What’s New: Update in Pediatric Dermatology

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Disclosures

• Consultant for Regeneron, Sanofi-Genzyme, Genentech, Novartis, Pfizer, Amgen, Incyte.
11 Minute High Yield Peds Update!

1. COVID
2. Atopic dermatitis
3. “New” to you

Pediatric COVID-19

- Multisystem inflammatory syndrome in children (MIS-C)
- Erythema +/- induration on the hands and feet.
- Oral mucositis
- Conjunctivitis
- Resembling Kawasaki disease.
COVID-19 MIS-C

• Most patients treated with IVIG (2 gram/kg) and steroids.
  – 3 largest observational studies found clinical benefit with IVIG plus glucocorticoids compared with IVIG alone

• Aspirin if patient meets criteria for incomplete Kawasaki’s.

• Most patients are PCR negative indicating it is a post-viral inflammatory syndrome.

COVID-19 MIS-C

• In a single-center, retrospective cohort study
  – 72 children with MIS-C, 20 children received IVIG alone (2 g/kg) as initial therapy, and 52 received IVIG plus infliximab (10 mg/kg).
  – Combined group had a higher percentage of patients with CA dilation and/or LV dysfunction on admission (71 versus 40 percent, respectively) and were more likely to have been admitted to the ICU (56 versus 10 percent, respectively).
  – After initial treatment, fewer patients who received IVIG and infliximab required additional therapy (31 versus 65 percent, respectively) or had new or worsening LV dysfunction (4 versus 20 percent, respectively). The patients on combination therapy also had a greater decrease in CRP levels at 24 and 48 hours after treatment initiation.

Pernio associated with COVID-19

- Pernio (chilblain) like erythematous-violaceous or purpuric macules of the feet, toes fingers.
- Adolescents and young adults.
- Asymptomatic or mild COVID symptoms, 1-4 weeks later develop rash.
- High potency topical steroids if symptomatic.

Perioral dermatitis

- “Maskne”
- Triggered by inhaled or topical steroids. Underlying cause is unknown.
- Oral antibiotics
  - Doxycycline 100 mg twice per day for 1-2 months in older than 9
  - Oral erythromycin 10-20 mg/kg/day divided q12 if younger than 9.
    Or
  - Topical erythromycin 1.5% solution, clindamycin 1% gel +/- calcineurin inhibitors.
  - NO STEROIDS
Irritant contact dermatitis

• Wet work
  – Glove wearing more than two hours per day.
  – Hand cleansing more than 20 times per day.

• Water is hypotonic and acts as a cytotoxic agent on eroded skin.

• Swelling of the stratum corneum, disruption of the intercellular lipids, and enhancement of skin permeability.

• Use of hand sanitizers, alcohol based cleansers.

Dupilumab (anti IL-4/IL-13) ("Dupixent") (Regeneron/Sanofi-Genzyme)

• FDA approved for moderate to severe atopic dermatitis ages 6 and up.

• Dosing:
  – 600 mg load then 300 mg once per month for 15 kg – 30 kg
  – 400 mg load then 200 mg every 2 weeks for 30 kg-60 kg.
**Dupixent 6 months – 5 years**

**LIBERTY AD PRE-SCHOOL Part B (Phase 3)**

- Dosed 300 mg every 4 weeks or 200 mg every 4 weeks based on weight.
- IGA 0 or 1: 28% vs. 4% with placebo.
- EASI-75: 53% vs. 11% with placebo.
- Average improvement in EASI from baseline: 70% vs. 20% placebo.
- Average improvement from baseline itch: 49% vs. 2% placebo.

**Dupixent 6 months – 5 years**

- Safety profile similar to prior experience.
- Conjunctivitis: 5% vs. 0% placebo.
- Injection site reaction: 2% vs. 3% placebo.
Tralokinumab (anti IL-13) (Leo)

- ECZTRA 6 trial (phase 3)
- 301 adolescent patients ages 12-17.
- Tralokinumab 150 mg or 300 mg (300 mg and 600 mg load) or placebo subcutaneously every two weeks for 16 weeks.

