Clinical and Immunologic Characteristics of European Patients Screened for PALISADE (Peanut Allergy Oral Immunotherapy Study of AR101 for Desensitization in Children and Adults)

Andrea Vereda,1 M. Dolores Ibáñez,2 Kirsten Beyer,3 A. Wesley Burks,4 Thomas Casale,5 Jonathan O’B. Hourihane,6 Stacie M. Jones,7 Amr Radwan,8 Brian P. Vickery,9 Daniel C. Adelman10

1Allergology Therapeutics, Brisbane, CA, United States; 2Nifs Jesus Children’s University Hospital, Madrid, Spain; 3University Children’s Hospital Charité, Berlin, Germany; 4University of North Carolina, Chapel Hill, NC, United States; 5University of South Florida, Tampa, FL, United States; 6University College Cork, Cork, Ireland; 7University of Arkansas for Medical Sciences and Arkansas Children’s Hospital, Little Rock, AR, United States

BACKGROUND

• Double-blind placebo-controlled food challenge (DBPCFC) is considered the gold standard in diagnosis of food allergy.7
• DBPCFCs were recently conducted during screening for PALISADE, a randomized, placebo-controlled, international, phase 3 trial of AR101 for peanut allergy.9
• Preliminary pre-randomization on data from different patients performing DBPCFC for PALISADE are summarized here.

METHODS

• Eligible subjects aged 4–55 years with a clinical history of IgE-mediated peanut allergy and evidence of peanut sensitization underwent a screening DBPCFC.
• The screening DBPCFC, an abbreviated version of the PRACTALL DBPCFC, progressed sequentially without repeating any dose (1, 10, 50, 100 mg of peanut protein). Doses were given at 24- to 72-hour intervals, but intervals could be increased to 10 days to observe emerging symptoms.
• DBPCFC stopping criteria were prospectively defined in the protocol, based on PRACTALL guidelines,9 and the required presence of 1 or more investigator-determined dose-limiting symptoms (DLS), which were generally objective.
• Investigators graded the severity of allergic symptoms during DBPCFC using National Cancer Institute Common Toxicity Criteria grading scales previously modified and established by the Consortium of Food Allergy Research.
• Subjects who did not react or had a manageable dose of peanut protein were eligible for the PALISADE study.

RESULTS

Table 1. European Subject Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Population (N=166)</th>
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<tbody>
<tr>
<td>Sex</td>
<td>Male: 102, Female: 64</td>
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<tr>
<td>Age</td>
<td>Median: 12; mean: 36.1, SD: 21.0</td>
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<tr>
<td>Peanut-specific IgE, median (Q1, Q3):</td>
<td>8.1 (1.0, 38.1)</td>
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<td>Peanut skin test, median (Q1, Q3):</td>
<td>10.5 (8.1, 12.3)</td>
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<td>Median, n (%)</td>
<td>Allergic reactions: 59 (35.4); Asthma: 81 (48.8); Atopic dermatitis, n (%) 86 (51.5); Allergy to foods other than peanut, n (%) 83 (50)</td>
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• 52% of the subjects were aged 4–11, 28% were aged 12–17, and 15% were adults.
• 62% of the subjects experienced DLS at a cumulative median dose of 44 mg (nonreactors).

Figure 1. Cumulative Amount of Peanut Protein Causing DLS During the Screening DBPCFC, by Age (N=166)

• Median peanut wheal diameter, peanut-specific IgE, and Ara h 2–specific IgE were statistically significantly greater in reactive subjects compared with nonreactive subjects (Figure 3A–C).

Figure 3. Immune Parameters Among Reactors and Nonreactors to the Screening DBPCFC

• Peanut-specific IgE, Ara h 2–specific IgE, and peanut mean wheal diameters were not different in subjects with severe symptoms compared with subjects with mild or moderate symptoms (Figure 5B).

Figure 5B. Immune Parameters by Severity of Most Severe Symptom During the Screening DBPCFC

CONCLUSIONS

• The majority of patients screened for PALISADE were children. Many of them were allergic to foods other than peanut, and most had at least one other atopic condition.
• The majority of the screened patients were highly sensitive to peanut, reacting to 144 mg (cumulative) or less of peanut protein, but 38% of patients did not react at this dose.
• Ara h 2–specific IgE, peanut-specific IgE, and peanut mean wheal diameters were significantly elevated in subjects reacting to the screening DBPCFC, compared with nonreactors. However, these parameters were not linked with the severity of the reaction.
• Sensitization to Ara h 2 or Ara h 3 did not discriminate between reactors and nonreactors in our sample population.
• Most of the symptoms appearing during the DBPCFC were either mild or moderate, and adrenaline was used in nearly 15% of the patients.

IMPLICATIONS/FUTURE DIRECTIONS

• Even if allergic to multiple foods, patients and their families are reluctant to allow their children to participate in the trial.
• The possibility of allowing higher amounts of peanut in the screening DBPCFC should be considered in future clinical trials with AR101.
• This unique dataset of DBPCFCs will provide valuable data for future study.