Exploring the role of JAK Inhibitors in Moderate-to-Severe ATOPIC DERMATITIS

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 educational grant from Pfizer.

Exploring the Role of JAK Inhibitors in Moderate to Severe Atopic Dermatitis

PROGRAM OVERVIEW

This live virtual activity will cover the care and treatment of patients with moderate to severe atopic dermatitis.

TARGET AUDIENCE

This live virtual activity is intended for dermatologists, allergists, advanced practitioners, and other health care professionals involved in the care and treatment of patients with moderate to severe atopic dermatitis.

LEARNING OBJECTIVES

On completing the program, attendees should be able to:

- Identify patients with moderate to severe atopic dermatitis (AD) who may benefit from systemic therapy
- Evaluate clinical trial data on the efficacy and safety of available and emerging JAK inhibitors for treating AD
- Develop individualized treatment plans for adolescent and adult patients with AD who require treatment intensification
- Recognize and manage adverse events associated with JAK inhibitors in managing AD

ACCREDITATION AND DESIGNATION STATEMENTS

PHYSICIAN
Med Learning Group is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

This CME activity was planned and produced in accordance with the ACCME Essentials.

Med Learning Group designates this live activity for a maximum of *1.0 AMA Category 1 Credit*™. Physicians should claim only the credit commensurate with the extent of their participation in the live activity.

NURSES
This program would be beneficial for nurses involved in treating and managing patients with moderate to severe atopic dermatitis.

CNE Credits:
1.0 ANCC Contact Hour

Ultimate Medical Academy/Complete Conference Management (CCM) is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

Awarded 1.0 contact hour of continuing nursing education of RNs and APNs.

FACULTY

Peter Lio, MD (Program Chair) Clinical Assistant Professor of Dermatology and Pediatrics Northwestern University Feinberg School of Medicine Chicago, Illinois		
Lisa Arkin, MD Assistant Professor and Director of Pediatric Dermatology University of Wisconsin-Madison Madison, Wisconsin	**Steven Feldman, MD** Professor of Dermatology, Pathology and Public Health Sciences Department of Dermatology Wake Forest School of Medicine Winston-Salem, North Carolina	**Jonathan I. Silverberg, MD, PhD, MPH** Associate Professor Director of Clinical Research and Patch Testing The George Washington University School of Medicine and Health Sciences Washington, DC
Jane S. Bellet, MD, FAAD Professor of Pediatrics and Dermatology Duke University School of Medicine Durham, North Carolina	**Howard Pride, MD** Director of Dermatology Service Line, Pediatric Dermatology Geisinger Health System Danville, Pennsylvania	**Lucia Diaz, MD** Assistant Professor Department of Internal Medicine Assistant Professor Department of Pediatrics Associate Program Director, Dermatology Residency The University of Texas at Austin Austin, Texas

DISCLOSURE OF UNLABELED USE

In accordance with the Accreditation Council for Continuing Medical Education (ACCME) Standards for Commercial Support, educational programs sponsored by Med Learning Group must demonstrate balance, independence, objectivity, and scientific rigor. All faculty, authors, editors, staff, and planning committee members participating in a MLG-sponsored activity are required to disclose any relevant financial interest or other relationship with the manufacturers of any commercial products and/or providers of commercial services that are discussed in an educational activity.

DISCLOSURE OF FINANCIAL RELATIONSHIPS

SPEAKER	RELATIONSHIP	MANUFACTURER
Lisa Arkin, MD	Consultant	Regeneron, AbbVie
	Principal Investigator	Amgen, Candela
Jane S. Bellet, MD, FAAD	Stock	Merck
Lucia Diaz, MD	Research	Pfizer, Janssen, Regeneron
	Royalty	UpToDate
Peter A. Lio, MD (Program Chair)	Consultant	Dermavant Sciences, Galderma, Pierre-Fabre, Level Ex, UCB, Regeneron/Sanofi Genzyme, Pfizer, Micreos, Johnson and Johnson, Menlo Therapeutics, IntraDerm, AOBiome, Realm Therapeutics, Altus Labs, Verrica, Arbonne, Bodewell, YobeeCare, My-Or Diagnostics, Kimberly-Clark
	Speaker	Unilever, Arbonne, Verrica, Burt's Bees, Galderma, Eli Lilly and Company, L'Oreal USA Inc.
	Advisory Board	Dermira, Pfizer, LEO Pharmaceuticals, AbbVie, Eli Lilly and Company, L'Oreal USA Inc., Pierre-Fabre, Level Ex, Unilever, Theraplex, Exeltis, AOBiome, Galderma, Amyris, Bodewell, YobeeCare, Burt's Bees, My-Or Diagnostics, and Kimberly-Clark
	Research	National Eczema Association, AOBiome, Regeneron/Sanofi Genzyme, AbbVi
	Patent Holder	Theraplex
	Stockholder	Micreos, YobeeCare, and Altus Labs
Howard Pride, MD	Not relevant relationships to report.	
Jonathan I. Silverberg, MD	Consultant	Abbvie, Afyx, Arena, Asana, BioMX, Bluefin, Bodewell, Boehringer-Ingelheim, Celgene, Dermavant, Dermira, Eli Lilly, Galderma, GlaxoSmithKline, Incyte, Kiniksa, Leo, Luna, Menlo, Novartis, Pfizer, RAPT, Regeneron, Sanofi
	Research	Galderma
	Speakers Bureau	Pfizer, Regeneron, Sanofi-Genzyme
Steven Feldman, MD	Speaker	AbbVie, Amgen/Celgene, Janssen, Leo Pharmaceuticals, Lilly, Novartis Pharmaceuticals, Pfizer Inc., Regeneron, Sanofi, Sun Pharma
	Consultant	AbbVie, Alvotech, Advance Medical, Almirall, Arena, Bristol-Myers Squibb, Caremark, Amgen/Celgene, Galderma, Gerson Lehrman Group, Guidepoint Global, Helsinn, Janssen, Kikaku, Leo Pharmaceuticals, Lilly, Merck and Co., Mylan, Novartis Pharmaceuticals, Ortho Dermatology, Pfizer Inc., Regeneron, Sanofi, Sienna, Sun Pharma, Suncare Research, Xenoport
	Grant Support	AbbVie, Amgen/Celgene, Janssen, Lilly, Novartis Pharmaceuticals, Pfizer Inc., Regeneron, Sanofi
	Royalties	Informa, UpToDate, Xlibris
	Stock	Causa Technologies, Medical Quality Enhancement Corporation Founder/Chief Technology Officer, Cause Technologies

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 independently peer reviewed.
The reviewer of this activity has nothing to disclose.

Planners
The staff, planners and managers reported the following financial relationships or relationships to products or devices they or their spouse/life partner have with commercial interests related to the content of this CME/CE activity:

Matthew Frese, General Manager of Med Learning Group, has nothing to disclose.
Christina Gallo, SVP, Educational Development for Med Learning Group, has nothing to disclose.
Marcello Morgan, Medical and Scientific Services for Med Learning Group, has nothing to disclose.
Lauren Welch, MA, VP of Accreditation and Outcomes for Med Learning Group, has nothing to disclose.
Russie Allen, Accreditation and Outcomes Coordinator for Med Learning Group, has nothing
Daniel Dasilva, Accreditation and Outcomes Coordinator for Med Learning Group, has nothing
Sharine Griggs, Senior Program Manager for Med Learning Group, has nothing to disclose.

DISCLOSURE OF UNLABELED USE

Med Learning Group requires that faculty participating in any CME activity disclose to the audience when discussing any unlabeled or investigational use of any commercial product or device not yet approved for use in the United States.

During this lecture, the faculty may mention the use of medications for both FDA-approved and nonapproved indications.

Method of Participation

There are no fees for participating in and receiving CME/CNE credit for this live activity. To receive CME/CNE credit participants must:

1. Read the CME/CNE information and faculty disclosures.
2. Participate in the live activity.
3. Complete pre and post survey.
4. Submit the evaluation form online.

You will receive your certificate as a downloadable file.

DISCLAIMER

Med Learning Group makes every effort to develop CME activities that are science-based. This activity is designed for educational purposes. Participants have a responsibility to use this information to enhance their professional development in an effort to improve patient outcomes. Conclusions drawn by the participants should be derived from careful consideration of all available scientific information. Participants should use their clinical judgment, knowledge, experience, and

diagnostic decision-making experience before applying any information, whether provided here or by others, for any professional use.

For CME questions, please contact Med Learning Group at info@medlearninggroup.com

Contact this CME provider at Med Learning Group for privacy and confidentiality policy statement information at http://www.medlearninggroup.com/privacy-policy/

AMERICANS WITH DISABILITIES ACT

Event staff will be glad to assist you with any special needs. Please contact Med Learning Group prior to the live event at info@medlearninggroup.com

Provided by Med Learning Group

Co-provided by Ultimate Medical Academy/Complete Conference Management (CCM)

Supported by an educational grant from Pfizer.

