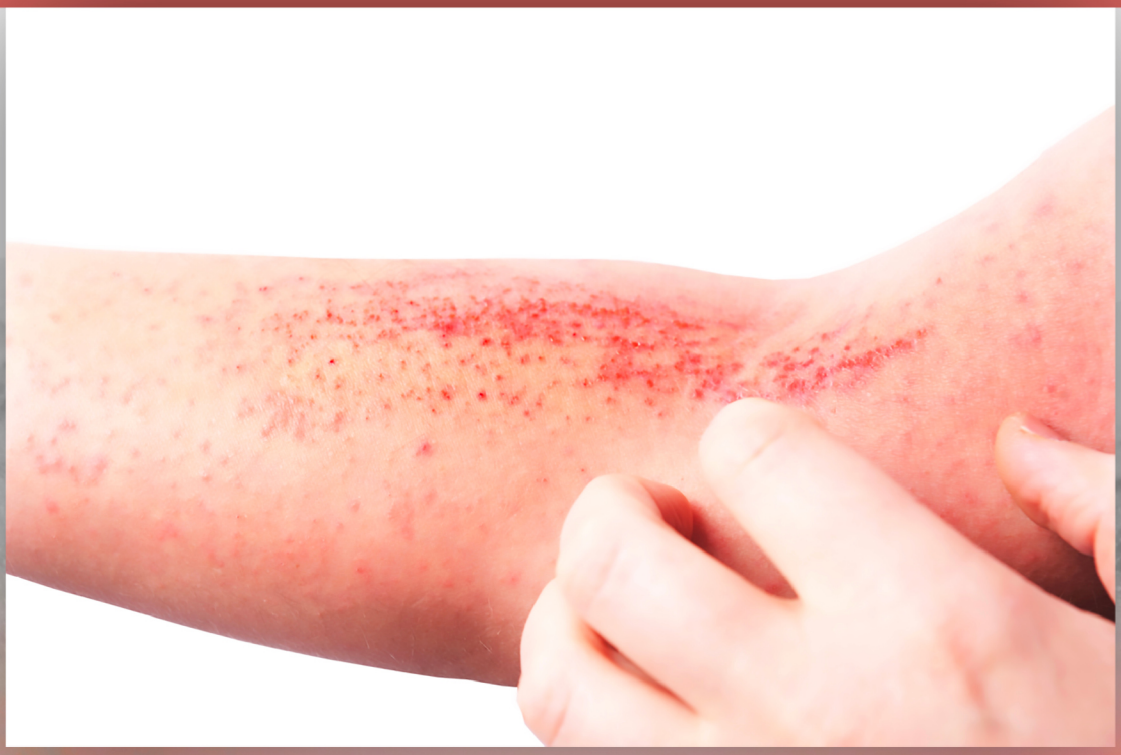
Advances in the Management of

MODERATE-TO-SEVERE ATOPIC DERMATITIS:

Incorporating Systemic Therapies into Clinical Practice



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

Advances in the Management of Moderate-to-Severe Atopic Dermatitis: Incorporating Systemic Therapies into Clinical Practice

FACULTY

Eric Simpson, MD (Program Manager) Professor, Dermatology School of Medicine Frances J. Storrs, M.D. Medical Dermatology Professor, Dermatology School of Medicine Oregon Health & Science University Portland, Oregon		
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** Assistant Professor Departments of Dermatology, Preventive Medicine, and Medical Social Sciences Director, Northwestern Medicine Multidisciplinary Eczema Center Director, Patch Testing Clinic Northwestern Memorial Hospital Chicago, IL
Peter Lio, MD Clinical Assistant Professor of Dermatology and Pediatrics Northwestern University Feinberg School of Medicine Chicago, Illinois	**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	

PROGRAM OVERVIEW

This program will explore the use of systemic therapies for the management of moderate-to-severe atopic dermatitis in pediatric and adult patients.

TARGET AUDIENCE

This activity is intended for dermatologists, allergists, immunologists, primary 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:

- Identify patients with moderate-to-severe atopic dermatitis who require step-up therapy
- Utilize guideline recommendations and clinical trial data to design treatment plans that address the symptoms and quality of life of patients with atopic dermatitis

- Review up-to-date guidance on the use of systemic therapies for atopic dermatitis in patients who are positive or negative for SARS-CoV-2

ACCREDITATION STATEMENT

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

CREDIT DESIGNATION STATEMENT

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

NURSING CREDIT INFORMATION

Purpose: This program would be beneficial for nurses involved in the care of patients with atopic dermatitis.
Credits: 1.0 ANCC Contact Hours

CNE ACCREDITATION STATEMENT

Ultimate Medical Academy/CCM is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. Awarded 1.0 contact hours of continuing nursing education of RNs and APNs.

DISCLOSURE POLICY STATEMENT

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 manufacturer(s) of any commercial product(s) and/or provider(s) of commercial services that are discussed in an educational activity.

DISCLOSURE OF CONFLICTS OF INTEREST

Speaker	Relationship	Manufacturer
Eric Simpson, MD (Program Chair)	Contracted research/Principal Investigator	AbbVie, Amgen, Eli Lilly, Incyte, Kyowa Hakko Kirin, Leo Pharmaceuticals, Merck
	Consulting Fee	AbbVie, Amgen, Arena Pharmaceuticals, Benevolent AI Bio Limited "BAI", BiomX Ltd, Bluefin Biomedicine Inc,
Lisa Arkin, MD	Consultant	Regeneron, AbbVie
	Principal Investigator	Amgen, Candela
Lucia Diaz, MD	Research	Pfizer, Janssen, Regeneron
	Royalty	UpToDate
Peter A. Lio, MD	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
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 peer reviewed by a nurse reviewer.

The reviewer of this activity has nothing to disclose.

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, MBA, General Manager of Med Learning Group, has nothing to disclose.

Christina Gallo, SVP, Educational Development for Med Learning Group, has nothing to disclose.

Sharine Griggs, Senior Program Manager for Med Learning Group, has nothing to disclose.

Diana Tommasi, PharmD, Director of Medical Services for Med Learning Group, has nothing to disclose.

Lauren Welch, MA, VP, Accreditation and Outcomes, has nothing to disclose.

Daniel Dasilva, Accreditation and Outcomes Coordinator, 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 non-approved indications.

METHOD OF PARTICIPATION

There are no fees for participating and receiving CME 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. Submit the evaluation form to Med Learning Group.

Participants will receive their certificate via email within 30 days.

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. The participant

should use his/her clinical judgment, knowledge, experience, and diagnostic decision-making 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://medlearninggroup.com/privacy-policy/

AMERICANS WITH DISABILITY ACT

Event staff will be glad to assist you with any special needs (eg, physical, dietary, etc.). Please contact Med Learning Group prior to the live event at info@medlearninggroup.com

Provided by Med Learning Group

This activity is co-provided by Ultimate Medical Academy/Complete Conference Management (CCM).

Supported by an educational grant from Sanofi Genzyme and Regeneron Pharmaceuticals.

