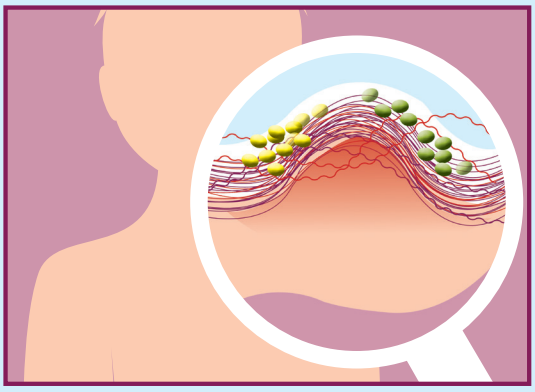
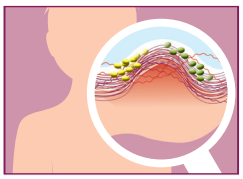


MILD TO MODERATE ATOPIC DERMATITIS:

Pathogenesis and Therapeutic Strategies for Improved Outcomes

This educational activity is jointly provided by The American Academy of CME, Spire Learning, and The Kansas Chapter, American Academy of Pediatrics.

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



MILD TO MODERATE ATOPIC DERMATITIS: Pathogenesis and Therapeutic Strategies for Improved Outcomes

PROGRAM OVERVIEW

This live meeting will address several important clinical practice gaps related to atopic dermatitis, including diagnosis, the importance of proper skin care in improving skin barrier dysfunction and reducing frequency of flare-ups, current knowledge of inflammatory pathways that contribute to the pathogenesis of atopic dermatitis, as well as the safety and efficacy of current and emerging therapies for the treatment of mild to moderate atopic dermatitis.

TARGET AUDIENCE

- Pediatricians
- Dermatologists
- Nurse Practitioners
- Physician Assistants

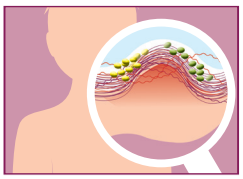
LEARNING OBJECTIVES

After participating in this activity, practitioners should be better able to:

- Summarize the role of skin barrier dysfunction and inflammatory responses in atopic dermatitis pathogenesis
- Describe the inflammatory/immunomodulating pathways in atopic dermatitis
- Evaluate the benefits and limitations of current therapies for mild to moderate atopic dermatitis
- Assess the efficacy and safety of emerging therapies and their potential role in treating atopic dermatitis

DISCLAIMER

The opinions expressed in this educational activity are those of the faculty and do not represent those of the Academy or Spire Learning. This activity is intended as a supplement to existing knowledge, published information, and practice guidelines. Learners should appraise the information presented critically and draw conclusions only after careful consideration of all available scientific information.



OFF-LABEL STATEMENT

This educational activity may contain discussion of published and/or investigational uses of therapies that are not indicated by the FDA, including roflumilast, OPA-15406, tofacitinib, SB011, and apremilast. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings. Further, participants are encouraged to consult appropriate resources for any product or device mentioned in this program.

CONFLICT OF INTEREST STATEMENTS

According to the disclosure policy of the Academy, all faculty, planning committee members, editors, managers, and other individuals who are in a position to control content are required to disclose any relevant relationships with any commercial interests related to this activity. The existence of these interests or relationships is not viewed as implying bias or decreasing the value of the presentation. All educational materials are reviewed for fair balance, scientific objectivity, and levels of evidence. Disclosures are as follows:

Faculty Presenters

Please refer to the Faculty Presenters section for each faculty member's affiliation and disclosure statement.

Educational Planning Committee

American Academy of CME, Inc.
John JD Juchniewicz, MCIS, CHCP: No relevant financial relationships with any commercial interests.

Spire Learning
Katie McGowan, Aisha Cobbs, PhD, and Jaime Symowicz, PhD: No relevant financial relationships with any commercial interests.

