A Phase 2 Study of Multi Oral Immunotherapy in Multi Food Allergic Patients to Test Immune Markers after Minimum Maintenance Dose using Xolair

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Introduction

- Food allergies affect approximately 8% of children1 and 10.8% of adults2 in the United States.
- 45% of patients are allergic to multiple foods3.
- Oral immunotherapy (OIT) has been well studied as a therapeutic option for treating food allergy.
- Numerous studies have indicated that sIgG4/sIgE ratio may be a more reliable indicator of desensitization than sIgG4 or sIgE alone3,4.
- The immune changes associated with varying maintenance doses in multi-allergen OIT (mOIT) have not been directly compared.
- This study assesses immunological changes associated with different low maintenance doses preceded by fixed dose ozalumab.

Methods

- Phase 2, multi-site mOIT trial
- Participants with 2-5 allergens (Table 1)
- Pretreated with 3 doses of ozalumab (150 mg) then randomized to receive mOIT to a maintenance dose of 300 or 1200 mg protein containing 2-5 food allergens (Fig 1)

Results

- Adverse events were also evaluated
- 60 participants (ages 4-20 years) were randomized 1:1 to 300 or 1200 mg treatment groups
- No significant differences in baseline characteristics by treatment arm (Table 1)

Table 1: Baseline Characteristics by mOIT Treatment Arm*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (n=60)</th>
<th>Treatment 300 mg (n=30)</th>
<th>Treatment 1200 mg (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>14 (4, 20)</td>
<td>14 (4, 20)</td>
<td>14 (4, 20)</td>
</tr>
<tr>
<td>Male</td>
<td>41 (68%)</td>
<td>21 (70%)</td>
<td>20 (67%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>1 (2%)</td>
<td>0</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Not Hispanic or Latino</td>
<td>59 (98%)</td>
<td>29 (97%)</td>
<td>30 (97%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>24 (40%)</td>
<td>15 (50%)</td>
<td>9 (30%)</td>
</tr>
<tr>
<td>Asian</td>
<td>22 (37%)</td>
<td>8 (27%)</td>
<td>14 (47%)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>1 (2%)</td>
<td>0</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Multiracial</td>
<td>10 (17%)</td>
<td>5 (17%)</td>
<td>5 (17%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (5%)</td>
<td>2 (7%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Allergic history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergic dermatitis</td>
<td>48 (80%)</td>
<td>24 (80%)</td>
<td>24 (80%)</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>39 (65%)</td>
<td>21 (70%)</td>
<td>18 (60%)</td>
</tr>
<tr>
<td>Allergic asthma</td>
<td>42 (70%)</td>
<td>20 (67%)</td>
<td>22 (73%)</td>
</tr>
<tr>
<td>Number of food allergens</td>
<td>7 [2, 14]</td>
<td>7 [3, 13]</td>
<td>7 [2, 14]</td>
</tr>
<tr>
<td>Treatment 300 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omalizumab dose ≥ 0.916 mg/kg/moL (standard dose)**</td>
<td>18 (30%)</td>
<td>9 (30%)</td>
<td>9 (30%)</td>
</tr>
</tbody>
</table>

* The probability of success and 95% CI was reported. To determine whether the probability of success differed by treatment arm, Fisher’s exact test was used to calculate the odds ratio.

- 70% of all participants showed a change in IgG4/IgE ratio in at least 2 allergens (Table 1)
- No differences in primary endpoint success, focused on the intention-to-treat (ITT) population, by treatment group, by ability to reach maintenance dose, or by number of allergens in the mOIT mix
- No differences in the percentage of doses associated with adverse events between the two treatment groups (19% vs. 17%, P = 0.69)

Figure 2: Change in Allergen-Specific IgG4/IgE Ratio by Maximum Per-Allergen Dose

Figure 3: Change in Specific IgG4/IgE Ratio by Maximum Per-Allergen Dose

Discussion

- Several publications have explored lower maintenance doses with small foods and showed evidence of immunological changes5.
- Our study is the first mOIT trial exploring different low maintenance doses over a short duration of time.
- Our data suggests that biomarker changes are induced early and at a lower maintenance dose than previously known.
- These findings are important when considering improvements to compliance in long-term dosing of OIT.
- Limitations include the lack of comparison to mOIT alone (without omalizumab), small sample size (but comparable to other OIT studies), and free IgE was not measured (ideal given omalizumab can elevate IgE values)

Conclusions

- Our data suggests that biomarker changes are induced early, even at a 300 mg dose for multiple allergens.
- Lower allergen maintenance doses will likely be better tolerated and preferred by patients, thus improving adherence.
- Larger phase 2 trials are needed to confirm these findings.

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References