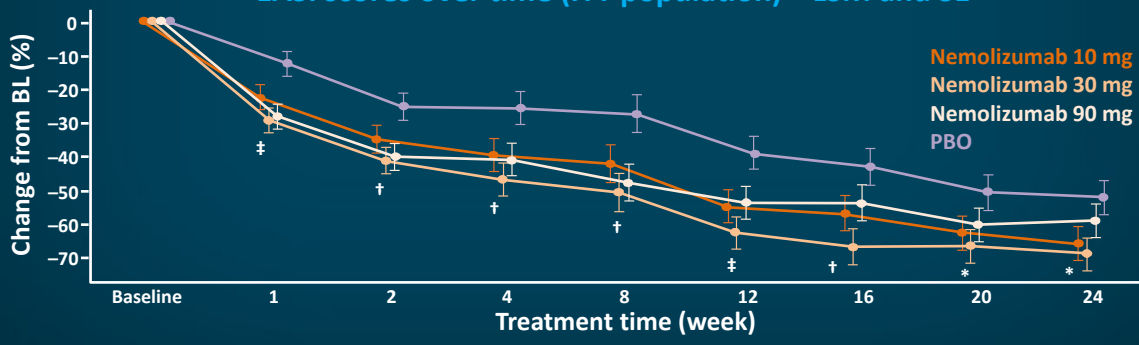
Guttman-Yassky E, et al. *JAMA Dermatol*. 2020;156:411-420.

56

Emerging Agent: Nemolizumab

- Phase 2b randomized trial in 226 adults with moderate-to-severe AD and severe pruritis, inadequately controlled with topical medications
- At week 24, EASI scores with nemolizumab (30mg) vs placebo were significantly reduced (–68.8% vs –52.1%; *P*= .016)

EASI scores over time (ITT population)—LSM and SE



*$P \leq .05$; †$P \leq .01$; ‡ $P \leq .001$, all vs placebo
ITT = intention-to-treat; SE = standard error.
Silverberg JI, et al. *J Allergy Clin Immunol*. 2020;145:173-182.

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AD and COVID-19

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Comorbidities Increase Risk of COVID-19–Associated Hospitalization and Death

- Immunosuppressive agents should not be **initiated** in patients with risk factors for severe COVID-19
- Immunosuppressive agents may be continued if COVID-19 negative
  - Weigh risk and benefits on case-by-case basis
  - Consider comorbidities that increase risk of COVID-19 complications

Factors That Increase the Risk of Progressing to Severe COVID-19

- Cancer
- Cardiovascular disease
- Chronic kidney disease
- Chronic lung diseases
- Diabetes (type 1 or 2)
- Immunocompromised state
- Overweight or obesity
- Older age (aged ≥65 years)
- Sickle cell disease or thalassemia
- Solid-organ or blood stem-cell transplant

US Centers for Disease Control and Prevention (CDC). Medical conditions. 2021 (www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html). American Academy of Dermatology Association (AADA). Guidance on the use of medications during COVID-19 outbreak. 2020 (https://assets.ctfassets.net/1ny4yoiyrqia/PicgNuD0IpYd9MSOwab47/2461e6c12cd88953632a13cd68952b71/Guidance_on_medications__10-12-20.pdf). Accessed 11/27/2021.

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AD and COVID-19

- Dupilumab is **not** associated with a significantly increased risk of viral infections
  - Dupilumab is an immunomodulator, not an immunosuppressant
- Dupilumab may even ***decrease the risk*** of severe COVID-19 symptoms
- Immunosuppressants may ***increase the risk*** of viral infection
  - Cyclosporine and azathioprine may ***slightly increase the risk***
  - Corticosteroid (prednisolone) at doses ≥20 mg daily ***increases the risk*** of SARS-CoV-2 infection and poor outcomes

International League of Dermatological Societies (ILDS). ILDS guidance. 2021 (https://ilds.org/covid-19/guidance-psoriasis-atopic-dermatitis). AADA. Guidance on the use of medications during COVID-19 outbreak. 2020 (https://assets.ctfassets.net/1ny4yoiyrqia/PicgNuD0IpYd9MSOwab47/2461e6c12cd88953632a13cd68952b71/Guidance_on_medications __10-12-20.pdf). Ungar B, et al. *J Allergy Clin Immunol Pract.* 2022;10:134-142. URLs accessed 1/16/2022.

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COVID Considerations

- No need to stop systemic therapy during pandemic
- If COVID-19-positive, unclear guidance on stopping therapy
  - AADA: **consider holding immunosuppressive agents until patient recovers**
- COVID vaccine guidance
  - ACR: No reason to stop therapies prior to vaccine
  - ACR: stop MTX and JAK inhibitors for 1 week after each vaccine dose
  - NPF: consider holding MTX for 2 weeks after single-dose vaccine
  - No need to stop cyclosporine

ACR = American College of Rheumatology; NPF = National Psoriasis Foundation.

AADA. (https://assets.ctfassets.net/1ny4yoiyrqia/PicgNuD0IpYd9MSOwab47/2461e6c12cd88953632a13cd68952b71/Guidance_on_medications__10-12-20.pdf). ACR. (www.rheumatology.org/Portals/0/Files/COVID-19-Vaccine-Clinical-Guidance-Rheumatic-Diseases-Summary.pdf). National Psoriasis Foundation (NPF). Updates to guidelines (www.psoriasis.org/covid-19-task-force-guidance-statements/). URLs accessed 11/27/2021. Poulsen NN, et al. *Am J Transplant*. 2020;20:2975-2982. Guisado-Vasco P, et al. *EClinicalMedicine*. 2020;28:100591. 3. 4. 5.

