Management of severe eosinophilic asthma in the biologics age: What does the patient journey look like?

Highlights from the Teva-sponsored symposium held at the European Respiratory Society (ERS) congress | 11 September 2017 | (17:15–19:15) | Milan, Italy

This symposium, chaired by Professor Ratko Djukanovic, University of Southampton, UK, focused on how patients with severe asthma present, and explored how asthma subtypes (based on clinical, functional and inflammatory parameters) can be used to tailor routine care and improve outcomes for individual patients. Topics at this session included:

- Defining the severe eosinophilic asthma (SEA) phenotype and remaining unmet needs
- Current approaches and targets for anti-IL-5 therapies
- Case studies showing which patients respond best to anti-IL-5 therapies

The symposium concluded with a panel discussion and questions from the audience.

EXPLORING SEVERE EOSINOPHILIC ASTHMA (SEA): WHO, WHEN AND HOW
Professor Stephen Holgate | University of Southampton, UK

A ‘one-size-fits-all’ approach does not work in managing patients with severe asthma, Professor Stephen Holgate stressed in the opening session of the symposium. Outlining the pathogenesis of SEA and detailing the differentiation of asthma phenotypes using clinical and inflammatory characteristics, and more granular biomarker and transcriptomic traits, Professor Holgate described how projects like U-BIOPRED are characterising the genomes of large cohorts of patients. These new techniques will further define subtypes of asthma, enabling linkage to biomarkers for targeted therapy selection and response assessment. The role of (local) IgE, for example in non-atopic asthma, needs further exploration, whereas eosinophilia clearly predicts response to anti-IL-5 therapy. In contrast, phenotypes where there are low levels of Th2 cells have no targeted therapies, but might benefit from emerging therapeutic options. While such therapies are an exciting prospect, in clinical practice important issues remain:

- Which biologic should be chosen, for whom and when?
- How should response be assessed?
- When should therapy be stopped, or switched?

Development of criteria to help guide such decisions was described, but the need to integrate these into current guidelines was also emphasised.

"It’s important to provide guidance on how to better define severe asthma and how to select patient treatment accordingly."

Professor Stephen Holgate

LEARNINGS AT A GLANCE

- Severe asthma is heterogeneous and a significant proportion of severe asthma is hypereosinophilic
- Early phenotyping of patients in practice can/ must be achieved to identify those who are most likely to respond to treatment with biologics
- Treatment with biologic agents targeting IgE, Th2, and ILC2 driven cytokines, particularly IL-5 are emerging as efficacious asthma therapies
- Effective patient phenotyping will be the foundation of a precision medicine approach in asthma management with increasing therapy choice for HCPs and patients
**APPROACHES AND TARGETS FOR ASTHMA BIOLOGIC THERAPIES**

**Professor Parameswaran Nair | McMaster University, Canada**

Clinical targets for asthma biologic therapies for treatment of severe eosinophilic asthma (including anti-IgE and anti-IL-5 therapies) were reviewed by **Professor Parameswaran Nair**. Beginning with a summary of data looking at the effect of available therapies on sputum and blood eosinophils, Professor Nair, showed how reduction of blood eosinophils after omalizumab treatment was associated with fewer exacerbations and that whilst both mepolizumab (100 mg SC) and reslizumab (3 mg/kg) can reduce blood eosinophil levels, IV weight-adjusted dosing of reslizumab suppresses sputum eosinophils better, and this is associated with greater improvement in asthma control and FEV₁ in patients with severe prednisone-dependent asthma. In patients where sputum eosinophil progenitor cells are more persistent, the investigational drug benralizumab was shown to have a reductive effect. It was concluded that, anti-IL-5 therapy is effective in ‘eosinophil-mediated asthma’ (blood or sputum eosinophils) independent of atopy, but as further therapeutic targets are identified and more treatments are developed, the place of these in the treatment paradigm will need to be addressed.

*Not yet licensed for use

**TARGETING THE RIGHT PATIENT: THE CASE OF ANTI-IL-5**

**Professor Roland Buhl | Johannes Gutenberg University of Mainz, Germany**

Choosing the right therapy for the right patient in clinical practice was the underlying theme of clinical cases presented by **Professor Roland Buhl**. The case of Frank, a 47-year-old never-smoker with history of asthma since 2005 and chronic rhinosinusitis with nasal polyposis, diagnosed with uncontrolled, non-allergic, eosinophilic asthma despite GINA step 4 treatment, highlighted how one of the main challenges in managing patients with severe asthma is early recognition of the phenotype, and that this patient type could benefit significantly from anti-IL-5 treatment. Professor Buhl also touched upon further subgroup analyses of clinical trials showing that these patients with late-onset disease, or chronic rhinosinusitis with nasal polyps, or who are GINA step 4/5 eligible, may respond better to anti-IL-5 therapy with reslizumab than comparison groups. However, he remarked that clinicians must first determine whether the asthma is uncontrolled or severe. Also, there is no universally accepted definition of response to treatment of severe asthma with biologics, with physicians routinely evaluating multiple aspects of response using a range of clinical tools. The next step is phenotype determination using biomarkers and other characteristics to help phenotype selection – for instance, allergic asthma tends to present in the young, whereas eosinophilic asthma tends to have a later onset, bringing the session into full circle.

**PANEL DISCUSSION AND CONCLUSION**

**Professor Djukanovic** (left) rounded up the session by chairing the panel discussion, and the faculty took questions from the audience. In conclusion:

- Targeted therapies have improved outcomes for SEA patients
- Further guidance on how best to prescribe and monitor these drugs is required

A better knowledge of asthma phenotypes together with the introduction of novel biological therapies will optimise treatment in patients with severe asthma.

**References**