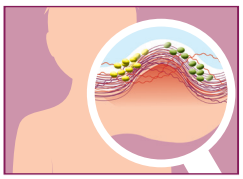
Jeanne Prater: Shareholder (spouse/partner): Johnson & Johnson; Employee (spouse/partner): Novo Nordisk.

LEVELS OF EVIDENCE

Two types of grades are provided for any treatment recommendations made in this presentation.

Level of Evidence	Strength of Clinical Recommendation
• Used to evaluate available evidence based on the quality of study methodology and the overall focus of the study	• Developed based on the best available evidence
I. Good-quality, patient-oriented evidence (ie, evidence measuring outcomes that matter to patients: morbidity, mortality, symptom improvement, cost reduction, and quality of life)	**A.** Recommendation based on consistent and good-quality, patient-oriented evidence
II. Limited-quality, patient-oriented evidence	**B.** Recommendation based on inconsistent or limited-quality, patient-oriented evidence
III. Other evidence including consensus guidelines, opinion, case studies, or disease-oriented evidence (ie, evidence measuring intermediate, physiologic, or surrogate endpoints that may or may not reflect improvements in patient outcomes)	**C.** Recommendation based on consensus, opinion, case studies, or disease-oriented evidence

Source: American Academy of Dermatology Guidelines of Care for the Management of Atopic Dermatitis



FACULTY PRESENTERS

Activity Co-Chair:
Adelaide A. Hebert, MD
Professor of Dermatology and Pediatrics
University of Texas Health Science Center at Houston
Professor, Section of Dermatology
University of Texas MD Anderson Cancer Center
Houston, TX

Adelaide A. Hebert, MD, is Professor of Dermatology and Pediatrics at the University of Texas Health Science Center at Houston (UTHealth). She is also a Professor in the Section of Dermatology at the University of Texas MD Anderson Cancer Center. After receiving her medical degree from Tulane University School of Medicine in New Orleans, Dr Hebert completed an internship in internal medicine and a residency in dermatology at the University of Texas Medical Branch in Galveston, followed by a pediatric dermatology fellowship at Northwestern University in Chicago.

Clinical research has been one of Dr Hebert's interests during her tenure at UTHealth. She has been involved in a wide array of research arenas with special focus on atopic dermatitis, psoriasis, hyperhidrosis, tuberous sclerosis, and neurofibromatosis. Her other areas of research interest have included skin and soft tissue infections; acne; wounds including pyoderma gangrenosa; fungal infections of the skin, scalp, and nails; diaper dermatitis; herpes simplex and herpes zoster infections; lupus erythematosus; rosacea; actinic keratosis; contact dermatitis; disorders of keratinization; and multiple sclerosis.

Dr Hebert is board certified in Dermatology, Pediatric Dermatology, and Wound Healing. In addition, she was President of the Society for Pediatric Dermatology in 2006-2007 and served on the Board of Directors for over 10 years. She served as the first Chair of the Society for Pediatric Dermatology Foundation. She is also a board member and co-founder of the International Hyperhidrosis Society. Dr Hebert currently serves as President of the Women's Dermatologic Society and has been on the Board of Directors for the past 4 years.

Disclosure Statement:

Advisory Board: Anacor Pharmaceuticals, Inc; Demira; Galderma Laboratories, LP; GlaxoSmithKline; PharmaDerm; Procter & Gamble; Promius Pharma, LLC; Shionogi, Inc; Stiefel, a GSK Company; Valeant Pharmaceuticals International
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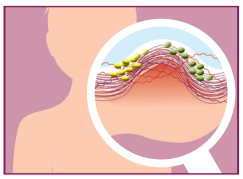
**All research funds paid to the UTHealth McGovern School of Medicine*



Activity Co-Chair:
Lawrence Eichenfield, MD
Professor of Dermatology and Pediatrics
Chief, Pediatric and Adolescent Dermatology
Vice Chair, Department of Dermatology
University of California, San Diego
Rady Children's Hospital, San Diego
San Diego, CA

Lawrence F. Eichenfield, MD, is Chief of Pediatric and Adolescent Dermatology at Rady Children's Hospital–San Diego, and Professor of Dermatology and Pediatrics at the University of California, San Diego (UCSD) School of Medicine. He received his medical degree from Mount Sinai School of Medicine in New York, was a pediatric resident and Chief Resident at Children's Hospital of Philadelphia, and completed his dermatology residency at the Hospital of the University of Pennsylvania.