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Case Study 3

- ***CC:*** *Tim is a 31-year-old Chinese man with a history of atopic dermatitis with recurrent skin infections; he is doing his post-doctoral work in the US*
  - He notes he is exhausted from many difficult nights of no sleep or poor sleep, and even when he does sleep, he is scratching
  - He is also fed up with the same treatment approaches over and over…

- **HPI**
  - Lifelong history of eczema, with patch development on cheeks before age 1; by age 5, he exhibited widespread disease
  - Multiple staph infections in last few years (some MRSA), requiring lengthy courses of oral antibiotics
  - Seasonal flares of eczema (particularly winter); avoids dairy due to symptom triggering
  - Difficulty getting and staying asleep due to scratching. He complains of difficulty concentrating at school and poor grades, as well as trouble keeping a job due to missing lots of work and being distracted.

Image courtesy of Dr. Peter Lio.

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Case Study 3: Current Therapy

- Triamcinolone 0.1% ointment 2–3x daily to affected areas
- Wet-wrap therapy with the triamcinolone at night (most nights of the week)
- Dilute bleach baths 3x per week
- Hydroxyzine 25 mg po qhs
- Cetirizine 10 mg po qAM
- Various moisturizing ointment and creams
- No current antibiotics, but most recent course of trimethoprim/sulfamethoxazole was approximately 1 month ago after scratching to infection

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Case Study 3: Question 1

- Tim has not received systemic therapy for his AD in the past, other than oral corticosteroids for intense flares
- What treatment course would you recommend to achieve symptom control?

A. Azathioprine
B. Phototherapy + medium potency TCS
C. Tralokinumab
D. Methotrexate + high-dose oral corticosteroids
E. Abrocitinib

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Case Study 3: Question 2

What other interventions would you recommend for this patient?

A. Brief hospitalization
B. Phototherapy to targeted areas
C. Topical calcineurin inhibitors to ”hot spots”
D. All of the above
E. None of the above

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Optimizing Long-Term Control

Address only intermittent flares

Prescription antibiotics, potent TCS, and prednisone

Yields alternating roller-coaster of improvements and flares

Practice daily skin care

Use adequate amounts of topical medication

Recognize and avoid triggers

Maintains control

Wollenberg A, et al. *J Eur Acad Dermatol Venereol.* 2016;30:729-747. Torrelo A, et al. *Actas Dermosifiliogr.* 2013;104:409-417. Thaci D, et al. *J Eur Acad Dermatol Venereol.* 2010;24:1040-1046. Sidbury R, et al. *J Am Acad Dermatol.* 2014;71:1218-1233.

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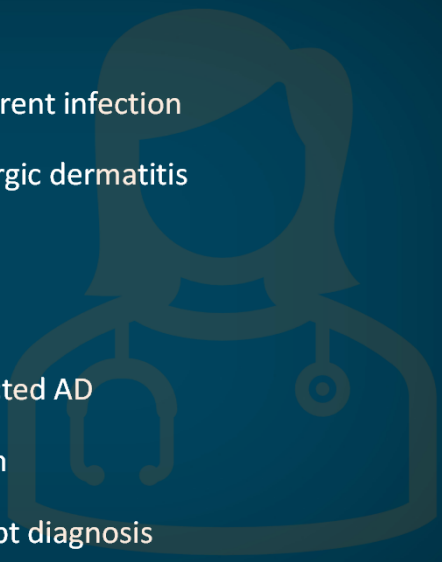
Who Needs the Care of an AD Specialist?

- Challenging skin presentations or uncertain diagnosis
- Refractory cases or cases associated with severe/recurrent infection
- Persistent symptoms related to suspected contact allergic dermatitis
- Moderate-to-severe AD with suspected food allergy
- AD causing significant quality-of-life impact
- ***Urgent referral*** for failed treatment of bacterially infected AD
- ***Immediate referral*** if suspicious of eczema herpeticum
- Telehealth may help increase access to care and prompt diagnosis



National Institute for Health and Care Excellence (NICE) guidance. Atopic eczema in under 12s: diagnosis and management (www.nice.org.uk/guidance/cg57/resources/atopic-eczema-in-under-12s-diagnosis-and-management-pdf-975512529349). Last updated 3/2/21. Eczema in skin of color: Social and economic factors. (https://eczemainskinofcolor.org/social-and-economic-factors/). Accessed 11/27/21.

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Conclusions

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Summary

- AD causes a significant societal and individual burden
- Evaluate patients and decide if they are true candidates for topical therapy
- *In addition to* signs and symptoms, *the* burden of topical regimens, TCS overuse, infection, and hyperpigmentation are factors which *may support a decision* to step-up to systemic therapy
- Traditional oral therapies cost less but lack sufficient or acceptable long-term safety or efficacy data; there are now multiple approved systemic therapies to treat moderate-to-severe AD
- Dupilumab provides effective therapy with proven long-term efficacy and safety in many types of AD patients and does not require laboratory monitoring
- Since AD is *more prevalent*, may be *more severe*, and frustratingly, is *more difficult to diagnose and evaluate* in patients with skin of color, extra care may be warranted in those patients with more richly-pigmented skin

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Q&A

Peter Lio, MD and Vivian Shi, MD, FAAD

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This activity is supported by an educational grant from Sanofi Genzyme and Regeneron Pharmaceuticals.

