

Highlights on the EAACI–WAO Congress 2013

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European Academy of Allergy and Clinical Immunology and World Allergy Organization. World Allergy and Asthma Congress. Milano, Italy, 22–26 June 2013

The European Academy of Allergy and Clinical Immunology and World Allergy Organization congress provided a meeting for researchers and clinicians interested in allergy and clinical immunology from all over the world and a unique opportunity to exchange experience with other professionals in this fields.

Lights went out on the European Academy of Allergy and Clinical Immunology (EAACI)–World Allergy Organization (WAO) Allergy and Asthma Congress that was held in Milano, Italy, on 22–26 June 2013. EAACI, under the Presidency of Cezmi Akdis, and WAO, under the Presidency of Ruby Pawankar, have combined their efforts to provide a meeting for allergist from all over the world. The congress, which was attended by more than 7,700 delegates from 100 countries worldwide, aimed to provide an update on the latest topics in allergy, asthma and clinical immunology. The program lasted for 5 days and was organized in many different session types, so a great amount of information was discussed among researchers and clinicians.

A major focus was on novel biomarkers for allergic diseases and the possible clinical setting in which they can be applied, like diagnosis, disease monitoring, prediction of disease expression and in particular whether they can serve as a guidance to treatment requirements and the subsequent response to intervention. About this topic, in his keynote lecture, Giorgio Walter Canonica (University of Genova, Italy) presented the possible role of new biomarkers like cytotoxic T lymphocyte-associated antigen 4 (CTLA4) as a marker of hymenoptera venom immunotherapy (VIT) efficacy and protection persistence. Serum CTLA4 levels are augmented in patients with autoimmune diseases such as systemic lupus erythematosus, thyroid diseases, Type 1 diabetes and in allergic asthma. High serum concentration of CTLA4 has also been observed in patients

with hymenoptera venom allergy and a decrease after VIT was detected, parallel with the increase of IL-10, whatever the protocol used [1]. Besides, the reduction in CTLA4 persists during VIT maintenance, differently from IL-10. In patients with allergic rhinitis also, soluble serum HLA-G and sHLA-A, -B, -C are significantly increased compared to normal subjects, and this increase is particularly evident for the sHLA-G molecule. Moreover, there is a very strong correlation between clinical severity, drug use and sHLA-G values and both sHLA-G and sHLA-A, -B, -C levels significantly diminish after sublingual immunotherapy (SLIT). Indeed, in allergic rhinitis, sHLA-G might be considered as a biomarker for evaluating clinical severity and a possible biomarker for monitoring sublingual immunotherapy [2].

Novel advances in the treatment of asthma also were one of the key points of the congress, and the new therapeutic approaches were reviewed in a symposium. Peter Barnes (Imperial College London, UK) discussed how existing drugs have recently been shown to have different mechanisms of action that could be exploited in the future for the treatment of asthma. For example, theophylline, which has long been used in asthma and COPD as bronchodilator, increases expression of histone deacetylase 2 – a key nuclear enzyme involved in the anti-inflammatory effects of corticosteroids whose expression is reduced in COPD patients. As results, low doses of theophylline can reduce steroids resistance and enhance the effectiveness of corticosteroids, so in a clinical

