Current Treatment Agents: Revolutionizing Atopic Dermatitis Management

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Post-doctoral Fellow
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The presenter for this activity has been required to disclose all relationships with any proprietary entity producing health care goods or services, with the exemption of non-government organizations and non-healthcare related companies.

No significant financial relationships with commercial entities were disclosed by the speaker.

(Please note any possible conflicts of interests or bias is to be disclosed early on and appropriate resolution taken or appropriately disclosed)
1. Describe the pathophysiology of atopic dermatitis
2. Evaluate the atopic dermatitis diagnostic scales and classification
3. Identify the signs, symptoms, and risk factors related to atopic dermatitis
4. Define the mechanism of action of treatment agents
PRE-TEST ACTIVITY
Atopic dermatitis is the most common, chronic, allergic inflammatory skin condition worldwide

A. True
B. False
Most cases of atopic dermatitis are seen in adults?
A. True
B. False
Mutation in the filaggrin gene is a contributor to all of the following EXCEPT?

A. Severe eczema
B. Delayed onset of atopic dermatitis
C. Increased risk of asthma
D. Development of food allergies
Skin fibrosis is commonly associated with which interleukin?
A. IL-4
B. IL-10
C. IL-5
D. IL-31
Which of the following is a major criteria in the diagnosis of atopic dermatitis?

A. Xerosis
B. Lichenification
C. Elevated serum IgE
D. Pruritus
ATOPIC DERMATITIS
EPIDEMIOLOGY
Atopic dermatitis (AD) also known as atopic eczema is the most common, chronic, allergic, inflammatory skin condition.\(^1,2\)

- In the United States, there are an estimated 17.8 million currently affected by AD.\(^3\)
  - In industrialized countries, there has been an increase in AD, affecting approximately 15% to 20% of children and 1% to 3% of adults worldwide.\(^4\)

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Analyzed a nationwide health register on prescription data to determine incidence rate (IR) of AD in an entire pediatric population

- Disease-specific prescriptions analyzed = 295,286

- All children residents in Norway < 6 years

- January 1, 2009 to December 31, 2015
• Overall incidence rate increased from 0.028 per PY (95% CI 0.028 - 0.029 per PY) in 2009 to 0.034 per PY (95% CI 0.050 - 0.053 PY) in 2014
DISEASE COMPONENTS

- Skin Barrier Dysfunction
- Environment
- Genetics
- Immunology
## Skin Barrier Dysfunction

<table>
<thead>
<tr>
<th>Epidermal barrier</th>
<th>Abnormalities</th>
<th>Functional effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transepidermal epithelial differentiation products</td>
<td>↓ filaggrin, loricrin, involucrin, corneodesmosin, keratin 1 and 10</td>
<td>↓ skin water content, enhanced allergen, microbial penetration and ↑ skin pH</td>
</tr>
<tr>
<td>Tight junctions</td>
<td>↓ claudin-1, 8 and 23</td>
<td>↑ transepidermal water loss (TEWL), enhanced allergen &amp; microbial penetration ↓ cohesion</td>
</tr>
<tr>
<td>Microbial barriers</td>
<td>Cutaneous dysbiosis</td>
<td>Skin inflammation, microbial skin infections, keratinocytes death and exacerbation of AD</td>
</tr>
</tbody>
</table>

### Skin Barrier Dysfunction

<table>
<thead>
<tr>
<th>Epidermal barrier</th>
<th>Abnormalities</th>
<th>Functional effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipids</td>
<td>Altered composition of epidermal lipids and ↓ ceramide</td>
<td>Staphylococcal infection, dry skin ↑ TEWL</td>
</tr>
<tr>
<td>Immune barrier</td>
<td>↓ cathelicidin, HBD-2, &amp; HBD-3</td>
<td>Recurrent microbial infections, skin dysbiosis and exacerbation of AD</td>
</tr>
</tbody>
</table>

Familial link

- Genetic risk of a child with a family history of allergies developing other allergic conditions related to the atopic march

- Dold et al

Questionnaire filled out by 6665 families

Data collected in population based cross sectional survey of 9-11 year old children in Munich and southern Bavaria

Results support the hypothesis that asthma, allergic rhinitis, and atopic dermatitis are multifactorial diseases brought about by various familial and environmental influences

