435 Long-Term Follow-up of Oral Immunotherapy for Multiple Food Allergies

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RATIONALE: To report long-term follow-up data describing frequency and quantity of home dosing of food allergens following desensitization with multi-OIT protocols as part of two previously published phase 1 clinical trials.

METHODS: A total of 73 participants completed two single-center phase 1 trials evaluating the safety of OIT for multiple food allergens using a mOIT protocol (n=43) or a rapid mOIT protocol with omalizimab (n=30). In both trials, subjects were instructed to maintain daily dosing and if skin test for the allergen became negative, dosing was decreased. Participants returned yearly for follow-up food challenges.

RESULTS: Long-term follow up data was available for 70 of 73 participants. The long-term follow-up period for participants who completed the mOIT protocol ranged from 18 to 73 months; 22 (56%) chose to consume 2g protein doses of each allergen, while 13 (33%) chose to consume between 300mg and 2g per allergen. In the rapid mOIT protocol, follow-up ranged from 11 to 46 months; 9 (30%) participants chose to consume 2g doses and 18 (60%) participants chose to consume doses between 300mg and 2g. All subjects in both groups remained desensitized to at least 2g protein of each of their food allergens on repeat food challenge, even those who chose to consume home doses as low as 300mg of their allergens three times per week.

CONCLUSIONS: Subjects who completed a mOIT protocol continue to consume regular doses that maintain desensitization to 2g of each allergen.

436 NMR-Based Metabolomics Analysis Reproducibly Identifies Unique Subject-Specific Profiles That Change during Peanut Oral Immunotherapy

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RATIONALE: Identification of a reliable biomarker of desensitization, and improved understanding of its biology, are major scientific goals in allergy research. We hypothesized that unbiased metabolomics analysis would identify specific signatures associated with allergen desensitization and uncover novel pathways.

METHODS: Plasma specimens were longitudinally obtained from peanut-allergic children (N=5) participating in an ongoing trial of short-term peanut oral immunotherapy (OIT) focused on identifying early changes indicative of desensitization. Cryopreserved samples were thawed and mixed with 0.9% saline solution in D_2O. ^1H NMR data were acquired in triplicate using a 700 MHz NMR. Data were manually phased, baseline-corrected, and referenced to formate. Processed spectra were binned using intelligent bucketing integration, and normalized to the total integral of each spectrum. Principle components analysis (PCA) was performed using pareto-scaling and mean centering in SIMCA 14.0 (Umetrics, Umeå, Sweden) software.

RESULTS: PCA of all samples demonstrated high reproducibility, with analytical variability less than biological variability at each time point and substantial between-subject variation in metabolic profiles. This variation was evident prior to the initial challenge and may reflect differences in each Subject's baseline IgE levels, indicative of their peanut sensitivity. Unsupervised multivariate analysis also clearly showed that over time, the individual metabolic profiles changed during peanut OIT.

CONCLUSIONS: NMR-based metabolomics identifies unique metabolic profiles with high reproducibility among children undergoing peanut OIT. The ability to work with small volumes of cryopreserved serum or plasma highlights the potential of this technology as an approach for biomarker discovery.

437 Safety of Viaskin Milk Epicutaneous Immunotherapy (EPIT) in IgE-Mediated Cow's Milk Allergy (CMA) in Children (MILES Study)

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RATIONALE: EPIT is a promising method for treating food allergy. A dose-finding phase 1/2 study is ongoing to evaluate the safety and efficacy of EPIT using an epicutaneous delivery system Viaskin containing milk proteins, in children aged 2-17 years with IgE-mediated CMA.

METHODS: The safety of EPIT in CMA children was evaluated in 3 successive cohorts of 6 subjects receiving Viaskin Milk (150μg, 300μg or 500μg cow's milk protein) versus placebo in a 2:1 ratio following a 3-week course of treatment.

RESULTS: Eighteen subjects with cow's milk sIgE≥10kU$_A$/L and reacting objectively at ≤300mg of cow's milk protein were randomized and remained double-blinded to treatment assignment. At study entry, the median age was 8 years, median cow's milk sIgE was 88kU$_A$/L and median cumulative milk protein reactive dose was 149mg. No serious adverse events occurred and no epinephrine was required for drug-related-AEs. Most subjects reported local itching (83.3%), redness (83.3%) or swelling (72.2%) at least once. One case of erythema with many or spreading papules was reported per investigator's assessment from Week1 and treated with 1% topical hydrocortisone. Three other cases of drug-related AEs were reported, all being exclusively skin reactions of mild or moderate intensity (application site urticaria, application site bruise and urticaria). There were no early withdrawals and all subjects are continuing treatment for efficacy assessment.

CONCLUSIONS: No safety concerns were noted at any of the 3 doses tested from the DSMB reviews. These safety results warrant continuation of all 3 doses for efficacy assessment of Viaskin Milk in children with CMA.

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