Agenda

I. Atopic Dermatitis: An Overview of Features and Impact

a. Epidemiology and burden of AD
   i. Introducing the Case Study
b. Evaluation and diagnosis
c. Pathophysiology of AD
   i. Epithelial barrier dysfunction
   ii. Dysregulation of the immune system
   (Animated theme – pathophysiology of atopic dermatitis)

II. Long-term Management of AD

a. Challenges in the management of AD
b. Current treatment guidelines for the management of moderate-to-severe AD
c. Evaluating therapeutic outcomes
d. Recognizing patients who would benefit from systemic therapy

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

a. Mechanism of action of approved and investigational agents
   (Animated theme – mechanism of action of available and emerging systemic agents for the management of AD)
b. Clinical trial data on the efficacy and safety of targeted therapies
   i. IL-4/IL-13–targeted therapy
   ii. Emerging JAK inhibitors
   iii. Others
c. Recognizing and managing adverse events with systemic therapy

IV. Shared Decision-Making and Patient Considerations in AD

a. Identifying patient- and disease-specific factors that impact treatment selection
b. Designing individualized treatment plans
c. Addressing barriers to therapy adherence

V. Revisiting the Case Study

VI. Conclusions

VII. Questions and Answers

Exploring the Role of JAK Inhibitors in Moderate-to-Severe Atopic Dermatitis

Disclosures

- During the course of this lecture, the faculty may mention the use of medications for both FDA-approved and non-approved indications

This activity is supported by an educational grant from Pfizer, Inc.

FDA = US Food and Drug Administration.

Learning Objectives

- Identify patients with moderate-to-severe AD who may benefit from systemic therapy
- Evaluate clinical trial data on the efficacy and safety of available and emerging JAK inhibitors for the treatment of AD
- Develop individualized treatment plans for adolescent and adult patients with AD who require treatment intensification
- Recognize and manage AEs associated with JAK inhibitors in the management of AD

AD = atopic dermatitis; AE = adverse event; JAK = Janus kinase.

Features and Impact

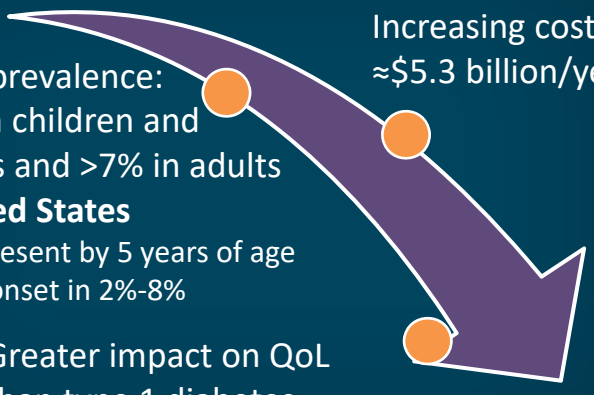
Features of Atopic Dermatitis (AD)

AD is a chronic, pruritic, inflammatory skin disease that typically involves:

- Childhood onset
- Familial occurrence
- Eczematous change
  - Erythema
  - Induration, papulation
  - Excoriation
  - 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.

Impact of AD



Increasing prevalence: 12%-13% in children and adolescents and >7% in adults in **the United States**

- 85% present by 5 years of age
- Adult onset in 2%-8%

Increasing costs: ≈$5.3 billion/year

Greater impact on QoL than type 1 diabetes

QoL = quality of life.

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.

Impact on QoL

- Consequences of ***sleep deprivation***
  - Exhaustion
  - Mood changes
  - Impaired psychosocial functioning
- Consequences of ***social isolation***
  - School avoidance
  - Depression
- **Restricted** lifestyle choices
  - Clothing, holidays, socializing, owning pets, and participating in sports

Lewis-Jones S. *Int J Clin Pract.* 2006;60:984-992.

Associated Comorbidities

Atopic	Others[1,2,6,7]
• **Allergic rhinitis** (≈50% prevalence)[1]	• **Mental/behavioral health**
• **Allergic conjunctivitis**[2]	• **Skin infections**
• **Asthma** (≈22%-30% prevalence)[1,3,4]	• **Allergic contact dermatitis**
• **Primary eosinophilic gastrointestinal disorders**[2]	• **Immune deficiency**
• **Food allergy**[5]	• **Cataracts**

1. Whiteley J, et al. *Curr Med Res Opin.* 2016;32:1645-1651. 2. Silverberg JI. *Cutis.* 2019;104:142-143. 3. Silverberg JI, Hanifin JM. *J Allergy Clin Immunol.* 2013;132:1132-1138. 4. Wang D, Beck LA. *Am J Clin Dermatol.* 2016;17:425-443. 5. Greenhawt M. *Allergy Asthma Proc.* 2010;31:392-297. 6. Silverberg NB. *Cutis.* 2016;97:408-412. 7. De Benedetto A, et al. *J Invest Dermatol.* 2009;129:14-30.

Case Study

- 19-year-old woman
- Lifelong history of moderate-to-severe AD
- Presents with worsening itch and frequent flares
- Physical exam
  - Widespread open, excoriated eczematous patches on arms, legs, and trunk
  - She is tired-appearing and scratching throughout the visit
- Medications
  - Triamcinolone 0.1% ointment twice daily when flaring (most of the time)
  - Tacrolimus 0.1% twice daily between flares
  - She has a bag full of moisturizers
  - Has been on antibiotics and oral prednisone in the past few months
- Laboratory tests
  - Has had allergy testing: + to cats and mold and dust mites
  - Has had patch testing: + nickel and + fragrance

BMI = body-mass index; mo = month(s); BP = blood pressure; HbA1c = glycosylated hemoglobin.

Evaluation and Diagnosis

Dermatitis Is a Phenotype

Characteristics

- Itch
- Skin lesions: poorly circumscribed erythema and induration with fine scale
  - Acute: edema/vesicles; quickly reversible
  - Subacute
  - Chronic: lichenification; persistent
- Histology
  - Epidermis: spongiosis, parakeratosis
  - Dermis: superficial perivascular infiltrate (lymphocytes/histiocytes > neutrophils/eosinophils)

Krafchik BR. Atopic dermatitis. In: Schachner LA, Hansen RC. *Pediatric Dermatology*. 4th ed. Elsevier: 2011;851-866.

AD: Diagnosis Features

Features to be considered in diagnosing patients with AD

- **ESSENTIAL FEATURES**, must be present:
  - Pruritus
  - Eczema (acute, subacute, chronic):
    - Typical morphology and age-specific patterns*
    - Chronic or relapsing history

**Patterns include:*
1) *Facial, neck, and extensor involvement in infants and children*
2) *Current or prior flexural lesions in any age group*
3) *Sparing of groin and axillary regions*

- **IMPORTANT FEATURES**, seen in most cases, adding support to the diagnosis:
  - Early age of onset
  - Atopy
    - Personal and/or family history
    - IgE reactivity
  - Xerosis
- **ASSOCIATED FEATURES**, these clinical associations help to suggest the diagnosis of AD but are too non-specific to be used for defining or detecting AD for research and epidemiologic studies:
  - Atypical vascular responses (eg, facial pallor, white dermographism, delayed blanch response)
  - Keratosis pilaris/pityriasis alba/hyperlinear palms/ichthyosis
  - Ocular/periorbital changes
  - Other regional findings (eg, perioral changes/periauricular lesions)
  - Perifollicular accentuation/lichenification/prurigo lesions
- **EXCLUSIONARY CONDITIONS**, it should be noted that a diagnosis of AD depends on excluding conditions such as:
  - Scabies
  - Seborrheic dermatitis
  - Contact dermatitis (irritant or allergic)
  - Ichthyoses
  - Cutaneous T-cell lymphoma
  - Psoriasis
  - Photosensitivity dermatoses
  - Immune deficiency diseases
  - Erythroderma of other causes

Ig = immunoglobulin.

Eichenfield LF, et al. *J Am Acad Dermatol.* 2003;49:1088-1095. Eichenfield LF, et al. *J Am Acad Dermatol.* 2014;70:338-351.

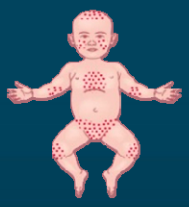
AD: Diagnosis

Clinical diagnosis

1. Pruritus
2. Eczematous eruption with characteristic pattern and morphology
3. Chronic or relapsing

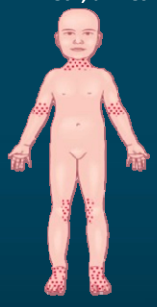
Infantile type

Face, scalp, trunk, extensor surfaces of extremities



Childhood type

Flexural folds of extensors (antecubital, popliteal fossa) neck, ankles



Adult type

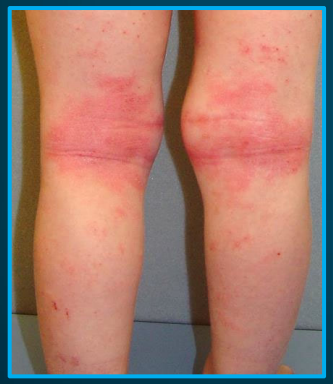
Upper arms, back, wrists, hands, fingers, feet, toes

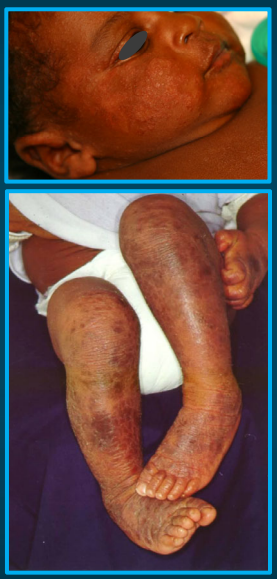
Eichenfield LF, et al. *J Am Acad Dermatol.* 2014;70:338-351. Napolitano M, et al. *G Ital Dermatol Venereol.* 2016;151:403-411.
Krafchik BR. Atopic dermatitis. In: Schachner LA, Hansen RC. *Pediatric Dermatology*. 4th ed. Elsevier: 2011;851-866.

