A Novel Characterized Peanut Allergen Formulation (AR101) for Oral Immunotherapy (OIT) Induces Desensitization in Peanut-Allergic Subjects: A Phase 2 Clinical Safety and Efficacy Study


EAACI Presentation by Wesley Burks, MD
June 7, 2015
Barcelona, Spain
Disclosure

In relation to this presentation, I declare the following, real or perceived conflicts of interest:

This study was sponsored by Aimmune Therapeutics

A conflict of interest is any situation in which a speaker or immediate family members have interests, and those may cause a conflict with the current presentation. Conflicts of interest do not preclude the delivery of the talk, but should be explicitly declared. These may include financial interests (eg. owning stocks of a related company, having received honoraria, consultancy fees), research interests (research support by grants or otherwise), organisational interests and gifts.
Study overview

Background

- Food allergy prevalence is increasing worldwide, including to peanut*
- Oral immunotherapy (OIT) has shown promise as treatment for a variety of food allergies, e.g., peanut, milk, and egg
- There are no approved drug products for peanut allergy

Objectives

- Assess clinical safety of a novel characterized peanut allergen formulation (AR101)
- Demonstrate AR101’s efficacy in inducing desensitization to peanut in peanut-allergic children and young adults undergoing peanut OIT

Primary Endpoint

- Number of subjects receiving AR101 vs. placebo in the intent-to-treat (ITT) population able to reach a maintenance dose of 300 mg/d, and to tolerate a cumulative amount of peanut protein at Exit DBPCFC ≥ 443 mg with no more than mild symptoms

*JACI. 2014;133:291-307
<table>
<thead>
<tr>
<th>Key Inclusion Criteria</th>
<th>Key Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Ages 4 to 26 years</td>
<td>• History of life-threatening anaphylaxis</td>
</tr>
<tr>
<td>• History of peanut allergy</td>
<td>• History of EGID</td>
</tr>
<tr>
<td>• Peanut-specific IgE &gt; 0.35 kU_{A}/L</td>
<td>• Severe asthma OR mild/moderate asthma if poorly controlled</td>
</tr>
<tr>
<td>• Peanut skin-prick test wheal diameter &gt; 3 mm</td>
<td></td>
</tr>
<tr>
<td>• Dose-limiting symptoms to ≤ 143 mg of peanut protein in DBPCFC</td>
<td></td>
</tr>
</tbody>
</table>
Study design: multi-center, randomized, double-blind, placebo-controlled

Dose increments of 1.2 to 2x

Initial Escalation

Screen / Rand

Fail DBPCFC at ≤ 143 mg

1 day

2-week intervals

Pass DBPCFC at 1043 mg

Additional Endpoint

DBPCFC

<table>
<thead>
<tr>
<th>Dose</th>
<th>Cumulative</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 mg</td>
<td>3 mg</td>
</tr>
<tr>
<td>10 mg</td>
<td>13 mg</td>
</tr>
<tr>
<td>30 mg</td>
<td>43 mg</td>
</tr>
<tr>
<td>100 mg</td>
<td>143 mg</td>
</tr>
<tr>
<td>300 mg</td>
<td>443 mg</td>
</tr>
<tr>
<td>600 mg</td>
<td>1043 mg</td>
</tr>
</tbody>
</table>

Open-Label

Pass DBPCFC at ≥ 443 mg

Primary Endpoint

Possible dose reductions and re-escalations
Enrollment and disposition

Screened
N = 67

Randomized
N = 56

Screen failures
N = 11

AR101
n = 29

Placebo
n = 27

Early Discontinuations
n = 6

Completers
AR101
n = 23

Completers
Placebo
n = 26

AR101
n = 29

ITT AR101
n = 29

ITT Placebo
n = 26

• 5 withdrew consent
• 4 tolerated 100 mg of peanut protein in DBPCFC
• 1 SAE of biphasic anaphylaxis
• 1 reacted to placebo in DBPCFC

• 4 due to GI AEs
• 1 withdrew consent
• 1 investigator decision
tolerability, compliance, & GI issues
No significant differences in demographic or baseline characteristics between treatment groups.

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Active (AR101)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n, ITT</td>
<td>26</td>
<td>29</td>
</tr>
<tr>
<td><strong>Age, Median</strong></td>
<td>8 years</td>
<td>7 years</td>
</tr>
<tr>
<td>(min, max)</td>
<td>4 to 14</td>
<td>4 to 21</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>16 male</td>
<td>20 male</td>
</tr>
<tr>
<td></td>
<td>10 female</td>
<td>9 female</td>
</tr>
<tr>
<td><strong>Peanut-specific IgE, Median</strong></td>
<td>100.0 (3.5 to &gt;100)</td>
<td>64.3 (0.8 to &gt;100)</td>
</tr>
<tr>
<td><strong>Wheal, Median</strong></td>
<td>13 mm (5 to 26)</td>
<td>14 mm (5 to 30)</td>
</tr>
<tr>
<td><strong>MTD, Cumulative, Median</strong></td>
<td>28 mg (3 to 30)</td>
<td>13 mg (3 to 30)</td>
</tr>
</tbody>
</table>

