L16 Validation of Peptide Immunotherapy as a New Approach in the Treatment of Allergic Rhinoconjunctivitis: The Clinical Benefits of Treatment with Amb a 1 Derived T cell Epitopes

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RATIONALE: A series of T-cell epitopes from cat allergen, Fel d1, formulated into a short-course peptide vaccine (ToleroMune Cat) was previously shown to significantly reduce allergic rhinoconjunctivitis symptoms shortly after vaccine therapy ended and persistently, one year after dosing start (tolerance). In this study, we evaluated the efficacy of a vaccine from a newly identified series of T-cell epitopes from ragweed allergen Amb a1 (ToleroMune Ragweed) on allergic rhinoconjunctivitis symptoms.

METHODS: Screened ragweed allergic subjects attended four consecutive 3-hour Baseline Challenges in an Environmental Exposure Chamber (EEC) where airborne ragweed pollen levels were controlled at 3500±500 grains/m^3 . Total Rhinoconjunctivitis Symptom Score (TRSS) was scored every 30 minutes on a scale of 0-24. 275 subjects were randomised to placebo, or one of four ToleroMune Ragweed treatment arms. Subjects returned to a series of 4 consecutive, 3-hour Post-Treatment EEC Challenges 18-22weeks after the start of treatment.

RESULTS: Treatment with ToleroMune Ragweed resulted in the largest changes in TRSS in the most symptomatic subjects who had the highest scores at Baseline. In this group, treatment with the highest dose of ToleroMune Ragweed showed a mean change in the TRSS score at the post treatment EEC visit of -5.77±5.31 versus a change of -2.93±5.31 on placebo ($p < 0.05$). The product was safe and well tolerated.

CONCLUSIONS: The efficacy of T cell epitope-based peptide immunotherapy has been demonstrated for cat and ragweed allergies. This new treatment modality offers an exciting alternative short-course immunotherapy with an enhanced safety profile that is potentially applicable across multiple allergens.

L17 Sequential IgE-Targeted Therapy Combining Immunapheresis And Omalizumab In Patients With Severe Atopic Dermatitis And Grossly Elevated Total Serum IgE Levels - A Pilot Trial

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RATIONALE: To evaluate the role of IgE in atopic dermatitis (AD) by combining immunoglobulin (Ig)-apheresis and anti-IgE-antibody omalizumab to reduce IgE in patients with severe, therapy-refractory AD and grossly elevated IgE levels.

METHODS: Investigator-initiated open-label pilot trial, treating 10 patients with Ig-apheresis prior to regular subcutaneous administration of 450 mg omalizumab every 2 weeks for 6 months followed by a 6 months follow-up. On every visit, total and free IgE and TARC (CCL17) were quantified and the severity of AD documented by standardized photos as well as rated by SCORAD and by the patients' personal evaluation on a severity and pruritus-scale.

RESULTS: Before starting treatment, IgE-levels ranged from 3,728 kU/L to 69,872 kU/L. IgE-levels were seen to be reduced significantly after the Ig-apheresis and to continuously drop in all patients during the anti-IgE-therapy (reaching free IgE levels <150 kU/L in 5/10 and <1,000 kU/L in 9/10 patients). A reverse trend was observed during the follow-up period. Parallel, a clear improvement of AD was seen during the treatment period in all patients followed by an aggravation during follow-up (SCORAD, pruritus, severityscale, TARC). Two patients dropped out after initial improvement due to acute exacerbation despite anti-IgE therapy and one patient was lost due to lack of compliance.

CONCLUSIONS: The sequential combination of Ig-apheresis and omalizumab is suitable to reduce grossly elevated serum IgE levels and improves clinical symptoms of severe refractory AD. Due to the limited number of patients included and the open-label design in our pilot trial, further studies are needed to strengthen this conclusion.

L18 Real-world Comparative Effectiveness Of Extrafine Hydrofluoroalkane-beclomethasone (EF HFA-BDP) Versus Inhaled Corticosteroid (ICS) / Long-acting Beta-agonist (LABA) Therapy In Pediatric Asthma

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RATIONALE: Uncertainty exists around LABA effectiveness in pediatric asthma. We compared the real-world effectiveness of EF HFA-BDP and ICS/LABA in children stepping-up ICS.

METHODS: Retrospective study using the UK General Practice and Optimum Patient Care Research Databases. Children (4-11 years) stepped-up existing ICS to (i) higher dose ICS (≥50% increase) as EF HFA-BDP or (ii) ICS/LABA (no ICS dose/drug change) as fixed-dose combination (FDC) or free-combination (FC) ICS/LABA. EF HFA-BDP patients were matched 1:2 (n=325:650) to FC and 1:1 (n=209:209) to FDC patients based on demographic and disease characteristics over the pre-step-up year. Outcomes evaluated over the post-step-up year included: severe exacerbations (ATS/ERS definition); asthma control (no: severe exacerbations; out-of-hours care; outpatient department attendance; antibiotics for lower respiratory infections); ICS adherence, SABA usage.

RESULTS: There were no significant differences between EF HFA-BDP and FDC in achieving asthma control (adjusted odds ratio[AOR] 95%CI: 0.96[0.51-1.80]); exacerbation rates (adjusted rate ratio[ARR] 95%CI: 1.00 [0.62-1.62]), or odds of higher adherence (0.77 [0.54-1.10]), but odds of higher SABA usage were significantly greater for EF HFA-BDP patients (1.49 [1.07-2.07]). Compared with FC, EF HFA-BDP patients had significantly higher odds of achieving asthma control (1.50 [1.04-2.16]); with no significant differences in exacerbation rates (0.91 [0.68-1.22]), adherence (EF HFA-BDP: 1.22 [0.95-1.56]) or SABA usage (EF HFA-BDP: 1.11 [0.86-1.43]). Median(IQR) doses were 137.0(82.2-219.2)mcg for EF HFA-BDP vs 82.2(41.1-137.0)mcg fluticasone-equivalent for FDC, and 137.0(82.2-219.2)mcg for EF HFA-BDP vs 98.7(65.6-148.0)mcg fluticasone-equivalent for FC.

CONCLUSION: Stepping-up ICS as EF HFA-BDP dose increase provides similar asthma control as FDC ICS/LABA therapy and substantial benefits over FC ICS/LABA.