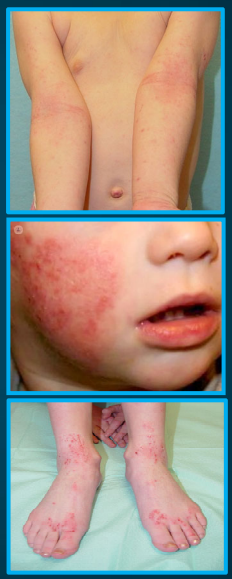
Classic AD Distribution Changes With Age

Infants:
Face, extensor extremities

Children:
Wrists, ankles, antecubital and popliteal fossae

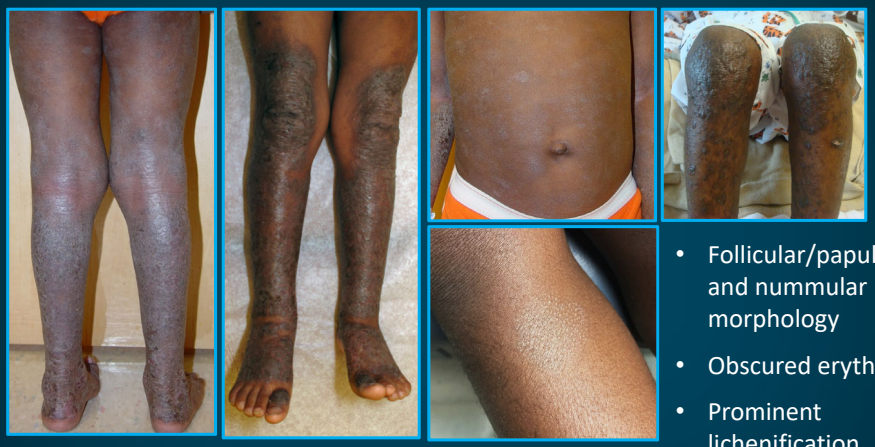






AD across the lifespan. 2017 (https://atopicdermatitis.net/across-lifespan). Accessed January 26, 2021.
Images courtesy of Dr. Peter Lio.

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.
Images courtesy of Dr. Peter Lio.

Phenotypic Mimics

Otherwise healthy

- Pityriasis alba
- Keratosis pilaris
- Ichthyosis vulgaris
- Lichen simplex chronicus
- Contact dermatitis
- Psoriasiform overlap
- Seborrheic dermatitis
- Tinea
- Scabies

Unhealthy

- Immune deficiencies
- Nutritional deficiencies
- Cutaneous T-cell lymphoma
- Genodermatoses

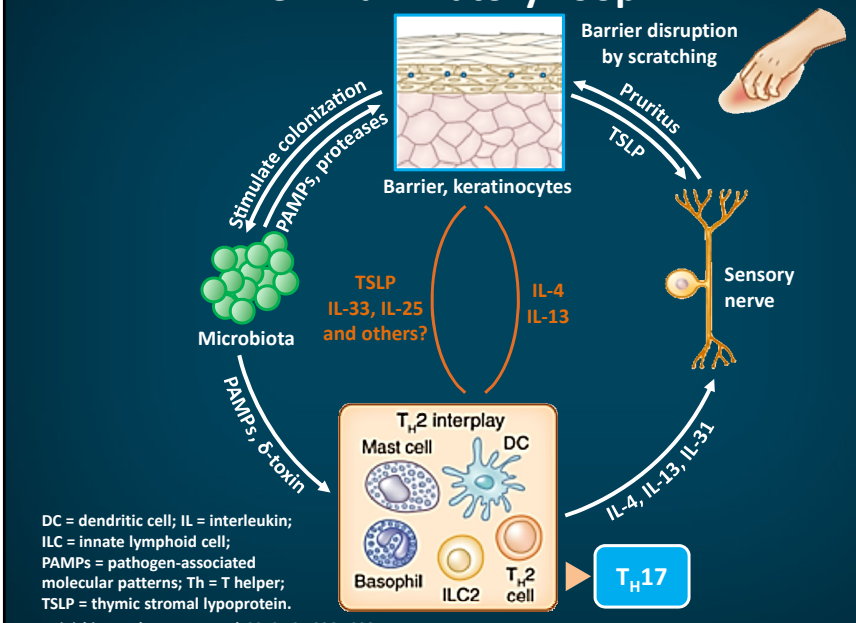
Siegfried EC, Hebert AA. *J Clin Med.* 2015;4:884-917. Wine SJ, Steinberg S. *Can Fam Physician.* 1972;18:65-66. Purohit MP. Lichen simplex chronicus. *DoveMed*. 2018 (www.dovemed.com/diseases-conditions/lichen-simplex-chronicus). Fields D. Types of genodermatoses. *NEWS Medical.* 2019 (www.news-medical.net/health/Types-of-Genodermatoses.aspx).
All URLs accessed August 1, 2020.

Pathogenesis

Animation #1: Pathogenesis

Pathology:
https://youtu.be/u9OLTf1uP2A

The Inflammatory Loop in AD



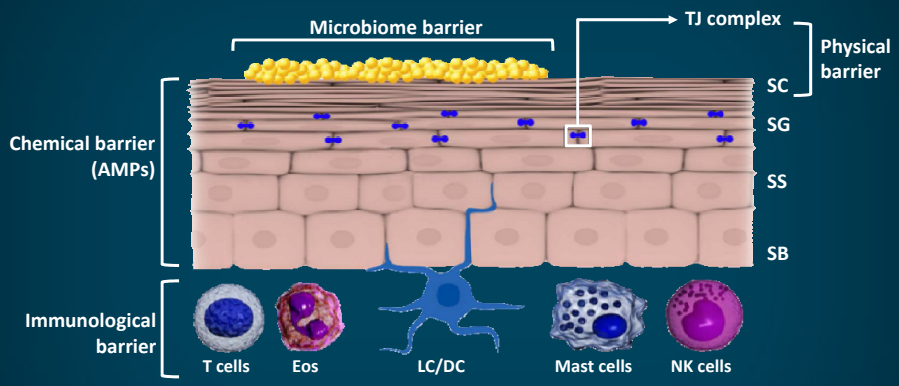
DC = dendritic cell; IL = interleukin; ILC = innate lymphoid cell; PAMPs = pathogen-associated molecular patterns; Th = T helper; TSLP = thymic stromal lypoprotein.

Dainichi T, et al. *Nat Immunol*. 2018;19:1286-1298.

AD: Pathophysiologic Overview

- **Barrier defect**
  - Barrier abnormality is not just an epiphenomenon
  - Initiator of the pathogenesis of the disease state
- Immune dysregulation

Normal Skin Versus Dry Skin



AMPs = antimicrobial peptides; Eos = eosinophil; LD = Langerhans cell; NK = natural killer; SB = stratum basale; SC = stratum corneum; SG = stratum granulosum; SS = stratum spinosum; TJ = tight junction.

Leung DY, Guttman-Yassky E. *J Allergy Clin Immunol.* 2014;134:769-779.

Itching

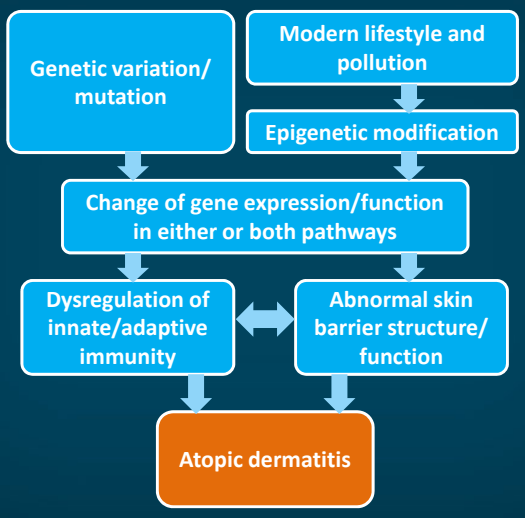
- A decrease of skin hydration of just 10% is crucial for the induction of itch
- Impaired skin barrier facilitates the entry of irritants and itch-causing agents

Lee C-H, et al. *Br J Dermatol.* 2006;154:1100-1107.

AD: Pathophysiologic Overview

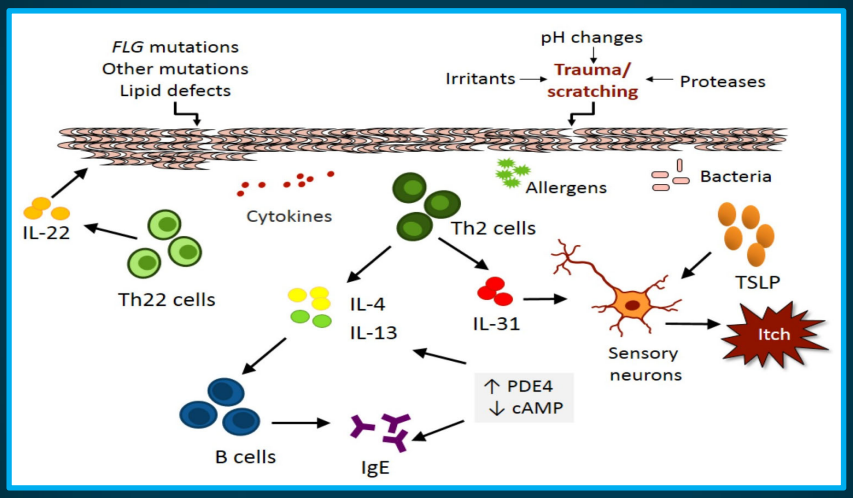
- Barrier defect
  - Barrier abnormality is not just an epiphenomenon
  - Initiator of the pathogenesis of the disease state
- **Immune dysregulation**

Dysregulation in AD



Bin L, Leung DYM. *Allergy Asthma Clin Immunol*. 2016;12:52.

