Respiratory Allergy, the best therapeutical choice: Lais® the carbamylated monomeric allergoid

Enrico Compalati[1], Marco Emanuele Bruno[2], Gianni Mistrello[2]

1. University of Genoa. Allergy & Respiratory Diseases department. Genoa. Italy
2. Lofarma SpA. Medical and Research departments. Milan. Italy

Allergen immunotherapy with standardized extracts is effective in treating respiratory allergy but the risk of side effects exist, mainly for subcutaneous immunotherapy (SCIT) (1). Sublingual immunotherapy (SLIT) in drop or tablets featured by a better safety profile, gained large diffusion in recent years in order to face this drawback, however a certain risk is associated also to this route of administration when the preparation contains native allergens. Eleven cases of anaphylaxis have been reported with these traditional vaccines (2).

Lais®, a carbamylated monomeric allergoid in tablets for SLIT, is a chemically modified allergen resulting in a substitution of ε-aminogroups of allergen lysine residues conferring reduced IgE-binding activity (3). The extremely selective carbamylation does not affect the structural conformation and size of the allergen molecule, making Lais® the only one allergoid suitable also for sublingual administration ('monomeric'). In fact other common allergoids ('polymerized') existing on the market, are characterized by a polymeric nature due to their modification with glutaraldehyde that determines a strong increase of the molecular dimension of the derived extracts preventing a sublingual absorption.
The reduced allergenic activity of Lais® improves the safety of the preparation as documented by numerous studies in adults and children with different administration regimens and with a large range of dosages (4-6). The tolerability of Lais® has been confirmed by post-marketing surveys showing an incidence of adverse reactions largely inferior to traditional extracts (6). No serious events have ever been reported with Lais®, even with short up-dosing regimens or without any up-dosing (7, 8). Of note, one study observed that Lais® is well tolerated also in children under the age of five (9).
The chemical modification however does not affect the immunological properties of this kind of vaccine, that has been demonstrated to immune-modulate the human's response to the allergen with production of IL-10 and reduction of Th-2 mediators (10). Lais® was associated with a down-regulation of specific IgE (without the early increase typical of SLIT with native allergens) and effectors cells (10). Moreover an early immune suppression has been shown correlated to rapid induction schemes (11).
These findings are accompanied by robust evidence of improvements in relevant clinical parameters. The SLIT position-paper of the World Allergy Organization (12) remarks the very first studies conducted with tablets in adults (Passalacqua. Lancet 1998) and children (Caffarelli. Allergy 2000) (13, 14); these two studies administered Lais®. Double-blind randomized placebo-controlled clinical trials administering house dust mites and grass pollen tablets or drops demonstrated the efficacy of Lais® in reducing the total and individual symptoms and the drug consumption in patients with allergic rhinitis and asthma (15-18). In some randomized controlled trials also a reduction in bronchial hypereactivity

was shown, together with the confirmed benefits for other extracts (birch, parietaria, cypress and olea allergoids) (16-23). Long-lasting and preventive (on asthma onset and new sensitizations) effects of Lais® in allergic rhinitis are documented in different observational studies (24-26). All the clinical results appeared correlated to relevant anti-inflammatory effects.

The peculiar chemical modification of the extract has another very important feature. It confers resistance to the proteolytic activity of gastroenteric enzymes, thus improves the bioavailability of the vaccine. Pharmacokinetics studies, on human volunteers using the sublingual administration of radiolabelled purified carbamylated allergoid, evidenced that a part of the molecule, after swallowing, is able to reach the systemic circulation, differently from the native unmodified allergen which is more likely digested by enzymes at gastro-intestinal level (27-30). In a mouse-model the intragastric-restricted administration of carbamyled allergoid stimulated gut-associated-lymphoid-tissue immune-changes, inducing a systemic tolerogenic response (31). Recently a clinical comparison between the three modalities of administration (sublingual-spit/oral/sublingual-swallow) confirmed that the benefits of Lais® are the results of the contribution of both the oro-mucosal and gastro-enteric adsorption. These observations suggest that Lais® can express its therapeutic effects through two concomitant actions, one involving local mechanism (due to its long persistence in the mouth) and the other through systemic mechanisms (due to the enteric contact and absorption). The resistance to the proteolytic activity of Lais® allows the administration of an optimized amount of effective dose unable to provoke side effects improving the global efficiency of the treatment and favoring patients' high adherence.

In summary the characteristics of the monomeric allergoid, its preserved molecular dimension suitable for sublingual administration, its reduced allergenic activity responsible for the optimal safety profile, its retained immunological activity responsible for the clinical efficacy, the improved bioavailability permitting the optimization of a safe and effective dosage, make Lais® a unique vaccine, suitable also for a very early treatment of allergic children, against the progression of the allergic march.

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