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Overview and Impact of Atopic Dermatitis

Abuabara K, Magyari A, McCulloch CE, Linos E, Margolis DJ, Langan SM. Prevalence of atopic eczema among patients seen in primary care: Data from The Health Improvement Network. *Ann Intern Med*. 2019;170:354-356.	https://www.acpjournals.org/doi/10.7326/M18-2246
Bin L, Leung DY. Genetic and epigenetic studies of atopic dermatitis. *Allergy Asthma Clin Immunol*. 2016;12:52.	https://aacijournal.biomedcentral.com/articles/10.1186/s13223-016-0158-5
Boguniewicz M, Leung DYM. Atopic dermatitis: A disease of altered skin barrier and immune dysregulation. *Immunol Rev.* 2011;242:233-246.	https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1600-065X.2011.01027.x
Czarnowicki T, He H, Krueger JG, Guttman-Yassky E. Atopic dermatitis endotypes and implications for targeted therapeutics. *J Allergy Clin Immunol*. 2019;143:1-11.	https://www.jacionline.org/article/S0091-6749(18)31572-0/fulltext
Drucker AM, Wang AR, Li WQ, Sevetson E, Block JK, Qureshi AA. The burden of atopic dermatitis: Summary of a report for the National Eczema Association. *J Invest Dermatol.* 2017;137:26-30.	https://www.jidonline.org/article/S0022-202X(16)32120-0/fulltext
Kiebert G, et al. Atopic dermatitis is associated with a decrement in health-related quality of life. *Int J Dermatol.* 2002;41:151-158.	https://onlinelibrary.wiley.com/doi/abs/10.1046/j.1365-4362.2002.01436.x
Leung DYM, Berdyshev E, Goleva. Cutaneous barrier dysfunction in allergic diseases. *J Allergy Clin Immunol.* 2020;145:1485-1497.	https://www.jacionline.org/article/S0091-6749(20)30274-8/fulltext
McKenzie C, Silverberg JI. The prevalence and persistence of atopic dermatitis in urban United States children. *Ann Allergy Asthma Immunol*. 2019;123:173-178.e1.	https://www.annallergy.org/article/S1081-1206(19)30371-0/fulltext
Siegfried EC, Hebert AA. Diagnosis of atopic dermatitis: Mimics, overlaps, and complications. *J Clin Med.* 2015;4:884-917.	https://www.mdpi.com/2077-0383/4/5/884
Silverberg JI. Comorbidities and the impact of atopic dermatitis. *Ann Allergy Asthma Immunol.* 2019;123:144-151.	https://www.annallergy.org/article/S1081-1206(19)30319-9/fulltext
Silverberg JI, et al. Patient burden and	https://www.annallergy.org/article/S1081-

quality of life in atopic dermatitis in US adults: A population-based cross-sectional study. *Ann Allergy Asthma Immunol.* 2018;121:340-347	1206(18)30567-2/fulltext
Simpson EL, Bieber T, Eckert L, et al. Patient burden of moderate to severe atopic dermatitis (AD): Insights from a phase 2b clinical trial of dupilumab in adults. *J Am Acad Dermatol.* 2016;74:491-498.	https://www.jaad.org/article/S0190-9622(15)02471-8/fulltext
Vakharia PP, Chopra R, Sacotte R, et al. Burden of skin pain in atopic dermatitis. *Ann Allergy Asthma Immunol*. 2017;119:548-552.e3.	https://www.annallergy.org/article/S1081-1206(17)31127-4/fulltext

AD and Skin of Color

Alexis AF, Sergay AB, Taylor SC. Common dermatologic disorders in skin of color: A comparative practice survey. *Cutis.* 2007;80:387-394.	https://cdn.mdedge.com/files/s3fs-public/Document/September-2017/080050387.pdf
American College of Allergy, Asthma & Immunology (ACAAI) and the Asthma & Allergy Network (AAN). Eczema in skin of color: Social and economic factors.	https://eczemainskinofcolor.org/social-and-economic-factors/
Brunner PM, Guttman-Yassky E. Racial differences in atopic dermatitis. *Ann Allergy Asthma Immunol*. 2019;122:449-455.	https://www.annallergy.org/article/S1081-1206(18)31420-0/fulltext
Jones VA, Clark KA, Shobajo MT, Cordova A, Tsoukas MM. Skin of color representation in medical education: An analysis of popular preparatory materials used for United States Medical Licensing Examinations. *J Am Acad Dermatol*. 2021;85:773-775.	https://www.jaad.org/article/S0190-9622(20)32315-X/fulltext
Montgomery SNB, Elbuluk N. A quantitative analysis of research publications focused on the top chief complaints in patients with skin of color. *J Am Acad Dermatol*. 2021;85:241-242.	https://www.jaad.org/article/S0190-9622(20)32421-X/fulltext
Nijhawan RI, Jacob SE, Woolery-Lloyd H. Skin of color education in dermatology residency programs: Does residency training	https://www.jaad.org/article/S0190-9622(08)00749-4/fulltext

reflect the changing demographics of the United States? *J Am Acad Dermatol*. 2008;59:615-618.	
Poladian K, De Souza B, McMichael AJ. Atopic dermatitis in adolescents with skin of color. *Cutis.* 2019;104:164-168.	https://www.mdedge.com/dermatology/article/207506/atopic-dermatitis/atopic-dermatitis-adolescents-skin-color
Taylor SC. Skin of color: Biology, structure, function, and implications for dermatologic disease. *J Am Acad Dermatol*. 2002;46(2 suppl):S41-62.	https://www.jaad.org/article/S0190-9622(02)32474-5/fulltext
Wan J, Margolis DJ, Mitra N, Hoffstad OJ, Takeshita J. Racial and ethnic differences in atopic dermatitis-related school absences among US children. *JAMA Dermatol*. 2019;155:973-975.	https://jamanetwork.com/journals/jamadermatology/fullarticle/2733223

