

# **SUBLINGUAL IMMUNOTHERAPY PRESENT AND FUTURE**

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The subcutaneous administration of specific immunotherapy (SCIT) remained for many decades the only available administration route. SCIT is effective and safe, when properly prescribed and administered, but some risk of severe side effects remain. This aspect lead to the search for safe routes, among which, the sublingual (SLIT), rapidly achieved credibility, and was introduced in the official documents as a viable alternative to the classic injection route (1, 2). Presently, SLIT is commercialized and routinely used in Europe and many other countries, and some products have been recently approved also in the USA. According to the more recent World Allergy (WAO) Position Paper (3), there are 77 randomized placebo controlled trials published, of which only 8 displayed negative results, 5 further trials were published after 2013. Some studies clearly showed a dose-dependent effect of SLIT (4, 5), and several meta-analyses are also available (6).

Provided that SLIT, in general, is effective, attempts to ameliorate it have been constantly made.

One of the most relevant novelties was the introduction of the chemically modified allergens

(allergoids). The chemical modification usually produce polymerized allergoids, which therefore profoundly differ from the native proteins. A new technique allowed to obtain a monomeric allergoid, which retains the capacity of interacting with antigen presenting cells, with a decreased capacity to bind specific IgE. The monomeric allergoid (LAIS, Lofarma spa, Milan, Italy) confirmed a satisfactory clinical effectiveness in clinical trials (7, 8). According to the immunological knowledge, it also retained a relevant safety profile, so that it was used firstly in children below the age of 5 years (9).

The mechanisms of action of SLIT and SCIT are similar, and converge in the stimulation of T regulatory cells which, in turn, downregulate the Th2 actions (10). It is also true that the mucosal administration involve the role of local antigen-presenting cells (dendritic cells). Nowadays, SLIT is recognized superior in safety as compared to SCIT. After more than 25 years no fatality was reported. Adverse events are usually local (mouth/tongue itching/swelling, nausea, stomach ache) and spontaneously disappear within few days. The rate of occurrence of side effects does not differ between adults and children (11)..

SLIT remains an important clinical option, and a fruitful model to investigate the interactions between mucosal surfaces and allergen. Owing to the fact that a direct mucosal presentation of the allergen keeps relevant, SLIT has been investigated also for non respiratory allergens and for food desensitization. As well, adjuvants have been associated to the sublingual administration- Finally, there is a relevant place in therapy of SLIT in food allergy, as optimistically shown (3).

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