DM-24: Advances in the Management of Moderate-to-Severe Atopic Dermatitis: Incorporating Systemic Therapies into Clinical Practice

1. **Atopic Dermatitis (AD): An Overview**
    a. Epidemiology of AD
    b. Type 2 comorbidities and the atopic march
    c. Pathophysiology of AD
        i. Epithelial barrier dysfunction
        ii. Dysregulation of the immune system
    d. Burden of AD
        i. Mental health comorbidities
        ii. Impact on quality of life and sleep
        iii. Other associated conditions

2. **Diagnosis and Long-term Management of AD**
    a. AD spectrum
    b. Clinical assessment tools
    c. Algorithm for "step-up" care
    d. Management of flares
    e. Deciding on when to use systemic therapies
        i. Patient factors to consider
        ii. Benefits and risks of therapy options

3. **Clinical Trial Data on Systemic Agents for the Management of AD**
    a. Mechanism of action of approved and investigational agents
    b. Clinical trial data on the efficacy and safety of:
        i. Dupilumab
        ii. Emerging therapies
    c. Recognizing and managing adverse events with systemic therapy

4. **Atopic Dermatitis and COVID-19**
    a. Risk factors for severe COVID-19
    b. Benefits and risks of immunosuppressants and immunomodulators
    c. Guidance on managing patients with COVID-19

5. **Case Study**

6. **Conclusions**

7. **Questions and Answers**

Advances in the Management of Moderate-to-Severe Atopic Dermatitis: Incorporating Systemic Therapies Into Clinical Practice

1

Disclosures

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

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

2

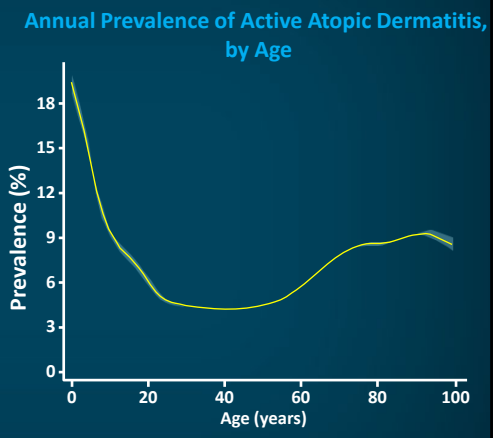
Learning Objectives

- Identify patients with moderate-to-severe atopic dermatitis who require step-up therapy
- Utilize guideline recommendations and clinical trial data to design treatment plans that address the symptoms and quality of life of patients with atopic dermatitis
- Review up-to-date guidance on the use of systemic therapies for atopic dermatitis in patients who are positive or negative for SARS-CoV-2

3

Atopic Dermatitis: A Highly Prevalent Disease

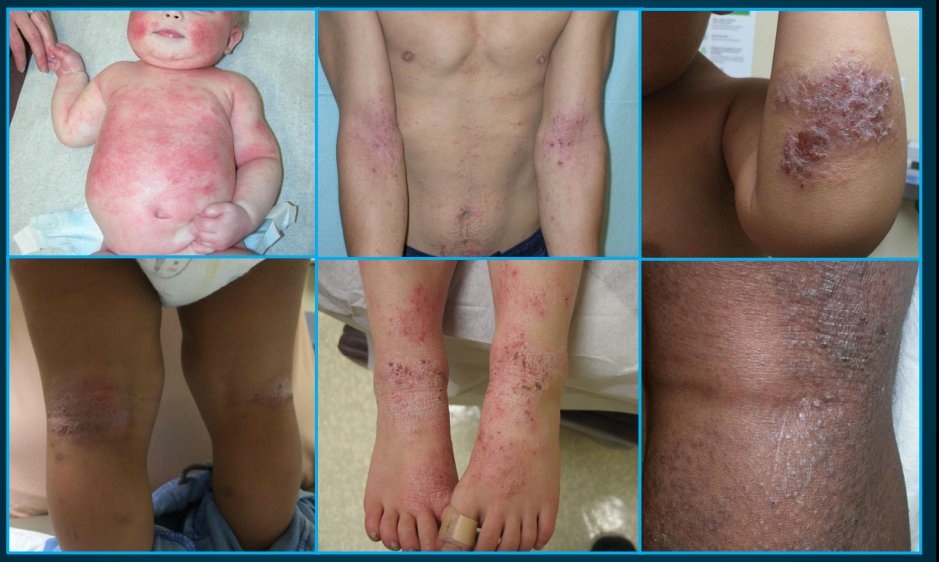
- 10%-25% prevalence in children
- 7.2% prevalence in adults
- Unknown prevalence in older adults
- Most commonly begins before age 5 and improves over time
- Multiple disease trajectories possible



Abuabara K, et al. *Ann Intern Med*. 2019;170:354-356. Schmitt J, et al. *J Allergy Clin Immunol.* 2007;120:1389-1398.

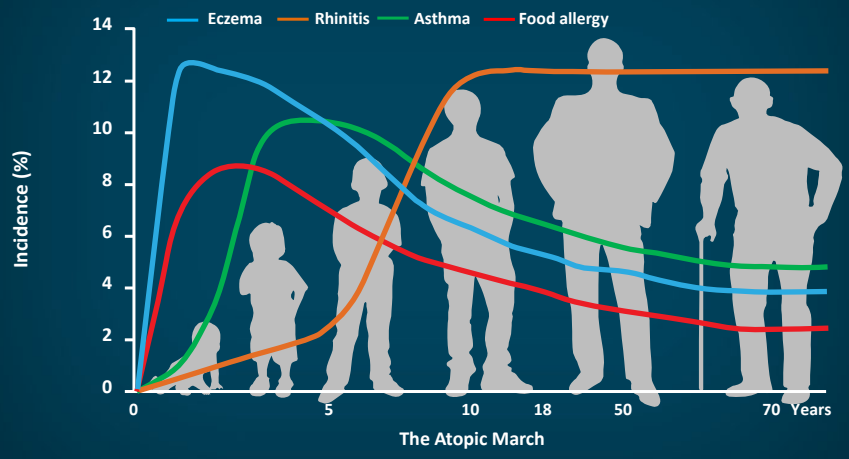
4

AD Is Heterogenous in Presentation



5

Atopic March

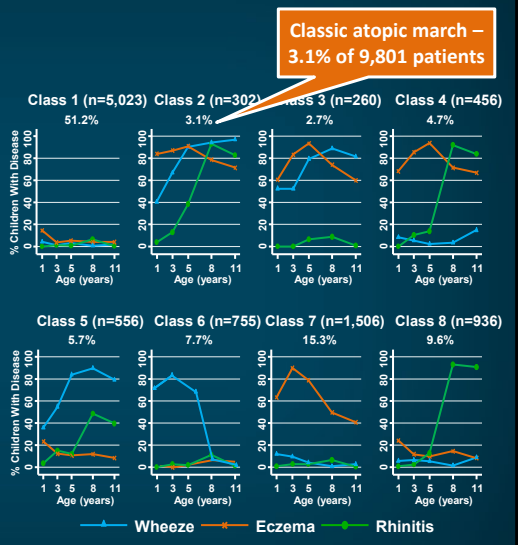


Zheng T, et al. *Allergy Asthma Immunol Res.* 2011;3:67-73. Czarnowicki T, et al. *J Allergy Clin Immunol.* 2017;139:1723-1734.

6

AD Is Associated With Type 2 Comorbidities

- Allergic comorbidities cluster together (multimorbidity)
- Polysensitization identifies multimorbidity risk, but:
  - IgE not the dominant causal mechanism
  - Various atopic disease trajectories
  - <4% follow classic atopic march pattern
- Proteomic network studies identified type 2 signaling pathways as important for multimorbidity phenotype



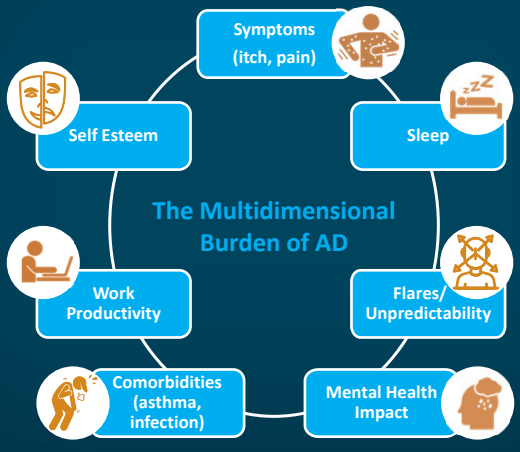
Ig = immunoglobulin.

Belgrave DCM, et al. *PLOS Med.* 2014;11:e1001748. Aguilar D, et al. *PLoS One.* 2017;12:e0179125. Bousquet J, et al. *Allergy.* 2011;66:596-604.

