Immunomodulation with Immunotherapy—“1911-2014”
Change the course of the disease.
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Allergy/Immunology/Pedi Pulmonology

Disclosures/COI

• Speakers Bureau/Consultant:
  • Astra Zeneca, Merck. Genentech/Novartis, Mylan, Teva, Boehringer Ingleheim, Baxter, Alcon, Sunovium
  • Consultant-G3B pharma,
  • Adjunct Clinical Prof Stanford/Lucille Packard Children’s Hospital

History

• “102 yrs”—last 25 notable
• “allergy”- Australian Pedi Clemens Freiherr von Pirquet—altered immune reactivity
• 1911-Leonard Noonan/John Freerman—grass immunotherapy—>SLIT, SCIT and Nonspecific IT—Anti IgE.....

• Goal—Control Sx of AR and Asthma, dec new sensitization and dec progression of As Sx.
Immunology-change the course of the disease

- Desensitization of the FceR1-bearing mast and baso-upreg of H2receptor w/ 6 hrs
- T Cell responses
- IgE and IgG4 responses
- Regulation of mast cells, basophils and eos
- Tolerance
- T and B cell responses

- Burks A.W. "Update on Allergy Immunotherapy: PRACTALL", JACI 2013:131:1288-96

Immunomodulation

- Immunological effects (lab)
- Clinical evaluation:
  - Patient selection: Sensitivity (mono, poly), age, Sx, disease severity
  - Antigen and route of delivery
  - Duration of therapy
  - Parameters evaluated—QOL, Sx control, PFTs, exacerbations—need a biomarker

Antigen

- Antigen—FDA, CBER
  - W/V, PNU, Standardized
- Protein, modified allergens (Chemical/Molecular)
- Adjuvants (incorporate immunostimulant molecules or co-mix adjuvant with allergen extract, viral-Capsids), Peptides, SLIT constructs
- Mix or individualized therapy (SCIT)
- Single allergen in Polysensitized subjects (SLIT)
## Antigen Delivery-Route

- Subcutaneous
- Sublingual
- Intralymphatic
- Epicutaneous-skin patches
- (Bronchial)
- (Nasal)
- (Oral)

## Dose --SIT

<table>
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<th>Extract Target Range</th>
<th>2007</th>
<th>2011</th>
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<tr>
<td>Short Ragweed</td>
<td>6-12 AgE U(ug)</td>
<td>6-12 AgE U (ug)</td>
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<tr>
<td>Cat</td>
<td>1-4,000 BAU</td>
<td>1-4,000 BAU</td>
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<tr>
<td>Dust Mite</td>
<td>500-2,000 AU</td>
<td>500-2,000 AU</td>
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<tr>
<td>Pasture Grasses</td>
<td>1-4,000 BAU</td>
<td>1-4,000 BAU</td>
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<td>Bermuda Grass</td>
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<td>Dog, AP</td>
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</table>


## Immunotherapy Parameters

- Task Force allergy Parameters-- AAAI, ACAAI, JCAAI
- Anaphylaxis, Immunotherapy, Insect Sensitivity, House Dust mite...
- Work group, Editorial team, Reviewers,
- Update q 3 yrs
- Document—Preamble
- Summary statements—"to do"
- References Graded
- Annals or JACI—pub, on line
- (Summary Cards)
- Allergyparameters.org
Dose SLIT

- FDA pending: Timothy
- Sgrass mix: Timothy, Kentucky Blue,
- Perennial Rye, Orchard, Sweet Vernal
- Ragweed
- HDM
- MonoRx in Polysensitized pt
- Dose Variable—SLIT daily dose equal to Monthly SCIT dose

Duration

- SCIT: 3-6 yrs (85%/85%)—remission 12 +yrs
- Buildup and then maintenance phase
- (Pre seasonal / Intermittent -adjuvants)
- SLIT: 2 yrs?
- Compliance/Knowledge: (Studies vs Patient surveys)
  - SLIT
  - SCIT

Clinical Efficacy

- SIT in AR pts dec late phase responses to local allergen challenge in skin and nasal mucosa.
- In asthmatics, nonspecific airway hyperreactivity and bronchial responses to inhaled allergen challenge were dec.
- Skin reactivity dec with SCIT and SLIT
How does Rx Schedule affect efficacy?

- Rush– Bee, IFA...
- Cluster
- Standard
- ? Increase reactions/safety
- ? Efficacy
- Administer in a Medically supervised facility
- Cox,L—Immunotherapy Parameter

Safety

- SCIT—Life threatening reaction 1.2.4 Million shots (0.1% mild reactions)—3-4 deaths per yr possibly attributed to shots—less over time.
- SLIT— oral mucosal 3x noted
- Anaphylaxis—Parameters—
  - Epinephrine
    - Epi Pen, AuviQ, (Twinject),Generic
    - IM Lateral thigh
    - Teach Patient, Family/Caregivers (teachers)
- Antihistamines treat the hives not the SSx
- Lieberman, Anaphylaxis Parameter

Summary—3 Key issues

- 1)
- 2)
- 3)
Thank you

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References

- Butler R, "Effect of vaccine IT on OT and FCT on Clinical and Lab Parameters in Children with AA and HS" JACI 2011;127:298-305
- Banks R, "Update on Allergy immunotherapy - PRACTALL" JACI 2011;127;S1-55
- Castle T, "Future forms of IT" JACI 2011;127;6-11
- Golden D, "Insect Hypersensitivity", JACI 2011, 127 (4); 851-4
- Grier T, "How I'm dosing!" Ann Allergy Asthma Immunol 2011;107(2):289-300
- Kiel M, "Real-life compliance and persistence among users of IT, PRACTALL" JACI 2011;127;6-11
- Lockey R, "Health economics of allergen-specific IT in the US", JACI 2011;127;6-11
- Mohapatra, "IT for allergies and asthma" Curr Opin Pharmacol, 2010;10(3):276-288, doi 10.1016/j.coph.2010.05.012
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- AAAI.org