Dr Eichenfield's clinical interests include atopic dermatitis, acne, psoriasis, vascular lesions including port wine stains and hemangiomas, neonatal dermatology, laser surgery, nevi, and skin signs of systemic disease. He has authored more than 300 journal articles, chapters, abstracts, and books on these topics and has served as the senior editor of *Neonatal and Infant Dermatology* published by Elsevier, as well as *The Eczemas* published by Summit Communications. He is also editor-in-chief of *Pediatric Dermatology* and serves on the editorial boards of multiple journals and periodicals.

Dr Eichenfield was honored as a member of the Alpha Omega Alpha Medical Honor Society during his time in medical school, a recipient of the Benjamin Ritter Award at Children's Hospital of Philadelphia, and a recipient of excellence in teaching awards from UCSD Pediatrics, UCSD Dermatology, and Rady Children's Hospital–San Diego. He has been named one of the "Best Doctors in America" since 1994. In addition, he is past President of the Society for Pediatric Dermatology, past board member of the American Academy of Dermatology, and Chair for the 69th Annual Meeting of the American Academy of Dermatology. Dr Eichenfield is also a founding board member of the American Acne and Rosacea Society and the Pediatric Dermatology Research Alliance (PeDRA), for which he also serves as Co-chair.

Disclosure Statement:
Consultant: Allergan, Inc; Anacor Pharmaceuticals, Inc/Pfizer Inc; DS Biopharma; Eli Lilly and Company; Galderma Labaratories, LP; Genentech, Inc; Otsuka/Medimetriks; Ralexar Therapeutics, Inc; Regeneron Pharmaceuticals, Inc/Sanofi; TopMD; Valeant Pharmaceuticals
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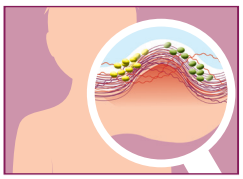
Advisory Board/Speaker: Valeant Pharmaceuticals



Anthony J. Mancini, MD, FAAP, FAAD
Head, Division of Dermatology
Ann & Robert H. Lurie Children's Hospital of Chicago
Professor of Pediatrics and Dermatology
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Anthony J. Mancini, MD, FAAP, FAAD, is Professor of Pediatrics and Dermatology at Northwestern University Feinberg School of Medicine, and Head of the Division of Pediatric Dermatology at Ann & Robert H. Lurie Children's Hospital of Chicago, where he directs the division's pediatric dermatology fellowship training program. He received his medical degree at the University of Arizona, and trained in pediatrics, pediatric dermatology, and dermatology at Stanford University, California.

Dr Mancini's clinical and research interests include infantile hemangiomas, infectious skin diseases, exanthems of childhood, and neonatal skin maturation and skin disorders. He has published more than 185 peer-reviewed articles, abstracts, books, and book chapters. He is coauthor of *Hurwitz Clinical Pediatric Dermatology* (3rd, 4th, and 5th editions), coeditor of the American Academy of Pediatrics (AAP) publication, *Pediatric Dermatology – A Quick Reference Guide* (1st, 2nd, and 3rd editions), and Section Editor of *Dermatology* (1st, 2nd, and 3rd editions). Dr Mancini just completed his term as President of the Society for Pediatric Dermatology. In addition, he previously served two 5-year terms as Secretary-Treasurer. In the past he has served on the AAP Executive Committee of the Section on Dermatology, the AAP Super CME Planning Group, and the AAP PediaLink Pediatric Dermatology Project Team.