7

The Burden of AD

- The full impact of AD cannot be estimated based on skin signs alone
- The burden of AD includes multiple factors; key among these are itch, pain, sleep, and QoL

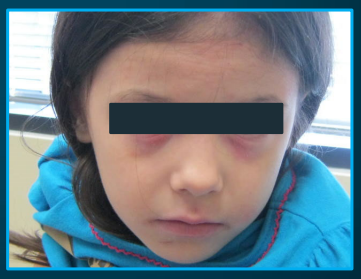


Schmitt J, et al. *J Allergy Clin Immunol*. 2007;120:1389-1398.

8

Mental Health Comorbidity

- Emotional and behavioral effects in children, including ADHD[1]
- Families of children with moderate-to-severe AD affected to a larger degree compared with families of children with diabetes[1,2]
- Anxiety and depression more common in children and adults with AD[1,3,4]
- Increased risk of suicide[3,4]
- Sleep loss[1]
- Feelings of isolation, guilt, or shame



ADHD = attention-deficit/hyperactivity disorder.

1. Chamlin SL, Chren MM. *Immunol Allergy Clin North Am.* 2010;30:281-288. 2. Su J, et al. *Arch Dis Child.* 1997;76:159-162. 3. Dieris-Hirche J et al. *Hautarzt.* 2009;60:641-646. 4. Lee S, Shin A. *BMC Psychiatry.* 2017;17:3. Image courtesy of Eric Simpson, MD.

9

Other Burdens for Patients

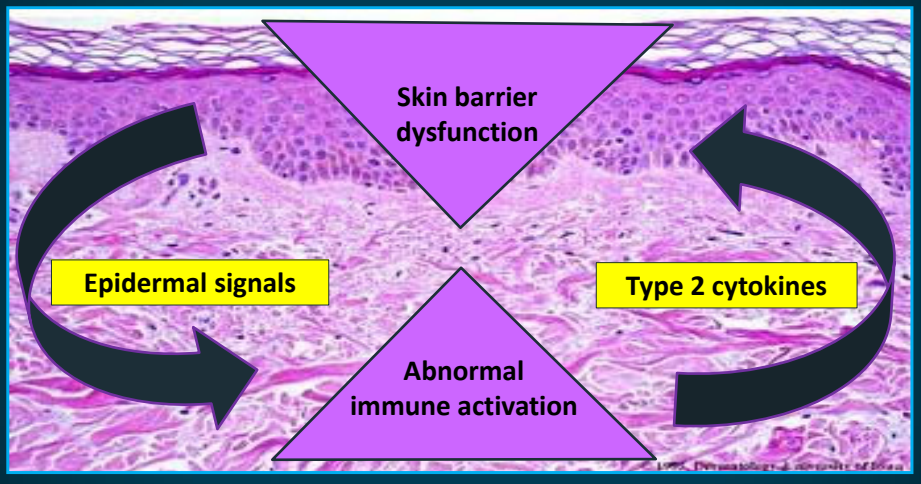
- Steroid phobia
- Mixed messaging by providers
- False positive IgE testing
- Complicated treatment regimens
- Internet misinformation
- Altered activities, lifestyle, and work and school difficulties
- Burden and stress on family
- Chasing the allergen/cause
- Physician disagreement
- Embarrassment
- Stigma
- Oral steroid toxicity

10

Pathophysiology

11

AD Pathogenesis



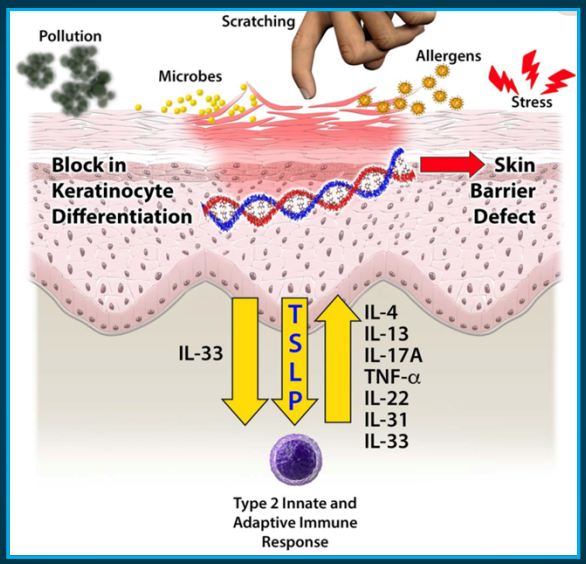
Bin L, Leung DYM. *Allergy Asthma Clin Immunol*. 2016;12:52. Boguniewicz M, et al. *Immunol Rev.* 2011;242:233-246.

12

Introduce whiteboard animation: Pathophysiology of AD

13

Factors Contributing to AD



TNF = tumor necrosis factor.

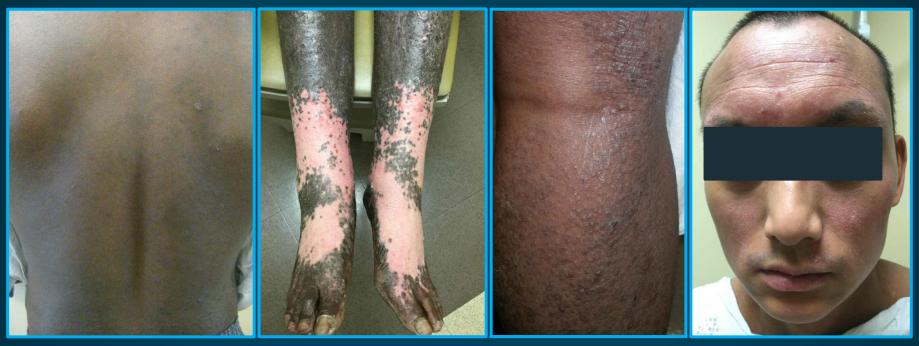
Leung DYM, et al. *J Allergy Clin Immunol.* 2020;145:1485-1497.

14

Disease Assessment

15

Dyspigmentation and Facial Dermatitis Add Additional Burden

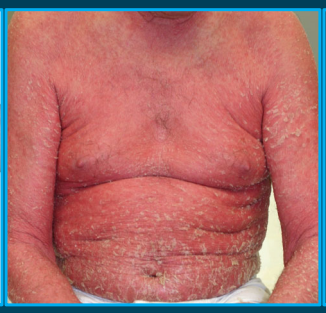


Kaufman BP, et al. *Exp Dermatol*. 2018;27:340-357.

16

Atopic Dermatitis Spectrum

Prurigo Nodularis

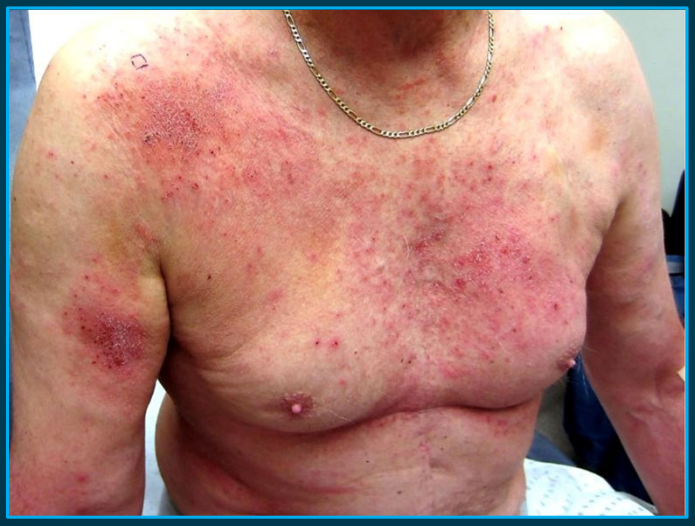


Erythroderma

Hand Eczema

17

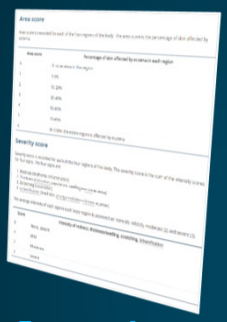
Chronic Eczematous Eruption of the Elderly



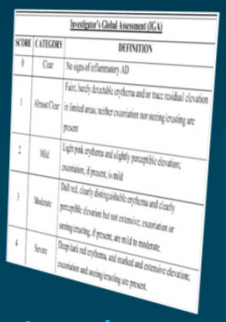
Brummer GC, et al. *Dermatol Online J*. 2018;24:13030.

