267 Consistent Treatment Effect with Birch Pollen SLIT-Tablets Also Across Hazel/Alder and Oak Pollen Seasons

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RATIONALE: Birch, alder, hazel, and oak are members of the birch homologous group based on IgE cross-reactivity to the major allergen Bet v 1. Treatment effects of tree sublingual immunotherapy (SLIT)-tablets containing standardized birch pollen extract in participants with birch pollen-induced allergic rhinitis with or without conjunctivitis (AR/C) were evaluated during alder/hazel and oak pollen seasons.

METHODS: In a randomized, multinational, double-blind trial (EudraCT-2015-004821-15), 634 participants (12-65 years) with birch pollen-induced AR/C with or without asthma received daily tree SLIT-tablets (12 SQ-Bet) or placebo before and during tree pollen season (TPS; start of alder/hazel pollen season through birch pollen season). Rescue medication was allowed. The primary endpoint was the total combined score (TCS; sum of rhinoconjunctivitis daily symptom score [DSS] and daily medication score [DMS]) during birch pollen season. TCS, DSS, and DMS during alder/hazel and oak pollen seasons and the continuous TPS (all days during TPS regardless of pollen counts) were analyzed post-hoc.

RESULTS: Relative improvements in TCS with tree SLIT-tablets versus placebo were 39.6%, 29.7%, and 36.0% during birch, alder/hazel, and oak pollen seasons, respectively, and 35.0% for continuous TPS (all $p \leq 0.002$). Relative improvements in DSS versus placebo were 36.8%, 26.0%, and 31.6% during birch, alder/hazel, and oak pollen seasons, and 31.6% for continuous TPS (all $p \leq 0.003$) and in DMS were 49.2%, 43.8%, 45.9%, and 45.3%, respectively (all $p \leq 0.002$).

CONCLUSIONS: Improvements with tree SLIT-tablets versus placebo during alder/hazel and oak pollen seasons showed internal consistency across seasons and support the clinical relevance of the immunologic cross-reactivity between birch pollen homologous allergens.

268 Formononetin Isolated from Ku Shen (Radix Sophorae Flavescentis) Inhibits B cell IgE Production by Inhibiting STAT 6 and NF-κB phosphorylation and XBP1 and IgE heavy chain expression

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RATIONALE: Formononetin isolated from Ku Shen one of the three herbs in ASHMI (Antiasthma Simplified Herbal Medicine Intervention) has been shown to decrease IgE in human B cells (U266 cells). In this study we investigated, the mechanism(s) involved in formononetin mediated inhibition of IgE in human B cells using U266 cells.

METHODS: U266 cells were cultured at 2.5×10^6 cells/mL and then incubated with formononetin at different concentrations of 20, 10, 5, 2.5, and 0 μg/mL for 12 hours, 72 hours. Supernatants were collected for measuring IgE levels by ELISA. Cell viability was determined using Trypan blue dye . The protein expression was determined for pSTAT6 and p-IκBα with GAPDH as control using western blotting after culture for 12 and 72 hours. mRNA expression was determined for Xbp1 and IgEH genes compared with GAPDH using RT-PCR after 6 days culture with or without formononetin.

RESULTS: Formononetin significantly decreased IgE production in U266 cells with maximal inhibition observed at 20 μg/mL without cytotoxicity. The protein expression of p-IκBα was inhibited at 12-72 hours and pSTAT6 at 72 hours in the culture treated with formononetin when compared with untreated culture. Formononetin decreased mRNA expression of IgEH and Xbp1 at 6 days when compared with untreated controls.

CONCLUSIONS: Formononetin decreased IgE production by human B cell by inhibiting STAT6, NF-κB phosphorylation, as well as Xbp1 and IgE heavy chain expression. It may be a potential for IgE mediated asthma and other allergic conditions.

269 Mannan-Allergoid Conjugate of House-Dust Mites: First Subcutaneous and Sublingual Dose-Finding Study in Humans

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RATIONALE: Polymerized-allergoids conjugated to nonoxidized-mannan (PM) have a better dendritic cell-uptake while promoting T-reg cell-induction, which may improve specific allergen immunotherapy (AIT).

A dose-finding study was conducted with PM (mites) to search the optimal dose for both subcutaneous (SC) and sublingual (SL) routes. The main outcome was the allergen-specific nasal provocation-test (NPT).

METHODS: A randomized multicentre, double-blind, double-dummy and placebo-controlled study of 4 months/patient (EudraCT:2015-000820-27) was conducted. Four concentrations (500, 1000, 3000 and 5000 mTU/mL) of PM (*D. pteronyssinus* and *D. farinae*) were evaluated. 186 patients (mean age:26 years, range:12-62), sensitized to house-dust mites were randomly allocated in 9 groups. One group received SC and SL placebo, 4 groups received SC-active and SL-placebo. The remaining groups received SL-active and SC-placebo. SL administration was 2 spray-puffs daily; SC was 0.2mL+0.3mL first day, followed by 0.5 mL/monthly.

NPT was assessed at baseline and at the end. A positive outcome was considered when a positive NPT was achieved with at least three times the allergen concentration needed at baseline.

Fisher's exact test was used for to compare to placebo the number of patients that experienced a positive outcome for each group.

RESULTS: Patients experiencing improvement were: placebo 16%; 500 mTU/mL, 45% SC ($p=0.082$), 44% SL ($p=0.079$); 1000 mTU/mL, 53% SC ($p=0.033$), 58% SL ($p=0.017$); 3000 mTU/mL, 62% SC ($p=0.021$), 61% SL ($p=0.007$); 5000 mTU/mL, 56% SC ($p=0.017$), 56% SL ($p=0.017$).

CONCLUSIONS: PM produced a significant clinical improvement, measured by NPT after 4 months of treatment, using concentrations above 500 mTU/mL, by both SL and SC routes.