Disclosure Statement:
Consultant: Anacor Pharmaceuticals, Inc; Galderma Laboratories, LP
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MILD TO MODERATE ATOPIC DERMATITIS:
Pathogenesis and Therapeutic Strategies For Improved Outcomes

Please complete the preassessment located in your handout before the program begins.

Epidemiology, Prevalence, and Pathogenesis

What's Your Diagnosis?

- 4-month-old infant presents with erythematous scaling dermatitis of the cheeks bilaterally
- Similar-appearing lesions over the posterior neck and extensor aspects of the extremities

Patient photo not available for handout.

Epidemiology in Children and Adolescents

- Affects 10%-20% of school-aged children in the US[1]
- Higher prevalence in African Americans, urban residents, and children living in homes with higher education levels[2]
- AD will persist into adulthood in up to 33% of children[1]

1. Silverberg NB. *Cutis*. 2016;97:267-271. 2. Wolter DY, et al. *Pediatr Clin North Am*. 2014;61(2):241-260.

Diagnostic Criteria for Atopic Dermatitis

- Pruritus (itching)
- Eczematous changes that are acute, subacute, or chronic
  - Age-specific distribution patterns
  - Intermittent course with flares and remissions

American Academy of Dermatology. *J Am Acad Dermatol*. 2014;70(2):338-351.

Primary Physical Findings

- Erythema
- Papules/plaques
- Excoriations
- Xerosis
- Erosions and crusting
- Lichenification
- Dyspigmentation

Patient photos not available for handout.

Eichenfield LF, et al. *Pediatrics*. 2015;136(3):554-565.
Siegfried EC, et al. *J Clin Med*. 2015;4(5):884-917.

Distribution of Atopic Dermatitis Varies With Age

- Infants
  - Face, trunk (except diaper area), extensor extremities
- Children
  - *Flexors (wrists, ankles, antecubital/popliteal fossae)*
- *Adolescents*
  - *Flexors, neck, wrists, hands, ankles*

Patient photos not available for handout.

Siegfried EC, et al. *J Clin Med*. 2015;4(5):884-917.
Weidinger S, et al. *Lancet*. 2016;387(10023):1109-1122.

Clinical Presentation in Children

- More than 7 million healthcare provider visits per year for AD[1]
- Approximately 67% of children have mild disease that can be managed by a primary care provider[2]
- Specialist referral is required in moderate (20%) and severe (2%) cases[3]

1. Horii KA, et al. *Pediatrics*. 2007;120(3):e527-e534.
2. Eichenfield LF, et al. *Pediatrics*. 2015;136(3):554-565.
3. Arkwright PD. *J Allergy Clin Immunol*. 2013;1(2):142-151.

Patient photos not available for handout.

Features in Darker Skin Types

- Follicular accentuation
- Pityriasis alba
- Erythema (hard to see due to pigmentation)
- Marked lichenification

Patient photos not available for handout.

Differential Diagnosis of Atopic Dermatitis: Common Disorders

- Seborrheic dermatitis
- Scabies
- Impetigo
- Contact dermatitis (allergic and irritant)
- Psoriasis
- Ichthyosis vulgaris
- Tinea corporis
- Keratosis pilaris

Patient photos not available for handout.

Differential Diagnosis of Atopic Dermatitis: Rare Disorders in Infancy and Childhood

Metabolic/nutritional/genetic disorders

- Acrodermatitis enteropathica
- Zinc deficiency (prematurity; breast milk deficient in zinc; cystic fibrosis)
- Other nutritional deficiencies (biotin, essential fatty acids)
- Netherton syndrome
- Phenylketonuria
- Omenn syndrome
- Prolidase deficiency
- Gluten sensitivity-related dermatitides
- Hurler syndrome

Differential Diagnosis of Atopic Dermatitis: Rare Disorders in Infancy and Childhood