18

Clinical Assessment Tools

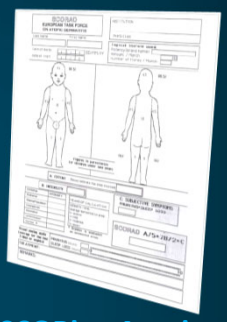


Eczema Area and Severity Index (EASI)[1]



Investigator Global Assessment (v-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. Severity scoring of atopic dermatitis: the SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis. *Dermatology*. 1993;186:23-31.

19

Validated Investigator Global Assessment Scale for Atopic Dermatitis (vIGA-AD)

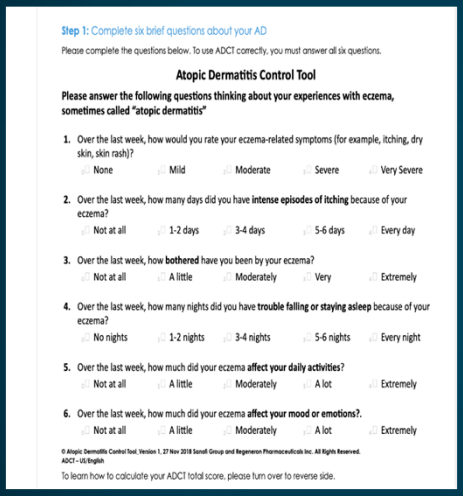
- Score is selected using descriptors that best describe overall appearance of lesion at a given time point
- It is not necessary for all characteristics under Morphological Description to be present

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

Simpson E, et al. *J Am Acad Dermatol.* 2020;83:839-846.

20

Atopic Dermatitis Control Tool



Step 1: Complete six brief questions about your AD

Please complete the questions below. To use ADCT correctly, you must answer all six questions.

Atopic Dermatitis Control Tool

Please answer the following questions thinking about your experiences with eczema, sometimes called "atopic dermatitis"

1. Over the last week, how would you rate your eczema-related symptoms (for example, itching, dry skin, skin rash)?
   ☐ None ☐ Mild ☐ Moderate ☐ Severe ☐ Very Severe
2. Over the last week, how many days did you have **intense episodes of itching** because of your eczema?
   ☐ Not at all ☐ 1-2 days ☐ 3-4 days ☐ 5-6 days ☐ Every day
3. Over the last week, how **bothered** have you been by your eczema?
   ☐ Not at all ☐ A little ☐ Moderately ☐ Very ☐ Extremely
4. Over the last week, how many nights did you have **trouble falling or staying asleep** because of your eczema?
   ☐ No nights ☐ 1-2 nights ☐ 3-4 nights ☐ 5-6 nights ☐ Every night
5. Over the last week, how much did your eczema **affect your daily activities**?
   ☐ Not at all ☐ A little ☐ Moderately ☐ A lot ☐ Extremely
6. Over the last week, how much did your eczema **affect your mood or emotions?**.
   ☐ Not at all ☐ A little ☐ Moderately ☐ A lot ☐ Extremely

ADCT – US/English

To learn how to calculate your ADCT total score, please turn over to reverse side.

- 6-item questionnaire
- Extensive validation (aged >12 years)
- Multiple domains
  - Sleep
  - Symptoms
  - Bother
  - Intense itching
  - Emotions
  - Activity

1. Pariser DM, et al. *Curr Med Res Opin*. 2020;36:367-376. 2. Simpson E, et al. *BMC Dermatol*. 2019;19:15. 3. Sanofi PRO Questionnaires. Atopic Dermatitis Control Tool (ADCT). 2017 (https://patient-questionnaires.sanofi.com/questionnaires/adct). Accessed July 6, 2021.

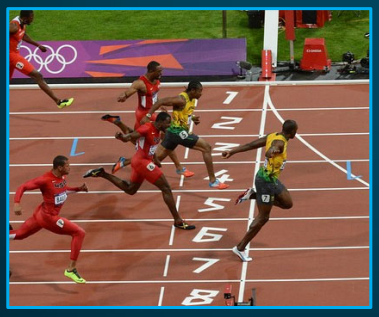
21

Management of AD

22

Overview for Topical Therapy

- Induce clearance (usually with TCS)
- Maintenance (many options, reactive, proactive, TCS or nonsteroidal treatments)
- Brief clearance protocol for flares



Sprint or a marathon?

TCS = topical corticosteroid.

23

Algorithm for "Step-up Care"

	MILD	MODERATE	SEVERE
Acute Treatment	**Apply TCS to Inflamed Skin** • Low-to-medium potency TCS, BID for 2 wk, QD for 1 wk, few days beyond clearance • Alternative: Consider crisaborole 2% or TCI	**Apply TCS to Inflamed Skin** • Medium-to-high potency TCS, BID for 2 wk, QD for 1 wk, twice per week to "hot spots" • Low potency for sensitive areas or consider crisaborole 2% or TCI	**Apply TCS to Inflamed Skin** • Medium-to-high potency TCS, BID for 3-7 days beyond clearance • Lower potency for sensitive areas or consider crisaborole 2% or TCI • **If unresolved after 7 days, reconsider next step**
Next Steps			• Nonadherence • Infection • Misdiagnosis • Contact allergy to medications • Referral
Basic and Maintenance Treatment	*(Basic management)* **1. Skin Care** – Liberal, frequent moisturizer use – Daily warm bath/shower, followed by moisturizer **2. Trigger Avoidance** – Common irritants; allergens if proven – Consider comorbidities	*(Basic management + topical medications)* **Maintenance TCS** – Medium potency, 2-3 times weekly ("proactive") to recurrently active areas of involvement – Low potency TCS several times weekly for sensitive areas OR **Maintenance TCI** – 2-3 times weekly up to BID (proactive approach) **Crisaborole 2%, BID** OR – Several times weekly **Consider: Add Bleach Baths** – 2-7 times weekly based on severity and tendency to develop crusting at sites of excoriation	*(Basic management + **REFERRAL** to AD Specialist)* **1. Phototherapy** **2. Dupilumab** **3. Systemic Immunosuppressants** – Cyclosporine A* – Methotrexate* – Mycophenolate mofetil* – Azathioprine* – Corticosteroids* **4. Consider acute treatment for some patients to help gain control** – Wet wrap therapy – Short-term hospitalization

Advance from mild to moderate when symptomatic despite appropriate use of TCS and adherence to basic management and/or persistence or frequent flaring

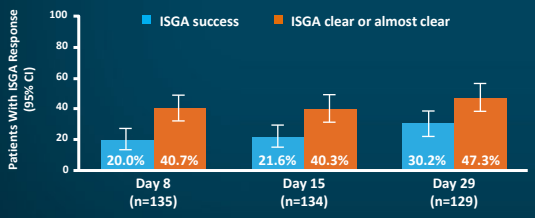
BID = twice daily; QD = daily; TCI = topical calcineurin inhibitor. * Not FDA-approved for the treatment of AD.

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

24

CrisADe CARE 1 Study

- 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
- Crisaborole is approved for mild-to-moderate AD in adult and pediatric patients aged ≥3 months



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; TEAE = treatment-emergent adverse event; URTI = upper respiratory tract infection.

Schlessinger J, et al. *Am J Clin Dermatol.* 2020;21:275-284.
Crisaborole (Eucrisa®) PI 2020 (http://labeling.pfizer.com/ShowLabeling.aspx?id=5331). Accessed July 1, 2021.

25

Maintenance and Management of Flares

- Preventing or at least increasing the time interval between flares is a critical goal of management[1]
- Important to act quickly and aggressively when treating flares[1]
- 2 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[6,7]
    - 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;71:327-349. 3. Eichenfield LF, et al. *Pediatrics*. 2015;136:554-565. 4. Schmitt J, et al. *Br J Dermatol*. 2011;164:415-428. 5. Chopra R, et al. *Ann Allergy Asthma Immunol*. 2017;119:435-440. 6. Suh L, et al. *Pediatr Dermatol*. 2008;25:528-534. 7. Kim J, et al. *Allergy Asthma Immunol Res*. 2019;11:593-603.

