

SUPPLEMENTARY FILE S1: Detailed Methods

Airway eosinophilia on bronchoalveolar lavage and the risk of exacerbations in COPD

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Detailed Methods

The Study to Investigate the Differential Effects of Inhaled Symbicort and Advair on Lung Microbiota (DISARM) trial: This randomized controlled trial was conducted to determine the effects of inhaled corticosteroid/long-acting beta-agonist (ICS/LABA) combination therapy on the lower airway microbiome in participants with COPD. The trial protocol was registered at clinicaltrials.gov (#NCT02833480) and the primary outcome results have recently been published.¹ Between October 2015 and June 2019, we recruited male and female participants

aged 40-85 years with COPD defined by a post-bronchodilator ratio of forced expiratory volume in 1 s to forced vital capacity (FEV1/FVC) <0.7, smoking history ≥10 pack years, and either FEV1 between 20% and 80% of predicted or clear evidence of emphysema on thoracic computed tomography. All participants were clinically stable without the use of systemic corticosteroids or antibiotics for at least 8 weeks prior to enrolment. Peripheral blood was collected at baseline. After ceasing any ICS therapy and undergoing a 4-week run-in period of LABA monotherapy (formoterol 12 microg via Turbuhaler twice daily), the purpose of which was to wash out any residual ICS, participants underwent bronchoscopy. One week after the bronchoscopy, participants were randomized 1:1:1 to receive formoterol 12 microg via Turbuhaler® twice daily, budesonide/formoterol 400/12 microg via Turbuhaler® twice daily, or fluticasone propionate/salmeterol 250/50 microg via Diskus® twice daily, for 12 weeks. At the end of the treatment period, participants returned for a second bronchoscopy. Neither the participants nor study coordinators were blinded to the treatment allocation, but study physicians assessing the participants during follow-up were unaware of their allocation. Acute exacerbations of COPD (AECOPD) were defined as acute worsening of symptoms requiring antibiotics and/or systemic corticosteroids. Data on AECOPD events and vital status were recorded prospectively after enrollment, for a minimum of one year. Data were confirmed from the electronic medical records following clinical review by specialist respiratory physicians.

Reference

1. Filho FSL, Takiguchi H, Akata K, Ra SW, Moon J-Y, Kim HK, et al. Effects of Inhaled Corticosteroid/Long-Acting β 2-Agonist Combination on the Airway Microbiome of Patients with Chronic Obstructive Pulmonary Disease: A Randomized Controlled Clinical Trial (DISARM). *Am J Respir Crit Care Med.* 2021;204(10):1143-52.