Pathogenesis: Immune Dysregulation



cAMP = cyclic adenosine monophosphate; FLG = filaggrin; PDE4 = phosphodiesterase type 4.

Adapted from Leung DYM, et al. *J Clin Invest*. 2004;113:651-657. Boguniewicz M, et al. *Ann Allergy Asthma Immunol*. 2018;120:10-22.e2. Paller AS, et al. *J Allergy Clin Immunol*. 2017;140:633-643.

Management

Disease Issues

- AD is a *chronic disease* with episodic flares
- There is **no cure;** the goal of treatment is to maintain control
- It has been suggested that early optimal and successful treatment of atopic dermatitis may prevent or attenuate the development of other atopic conditions[1]

Johns Hopkins Medicine. Eczema (https://www.hopkinsmedicine.org/health/conditions-and-diseases/eczema). Accessed August 26, 2020. Tollefson MM, Bruckner AL. *Pediatrics.* 2014;134:e1735-e1744. 1. Tan RA, Corren J. *Immunol Allergy Clin North Am*. 2011;31(3):481–491.

Management Issues

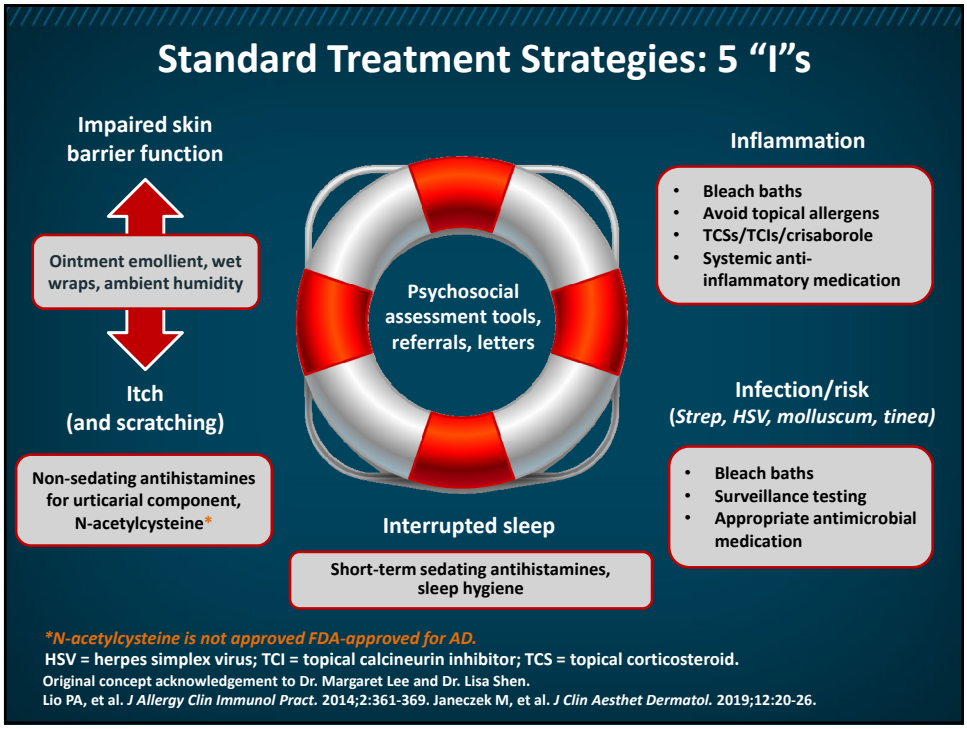
Variables impacting treatment choice

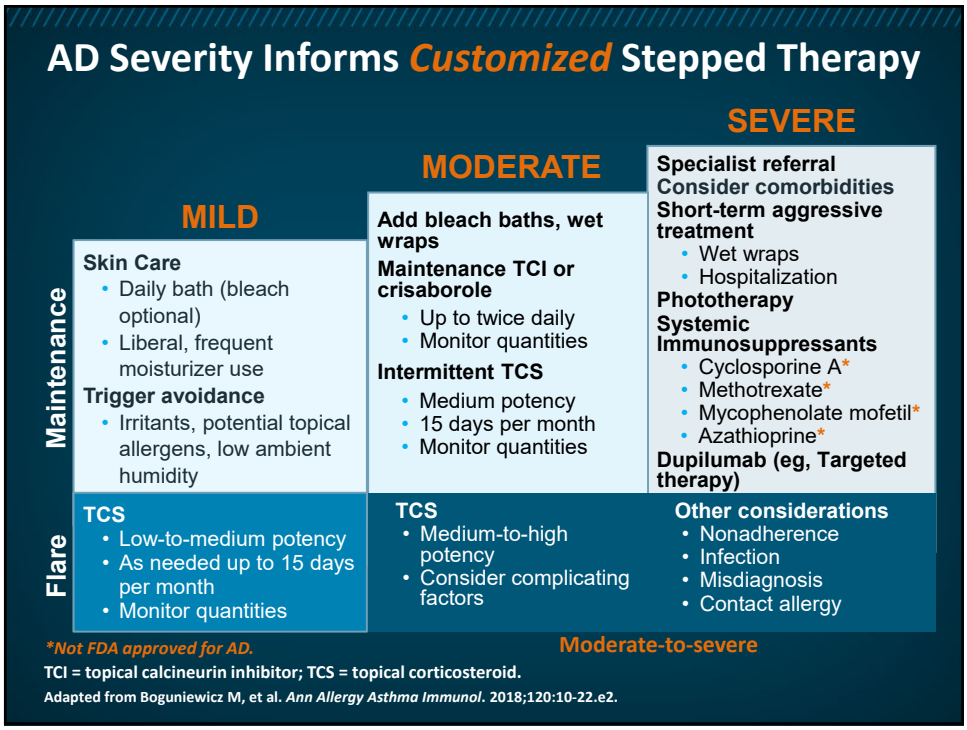
- Patient preference and ability
- Safety and efficacy
- Cost and access
- Comorbidities

Therapeutic goals

- To reduce symptoms, prevent exacerbations, and minimize therapeutic risks
- Prolonged remission and infrequent flares
  - Improved adherence through affordable, easy-to-use and effective regimen
  - Resultant improved QoL, including restful sleep and undisturbed activities of daily living

Retzler J, et al. *Qual Life Res.* 2019;28:2373-2381. Tollefson MM, Bruckner AL. *Pediatrics.* 2014;134:e1735-e1744. Weston WL, Howe W. Treatment of atopic dermatitis. 2020 (https://www.uptodate.com/contents/treatment-of-atopic-dermatitis-eczema). Avena-Woods C. *Am J Manag Care.* 2017;23:S115-S123 (https://www.ajmc.com/view/overview-of-atopic-dermatitis-article). All URLs accessed August 26, 2020.


Standard Treatment Strategies: 5 "I"s
Impaired skin barrier function
Ointment emollient, wet wraps, ambient humidity
Itch (and scratching)
Non-sedating antihistamines for urticarial component, N-acetylcysteine*
Psychosocial assessment tools, referrals, letters
Inflammation
Bleach baths
Avoid topical allergens
TCSs/TCIs/crisaborole
Systemic anti-inflammatory medication
Infection/risk (Strep, HSV, molluscum, tinea)
Bleach baths
Surveillance testing
Appropriate antimicrobial medication
Interrupted sleep
Short-term sedating antihistamines, sleep hygiene
*N-acetylcysteine is not approved FDA-approved for AD.
HSV = herpes simplex virus; TCI = topical calcineurin inhibitor; TCS = topical corticosteroid.
Original concept acknowledgement to Dr. Margaret Lee and Dr. Lisa Shen.
Lio PA, et al. J Allergy Clin Immunol Pract. 2014;2:361-369. Janeczek M, et al. J Clin Aesthet Dermatol. 2019;12:20-26.


AD Severity Informs Customized Stepped Therapy
MILD
MODERATE
SEVERE
Maintenance
Skin Care
Daily bath (bleach optional)
Liberal, frequent moisturizer use
Trigger avoidance
Irritants, potential topical allergens, low ambient humidity
Add bleach baths, wet wraps
Maintenance TCI or crisaborole
Up to twice daily
Monitor quantities
Intermittent TCS
Medium potency
15 days per month
Monitor quantities
Specialist referral
Consider comorbidities
Short-term aggressive treatment
Wet wraps
Hospitalization
Phototherapy
Systemic Immunosuppressants
Cyclosporine A*
Methotrexate*
Mycophenolate mofetil*
Azathioprine*
Dupilumab (eg, Targeted therapy)
Flare
TCS
Low-to-medium potency
As needed up to 15 days per month
Monitor quantities
TCS
Medium-to-high potency
Consider complicating factors
Other considerations
Nonadherence
Infection
Misdiagnosis
Contact allergy
*Not FDA approved for AD.
Moderate-to-severe
TCI = topical calcineurin inhibitor; TCS = topical corticosteroid.
Adapted from Boguniewicz M, et al. Ann Allergy Asthma Immunol. 2018;120:10-22.e2.