Immune disorders

- Hyperimmunoglobulin E syndrome
- Severe combined immunodeficiency disorder
- Wiskott-Aldrich syndrome
- Agammaglobulinemia
- Ataxia-telangiectasia
- Neonatal lupus erythematosus

Proliferative disorders

- Langerhans cell histiocytosis

Differential Diagnosis of Atopic Dermatitis: Rare Disorders in Adolescents and Adults

- Cutaneous T-cell lymphoma (Mycosis fungoides or Sézary syndrome)
- HIV-associated dermatoses
- Dermatomyositis
- Graft-versus-host disease
- Lupus erythematosus
- Pemphigus foliaceus
- Drug eruptions

Pathogenesis

Complex, heterogeneous pathogenesis

- Skin barrier dysfunction
  - Filaggrin mutations
  - Diminished ceramides
- Inflammation
- Pruritus/scratching
- Microbial colonization
- Allergy

Colonization by *Staphylococcus aureus*

- Worsens disease status
- Renders disease harder to control
- Patients do not have to be infected to be adversely impacted by *S. aureus*
- Skin that is colonized has a true trigger for disease flares

Image not available for handout.

Bieber T. *N Engl J Med.* 2008;358(14):1483-1494.

Boguniewicz M, et al. *J Allergy Clin Immunol.* 2010;125:4-13.

Immunopathogenesis of Atopic Dermatitis

Image not available for handout.

Harskamp CT, et al. *Semin Cutan Med Surg.* 2013;32:132-139.

Pathogenesis of Atopic Dermatitis

Image not
available for handout.

Gittler JK, et al. *J Allergy Clin Immunol.* 2012;130(6):1344-1354.

Burden of Disease

- **Quality of Life**
  - An average of 9 flares per year, each lasting 15 days[1]
  - Poor quality of sleep[2]
    - Sleep disturbances ~7.3 nights per flare[1]
    - Increased co-sleeping (up to 30% in one study)[3]
    - Polysomnography showing high number of arousals in AD children, independent of scratching[4]
  - Itching[5]
    - 87% experience itching daily
    - Itching lasts ≥ 18 hours in 41.5% of patients

1. Zuberbier T. *J Allergy Clin Immunol.* 2006;118:226-232.
2. Shani-Adir A, et al. *Pediatr Dermatol.* 2009;26(2):143-149.
3. Chamlin SL, et al. *Arch Pediatr Adolesc Med.* 2005;159:745-750.
4. Reuveni H, et al. *Arch Pediatr Adolesc Med.* 1999;153:249-253.
5. Simpson EL, et al. *J Am Acad Dermatol.* 2016;74(3):491-498.

Impact of Comorbidities

- Asthma
- Allergic rhinitis
- Food allergy
- Contact dermatitis
- Emerging comorbidities
  - Obesity
  - Hypertension

Simpson EL. *Curr Dermatol Rep.* 2012;1(1):29-38.

Available Therapies and Management Strategies

Case 2

Patient photo not available for handout.

Case 2: Therapy Recommendations

- Apply mild to moderate potency topical steroids twice daily (A,I) for 1-2 weeks, several days beyond clearing for flare control
- Emollients 2 to 3 times per day (A,I)
- Sedating antihistamines can be considered if sleep is disturbed….BUT…skin-directed therapy should be emphasized!

*Against use of systemic antihistamines: sedating C, III, and nonsedating A, II.
Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;71:116-132.
Sidbury R, et al. *J Am Acad Dermatol*. 2014;71:327-349.
Stein SL, et al. *JAMA*. 2016;315:1510-1511.

Maintenance Therapies for Atopic Dermatitis

- Skin care
  - Liberal and frequent application of moisturizers
  - Warm baths/showers (<5 min) using nonsoap cleansers or mild soaps
- Antiseptic measures
  - Dilute bleach baths
- Trigger avoidance

Eichenfield LF, et al. *Pediatrics*. 2015;136(3):554-565.