26

When to Use Systemic Therapy

International Eczema Council Panel Recommendations

If aggressive topical therapy is not achieving adequate control of the disease

AND

- Adequate education delivered
- Infection addressed
- Large impact on QoL
- Reconsidered diagnosis: Cutaneous T-cell lymphoma? Allergic contact dermatitis?
- Consider phototherapy

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

27

Systemic Therapy

28

Factors to Consider When Choosing a Systemic Therapy

29

Cyclosporine* ≈50%-90% Reduction in Eczema at 16 Weeks

When to Use

- Rapid relief needed
- To get off steroid roller coaster
- Failed dupilumab or not covered
- Pediatric patient aged <6 years
- Topical steroid withdrawal
- Start at 5 mg/kg!
- Can overlap or combine with dupilumab

When **NOT** to Use

- Older adults and polypharmacy
- Hypertension
- History of cancer or serious infection
- Should not use for >1 year
- Breastfeeding

* Not FDA-approved for the treatment of AD.

Schmitt J, et al. *J Eur Acad Dermatol Venereol*. 2007;21:606-619.

30

Methotrexate* ≈40%-50% Reduction in Eczema at 16 Weeks

When to Use

- Moderate patient
- Transition from cyclosporine
- Dupilumab not covered/Medicare patient
- As add-on to dupilumab
- Not sure about diagnosis
- 0.2-0.6 mg/kg/wk in children

When **NOT** to Use

- Liver comorbidities
- Women of child-bearing potential without contraception
- Chronic and frequent alcohol use

* Not FDA-approved for the treatment of AD.

Schram ME, et al. *J Allergy Clin Immunol*. 2011;128:353-359. El-Khalawny MA, et al. *Eur J Pediatr*. 2013;172:351-356.

31

Dupilumab ≈65%-80% Reduction in Eczema

When to Use

- Any patient without adequate disease control using topical therapy aged ≥6 years
- Need long-term approach

When to **NOT** Use

- Needle-phobic patients

Dupilumab is the only FDA-approved therapy for those aged ≥6 years with moderate-to-severe AD

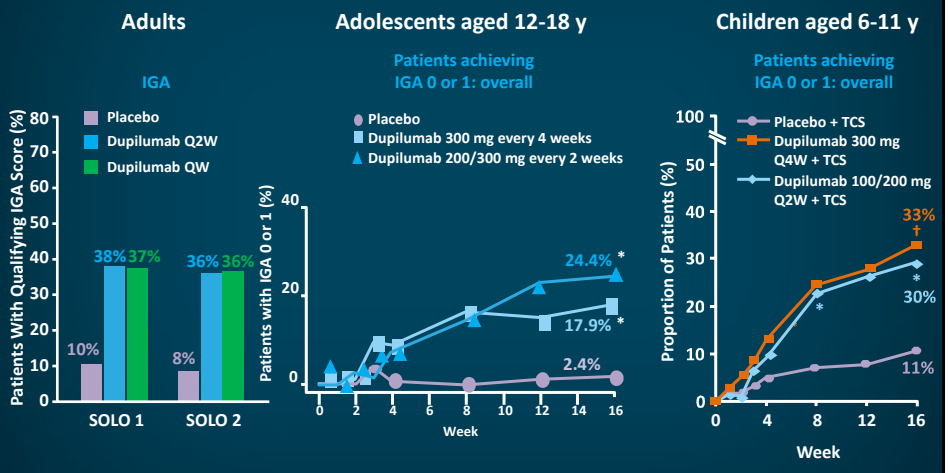
Simpson EL, et al. *N Engl J Med*. 2016;375:2335-2348. Dupilumab (Dupixent®) PI 2020 (https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761055s020lbl.pdf). Accessed July 1, 2021.

32

Introduce whiteboard animation: MOA of novel systemic therapies

33

Dupilumab: Improvements in IGA in 3 Age Cohorts

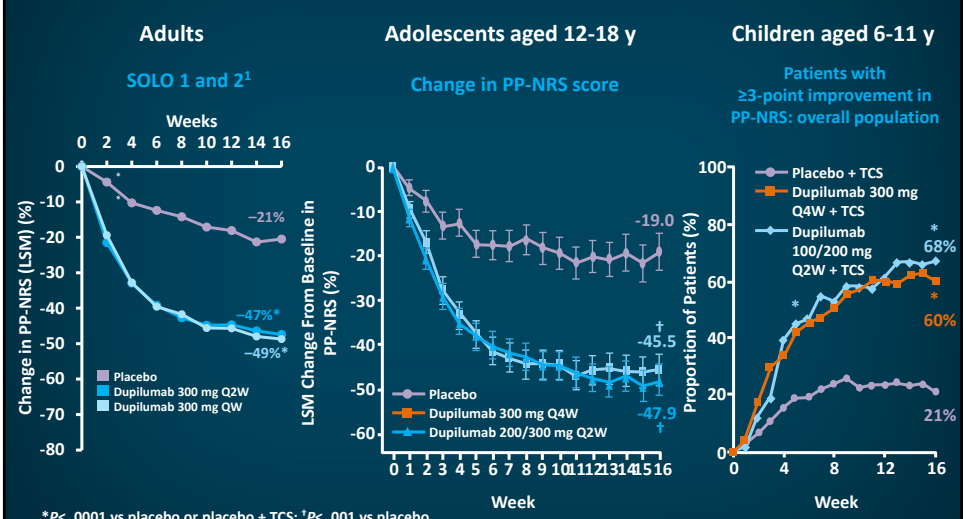


*P< .001 and †P< .0001 vs placebo. Q2W = every 2 weeks; Q4W = every 4 weeks; QW = every week.

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

34

Dupilumab: Impact on Pruritus

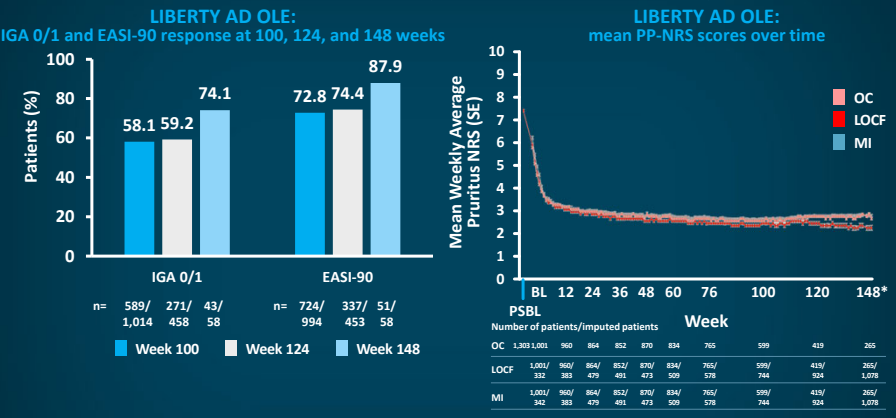


*P< .0001 vs placebo or placebo + TCS; †P< .001 vs placebo.
LSM = least squares mean; PP-NRS = Peak Pruritus Numerical Rating Scale.

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

35

Liberty AD OLE: Dupilumab Provided Long-term Sustained Clinical Efficacy in Adults for up to 3 Years



Dupilumab 300 mg QW (approved dose Q2W) evaluation in the OLE study showed long-term, sustained efficacy in signs, symptoms, and QoL for up to 3 years[1]

BL = baseline; MI = multiple imputation; OC = observed cohort; OLE = open-label extension study; PSBL = parent study baseline.

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

36

Dupilumab: Long-term Sustained Safety Up to 3 Years

	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	9.29	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/PY = number of patients per patient-years; TEAE = treatment-emergent adverse event.
Beck LA, et al. *Am J Clin Dermatol.* 2020;21:567-577.

37

One-Year Experience of Dupilumab on Different AD Phenotypes

A significant improvement after 16 weeks of treatment (*P*< .0001) was found in all 6 phenotypes for all the assessed scores mentioned below, persisting up to week 52.

