Pleiotropic effects of modern biological therapies of severe asthma in terms of mediation of alarmins (IL-25, IL-33 TSLP) and soluble ST2 receptor levels and airway remodeling

Asthma is one of the most common chronic respiratory diseases. It is mainly caused by allergic mechanisms in response to external stimuli such as inhalant allergens (pollen from trees, grasses, animal hair, mites), but can also develop on non-allergic grounds. Symptoms of asthma include shortness of breath, coughing, wheezing, chest tightness and many oher.

Immune system reactions play a key role in the pathogenesis of asthma. Cells of this system, under the influence of external or internal stimuli secrete a number of signaling molecules (cytokines), which are responsible for the development of the inflammatory process in the bronchi, which is the basis of the pathogenesis of asthma. Among many such cytokines, the so-called 'alarmins', i.e. particles released by respiratory epithelial cells under the influence of an external stimulus and leading to the further development of inflammation in the bronchi. This results in a chronic inflammation that leads to bronchial asthma symptoms. Among the consequences of this phenomenon, we can distinguish the airway remodeling process, i.e. the gradual reconstruction of the composition and structure of the airways. The long-term consequences of this phenomenon are the persistent reduction in lung function and limited response to drugs.

In the treatment of asthma, inhaled drugs - bronchodilators (β2-mimetics) and anti-inflammatory agents (glucocorticosteroids) play a dominant role. The most severely ill may currently use modern methods of treatment of severe asthma, which are biological drugs - monoclonal antibodies blocking key cytokines of asthma pathogenesis. In the literature so far, we will find only few and incomplete studies in the field of assessing the effect of biological treatment of severe asthma with omalizumab, mepolizumab or benralizumab on the level of key inflammatory cytokines, which are alarmins, as well as their impact on airway remodeling.

This project is an attempt to answer the question whether modern biological drugs used in severe asthma (omalizumab, mepolizumab and benralizumab), in addition to their proven effect on the course of the disease, have other (pleiotropic) effects in the field of modulation of alarmins levels (IL-25, IL - 33 and TSLP) and free IL-33 receptor - sST2 and airway remodeling.

To answer the research question, we will follow up in 6 months 45 patients undergoing treatment with omalizumab, mepolizumab or benralizumab. We will assess the concentration of alarmins and sST2 receptor in blood and bronchoalveolar lavage as well as histological structure of the bronchial wall (in bronchial biopsy) and immuno-expression of alarmins in bronchial epithelial cells before the start of biological treatment of severe asthma and after 6 months of biological treatment.

The project will assess whether biological drugs currently used in the treatment of severe asthma significantly affect the key cytokines (alarmins) that are crucial in the development of chronic bronchial inflammation. We will also learn the answer to the question of whether these drugs significantly reduce airway remodeling, i.e. the process of long-term and well-established remodeling of bronchial walls. We will also find out whether the level of airway remodeling correlates with the level of important inflammatory cytokines, which are alarms. This will fill the gap in knowledge about the additional actions of these modern drugs and assess the effectiveness of their use in the modulation of long-term sequelae of asthma