Management of Acute Flares

- Avoid trigger factors
- Restore barrier integrity
- Control itching
- Treat infection/control colonization

Eichenfield LF, et al. *Pediatrics*. 2015;136(3):554-565.

Barrier Defect

Repairing Barrier Integrity Requires Fundamental Skin Care

- Gently cleanse twice a day
- Use mild, nonsoap cleansers (syndets)
  - Eg, CeraVe®, Cetaphil®, Equate®, etc
- Use an effective moisturizer every day after cleansing

Eichenfield LF, et al. *Pediatrics*. 2015;136(3):554-565.
Nicol NH. *Cutis*. 2005;76(suppl 6):26-31.

Water: Irritant or Treatment?

- **Water *irritates* skin IF:**
  - Skin is frequently wet, without immediate application of effective moisturizer
  - Moisture evaporates, causing skin barrier to become dry, irritated
- **Water *hydrates* skin IF:**
  - Effective moisturizer is applied and hydration is retained, keeping skin barrier intact and flexible

Importance of Barrier Integrity

Topical Corticosteroids (TCS): Benefits and Limitations

Benefits:

- Highly effective at treating inflammation
- Rapid onset of action
- Multiple potency and delivery vehicles
  - Varied potency frequently required per patient

Limitations:

- Product-specific age limits (although often used off-label)
- Potential for local and systemic side effects (but rare when used appropriately):
  - Local: striae, telangiectasias, skin atrophy, dyspigmentation, periorificial dermatitis, acne rosacea
  - Systemic: HPA axis suppression
  - Periorbital administration: cataracts, glaucoma

HPA, hypothalamic-pituitary-adrenal.
Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;71:116-132.
Stein SL, et al. *JAMA*. 2016;315:1510-1511.

Relative Potencies of Topical Corticosteroids

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available for handout.

Adapted from Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;71:116-132.

Topical Corticosteroids

- Low potency: hydrocortisone 1%-2.5% or desonide 0.05%
- Mid potency: triamcinolone 0.1%
- High potency: fluocinonide 0.05%

Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;71:116-132.

Topical Calcineurin Inhibitors (TCI) Benefits

- Extensive clinical trials experience
- Steroid-sparing
- Good efficacy for mild, moderate, and severe AD
- Used for acute and maintenance therapies
- Little systemic absorption
- Can be applied to face (including periorbital regions), extremities, and genital area

Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;71:116-132.
Stein SL, et al. *JAMA*. 2016;315:1510-1511.

Available TCIs

TCI	Vehicle	Indications
Pimecrolimus (1%)	Cream	Approved for mild to moderate AD (2 years and older)
Tacrolimus (0.03% and 0.1%)	Ointment	Approved for moderate to severe AD (0.03%: 2 years and older; 0.1%: 15 years and older)

- Both TCIs were shown to be more effective than vehicle in short-term (3-12 weeks) and long-term studies (up to 12 months) in adults and children with active disease
  - Decline in Eczema Area and Severity Index (EASI) score
  - Decrease in percent body surface involved
  - Reduction in patient evaluated symptoms and signs of disease

Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;71:116-132.
Stein SL, et al. *JAMA*. 2016;315:1510-1511.

TCI Limitations and Potential Adverse Events

- Not indicated for use in children <2 years of age
- Not indicated for long-term continuous therapy
- Second-line agents
- Limited range of vehicles available vs TCSs
- Stinging and burning in a small subset of patients
- FDA-mandated black box warning and medication guide
- The only time in FDA history that a black box was given for potential risk

Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;71:116-132.
Stein SL, et al. *JAMA*. 2016;315:1510-1511.

Phosphodiesterase Type 4 (PDE4)

- Elevated in patients with AD compared with control patients[1]
- Reduces intracellular cyclic adenosine monophosphate (cAMP) and suppresses protein kinase A, leading to increased levels of proinflammatory cytokines[1]
- Topical and oral PDE4 inhibitors currently under clinical investigation

1. Hanifin JM, et al. *J Invest Dermatol*. 1996;107:51-56.

Image not
available for handout.

