
Participants in this month’s Asthma Institute Support Group had the privilege of participating in a discussion/study session with Dr. Sally Wenzel, Director of UPMC’s Asthma Institute, on new and experimental approaches for treating severe asthma.

Dr. Wenzel introduced the concept of the **asthma phenotype**: the set of characteristics that show the interaction between a person’s genetic background and their environment. One may be pre-disposed to developing asthma for genetic reasons. When different asthma patients present differently we then ask and observe: Does the patient have sinus disease? Skin problems? Are they an adult or child-onset asthmatic? And so on, to identify different subgroups of asthmatics, and these help us to understand the different phenotypes. Well-recognized subgroups include child-onset asthmatics who tend to be more allergic vs. adult-onset asthmatics who tend to be less so.

We then must ask: Can we better treat patients if their phenotypes are well known? Do patients with different phenotypes respond differently to medications? Even among adult severe and hard-to-treat asthmatics, different phenotypes exist. Participants in SARP, the Asthma Institute’s Severe Asthma Research Project have had lung biopsies, and researchers now have molecular profiles of their phenotypes, with the aim to better answer the above questions. The term "personalized medicine" refers to the new focus in medicine on tailoring treatment not only to disease but also to the patient’s *presentation* of the disease. Ideally, one day, a blood test will be able to identify your type of asthma and point towards the most effective treatment for you.

Following is a review of newer medications designed to target specific molecular phenotypes:

- **Xolair**, which is available by prescription, was developed for asthmatics who are very allergic. Xolair blocks IgE, or Immunoglobulin E, an antibody associated with allergic reactions. Thirty-forty percent of severe allergic asthmatics will improve somewhat with it, although the degree of response is highly variable.

The following two drugs are in the clinical trial phase of development:

- **Anti-Interleukin (IL)-5** blocks eosinophils, white blood cells in the lung associated with asthma. It has been found that high levels of eosinophils are associated with asthma exacerbations, although not all asthma patients have high eosinophils. For patients who do have them, their asthma can improve.

- **Anti-Interleukin (IL)-13** is a drug being developed to block IL-13, a chemical in the body that promotes inflammation and scarring in asthma patients.
Dr Wenzel stressed that these medications are for severe asthmatics, not for patients with mild forms of the illness. However, many of the most severely ill asthmatics are too sick to enter clinical trials because they are at risk for multiple complications that could complicate trial findings.

Non-allergic types of asthma are less targeted by newer drugs. Dr. Wenzel did cite a new pill that blocks mast cells, cells that can promote inflammation often seen in asthmatics.

- **CRTH2 antagonists** are in development to block one of the chemicals, produced by mast cells, that has been linked to inflammation and wheezing.

- Another medication, **Imuran**, is a potent anti-inflammatory medication that is used to treat multiple medical conditions. In some distinct types of asthma, it has reduced patients' need for prednisone.

A final word about, **bronchothermoplasty**, a procedure conceived to treat the narrowing of airways in asthma by heating up the airway in order to melt away smooth muscle: According to Dr. Wenzel, although this procedure has been proven effective, the improvements are very modest, and in severe asthmatics the procedure itself can even *cause* exacerbations. Further, the procedure affects the large airways only and so does not have any effect on patients with small airway obstruction.