

ORIGINAL ARTICLE

Treatment of respiratory allergy with allergy immunotherapy tablets

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Abstract

Allergy immunotherapy tablets (AIT) have expanded the treatment options for patients suffering from respiratory allergies. Efficacy is established in adults and children for two different commercially available grass AITs. The ALK grass AIT has an efficacy comparable to subcutaneous immunotherapy (SCIT), with a proven disease-modifying effect after treatment completion. Safety profiles favour AIT over SCIT. Studies suggest that tablets in all aspects are superior to sublingual drops. AITs for other allergies including house dust mite and birch and ragweed pollen are in development.

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An enormous amount of research is currently underway on allergy immunotherapy in well-designed studies with hundreds of patients. The research programmes fit together through preclinical, phase I, II, and III trials. The benefits will not only affect patients with grass pollen-induced allergies but also those who suffer from allergies to house dust mite, ragweed, tree pollen, or cats. The most common indoor and outdoor allergens in Europe and the USA will be covered by allergy immunotherapy tablets (AIT) in the near future.

From ALK, grass pollen tablets are now marketed in the European Union and phase III trials in the US have been concluded for both adults and children. House dust mite and ragweed tablets are in phase III trials and birch pollen phase II trials are being prepared. Recombinant therapy for cat allergy is in early development. Stallergènes has a similar AIT programme covering the same allergens, plus Japanese cedar.

Trial results for grass allergy immunotherapy tablets

Trial results show substantial reductions in symptoms for ALK's Grazax[®] and Stallergènes' Oralair (1, 2). Although comparing results from different trials is difficult, the quality of the trials is high. Median reductions in symptom scores for both products are 34–37%, and reduction in medication

scores is 46–53%. The true message of the studies is that the principle of AIT works. In terms of efficacy, in adults as well as in children (3–5), both products demonstrate significant benefit in reduction of both symptom and medication scores during the pollen season.

Many patients experience side effects, with the most common being local oral and ear pruritus, mouth oedema, and throat irritation. These are not long lasting, usually occurring on a time scale of minutes (6). Resolution, defined as days from first intake until the event no longer occurs, is also fast, for example with 5 days for oral pruritus. The events occur in the beginning of treatment for which the patients can be prepared. Data show that in the second and third years of treatment, side effects are not significantly different from placebo.

Postmarketing surveillance of Grazax[®] by ALK has data on more than 50 000 treatment years. Preliminary analysis of data based on more than 17 000 treatment years of exposure to Grazax[®] (7) shows 12 serious systemic allergic reactions reported, corresponding to a frequency of 0.7 per 1000 treatment years. No reactions were life-threatening. Nine of the serious systemic allergic reactions occurred at first intake and concomitant contributing factors were present for the remainder. This means that the first tablet should be taken in the doctor's office. In patients who have previously had a systemic reaction to grass subcutaneous immunotherapy (SCIT),

the risk of experiencing a severe reaction with Grazax[®] may be increased. Initiation of Grazax[®] should be carefully considered and measures to treat reactions should be available at first tablet intake.

A current discussion concerning the ALK and Stallergènes products is seasonal vs continuous therapy. For Grazax[®], six phase II and III trials are published (8–11) using seasonal and pre-seasonal regimens. Just looking at symptoms, a seasonal/preseasonal dose regimen has beneficial effect on symptoms for both Grazax[®] and Oralair (2, 4). Long-term effects were shown in a trial using a continuous treatment regimen for Grazax[®] (12). A long-term trial with a seasonal/pre-seasonal approach is underway for Oralair. Choice of treatment regimens in the future is likely to be determined by local preferences.

Grass AITs are without a doubt effective in adults and children. Long-term efficacy during treatment has been shown for 3 years of treatment with both Grazax[®] and Oralair, and disease-modifying effects are reported for Grazax[®], although not yet for Oralair. It is likely that an effect for 2 years after the completion of treatment will be reported in the near future. In any case, results so far support the principle of the concept. The preventive effects will be studied by the ongoing Grazax[®] Asthma Prevention trial. This opens the possibility of modifying indications for AIT in the near future.

Allergy immunotherapy tablets with other allergens

Clinical proof-of-concept has been reported for the effectiveness of house dust mite AIT from ALK against asthma (13). Stallergènes' house dust mite tablet has reported phase IIb/III data for allergic rhinoconjunctivitis. Reduction in an average adjusted symptom score is reported compared to placebo. A moderate effect is seen in reduction of symptoms for two concentrations of treatment. Therefore, we expect to have more possibilities for treating patients with house dust mite allergy. Birch AIT phase II clinical trials are being planned

by ALK, and are in phase IIb/III trials for the Stallergènes product. A 25% reduction in average adjusted symptoms score has been reported.

Debates about SCIT vs sublingual immunotherapy (SLIT) should be disregarded in favour of looking at individual products. A Cochrane meta-analysis (14) comparing standardised mean differences in median symptom scores showed that both SCIT and SLIT are better than placebo, but SCIT seemed to be more efficacious. This led to SCIT as the first choice and gold standard in most guidelines. However, evaluation of the meta-analysis shows heterogeneity with a wide range of different allergens and treatment regimens and classes. Reporting the efficacy of individual products would produce more useful results in terms of serving as the basis for decision making.

If we compare SCIT and SLIT treatment for grass pollen allergic rhinoconjunctivitis only (15), a meta-analysis of randomised double-blind placebo-controlled peer-reviewed studies showed that both SCIT and SLIT are beneficial, and that AIT is better than SLIT drops. However, again we see heterogeneity in the studies, so these results are not necessarily applicable for all products. The basic message is that AIT has benefits that are near, if not overlapping or identical, to SCIT. Studies on Alutard[®] (16) and Grazax[®] showed similar reductions in symptom and medication scores. In conclusion, available efficacy data indicates that AITs are comparable to SCIT. In general, the current time is very exciting with several new products being developed, and new products appear with a hitherto unseen documentation. This development is more than likely to change current practice to the benefit of our patients.

Conflict of interest

Claus Bachert has received research grants from ALK-Abelló as well as consultancy fees and lecture fees from ALK-Abelló, Stallergènes, Allergopharma and Novartis.

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