### Genetic Risk Of Asthma, Allergic Rhinitis, And Atopic Dermatitis

<table>
<thead>
<tr>
<th>Family history</th>
<th>Boys (%)</th>
<th>Girls (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No allergic family history</td>
<td>14</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td>One parent with AD</td>
<td>38</td>
<td>37</td>
<td>38</td>
</tr>
<tr>
<td><strong>OR (95% CI)</strong></td>
<td><strong>3.8 (2.7 to 5.5)</strong></td>
<td><strong>3.2 (2.2 to 4.5)</strong></td>
<td><strong>3.4 (2.6 to 4.4)</strong></td>
</tr>
<tr>
<td>One parent with allergic rhinitis</td>
<td>18</td>
<td>23</td>
<td>20</td>
</tr>
<tr>
<td><strong>OR (95% CI)</strong></td>
<td><strong>1.3 (0.9 to 1.8)</strong></td>
<td><strong>1.5 (1.2 to 2.1)</strong></td>
<td><strong>1.4 (1.1 to 1.8)</strong></td>
</tr>
<tr>
<td>One parent with asthma</td>
<td>14</td>
<td>27</td>
<td>21</td>
</tr>
<tr>
<td><strong>OR (95% CI)</strong></td>
<td><strong>1.0 (0.5 to 1.9)</strong></td>
<td><strong>2.0 (1.2 to 3.3)</strong></td>
<td><strong>1.5 (1.0 to 2.2)</strong></td>
</tr>
</tbody>
</table>

**Child’s Atopic Dermatitis (Ad) In Relation To One Of The Parent With AD**

FILAGGRIN (FLG)

- Crucial protein in skin barrier
- Most frequent mutation involving variation in genes
- Observed in 10% - 50% of patients with AD worldwide
- Margolis et al.
- Contributor to the atopic march
  - Associated with severe eczema, early onset AD, ↑ risk of asthma

Evaluated the effect of individual FLG null mutation on the persistence of AD

Multiyear, prospective cohort study

Children with respect the FLG null mutations

857 subjects

Individuals with a FLG null mutation were less likely to report that their skin was symptom-free at any time as compared to those without a FLG null mutation [OR: 0.54 (95% CI 0.41 - 0.71)]
Also referred to as the “allergic march”

Early development of atopic dermatitis during infancy, followed by the progression of IgE-mediated allergic rhinitis, food allergies and asthma later in childhood.

IMMUNE RESPONSE

- Key cells involved in the innate immunity for the skin: keratinocytes & dendritic cells (DCs)
- Defects in the innate immunity associated with increased bacterial & viral infections in AD
- Epidermal DCs carry a high-affinity receptor (FcεRI) for IgE
  - IgE plays a role in allergen presentation to T-helper type (Th2) cells via Langerhans cells
  - LCs cells with FcεRI that bear IgE are necessary to provoke eczematous skin lesions in unprovoked AD of skin
- Keratinocytes produce antimicrobial peptides (AMPs)
  - ↓ AMP = ↑ Staphylococcus aureus infections

TH2 CYTOKINES INVOLVED IN ATOPIC DERMATITIS

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Abnormality in AD</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-4</td>
<td>↑ IL-4 = pruritus, ↑ inflammatory cells in skin, ↑ bacterial infection, ↑ IgE</td>
</tr>
<tr>
<td>IL-13</td>
<td>↑ IL-13 = pruritic dermatitis, ↑ IgG1 and IgE levels, inflammatory cell infiltration into the skin, skin fibrosis</td>
</tr>
<tr>
<td>IL-5</td>
<td>↑ IL-5 = ↑ eosinophilia</td>
</tr>
<tr>
<td>IL-31</td>
<td>↑ IL-31 = severe pruritus, skin lesions</td>
</tr>
<tr>
<td>IL-10</td>
<td>Potentially modulates disease severity?</td>
</tr>
</tbody>
</table>

ENVIRONMENT & LIFESTYLE FACTORS
• Worldwide data collected from 146 centers of the International Study of Asthma and Allergies in Childhood (ISAAC)

• 155 study centers in 56 countries on six countries

• Involved 463,801 children in this age group and had a participation of more than 85% in most study centers

• Prevalence of eczema symptoms correlated with latitude (positively) and mean annual outdoor temperature (negatively)

FOOD ALLERGIES

• Certain foods can trigger IgE-mediated hypersensitivity reactions as well as eczematous lesions either immediately

