Efficacy and Safety of AR101 in Oral Immunotherapy for Peanut Allergy: Results of ARC001, a Randomized, Double-Blind, Placebo-Controlled Phase 2 Clinical Trial


PURPOSE OF THE STUDY. To investigate the efficacy and safety of the novel oral biologic peanut oral immunotherapy (OIT) drug product, AR101, in a phase II multicenter study.

STUDY POPULATION. Subjects aged 4 to 26 years meeting the following criteria were included: a clinical history of peanut allergy, positive skin or blood peanut immunoglobulin E test result, and reaction to <143 mg of peanut protein in the screening double-blind, placebo-controlled food challenge (DBPCFC). Subjects with a history of life-threatening anaphylaxis or poorly controlled asthma were excluded.

METHODS. In this randomized controlled trial, subjects were randomly assigned 1:1 to receive either AR101 (a defatted peanut flour capsule) or a placebo, with gradual updosing from 0.5 to 300 mg daily over 20 to 34 weeks. After 2 weeks on a 300 mg maintenance dose, repeat DBPCFC was performed. The primary end point was successful consumption of ≥443 mg of cumulative peanut protein, a level exceeding the amount of peanut typically required to trigger a reaction with accidental ingestion. The number of subjects tolerating 1043 mg of cumulative peanut protein was also recorded.

RESULTS. Fifty-five subjects (29 AR101 and 26 placebo) were enrolled. Six subjects who were randomly assigned to AR101 withdrew, primarily because of adverse gastrointestinal side effects. In intention-to-treat analysis, 23 of 29 (79%) and 18 of 29 (62%) AR101 subjects tolerated 443 mg and 1043 mg at exit DBPCFC, respectively, versus 5 of 26 (19%) and 0 of 26 (0%) subjects on a placebo. AR101 increased the maximum tolerated dose of peanut by 18-fold. Most treatment-emergent adverse events were graded as mild, and no severe treatment-emergent adverse events occurred in either group.

CONCLUSIONS. Compared with a placebo, AR101 significantly increased the ability to tolerate peanut protein in subjects with a peanut allergy and was safe and well tolerated.

REVIEWER COMMENTS. In this phase 2 randomized controlled trial of peanut OIT with exit and entry DBPCFCs using a Current Good Manufacturing Practice drug product, we provide proof of concept of the effectiveness of AR101. Resoundingly, all the 26 subjects who completed treatment were able to tolerate 443 mg of peanut. Notably, all 6 who withdrew from the study had initial peanut serum immunoglobulin E >100 killiunits/L, and all gastrointestinal complaints resolved within 3 weeks of discontinuation. A case of new-onset eosinophilic esophagitis noted in a treatment group participant is consistent with previous OIT studies. Eosinophilic esophagitis should be suspected in future patients receiving peanut OIT who complain of chronic, recurrent gastrointestinal symptoms. Overall, in this phase 2 study, AR101 demonstrated the clinical and safety characteristics of a feasible immunomodulatory treatment option in individuals with a peanut allergy 4 to 26 years of age. An active phase 3 study (identifier NCT02635776) has shown similar results, and Aimmune Therapeutics is widely expected to file a biologic license application for AR101 late this year. Although not a cure for peanut allergy, AR101 could be a viable option for patients wishing to reduce the risk of anaphylaxis from accidental peanut protein consumption.

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Changes in Patient Quality of Life During Oral Immunotherapy for Food Allergy


PURPOSE OF THE STUDY. In this study, the authors examined how quality of life (QoL) changes for children with food allergy during the up-dosing build phase of oral immunotherapy (OIT).

STUDY POPULATION. There were 155 children age 4 to 12 years (median age: 5 years) with immunoglobulin E–mediated food allergy to milk, peanuts, or eggs enrolled in OIT, and 41 age-matched children (median age: 7 years) with food allergy who did not undergo OIT were included as controls.

METHODS. During the OIT induction phases, the maximal-tolerated dose (MTD) without a reaction was established for each child, and this dose was consumed twice daily during the home-treatment phase until the next induction cycle, at which time the MTD was increased as tolerated. Parents completed the Food Allergy Quality of Life Questionnaire Parent Form during the initial induction week and again at the median time point (4 months). QoL of controls were measured at 2 time points 16 months apart.