Jarnagin K, et al. *J Drugs Dermatol*. 2016;15(4):390-396.

Crisaborole 2% Ointment

- A nonsteroidal, boron-based PDE4 inhibitor
- Approved for mild to moderate AD in adults and children ≥2 years in December 2016
- Reduces inflammation and itching
- Maintains skin barrier

Crisaborole 48-Week Safety Study

- Open-label study (after Phase 3), 517 patients
- Disease severity assessed every 4 weeks using ISGA scale
- Patients received 4-week cycles of crisaborole as needed
- Safety measures: local tolerability, adverse events, serious adverse events, clinical laboratory results, vital signs, physical examinations

Eichenfield LF, et al. Presented at: 13th ESPD; May 26, 2016; Paris, France.

Crisaborole 48-Week Safety Study, cont'd

	AD-301 (Crisaborole/Vehicle) N = 503/256	AD-302 (Crisaborole/Vehicle) N = 513/250
Primary Efficacy Endpoint[1] • Percentage of patients who achieved success in ISGA (defined as score of 0 [clear] or 1 [almost clear] with a minimum 2-grade improvement) at Day 29	**32.8%/25.4%** (*P* = .038)	**31.4%/18.0%** (*P* < .001)
Secondary Efficacy Endpoint[1] • Percentage of patients achieving ISGA clear (0) or almost clear (1) at Day 29	**51.7%/40.6%** (*P* = .005)	**48.5%/29.7%** (*P* < .001)

50% of patients treated with crisaborole achieved improvement in pruritus by 1.37 days (compared with 1.73 days for the vehicle group, *P* = .001)[2]

ISGA, Investigator's Static Global Assessment.
1. Paller AS, et al. Presented at: Fall Clinical Dermatology Conference; October 1-4, 2015; Las Vegas, NV.
2. Hebert AA, et al. Presented at: Fall Clinical Dermatology Conference; October 1-4, 2015; Las Vegas, NV,

Crisaborole Safety Profile

- Favorable safety profile over 48-week study
  - Treatment-related TEAEs in ≥1% of patients: AD (3.1%), application site pain (2.3%), application site infection (1.2%)[1]
  - TEAEs in at least 5% of patients: AD (11.2%), upper respiratory tract infection (10.3%), nasopharyngitis (7.7%), cough (6.8%), and pyrexia (5.6%)[1]
  - Limited systemic exposure[2]
  - No atrophy, telangiectasia, hypopigmentation

TEAE, treatment-emergent adverse event.
1. Eichenfield LF, et al. Presented at: Winter Clinical Dermatology Conference; January 15-20, 2016; Koloa, HI.
2. Tom WL, et al. *Pediatr Dermatol.* 2016;33(2):150-159.

Dupilumab

- Approved March 2017
- Injectable biologic therapy
- Blocks cytokines IL-4 and IL-13
- Indicated for adults with moderate to severe AD

Beck LA, et al. *N Engl J Med*. 2014;371:130-139.

Controlling the Itch

- Frequent moisturization to reduce dryness
- Apply low- to mid-potency TCSs to control inflammation
- Antihistamines are not effective at alleviating itching
  - Sedating antihistamines can be used to improve sleep

Tollefson MM, et al. *Pediatrics*. 134(6):e1735-e1744.

Antihistamines in Atopic Dermatitis

Agent	Vehicle	Properties
Diphenhydramine*	**Oral**	Sedating antihistamine
Hydroxyzine	**Oral**	Sedating antihistamine
Doxepin	**Oral, L**	Sedating antihistamine
Cetirizine*	**Oral**	Non-sedating antihistamine
Fexofenadine*	**Oral**	Non-sedating antihistamine
Loratadine	**Oral**	Non-sedating antihistamine

C, cream; L, lotion.
*Available over the counter.