- Classic: Lichenified/exudative flexural dermatitis
- Generalized eczema with an inflammatory pattern
- Generalized eczema with a lichenoid pattern
- Prurigo
- Erythroderma
- Nummular

Tavecchio S, et al. *J Clin Med*. 2020;9:2684.

38

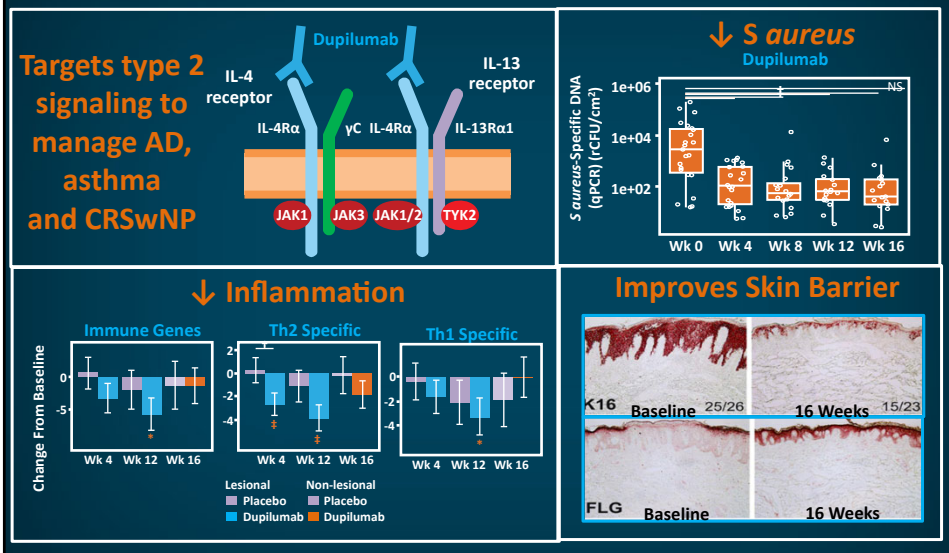
Key Dupilumab Clinical Updates

- Long-term safety excellent over 3 years[1]
- No immunosuppression
- Adolescent and pediatric patients continue to improve over 12 months
- AD safe and effective in elderly[2]
- Efficacy improves over time in "non-responders"
- Reports of safety in patients with HIV and hepatitis B virus[3,4]

1. Beck LA, et al. *Am J Clin Dermatol*. 2020;21:567-577. 2. Russo F, et al. *Dermatitis*. 2020 (doi:10.1097/DER.0000000000000686). Accessed July 1, 2021. 3. Ly K, et al. *JAAD Case Rep*. 2019;5:624-626.
4. Alawadhi A, et al. *JAAD Case Rep*. 2020;6:1356-1359.

39

Other Effects of Dupilumab

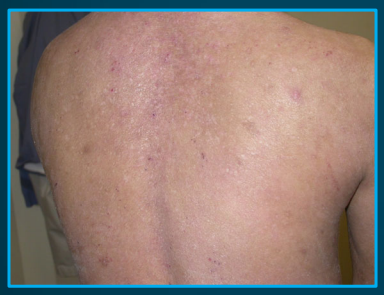


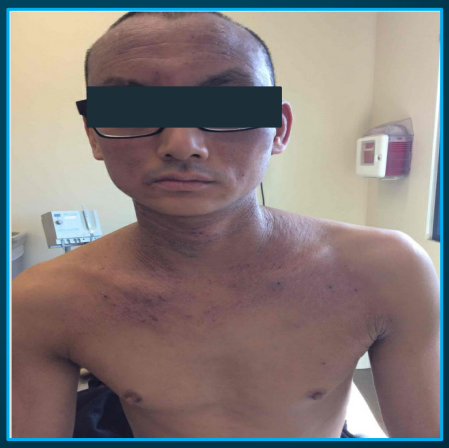
*P< .01; †P< .05; ‡P< .001.
CRSwNP = chronic rhinosinusitis with nasal polyposis; JAK = Janus kinase; qPCR = quantitative polymerase chain reaction; R = receptor.
Callewaert C, et al. *J Invest Dermatol*. 2020;140:191-202.e7. Guttman-Yassky E, et al. *J Allergy Clin Immunol*. 2019;143:155-172.

40

Case Study #1

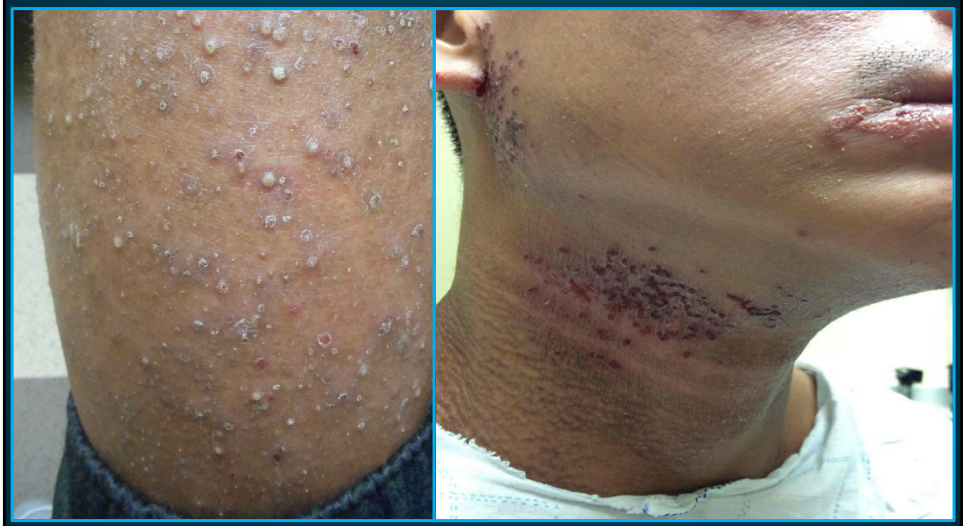
- 32-year-old patient with AD his whole life
- Not well-controlled on topical steroids or prednisone from primary care





41

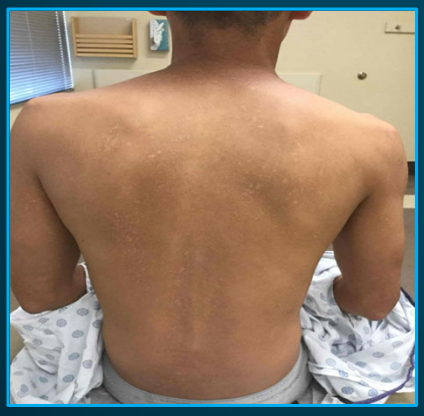
With a History of Multiple Infections, What Is the Best Treatment Option for This Patient?

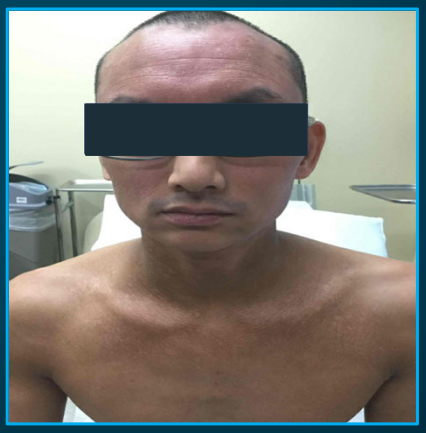


42

Case Study (continued)

- 1.5 years on dupilumab
- Off all other systemics in the first 2 months of dupilumab



