EDITORIAL

# Chronic urticaria: new hope for an old disease

Chronic urticaria (CU) is a well-known disease with two faces: so easy to diagnose and so difficult to treat. Having seen certainly more than 1000 urticaria patients, I tell students some sayings shared with other experienced dermatologists, such as 'If you don't know the cause or elicitor of urticaria within the first minute of talking to the patient, you will probably not find it out in the next 10 years!' or 'If you have a colleague whom you really don't like, just recommend him as an expert for chronic urticaria'. These are the frustrations of the past.

Urticaria is one of the most common skin diseases; approximately, every second person suffers from acute urticaria at least once in their lifetime. Estimates range from 1% to 3% of the population affected by CU, defined as the occurrence of wheals and/or angioedema for 6 weeks or more. There is immense individual suffering, not only due to the excruciating itch but also due to the impact on the patient's whole personal life of an urticaria flare up. At the same time, considerable socioeconomic losses are caused by this disease, with duration times ranging over a average of 5–7 years and up to 50 years in some patients.

Therefore, it is a major progression that new and effective treatment options are finally available, especially with monoclonal antibodies against human immunoglobulin (Ig) E (omalizumab), which has been around for the treatment of asthma for many years.

This supplement reflects a summary of the topics and lectures given at the recent Global Urticaria Forum in November 2015 in Berlin, where international experts from Germany, Spain, UK, Denmark, Israel, Canada and New Zealand met and discussed the state of the art, actual problems, new opportunities and future developments in the field. It is thanks to the continuous efforts and the immense experience of Ana Giménez-Arnau at Hospital del Mar, Barcelona and Marcus Maurer at Charité – Universitätsmedizin Berlin that this symposium has been made possible.

Regarding the clinical picture, Maurer *et al.*[1] report surprising findings in that almost 50% of patients with chronic spontaneous urticaria (CSU) also have episodes of angioedema. There is a significant predominance of the female sex, with approximately 70% women affected.

The mast cell is at the centre of the pathophysiology of this disease. There has been tremendous progress in the last decade with regard to mechanisms of mast cell activation and signal transduction. However, the question as to what is the causal stimulus activating the mast cell in CSU is still open.

Probably the greatest progress in the new millennium in CU was the discovery that anti-IgE, which had been registered for the treatment of allergic bronchial asthma, also works in CU. This observation led to a rapid spread of this new kind of therapy, so that from 2015, there are already 17 000 patient treatment-years with omalizumab which can be evaluated. Interestingly, there seem to be two types of responder to omalizumab treatment: namely fast responders, in which the wheals disappear within days after the injection, and gradual responders, where it takes a longer time until the clinical effect shows.

As to the mechanism of this treatment, the binding of omalizumab to the C-epsilon-3 domain of human IgE is thought to block the binding of IgE to the Fc-epsilon receptor on the surface of mast cells and basophil leukocytes. Another possible mechanism might be in regulatory effects of IgE–anti-IgE complexes.

In their article, Staubach *et al.*[2] reflect on controversial issues and challenges in practical management with regard to difficult groups of patients, such as children with CU, case studies with physical urticaria, solar urticaria or urticarial vasculitis. Autoinflammatory syndromes are also covered, where new monoclonal antibodies against interleukin 1ß (canakinumab) have been shown to be effective in some patients.

The practical clinical management of omalizumab therapy in CSU is highlighted by Giménez-Arnau *et al.*,[3] who gave an algorithm with three steps for urticaria, based on current guidelines and evidence-based criteria.

Unfortunately, many patients who respond very well to omalizumab relapse after treatment is stopped, within an interval of 3–8 weeks. There are still open questions with regard to stopping omalizumab therapy in CSU. Data are available from studies up to 6 months. Long-term studies are on the way. Some studies estimate a duration of treatment of between 6 and 18 months, others between 17 and 112 months. At the moment, there is no clear-cut diagnostic or prognostic criterion which would tell us when the therapy can be stopped. Therefore, the search for biomarkers in the blood is ongoing. Basophil upregulating activity (increased CD63 or CD203) after incubation with patients' serum has been found in sera of patients who will relapse rather quickly.

International cooperation will be facilitated by a registry – Chronic Urticaria Registry (CURE) – and the global network of GA$^2$LEN Urticaria Centers of Reference and Excellence (UCAREs).

Taken together, this new therapy really represents a major step forward in urticaria management. As Editor-in-Chief of the *Journal of the European Academy for Dermatology and Venerology*


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(JEADV), I recommend this supplement to our readers and to all people interested in CU. There is really good news for this chronic disease!

## Conflicts of interest

The author declares that he has no conflicts of interest.

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