• Food allergies are seen in roughly, 1/3 of children with moderate to severe AD

• Most common food allergens observed in ≥ 90% of individuals with AD: cow’s milk, nuts, wheat, hen’s eggs and fish

• Once a potential allergen is identified, it is recommended to avoid the agent in an effort to minimize AD exacerbation

• Investigated the association between AD, body weight and serum lipid levels

• 239 children under the age of 14

• Mean body mass index (BMI) was slightly higher in AD patients compared to healthy controls

• Additionally, slightly higher in AD patients aged 0-2 years and 12-14 years

• BMI was significantly higher in those with severe atopic dermatitis in the 9-12 age group (P=0.03) and 12 -14 age group (P=0.01)
### Body Mass Index (BMI)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Mild AD</th>
<th>Moderate AD</th>
<th>Severe AD</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>15.0</td>
<td>17.3</td>
<td>15.8</td>
<td>NS</td>
</tr>
<tr>
<td>2-5</td>
<td>18.7</td>
<td>15.9</td>
<td>15.2</td>
<td>NS</td>
</tr>
<tr>
<td>5-9</td>
<td>17.7</td>
<td>17.6</td>
<td>16.3</td>
<td>NS</td>
</tr>
<tr>
<td>9-12</td>
<td>18.8</td>
<td>19.3</td>
<td>24.4</td>
<td>0.03</td>
</tr>
<tr>
<td>12-14</td>
<td>-</td>
<td>21.9</td>
<td>27.8</td>
<td>0.01</td>
</tr>
</tbody>
</table>

NS = Not significant

BMI was significantly higher in those with severe atopic dermatitis in the 9-12 age group (P=0.03) and 12-14 age group (P=0.01)

MULTIFACTORIAL DISEASE

SIGNS, SYMPTOMS & RISK FACTORS
SIGNS & SYMPTOMS

- Usually presents within the first 5 years of life in 90% of patients
- In infants and children, the face, scalp and extensor regions of the body is affected
- Older children and adults are affected in mainly in the flexural areas
- Most common symptom related to AD is pruritus
  - Another important symptom is xerosis reported across both children and adults

## SELECTED DIAGNOSTIC CRITERIA

<table>
<thead>
<tr>
<th>MAJOR CRITERIA</th>
<th>MINOR CRITERIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pruritus</td>
<td>Early age of onset</td>
</tr>
<tr>
<td>Characteristic morphology and distribution:</td>
<td>Xerosis</td>
</tr>
<tr>
<td>• Facial and extensor involvement in infants and children; flexural involvement with lichenification in adults</td>
<td>Palmar hyperlinearity, ichthyosis, keratosis pilaris</td>
</tr>
<tr>
<td>Chronic or chronic, relapsing course</td>
<td>Elevated serum IgE</td>
</tr>
<tr>
<td>Personal or family history of atopy, including asthma, allergic rhinitis, atopic dermatitis</td>
<td>Cutaneous infection</td>
</tr>
<tr>
<td></td>
<td>Cheilitis/Pityriasis alba</td>
</tr>
<tr>
<td></td>
<td>Facial erythema or pallor</td>
</tr>
</tbody>
</table>

Two major risk factors associated with the development of AD:
1. A family history of atopy
2. Loss of function mutations in the filaggrin (FLG) gene
DIAGNOSTIC TOOLS
<table>
<thead>
<tr>
<th>SCORING SYSTEM</th>
<th>DESCRIPTION</th>
<th>SEVERITY RATING</th>
</tr>
</thead>
</table>
| SCORing Atopic Dermatitis (SCORAD) | 3 components:  
(A) Extent—sites affected  
(B) Intensity score for redness, swelling, crusting or oozing, skin thickening (lichenification), dryness, scratch marks  
(C) Subjective score for sleeplessness and itch  

SCORAD total score = A/5 + 7B/2 + C (maximum 103) | Mild <25, moderate >25 to <50, severe >50 |
| Eczema Area and Severity Index (EASI) | 2 components:  
(A) Area score recorded for 4 regions  
(B) Severity score for each region calculated based on intensity of redness, thickness or swelling, scratching, lichenification  