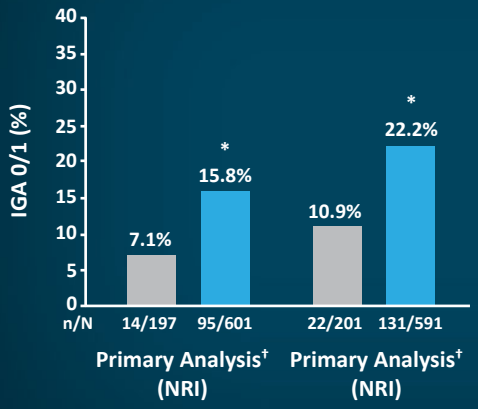


43

Emerging Topical and Systemic Therapies

44

Tralokinumab (Anti–IL-13): IGA 0/1 at Week 16



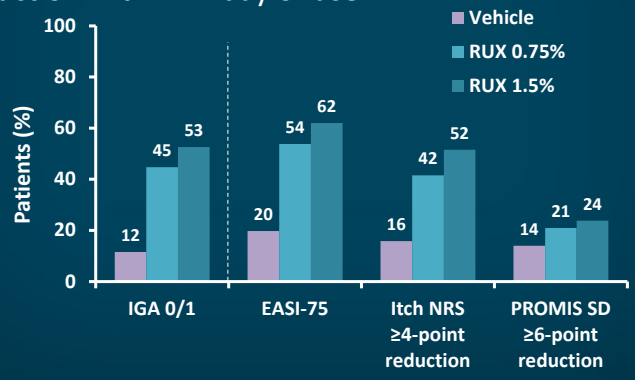
- IL-13 cytokine blocking agent
- Q2W and possible Q4W dosing
- Common AE: conjunctivitis
- Improved efficacy beyond week 16 with Q4W dosing possible for some patients

*P< .01 vs placebo. †Use of rescue medication considered as nonresponse and missing data imputed as nonresponse.
NRI = non-responder imputation.
1. Simpson E, et al. AAD VMX. 2020 (https://jofskin.org/index.php/skin/article/view/1066/pdf). Accessed July 1, 2021.
2. Weidinger S, et al. AAD VMX. 2020 (https://jofskin.org/index.php/skin/article/view/1079/pdf). Accessed July 1, 2021.

45

Topical JAK Inhibitor: Ruxolitinib

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



AE = adverse event; PROMIS SD = Patient-Reported Outcomes Measurement Information System Sleep Disturbance; RUX = ruxolitinib.
Papp K, et al. *J Am Acad Dermatol*. 2021;Epub ahead of print.

46

General Statements on Systemic JAK Inhibitors for AD

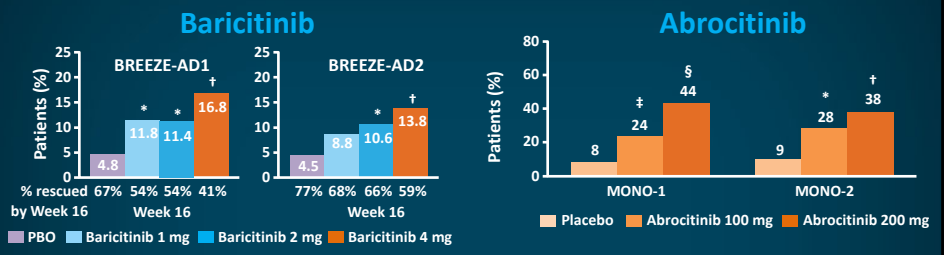
- ALL improve itch rapidly within days (+ skin rash and QoL)
- Efficacy, tolerability, and safety depend on molecule and dose
- JAK inhibitors may be appropriate as first-line systemic therapy with proper shared decision-making process and patient selection
  - JAK inhibitors not FDA-approved for the treatment of AD
- Safety and tolerability outcomes to pay attention to:
  - Headache and nausea/vomiting
  - Acne
  - Herpes simplex and herpes zoster viruses
  - Serious infection
  - Venous thrombosis: avoid in at-risk patients (elderly, family history)
  - Major adverse cardiovascular events: stroke and heart attack
  - Malignancy

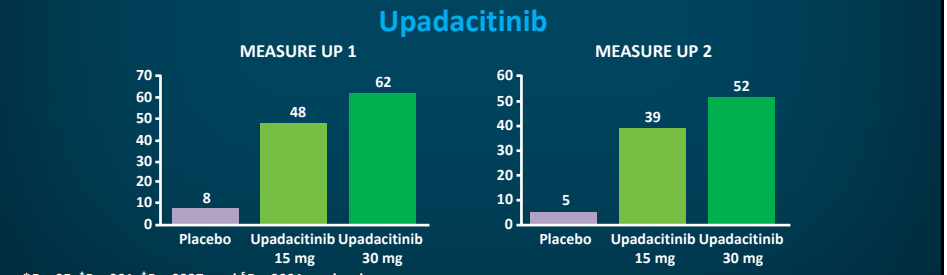
Simpson EL, et al. *Br J Dermatol*. 2020;183:242-255. Guttman-Yassky E, et al. *Lancet*. 2021;397:2151-2168. Simpson EL, et al. *Lancet*. 2020;396:255-266. Silverberg JI, et al. *JAMA Dermatol*. 2020;156:863-873.

47

JAK Inhibitors in AD

Proportion of Clear/Almost Clear at Week 12/16 (Monotherapy)





*P< .05, †P< .001, ‡P= .0037, and §P< .0001 vs placebo.

Simpson EL, et al. *Br J Dermatol*. 2020;183:242-255. Guttman-Yassky E, et al. *Lancet*. 2021;397:2151-2168. Simpson EL, et al. *Lancet*. 2020;396:255-266. Silverberg JI, et al. *JAMA Dermatol*. 2020;156:863-873.

48

Abrocitinib vs. Dupilumab

	IGA response (improvement of ≥2 points at 12 weeks)	EASI-75 response (≥75% improvement at 12 weeks)
Abrocitinib, 200 mg/day (oral; n = 226)	48.4%	70.3%
Abrocitinib, 100 mg/day (oral; n= 238)	36.6%	58.7%
Dupilumab, 300 mg Q2W (SQ; n = 243)	36.5%	58.1%
Placebo (n = 131)	14.0%	27.1%

- The 200-mg dose of abrocitinib reduced itch at 2 weeks as compared with dupilumab but did not differ in most other secondary end points.

Bieber T, et al. *N Engl J Med*. 2021;384:1101-1112.

49

Heads Up Trial Results

Heads Up Results at Week 16*

	Dupilumab 300 mg (n=344)	Upadacitinib 30 mg (n=348)
EASI-75	61%	71%
EASI-90	39%	61%
EASI-100	8%	28%
Percent change from baseline in worst pruritus NRS	-49%	-67%
Worst pruritus NRS improvement ≥4 (dupilumab, n=336) (upadacitinib, n=340)	36%	55%

Blauvelt A, et al. ISAD 2021. Abstract PT29.

50

Systemic JAK Inhibitors*

When to Use

- Possible first-line systemic agents?
- Preference for oral and flexible dosing
- For patients wanting very quick response (within first week)
- Inadequate or loss of response to dupilumab

When to **NOT** Use

- History of malignancy
- History of severe infection
- History of thrombosis
- Severe renal or liver disease
- Pregnant or breastfeeding
- Elderly: use lower dose
- Patient with low tolerance for rare risk

* Not FDA-approved for the treatment of AD.

Baricitinib (Olumiant®) prescribing information. Indianapolis, IN: Eli Lilly;2020. He H, et al. *Am J Clin Dermatol.* 2019;20:181-192.

51

AD and COVID-19

52

Increased Risk of COVID-19–Associated Hospitalization and Death With Certain Comorbidities

- It is recommended that immunosuppressive agents should not be **initiated** in patients with risk factors for severe COVID-19
- Patients on immunosuppressive agents should continue therapy if they do not have COVID-19
  - Risks and benefits of continued immunosuppressive therapy should be weighed on case-by-case basis and should 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). Accessed June 2, 2021. American Academy of Dermatology Association. 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 July 1, 2021.

53

AD and COVID-19

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

American Academy of Dermatology Association. 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 July 1, 2021. International League of Dermatological Societies (ILDS). ILDS guidance. 2021 (https://ilds.org/covid-19/guidance-psoriasis-atopic-dermatitis). Accessed July 1, 2021.