AD and Urban Communities

Fiscella K, Williams DR. Health disparities based on socioeconomic inequities: Implications for urban health care. *Acad Med*. 2004;79:1139-1147.	https://journals.lww.com/academicmedicine/Fulltext/2004/12000/Health_Disparities_Based_on_Socioeconomic.4.aspx
Hendricks AJ, Eichenfield LF, Shi VY. The impact of airborne pollution on atopic dermatitis: A literature review. *Br J Dermatol*. 2020;183:16-23.	https://onlinelibrary.wiley.com/doi/10.1111/bjd.18781
Kjellstrom T, Mercado S, Sami M, Havemann K, Iwao S. Achieving health equity in urban settings. *J Urban Health.* 2007;84(3 suppl):1-6.	https://link.springer.com/article/10.1007%2Fs11524-007-9192-4
Saha S, Feldman JM. Neighborhood-level racial/ethnic and economic inequities in COVID-19 burden within urban areas in the US and Canada. *medRxiv.* 2020. 12.07.20241018.	https://www.medrxiv.org/content/10.1101/2020.12.07.20241018v1
World Health Organization (WHO). *Hidden cities: unmasking and overcoming health inequities in urban settings*. September 14, 2010.	https://www.who.int/publications/i/item/9789241548038

AD Disease Severity Clinical Assessment Tools

Charman CR, Venn AJ, Williams HC. The patient-oriented eczema measure: Development and initial validation of a new tool for measuring atopic eczema severity from the patients' perspective. *Arch Dermatol*. 2004;140:1513-1519.	https://jamanetwork.com/journals/jamadermatology/fullarticle/480876
Charman CR, Venn AJ, Ravenscroft JC, Williams HC. Translating Patient-Oriented Eczema Measure (POEM) scores into clinical practice by suggesting severity strata derived using anchor-based methods. *Br J Dermatol*. 2013;169:1326-1332.	https://onlinelibrary.wiley.com/doi/10.1111/bjd.12590
Futamura M, Leshem YA, Thomas KS, Nankervis H, Williams HC, Simpson EL. A systematic review of Investigator Global Assessment (IGA) in atopic dermatitis (AD) trials: Many options, no standards. *J Am Acad Dermatol*. 2016;74:288-294.	https://www.jaad.org/article/S0190-9622(15)02284-7/fulltext
Hanifin JM, Thurston M, Omoto M, Cherill R, Tofte SJ, Graeber M. The eczema area and severity index (EASI): Assessment of reliability in atopic dermatitis. EASI Evaluator Group. *Exp Dermatol*. 2001;10:11-18.	https://onlinelibrary.wiley.com/doi/abs/10.1034/j.1600-0625.2001.100102
Severity scoring of atopic dermatitis: The SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis. *Dermatology*. 1993;186:23-31.	https://www.karger.com/Article/Abstract/247298
Simpson E, Bissonnette R, Eichenfield LF, et al. The Validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD): The development and reliability testing of a novel clinical outcome measurement instrument for the severity of atopic dermatitis. *J Am Acad Dermatol.* 2020;83:839-846.	https://www.jaad.org/article/S0190-9622(20)30720-9/fulltext

Treatment of Atopic Dermatitis

Resource	Address
Agusti-Mejias A, Messeguer F, García R, Febrer I. Severe Refractory Atopic Dermatitis in an Adolescent Patient Successfully Treated With Ustekinumab. *Ann Dermatol.* 2013;25:368-370.	https://anndermatol.org/DOIx.php?id=10.5021/ad.2013.25.3.368
Arkwright PD, Motala C, Subramanian H, et al. Management of difficult-to-treat atopic dermatitis. *J Allergy Clin Immunol Pract.* 2013;1:142-151.	https://www.sciencedirect.com/science/article/abs/pii/S221321981200013X
Ariëns LFM, Gadkari A, van Os-Medendorp H, et al. Dupilumab versus cyclosporine for the treatment of moderate-to-severe atopic dermatitis in adults: Indirect comparison using the eczema area and severity index. *Acta Derm Venereol.* 2019;99:851-857.	https://www.medicaljournals.se/acta/content/abstract/10.2340/00015555-3219
Barnes TM, Greive KA. Use of bleach baths for treatment of infected atopic eczema. *Australas J Dermatol. 2013;54:251-258.*	https://pubmed.ncbi.nlm.nih.gov/23330843/
Bass AM, Anderson KL, Feldman SR. Interventions to increase treatment adherence in pediatric atopic dermatitis: A systematic review. *J Clin Med.* 2015;4:231-242.	https://www.mdpi.com/2077-0383/4/2/231
Beattie PE, Lewis-Jones MS. Parental knowledge of topical therapies in the treatment of childhood atopic dermatitis. *Clin Exp Dermatol.* 2003;28:549-553.	https://onlinelibrary.wiley.com/doi/abs/10.1046/j.1365-2230.2003.01357.x
Beck LA, Thaçi D, Deleuran M, et al. Dupilumab provides favorable safety and sustained efficacy for up to 3 years in an open-label study of adults with moderate-to-severe atopic dermatitis. *Am J Clin Dermatol*. 2020;21:567-577.	https://link.springer.com/article/10.1007%2Fs40257-020-00527-x
Bender B, Milgrom H. Neuropsychiatric effects of medications for allergic diseases. *J Allergy Clin Immunol.* 1995;95:523-528.	https://pubmed.ncbi.nlm.nih.gov/7852668/
Bissonnette R, et al. Topical tofacitinib for atopic dermatitis: A phase IIa randomized trial. *Br J Dermatol*. 2016;175:902-911.	https://onlinelibrary.wiley.com/doi/full/10.1111/bjd.14871
Blauvelt A, de Bruin-Weller M, Gooderham M, et al. Long-term management of moderate-to-severe atopic dermatitis with	https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)31191-1/fulltext

dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): A 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial. *Lancet.* 2017;389:2287-2303.	
Boguniewicz M, Fonacier L, Guttman-Yassky E, Ong PY, Silverberg J, Farrar JR. Atopic dermatitis yardstick: Practical recommendations for an evolving therapeutic landscape. *Ann Allergy Asthma Immunol*. 2018;120:10-22.e2.	https://www.annallergy.org/article/S1081-1206(17)31260-7/fulltext
Boguniewicz M, Alexis AF, Beck LA, et al. Expert perspectives on management of moderate-to-severe atopic dermatitis: A multidisciplinary consensus addressing current and emerging therapies. *J Allergy Clin Immunol Pract.* 2017;5:1519-1531.	https://www.jaci-inpractice.org/article/S2213-2198(17)30615-3/fulltext
Brar KK, Nicol NH, Boguniewicz M. Strategies for successful management of severe atopic dermatitis. *J Allergy Clin Immunol Pract*. 2019;7:1-16.	https://www.sciencedirect.com/science/article/abs/pii/S2213219818306780
Cotter DG, Schairer D, Eichenfield L. Emerging therapies for atopic dermatitis: JAK inhibitors. *J Am Acad Dermatol*. 2018;78(suppl 1):S53-S62.	https://www.jaad.org/article/S0190-9622(17)32820-7/fulltext
Czarnowicki T, He H, Krueger JG, Guttman-Yassky E. Atopic dermatitis endotypes and implications for targeted therapeutics. *J Allergy Clin Immunol*. 2019;143:1-11.	https://www.jacionline.org/article/S0091-6749(18)31572-0/fulltext
Czarnowicki T, Krueger JG, Guttman-Yassky E. Novel concepts of prevention and treatment of atopic dermatitis through barrier and immune manipulations with implications for the atopic march. *J Allergy Clin Immunol.* 2017;139:1723-1734.	https://www.jacionline.org/article/S0091-6749(17)30665-6/fulltext
Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: Section 1. diagnosis and assessment of atopic dermatitis. *J Am Acad Dermatol*. 2014;70:338-351.	https://www.jaad.org/article/S0190-9622(13)01095-5/fulltext
Eichenfield LF, Boguniewicz M, Simpson EL, et al. Translating atopic dermatitis management guidelines into practice for	https://publications.aap.org/pediatrics/article-abstract/136/3/554/61253/Translating-Atopic-Dermatitis-

primary care providers. *Pediatrics*. 2015;136:554-565.	Management?redirectedFrom=fulltext
Ellis RM, Koch LH, McGuire E, Williams JV. Potential barriers to adherence in pediatric dermatology. *Pediatr Dermatol.* 2011;28:242-244.	https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1525-1470.2011.01493.x
Fleming P, Drucker AM. Risk of infection in patients with atopic dermatitis treated with dupilumab: A meta-analysis of randomized controlled trials. *J Am Acad Dermatol.* 2018;78:62-69.e1	https://www.jaad.org/article/S0190-9622(17)32457-X/fulltext
Gori N, Chiricozzi A, Malvaso D, et al. Successful combination of systemic agents for the treatment of atopic dermatitis resistant to dupilumab therapy. *Dermatology.* 2021;237:535-541.	https://www.karger.com/Article/Abstract/512890
Guttman-Yassky E, Silverberg JI, Nemoto O, et al. Baricitinib in adult patients with moderate-to-severe atopic dermatitis: A phase 2 parallel, double-blinded, randomized placebo-controlled multiple-dose study. *J Am Acad Dermatol.* 2019;80:913-921.e9.	https://www.jaad.org/article/S0190-9622(18)30129-4/fulltext
Guttman-Yassky E, et al. Efficacy and safety of lebrikizumab, a high-affinity interleukin 13 inhibitor, in adults with moderate to severe atopic dermatitis: A phase 2b randomized clinical trial. *JAMA Dermatol*. 2020;156:411-420.	https://jamanetwork.com/journals/jamadermatology/fullarticle/2761466
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;397:2151-2168.	https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00588-2/fulltext
Janeczek M, Moy L, Riopelle A, et al. The potential uses of N-acetylcysteine in dermatology: A review. *J Clin Aesthet Dermatol.* 2019;12:20-26.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6561714/
Jarnagin K, Chanda S, Coronado D, et al. Crisaborole topical ointment, 2%: A nonsteroidal, topical, anti-inflammatory	https://jddonline.com/articles/dermatology/S1545961616P0390X

