At present, there are numerous inaccurate and stereotyped ideas about allergen immunotherapy (AIT). These false beliefs have often become ingrained in doctors’ mind because of the early empiric nature of clinical investigation and practice that have dominated AIT for a century. Since the original clinical studies by Noon and Freeman,¹,² careful methods and detailed case reports, standardization and outcome measures have been proposed.³ However, individual rigour is no substitute for large-scale, robust, well-designed clinical trials, which have been mainly conducted in the last decade.³ The expected heterogeneity observed in meta-analyses of both subcutaneous (SCIT) and sublingual (SLIT) AIT trials has sometimes been exaggerated to muddle the issue and reinforce if not create some of the dogmas, fallacies and misconceptions.

One fallacy among physicians and patients sometimes is that “allergic rhinoconjunctivitis is a trivial and homogenous disease”. Firstly, over half of all allergic rhinitis sufferers do not seek medical help for their allergic condition.⁴ The majority of these people have mild symptoms that are easily treated with occasional symptomatic medications but about one third of allergic rhinitis patients in Europe have moderate to severe symptoms with an impact on their daily activities, sleep and quality of life.⁵,⁶ Furthermore, physicians tend to downplay the severity of symptoms as well, with a risk of under-diagnosis and under-treatment as reported in a Danish survey, where 83% of patients with moderate-to-severe rhinitis were undertreated.⁷ It is clear that many physicians consider that “AIT in general (either SCIT or SLIT) is less effective than pharmacotherapy” in terms of relieving the symptoms of allergic rhinitis. That argument just does not hold up when we look at the evidence. In a meta-analyses conducted by Benninger et al.⁸ it was found that the median percentage changes from baseline for the total nasal symptom score (TNSS) in seasonal allergic rhinitis were 22.2% for nasal antihistamines, 23.5% for oral antihistamines and 40.7% for intranasal steroids. The median reduction in the TNSS with placebo alone was 15%, which significantly reduces the apparent magnitude of efficacy for these medications vs. placebo. Similarly, Wilson et al.⁹ found that leukotriene receptor antagonists reduced mean daily rhinitis symptom scores (in absolute terms) by just 5% more than the placebo did. These figures for symptomatic medications are no better than the percentage reductions vs. placebo in total rhinitis symptom scores - including eye symptoms - for SLIT¹⁰ and are well below the efficacy values recorded in the recent “big trials” of sublingual tablets in particular.¹¹,¹² There are methodological factors that complicate head-to-head AIT vs. drug comparisons but most of these tend to disfavour AIT. The efficacy of symptom relief by AIT is usually judged over several months’ period, during which allergen levels (and thus disease activity) can fluctuate and in patients with no symptoms at inclusion; this dilutes the positive effects of AIT. In contrast, symptomatic drugs tend to be evaluated over two weeks in patients with severe symptoms at inclusion. But even with these “advantages”, the effect size of symptomatic drugs is relatively modest. Moreover, AIT is never tested against a placebo since rescue medications are always allowed.³
Some physicians seem to think that "allergen preparations are being formulated just as Noon and Freeman did in 1911 and they are not proper medications". Those days are over, in Europe at least, where there are now very strict regulatory guidelines that benefit patients and allergists alike. The European Medicines Agency’s 2008 Guidelines, recommend that modern AIT products have to meet the same standards for quality, safety and efficacy as licensed pharmaceutical, because they are licensed pharmaceuticals.

Another dogma held by allergists is whether “SCIT is harmless in trained hands and allows a better compliance compared to SLIT”. SLIT obviously has a far better safety profile – but people continue to say that it is safe because it is not effective. The "big trials" and the meta-analyses show without doubt that SLIT is effective. Head-to-head SLIT vs. SCIT comparisons are rare but the available evidence says that both formulations (when correctly administered) have similar levels of efficacy. Considering that the two routes have similar clinical efficacy and depending on the availability of suitable products, we believe that the choice of SCIT or SLIT should result from an evidence-based treatment decision taken in conjunction with the patient. For grass pollen AIT formulations in general, the application of an evidence-based medicine approach for reviewing the level and quality of research evidence has lead to similar conclusions. Compliance in AIT is an important issue because we are talking about seasonal or continuous administration for several years. In a recent systematic review of in AIT, compliance in the early studies of SCIT ranged from 45 to 60%, with higher values for more recent trials (up to 89%). The values for SLIT ranged from 75 to 95%. Sieber et al. have retrospectively tracked individual prescriptions for SCIT and SLIT preparations in a representative German, nationwide database over several years and used prescription renewal rates (persistency), as a proxy for compliance. They found that persistency rates for natural extract SLIT (51%, after two years) were significantly higher than those for natural extract SCIT (34%). This is strong evidence, not biased by patient nor doctor characteristics since it was performed retrospectively from the social security database.

To conclude, we would encourage doctors and allergist colleagues to base their AIT decisions on evidence-based information which is robust and objective instead of perceptions.

References