ONLINE SUPPLEMENT

Supplementary Table 1

Study	Study design	Sample size	Main outcomes
Bafadhel et al[1]	Prospective study examining sputum mediators of subjects with asthma and COPD	Subjects with asthma and COPD (n = 54 and n = 49)	Recovery of sputum mediators sensitive to DTT can be improved using the described sputum processing technique. Within airway inflammatory sub-phenotypes there is a differential pattern of mediator expression that is independent of disease.
Pavord et al[2]	Two phase 3, randomized, placebo-controlled, double-blind, parallel-group trials comparing mepolizumab (100 mg in METREX, 100 or 300 mg in METREO) with placebo	Patients were 40 years of age or older and had a documented diagnosis of COPD for at least 1 year (based on the ATS–ERS 2004 definition) METREX = 462 patients METREO = 674 patients	Mepolizumab at a dose of 100 mg was associated with a lower annual rate of moderate or severe exacerbations than placebo among patients with COPD and an eosinophilic phenotype.
Criner et al [3]	GALATHEA and TERRANOVA were phase 3, randomized, double-blind, placebo-controlled, parallel-group trials	Patients who were 40 to 85 years of age and had moderate to very severe COPD Primary analysis populations (1120 patients in GALATHEA and 1545 patients in TERRANOVA had baseline blood eosinophil counts of ≥220 per cubic millimeter) and in the overall study populations (1656 in GALATHEA and 2254 in TERRANOVA)	Add-on benralizumab was not associated with a lower annualized rate of COPD exacerbations than placebo among patients with moderate to very severe COPD, a history of frequent moderate or severe exacerbations, and blood eosinophil counts of 220 per cubic millimeter or greater
Bafadhel et al[4]	Post-hoc analysis of three randomised,	Patients with COPD, who had blood eosinophils	In patients with COPD treated with formoterol,

	double-blind, double-dummy, parallel-group, multicentre trials of budesonide–formoterol fixed-dose combination	collected at the screening visit Of the 4612 patients (excluding patients allocated to budesonide 160 µg alone) randomised in the three studies, 4528 had available baseline eosinophil counts and were included in the pooled analysis	blood eosinophil count predicts exacerbation risk and the clinical response to ICS
Burge et al (The ISOLDE study) [5]	Randomised, Double Blind, Placebo Controlled Study	A total of 751 men and women aged between 40 and 75 years with mean forced expiratory volume in one second (FEV(1)) 50% of predicted normal	Fluticasone propionate 500 microgram twice daily did not affect the rate of decline in FEV(1) but did produce a small increase in FEV(1). Patients on fluticasone propionate had fewer exacerbations and a slower decline in health status
Hastie et al and Couper et al (The SPIROMICS investigation) [6,7]	Prospective cohort study	3,200 participants were split into four strata (Non-smokers, Smokers without airflow obstruction, Mild/Moderate COPD, and Severe COPD)	High concentrations of sputum eosinophils were a better biomarker than high concentrations of blood eosinophils to identify a patient subgroup with more severe disease, more frequent exacerbations, and increased emphysema by quantitative computed tomography

A. Summary of GlaxoSmithKline plc.'s scientific engagement protocols and reinforcement of non-promotional nature of collaboration/sponsorship

Scientific collaboration between GlaxoSmithKline plc. and diverse groups of experts (academia, industry, regulators, public health authorities, etc) is necessary to advance key medical/scientific discussions and to contribute and share GlaxoSmithKline plc.'s broad scientific knowledge and experience in various settings.

GlaxoSmithKline plc.'s scientific engagement may take the form of a scientific workshop as a standalone meeting with the purpose of discussing or debating disease-related scientific topics. These topics are driven by healthcare professionals/other healthcare staff needs and interests. Participants are healthcare professionals/other healthcare staff or other experts who have relevant expertise and recent or current interest in the proposed topics. GlaxoSmithKline plc. staff with a defined role to play may participate and GlaxoSmithKline plc. may arrange and pay for reasonable travel and accommodation for participants of a meeting.

B. Standardisation of measurement of eosinophils

The eosinophil has a role in host defence against parasitic infections, which affect millions of individuals worldwide and the natural distribution of which goes far beyond endemic areas.[8] While the prevalence of parasitic infections may differ between populations and geographic regions, the range of peripheral blood eosinophils reported across diverse countries is generally very similar in 'healthy' individuals. Commonly, blood eosinophil levels are considered within the normal range when the percentage of eosinophils in the blood is 1–4%[9] or the absolute blood eosinophil count is 30–350 cells/μL.[10] These ranges may vary slightly between laboratories. Studies investigating the relationship between eosinophils and COPD have variably used sputum or blood and absolute or relative counts to measure eosinophil levels. While each approach has its merits, the discordance in methods makes it difficult to compare studies or conduct meta-analyses. Furthermore, neither absolute nor relative cell counts predict phenotype or determine eosinophil activation state, while the importance of the relationship between blood eosinophil count and eosinophil levels in the tissues is currently under debate. The development and use of standardised parameters, which are likely to differ dependent on the outcome of interest, could be an aid to the effective adoption of eosinophils as a biomarker in COPD, to be used in conjunction with other factors such as clinical assessment. The suitability of the eosinophil count to be incorporated into a composite clinical scoring system that includes additional clinical parameters, analogous to the QRISK approach in cardiovascular disease,[11] remains to be determined.

C. Relationship with infectious disease

Bacterial and viral respiratory infections are thought to have an important role in most COPD exacerbations.[12-15] Exacerbation phenotypes associated with bacteria, virus and sputum eosinophilia have been described, with co-existence of bacteria- and sputum eosinophil-associated exacerbations rarely observed.[16] Patients with eosinophilic exacerbations have been shown to have an altered and distinct lung microbiome profile compared with other exacerbation phenotypes that discriminated these events from bacterial exacerbations.[17] One UK study showed patients with COPD with blood eosinophils ≥2% at exacerbation and eosinophil predominance during stable disease had a lower risk of bacterial presence at exacerbation;[18] there was seasonality in the occurrence of bacterial infection at exacerbation (winter vs summer, odds ratio 4.74, p=0.011), which was most apparent in the predominantly eosinophilic patients.[18] Eosinophil counts of <2% are potential indicators of bacterial infection in acute exacerbations, implying that eosinophil count may be helpful in deciding whether to prescribe antibiotics.[19]

David B, *et al. Thorax* 2020;0:1–8. doi: 10.1136/thoraxjnl-2020-215167

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