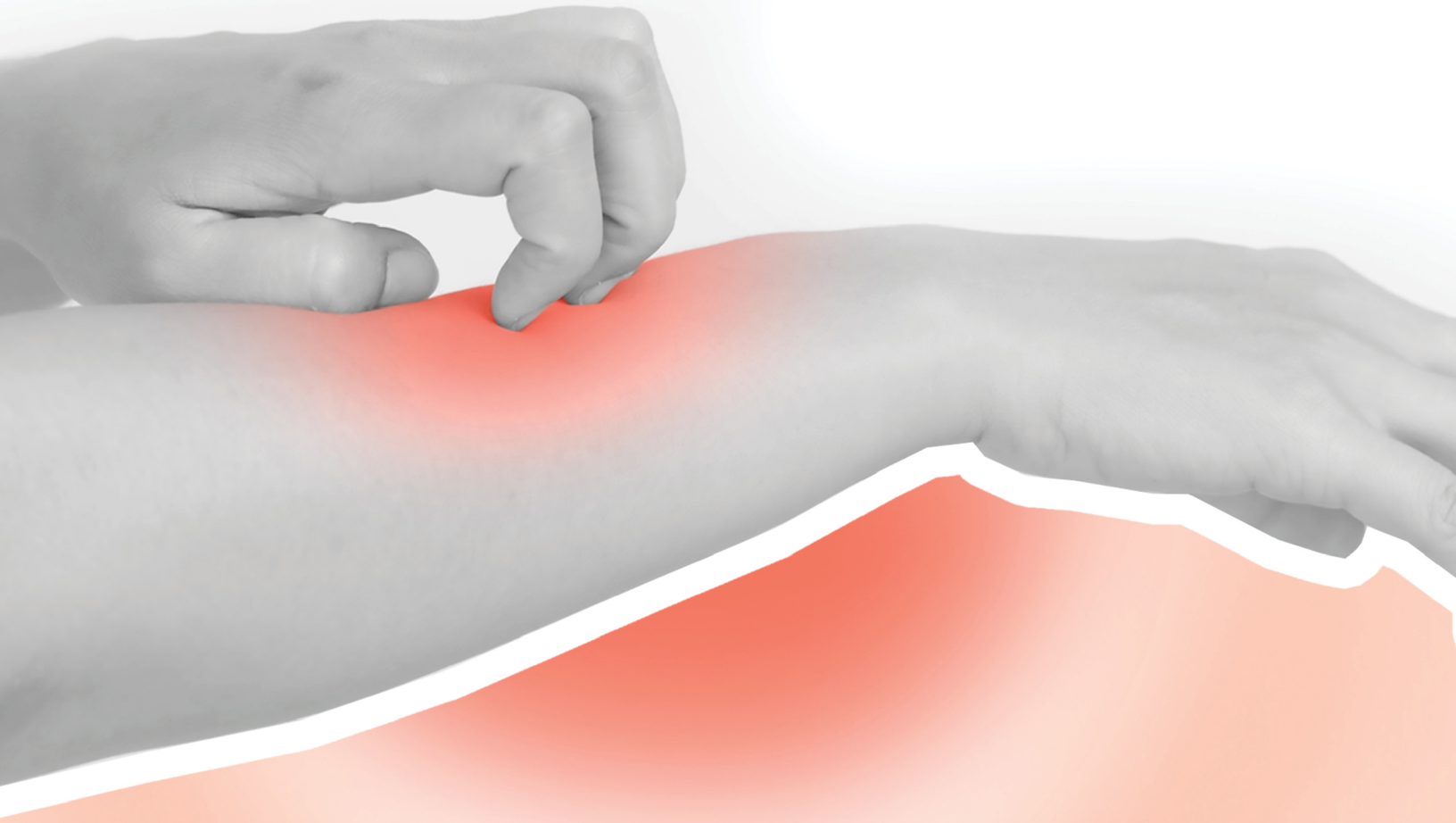

Multidisciplinary Care of Pediatricand Adolescent Patients with Moderate-to-Severe

ATOPIC DERMATITIS

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

Multidisciplinary Care of Pediatric and Adolescent Patients with Moderate to Severe Atopic Dermatitis

PROGRAM OVERVIEW

This live activity will cover treating and managing atopic dermatitis in pediatric and adolescent patients.

TARGET AUDIENCE

This activity is intended for dermatologists, pediatric dermatologists, pediatricians, primary care physicians, and other health care professionals involved in managing pediatric and adolescent patients with atopic dermatitis.

LEARNING OBJECTIVES

On completing the program, attendees should be able to:

- Develop treatment plans for the management of atopic dermatitis in pediatric and adolescent patients that incorporate guideline recommendations, evidence from clinical trials, and patient-specific factors
- Identify patients who would benefit from treatment intensification based on disease severity, failure of prior therapy, and comorbid conditions
- Incorporate strategies into clinical practice that encourage patient-centered and multidisciplinary care of atopic dermatitis

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 the treatment and management of pediatric and adolescent patients with atopic dermatitis.

CNE Credits:
1.0 ANCC Contact Hour

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 hour of continuing nursing education of RNs and APNs.

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DISCLOSURE OF FINANCIAL RELATIONSHIPS

SPEAKER	RELATIONSHIP	RELATIONSHIPS
Amy Paller, MD (Program Chair)	Not Applicable	
Jane S. Bellet, MD, FAAD	Stock	Merck
Heather Brandling-Bennett, MD	**Not Applicable**	
Lucia Diaz, MD	Research	Pfizer, Janssen, & Regeneron
	Royalty	UpToDate
Peter A. Lio, MD	Consultant	L'Oreal USA Inc., Franklin BioScience, AbbVie, Kiniksa Pharmaceuticals, Ltd, Eli Lilly and Company, Unilever, Dermira, TopMD, Amyris, Inc. LEO Laboratories Ltd (LEO Pharma), Odeza LLC, Theraplex, Exeltis, and Burt's Bees
	Speaker	La Roche-Posay Laboratorie Pharmaceutique, Pierre Fabre Dermatologie, Regeneron, Theraplex, and Pfizer Inc.
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Howard Pride, MD	**Not Applicable**	
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	Research	Galderma
	Speakers Bureau	Regeneron, Sanofi-Genzyme

CME Content Review

The content of this activity was independently peer reviewed.

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2. Participate in the live activity.
3. Complete pre and post survey.
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You will receive your certificate as a downloadable file.

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Provided by Med Learning Group

Co-provided by Ultimate Medical Academy/CCM.

Supported by an educational grant from Pfizer.

Agenda

I. Atopic dermatitis in pediatric and adolescent patients: an overview

a. Prevalence and burden of AD
b. Pathogenesis of AD
    i. Whiteboard theme – pathophysiology of atopic dermatitis
    ii. Role of filaggrin and epidermal barrier dysfunction
    iii. Immune dysregulation and type 2 inflammation
c. Comorbid conditions
a. Challenges in the management of AD
b. Psychosocial and developmental impact of AD in children and adults

II. **Diagnosis and long-term management of AD in pediatric and adolescent patients**

a. Diagnostic features of AD in pediatric and adolescent patients
b. Current guideline recommendations for the management of AD in pediatric and adolescent patients
c. Incorporating quality of life and psychosocial concerns into treatment plans
d. Assessing disease severity and intensifying therapy
e. Developing a personalized treatment plan for patients with atopic dermatitis

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

a. Mechanism of action of approved and investigational agents
b. Whiteboard theme – mechanism of action of available agents for the management of AD
c. Crisaborole
d. Dupilumab
e. Emerging agents

IV. Collaborative Care in the Management of AD

a. Identifying patients who require a referral to a specialist
b. Best practices for co-management of pediatric patients
c. Communication between providers
d. Monitoring for adverse events
e. Patient education and counseling
f. Incorporating shared-decision making into clinical practice

V. Case Study

VI. Conclusions

Multidisciplinary Care of Pediatric and Adolescent Patients with Moderate-to-Severe Atopic Dermatitis

Disclosures

- Amy S. Paller, MD, has received consulting fees from AbbVie, Almirall, AnaptysBio, Asana, Boehringer-Ingelheim, Dermavant, Dermira, Eli Lilly, Forte, Galderma, Leo, Novartis, Pfizer, Regeneron, Sanofi-Genzyme, and Sol Gel.
- During the course of this lecture, the faculty may mention the use of medications for both FDA-approved and non-approved indications.

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Learning Objectives

- Develop treatment plans for the management of atopic dermatitis in pediatric and adolescent patients that incorporate guideline recommendations, evidence from clinical trials, and patient-specific factors
- Identify patients who would benefit from treatment intensification based on disease severity, failure of prior therapy, and comorbid conditions
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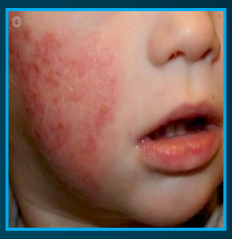
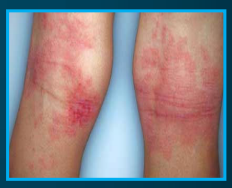
Atopic Dermatitis: Overview and Diagnosis

Atopic Dermatitis (or Atopic Eczema)

- AD is chronic, pruritic, systemic inflammatory disease with periods of acute disease flares[1,2]
  - Characterized by erythematous, scaly, excoriated, and lichenified papules and plaques[3]
- Frequently begins in children and tends to occur in families with other atopic diseases (eg, asthma, allergic rhinitis, food allergies)[1,3]
- AD has detrimental effects on patient QoL[1–5]
  - Social, psychological (eg, self-esteem, mood), occupational, and financial impacts
  - Results in decreased productivity and increased absenteeism[5–7]





AD = atopic dermatitis; QoL = quality of life.