setting, it may improve responses to inhaled corticosteroids in patients with COPD and smoking asthmatics patients. The molecular target of theophylline, which allows to obtain such effect, is phosphoinositide-3-kinase- δ (PI3K) [3]. Other drugs that reverse steroids resistance by inhibiting the PI3K are nortriptyline, a tricyclic antidepressant and macrolides. For this reason, nonantibiotic macrolides are now in clinical development [4]. The application of bronchial thermoplasty has been discussed by Gerard Cox (McMaster University, Canada). This is a new procedure, performed at fiberoptic bronchoscopy, which reduces the mass of muscle in the airway wall through the direct application of heat. Multiple studies support the effectiveness of thermoplasty, the efficacy and safety were demonstrated in three randomized controlled trials: Asthma Intervention Research (AIR), Research in Severe Asthma and the AIR2 trial [5–7]. About safety, a 5 years follow-up in trials with annual high-resolution computerized tomography showed no parenchymal variations. So the bronchial thermoplasty is helpful in adult patients with severe asthma not controlled despite therapy and is promising as disease-modifying treatment according to the persistence of benefits for 5 years. Moreover, biological therapies that target cytokines are potentially useful for the treatment of asthma, like recent advances in knowledge of the pathobiology suggest, but must be considered that this is a complex and heterogeneous disease and an appropriate selection of patients is needed [8]. An accurate characterization of the different asthma phenotypes is in fact essential for the therapeutic response to biologicals. William Busse (University of Wisconsin, USA) showed data from recent trials about biologicals in asthma. A double-blind placebo-controlled trial showed that the anti-IL-5 antibody mepolizumab is effective in reducing exacerbations in patients with severe eosinophilic asthma defined as having sputum eosinophils $\geq 3\%$, fractional exhaled nitric oxide ≥ 50 ppb and blood eosinophils $\geq 300/\text{cc}$ [9]. Also anti-IL-4 α -subunit receptor antibody Dupilumab was associated with fewer asthma exacerbations in patients with persistent, moderate-to-severe asthma and elevated eosinophil levels [10]. Treatment with lebrikizumab (anti-IL-3 antibody) was greater effective in patients with high serum periostin levels than in patients with low periostin levels with a higher increase of forced expiratory volume in 1 second and a higher decrease in fractional exhaled nitric oxide in this subgroup of patients; these findings suggest a possible use of serum periostin as a marker able to identify patients that will respond to Lebrikizumab [11].

With regard to biologicals, another field of great interest to the allergist is represented by the side effects. These have been discussed by Onur Boyman (University Hospital Zurich, Switzerland) and Alessandra Vultaggio (AOU Careggi, Italy). The latter reported how different mechanisms can sustain hypersensitivity reactions toward this drugs and how their recognition may allow a correct risk assessment. This is not always easy for the clinician considering that symptoms due to the cytokine release syndrome, an antibody-independent massive cytokine release by different types of immune cells and symptoms due to an IgE-mediated reaction significantly overlap. Some infusion reactions are the

result of an antibody-mediated reaction; all the biologicals are in fact intrinsically immunogenic and can induce the development of specific antidrug antibodies that are mostly represented by IgG isotype, but a proportion of them may belong to IgE isotype [12].

About specific immunotherapy, Thomas Kundig (University Hospital Zurich, Switzerland) presented the novel emerging modalities. Intralymphatic administration was tested as regards safety, immunogenicity and efficacy in a randomized controlled trial in patients with hay fever due to grass pollen allergy. Intralymphatic immunotherapy was found to be safe and to give an amelioration of allergy symptoms after only three intralymphatic injections that were long lasting and comparable to that achieved after 3 years of conventional immunotherapy [13]. Also epicutaneous administration was investigated in a placebo-controlled, double-blind trial in patients with allergic rhinoconjunctivitis: epicutaneous immunotherapy was safe, well tolerated and caused significantly symptoms amelioration than placebo [14]. Finally, allergens coupled to virus-like particles can be used to enhance the efficiency of allergen-specific immunotherapy; in a Phase I trial on 24 healthy volunteers, vaccination with a Der p1 covalently coupled to highly repetitive virus-like particles induced a significant IgG responses 4 weeks after a single injection [15]. An updated WAO SLIT position paper is now in press, GW Canonica presented the novelties contained in it. Different speakers also focused on the specific immunotherapy for the treatment of food allergy. SLIT seems to be a promising therapeutic option for the treatment of food allergy. Giovanni Passalacqua (University of Genova, Italy) in his lecture on advances in SLIT delved into this aspect. Considering peanut allergy, in a double-blind placebo-controlled study in children, SLIT-induced clinical desensitization with evidence of immunologic changes suggesting a significant change in the allergic response [16]. SLIT for the peach lipid transfer protein Pru p 3, a highly prevalent allergen in the Mediterranean area, allergy was also investigated in a randomized, double-blind, placebo-controlled clinical trial. After SLIT, patients in the active group tolerated a significantly higher amount of peach and a significant increase in IgG4 to Pru p 3 was observed [17]. Also, the role of anti-IgE therapy in food allergy was not forgotten, in particular its use in combination with oral immunotherapy. Kari Nadeau (Stanford University, USA) showed the results of pilot study included 11 subjects, which indicates that in patients with IgE-mediated cow's milk, allergy pretreatment with omalizumab was safe and allowed for rapid oral desensitization [18].

A large space has also been reserved for EAACI junior members with a poster session in which over 200 posters were presented exclusively by juniors, a case reports session, an educational session and a scientific symposium focused on patient's quality of life.

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