phosphodiesterase 4 inhibitor in clinical development for the treatment of atopic dermatitis. *J Drugs Dermatol.* 2016;15:390-396.	
Kabashima K, Furue M, Hanifin JM, et al. Nemolizumab in patients with moderate-to-severe atopic dermatitis: Randomized, phase II, long-term extension study. *J Allergy Clin Immunol.* 2018;142:1121-1130.e7.	https://www.jacionline.org/article/S0091-6749(18)30698-5/fulltext
Khattri S, Brunner PM, Garcet S, et al. Efficacy and safety of ustekinumab treatment in adults with moderate-to-severe atopic dermatitis. *Exp Dermatol*. 2017;26:28-35.	https://onlinelibrary.wiley.com/doi/abs/10.1111/exd.13112
Kim J, Kim BE, Ahn K, Leung DYM. Interactions between atopic dermatitis and *Staphylococcus aureus* infection: Clinical implications. *Allergy Asthma Immunol Res.* 2019;11:593-603.	https://e-aair.org/DOIx.php?id=10.4168/aair.2019.11.5.593
Lewis KE, Holdren MS, Maurer MF, et al. Interleukin (IL) 31 induces in cynomolgus monkeys a rapid and intense itch response that can be inhibited by an IL-31 neutralizing antibody. *J Eur Acad Dermatol Venereol.* 2017;31:142-150.	https://onlinelibrary.wiley.com/doi/abs/10.1111/jdv.13794
Li AW, Yin ES, Antaya RJ. Topical corticosteroid phobia in atopic dermatitis: A systematic review. *JAMA Dermatol*. 2017;153:1036-1042.	https://jamanetwork.com/journals/jamadermatology/article-abstract/2643740
Lio PA, Lee M, LeBovidge J, Timmons KG, Schneider L. Clinical management of atopic dermatitis: Practical highlights and updates from the atopic dermatitis practice parameter 2012. *J Allergy Clin Immunol Pract.* 2014;2:361-369.	https://www.sciencedirect.com/science/article/abs/pii/S2213219814000889
Lyons JJ, Milner JD, Stone KD. Atopic dermatitis in children: Clinical features, pathophysiology, and treatment. *Immunol Allergy Clin North Am.* 2015;35:161-183.	https://www.sciencedirect.com/science/article/abs/pii/S0889856114001088
Malajian D, Guttman-Yassky E. New pathogenic and therapeutic paradigms in atopic dermatitis. *Cytokine.* 2015;73:311-	https://www.sciencedirect.com/science/article/abs/pii/S1043466614006061

318.	
Maliyar KB, Sibbald C, Pope E, Gary Sibbald R. Diagnosis and management of atopic dermatitis: A review. *Adv Skin Wound Care.* 2018;31:538-550.	https://journals.lww.com/aswcjournal/Fulltext/2018/12000/Diagnosis_and_Management_of_Atopic_Dermatitis__A.3.aspx
Mobasher P, Heydari Seradj M, Raffi J, Juhasz M, Atanaskova Mesinkovska N. Oral small molecules for the treatment of atopic dermatitis: A systematic review. *J Dermatolog Treat.* 2019;30:550-557.	https://www.tandfonline.com/doi/full/10.1080/09546634.2018.1544412
Nieburhr M, Mai U, Kapp A, Werfel T. Antibiotic treatment of cutaneous infections with Staphylococcus aureus in patients with atopic dermatitis: Current antimicrobial resistances and susceptibilities. *Exp Dermatol*. 2008;17:953-957.	https://onlinelibrary.wiley.com/doi/10.1111/j.1600-0625.2008.00734.x
Nemoto O, Furue M, Nakagawa H, et al. The first trial of CIM331, a humanized qntihuman interleukin-31 receptor A antibody, in healthy volunteers and patients with atopic dermatitis to evaluate safety, tolerability and pharmacokinetics of a single dose in a randomized, double-blind, placebo-controlled study. *Br J Dermatol.* 2016;174:296-304.	https://onlinelibrary.wiley.com/doi/full/10.1111/bjd.14207
Paller AS, Siegfried EC, Simpson EL, et al. A phase 2, open-label study of single-dose dupilumab in children aged 6 months to <6 years with severe uncontrolled atopic dermatitis: Pharmacokinetics, safety and efficacy. *J Eur Acad Dermatol Venereol*. 2021;35:464-475.	https://onlinelibrary.wiley.com/doi/10.1111/jdv.16928
Paller AS, Tom WL, Lebwohl MG, et al. Efficacy and safety of crisaborole ointment, a novel, nonsteroidal phosphodiesterase 4 (PDE4) inhibitor for the topical treatment of atopic dermatitis (AD) in children and adults. *J Am Acad Dermatol.* 2016;75:494-503.e6.	https://www.jaad.org/article/S0190-9622(16)30330-9/fulltext
Paller AS, Siegfried EC, Thaçi D, et al. Efficacy and safety of dupilumab with concomitant topical corticosteroids in children 6 to 11 years old with severe atopic dermatitis: A	https://www.jaad.org/article/S0190-9622(20)31152-X/fulltext