1. Holm JG, et al. *J Eur Acad Dermatol Venereol.* 2016;30:1760-1767. 2. Simpson EL, et al. *J Am Acad Dermatol.* 2016;74:491-498. 3. Whiteley J, et al. *Curr Med Res Opin.* 2016;32:1645-1651. 4. Drucker AM, et al. *J Invest Dermatol.* 2017;137:26-30. 5. Zuberbier T, et al. *J Allergy Clin Immunol.* 2006;118:226-232. 6. van Os-Medendorp H, et al. *J Clin Med.* 2015;4:535-547. 7. Dickel H, et al. *J Invest Dermatol.* 2003;121:37-40.

Pediatric Atopic Dermatitis in United States

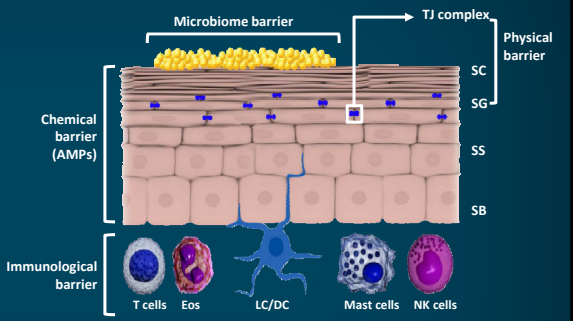
- Since 1970s, there has been a 3-fold increase in AD incidence[1]
  - Prevalence for US children = ~10.7%[1]
- More than 1 million school-aged children have AD[2]
  - 60% manifest symptoms in first year of life[1]
  - 90% within first 5 years[1]
- Overall health-related costs in 2015 estimated at $5.3 billion[3]
  - $349 per AD patient per month vs $261 for controls*[4]
- 86% of pediatric dermatology admissions to hospital are for AD[3]

***Data from 1998–2005**

1. Avena-Woods C. *Am J Manag Care.* 2017;23(8 suppl):S115-S123. 2. National Eczema Association (https://nationaleczema.org/school-tools-eczema-kids/). Accessed 2/22/2020. 3. Drucker AM, et al. *J Invest Dermatol.* 2017;137:26-30. 4. Zane LT, et al. *Immunotherapy.* 2016;8:853-866.

Pathogenesis of Atopic Dermatitis

- Complex pathogenesis
- No one conceptual model works (eg, extrinsic, intrinsic, inside-out, outside-in)
- Interplay among multiple factors:
  - Skin-barrier dysfunction
  - Immune dysregulation
  - Environmental exposures
  - Gene-environment interactions

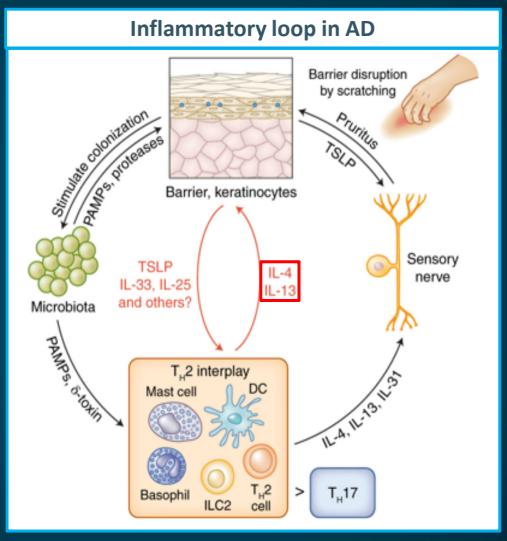


AMP = antimicrobial peptide; TJ = tight junction; SC = stratum corneum; SG = stratum granulosum; SS = stratum spinosum; SB = stratum basale; Eos = eosinophils; LC = Langerhans cells; DC = dendritic cells; NK = natural killer.

Novak N, Bieber T. *J Allergy Clin Immunol.* 2003;112:252-262. Napolitano M, et al. *G Ital Dermatol Venereol.* 2016;151:403-411. McLean WH. *Br J Dermatol.* 2016;175(suppl 2):4-7. Palmer CN, et al. *Nat Genet.* 2006;38:441-446. Paternoster L, et al. *Nat Genet.* 2015;47:1449-1456. Tamari M, Hirota T. *J Dermatol.* 2014;41:213-220. Sasaki T, et al. *J Dermatol Sci.* 2014;76:10-15. Leung DY, Guttman-Yassky E. *J Allergy Clin Immunol.* 2014;134:769-779. Wang D, Beck LA. *Am J Clin Dermatol.* 2016;17:425-443.

Inflammatory Loop in Atopic Dermatitis

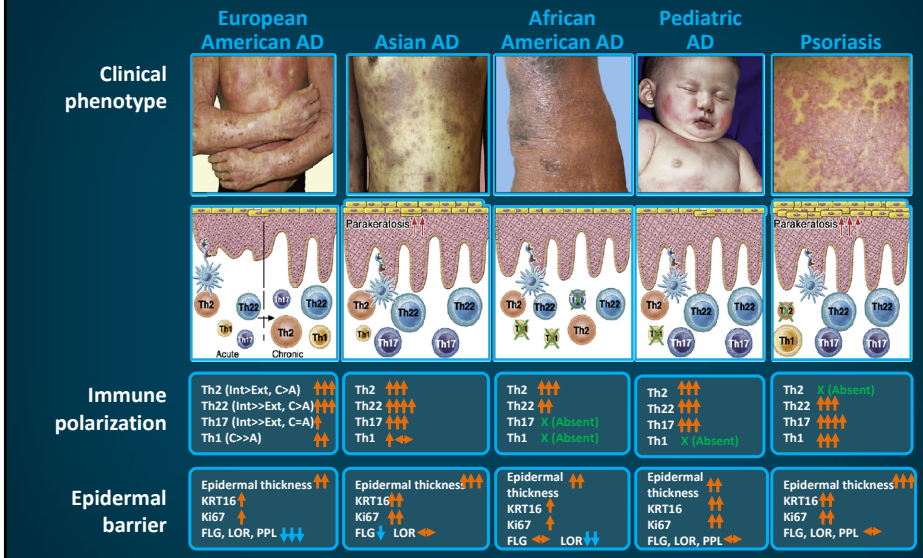
- In AD, a defective barrier and microbial dysbiosis drive a type 2 cytokine loop (IL-4/-13)
- Predominating factor is probably specific to each patient, reflecting heterogeneity of AD



IL = interleukin; TSLP = thymic stromal lymphopoietin; PAMPs = pathogen-associated molecular patterns

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

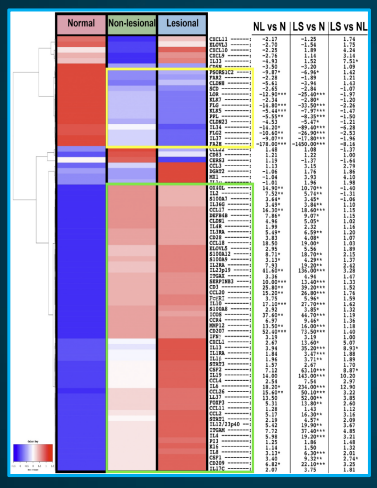
AD Phenotypes and Related Endotypes



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

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

Subphenotyping AD: Big Data Analysis from Biopsies and Tape Strips



- **Tape strips: painless for kids**
  - Tape stripping (x20) reaches upper SG
  - qRT-PCR: 77/79 genes detectable and in ~100% of children sampled
  - Largely same patterns as biopsy
  - Increases in Th2 and Th17 expression
  - Reductions in genes for lipid synthesis, TJ proteins, proteins of differentiation (eg, FLG, LOR, PPL), and negative-immune regulators (IL-34, IL-37)
  - Sufficient RNA to run all samples for RNASeq for an expanded signature
- **Opportunity to predict natural history, development of comorbidities, and therapeutic responses**

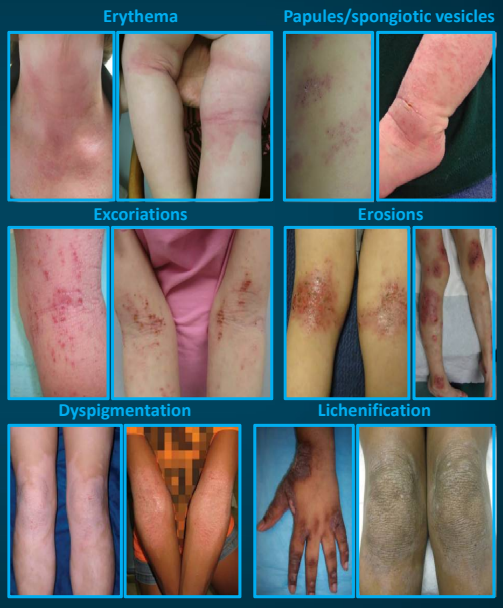
qRT-PCR = quantitative real-time polymerase chain reaction; RNA = ribonucleic acid; RNASeq = RNA sequencing.

Guttman-Yassky E, et al. *JAMA Dermatol.* 2019;155:1358-1370. Pavel AB, et al. *Allergy.* 2020 Jul 8;Epub ahead of print.

