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Comments on: “Allergen immunotherapy as a drug: the new deal of grass allergen tablets from clinical trials to current practice”

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In their recent article (1) published in *European Annals of Allergy and Clinical Immunology*, Manzotti and Lombardi evaluated the available trials with Grazax[®] and Oralair[®] to support their use in clinical practice.

First, we have noted with particular interest the position of the authors regarding the pre-seasonal and co-seasonal schedule. They consider it to be: “*the most suitable schedule for pollens in clinical practice instead of continuous immunotherapy*”. Though, the efficacy of Grazax[®] has been assessed with a continuous protocol over the 3 years of treatment, its long-term efficacy and safety when administered discontinuously has yet to be assessed. To date, Oralair[®] is the only allergen immunotherapy sublingual tablet with demonstrated efficacy and safety using a pre-seasonal and co-seasonal treatment regimen.

Moreover, the authors stated that “*Oralair[®] has been shown to be effective and safe in two Phases III double-blind placebo controlled trials*” ... “*and in a trial based in an allergen challenge chamber.*” In fact, since Oralair[®] has been marketed in 2008, two additional clinical trials (VO53.06 and VO61.08USA) have been completed, bringing the total to four natural field studies including 2012 patients, in addition to the 89 patients in the allergen challenge chamber study (VO56.07A).

Study VO53.06, a multicenter, randomized, controlled trial, evaluated the long-term effect of pre-seasonal and co-seasonal administration of Oralair[®] over a period of three consecutive pollen seasons followed by an observation time. The clinically relevant efficacy shown during the first three years (2) was maintained during the first treatment-free follow-up year, indicating post-treatment long-term efficacy (3).

Table 2 - Oralair[®] study in pollen chamber

| Trial | No. of pts | Type of pts / +Type of the disease of pts included in the study | Onset of action | | | Oralair [®] Improvement vs. Placebo at 4 months |
|-------------------|------------|---|----------------------------------|---------------------------------|----------------------------------|--|
| | | | ARTSS after 1 month | ARTSS after 2 months | ARTSS after 4 months | |
| Horak et al, 2009 | 89 | Adults / Grass pollen-induced rhinoconjunctivitis | -5.89±2.431 <i>p</i> = 0.0042 | -5.09±2.088 <i>p</i> = 0.200 | -4.85±1.995 <i>p</i> = 0.0007 | 29.3% |

The VO61.08USA trial (4) conducted in US adult patients with grass pollen-induced allergic rhinoconjunctivitis showed that pre-seasonal and co-seasonal treatment with Oralair® demonstrated clinically meaningful efficacy.

With respect to **table 2** - Synopsis of Phase III Oralair® studies, we note a number of errors with respect to the results of study VO56.07. We have provided the corrected data. In addition, the correct reference is “*Horak F, Zieglmayer P, Zieglmayer R, Lemell P, Devillier P, et al. Early onset of action of a 5-grass-pollen 300-IR sublingual immunotherapy tablet evaluated in an allergen challenge chamber. J Allergy Clin Immunol. 2009 Sep;124(3):471-7, 477.e1*”.

Lastly, the authors have noted that “*in fact, an extract with only Phleum pratense seems adequate for patients living in Northern Europe but not for patients living in Mediterranean areas.*” Actually, the 5-grass pollen extract better represents natural exposure conditions encountered by grass pollen-allergic patients, because the 5 species are broadly distributed throughout Europe and North America and their allergen content has been well characterized (5).

References

1. Manzotti G, Lombardi C. Allergen immunotherapy as a drug: the new deal of grass allergen tablets from clinical trials to current practice. *Eur Ann Allergy Clin Immunol.* 2013;45(2):34-42.
2. Didier A, Worm M, Horak F, Sussman G, de Beaumont O et al. Sustained 3-year efficacy of pre- and co-seasonal 5-grass-pollen sublingual immunotherapy tablets in patients with grass pollen-induced rhinoconjunctivitis. *J Allergy Clin Immunol.* 2011;128(3):559-66.
3. Didier A, Malling HJ, Worm M, Horak F, Sussman G et al. Post-treatment efficacy of discontinuous treatment with 300IR 5-grass pollen sublingual tablet in adults with grass pollen-induced allergic rhinoconjunctivitis. *Clin Exp Allergy.* 2013;43(5):568-77.
4. Cox LS, Casale TB, Nayak AS, Bernstein DI, Creticos PS, et al. Clinical efficacy of 300IR 5-grass pollen sublingual tablet in a US study: the importance of allergen-specific serum IgE. *J Allergy Clin Immunol.* 2012;130(6):1327-34e1.
5. Moingeon P, Hrabina M, Bergmann KC, Jaeger S, Frati F et al. Specific immunotherapy for common grass pollen allergies: pertinence of a five grass pollen vaccine. *Int Arch Allergy Immunol.* 2008;146(4):338-42.