Maximum score of 12 for each region | Mild 1.1–7, moderate 7.1–21, severe 21.1–50, very severe 50.1–72 |
| Investigator Global Assessment (IGA) | Utilized by the FDA to categorize AD severity based on investigator's subjective assessment of a lesion according to erythema, induration or papulation, and/or oozing or crusting. | 0 = clear to 4 = severe |
| Dermatology Life and Quality Index (DLQI) | 10-question validated questionnaire providing patient's perception of the impact of AD on quality of life in past week | Each question is answered according to ratings: 0 = not at all, 1 = a little, 2 = a lot, 3 = very much; maximum 30 |

NON-PHARMACOLOGIC AGENTS
EMOLLIENTS & MOISTURIZERS

- Mainstay of therapy
- Form a thin hydrophobic surface on the skin that ↓ transepidermal water loss (TEWL) and ↑ skin hydration
- Mimic components found on the skin:
  - ceramides, cholesterol and free fatty acids
- Loden et al

• The use of urea-containing moisturizers on the barrier properties of atopic skin

• N= 15 patients

• AD patients treated one of their forearms BID with a moisturizing cream for 20 days

• Measured skin capacitance and TEWL at baseline, Day 10 and Day 20
  ○ Irritant exposure – sodium lauryl sulfate: Day 21
RESULTS IN THE TREATED ARM

The moisturizer had no meaningful effect on TEWL. However, there was significant improvement in skin capacitance.

RESULTS IN THE TREATED ARM

Irritative response: measured by TEWL and superficial skin blood flow

Prophylactic treatment with a urea-containing moisturizer showed improvement in barrier properties of atopic skin

### EMOLLIENTS & MOISTURIZERS

<table>
<thead>
<tr>
<th>Agents</th>
<th>Ingredients</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emollients</td>
<td>Glycol and glyceryl stearate, soy sterols</td>
<td>Lubricate and soften the skin</td>
</tr>
<tr>
<td>Occlusive Agents</td>
<td>Petrolatum, dimethicone, mineral oil, lanolin, liquid paraffin</td>
<td>Form a layer to retard evaporation of water</td>
</tr>
<tr>
<td>Humectants</td>
<td>Glycerol, lactic acid, urea, propylene glycol</td>
<td>Attract and hold water</td>
</tr>
</tbody>
</table>

The efficacy of moisturizing is greater following twice daily application (morning and evening) compared to once daily. It is recommended to apply emollients immediately after bathing.\textsuperscript{35-36} For patients with mild AD moisturizers can be the main primary therapy; and should be added as part of the regimen for patients with moderate to severe AD.\textsuperscript{37} Currently, there are a variety of emollients and moisturizers on the market that can be used in the management of AD. They are available in multiple formulations ranging from creams to ointments.
PHARMACOLOGIC AGENTS
TOPICAL CORTICOSTEROIDS (TCS)

- Approved for both children and adults with AD
- Primarily used in the management of AD flares and in the prevention of relapses
- Mainstay of anti-inflammatory therapy
  - Acts on multiple immune cells: T-lymphocytes, macrophages and DCs
  - Suppress the release of pro-inflammatory cytokines
  - Interferes with antigen processing
- Available in low to high potency range

• Multicenter, double-masked, placebo-controlled, randomized study

• Evaluated the efficacy, safety, tolerability and cosmetic acceptability of hydrocortisone buteprate 0.1% cream
  ○ N=194 adults

• Hydrocortisone buteprate 0.1% cream or placebo (cream base of the medication) applied topically once daily for 14 days

• Investigators assessed the severity of dermatitis signs on a 4-point scale at baseline and on Days 3, 7 and 14

• Most commonly reported adverse event was burning sensation
Hydrocortisone buteprate 0.1% was rated as having greater overall improvement at each efficacy level versus placebo.