Diagnosis and Treatment

Atopic Dermatitis: Clinical Diagnosis

- Age-specific clinical criteria
  - Infants: face, trunk, and/or extensor extremities
  - Children: flexors (wrists, ankles, antecubital/popliteal fossae)
  - Adults: hands
  - Groin and axillae typically spared
- Generalized xerosis
- Interval flares, often without obvious triggers
- Skin lesions typically diffuse and very pruritic



Siegfried EC, Hebert AA. *J Clin Med*. 2015;4:884-917.

Atopic Dermatitis: 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 (e.g., facial pallor, white dermographism, delayed blanch response)
  - Keratosis pilaris / pityriasis alba / hyperlinear palms / ichthyosis
  - Ocular / periorbital changes
  - Other regional findings (e.g., 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

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

Pillars of Atopic Dermatitis Management

- Avoid environmental triggers if possible
- Restore the disturbed skin barrier
  - Skin care regimen and hydration (eg, emollients, especially after bathing)
- Reduce inflammation and itch
  - Aggressive early treatment, appropriate for severity, eg:
    - Anti-inflammatory topicals (TCS, TCI, PDE-4i)
    - Systemic (CsA*, MTX*, MMF*, AZA*, OCS*, and dupilumab)
    - Phototherapy (narrowband UV-B)
  - Adjunctive agents for sleep (eg, oral antihistamines), infection (eg, oral antibiotics), and concomitant allergic disorders (eg, non-sedating antihistamines)
  - Other adjunctive agents: wet wraps, dilute bleach baths
  - Rarely, other systemic immunosuppressants, IVIG, or omalizumab have been used

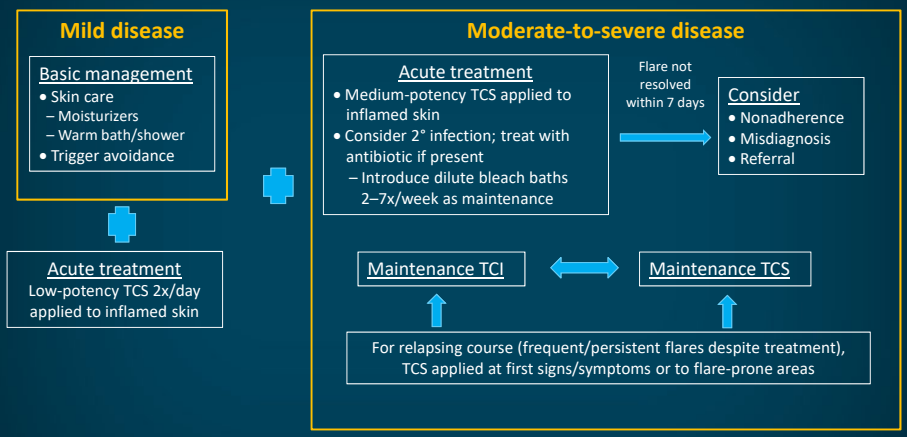
AD management

TCS = topical corticosteroid; TCI = topical calcineurin inhibitor; PDE-4 = phosphodiesterase-4; PDE-4i = PDE-4 inhibitor; OCS = oral corticosteroid; CsA = cyclosporine A; MTX = methotrexate; MMF = mycophenolate mofetil; AZA = azathioprine; UV-B = ultraviolet B; IVIG = intravenous immunoglobulin.

Wang D, Beck LA. *Am J Clin Dermatol.* 2016;17:425-443. Saeki H, et al. *J Dermatol.* 2016;43:1117-1145. Ring J, et al. *J Eur Acad Dermatol Venereol.* 2012;26:1045-1060. Ring J, et al. *J Eur Acad Dermatol Venereol.* 2012;26:1176-1193. Roekevisch E, et al. *J Allergy Clin Immunol.* 2014;133:429-438. Mohan GC, Lio PA. *JAMA Dermatol.* 2015;151:1009-1013. Wollenberg A, et al. *J Eur Acad Dermatol Venereol.* 2016;30:729-747.

*** Not an FDA-approved indication.**

Overview of Atopic Dermatitis Management



Modified from Eichenfield LF, et al. *Pediatrics*. 2015;136:554-565.

Topical Corticosteroids

- TCS is recommended if AD symptoms are not controlled by moisturizers alone
- Low-potency
  - Maintenance therapy to prevent exacerbations
- Intermediate- and high-potency (halogenated)
  - Exacerbations for short period or proactive therapy
- Ultra-high-potency
  - No more than 1–2 weeks
  - Non-facial, non-skinfold areas
- Potent, fluorinated corticosteroids should not be used beyond a few days on mucous membranes, face, eyelids, genitalia, and intertriginous areas or in young infants

Schneider L, et al. *J Allergy Clin Immunol*. 2013;131:295-299.e1-27. Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;71:116-132.

Topical Calcineurin Inhibitors

- TCIs include[1]:
  - Pimecrolimus cream 1% (≥2 years of age)
  - Tacrolimus 0.03% (≥2 years of age)
  - Tacrolimus 0.1% ointment (≥16 years of age)
- Block production of proinflammatory cytokines and other inflammatory mediators[1,2]
- TCI advantages vs TCS[1–3]
  - For face, anogenital, skin folds, or other sensitive areas
  - No atrophogenic properties; can reverse steroid-induced atrophy
  - Steroid-sparing: reduce overall TCS when used for maintenance

1. Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;71:116-132. 2. Schneider L, et al. *J Allergy Clin Immunol*. 2013;131:295-299.e1-27.
3. Siegfried EC, et al. *BMC Pediatr*. 2016;16:75.

Are You Dispensing Enough?

Estimates for Quick Memorization	
Recommended amount per dose	
Total BSA of a 5-month-old baby	5 gm
Total BSA of a 5–10-year-old child	10 gm
Total BSA of an adult	30 gm
Do the math for 2 weeks if 100% BSA...	
5 mo old: 100% BSA = 5 gm BID = 10 gm x 14 days = 140 gm	
7 yo: 100% BSA = 10 gm BID = 20 gm x 14 days = 280 gm	

BSA = body-surface area; mo = month(s) old; yo = year(s) old; BID = twice daily.

Management of Flares

- Preventing or at least increasing time interval between flares is critical goal of management[1]
- Important to act quickly and aggressively in treating flares[1]
- Two approaches (with continued basic management)[1–4]

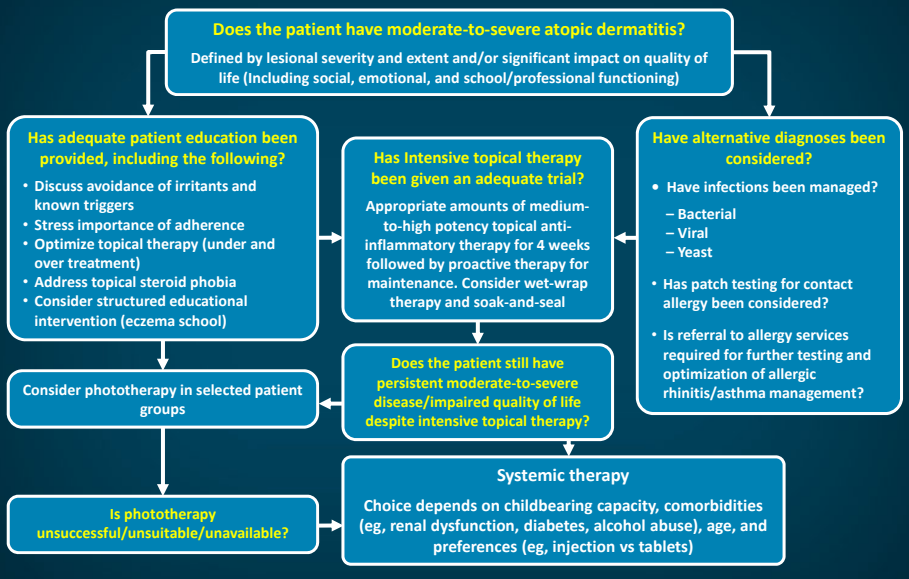
Reactive	Proactive
TCI or TCS applied at first signs/symptoms of flare	TCS 2–3 times/week or TCI 2–3 times/week

- Antiseptic/antibiotic therapy
  - Topical—dilute bleach bath (minimally twice-weekly; severe flares may require daily baths)[5]
  - Systemic—*S. aureus* most common pathogen[2]; MSSA >> MRSA[6,7]
    - Oral cephalosporin; amoxicillin/clavulanate

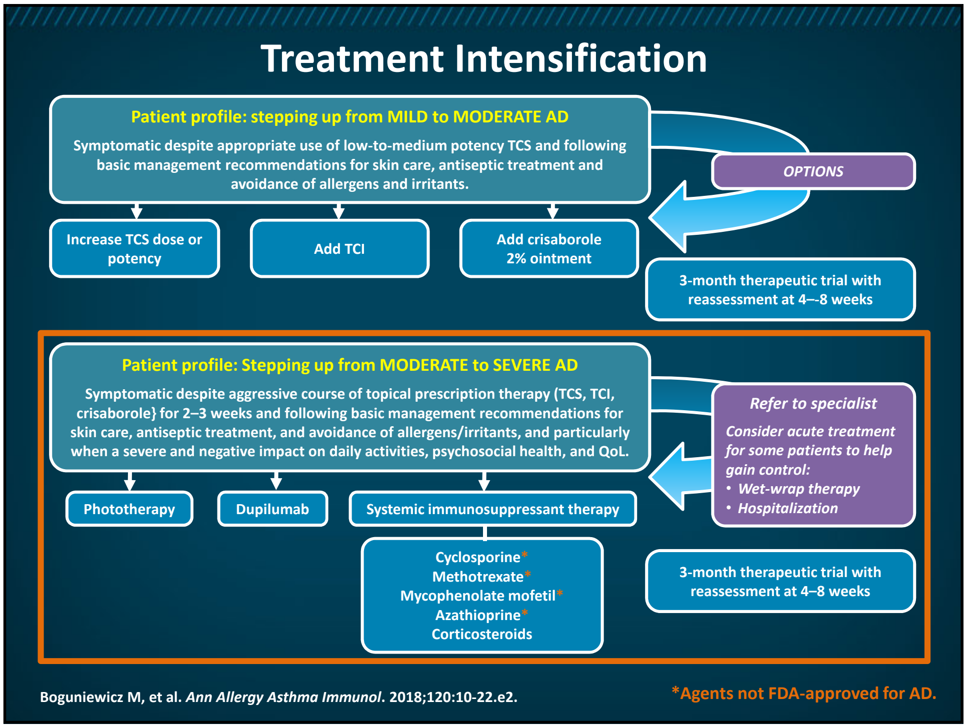
MSSA = methicillin-sensitive *S. (staphylococcus) aureus*; MRSA = methicillin-resistant *S. aureus*.