randomized, double-blinded, placebo-controlled phase 3 trial. *J Am Acad Dermatol*. 2020;83:1282-1293.	
Pan Y, Xu L, Qiao J, Fang H. A systematic review of ustekinumab in the treatment of atopic dermatitis. *J Dermatolog Treat*. 2018:29:539-541.	https://www.tandfonline.com/doi/full/10.1080/09546634.2017.1406894
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;85:863-872.	https://www.jaad.org/article/S0190-9622(21)00931-2/fulltext
Pena-Robichaux V, Kvedar JC, Watson AJ. Text messages as a reminder aid and educational tool in adults and adolescents with atopic dermatitis: A pilot study. *Dermatol Res Pract.* 2010;2010:894258.	https://www.hindawi.com/journals/drp/2010/894258/
Politiek K, van der Schaft J, Coenraads PJ, de Bruin-Weller MS, Schuttelaar ML. Drug survival for methotrexate in a daily practice cohort of adult patients with severe atopic dermatitis. *Br J Dermatol*. 2016;174:201-203.	https://onlinelibrary.wiley.com/doi/10.1111/bjd.13961
Puya R, Alvarez-López M, Velez A, Casas Asuncion E, Moreno JC. Treatment of severe refractory adult atopic dermatitis with ustekinumab. *Int J Dermatol.* 2012;51:115-116.	https://onlinelibrary.wiley.com/doi/full/10.1111/j.1365-4632.2011.05195.x
Raffin D, Giraudeau B, Samimi M, Machet L, Pourrat X, Maruani A. Corticosteroid phobia among pharmacists regarding atopic dermatitis in children: A national French survey. *Acta Derm Venereol*. 2016;96:177-180.	https://www.medicaljournals.se/acta/content/abstract/10.2340/00015555-2157
Ring J, Alomar A, Bieber T, et al. Guidelines for treatment of atopic eczema (atopic dermatitis) part I. *J Eur Acad Dermatol Venereol.* 2012;26:1045-1060.	https://onlinelibrary.wiley.com/doi/full/10.1111/j.1468-3083.2012.04635.x
Ruzicka T, Hanifin JM, Furue M, et al. Anti-interleukin-31 receptor A antibody for atopic dermatitis. *N Engl J Med.* 2017;376;826-835.	https://www.nejm.org/doi/10.1056/NEJMoa1606490

Samorano LP, Hanifin JM, Simpson EL, Leshem YA. Inadequate response to ustekinumab in atopic dermatitis - A report of two patients. *J Eur Acad Dermatol Venereol.* 2016;30:522-523.	https://onlinelibrary.wiley.com/doi/abs/10.1111/jdv.12918
Schaefer P. Acute and chronic urticaria: Evaluation and treatment. *Am Fam Physician*. 2017;95:717-724	https://pubmed.ncbi.nlm.nih.gov/28671445/
Schlessinger J, Shepard JS, Gower R, et al. Safety, effectiveness, and pharmacokinetics of crisaborole in infants aged 3 to < 24 months with mild-to-moderate atopic dermatitis: A phase IV open-label study (CrisADe CARE 1). *Am J Clin Dermatol.* 2020;21:275-284.	https://link.springer.com/article/10.1007/s40257-020-00510-6
Schmitt J, von Kobyletzki L, Svensson A, Apfelbacher C. Efficacy and tolerability of proactive treatment with topical corticosteroids and calcineurin inhibitors for atopic eczema: Systematic review and meta-analysis of randomized controlled trials. *Br J Dermatol*. 2011;164:415-428.	https://onlinelibrary.wiley.com/doi/10.1111/j.1365-2133.2010.10030.x
Scudder L, Seymour S, Torjusen E. Montelukast's underrecognized adverse drug events. *Medscape*. March 2, 2015.	https://www.medscape.com/viewarticle/840302
Shi VY, Nanda S, Lee K, Armstrong AW, Lio PA. Improving patient education with an eczema action plan: A randomized controlled trial. *JAMA Dermatol.* 2013;149:481-483.	https://jamanetwork.com/journals/jamadermatology/fullarticle/1670411
Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis: Section 3. Management and treatment with phototherapy and systemic agents. *J Am Acad Dermatol.* 2014;71:327-349.	https://www.jaad.org/article/S0190-9622(14)01264-X/fulltext
Siegfried EC, Jaworski JC, Eichenfield LF, et al. Developing drugs for treatment of atopic dermatitis in children (≥3 months to <18 years of age): Draft guidance for industry. *Pediatr Dermatol.* 2018;35:303-322.	https://onlinelibrary.wiley.com/doi/abs/10.1111/pde.13452
Silverberg JI, Simpson EL, Thyssen JP, et al. Efficacy and safety of abrocitinib in patients	https://jamanetwork.com/journals/jamadermatology/fullarticle/2766772

with moderate-to-severe atopic dermatitis: A randomized clinical trial. *JAMA Dermatol*. 2020;156:863-873.	
Silverberg JI, Pinter A, Pulka G, et al. Phase 2B randomized study of nemolizumab in adults with moderate-to-severe atopic dermatitis and severe pruritus. *J Allergy Clin Immunol*. 2020;145:173-182.	https://www.jacionline.org/article/S0091-6749(19)31099-1/fulltext
Simpson EL, Imafuku S, Poulin Y, et al. A phase 2 randomized trial of apremilast in patients with atopic dermatitis. *J Invest Dermatol*. 2019;139:1063-1072.	https://www.jidonline.org/article/S0022-202X(18)32905-1/fulltext
Simpson EL, Lacour JP, Spelman L, et al. Baricitinib in patients with moderate-to-severe atopic dermatitis and inadequate response to topical corticosteroids: Results from two randomized monotherapy phase III trials. *Br J Dermatol*. 2020;183:242-255.	https://onlinelibrary.wiley.com/doi/10.1111/bjd.18898
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;396:255-266.	https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30732-7/fulltext
Simpson EL, Paller AS, Siegfried EC, et al. Efficacy and safety of dupilumab in adolescents with uncontrolled moderate to severe atopic dermatitis: A phase 3 randomized clinical trial. *JAMA Dermatol*. 2020;156:44-56.	https://jamanetwork.com/journals/jamadermatology/fullarticle/2753673
Simpson EL, Flohr C, Eichenfield LF, et al. Efficacy and safety of lebrikizumab (an anti-IL-13 monoclonal antibody) in adults with moderate-to-severe atopic dermatitis inadequately controlled by topical corticosteroids: A randomized, placebo-controlled phase II trial (TREBLE). *J Am Acad Dermatol.* 2018;78:863-871.e11.	https://www.jaad.org/article/S0190-9622(18)30102-6/fulltext
Simpson EL, Bieber T, Eckert L, et al. Patient burden of moderate to severe atopic dermatitis (AD): Insights from a phase 2b clinical trial of dupilumab in adults. *J Am*	https://www.jaad.org/article/S0190-9622(15)02471-8/fulltext