Dilute Bleach Baths

- Mechanism of action still unclear
  - Anti-inflammatory actions or suppression of *S. aureus* overgrowth?[1]
- Preparation: ⅛ -½ cup of bleach per standard bathtub, at least 2 times per week[2]
- Supporting evidence: see references 1-3

1. Hon KL, et al. *J Dermatolog Treat*. 2016;27:156-162.
2. Huang JT, et al. *Pediatrics*. 2009;123:e808-e814.
3. Wong SM, et al. *J Dermatol*. 2013;40:874-880.

Case 3

Patient photos not available for handout.

Case 3: Therapy Recommendations

Initial therapy

- Disease control
  - Face: low-potency TCS or TCI (A,I)
  - Body: mid-potency TCS, with or without wet wraps (A,I)
- Emollients 2-3 times per day (A,I)
- Antihistamines if necessary/desired*
- Dilute bleach baths if skin is red and crusted (B,II)

After-flare control

- Intermittent treatment with TCS, TCI (A,I)

*Against use of systemic antihistamines: sedating C, III, and nonsedating A, II.

Eichenfield LF, et al. *J Am Acad Dermatol*. 2014;71:116-132.
Sidbury R, et al. *J Am Acad Dermatol*. 2014;71:327-349.
Stein SL, et al. *JAMA*. 2016;315:1510-1511.

Patient and Caregiver Education

- Written treatment plan increases likelihood of adherence
- Moisturize frequently throughout the day
- Topical medications do not take the place of moisturizers
- Continue maintenance therapies, even if skin “appears” healthy
- Appearance of AD changes with age

Specialty Referral

- Early referral in the case of severe, persistent disease
- Otherwise, refer if the patient is not responding to conservative measures and standard treatment modalities
- For food allergy evaluation for milk, egg, peanut, wheat, and soy if at least 1 of the following conditions is met:
  - Persistent AD in spite of optimized management and topical therapy
  - Reliable history of immediate reaction after ingestion of a specific food

Eczema Herpeticum

Patient photos not available for handout.

Emerging Therapies for Atopic Dermatitis

Other Emerging Treatments for Atopic Dermatitis

- Topical therapies
  - PDE4 inhibitors (eg, roflumilast,[1] OPA-15406[2])
  - Janus kinase inhibitors: tofacitinib ointment[3]
    - Phase 2 trial results (2% ointment, BID)
      - EASI score for tofacitinib -87.7% (compared with -29.9% with vehicle, *P*<0.001)
      - Significant improvements in EASI, PGA, and BSA by week 1, pruritus by day 2 with tofacitinib
      - More AEs were observed for vehicle (55.9%) vs tofacitinib (31.4%)
      - No patients treated with tofacitinib discontinued treatment due to AEs
      - No SAEs were reported in either group
      - Fewer TEAEs reported for tofacitinib (5.7%) vs vehicle (11.8%)
  - Calcineurin inhibitor: SB011[4]

EASI, Eczema Area and Severity Index; PGA, Physician's Global Assessment; BSA, Body Surface Area; AE, adverse event; SAE, serious adverse event; TEAE, treatment-emergent adverse event.
1. ClinicalTrials.gov Identifier: NCT01856764. 2. ClinicalTrials.gov Identifier: NCT01702181.
3. Bissonnette R, et al. *Br J Dermatol*. 2016.175(5):902-911. 4. ClinicalTrials.gov Identifier: NCT02079688.

Other Emerging Treatments for Atopic Dermatitis

- Systemic therapies
  - Apremilast: an oral PDE4 inhibitor[1]
- Other new agents on the horizon that look promising

1. ClinicalTrials.gov Identifier: NCT02087943.

Clinical Pearls

- Do not undertreat the disease
- Stress the importance of moisturization in disease control to patients/parents
- Control infection/colonization
- Oral steroids are very rarely indicated in the treatment of AD

Questions

Thank You

Please complete the **postassessment and evaluation** located in your meeting handout.