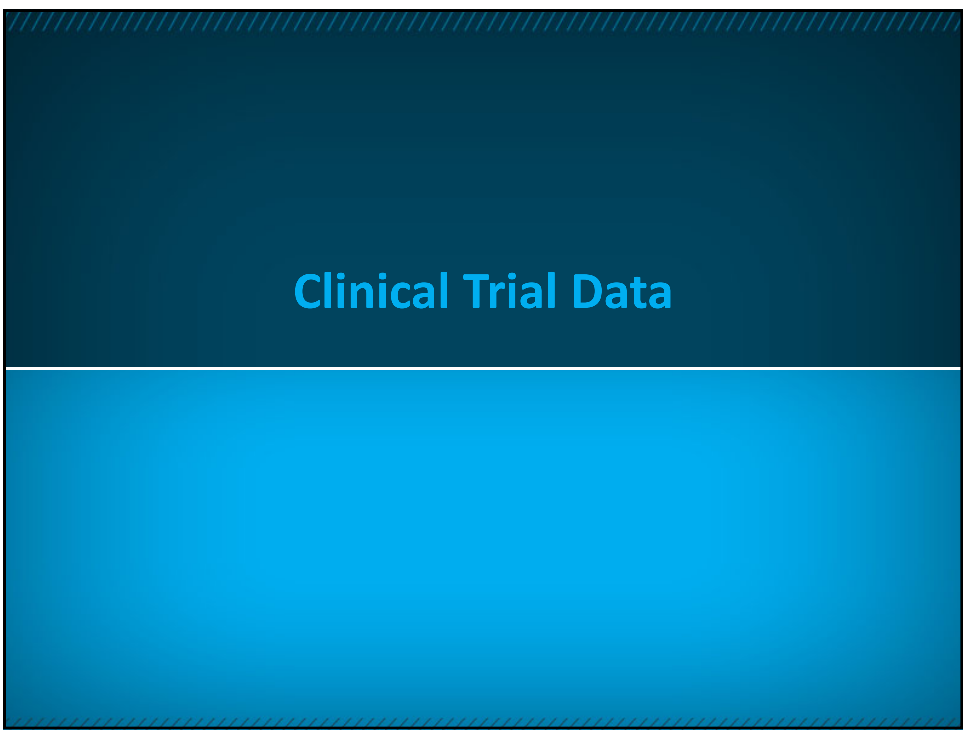
1. Wollenberg A, et al. *J Eur Acad Dermatol Venereol*. 2016;30:729-747. 2. Sidbury R, et al. *J Am Acad Dermatol*. 2014;71:327-349. 3. Eichenfield LF, et al. *Pediatrics*. 2015;136:554-565. 4. Schmitt J, et al. *Br J Dermatol*. 2011;164:415-428. 5. Chopra R, et al. *Ann Allergy Asthma Immunol*. 2017;119:435-440. 6. Suh S, et al. *Pediat Dermatol*. 2008;25:528-534. 7. Kim J, et al. *Allergy Asthma Immunol Res*. 2019;11:593-603.

When Is Systemic Therapy Warranted?



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


Treatment Intensification
Patient profile: stepping up from MILD to MODERATE AD
Symptomatic despite appropriate use of low-to-medium potency TCS and following basic management recommendations for skin care, antiseptic treatment and avoidance of allergens and irritants.
OPTIONS
Increase TCS dose or potency
Add TCI
Add crisaborole 2% ointment
3-month therapeutic trial with reassessment at 4–-8 weeks
Patient profile: Stepping up from MODERATE to SEVERE AD
Symptomatic despite aggressive course of topical prescription therapy (TCS, TCI, crisaborole} for 2–3 weeks and following basic management recommendations for skin care, antiseptic treatment, and avoidance of allergens/irritants, and particularly when a severe and negative impact on daily activities, psychosocial health, and QoL.
Refer to specialist
Consider acute treatment for some patients to help gain control:
• Wet-wrap therapy
• Hospitalization
Phototherapy
Dupilumab
Systemic immunosuppressant therapy
Cyclosporine*
Methotrexate*
Mycophenolate mofetil*
Azathioprine*
Corticosteroids
3-month therapeutic trial with reassessment at 4–8 weeks
Boguniewicz M, et al. Ann Allergy Asthma Immunol. 2018;120:10-22.e2.
*Agents not FDA-approved for AD.

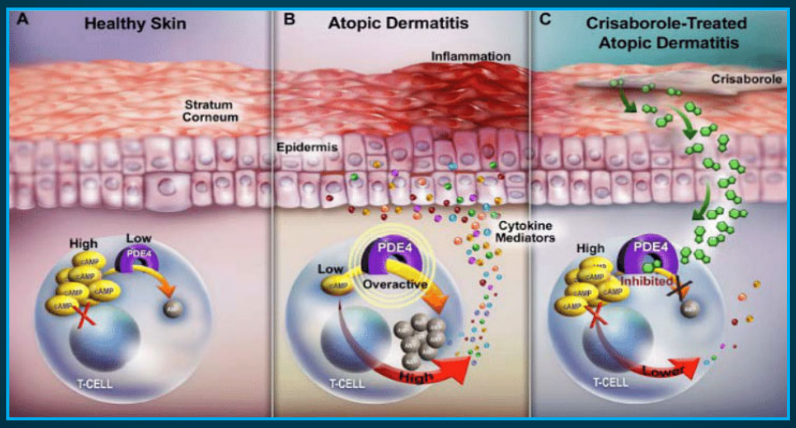

Clinical Trial Data

New Therapeutic Targets

Topical Agents: Crisaborole Ointment 2%

Non-steroidal, topical PDE-4 inhibitor

cAMP-activated intracellular signaling in (A) normal healthy skin, (B) untreated atopic dermatitis, and (C) atopic dermatitis treated with the PDE-4 inhibitor crisaborole



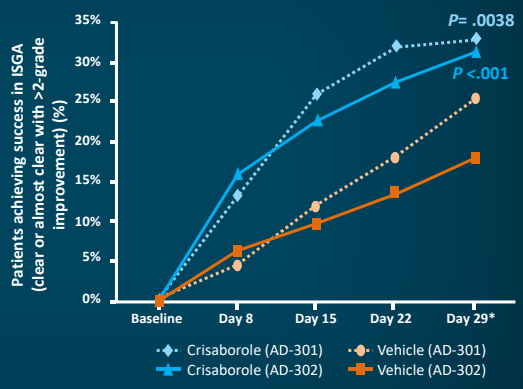
AMP = adenosine monophosphate; cAMP = cyclic AMP.

Jarnagin K et al. *J Drugs Dermatol*. 2016;15:390-396.

Phase 3 Data for Crisaborole

- 31–33% of patients achieved ISGA score of 0 or 1 (clear or mostly clear) with ≥2-grade improvement compared with 18–25% in placebo group.
- Good long-term safety; most common AE is application-site reactions

Crisaborole demonstrated early and continued separation from vehicle across treatment period



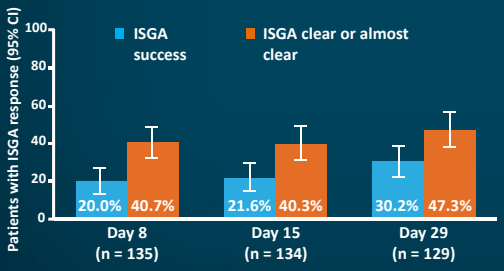
Symptoms of systemic PDE-4 inhibitors (eg, nausea, vomiting, and headache) were rare.

ISGA = Investigator's Static Global Assessment; AE = adverse event.

Paller AS, et al. *J Am Acad Dermatol.* 2016;75:494-503.e6.