### SELECTED TOPICAL CORTICOSTEROIDS USED IN ATOPIC DERMATITIS

<table>
<thead>
<tr>
<th>Potency</th>
<th>Drug</th>
<th>Formulation(s)</th>
<th>Strength (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Very High</td>
<td>Augmented betamethasone dipropionate</td>
<td>Ointment</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>Clobetasol propionate</td>
<td>Cream, foam, ointment</td>
<td>0.05</td>
</tr>
<tr>
<td>II. High</td>
<td>Augmented betamethasone dipropionate</td>
<td>Cream</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone acetonide</td>
<td>Cream, ointment</td>
<td>0.5</td>
</tr>
<tr>
<td>III-IV. Medium</td>
<td>Betamethasone valerate</td>
<td>Cream, foam, lotion, ointment</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Mometasone furoate</td>
<td>Cream</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Triamcinolone acetonide</td>
<td>Cream, ointment</td>
<td>0.1</td>
</tr>
<tr>
<td>V. Lower-medium</td>
<td>Hydrocortisone butyrate</td>
<td>Cream, ointment, solution</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone probutate</td>
<td>Cream</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>Hydrocortisone valerate</td>
<td>Cream, ointment</td>
<td>0.2</td>
</tr>
<tr>
<td>VI. Low</td>
<td>Alclometasone dipropionate</td>
<td>Cream, ointment</td>
<td>0.05</td>
</tr>
</tbody>
</table>

**ADMINISTRATION**

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**Quantity of Ointment per Application per Body Area by Age Group**

**Weekly/Monthly Quantities by Age Group (Whole Body Application)**

<table>
<thead>
<tr>
<th>Moisturizer</th>
<th>Basic Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant</td>
<td>100 g/week</td>
</tr>
<tr>
<td>Child</td>
<td>150–200 g/week[^4]</td>
</tr>
<tr>
<td>Adolescent/Adult</td>
<td>500 g/week[^5]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ointment</th>
<th>Acute Treatment[^5][^6]</th>
<th>Maintenance Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant</td>
<td>60–100 g/week</td>
<td>10 g/month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>15 g/month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>75 g/month</td>
</tr>
<tr>
<td>Child</td>
<td>125–250 g/week</td>
<td>20 g/month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30 g/month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>150 g/month</td>
</tr>
<tr>
<td>Adolescent/Adult</td>
<td>260–300 g/week</td>
<td>40–60 g/month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60–90 g/month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>300–450 g/month</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cream[^3]</th>
<th>Acute Treatment</th>
<th>Maintenance Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant</td>
<td>66–110 g/week</td>
<td>15 g/month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20 g/month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>100 g/month</td>
</tr>
<tr>
<td>Child</td>
<td>140–275 g/week</td>
<td>25 g/month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>35 g/month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>175 g/month</td>
</tr>
<tr>
<td>Adolescent/Adult</td>
<td>290–330 g/week</td>
<td>45–70 g/month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>70–100 g/month</td>
</tr>
<tr>
<td></td>
<td></td>
<td>350–500 g/month</td>
</tr>
</tbody>
</table>

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[^1]: 1 FTU = adequate amount of ointment for “thin and even” application to an area of skin equal to “2 adult hands” (fingers together)

[^2]: FTUs = amount of ointment expressed from a tube with a 5-mm diameter nozzle measured from the distal skin crease to the tip of the palmar surface of an adult’s index finger (~0.5 g)

[^3]: Ointment or cream can be used interchangeably

[^4]: For children over 12 years of age

[^5]: For adolescents and adults

[^6]: For infants and children under 2 years of age
TOPICAL CALCINEURIN INHIBITORS (TCIs)

- Tacrolimus and pimecrolimus are approved for short-term or chronic intermittent AD in patients ≥ 2 years of age who have failed other treatment agents.

- Macrolactams that suppress the immune system by inhibiting the action of T-lymphocytes thus decreasing the release of pro-inflammatory cytokines.

- Both agents inhibit mast cell and neutrophil activation and release of inflammatory mediators.

- Tacrolimus has additional effects on basophils and eosinophils function.

- Black Box warning on TCIs for the lack of long-term safety data and the potential risk of the development of malignancies.

• Pimecrolimus is approved for mild-to-moderate AD when TCS are not well tolerated or contraindicated

• Tacrolimus is approved for patients with moderate-to-severe AD when there is minimal response to other treatment options including TCS

• Additional usages:
  ○ To prevent relapses and prevent flares in patients experiencing ≥ four exacerbations per year, who previously responded to treatment with tacrolimus ointment 2 times a day for maximum 6 weeks
# Selected Topical Calcineurin Inhibitors Used in Atopic Dermatitis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation(s)</th>
<th>Strength(s)</th>
<th>Administration</th>
</tr>
</thead>
</table>
| Tacrolimus      | Ointment       | 0.1%, 0.03% | • Ages 2 to 16 years, first 0.03% ointment twice daily for 3 weeks, then once daily until disappearance of lesions  
|                 |                |             | • From the age of 16 years, 0.1% ointment until disappearance of lesions |
| Pimecrolimus    | Cream          | 1%          | • Adults and children older than 2 years, twice daily until lesions disappear, not longer than 6 weeks |

