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Ultra-short-course booster allergen immunotherapy

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“these results demonstrated the efficacy of the ultra-short-course subcutaneous AIT with MPL[®] as a booster therapy for patients with recurrent grass pollen-induced allergic rhinoconjunctivitis after a previous SCIT or SLIT”

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Allergen immunotherapy (AIT) represents the only treatment option with a disease-modifying effect on the IgE-mediated inflammatory immune response in allergic patients [1–5]. Both routes of administration, sublingual (SLIT) and subcutaneous immunotherapy (SCIT), had demonstrated clinical efficacy and safety [6–8]. However, despite initially reported alleviation of allergic complaints, a relevant proportion of patients suffered from recurrent symptoms some years after the cessation of the AIT [9–11].

Several innovative approaches in AIT, including adjuvant vaccines, have been developed and already moved into the clinical phase [12]. The ultra-short course subcutaneous AIT (POLLINEX[®] Quattro Plus 1.0 ml; Bencard[®] Allergy GmbH, Munich, Germany) using tyrosine-adsorbed grass pollen allergoids and monophosphoryl lipid A (MPL[®]) as an adjuvant has proven its clinical efficacy and safety in pollen-allergic patients [13–16]. The treatment consists of four pre-seasonal injections of 300 SU, 800 SU and 2000 SU (twice), according to the summary of product characteristics [17].

Recently, we investigated this ultra-short-course subcutaneous AIT as a booster therapy in patients with grass pollen-induced allergic rhinoconjunctivitis who had completed any kind of grass pollen AIT (SLIT or SCIT) at least 5 years prior to study start with initial reduction of symptoms in the first years after the treatment, but then suffered from recurrent symptoms of grass pollen allergy [18]. The study was designed as a prospective, controlled, non-randomized, patient-preference, non-interventional study (NIS) carried out in 14 study centers in Germany from March to September 2015. After consulting with their allergists, patients (12 years of age or older) chose whether they received one course of ultra-short AIT before the grass pollen season or not. During the season, all patients received (standardized) symptomatic medication according to the EAACI Position Paper [19] free of charge via an Internet pharmacy. 56 (52.3%) patients chose the booster AIT in combination with symptomatic medication if needed during the grass pollen season (booster AIT group) and 51 (47.7%) preferred to take symptomatic medication exclusively (control group). The study consisted of seven visits for booster AIT patients: four treatment visits (V1 to V4) before and three visits during the grass pollen season (V5 at the beginning of the season, V6 during the peak season, and V7 at the end of the season). Patients of the control group had four visits: one (V1) at the study start and three (V5 to V7) during the grass pollen period.

The definition of the peak pollen period was based on data from the German Weather Service, Medicine Meteorology (Deutscher Wetterdienst Meteorologie; www.dwd.de). The regional peak pollen period was defined as those consecutive 30 days with the highest pollen concentration, starting from the first detection of moderate-to-high pollen counts (stage 2–3) in the nearest pollen count station.

Patients were asked to keep a diary that provided data for the daily symptom score (dSS), the daily medication score (dMS) and the combined symptom and medication score (CSMS) [19]. During the 30-day peak pollen period, the daily mean CSMS was consistently lower in the booster AIT group than in the control group. The average daily mean CSMS in the booster AIT group and in the control group was 1.17 ± 0.93 and 1.9 ± 1.14 , respectively. The difference of 38.4% was statistically significant in favor of the booster AIT group ($p < 0.01$). Likewise, the dSS and the dMS were 29.3% and 46.9% lower in the booster AIT group, respectively. Comparing the booster AIT and the control group, the differences were statistically significant ($p < 0.05$ and $p < 0.01$).

Retrospective assessments of the intensity of allergic complaints during the grass pollen season 2014 and 2015 were enquired from the patients at the first and last visit, respectively [20]. From 2014 to 2015, the intensity decreased by 57% in the booster AIT group and by 30% in the control group. These reductions were statistically significant (each $p < 0.001$). Remarkably, the reduction of the intensity of allergic symptoms in the booster AIT group was almost twice as much as that in the control group and was statistically significant ($p < 0.05$) when compared with control.

Analysis of medication intake revealed that the proportion of patients in the booster AIT group who did not use any symptomatic medication during the grass pollen period increased by 30% from 2014 to 2015. In the control group, these proportions were almost identical in both years. The difference between the booster AIT group (34.0%) and the control group (2.0%) in 2015 was statistically significant ($p < 0.001$).

The above mentioned results were supported by the patients' assessment of their state of health in 2015 in comparison with that in the previous year using the following scale: 'significantly better', 'slightly better', 'unchanged', and 'worse' [21]. The great majority (92%) of booster AIT patients evaluated their state of health in 2015 as significantly or slightly better. In contrast, in the control group, only 46% of patients made a similar assessment.

In order to gain information about the impact of the grass pollen allergy on patients' daily life, we asked study participants to complete the Mini Rhinoconjunctivitis Quality of Life Questionnaire (MiniRQLQ) [22] at V1 at the study start (before the grass pollen season) as well as at V5, V6 and V7 during the grass pollen season. The analysis of the MiniRQLQ demonstrated consistently and significantly better quality of life in the booster AIT group than that in the control group at V5, V6, and V7 (Mean outcome: 0.99, 0.87 and 0.48 versus 1.88, 1.43 and 0.94, respectively), whereas the outcome of this questionnaire was similar between the two groups at V1.

In conclusion, these results demonstrated the efficacy of the ultra-short-course subcutaneous AIT with MPL® as a booster therapy for patients with recurrent grass pollen-induced allergic rhinoconjunctivitis after a previous SCIT or SLIT that was completed at least 5 years prior to this investigation. Although patients of both treatment groups had access to highly effective symptomatic medication during the pollen season, the booster AIT group showed a greater benefit than the control group, clearly demonstrating the superiority of the booster therapy over the pharmacological treatment alone. The significance of the trial was supported by the analysis of end point variables like CSMS and the MiniRQLQ, as recommended by the EAACI for field trials in AIT [19].

Furthermore, a large proportion of AIT patients evaluated the tolerability of the four injections as 'very good' or 'good' (77 to 84% for each injection). Local reactions at the injection site such as itching and swelling were reported by only 28.6% of patients. In all, two patients suffered from a mild, grade 1 systemic adverse reaction each. A great majority (96.4%) of AIT patients did not report any adverse event besides minor discomforts at the injection site. These results, together with the absence of serious adverse events, cases of fatality, anaphylaxis, and the use of epinephrine demonstrated the good safety profile of MPL® enhanced booster therapy.

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