

Methods In this 26-week, multicenter, double-blind study, patients ≥ 40 years with COPD (forced expiratory volume in 1 second [FEV₁] $\geq 40\%$ to $<80\%$ predicted and no history of exacerbations in the previous year) were randomised (1:1) to QVA149 110/50 g or SFC 50/500 g. In this post hoc analysis, we report the rate of mild, moderate or severe COPD exacerbations during 26 weeks of treatment with QVA149 or SFC.

Results Of 522 patients randomised [QVA149 (n = 258), SFC (n = 264); mean age: 63.3 years; mean post-bronchodilator FEV₁: 60.2% predicted], 82.6% completed. Rate ratio of QVA149 versus SFC [RR] of moderate or severe exacerbations was 0.80 (95% confidence interval [CI]: 0.41–1.56) and for all COPD exacerbations (mild, moderate, and severe), RR was 0.69 (95% CI: 0.44–1.07) (neither statistically significant).

Conclusion Risk of exacerbations with once-daily QVA149 was numerically, but not statistically significantly, lower than twice-daily SFC in patients with moderate-to-severe COPD and no previous history of exacerbations. The LABA/LAMA combination QVA149 has the potential to be an alternative to LABA/ICS in preventing COPD exacerbations.

REFERENCE

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Pulmonary infection

P238 ROLE OF NATURALLY-ACQUIRED IGG IN PROTECTION FROM *S. PNEUMONIAE* LUNG INFECTION

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Preventing *Streptococcus pneumoniae* lung infections will have substantial health benefits, yet existing polysaccharide vaccines are not effective against pneumonia. Identifying the mechanisms of naturally-acquired immunity to *S. pneumoniae* lung infections could indicate alternative preventative strategies. Human intravenous immunoglobulin (IVIG) preparations pooled from >1000 donors prevent respiratory infections in patients with hypogammaglobulinaemia. IVIG therefore provides a tool to investigate the naturally-acquired antibody responses to *S. pneumoniae* within a population. We have used mouse models and *in vitro* assays to assess the efficacy of IVIG for preventing *S. pneumoniae* lung infections and to identify the immunodominant target antigens.

In a mouse pneumonia model, IVIG treatment was highly protective against bacteraemia (17% septicaemia v. 100% in controls, $P = 0.015$) and partially protected against lung infection (lung CFU log₁₀ 3.7 for IVIG v. 6.3 for controls, $P = 0.041$) but not against nasopharyngeal colonisation. Depletion of phagocyte subsets demonstrated that IVIG-mediated protection required neutrophils and macrophages for lungs and blood respectively. Flow-cytometry assays demonstrated that IgG within IVIG preparations opsonised *S. pneumoniae* effectively. Importantly, IgG opsonisation was reduced by pre-treatment of bacteria with pronase to remove bacterial surface proteins but not by depletion of anti-capsular antibody. Furthermore, *in vitro* assays demonstrated that IVIG facilitated phagocytosis, growth impairment and bacterial agglutination of capsule-deficient *S. pneumoniae* mutants, in mice IVIG depleted of anti-capsular antibody remained protective against lung infection and septicaemia. These results

demonstrate that surface proteins rather than the capsule are targets for naturally-acquired adaptive immunity to *S. pneumoniae*. The potential *S. pneumoniae* protein antigen targets in IVIG were assessed using a semi-quantitative assay against 18 recombinant pneumococcal proteins. The results demonstrated significant IgG responses to the conserved pneumococcal protein antigens PhtD, PspC, PspA and PsaA. Interestingly, antibody titres to some of these antigens were reduced in sera from elderly compared to younger subjects, potentially identifying people at higher risk of *S. pneumoniae* infection. Our data demonstrate that the accepted paradigm that naturally-acquired immunity to *S. pneumoniae* depends on anti-capsular antigen is inaccurate, and instead antibody to proteins is dominant. These data will allow better evaluation of those at risk of *S. pneumoniae* infection and improved vaccine design.

P239 A ROLE FOR POLYCYSTINS IN AIRWAY MUCOCILIARY CLEARANCE?

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Polycystins 1 and 2 are the gene products of the mutated genes PKD1 and PKD2 in autosomal dominant polycystic kidney disease (ADPKD). They are localised to primary cilia in the kidney and thought to detect fluid flow. Recently patients with ADPKD have been shown to have an increased incidence of radiological findings of bronchiectasis, an abnormal dilatation of the bronchioles involving impaired mucociliary clearance (Driscoll *et al* 2009). We hypothesise that proteins from the polycystin pathway are present in respiratory epithelium and that this pathway is defective in bronchiectasis.

We demonstrate using immunofluorescent antibodies that the extracellular portion of polycystin 1 and the n terminal tail of polycystin 2 consistently localise to cilia of nasal epithelial cells from healthy individuals and that blocking polycystin 1 with antibodies can alter ciliary beat. Contrary to our hypothesis there were no differences in the distribution of these proteins in a group of patients with bronchiectasis (n = 13)

In conclusion we have shown that polycystins 1 and 2 are present in the motile cilia of the airways and may be involved in ciliary beat frequency regulation. We did not find any evidence of disruption of the polycystin proteins in a small population of patients with bronchiectasis.

P240 DOES A RELATIONSHIP EXIST BETWEEN SERUM ALBUMIN AND LACTATE WITH THE LENGTH OF STAY IN PATIENTS ADMITTED WITH COMMUNITY ACQUIRED PNEUMONIA?

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Introduction Previous studies have shown that high lactate and CURB65 scores are associated with increased mortality and morbidity in patients with community acquired pneumonia (CAP). We attempted to investigate a simple way to identify those patients who are likely to have prolonged hospital admission from CAP by using different biomarker.

Method We included first 50 patients who were diagnosed to have CAP by respiratory physicians on admission at Russell's