

## Chronic Obstructive Pulmonary Disease (COPD) Phenotyping and Evolution in its Management

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### Abstract

Emerging scientific evidence behind progression and root cause of COPD has been evolved during the last decade. Despite it has been proven that the COPD is an inflammatory condition; however, there is a quite variation in treatment approaches for COPD patients.

Previously COPD stages was determined only by through using lung function (spirometry), however with evolving the concept of phenotypes and biomarkers, treatment strategy is now moving from Traditional medicines to all patients towards Stratified medicines to homogeneous groups of patients according to biomarkers and phenotypes. This concept will pave the way towards a different approach which is Personalized treatment to single individuals of patients with similar condition and risk factor(s) rather than different groups.

**Keywords:** COPD; Phenotypes; Exacerbator; COPD Biomarkers

### Introduction

COPD is a disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles and gases [1].

The pathology of COPD is due to the Oxidative stress that produced by high concentrations of free radicals in tobacco smoke and released by inflammatory cells. Protease - Anti protease imbalance Leads to destruction of connective tissue. Also Inflammatory mediators such as chemokines, cytokines, and growth factors and elastase are leading to alveolar destruction and fibrosis [2].

Not all COPD patients are presented with same symptoms and clinical manifestations. Repeated exacerbations could be the main clinical presentation for a COPD patient, on the other hand Co morbidity or breathlessness might be the main symptoms for other patients.

### Phenotypes in COPD

The definition of Phenotype is A single or combination of disease attributes, that describe differences between individuals with COPD as they related to clinically meaningful outcomes.

Phenotypes are defined by symptoms, Investigation (LF/ X-Ray/ CT Scan) and Biomarkers.

The importance of understanding the phenotype, is to foresee and predict the response to treatment in different COPD Patient as it is not the same, and also to understand the prognosis of the condition, also through clinical presentation, pathological/ radiological findings [3,4].

Historically, Dornhorst in 1955 for the first time described two clinical phenotypes of COPD the classic 'Blue Bloaters' and 'Pink Puffers' [3,4].

Now, there are other types of phenotypes have been described [5,6], such of these phenotypes are:

- “Overlap” or mixed COPD-asthma phenotype
- Emphysema hyperinflation phenotype
- Chronic bronchitis phenotype
- Bronchiectasis
- Exacerbator phenotype
- Co-morbidities

### Exacerbator Phenotype

In General, assessment of COPD patient is based on patients' level of symptoms, future risk of exacerbations, the severity of spirometric abnormality and the identification of comorbidities [1].

Exacerbations are often triggered by infection with bacteria or virus, environmental pollution or other factors. Exacerbations have a great impact on health status and affect the quality of patient's life and represent a serious threatening to COPD patients' life [1].

Also and added to health impact there is a significant economic burden on health care utilization and cost of treatment due to exacerbations [1].

Therefore, it was needed to understand the risk factors and the “exacerbative phenotype COPD patients”. Hurst., *et al.* analysed the frequency and associations of exacerbation in 2138 patients enrolled in the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) study [7].

The ECLIPSE study was designed to determine the underlying mechanisms of disease progression and identify biomarkers that may serve as surrogate endpoints and therefore measures of disease progression.

### The Results are

- a. Exacerbations became more frequent (and more severe) as the severity of COPD increased.
- b. Here is a frequent-exacerbation phenotype of COPD that is independent of disease severity.
- c. 22% of patients with stage 2 disease, 33% with stage 3, and 47% with stage 4 had frequent exacerbations.
- d. The single best predictor of exacerbations, across all GOLD stages, was a history of exacerbations.
- e. With evidence of importance of understanding of COPD phenotypes, there is a growing concept behind it, which is biomarkers.

### COPD Biomarkers

COPD biomarker, is a biological molecule that can provide an insight in the pathophysiological mechanisms of COPD. In systematic review for Pulmonary Biomarkers of CROD Exacerbation searching in biomarkers from exhaled air, sputum, Broncho alveolar lavage (BAL) and lung biopsies might correlate the clinical variables and predict clinical outcomes [3].

In conclusion, pulmonary biomarkers have the potential to provide information on the mechanisms underlying ECOPD. However, on the basis of published evidence, no single molecule is adequately validated for wide clinical use. Most prominent Biomarker which is correlated with clinical outcome is sputum analysis [3].

Despite the above conclusion, there is still a need to easily identify a biomarker to direct treatment in COPD, to support a more individualized treatment approach; one such possible biomarker are eosinophils.

### Blood Eosinophils

Blood eosinophil count is readily available and is highly sensitive for predicting sputum eosinophil count [8].

Blood eosinophil count measured at point of exacerbation has been shown to predict treatment response to oral corticosteroids [9].

Post hoc analyses suggest that COPD patients with blood eosinophils  $\geq 2\%$  or  $\geq 150/\text{mm}^3$  are at higher risk of exacerbations and have greater benefit from exacerbation reduction with the addition of Inhaled Corticosteroids to Bronchodilators (ICs/LABA) compared to patients with lower eosinophil counts [10].

Another Post-hoc analyses suggest that COPD patients with blood eosinophils  $\geq 2\%$  or  $\geq 150/\text{mm}^3$  compared to patients with levels  $< 2\%$ / $< 150/\text{mm}^3$  [11] will derive greater benefit from exacerbation reduction with Inhaled Corticosteroids and long acting Bronchodilators (ICs/LABA) compared to Anticholinergics alone and placebo [11].

### Conclusion

COPD management is moving from Traditional treatment based on classes of medicines, to stratified treatment based on phenotypes and biomarkers. It's very important to identify the phenotype of COPD patient in order to understand the underlying mechanism, identify the right treatment and predict the disease progression. Biomarkers are very important and might lead to determine the COPD phenotype.

### Disclosure

I'm working as Franchise Medical Lead in GSK / Egypt.

The above article is only representing my Medical opinion and review. It's neither representing GSK Medical insight / opinion nor on behalf of GSK.

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