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 a >2-grade improvement on ISGA was achieved by 30.2% of patients at day 29
- Crisaborole approved for mild-to-moderate AD in patients ≥3 months of age



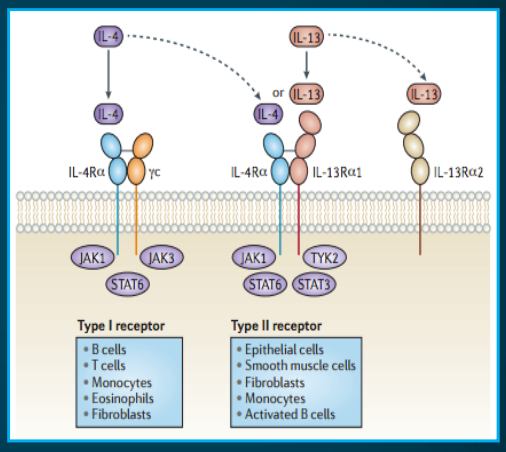
TEAEs Reported for ≥2.5% of Patients		
Overall TEAEs, n (%)	All-cause	Treatment-related
Pyrexia	13 (9.5)	0
URTI	10 (7.3)	1 (0.7)
Diarrhea	10 (7.3)	0
Atopic dermatitis	9 (6.6)	0
Dermatitis, diaper	9 (6.6)	0
Cough	7 (5.1)	0
Otis media	6 (4.4)	1 (0.7)
Eczema	5 (3.6)	2 (1.5)
App-S pain	5 (3.6)	5 (3.6)
Conjunctivitis	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
App-S discomfort	4 (2.9)	4 (2.9)
App-S erythema	4 (2.9)	3 (2.2)
Ear infection	4 (2.9)	0
Nasopharyngitis	4 (2.9)	0
Teething	4 (2.9)	0

TEAE = treatment-emergent AE; URTI = upper respiratory tract infection; App-S = application-site; CI = confidence interval.

Schlessinger J, et al. *Am J Clin Dermatol.* 2020;21:275-284. Crisaborole (Eucrisa®) prescribing information (PI) 2020 (http://labeling.pfizer.com/ShowLabeling.aspx?id=5331). Accessed 9/4/2020.

New Therapeutic Targets: Dupilumab
Systemic Agents/Biologics

- Dupilumab is a humanized monoclonal antibody against IL-4Rα that blocks activity of IL-4 and IL-13.
- FDA-approved for treatment of patients ≥6 years with moderate-to-severe AD whose disease is not adequately controlled with topical therapies or when those therapies are not advised
  - May be used with or without topical corticosteroids

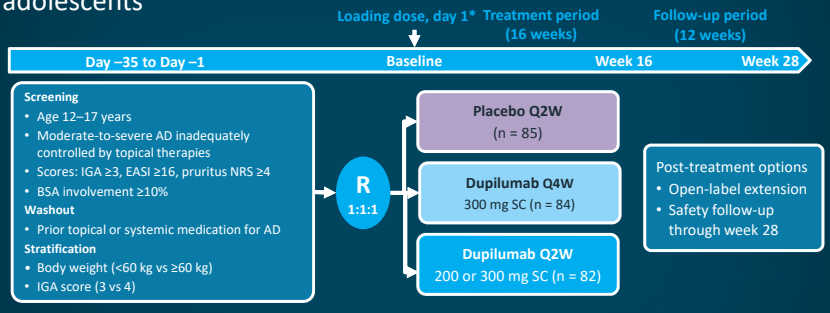


JAK = Janus kinase; STAT = signal transducer and activator of transcription; TYK = tyrosine kinase.

Adapted from Paller AS, et al. *J Allergy Clin Immunol.* 2017;140:633-643. Dupilumab (Dupixent®) PI 2020 (www.regeneron.com/sites/default/files/Dupixent_FPI.pdf). Accessed 9/4/2020.

Dupilumab in Adolescents with Uncontrolled Moderate-to-Severe AD

- Randomized, double-blind, parallel-group, phase 3 trial of 251 adolescents



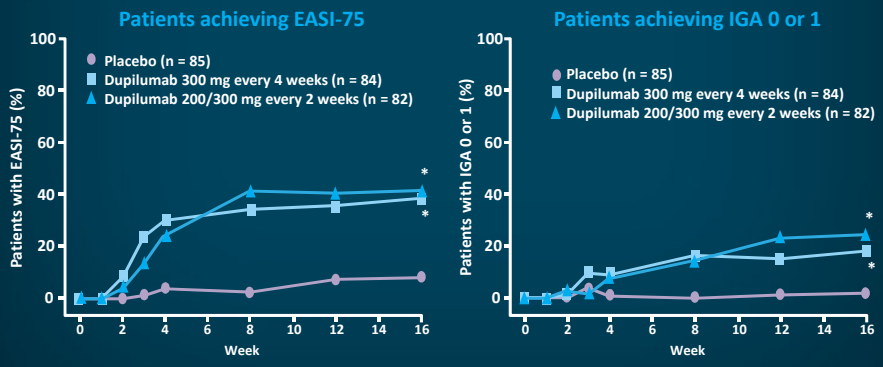
- Majority of patients had comorbid type 2 disease (asthma, 53.6%; food allergies, 60.8%; allergic rhinitis, 65.6%)

*600 mg loading dose (LD) followed by 300 mg for patients weighing ≥60 kg; 400 mg LD followed by 200 mg for <60 kg. BSA = body surface area; IGA = Investigator's Global Assessment; EASI = Eczema Area and Severity Score; NRS = Numerical Rating Scale; Q4W = every 4 weeks; Q2W = every 2 weeks; R = randomization; SC = subcutaneous.

Simpson EL, et al. *JAMA Dermatol*. 2020;156:44-56 and supplement.

Dupilumab in Adolescents with Uncontrolled Moderate-to-Severe AD: EASI-75 and IGA

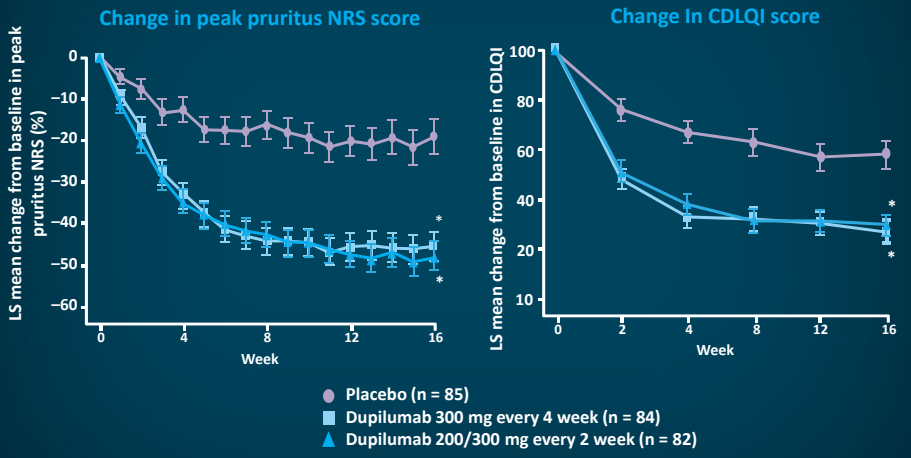
Significantly higher proportion of patients reached EASI-75 and IGA 0 or 1 at week 16 in both dupilumab Q2W and Q4W groups compared with placebo



*P <.001 vs placebo.

Simpson EL, et al. *JAMA Dermatol*. 2020;156:44-56.

Dupilumab in Adolescents with Uncontrolled Moderate-to-Severe AD: Pruritus and QoL



*P <.001 vs placebo.
CDLQI = Children's Dermatology Life Quality Index; LSM = least squares mean; BL = baseline.

Simpson EL, et al. *JAMA Dermatol*. 2020;156:44-56.

Dupilumab in Adolescents with Uncontrolled Moderate-to-Severe AD: Adverse Events

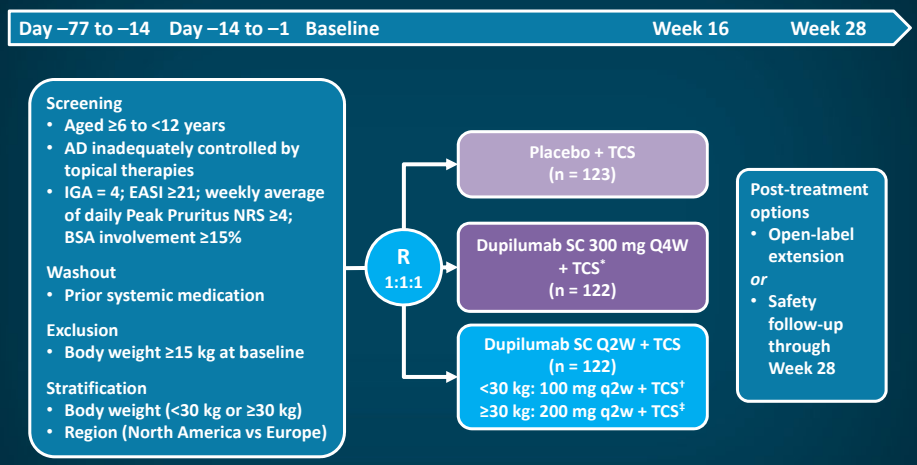
AEs during study treatment period showed no new signals.

Adverse events, n (%)	Placebo (n = 85)	Dupilumab 300 mg Q4W (n = 83)	Dupilumab 200/300 mg Q2W (n = 82)
Patients with TEAE	59 (69.4)	53 (63.9)	59 (72.0)
Permanent discontinuation of study drug d/t TEAE	1 (1.2)	0	0
Serious TEAE	1 (1.2)	0	0
Death	0	0	0
Most common TEAEs (≥5% of patients in any group)			
Atopic dermatitis	21 (24.7)	15 (18.1)	15 (18.3)
Skin infections (adjudicated)	17 (20.0)	11 (13.3)	9 (11.0)
Excluding herpetic skin infections (adjudicated)	16 (18.8)	8 (9.6)	8 (9.8)
Upper respiratory tract infection	15 (17.6)	6 (7.2)	10 (12.2)
Headache	9 (10.6)	4 (4.8)	9 (11.0)
Conjunctivitis*	4 (4.7)	9 (10.8)	8 (9.8)
Nasopharyngitis	4 (4.7)	9 (10.8)	3 (3.7)
Infections and infestations (SOC)	37 (43.5)	38 (45.8)	34 (41.5)
Injection-site reactions (HLT)	3 (3.5)	5 (6.0)	7 (8.5)
Herpes viral infections (HLT)	3 (3.5)	4 (4.8)	1 (1.2)

*Includes atopic keratoconjunctivitis, conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, and conjunctivitis viral.
AE = adverse event; d/t = due to; HLT = high-level term; SOC = system organ class.

Simpson EL, et al. *JAMA Dermatol*. 2020;156:44-56.

Phase 3 LIBERTY AD PEDS Trial



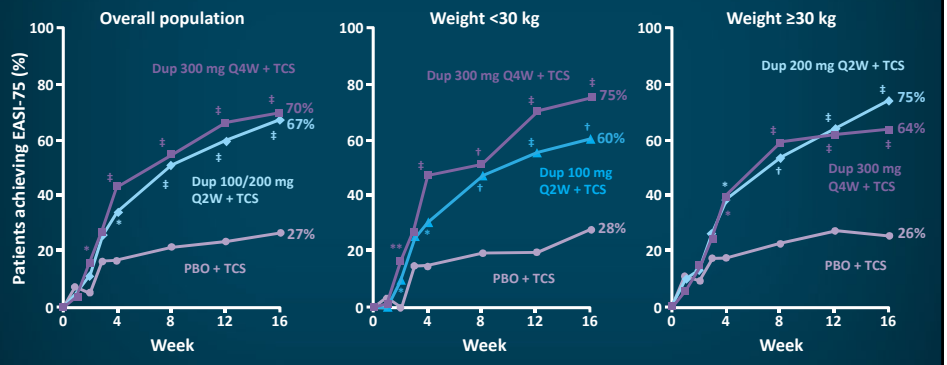
*600 mq loading dose; †200 mg loading dose; ‡400 mg loading dose.

Paller AS, et al. *J Am Acad Dermatol.* 2020;Jun 20: Epub ahead of print. Paller AS, et al. Poster 215. Presented at the Revolutionizing Atopic Dermatitis (RAD) Conference 2020.

LIBERTY AD PEDS Results: IGA and EASI-75

IGA score of 0/1 achieved by 32.8% of patients in Q4W +TCS group, 29.5% in the Q2W + TCS group, and 11.4% in the placebo + TCS group

Proportions of patients achieving EASI-75 over time



*P <.05; †P <.001; ‡P <.0001.

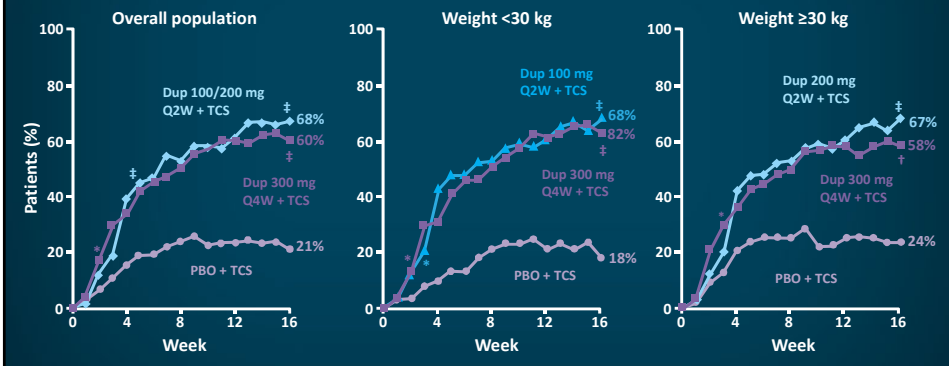
Dup = dupilumab; PBO = placebo

Paller AS, et al. *J Am Acad Dermatol.* 2020;Jun 20: Epub ahead of print. Paller AS, et al. Poster 215. Presented at RAD Conference 2020.

LIBERTY AD PEDS Results: Peak Pruritus

Optimal dosing for efficacy and safety was 300 mg Q4W in children <30 kg and 200 mg Q2W in children ≥30 kg

Proportions of patients with ≥3-point improvement in Peak Pruritus NRS



*P <.05; †P <.001; ‡P <.0001.

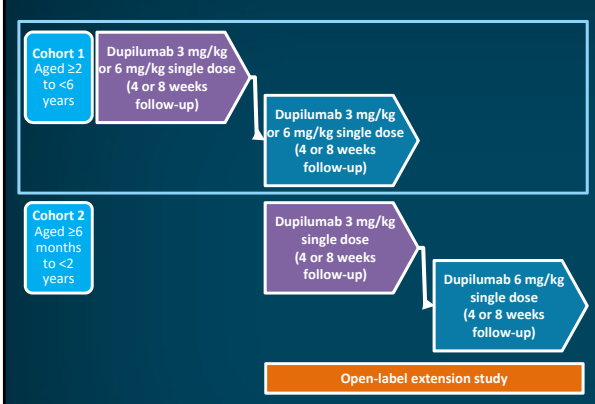
Paller AS, et al. *J Am Acad Dermatol*. 2020;Jun 20: Epub ahead of print. Paller AS, et al. Poster 215. Presented at RAD Conference 2020.

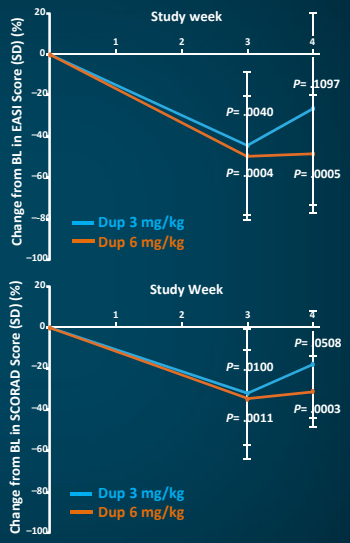
LIBERTY AD PEDS Safety Data

AE/TEAE, n (%)	PBO + TCS (n = 120)	Dup 300 mg Q4W + TCS (n = 120)	Dup 100/200 mg Q2W + TCS (n = 122)
Patients with ≥1 TEAE	88 (73.3)	78 (65.0)	82 (67.2)
Patients with ≥1 serious TEAE	2 (1.7)	2 (1.7)	0
Discontinuation of treatment d/t TEAE	2 (1.7)	0	2 (1.6)
Deaths	0	0	0
TEAEs reported in ≥5% of patients			
Dermatitis atopic, exacerbation	17 (14.2)	8 (6.7)	10 (8.2)
Asthma	12 (10.0)	2 (1.7)	4 (3.3)
Nasopharyngitis	8 (6.7)	15 (12.5)	8 (6.6)
URTI	12 (10.0)	13 (10.8)	10 (8.2)
Viral URTI	6 (5.0)	2 (1.7)	1 (0.8)
Vomiting	8 (6.7)	6 (5.0)	6 (4.9)
Cough	9 (7.5)	3 (2.5)	5 (4.1)
Headache	10 (8.3)	6 (5.0)	7 (5.7)
Other AEs			
Infections and infestations (SOC)	61 (50.8)	52 (43.3)	49 (40.2)
Conjunctivitis cluster	5 (4.2)	8 (6.7)	18 (14.8)
Keratitis cluster	0	0	1 (0.8)
Skin infection (adjudicated)	16 (13.3)	7 (5.8)	10 (8.2)
Injection-site reactions	7 (5.8)	12 (10.0)	13 (10.7)
Herpes viral infections (HLT)	6 (5.0)	2 (1.7)	4 (3.3)

Paller AS, et al. *J Am Acad Dermatol*. 2020;Jun 20: Epub ahead of print. Paller AS, et al. Poster 215. Presented at the Revolutionizing Atopic Dermatitis (RAD) Conference 2020.

Phase 2/3 LIBERTY AD PRE-SCHOOL Trial





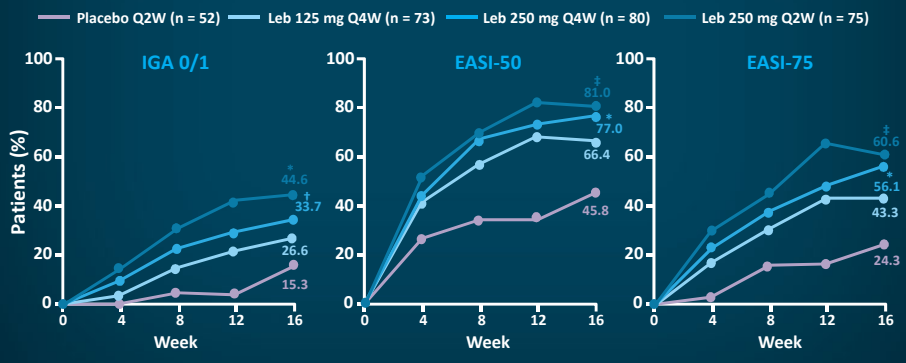
Dupilumab is not FDA-approved in patient <6 years

OLE = open-label extension; SCORAD = Scoring AD; SD = standard deviation.

Simpson EL, et al. Poster 128. Presented at the RAD Conference 2020.

