



Urticaria and Beyond

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HONING in on urticaria and other mast cell driven diseases, experts at the European Academy of Allergy and Clinical Immunology (EAACI) Congress 2023 presented a forward-thinking session in one of the most insightful symposia from the hybrid meeting hosted in Hamburg, Germany. Feeding into the over-arching congress motto, “pathways from precision medicine to personalised healthcare in allergy and asthma,” the speakers outlined what the future holds for targeting cells and identifying remission, amongst other topics in this field.

TARGETING MAST CELLS

There are many mast cell targeting drugs currently available, and Martin Metz, Charité – Universitätsmedizin Berlin, Germany, began by presenting these alongside the many more drugs in development and in ongoing clinical trials, which are likely to become available soon. Metz arranged these treatments into four main categories: those that block mast cell mediators, inhibit mast cell activation, silence, and deplete mast cells.

Presenting data for three different modes of action: remibrutinib targeting Bruton’s tyrosine kinase, barzolvolimab targeting KIT, and dupilumab targeting IL-4 receptor, Metz promised that there is much more to come, and outlined future applications for urticaria. Describing the surprising efficacy of dupilumab as a drug for urticaria, Metz expressed that, “we have to rethink the role of mast cells in many diseases and see the targets on these cells as being interesting in mast cell-driven diseases.” They went on to describe the biology behind barzolvolimab as a “super fascinating” drug, depleting mast cells through encouraging apoptosis and producing symptom-free patients.

Looking beyond urticaria, Metz offered insight into the future applications for the targeting of mast cells. Mastocytosis and mast cell-activation syndrome were among the first and most direct pathways to explore.

Metz went on to provide an extensive list where there is evidence that targeting therapy could be helpful, ranging from asthma, psoriasis, and rheumatoid arthritis to inflammatory bowel diseases, migraine, and autism spectrum disorder. This presentation confirmed there are multiple inter-specialty avenues to explore where the role of mast cells is not yet clearly defined.

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IDENTIFYING REMISSION AND DISCONTINUING TREATMENT

Massimo Triggiani, Università degli Studi di Salerno, Italy, began by acknowledging the complex and heterogeneous mechanisms that are involved with the common clinical conditions chronic spontaneous urticaria (CSU) and angioedema. Triggiani went on to define ‘control’ and ‘remission’ for CSU, differentiating between the two as an absence of disease during treatment, and 6 months after the treatment ceased.

Triggiani underlined that attempts to stop CSU treatment when the disease is well controlled should always be made.



The presentation touched on the methods for assessment of control, recommending that clinicians undertake frequent and specific disease evaluations with their patients, alongside questionnaires for patient quality of life. Triggiani shared the criteria for complete, good, partial, and absence of control, referencing several studies which have looked at the risk factors of CSU persistence and tracked clinical course. Triggiani acknowledged a gap in literature studying paediatric populations by discussing an investigation that compared male and female data on remission, and noted the interesting co-interaction of chronic urticaria in children with atopic dermatitis, allergic rhinitis, and asthma. A key point from this section was the finding that a high eosinophil count is a protective factor.

Presenting longitudinal data spanning 10 years from the Università degli Studi di Salerno, Triggiani spoke about the responsiveness of patients to antihistamines. Discussion then shifted to dermographism and its transient nature, detectable in about half of patients with CSU, and not usually associated with pruritis. "I do not know really if dermographies can be intended as a way to assess mast cell reactivity *in vivo*, was the honest statement that Triggiani opened to the floor, but they followed up by confirming that, "certainly, most of the patients that enter into remission, are patients who lose steadily their dermography characteristics."

Triggiani outlined the factors that are useful in predicting time to CSU remission, some with conflicting data and caveats. Data showed that female gender and the age of a patient were among the factors predicting a longer time to remission; the same was observed for a higher severity of CSU, longer duration of disease, and concomitant angioedema. More research is warranted on responses to antihistamines as the predictive value of this is unknown. The same is seen for eosinophilia and basopenia, but for total serum IgE the predictive value is limited.

"Triggiani outlined the factors that are useful in predicting time to CSU remission."

Triggiani finished their talk by bringing all the topics they had discussed together, with the help of a large study that employed machine learning to assess clinical remission. Triggiani recognised there is no full agreement on a definition for remission, but promoted this integrated analysis as an artificial intelligence model for predicting CSU recurrence. A real takeaway from this segment for clinicians was that patients should be informed that recurrence of urticaria is the rule rather than the exception, and reassurance should be provided that in the case of recurrence previous treatment will be as safe and effective as it was before.

CONCLUDING REMARKS

“The neglected duckling of urticaria,” was the way Marcus Maurer, Charité – Universitätsmedizin Berlin, Germany, described chronic inducible urticaria when concluding this session. Maurer highlighted differences compared with CSU, its more common counterpart, and brought real energy to the stage providing guidance for physicians dealing with patients with this disease. Maurer encouraged development of better drugs for chronic inducible urticaria, advising threshold testing to assess disease activity, aiming for complete control until remission, and starting with non-sedating antihistamines.

Finally, Maurer recommended a higher than standard dose for patients, if required; omalizumab when antihistamines fail; and that patients are guided towards clinical trials.

The cutting-edge contributions in this session will have significant impact on the decision-making and practice of clinicians as they go back to their work, providing a satisfying ‘itch’ for those specialising in the field of and living with urticaria. What is clear from this talk is that although great advances are being made, there is a great deal to be uncovered still with this complex condition, as we move towards more precise medicine and provision of care. ●