Assessment of Disease Severity

- Validated AD-specific severity scales
  - **SCORAD** (**SCOR**ing **A**topic **D**ermatitis index): includes extent, sleep, and itch
  - **EASI** (**E**czema **A**rea and **S**everity **I**ndex): includes extent
  - **IGA** (**I**nvestigator's **G**lobal **A**ssessment): simple 0- to 5-point scale
- Modified forms used in clinical trials
- SCORAD and EASI are too cumbersome for clinical practice
  - But may be important for insurance documentation
- IGA is simple, useful, and may be required for insurance authorization

Siegfried EC, et al. *Pediatr Dermatol.* 2018;35:303-322. Chopra R, et al. *Br J Dermatol.* 2017;177:1316-1321. Brunk D. *Dermatol News.* 2020 (www.mdedge.com/dermatology/article/220713/atopic-dermatitis/expert-discusses-her-approach-using-systemic-agents). Accessed March 1, 2021. Silverberg JI, et al. *Br J Dermatol.* 2019;181:80-87.

AD: Current Treatment Options
Considerations for Treatment

- Majority of patients with mild AD can expect to obtain clinical improvement and disease control with use of emollients, conventional topical therapies (TCS and/or TCI), and environmental and/or occupational modifications, when necessary
- These interventions may not be sufficient for patients with moderate-to-severe or difficult-to-control disease

Sidbury R, et al. *J Am Acad Dermatol.* 2014;71:327-349. Wollenberg A, et al. *J Eur Acad Dermatol Venereol.* 2016;30:729-747. Saeki H, et al. *J Dermatol.* 2016;43:1117-1145.

Optimizing Long-term Control

Address only intermittent flares

Prescription antibiotics, potent TCS, and prednisone

Yields alternating roller-coaster improvement 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.

Adherence

- The ***most important contributory factor*** to successful treatment
- Barriers
  - Time constraints
  - Unclear or difficult-to-follow instructions
  - Medication phobia
  - Cost/access
- Confirming medication use will inform therapeutic response

Strategies for Improvement

- **Consistent messaging across providers**
- **Frequent follow-up visits**
- **Patient/parent education**
- **Give specific skin care instructions**
- **Prescribe adequate quantities**
- **Monitor medication use**
- **Electronic reminders (eg, email, text messages)**
- **Experience positive outcomes**

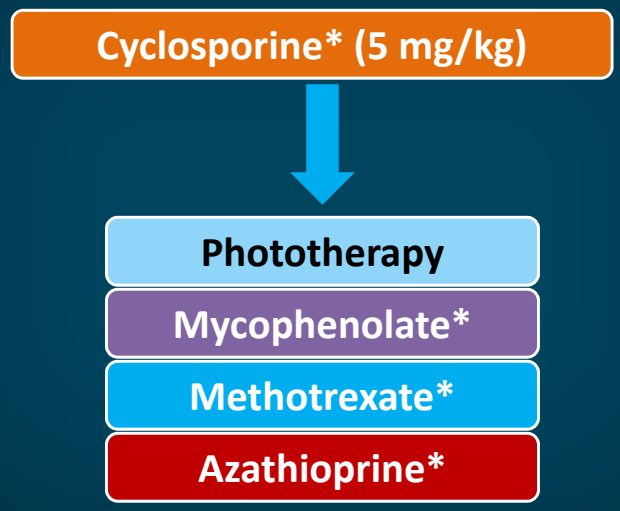
Bass AM, et al. *J Clin Med.* 2015;4:231-242. Snyder A, et al. *Cutis.* 2015;96:397-401. Ellis RM, et al. *Pediatr Dermatol.* 2011;28:242-244. Smith SD, et al. *Med J Aust.* 2013;199:467-469. Shi VY, et al. *JAMA Dermatol.* 2013;149:481-483. Pena-Robichaux V, et al. *Dermatol Res Pract.* 2010;2010:894258. Pérez-Jover V, et al. *J Med Internet Res.* 2019;21:e12505.

Systemic Agents

Animation #2: MOAs of Current and Emerging Targeted Therapies for AD

MOA: https://youtu.be/UfKs4V4Ui3s

Conventional Systemic Treatment Algorithm



*Off-label use; Not FDA-approved for use in atopic dermatitis.

Discontinuation Rates of Immunosuppressive Therapies

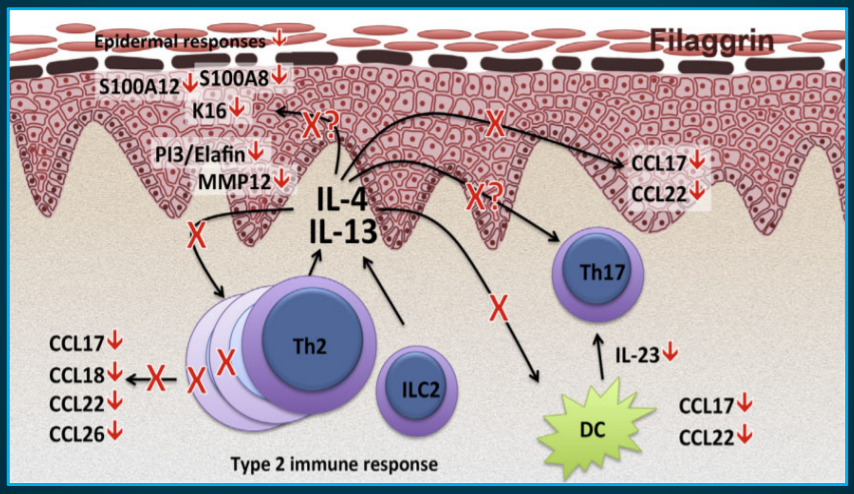
	CsA* (N=356) (at 6-year follow-up)[1]	AZA* (N=94) (at 3-year follow-up)[2]	MTX* (N=89) (at 2-year follow-up)[3]	EC-MPS* (N=84) (at 3-year follow-up)[2]
AE	22%	36%	25%	14%
Inefficacy	16%	19%	15%	38%
Controlled AD	26%	11%	6%	11%
Other reasons	11%	6%	7%	4%

*Off-label use; Not FDA-approved for use in atopic dermatitis.

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

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.

AD Targets: IL-4/IL-13



Brunner PM, et al. *J Allergy Clin Immunol*. 2017;139(4 suppl):S65-S76.

Dupilumab

- A human monoclonal antibody against IL-4Rα
- Inhibits signaling of IL-4 and IL-13
- FDA approved for moderate-to-severe AD in adults in March 2017, for aged ≥12 years in 2019, and for aged ≥6 years in 2020
- Also FDA approved for moderate-to-severe eosinophilic asthma (aged ≥12 years) and for add-on maintenance therapy for CRSwNP (adults)
- Subcutaneous injection Q2W (Q4W in those weighing <30 kg)

CRSwNP = chronic rhinosinusitis with nasal polyposis; Q2W = every 2 weeks; Q4W = every 4 weeks; Rα = receptor α.

Dupilumab (Dupixent®) PI 2020 (https://www.regeneron.com/sites/default/files/Dupixent_FPI.pdf). Sanofi dupilumab press release. March 11, 2019 (http://www.news.sanofi.us/2019-03-11-FDA-approves-Dupixent-R-dupilumab-for-moderate-to-severe-atopic-dermatitis-in-adolescents#:~:text=and%20TARRYTOWN%2C%20N.Y.%2C%20March%2011,prescription%20therapies%2C%20or%20when%20those). Regeneron dupilumab press release. May 26, 2020 (https://www.prnewswire.com/news-releases/fda-approves-dupixent-dupilumab-as-first-biologic-medicine-for-children-aged-6-to-11-years-with-moderate-to-severe-atopic-dermatitis-301065273.html). All URLs accessed February 18, 2021.

Dupilumab in Children Aged 6 to 11 Years

- Phase 3 RCT double-blind, placebo-controlled trial in 367 children with severe AD
- 90% had >1 atopic comorbidity
- Results at 16 weeks:
  - 33% of patients who received dupilumab Q4W (300 mg regardless of weight) and 30% of patients who received dupilumab Q2W (100 mg or 200 mg based on weight) achieved clear or almost clear skin (IGA 0 or 1) compared with 11% for TCSs alone ($P \leq .0001$ and $P \leq .001$, respectively)
  - 70% of patients who received Q4W drug and 67% who received Q2W drug achieved EASI-75 compared with 27% TCSs alone ($P \leq .0001$ for both)
  - AEs: conjunctivitis, nasopharyngitis, and injection site reactions

EASI-75 = 75% reduction from baseline in EASI.

Paller AS, et al. 2020 Revolutionizing Atopic Dermatitis (RAD) Virtual Symposium. Abstract 215. https://revolutionizingad.com/education-resources/2020-virtual/2020-virtual-abstracts-5. Paller AS, et al. *J Am Acad Dermatol*. 2020;83:1282-1293.

Dupilumab

- It appears much safer than conventional immunosuppressants, but other potential considerations include:
  - Conjunctivitis in up to 10% of patients
  - Injection site reaction/systemic reactions
  - Cost may be a factor
  - Injection
  - Currently approved for individuals as young as 6 years of age, but younger groups are being studied

Paller AS, etal. *J Am Acad Dermatol*. 2020;83:1282-1293.

Pipeline: Selected Agents

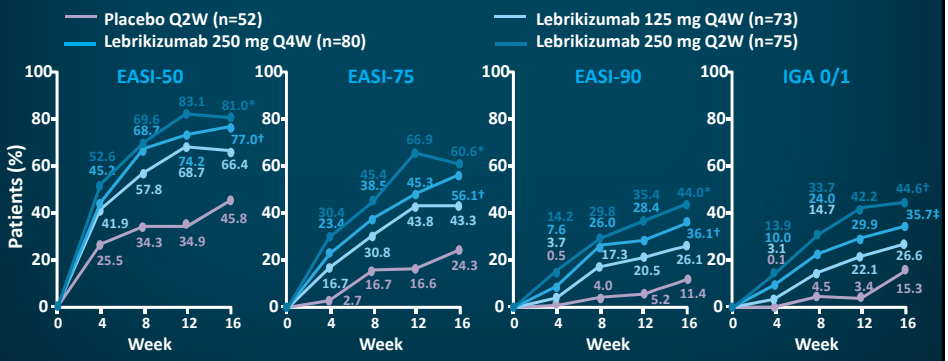
Drug	Target
TOPICAL	
Delgocitinib	JAK1, JAK2, JAK3, TYK2
E6005	PDE4
OPA-15406	PDE4
Ruxolitinub	JAK1 and JAK2
Tapinarof	AHR ligand
ORAL	
Abrocitinib	JAK1
ASN002	JAK, SYK
Baricitinib	JAK1 and JAK2
Upadacitinib	JAK1
SYSTEMIC INJECTION	
Lebrikizumab	IL-13
Nemolizumab	IL-31
Tralokinumab	IL-13

AHR = aryl hydrocarbon receptor; TYK2 = tyrosine kinase 2; SYK = spleen tyrosine kinase.

National Eczema Association. Eczema treatments in development (https://nationaleczema.org/research/eczema-treatment-research). Accessed September 19, 2019. Vakharia PP, Silverberg JI. *Lancet Child Adolesc Health*. 2019;3:343-353.

Emerging Agent: Lebrikizumab (Anti–IL-13)

- A phase 2b, randomized, monotherapy trial in 280 adults with moderate-to-severe AD inadequately controlled with TCS
- At week 12, significantly more patients achieved EASI-50/-75/-90 with lebrikizumab 250 mg Q2W or Q4W vs placebo



*P< .001; †P< .01; ‡P< .05 vs placebo. EASI-50/-90 = 50%/90% improvement from baseline EASI.

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

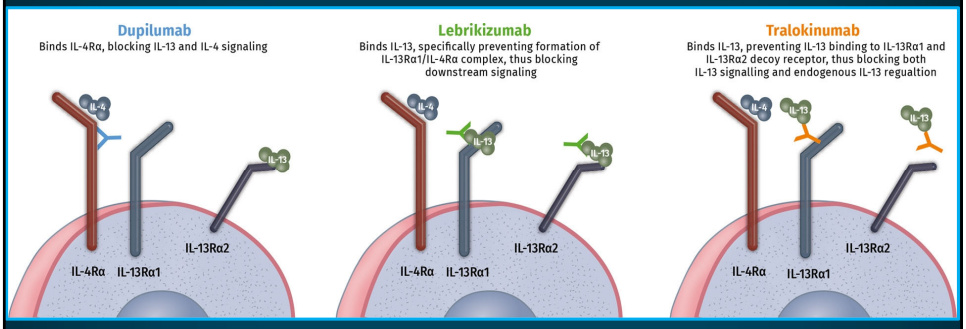
Emerging Agent: Tralokinumab (Anti–IL-13)

Study	Treatment	IGA 0/1 Response at Week 16	EASI-75 Response at Week 16
ECZTRA 1[1]	Tralokinumab	16%	25%
	Placebo	7%	13%
	Placebo-adjusted response	**9%**	**12%**
ECZTRA 2[1]	Tralokinumab	22%	33%
	Placebo	11%	11%
	Placebo-adjusted response	**11%**	**22%**
ECZTRA 3[2]	Tralokinumab	39%	56%
	Placebo	26%	36%
	Placebo-adjusted response	**12%**	**20%**

- ECZTRA 1/2: 51%-60% maintained response over 52 weeks
- ECZTRA 3: 78%-93% maintained response over 32 weeks

1. Wollenberg A, et al. *Br J Dermatol*. 2020. doi:10.1111/bjd.19574. 2. Silverberg J, et al. *Br J Dermatol*. 2020. doi:10.1111/bjd.19573.

Not Identical Mechanisms



Lebrikizumab does not prevent binding to Rα2 → no increased levels of IL-13

Tralokinumab prevents the binding to Rα2 → thus increased total IL-13 levels

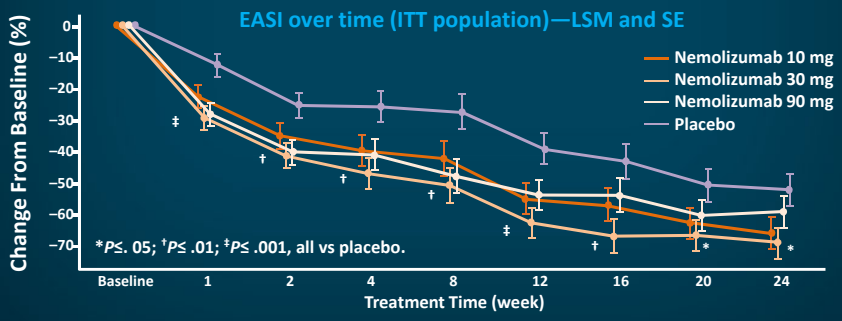
What does this mean?

We don't know!

Moyle M, et al. *Exp Dermatol*. 2019;28:756-768.

Emerging Agent: Nemolizumab (Anti–IL-31)

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

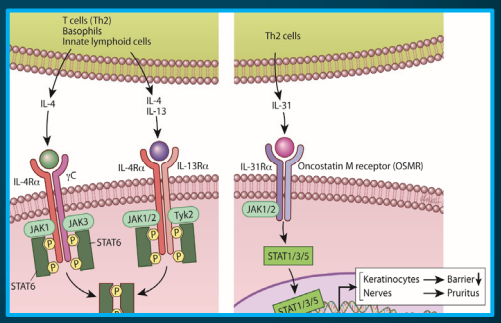


ITT = intention-to-treat; LSM = least squares mean.

Silverberg JI, et al. *J Allergy Clin Immunol*. 2020;145:173-182.

Janus Associated Kinase

- JAK-STAT pathway is a conserved master regulator of immunity and myeloproliferation
- JAK inhibitors are used to treat several hematologic and inflammatory diseases
- Small molecules (including JAK inhibitors) show improvement in AD disease scores, patient-reported outcomes, and QoL



STAT = signal transducer and activator of transcription.

Cotter DG, et al. *J Am Acad Dermatol*. 2018;78:S53-S62. Mobasher P, et al. *J Dermatolog Treat*. 2019;30:550-557.

Paller AS, et al. *J Allergy Clin Immunol*. 2017;140:633-643.

JAK Inhibitors: Systemic

- **Abrocitinib**[1]
  - Received breakthrough therapy designation in February 2018
  - Positive topline results from phase 3 trial in patients aged ≥12 years with severe disease
    - By week 12, percentage of patients who met each co-primary efficacy endpoint and each key secondary endpoint with either dose, 100 mg or 200 mg, was significantly higher than placebo
- **Baricitinib**[2]
  - In a phase 2 trial more subjects achieved an EASI-50 score on daily 4-mg dose than placebo at 16 weeks
    - All patients were using TCSs for 1 month prior to initiation
    - Side effects included lymphopenia, neutropenia, AD exacerbation, and headache with no serious AEs
  - Multiple phase 3 trials for adults are evaluating safety and efficacy and use as monotherapy
- **Upadacitinib**[3,4]
  - Received breakthrough therapy designation in January 2018
  - Phase 2b trial revealed that 30-mg dose was superior to placebo in EASI score improvement and pruritus reduction
  - Phase 3 trials underway

1. Terry M. BioSpace.com. May 15, 2019 (https://www.biospace.com/article/pfizer-s-abrocitinib-hits-primary-endpoints-in-atopic-dermatitis-trial). 2. Guttman-Yassky E, et al. *J Am Acad Dermatol*. 2019;80:913-921. 3. Guttman-Yassky E, et al. *J Allergy Clin Immunol*. 2020;145:877-884. 4. Abbvie upadacitinib release. January 8, 2018 (https://news.abbvie.com/news/abbvies-upadacitinib-granted-breakthrough-therapy-designation-from-us-food-and-drug-administration-for-atopic-dermatitis.htm). All URLs accessed February 23, 2021.

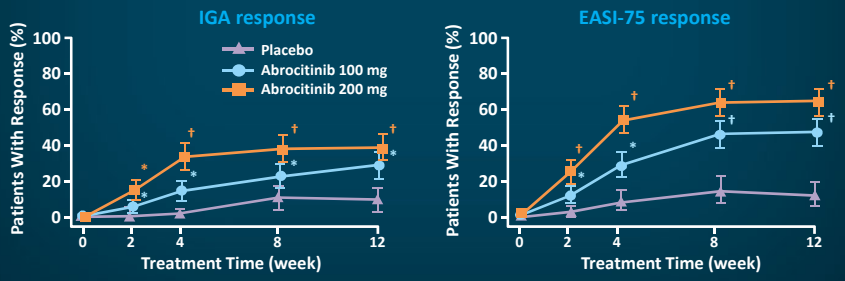
JAK Inhibitors: Topical

- **Delgocitinib**[1,2]
  - Dose-ranging (0.25%-3%) ointment vs vehicle vs tacrolimus 0.1% twice daily x 4 weeks
  - All doses > vehicle in EASI (73% vs 12% in 3% group)
  - Tacrolimus = 62% reduction
  - No serious AEs
- **Ruxolitinib**
  - Phase 2 randomized, dose-ranging, vehicle- and active-controlled study to evaluate safety and efficacy in adult patients[3]
    - 1.5% twice-daily group > vehicle in EASI (71.6% improvement at 4 weeks) and noninferior to triamcinolone cream 0.1%
  - Phase 1 study in children aged 2-7 years and 2 phase 3 studies in patients aged ≥12 years (TruE-AD1 and TruE-AD2) are underway

1. Nakagawa H, et al. *Br J Dermatol*. 2018;178:428-432. 2. Bissonnette R. *Br J Dermatol*. 2018;178:321. 3. Kim BS, et al. *J Am Acad Dermatol*. 2020;82(6):1305-1313.

