Use of Biomarkers in Severe Asthma

Session 4002

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Learning Objectives:

1) Review and understand the utility specific biomarkers (blood and sputum eosinophils, FeNO, peristin, urine leukotrienes, exhaled breath condensate).

2) Describe the relationship of these markers to specific asthma phenotypes and endotypes.

3) Explore the use of these markers as predictors of efficacies of specific therapies.

Summary of Discussion Topics:

Asthma is a heterogeneous disease comprised of subtypes that encompass various mechanisms of lung inflammation. Response to medications may vary depending on asthma phenotypes, and the use of non-invasive biomarkers to characterize asthmatic inflammation and predict treatment responses is emerging as a crucial aspect of disease management. Sources of biomarkers include blood, sputum, exhaled gas, and bronchial fluid. In the session, the utility of biomarkers in each of these compartments will be discussed.

Fractional excretion of nitric oxide (FeNO): Exhaled nitric oxide has been widely studied as a rapid and easily measured tool to assess airway inflammation. Elevated FeNO correlates with eosinophilic airway inflammation and can predict glucocorticoid responsiveness (1-3).

Sputum Biomarkers: Induced sputum is a non-invasive method of obtaining cells and other mediators from the lower lung. The presence of sputum eosinophils (>2-3%) is characteristic of Th2 inflammation. Low or absent sputum eosinophils may correlate with poor response to inhaled glucocorticoids (4). In addition, the presence of sputum or serum eosinophilia may also be used to consider emerging therapies, such as anti-IL5 (5).

Serum Biomarkers: Peristin is a ~90kDa protein that is induced by Th2 cytokines and can be found in the serum. It may be a marker of Th2-predominant asthma, and can be used as tool to predict response to Th2-targeted therapy, such as anti-IL-13 (6).

Exhaled breath condensate (EBC): Physiologically, the exhaled breath is constituted predominately by water vapor and aerosolized particles, generated by airway lining fluid (ALF). By cooling breath vapor, EBC can be collected and its biochemical composition has been found to be very similar to ALF (7). Numerous mediators have been detected in EBC, and as detection methods have improved with better technologies in the past few years, it is now possible to quantitatively measure cytokines, nucleic acids, leukotrienes, pH, and other small molecules. Quantitation of these mediators is emerging as a means of phenotyping asthma. Measurement of eicosinoids in EBC has been demonstrated to differentiate aspirin-sensitive
and aspirin-tolerant asthmatics (8). Cytokine profiling has been shown to identify Th2 signatures and may be useful to distinguish Th2 high and Th2 low phenotypes (9). MicroRNAs (miRNAs) have also emerged as novel potential biomarkers. MiRNAs are small, non-coding RNAs, that are present in all biofluids. We have identified signatures of miRNAs which correspond to Th2 inflammation and are different in EBC of asthmatics, patients with COPD, and healthy subjects (10). MiRNAs are also found in serum and saliva, and measurement of their expression from these sources have also been shown have utility in asthma (11).

References: