Food Allergy Clinical Trials

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Outline

• Introduction
• Approaches to therapy
• Food allergy clinical trials in Chicago
  – Food Allergy Herbal Formula-2 (FAHF-2)
  – Viaskin® (VIPES)
  – Oral Immunotherapy for Wheat Allergy (Wheat OIT)
  – Peanut Reactivity Reduced by Oral Tolerance in an anti-IgE Clinical Trial (PRROTECT)
Overview of Approaches to Treatment

• Food-allergen specific
  – Treatment aimed at a particular allergen
  – Analogy: allergen immunotherapy (IT) for environmental allergens

• Allergen non-specific
  – May impact multiple different allergens

• Adjunctive therapies
  – Being developed to reduce risk of adverse reactions
Food-allergen specific approaches

- Native allergens and mutated recombinant proteins
- Oral IT (OIT)
- Sublingual IT (SLIT)
- Epicutaneous IT (EPIT)
Non-specific approaches

• Humanized monoclonal anti-IgE (omalizumab/Xolair®)*
• Chinese herbal medicine (FAHF-2)

*may also be useful to reduce severity of adverse reactions to food immunotherapy
Desensitization vs Tolerance

• Desensitization: change in the amount of allergen that causes symptoms while on treatment

• Tolerance: long-lasting effects of treatment, in which the patient can eat the food without problems after finishing treatment
New therapies in clinical trials

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Stage of study</th>
<th>Allergen studied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-allergen-specific therapy</td>
<td></td>
<td></td>
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<tr>
<td>Anti-IgE therapy</td>
<td>Phase II</td>
<td>Peanut, milk</td>
</tr>
<tr>
<td>Traditional Chinese medicine</td>
<td>Phase II</td>
<td>Peanut, tree nut, fish, shellfish, sesame</td>
</tr>
<tr>
<td>Allergen-specific therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral IT</td>
<td>Phase II-III</td>
<td>Peanut, milk, egg, tree nuts, wheat</td>
</tr>
<tr>
<td>Sublingual IT</td>
<td>Phase II</td>
<td>Peanut, milk, hazelnut, kiwi, peach</td>
</tr>
<tr>
<td>Heated antigen</td>
<td>Phase II</td>
<td>Egg, milk</td>
</tr>
<tr>
<td>Epicutaneous IT</td>
<td>Phase II</td>
<td>Peanut, milk</td>
</tr>
<tr>
<td>Recombinant protein IT</td>
<td>Phase I</td>
<td>Peanut</td>
</tr>
<tr>
<td>Combination therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-IgE plus oral IT</td>
<td>Phase II</td>
<td>Milk, peanut</td>
</tr>
</tbody>
</table>

Jones & Burks J Allergy Clin Immunol 2013; 131:3-11
Principles of and responses to food OIT

Nowak-Wegrzyn and Sampson J Allergy Clin Immunol 2011;127:558-73
OIT

- Growing body of evidence to support this approach
- Studied for milk, egg and peanut to date
- Appears to have good clinical (and immunologic) outcomes
- Side effects remain a concern (allergic reactions)
  - Usually mild (oral symptoms)
  - More severe allergic reactions have occurred
  - GI side effects in 10-20%, which have required stopping OIT
  - Risk factors: viral infections, menstruation, exercise
Summary of how much of food allergen was ingested in various clinical trials of OIT and SLIT

<table>
<thead>
<tr>
<th></th>
<th>Placebo Group</th>
<th>Active Treatment Group</th>
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</thead>
<tbody>
<tr>
<td>Peanut OIT</td>
<td>280 mg</td>
<td>5000 mg</td>
</tr>
<tr>
<td>Milk OIT</td>
<td>500 mg</td>
<td>5100 mg</td>
</tr>
<tr>
<td>Egg OIT</td>
<td>250 mg</td>
<td>5000-10,000 mg</td>
</tr>
<tr>
<td>(Peanut SLIT)</td>
<td>85 mg</td>
<td>1710 mg</td>
</tr>
</tbody>
</table>
### Table 2. Success Rates on Oral Food Challenge.

<table>
<thead>
<tr>
<th>Challenge</th>
<th>Participants Tested*</th>
<th>Response Rate</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo (N=15)</td>
<td>Oral Immunotherapy (N=40)</td>
<td>Placebo (N=15)</td>
</tr>
<tr>
<td></td>
<td>number</td>
<td>number (percent)</td>
<td></td>
</tr>
<tr>
<td>Desensitization, 5 g at 10 mo</td>
<td>13</td>
<td>35</td>
<td>0</td>
</tr>
<tr>
<td>Desensitization, 10 g at 22 mo</td>
<td>1†</td>
<td>34</td>
<td>0</td>
</tr>
<tr>
<td>Sustained unresponsiveness at 24 mo‡</td>
<td>0</td>
<td>29§</td>
<td>0</td>
</tr>
</tbody>
</table>
Peanut OIT
Varshney J Allergy Clin Immunol 2011;127:654-60

Cumulative amount of ingested peanut protein during oral food challenge after 12 months of OIT

Skin prick tests at baseline and after 12 months of OIT
Anti-IgE (omalizumab/Xolair®)

- Pilot study in 11 patients with milk allergy
- Study showed that pre-treatment with omalizumab before and during milk OIT decreased side effects and accelerated time needed to reach maintenance OIT dose
Multi-center studies being performed at Ann and Robert H. Lurie Hospital of Chicago
FAHF-2 (Chinese herbal formula)

- Phase 1 study showed FAHF-2 was safe and well tolerated (mild GI side effects)
- Phase 2 study
  - Randomized, double-blind placebo controlled trial
  - 68 subjects aged 12-45 years
  - Allergy to peanut, tree nut, sesame, fish or shellfish
  - 6 month intervention of 9 herbs taken 3 times a day
- Study will be completed this summer
Viaskin®/VIPES

- Phase 1 study showed Viaskin® to be safe and well tolerated
- Phase 2 study
  - International, randomized, double-blind placebo controlled trial
  - 220 subjects aged 6-55 years
  - Allergy to peanut
  - 12 month intervention of daily application of Viaskin®
Wheat OIT

- No published studies of wheat OIT exist
- Randomized, double-blind placebo controlled, crossover trial
- 48 subjects aged 4-30 years with history of wheat allergy
- 24 month intervention for active group; 12 month intervention for crossover group
PRROTECT

- Randomized, double-blind, multicenter study
- Objective: to learn if pre-treatment with omalizumab (Xolair®) helps peanut OIT to be done more safely and quickly
  - All participants will receive peanut OIT
  - In the beginning, some will receive omalizumab and others will receive placebo shots. Placebo participants will be offered the chance to receive omalizumab during the trial.
- 36 subjects (9 per site) aged 7-24 years
- Study duration: approximately 1 year
Summary

• Multiple treatment modalities are in development and testing
• Results appear to be promising in terms of safety and results, though different patterns of response have been seen
• Need to identify who is likely to respond to a particular treatment
• The duration of treatment and whether long term tolerance is achievable are still unclear
Contact Information for Food Allergy Studies at Lurie Children’s:

Phone: 1.888.573.1833
Email: allergystudy@luriechildrens.org
Website: http://www.luriechildrensresearch.org/allergy/

Thank you!