Emerging Agent: Abrocitinib

- Phase 3 randomized trial of 391 patients aged ≥12 years with moderate-to-severe AD for ≥1 year and inadequate response to topical medication for ≥4 weeks within 6 months
- At week 12, IGA 0/1 was achieved in greater proportion of patients in the 200- and 100-mg abrocitinib groups vs placebo (38.1% and 28.4% vs 9.1%, respectively; *P*< .001)

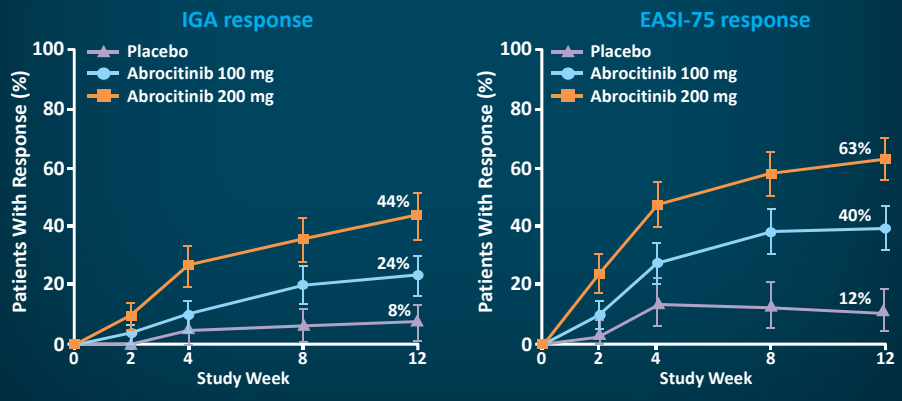


*P< .05; †P< .001 vs placebo. Note: 95% CI graphed.

Silverberg JI, et al. *JAMA Dermatol*. 2020;156:863-873.

Abrocitinib: JADE MONO-1

- Phase 3 trial, 387 patients aged ≥12 years with moderate-to-severe AD
- Primary endpoint of IGA 0/1 achieved by 24% with abrocitinib 100 mg (*P*= .0037), 44% with 200 mg (*P*< .0001), and 8% with placebo



Simpson EL, et al. *Lancet*. 2020;396:255-266.

Abrocitinib in Pediatric AD

- Inhibits IL-13, IL-31, interferon γ STAT1, IL-15 STAT5, and IL-4 STAT6[1]
- Phase 3 JADE program in patients with moderate-to-severe AD[2-4]
  - The 12-week study compared abrocitinib (PF-04965842; B7451012) 200 mg and 100 mg with placebo in 387 patients aged ≥12 years
  - Primary endpoint: proportion of patients experiencing an IGA score of clear (0) or almost clear (1) skin and ≥2-point improvement relative to baseline
  - Co-primary endpoint: proportion of participants achieving ≥75% change in EASI score from baseline

1. Gooderham MJ, et al. *JAMA Dermatol*. 2019;e192855. 2. Clinical Trials Arena. Press release. October 14, 2019 (www.clinicaltrialsarena.com/news/pfizer-abrocitinib-mono1-data). Accessed January 3, 2020. 3. Silverberg JI, et al. RAD 2020. Abstract 148. 4. Simpson EL, et al. RAD 2020. Abstract 166.

Abrocitinib in Pediatric AD (continued)

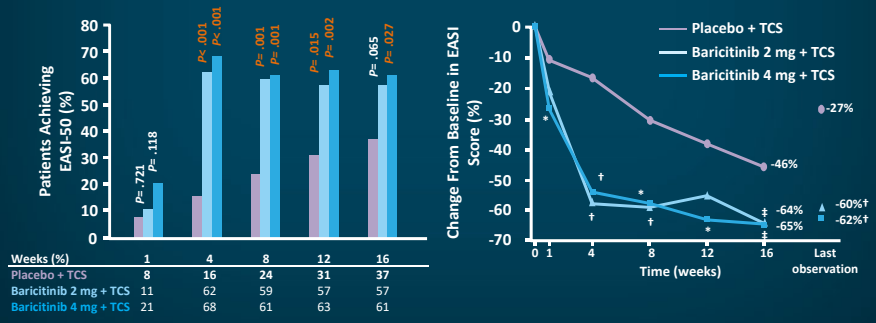
- Key secondary endpoints
  - ≥4-point decrease in itch severity on pruritus NRS
  - Magnitude of reduction in PSAAD scale
- Abrocitinib met all co-primary and secondary endpoints
- Abrocitinib displayed significant improvements compared with placebo in the following response rates: IGA, EASI-75, EASI-90, and NRS ≥4-point
- Improvements were observed to be significantly greater with both doses

NRS = Numerical Rating Scale; PSAAD = Pruritus and Symptoms Assessment for Atopic Dermatitis.

Clinical Trials Arena. Press release. October 14, 2019 (www.clinicaltrialsarena.com/news/pfizer-abrocitinib-mono1-data). Accessed January 3, 2020. Silverberg JI, et al. RAD 2020. Abstract 148. 4. Simpson EL, et al. RAD 2020. Abstract 166.

Emerging Agents: Baricitinib

- Phase 2 trial of 124 patients with moderate-to-severe AD who applied topical steroids for 4 weeks before randomization to baricitinib 2 mg or 4 mg or to placebo
- Significantly more patients who received baricitinib 4 mg achieved EASI-50 than those who received placebo (61% vs 37%; *P*= .027) at 16 weeks
- Treatment-emergent AEs were reported in 71% of baricitinib 4 mg and 49% of placebo recipients (Most common: headache, increased creatine phosphokinase, nasopharyngitis)



*P≤ .01; †P≤ .001; ‡P< .05.

Guttman-Yassky E, et al. *J Am Acad Dermatol*. 2019;80:913-921.e9.

Baricitinib: BREEZE-AD5 Trial

- Phase 3 trial of 440 adults with moderate-to-severe AD for ≥12 months and inadequate response or intolerance to topical medications <6 months prior to screening

Responses at Week 16	Baricitinib 1 mg	Baricitinib 2 mg	Placebo
Patients achieving EASI-75	13%	30%*	8%
Patients achieving a vIGA-AD of 0/1	13%†	24%*	5%
Patients achieving ≥4-point improvement on Itch NRS	16%†	25%*	6%
Mean change in DLQI	-5.5	-7.5‡	-4.0

- Improvement in proportion of patients who achieved ≥4-point improvement on Itch NRS statistically significant as early as week 2 for both baricitinib arms

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

DLQI = Dermatology Life Quality Index; vIGA = validated IGA for AD.

Simpson EL, et al. RAD 2020. Abstract 130.

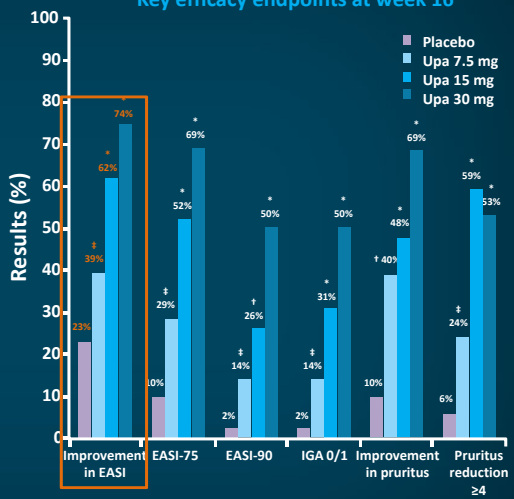
Emerging Agents: Upadacitinib

- Phase 2b trial in 167 adults with moderate-to-severe AD inadequately controlled by topical treatment[1]
- Significant improvement in EASI from baseline to week 16 with upadacitinib[1]

Top-Line Results: Measure Up Phase 3 Studies Patients Achieving EASI-75 at Week 16[2,3]

Study	Upa 15 mg	Upa 30 mg	Placebo	*P*
Measure Up 1	70%	80%	16%	< .001
Measure Up 2	60%	73%	13%	< .001

Key efficacy endpoints at week 16[1]



*$P \leq .001$; †$P \leq .01$; ‡$P \leq .05$.

Upa = upadacitinib.

1. Guttman-Yassky E, et al. *J Allergy Clin Immunol*. 2020;145:877-884. 2. AbbVie. Measure Up 1 press release. June 18, 2020 (https://news.abbvie.com/news/press-releases/rinvoq-upadacitinib-monotherapy-shows-improvement-in-skin-clearance-and-itch-in-first-phase-3-study-for-atopic-dermatitis.htm#:~:text=Measure%20Up%201%20is%20the,significant%20improvement%20in%20skin%20clearance). 2. AbbVie. Measure Up 2 press release. July 21, 2020 (https://news.abbvie.com/news/press-releases/rinvoq-upadacitinib-monotherapy-meets-all-primary-and-secondary-endpoints-in-second-phase-3-study-for-atopic-dermatitis.htm). All URLs accessed February 18, 2021.