Emerging Agent: Lebrikizumab (anti-IL-13)

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

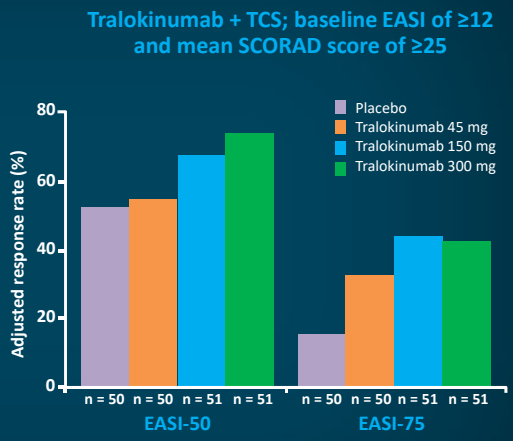


***P< .01; †P< .05; ‡P< .001 vs placebo.**

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

Emerging Agent: Tralokinumab

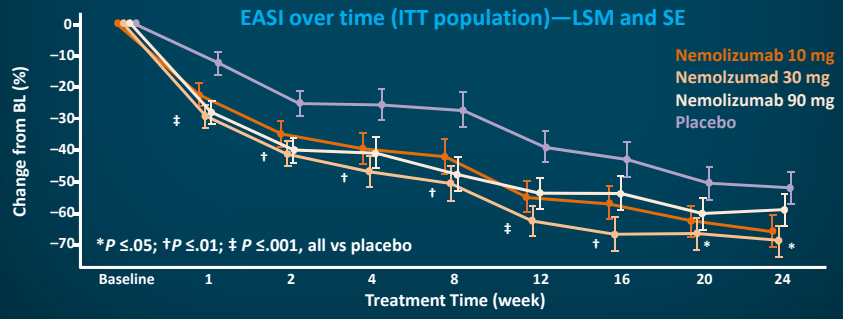
- Phase 2b randomized trial in 204 adults with moderate-to-severe AD inadequately controlled with TCS
- Subjects required to use TCS at least once daily
- At week 12, significantly more patients achieved EASI-50 with tralokinumab 300 mg Q2W than placebo



Wollenberg A, et al. *J Allergy Clin Immunol*. 2019:143:135-141.

Emerging Agent: Nemolizumab

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



ITT = intention-to-treat; SE = standard error.

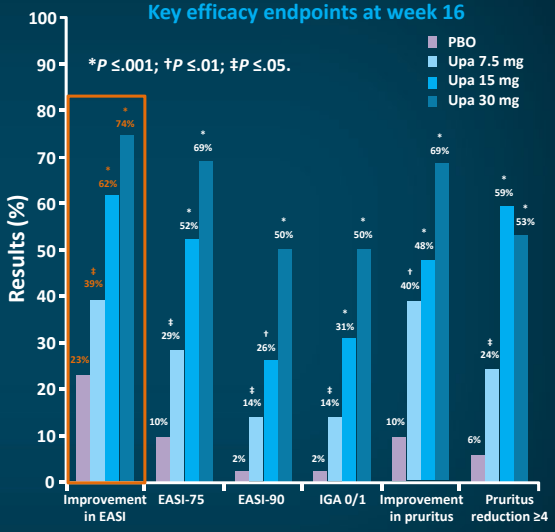
Silverberg JI, et al. *J Allergy Clin Immunol*. 2020;145:173-182.

Emerging Agents: Upadacitinib (Upa)

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

Top-Line Results: Measure Up Studies
Patients Achieving EASI-75 at Week 16

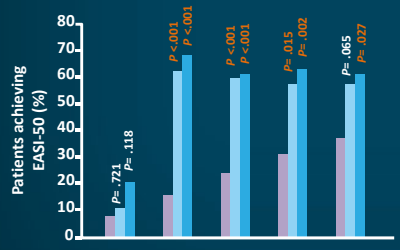
Study	Upa 15 mg	Upa 30 mg	PBO	*P*-value
Measure Up 1	70%	80%	16%	<.001
Measure Up 2	60%	73%	13%	<.001



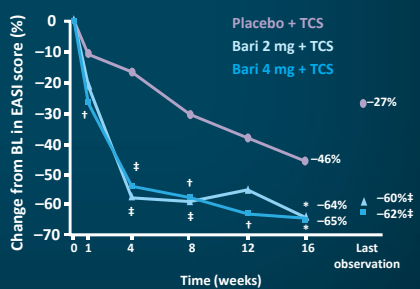
Guttman-Yassky E, et al. *J Allergy Clin Immunol.* 2020;145:877-884. AbbVie press release (PR). (https://news.abbvie.com/news/press-releases/rinvoq-upadacitinib-monotherapy-shows-improvement-in-skin-clearance-and-itch-in-first-phase-3-study-for-atopic-dermatitis.htm#:~:text=Measure%20 Up%201%20is%20a,are%20candidates%20for%20systemic%20treatment. AbbVie PR. (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)

Emerging Agents: Baricitinib (Bari)

- 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.
- TEAEs were reported in 71% of baricitinib 4 mg and 49% of placebo recipients



Weeks	1	4	8	12	16
PBO + TCS	8	16	24	31	37
Bari 2 mg + TCS	11	62	59	57	57
Bari 4 mg + TCS	21	68	61	63	61



*P <.05; †P ≤.01; ‡P ≤.001.

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 24-point improvement on Itch NRS	16%†	25%*	6%
Mean change in DLQI	–5.5	–7.5‡	–4.0

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

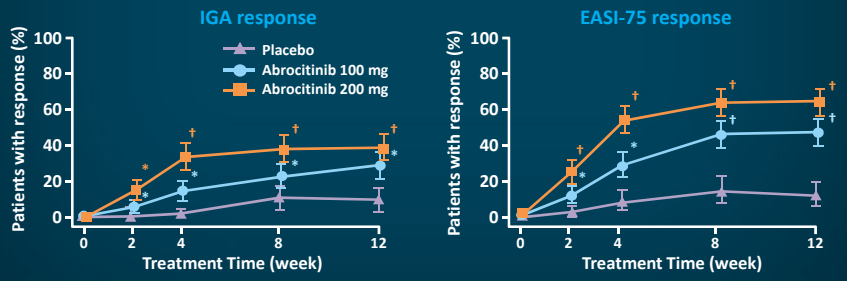
- Improvement in proportion of patients who achieved ≥4-point improvement on itch NRS statistically significant as early as week 2 for both baricitinib arms

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

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

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)

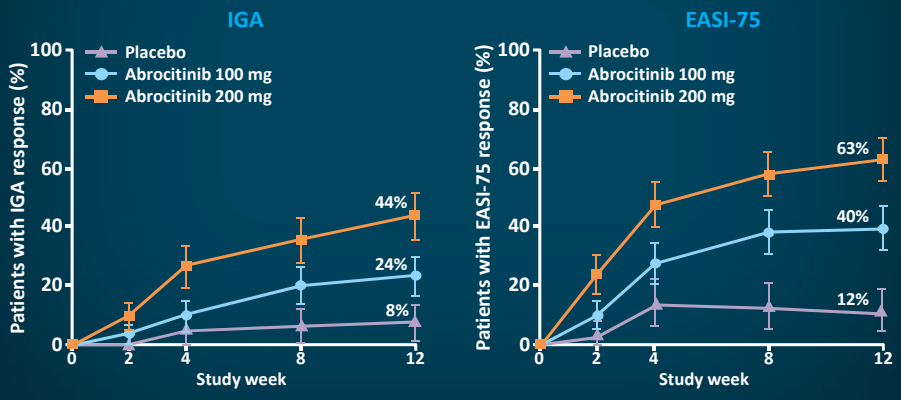


*P <.05; †P <.001 vs placebo. Note: 95% CI graphed.

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

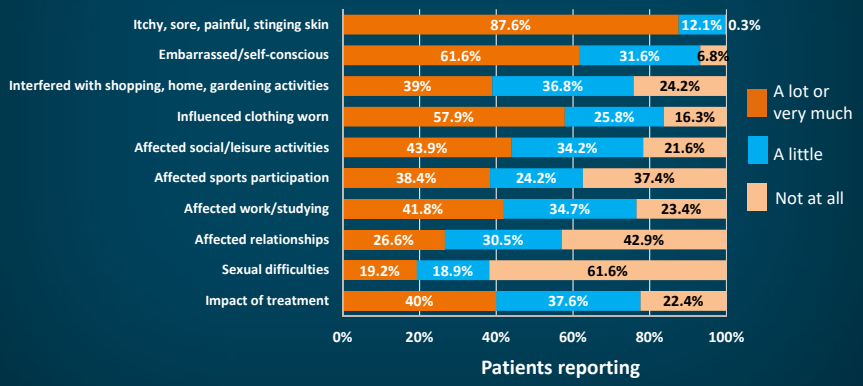


Simpson EL, et al. *Lancet*. 2020;396:255-266.

Patient Considerations in AD

AD Has a Very Large Impact on QoL: DLQI

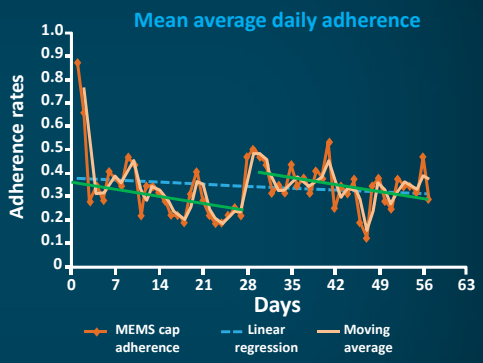
Total DLQI score was 14.3, consistent with a very large impact on patients' lives



Simpson EL, et al. *J Am Acad Dermatol*. 2016;74:491-498.