54

COVID Considerations

- No need to stop systemic therapy during pandemic
- If COVID-19-positive, unclear guidance on stopping therapy
  - AAD: consider holding immunosuppressive agents until patient recovers
- COVID vaccine guidance (ACR Guidance February 2021)
  - No reason to stop therapies prior to vaccine
  - Methotrexate and JAK inhibitors: stop for 1 week after each vaccine dose
    - NPF: consider holding methotrexate for 2 weeks after single-dose vaccine
  - No need to stop cyclosporine

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

1. Poulsen NN, et al. *Am J Transplant*. 2020;20:2975-2982. 2. Guisado-Vasco P, et al. *EClinicalMedicine*. 2020;28:100591. 3. American College of Rheumatology. (https://www.rheumatology.org/Portals/0/Files/COVID-19-Vaccine-Clinical-Guidance-Rheumatic-Diseases-Summary.pdf). 4. National Psoriasis Foundation. (https://www.psoriasis.org/covid-19-task-force-guidance-statements/). 5. American Academy of Dermatology Association. (https://assets.ctfassets.net/1ny4yoiyrqia/PicgNuD0IpYd9MSOwab47/2461e6c12cd88953632a13cd68952b71/Guidance_on_medications__10-12-20.pdf).

Case Study #2

- Paul is an 8-year-old boy with a history of chronic AD
- Eczematous lesions on arms, legs, abdomen, and hands (BSA: 40%)
  - Lichenification of popliteal and antecubital fossae
  - Excoriations on back of hands and forearms
- Mother reports generous use of emollients at bath and bedtime and adherence to therapy regimen

Medication	Dose	Sig	Dates
Fluocinolone acetonide ointment	0.025%	Apply to affected areas 2 times/week	7/20/19–current
Pimecrolimus ointment	1%	Apply to affected areas 3 times/week	7/20/19–current

How would you manage Paul's AD?

BSA = body surface area.

Case Study: Flare-up

- Fluocinolone increased to 2x daily
- Wet wraps recommended
- Paul reported improvement in itch and rashes

- After 2 weeks, Paul began to use fluocinolone 3x/week and symptoms flared again

How would you manage Paul's AD?

57

Summary

- AD causes a significant societal and individual burden
- Evaluate and decide if patients are true candidates for topical therapy
- In addition to signs and symptoms, burden of topical regimen, TCS overuse, infection, and hyperpigmentation should play a role in decision of whether to offer systemic therapy
- Traditional oral therapies cost less, but do not have sufficient or acceptable long-term safety or efficacy data
- Dupilumab provides effective therapy with proven long-term efficacy and safety in many types of patients with AD and scenarios without laboratory monitoring
- The investigational drug tralokinumab may provide a new alternative biologic with a safety profile similar to dupilumab, but it may be less effective
- JAKs coming that may be advantageous in some patient situations but careful patient selection important

58

Advances in the Management of Moderate-to-Severe Atopic Dermatitis: Incorporating Systemic Therapies into Clinical Practice

Resource	Address
Eichenfield LF, 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://pubmed.ncbi.nlm.nih.gov/24290431/
Wollenberg A, et al. **Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I.** *J Eur Acad Dermarol Venereol*. 2018;32:657-682.	https://pubmed.ncbi.nlm.nih.gov/29676534/
Boguniewicz M, et al. **Atopic dermatitis yardstick: Practical recommendations for an evolving therapeutic landscape.** *Ann Allergy Asthma Immunol*. 2018;120(1):10-22.	https://pubmed.ncbi.nlm.nih.gov/29273118/
Simpson EL, 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://pubmed.ncbi.nlm.nih.gov/28803668/
Silverberg JI. **Comorbidities and the impact of atopic dermatitis.** *Ann Allergy Asthma Immunol.* 2019;123:144-151.	https://pubmed.ncbi.nlm.nih.gov/31034875/
Simpson EL, 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://pubmed.ncbi.nlm.nih.gov/26777100/
Belgrave DCM, et al. **Developmental Profiles of Eczema, Wheeze, and Rhinitis: Two Population-Based Birth Cohort Studies**. *PLOS Medicine*. 2014;11: e1001748.	https://pubmed.ncbi.nlm.nih.gov/25335105/
Wang D, Beck LA. **Immunologic Targets in Atopic Dermatitis and Emerging Therapies: An Update.** *Am J Clin Dermatol.* 2016;17:425-443.	https://pubmed.ncbi.nlm.nih.gov/27371134/
Gandhi NA, et al. **Targeting key proximal drivers of type 2 inflammation in disease.** *Nat Rev Drug Discov.* 2016;15:35-50.	https://pubmed.ncbi.nlm.nih.gov/26471366/
Saeki H, et al. **Clinical Practice Guidelines for the Management of Atopic Dermatitis 2016.** *J Dermatol.* 2016;43:1117-1145.	https://pubmed.ncbi.nlm.nih.gov/27076388/
Shi VY, et al. **Improving patient education with an eczema action plan: a randomized controlled trial.** *JAMA Dermatol.* 2013;149:481-483.	https://pubmed.ncbi.nlm.nih.gov/23553035/
Paller AS, et al. **Efficacy and safety of crisaborole ointment, a novel, nonsteroidal phosphodiesterase 4 (PDE4) inhibitor for the topical treatment of atopic**	https://pubmed.ncbi.nlm.nih.gov/27417017/

dermatitis (AD) in children and adults. *J Am Acad Dermatol.* 2016;75:494-503.	
Schlessinger J, 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://pubmed.ncbi.nlm.nih.gov/32212104/
Simpson EL, 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://pubmed.ncbi.nlm.nih.gov/31693077/
Paller AS, et al. **Efficacy and safety of dupilumab with concomitant topical corticosteroids in children 6 to 11 years old with severe atopic dermatitis: A randomized, double-blinded, placebo-controlled phase 3 trial.** *J Am Acad Dermatol.* 2020;Jun 20: Epub ahead of print.	https://pubmed.ncbi.nlm.nih.gov/32574587/
Simpson EL, et al. **Two Phase 3 Trials of Dupilumab versus Placebo in Atopic Dermatitis.** *N Engl J Med.* 2016;375:2335-2348.	https://pubmed.ncbi.nlm.nih.gov/27690741/
Blauvelt A, et al. **Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial.** *Lancet*. 2017;389:2287-2303.	https://pubmed.ncbi.nlm.nih.gov/28478972/
de Bruin-Weller M, et al. **Dupilumab with concomitant topical corticosteroid treatment in adults with atopic dermatitis with an inadequate response or intolerance to ciclosporin A or when this treatment is medically inadvisable: a placebo-controlled, randomized phase III clinical trial (LIBERTY AD CAFÉ).** *Br J Dermatol*. 2018;178:1083-1101.	https://pubmed.ncbi.nlm.nih.gov/29193016/
Deleuran M, et al. **Dupilumab shows long-term safety and efficacy in patients with moderate to severe atopic dermatitis enrolled in a phase 3 open-label extension study.** *J Am Acad Dermatol*. 2020;82:377-388.	https://pubmed.ncbi.nlm.nih.gov/31374300/
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://pubmed.ncbi.nlm.nih.gov/32101256/
Wollenberg A, et al. **Treatment of atopic dermatitis with tralokinumab, an anti-IL-13 mAb.** *J Allergy Clin Immunol*. 2019:143:135-141.	https://pubmed.ncbi.nlm.nih.gov/29906525/

Silverberg JI, 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://pubmed.ncbi.nlm.nih.gov/31449914/
Guttman-Yassky E, et al. **Upadacitinib in adults with moderate to severe atopic dermatitis: 16-week results from a randomized, placebo-controlled trial.** *J Allergy Clin Immunol*. 2020;145:877-884.	https://pubmed.ncbi.nlm.nih.gov/31786154/
Guttman-Yassky E, 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://pubmed.ncbi.nlm.nih.gov/29410014/
Silverberg JI, et al. **Efficacy and Safety of Abrocitinib in Patients With Moderate-to-Severe Atopic Dermatitis: A Randomized Clinical Trial.** *JAMA Dermatol*. 2020;e201406.	https://pubmed.ncbi.nlm.nih.gov/32492087/