Tralokinumab (anti IL-13) (Leo)

- IGA 0 or 1 at week 16
  - 21.4% in the 150 mg group
  - 17.5% in the 300 mg group
  - 4.3% of the placebo group.

- EASI75 responses:
  - 28.6% of the 150 mg group
  - 27.8% of the 300 mg group
  - vs. 6.4% of the placebo group.
Lebrikizumab (anti IL-13) (Lilly)

- ADvocate 1 and Advocate 2 are ongoing 52-week randomized, double-blind, placebo-controlled, parallel-group, Phase 3 studies designed to evaluate lebrikizumab as monotherapy in adult and adolescent patients (aged 12 to less than 18 years of age and weighing at least 40 kg) with moderate-to-severe AD.

Abrocitinib (JAK1)(Pfizer)

- JADE TEEN trial included 285 adolescents (50.9% boys; median age, 15 years) with AD, of which 273 completed the trial. At 12 weeks
- IGA 0 or 1:
  - Abrocitinib 200 mg daily + TCS: 46%
  - Abrocitinib 100 mg daily + TCS: 41%
  - Placebo + TCS: 24%
- EASI75:
  - Abrocitinib 200 mg daily + TCS: 72%
  - Abrocitinib 100 mg daily + TCS: 68%
  - Placebo + TCS: 41%
Abrocitinib (JAK1)(Pfizer)

- 100 mg: 3 acne, 1 herpes zoster, 1 oral herpes, 1 eczema herpeticum
- 200 mg: 5 acne, 2 herpes simplex, 2 oral herpes
- Placebo: 1 conjunctivitis, 1 acne

Upadacitinib (JAK1) ("Rinvoq") (Abbvie)

- Open label multiple dose study.
  - To evaluate pharmacokinetics, safety and tolerability in pediatric subjects.
- Age 6 months to 12 years with IGA = 4 (severe atopic dermatitis).
- N = 40.
- Endpoints
  - Maximum plasma concentration
  - Time to maximum observed plasma concentration
  - Area under the plasma concentration time curve within a dosing interval
  - Number of participants with treatment emergent adverse events.
Topical Ruxolitinib (JAK1/JAK2) (Incyte)(“Opzelura”)

- FDA approved: indicated for the topical short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis in non-immunocompromised patients 12 years of age and older whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

- 1249 adult and adolescent patients ≥12 years of age in 2 identically designed double-blind, randomized, vehicle-controlled trials.

Topical Ruxolitinib (Opzelura)

- SERIOUS INFECTIONS
- Patients treated with oral Janus kinase inhibitors for inflammatory conditions are at risk for developing serious infections that may lead to hospitalization or death. Reported infections include:
  - Active tuberculosis, which may present with pulmonary or extrapulmonary disease.
  - Invasive fungal infections, including candidiasis and pneumocystosis.
  - Bacterial, viral, and other infections due to opportunistic pathogens.

- Avoid use of OPZELURA in patients with an active, serious infection, including localized infections. If a serious infection develops, interrupt OPZELURA until the infection is controlled. Carefully consider the benefits and risks of treatment prior to initiating OPZELURA in patients with chronic or recurrent infection. Closely monitor patients for the development of signs and symptoms of infection during and after treatment with OPZELURA.
Topical Ruxolitinib (Opzelura)

• Other warning associated with oral JAK inhibitors:
  – High rate of all-cause mortality.
  – Higher rate of MACE (major adverse cardiovascular events)
  – Higher rate of thrombosis.
  – Higher rate of thrombocytopenia, anemia and neutropenia.
  – Lipid elevations.

Topical Ruxolitinib (Opzelura)

• IGA 0 or 1: 53% (Opzelura) vs. 15% (vehicle) and 51% vs. 7% at week 8.

• EASI-75: 62% vs. 24% and 61% vs. 14%.

• NRS 4 point improvement: 52% vs. 15% and 50% vs. 16%.

• Burning 0.8% vs. 4.4%
• Pruritus 0% vs. 2.4%
Topical Ruxolitinib (Opzelura)

**ADVERSE REACTIONS OCCURRING IN $\geq$1% OF PATIENTS THROUGH WEEK 8 IN TRuE-AD1 AND TRuE-AD2:**

<table>
<thead>
<tr>
<th>Adverse reaction</th>
<th>OPZELURA (n=499)</th>
<th>Vehicle (n=250)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with any TEAE</td>
<td>27%</td>
<td>33%</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>1%</td>
<td>0%</td>
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<tr>
<td>Ear infection</td>
<td>1%</td>
<td>0%</td>
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<tr>
<td>Eosinophil count increased</td>
<td>1%</td>
<td>0%</td>
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<tr>
<td>Urticaria</td>
<td>1%</td>
<td>0%</td>
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<tr>
<td>Diarrhea</td>
<td>1%</td>
<td>&lt;1%</td>
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<tr>
<td>Folliculitis</td>
<td>1%</td>
<td>0%</td>
</tr>
<tr>
<td>Tonsillitis</td>
<td>1%</td>
<td>0%</td>
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<tr>
<td>Rhinorrhea</td>
<td>1%</td>
<td>&lt;1%</td>
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Crisaborole (Eucrisa) (Pfizer)

- Small molecule topical phosphodiesterase 4 (PDE-4) inhibitor.
- FDA approved for mild to moderate atopic dermatitis in 3 months and older.
- Available commercially as 2% ointment in a proprietary emollient base.
Crisaborole

- In two Phase 3 trials Crisaborole patients achieved greater success compared to placebo. Patient achieving clear or almost clear skin with a 2 point improvement in IGA score:
  - 32.8% (crisaborole) vs. 25.4% (vehicle)
  - 31.4% (crisaborole) vs. 18% (vehicle)

- 4% of patients experiencing burning/stinging with 78% resolving within the first 24 hours.


Secukinumab (“Cosentyx”) (Novartis) for plaque psoriasis

- FDA approved for moderate to severe plaque psoriasis age 6 and up.
- Inhibits IL-17.
- Adds to pediatric options: Enbrel (Amgen), Humira (Abbvie), Stelara (Janssen).

- 52-week (236 weeks total), 162 children.
- 75mg for <50kg and 150mg for ≥50kg once per month.

- PASI-75:
  - Cosentyx 75 mg: 55% vs 10% placebo
  - Cosentyx 150 mg: 86% vs 19% placebo

- PGA:
  - Cosentyx 75 mg 32% vs 5% placebo,
  - Cosentyx 150 m 81% g vs 5% placebo
• **Etanercept therapy for toxic epidermal necrolysis.**
  
• (Approved for 4 years and older in plaque psoriasis.)

• 10 patients.
• 50 mg of etanercept was administered in a single subcutaneous injection
• All patients promptly responded to treatment, reaching complete re-epithelialization without complications or side effects. The median time to healing was 8.5 days.

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**Systemic review of 91 patients:**
• 79 patients (86%) responded well and discharged with few side effects and complications

**Biologic TNF-alpha inhibitors in the treatment of Stevens-Johnson syndrome and toxic epidermal necrolysis: a systemic review**
Shan Zhang 1, Shuwei Yang 1, Sheng Li 1, Yupei Pan 3, Yingguo Diao 3
Affiliations + expand
PMCID: 3072266 DOI: 10.1088/09646647/10.10/677548

**Systemic review or 38 articles:**
• "Reviewed studies presented a strong case for biologic treatment, both monotherapy and combination use, in SJS/TEN treatment.”
• Biologic therapy as monotherapy may be a safer option based on the number of fatal adverse events.

**A Systematic Review of Efficacy and Safety of Monotherapy and Combination Therapy With Biologic for Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis**
Muskan Goelhria 1, Khalid Matyaj 1, Markia G Porco 1
Affiliations + expand
PMID: 33531910 DOI: 10.1077/10547754219983779
Intralesional Candida For Molluscum

• Retrospective chart review was conducted to examine the efficacy of intralesional injection of Candida antigen into a maximum of three individual molluscum lesions.
  – 29 patients
  – 55% had complete resolution
  – 37.9% experienced partial resolution
  – Overall response rate of 93%
  – 2/9 failed to respond (6.9%)

• My treatment of choice of molluscum.


Thank you!

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