RESULTS. Food anxiety, social and dietary limitation, and total Food Allergy Quality of Life Questionnaire Parent Form scores improved in children enrolled in OIT but not in controls; emotional impact did not improve. Food
anxiety and labeling concerns improved clinically, and limitation placed by food allergy on the child’s life was the single question revealing deterioration. Children with worse QoL at baseline deteriorated. Participant QoL scores were divided into 3 groups: significant worsening (23%), nonsignificant change (37%), and significant improvement (39%). Demographics, pre-OIT reaction severity, pace of advancing through OIT, build-up versus maintenance phase of OIT, MTD, and rate of reactions or epinephrine use during OIT did not differ among the 3 groups.

CONCLUSIONS. Despite the burden of treatment, QoL of children with food allergy improved during OIT in those with impaired QoL at baseline. QoL of children who started with better QoL at baseline deteriorated during OIT, suggesting that physicians should better prepare families for OIT.

REVIEWER COMMENTS. QoL of children and families has been shown to improve after the successful completion of OIT. In this study, the authors examined QoL changes among individual children still in the build-up phase of OIT compared with their baseline QoL and showed that QoL may deteriorate during OIT, particularly in children who start with better QoL and regarding limitations placed by food allergy on the child’s life. Deteriorating QoL may significantly affect adherence, a known limitation of OIT. Providing relevant counseling on the challenges of OIT and its impact on QoL, in conjunction with professional emotional and psychological support, may have a pivotal role in improving adherence. These findings may be used to guide the selection of families who will need more support during OIT when the support is most needed. Additional data regarding the short- and long-term changes in QoL during OIT may help to improve its effectiveness.

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NON-IGE MEDIATED FOOD ALLERGY

Food Protein-Induced Enterocolitis Syndrome in Australia: A Population-Based Study, 2012–2014

PURPOSE OF THE STUDY. To prospectively evaluate the incidence of acute food protein-induced enterocolitis syndrome (FPIES) in Australian children and to identify the clinical characteristics of infants with FPIES.

STUDY POPULATION. Acute FPIES cases (based on a standardized previously published definition, details of which are found and referenced in the article) were reported by using monthly surveillance reports emailed to pediatric practitioners.

METHODS. Anonymous detailed questionnaires were completed for new suspect cases, and follow-up with reporting clinicians was undertaken to confirm the case definition and to complete missing data.

RESULTS. The final inclusion criteria were met by 235 children <24 months old during the 29-month study period, a new case incidence of 15.4 out of 100 000 per year. Boys and girls were equally represented. Other allergic disorders were reported in 113 children (49%), and 33 children (14%) had ≥2 other allergic disorders. As compared with those without eczema, infants with FPIES and eczema were more likely to also have an immunoglobulin E (IgE)–mediated food allergy (P < .0001). Only 11 infants (5%) developed FPIES while exclusively breastfeeding, of whom 8 were first triggered by cow’s milk and 7 of whom ultimately had >1 food trigger. Overall, 350 FPIES triggers were identified to 40 different foods in 230 infants. More than 1 trigger was identified in 32% of children. Timing of solid food introduction was available in 215 subjects, with most starting between 4 and 6 months old. The type of first solid food and the median time before formula introduction were not associated with an increased risk of FPIES. The median time from the first episode (5 months) to diagnosis (7 months) was 1.5 months. Only 25% were diagnosed after the first episode, whereas 44% were diagnosed after the second event and 30% after ≥3 episodes. About half reacted after their first known ingestion. Median time from ingestion to onset of symptoms was 2 hours, independent of trigger, with the classic presentation of profuse vomiting (100%), pallor (78%), lethargy (75%), floppiness (70%), diarrhea (35% and 6% with bloody diarrhea), hypotension (16%), and/or hypothermia (10%). The most common individual food triggers were rice (45%), cow’s milk (33%), and egg (12%), with numerous other foods accounting for the rest. Infants with triggers from >1 food group were younger at initial presentation compared with those with triggers from only 1 food group (5 vs 5.5 months; P = .0049). A higher proportion of infants with FPIES to fruits or vegetables had triggers from multiple food groups as compared with those without fruit or vegetable triggers (66% vs 21%; P < .0001).

CONCLUSIONS. The incidence of acute FPIES in Australia was 15.4 out of 100 000 per year. Rice was the most common trigger in this population. Earlier onset of symptoms and reactions to fruits or vegetables was associated with a greater likelihood of triggers from >1 food group.

REVIEWER COMMENTS. FPIES is a non-IgE–mediated disease and is far less common than immediate (type I, IgE-mediated)
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