Adherence to Therapy

- Lack of adherence can result in poor disease control, worse clinical outcomes, and lack of medication efficacy
  - Poor adherence may be misconstrued as a poor treatment response.
- Poor compliance can also result from:
  - Time constraints
  - Unclear or difficult-to-follow instructions
  - Alternative health beliefs
  - Steroid-phobia or fear of other side effects
  - Medication cost



MEMS = medication event monitoring system (cap on medication bottle).

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. Krejci-Manwaring J, et al. *J Am Acad Dermatol*. 2007;56 :211-216.

Patient Education

- Treatment plan education
  - Chronic nature of disease, exacerbating factors, and efficacy and safety of treatments
  - Demonstrate skin-care techniques
  - Provide written treatment plan
  - Explore adherence issues and counsel to avoid "steroid phobia"
- Identify comorbidities and impact on patient and family quality of life
  - Refer to other healthcare providers for team-based approach as needed
    - For behavioral disorders, sleep disturbances, and comorbidities (PCP, allergy/immunology, pulmonology, sleep specialists, psychologists, and psychiatrists)
  - Include support and additional education from nurses, pharmacists, and dietitians

PCP = primary care physician/provider.

Schneider L, et al. *J Allergy Clin Immunol*. 2013;131:295-299.e.1-27. Smith SD, et al. *Med J Aust*. 2013;199:467-469.

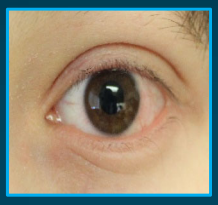
Potential Adverse Events

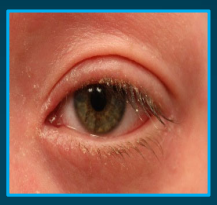
- Cutaneous side effects from TCS use include purpura, telangiectasia, striae, focal hypertrichosis, acneiform, and skin atrophy
  - Usually resolves with TCS discontinuation
- Topical calcineurin inhibitor
  - More local adverse effects than TCS (stinging, burning), especially if more inflamed
  - Black box warning persists for theoretical risk of malignancy (lymphoma, NMSC), although no evidence for a causal relationship to date; requires reassurance when prescribed
- Crisaborole
  - Application-site pain, burning, stinging
  - Resolves within 1 day of onset in majority of patients

NMSC = nonmelanoma skin cancer.

Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;71:116-132. Paller AS, et al. *J Am Acad Dermatol*. 2016;75:494-503.e6.

Potential Adverse Events with Dupilumab
Conjunctivitis

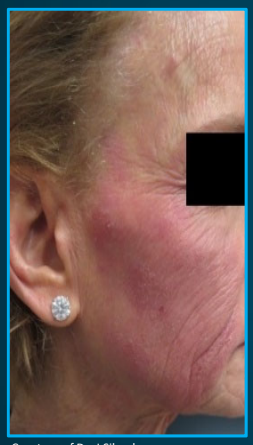




- In real-life study of adult AD (France), 38% of 241 patients developed conjunctivitis (awareness bias)
- Ask about history of conjunctivitis, but it is not a contraindication to starting dupilumab
- Some suggest eye lubricants as prophylaxis, but no evidence yet to support use
- Have consultant referral if conjunctivitis occurs; can be treated and tends to improve
- Topical treatment of eyelids with TCI may be helpful

Akinlade B, et al. *Br J Dermatol.* 2019;18:459-473. Faiz S, et al. *J Am Acad Dermatol.* 2019;81:143-151. Thyssen JP, et al. *J Eur Acad Dermatol Venereol.* 2019;33:1224-1231.

Other Cutaneous Issues with Dupilumab
Persistent Red Face (PRF)

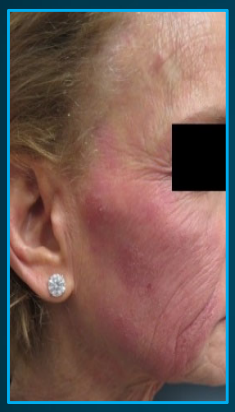


Courtesy of Dr. J Silverberg

- Paradoxical erythema of head and neck
- AD generally responds well to dupilumab elsewhere on the body
- Typically 10–40 weeks after starting treatment
- Sharply demarcated and patchy without increased scaling; variable associated itch
- Poor response to topical and systemic meds
- Rarely leads to dupilumab discontinuation

Stout M, Silverberg JI. *J Am Acad Dermatol.* 2019;81:157-162. Suresh R, Murase JE. *JAAD Case Rep.* 2018;4:899-904. de Beer FSA, et al. *JAAD Case Rep.* 2019;5:888-891.

Other Cutaneous Issues with Dupilumab: PRF



Courtesy of Dr. J Silverberg

- Insufficient dosing? Go to weekly dosing?*
- Comprehensive patch testing is first step
  - Being on dupilumab does not preclude patch testing and may improve responses upon repeat
- Consider *Malassezia* hypersensitivity
  - Trial of itraconazole 200 mg daily for 1–2 months, then continue 2–3x/week as needed if effective
- Consider:
  - Demodex-associated rosacea
  - Photosensitivity reaction
  - Sorbitan sesquioleate, 20% pet (1+)
  - Cosmetics (foundation and blush)

*** Not FDA approved.**

Stout M, Silverberg JI. *J Am Acad Dermatol.* 2019;81:157-162. Suresh R, Murase JE. *JAAD Case Rep.* 2018;4:899-904. de Beer FSA, et al. *JAAD Case Rep.* 2019;5:888-891. Zhu GA, et al. *JAAD Case Rep.* 2019;5:336-338.

Practical Considerations for Dupilumab

- Transition from another systemic medication during first 1–2 months (eg, full dose for 1st month then half for next month), and combine with TCS throughout as needed
- Continue trial for 3–4 months, monitoring change in severity, itch, and QoL
- Likely to be continued improvement during initial 6 months, but flares may also occur
  - Discuss potential risks upfront
- Mention low risk of injection-site reaction
- Review other risks: PRF, psoriasiform reactions, alopecia areata

Multidisciplinary Approach to AD

- Individuals with AD often have asthma, hay fever, sleep disorders, and psychological issues, eg, depression
- Eczema can exacerbate these associated comorbidities

Silverberg JI. *Ann Allergy Asthma Immunol.* 2019;123:144-151. Nataloni R. *Dermatologist.* 2016;24. (www.the-dermatologist.com/article/multidisciplinary-approach-eczema-treatment). Accessed 9/4/2020.

Multidisciplinary Team in Management of AD

- Proper management of direct and indirect effects of AD often requires expertise beyond scope of dermatology
- Multidisciplinary approach can:
  - Treat common comorbidities
  - Improve patient QoL
  - Reduce polypharmacy
  - Improve communication between providers

Nataloni R. *Dermatologist.* 2016;24. (www.the-dermatologist.com/article/multidisciplinary-approach-eczema-treatment). Accessed 9/4/2020.

Case Study

Case Study

- 8-year old girl presents with eczematous lesions covering 30% of BSA
  - First diagnosed with AD at 6 months of age
  - Thick, lichenified plaques found on knees, ankles, and wrists
  - Patient complains of uncontrolled itching leading to poor sleep quality
  - Patient weighs 31 kg
- Prior medical history significant for:
  - Two prior staph infections treated with cephalexin
  - Asthma; albuterol use twice/week for shortness of breath or coughing
  - Allergies to dust mites, cat dander, and mixed tree and weed pollen
- Current therapy includes triamcinolone 0.1% ointment for extremities and pimecrolimus 1% cream for face

What treatment options would you recommend for this patient?

Case Study: Intensified Therapy

- Frequency of triamcinolone application is increased to twice daily to control her flares
  - Patient sees improvement after 1 week
- Crisaborole 2% topical ointment is added to her regimen as maintenance therapy and the frequency of steroid application is reduced to twice weekly
  - The patient initially sees an improvement with crisaborole but returns 1 month later with worsening symptoms

What treatment options would you recommend for this patient?

Case Study: Further Treatment

Patient started on dupilumab 400 mg loading dose and 200 mg every 2 weeks

- Lichenified lesions begin to resolve after 1 month of therapy
- Near complete resolution of all skin lesions after 3 months of therapy
- Decreased pruritus and improved sleep quality was noted after 2 weeks

Conclusions

Conclusions

- Atopic dermatitis is a chronic disease that is challenging to treat and often significantly impairs a patient's quality of life
- Paradigm in the diagnosis and treatment of patients with atopic dermatitis:
  - Increased understanding of the pathogenesis of AD
  - Expansion in treatment alternatives
  - Newer interventions with improved efficacy and safety
- Appropriate management, including advancing to more aggressive therapy as needed, can be life-changing for pediatric and adolescent patients with AD
- Dupilumab is first FDA-approved systemic treatment for patients ≥6 years old with moderate-to-severe AD whose disease is not adequately controlled with topical therapies or when those therapies are not advised; other systemic agents are in trials
- Collaboration among dermatologists, allergists, pharmacists, nurses, other healthcare professionals, and patients can ensure safe, effective, and affordable treatment

Thank you!

Questions/Answers

Multidisciplinary Care of Pediatric and Adolescent Patients with Moderate to Severe Atopic Dermatitis

Resource	Address
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/
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/
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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/
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/
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 dermatitis (AD) in children and adults. *J Am Acad Dermatol.* 2016;75:494-503.	https://pubmed.ncbi.nlm.nih.gov/27417017/
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/
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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/