***Acad Dermatol*. 2016;74:491-498.**	
Simpson EL, Parnes JR, She D, et al. Tezepelumab, an anti-thymic stromal lymphopoietin monoclonal antibody, in the treatment of moderate to severe atopic dermatitis: A randomized phase 2a clinical trial. *J Am Acad Dermatol*. 2019;80:1013-1021.	https://www.jaad.org/article/S0190-9622(18)33050-0/fulltext
Simpson EL, Bieber T, Guttman-Yassky E, et al. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. *N Engl J Med.* 2016;375:2335-2348.	https://www.nejm.org/doi/10.1056/NEJMoa1610020
Simpson EL, Bruin-Weller M, Flohr C, et al. When does atopic dermatitis warrant systemic therapy? Recommendations from an expert panel of the International Eczema Council. *J Am Acad Dermatol*. 2017;77:623-633.	https://www.jaad.org/article/S0190-9622(17)31944-8/fulltext
Smith SD, Stephens AM, Werren JC, Fischer GO. Treatment failure in atopic dermatitis as a result of parental health belief. *Med J Aust.* 2013;199:467-469.	https://pubmed.ncbi.nlm.nih.gov/24099206/
Snyder A, Farhangian M, Feldman. A review of patient adherence to topical therapies for treatment of atopic dermatitis. *Cutis.* 2015;96:397-401.	https://pubmed.ncbi.nlm.nih.gov/26761934/
Suh L, Coffin S, Leckerman KH, Gelfand JM, Honig PJ, Yan AC. Methicillin-resistant Staphylococcus aureus colonization in children with atopic dermatitis. *Pediatr Dermatol.* 2008;25:528-534.	https://onlinelibrary.wiley.com/doi/10.1111/j.1525-1470.2008.00768.x
Thyssen JP, de Bruin-Weller MS, Paller AS, et al. Conjunctivitis in atopic dermatitis patients with and without dupilumab therapy - international eczema council survey and opinion. *J Eur Acad Dermatol Venereol*. 2019;33:1224-1231.	https://onlinelibrary.wiley.com/doi/full/10.1111/jdv.15608
Thaci D, Chambers C, Sidhu M, Dorsch B, Ehlken B, Fuchs. Twice-weekly treatment with tacrolimus 0.03% ointment in children with atopic dermatitis: Clinical efficacy and economic impact over 12 months. *J Eur Acad Dermatol Venereol.* 2010;24:1040-1046.	https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1468-3083.2010.03577.x

Thurmond RL, Kazerouni K, Chaplan SR, et al. Peripheral neuronal mechanism of itch: Histamine and Itch. In: Carstens E, Akiyama T, eds. *Itch: Mechanisms and Treatment*. CRC Press/Taylor & Francis; 2014. Chapter 10.	https://www.ncbi.nlm.nih.gov/books/NBK200934/
Torrelo A, Ortiz J, Alomar A, Ros S, Pedrosa E, Cuervo J. Health-related quality of life, patient satisfaction, and adherence to treatment in patients with moderate or severe atopic dermatitis on maintenance therapy: The CONDA-SAT study. *Actas Dermosifiliogr*. 2013;104:409-417.	https://www.actasdermo.org/en-linkresolver-health-related-quality-life-patient-satisfaction-S1578219013000954
Treister AD, Lio PA. Long-term off-label dupilumab in pediatric atopic dermatitis: A case series. *Pediatr Dermatol.* 2019;36:85-88.	https://onlinelibrary.wiley.com/doi/abs/10.1111/pde.13697
van der Schaft J, Politiek K, van den Reek JM, et al. Drug survival for azathioprine and enteric-coated mycophenolate sodium in a long-term daily practice cohort of adult patients with atopic dermatitis. *Br J Dermatol*. 2016;175:199-202.	https://onlinelibrary.wiley.com/doi/10.1111/bjd.14398
van der Schaft J, et al. Drug survival for ciclosporin A in a long-term daily practice cohort of adult patients with atopic dermatitis. *Br J Dermatol*. 2015;172:1621-1627.	https://pubmed.ncbi.nlm.nih.gov/25683671/
Wang D, Beck LA. Immunologic targets in atopic dermatitis and emerging therapies: An update. *Am J Clin Dermatol.* 2016;17:425-443.	https://link.springer.com/article/10.1007/s40257-016-0205-5
Wollenberg A, Oranje A, Deleuran M, et al. ETFAD/EADV Eczema task force 2015 position paper on diagnosis and treatment of atopic dermatitis in adult and paediatric patients. *J Eur Acad Dermatol Venereol.* 2016;30:729-747.	https://onlinelibrary.wiley.com/doi/full/10.1111/jdv.13599
Zuberbier T, Orlow SJ, Paller AS, et al. Patient perspectives on the management of atopic dermatitis. *J Allergy Clin Immunol*. 2006;118:226-232.	https://www.jacionline.org/article/S0091-6749(06)00450-7/fulltext