

“Subcutaneous Immunotherapy: Perspectives of Treatment Practices in the US and Europe”

Prof. Dr. med. Oliver Pfaar, Department of Otorhinolaryngology, Head and Neck Surgery, Center for Rhinology and Allergology, University Hospital Mannheim, Wiesbaden, Germany.
Tel.: +49-611-308 608 0
Fax: +49-611-308 608 255
E-mail: oliver.pfaar@allergiezentrum.org

Allergen-specific immunotherapy (AIT) has been firstly described in the „Lancet“ by Noon in 1911 ¹ and is considered as the only available causal, disease-modifying therapeutic option in the treatment of allergic patients since then ^{2 3}. Though the principle of this therapy is the same all over the world with similarities in standards of AIT, some differences of the principles of AIT have emerged between the United States and Europe (reviewed in ⁴).

For both U.S. and Europe standards for practical immunotherapy have been published ^{5 6}. In 2013, as part of the PRACTALL initiatives, the European Academy of Allergy and Clinical Immunology (EAACI) and the American Academy of Allergy, Asthma & Immunology (AAAAI) have developed consented recommendations of clinical practise in AIT aimed to create harmonization of standards ⁷.

The following outlines examples of similarities and differences as reported in the current guidelines of EAACI and AAAAI (^{5 6 7}, partly reviewed by Cox and Jacobsen in ⁴):

1. Dosing, Potency Determination and Preparation

In the European practices, (subcutaneous) AIT is commonly performed with a single allergen (in the respective formulation) as in the US multiple allergens are included in the extract formulation. Moreover, there is a difference about the preparation-process of

the allergen-formulations which are prepared in the physicians' offices in the US whereas they are fully prepared by the manufacturer in Europe. Potency units for allergen content varies in Europe as manufactures use different units determined by different standardization and validation processes.

2. Patient age and initiation of AIT

The US-parameters report that there is now lower limit of age for the beginning of AIT as well as no specific recommendation is given for elderly patients. However, the „risk/benefit assessment must be evaluated in every situation.“ The EAACI-standards report that subcutaneous AIT is primarily restricted to children above the age of 5 years and should be considered in younger children only by a highly experienced physician. Moreover, it is stated that “subcutaneous immunotherapy is rarely used after the age of 60 years“ without further recommendations.

3. Special Considerations for AIT

For pregnant patients the US parameters point out that “(AIT) can be continued but usually is not initiated..“ which is in line with the EAACI-standards which assess pregnancy as a relative contraindication (for AIT with inhalant allergens). For patients with HIV infection and autoimmune disorders the US summary statement is that AIT “can be considered“ but also includes and discusses current published literature. The indication and contraindication for initiation of AIT are in general comparable to the European standards and are also broadly addressed in the current ARIA-guidelines³ and in the recently published PRACTALL consensus report⁷.

4. Safety issues on (subcutaneous) AIT

In both US and European-recommendations an observation period of 30 minutes is recommended after the injection. The European standards also emphasize the importance of “regular training in safety procedures ... of each individual staff member“ and a logbook for emergency equipment. Premedication for AIT is recommended in both position-papers. However, the European standards report the possibility of masking a mild reaction which may lead to a dose modification at the subsequent injection.

Heterogeneity exists in classifying the grading of systemic reactions in the two statements. In this context, emphasize must be given to the fact that there is a harmonized and uniform grading system for classifying of systemic reactions after AIT proposed by WAO in 2010 ⁸ which is already addressed in the US parameters.

In conclusion, these examples underline that similarities as well as differences in the clinical practice of AIT are found in the current recommendations and consensus-reports of the two continents. The lecture at WAO-Symposium will analyze and evaluate pro's and con's on different of these aspects.

References

1. Noon L, Cantar B. Prophylactic Inoculation against Hay Fever. *Lancet* 1911; (1): 1572-3.
2. Bousquet J, Lockey R, Malling HJ. Allergen immunotherapy: therapeutic vaccines for allergic diseases. A WHO position paper. *J Allergy Clin Immunol* 1998; **102**(4 Pt 1): 558-62.
3. Bousquet J, Khaltsev N, Cruz AA, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy* 2008; **63 Suppl 86**: 8-160.
4. Cox L, Jacobsen L. Comparison of allergen immunotherapy practice patterns in the United States and Europe. *Ann Allergy Asthma Immunol* 2009; **103**(6): 451-59; quiz 9-61, 95.
5. Cox L, Nelson H, Lockey R, et al. Allergen immunotherapy: a practice parameter third update. *J Allergy Clin Immunol* 2011; **127**(1 Suppl): S1-55.
6. Alvarez-Cuesta E, Bousquet J, Canonica GW, Durham SR, Malling HJ, Valovirta E. Standards for practical allergen-specific immunotherapy. *Allergy* 2006; **61 Suppl 82**: 1-20.
7. Burks AW, Calderon MA, Casale T, et al. Update on allergy immunotherapy: American Academy of Allergy, Asthma & Immunology/European Academy of Allergy and Clinical Immunology/PRACTALL consensus report. *J Allergy Clin Immunol* 2013.
8. Cox L, Larenas-Linnemann D, Lockey RF, Passalacqua G. Speaking the same language: The World Allergy Organization Subcutaneous Immunotherapy Systemic Reaction Grading System. *J Allergy Clin Immunol* 2010; **125**(3): 569-74, 74 e1-74 e7.