MTD = maximum tolerated dose of peanut protein in Screening DBPCFC
Significantly more AR101 than placebo subjects tolerate top doses in the Exit DBPCFC

Percent of Subjects Tolerating Dose at Exit

![Graph showing the percentage of subjects tolerating different doses of AR101 and placebo. The graph includes ITT and Completer analysis populations.](image)

Analysis population
Safety Overview

Median time to reach DBPCFC: 22 weeks for both Placebo and AR101

6 Early Discontinuations from Active; None from Placebo
• 4 due to AEs of recurrent abdominal pain, nausea, and/or emesis
  ‒ 1 confirmed EoE by endoscopic biopsy
• 2 due to multiple factors, including taste, compliance, and GI

• Onset of GI symptoms at 3 to 12 mg; tended to lead to early withdrawal
• Symptoms often not closely associated with time of dose administration
• Symptoms resolved within 1 to 3 weeks of AR101 discontinuation
• Consistent with previous literature reports of GI side effects with OIT

Adverse Event Profile during OIT
• The most common treatment-related symptoms were GI: AR101 = 72%; Plbo = 27%
• 1 serious adverse event of anaphylaxis
• Only 1 epinephrine administration
• Majority of AEs graded as mild; no AEs graded as severe

Percent of completers with given symptom severity grade: less for AR101 group at each DBPCFC dose

**Placebo group** – Symptom severity in exit DBPCFC

<table>
<thead>
<tr>
<th>Challenge dose</th>
<th>Cumulative challenge dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td>3 mg</td>
<td>100 mg</td>
</tr>
<tr>
<td>30 mg</td>
<td>100 mg</td>
</tr>
<tr>
<td>30 mg</td>
<td>300 mg</td>
</tr>
<tr>
<td>100 mg</td>
<td>300 mg</td>
</tr>
<tr>
<td>100 mg</td>
<td>600 mg</td>
</tr>
<tr>
<td>3 mg</td>
<td>600 mg</td>
</tr>
<tr>
<td>13 mg</td>
<td>600 mg</td>
</tr>
<tr>
<td>43 mg</td>
<td>600 mg</td>
</tr>
<tr>
<td>143 mg</td>
<td>600 mg</td>
</tr>
<tr>
<td>443 mg</td>
<td>600 mg</td>
</tr>
<tr>
<td>1043 mg</td>
<td>600 mg</td>
</tr>
</tbody>
</table>

**Maximal symptom severity**
- severe
- mild
- moderate
- none

DBPCFC reactions requiring epinephrine
- **Placebo**: 11 subjects (3 requiring 2 injections)
- **AR101**: 2 subjects (0 requiring 2 injections)

**AR101 group** – Symptom severity in exit DBPCFC

- **Placebo** group
  - n=26
  - n=23
  - n=17
  - n=12
  - n=6

- **AR101** group
  - n=23
  - n=23
  - n=23
  - n=23
  - n=23
  - n=23

- **Maximal symptom severity**
  - severe
  - mild
  - moderate
  - none
Summary

AR101 had an acceptable overall safety and tolerability profile, consistent with previously reported OIT studies.

79% of subjects tolerated up-dosing to a maintenance of 300 mg/d.

Of those who embarked on therapy (including those who discontinued prematurely), the chances of tolerating a cumulative dose of peanut protein on DBPCFC were:

- 79% for 443 mg;
- 62% for 1043 mg.

For those who achieved maintenance dosing, the chances of tolerating a cumulative dose of peanut protein on DBPCFC were:

- 100% for 443 mg;
- 78% for 1043 mg.
Conclusion and next steps

**Conclusion**

- AR101 appears to be a safe and effective treatment option for peanut allergic individuals when used in a controlled OIT regimen

**Next Steps**

- Completion of ongoing open-label follow-on study (ARC002) with an extended maintenance dosing period
- Phase 3 trial of AR101 characterized oral desensitization therapy
Thank you for your attention

**Special thanks to our study volunteers and their families**

**Thanks also to the dedicated physicians, nurses, and staff at:**

- Allergy & Asthma Medical Group, San Diego - Mary Vales and Sarah Holland
- Arkansas Children's Hospital - Denise Pearson
- Boston Children’s Hospital - Heather Biehl and Sara Little
- Children's Hospital of Philadelphia - Deirdre Burke
- Children’s Medical Center of Dallas - Amy Arneson
- Cincinnati Children's Hospital Medical Center - Lisa Clark
- Icahn School of Medicine at Mount Sinai - Sally Noone
- University of North Carolina School of Medicine - Jill French and Pamela Steele

*The ARC001 study was sponsored by Aimmune Therapeutics, a company formerly known as Allergen Research Corporation (ARC)*