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CRISABOROLE 2% TOPICAL OINTMENT

- Crisaborole is a nonsteroidal, phosphodiesterase 4 (PDE-4) inhibitor
- Inhibition of PDE-4 results in increased intracellular cyclic adenosine monophosphate (cAMP) levels
  - The overall mechanism of action of crisaborole on AD lesions is not well understood
- Crisaborole is indicated for mild-to-moderate AD in patients aged 2 years and older.
- Most common adverse event note is application site pain

CRISABOROLE

- Approved December 14th 2016

- PDE4 is a key regulator of inflammatory cytokine production in AD through the breakdown of cAMP

- The inhibition of PDE4 in monocytes in vitro has demonstrated reduction in the release of proinflammatory cytokines.

- Crisaborole is indicated for mild-to-moderate AD in patients aged 2 years and older. A thin layer is applied twice daily to affected areas on the skin.

- Most common adverse event note is application site pain.
Efficacy And Safety Of Crisaborole Ointment, A Novel, Nonsteroidal Phosphodiesterase 4 (PDE-4) Inhibitor For The Topical Treatment Of Atopic Dermatitis (AD) In Children And Adults

- Two identically designed multicenter, randomized, double-blind, vehicle-controlled phase III clinical studies

- Assessed the efficacy and safety of crisaborole in patients with mild to moderate AD

- Patients were instructed to apply a layer of study drug to cover each lesion twice daily for 28 days

- The primary efficacy end point of success in ISGA score at day 29 was defined as clear (0) or almost clear (1) with a 2-grade or more improvement from baseline
RESULTS

• Patients in the crisaborole treatment arm achieved a higher ISGA score success and improvement in pruritus (clear/almost clear with ≥2-grade improvement)

• AD-301: 32.8% vs 25.4%, P = 0.038

• AD-302: 31.4% vs 18.0%, P < 0.001
DUPILUMAB

- Approved March 28th, 2017
- First biologic agent approved for the treatment of AD
- Subcutaneous administration for the treatment of patients aged 12 years or older with moderate-to-severe AD
- 400-mg loading dose followed by 200 mg every 2 weeks with baseline body weight <60 kg or a 600-mg loading dose followed by 300 mg every 2 weeks in patients weighing ≥60 kg or more with moderate to severe AD inadequately controlled with topical prescription therapies or when those therapies are not advisable
- Most common adverse reaction associated with dupilumab is injection site reaction and conjunctivitis

A Fully Human Monoclonal Antibody That Binds Specifically To The Shared Alpha Chain Subunit Of The Interleukin-4 (IL-4) And Interleukin-13 (IL-13) Receptors, Thereby Inhibiting The Signaling Of Both Interleukin

Two Phase 3 Trials of Dupilumab versus Placebo in Atopic Dermatitis

- Two identical, randomized, placebo-controlled, phase 3 trials of dupilumab versus placebo in atopic dermatitis (SOLO 1 and SOLO 2)

- Adults with moderate-to-severe atopic dermatitis whose disease was inadequately controlled by topical treatment were enrolled into the study

- Subjects received subcutaneous dupilumab (300 mg) or placebo weekly or the same dose of dupilumab every other week alternating with placebo based on 1:1:1 randomization for 16 weeks

- The primary outcome was the proportion of patients who had both a score of 0 or 1 (clear or almost clear) on the IGA and a reduction of 2 points or more in that score from baseline at week 16.
RESULTS

• Similar results were observed between both SOLO 1 and SOLO 2
• Dupilumab showed significant improvement in AD signs and symptoms
• The most frequently reported adverse event related to dupilumab was conjunctivitis and injection-site pain
Atopic dermatitis is a chronic, allergic, inflammatory skin condition that has increased incidence rates in industrialized countries.

AD is multifactorial

Emollients and moisturizers as a mainstay of therapy with the addition of other agents to manage symptoms, reduce relapses and decrease flares.

Topical corticosteroids and calcineurin are among the agents utilized in the treatment paradigm

Novel agents such as crisaborole and dupilumab have recently been approved to provide additional treatment options to patients.
Have you seen Atopic Dermatitis at your Practice?
REFERENCES


Follow-up comments & questions can be emailed to:
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