Team-Based Care and Shared Decision-Making

The Importance of Patient and Caregiver Education in AD

5 Essential Steps of SDM

SHARE Approach

1. **S**eek your patient's participation
2. **H**elp your patient explore and compare treatment options
3. **A**ssess your patient's values and preferences
4. **R**each a decision with your patient
5. **E**valuate your patient's decision

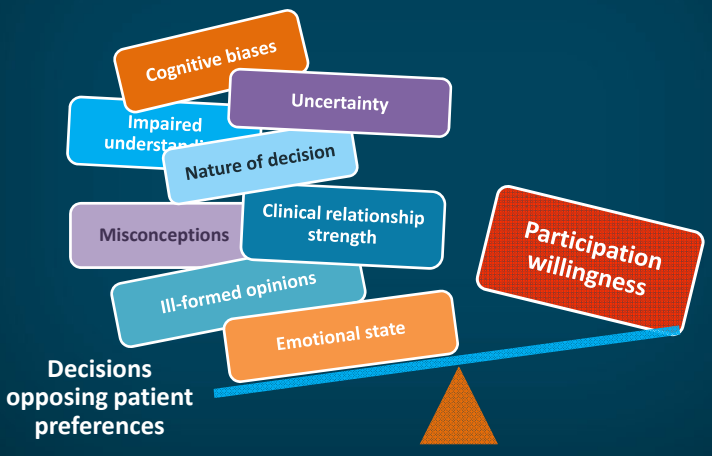
It's all about communication!

SDM = shared decision-making.

AHRQ. Share Approach (www.ahrq.gov/sites/default/files/publications/files/share-approach_factsheet.pdf). Accessed January 3, 2020.

Patient Barriers

Factors that can influence the patient's preference and participation in SDM overall



Fisher KA, et al. *Patient Educ Couns.* 2018;101:2195-2201.

SDM in Managing AD

- Questions to ask:
  - What factors improve or worsen your (or your child's) condition?
  - What things does your condition make it harder for you (or your child) to do?
  - What aspects bother you or your child the most?
  - What is the cause, in your opinion?
  - How is treatment going? Describe what you do in detail.
  - What concerns do you have about treatment?
  - What gets in the way of treatment?

LeBovidge JS, et al. *J Allergy Clin Immunol*. 2016;138:325-334.

SDM Take-Aways

Involve the patient and other members of the healthcare team in the SDM process

Intervention options should be **neutrally presented** and include discussion of risks, benefits, and no intervention

Use decision aids to enhance patient understanding and communication with the healthcare team

Complete **all steps** in the SDM process

SDM Take-Aways (continued)

- The final shared decision should harmonize with the patient's values and goals
- Fostering "choice awareness" in your patient interactions can help facilitate SDM
- SDM can be a **positive process** for both the healthcare team *and* the patient

Revisiting the Case

Case Study

- 19-year-old woman
- Lifelong history of moderate-to-severe AD
- Presents with worsening itch and frequent flares
- Physical exam
  - Widespread open, excoriated eczematous patches on arms, legs, and trunk
  - She is tired-appearing and scratching throughout the visit
- Medications
  - Triamcinolone 0.1% ointment twice daily when flaring (most of the time)
  - Tacrolimus 0.1% twice daily between flares
  - She has a bag full of moisturizers
  - Has been on antibiotics and oral prednisone in the past few months
- Laboratory tests
  - Has had allergy testing: + to cats and mold and dust mites
  - Has had patch testing: + nickel and + fragrance

BMI = body-mass index; mo = month(s); BP = blood pressure; HbA1c = glycosylated hemoglobin.

What Would You Do?

- She is doing a lot of topicals
- She is concerned about steroid overuse and side effects
- She has had oral prednisone which also signals severe disease

Options

- Phototherapy
- Systemic agent
  - Conventional immunosuppressant
  - Targeted therapy

Conclusions

- AD is a chronic disease with a significant impact on QoL
- **A pro**active approach is more effective than **re**active treatment
- Proactive treatment is stepwise and based on severity
- Management can be ***difficult*** and potentially complicated by conflicting messages from different care team members (clinicians and family)
- **Adherence** is **key** to successful therapy
- Evolving biomarkers and targeted treatments promise to revolutionize treatment

Thank You!

Exploring the Role of JAK Inhibitors in Moderate to Severe Atopic Dermatitis
TOOLKIT

Additional Reading

Current guidelines for the evaluation and management of atopic dermatitis: a comparison of the Joint Task Force Practice Parameter and American Academy of Dermatology guidelines. **(Eichenfield LF, Ahluwalia J, Waldman A, et al. *J Allergy Clin Immunol*. 2017;139(4 suppl):S49-S57)**	https://www.ncbi.nlm.nih.gov/pubmed/28390477
The burden of atopic dermatitis: summary of a report for the National Eczema Association. **(Drucker AM, Wang AR, Li WQ, et al. *J Invest Dermatol*. 2017;137:26-30)**	https://www.ncbi.nlm.nih.gov/pubmed/27616422
Expert perspectives on management of moderate-to-severe atopic dermatitis: a multidisciplinary consensus addressing current and emerging therapies. **(Boguniewicz M, Alexis AF, Beck LA, et al. *J Allergy Clin Immunol Pract*. 2017;5:1519-1531)**	https://www.ncbi.nlm.nih.gov/pubmed/28970084
Health outcome measures in atopic dermatitis: a systematic review of trends in disease severity and quality-of-life instruments 1985-2010. **(Rehal B, Armstrong A. *PLoS One*. 2011;6:e17520)**	https://www.ncbi.nlm.nih.gov/pubmed/21533286
Deciphering the complexities of atopic dermatitis: shifting paradigms in treatment approaches. **(Leung DY, Guttman-Yassky E. *J Allergy Clin Immunol*. 2014;134:76-779)**	https://www.ncbi.nlm.nih.gov/pubmed/25282559
Approach to the Assessment and Management of Pediatric Patients With Atopic Dermatitis: A Consensus Document. Section III: Treatment Options for Pediatric Atopic Dermatitis. **(Lansang P, Lam JM, Marcoux D, et al. *J Cutan Med Surg*. 2019;23(5 suppl):19S-31S)**	https://journals.sagepub.com/doi/full/10.1177/1203475419882647

Multidisciplinary interventions in the management of atopic dermatitis. **(LeBovidge JS, Elverson W , Timmons KG, et al. *J Allergy Clin Immunol*. 2016;138(2):325-334)**	https://www.ncbi.nlm.nih.gov/pubmed/27497275
Emerging therapies for atopic dermatitis: JAK inhibitors. **(Cotter DG, Schairer D , Eichenfield L. *J Am Acad Dermatol*. 2018 Mar;78(3 Suppl 1):S53-S62)**	https://pubmed.ncbi.nlm.nih.gov/29248518/
Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. **(Eichenfield LF, Wynnis LT, Chamlin SL, et al. *J Am Acad Dermatol*. 2014;70:338-351)**	https://pubmed.ncbi.nlm.nih.gov/24290431/
Comorbidities and the impact of atopic dermatitis. **(Silverberg JI. *Ann Allergy Asthma Immunol.* 2019;123:144-151)**	https://pubmed.ncbi.nlm.nih.gov/31034875/
New and emerging therapies for paediatric atopic dermatitis. **(Vakharia PP, Silverberg JI. *Lancet Child Adolesc Health*. 2019;3:343-353)**	https://pubmed.ncbi.nlm.nih.gov/30904349/
Quality of life and childhood atopic dermatitis: the misery of living with childhood eczema. **(Lewis-Jones S. *Int J Clin Pract*. 2006;60:984-992)**	https://pubmed.ncbi.nlm.nih.gov/16893440/

Selected Ongoing Clinical Trials

Systemic Therapies for Pediatric Atopic Dermatitis **NCT01447381**	https://clinicaltrials.gov/ct2/show/NCT01447381
Defining the Skin and Blood Biomarkers of Pediatric Atopic Dermatitis **NCT01782703**	https://clinicaltrials.gov/ct2/show/NCT01782703

A Pharmacokinetic Study of Ruxolitinib Phosphate Cream in Pediatric Subjects With Atopic Dermatitis NCT03257644	https://clinicaltrials.gov/ct2/show/NCT03257644
A Study to Evaluate the Pharmacokinetics, Safety and Tolerability of Upadacitinib in Pediatric Subjects With Severe Atopic Dermatitis NCT03646604	https://clinicaltrials.gov/ct2/show/NCT03646604
A Study of Baricitinib (LY3009104) in Participants With Moderate to Severe Atopic Dermatitis NCT03559270	https://clinicaltrials.gov/ct2/show/NCT03559270
Study of Abrocitinib Compared With Dupilumab in Adults With Moderate to Severe Atopic Dermatitis on Background Topical Therapy NCT04345367	https://clinicaltrials.gov/ct2/show/NCT04345367

Resources for Clinicians and Patients

American Academy of Pediatrics (AAP)	https://www.aap.org/en-us/Pages/Default.aspx
American Academy of Dermatology (AAD)	www.aad.org/public/diseases/eczema/atopic-dermatitis
The American Academy of Allergy, Asthma and Immunology (AAAAI)	https://www.aaaai.org/
Asthma and Allergy Foundation of America	www.aafa.org/page/eczema.aspx
Children's National	https://childrensnational.org/visit/conditions-and-treatments/allergies-immunology/eczema-atopic-dermatitis
National Eczema Association	https://nationaleczema.org/
National Eczema Society	www.eczema.org/atopic-eczema
NIH. National Institute of Allergy and Infectious Diseases (NIAID)	https://www.niaid.nih.gov/diseases-conditions/eczema-atopic-dermatitis