AEDV HIGHLIGHTS
27TH EADV CONGRESS
12-16 September 2018
PARIS, France
Systemic diseases

Dra. Raquel Rivera Díaz
Atopic Dermatitis
Dr. T Biedermann

- Key triangle in AD pathogenesis
  - Barrier function down
  - Th2 response up
  - Microbial dysbiosis
- Targeting Th2 - exit strategy for AD
- Targeting the microbioma to stabilize the skin

Dry Skin
Reduce barrier

“Allergy”
Th2 disease

“Infections”
Cutaneous dysbiosis
Increasing Comorbidities Suggest that Atopic Dermatitis is a Systemic Disorder

- Beyond the march to allergic conditions (food allergy, asthma, allergic rhinitis, allergic conjunctivitis, and eosinophilic esophagitis)
- Propensity to both skin and systemic infections
- Associations with cardiovascular, neuropsychiatric, and malignant diseases were increasingly reported

“AD as a systemic disease need for systemic treatment aproaches for severe AD patient”
Dra. E. Guttman

Journal of Investigative Dermatology (2017) 137, 18e25
Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children

- Treatment recommendation for atopic eczema: adult

**SEVERE:** SCORAD >50 / or persistent eczema
- Hospitalization; systemic immunosuppression: cyclosporine A, short course of oral glucocorticosteroids, dupilumab, methotrexate, azathioprine, mycophenolate mofetil; PUVA; alitretinoin

**MODERATE:** SCORAD 25-50 / or recurrent eczema
- Proactive therapy with topical tacrolimus or class II or class III topical glucocorticosteroids, wet wrap therapy, UV therapy (UVB 311 nm, medium dose UVA1), psychosomatic counseling, climate therapy

**MILD:** SCORAD <25 / or transient eczema
- Reactive therapy with topical glucocorticosteroids class II or depending on local cofactors: topical calcineurin inhibitors, antiseptics incl. silver, silver coated textiles

**BASELINE:** Basic therapy
- Educational programmes, emollients, bath oils, avoidance of clinically relevant allergens (encasings, if diagnosed by allergy tests)
Novel systemic drugs in treatment of atopic dermatitis: results from phase II and phase III studies published in 2017/2018

<table>
<thead>
<tr>
<th>Substance</th>
<th>Target molecule</th>
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<tbody>
<tr>
<td>Dupilumab</td>
<td>IL-4 receptor, IL-13 receptor</td>
</tr>
<tr>
<td>Lebrikizumab</td>
<td>IL-13</td>
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<tr>
<td>Tralokinumab</td>
<td>IL-13</td>
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<tr>
<td>Nemolizumab</td>
<td>IL-31 receptor</td>
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<tr>
<td>Fezakinumab</td>
<td>IL-22</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>IL-12/IL-23p40</td>
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<tr>
<td>Baricitinib</td>
<td>JAK 1/JAK 2</td>
</tr>
<tr>
<td>ZPL3893787</td>
<td>Histamine 4 receptor</td>
</tr>
</tbody>
</table>

Werfel. Curr Opinion Allergy Clin Immunol 2018
NEW THERAPIES...

ARE WE GETTING EXCITED TOO EARLY?
Systemic treatments of AD
Dr. Carsten Flohr

WE STILL HAVE A WAY TO GO...

- Treatment Registries
- H2H Trials
- (Living) Network Meta-Analysis
- Novel Therapy Trials
- Conventional Systemics Trials
- Stratification
- Personalised Medicine
Targeting the JAK/STAT pathway: Expert Forum

• JAK 1 inhibitors (alone or in combination with inhibition of JAK 2, JAK 3 or other molecules) were beneficial upon oral or topical application in phase 2 studies for the treatment of Atopic Dermatitis
  • Upadacitinib (JAK 1)
  • PF-04965842 (JAK 1)
  • Baricitinib (JAK 1,2)

• Tofacitinib and Ruxolitinib are effective for severe Alopecia Areta (unclear if topical JAKi will be effective for AA)
• Tofacitinib and Ruxolitinib, in combination with UVL, are effective for vitiligo
**Acquired AO +++**
- immediate hypersensitivity (IgE) +++
  drug, food, latex, insect; ± effort
- Anaphylactoid reaction +++
  drug, contrast medium
- « idiopathic » (auto-immune)
- inducible: vibration, pressure etc.

- pharmacological
  - NSAID
  - ACEi ++; ARB; aliskiren; gliptins...
- with C1inh deficiency (C1INH-AAO)

**Hereditary AO**
- with C1inh deficiency and mutation in SERPING1 (C1INH-HAO)
- without mutation in SERPING1
  - F12 (F12-HAO)
  - others

→ bradykinin vs histamine