

**Abstract S33 Table 1** Spearman's correlation for sputum colour at all exacerbations

	Sputum Colour	
	rho	p value
FEV1%	0.26	<0.01
Sputum		
Neutrophils (count)	0.66	<0.01
Neutrophils (%)	0.62	<0.01
Macrophages (count)	-0.38	<0.01
Macrophages (%)	-0.48	<0.01
Lymphocytes (count)	-0.22	<0.05
Lymphocytes (%)	-0.23	<0.05
Blood		
Neutrophils (10 <sup>9</sup> /L)	0.20	<0.05
CRP (mg/L)	0.47	<0.01
Fibrinogen (g/L)	0.32	<0.01
Procalcitonin (ng/ml)	NS	NS
EXACT-PRO	NS	NS
CAT	NS	NS

FEV1: Forced Expiratory Volume in 1 second; CRP: C Reactive Protein; EXACT-PRO: The Exacerbations of Chronic Pulmonary Disease Tool Patient Reported Outcome; CAT: The COPD Assessment Tool; NS: No significance

**Introduction** Acute exacerbations of COPD have a major impact on patients' health related quality of life (HRQoL), and the utilisation of health care resources. Current guidelines recommend oral corticosteroids and/or antibiotics for the treatment of acute exacerbations of COPD based on patients' symptoms. With increasing bacterial resistance to antibiotics and the rising costs of COPD treatment, further research into diagnostic tools to aid the management of COPD in its stable and exacerbating states is required. Sputum colour (SC) is an accessible marker of underlying bronchial inflammation. We investigated the contribution of objective measures of SC as a component of the clinical assessment of exacerbations and relationships with symptom severity.

**Methods** Data from 36 patients with moderate to very severe COPD was assessed in this prospective observational cohort study (AERIS). There were 122 exacerbations in total over a year. Sputum and blood sampling were performed at enrolment, routine follow up and exacerbation visits. A five-point sputum colour chart was developed to objectively report the SC. Sputum samples from all visits were graded against this chart by the trained laboratory staff. Data from mild, moderate and severe exacerbations were included in the analysis.

**Results** We found a correlation between SC at exacerbations and disease severity (FEV1%) at exacerbations. SC was also related to sputum neutrophilia at exacerbations. SC was significantly associated with systemic markers such as blood neutrophilia, CRP and fibrinogen. Interestingly, we observed no statistically significant correlation between SC and Procalcitonin levels. We also found no statistically significant relationship between SC and symptom scores (CAT and EXACT-PRO) at exacerbations. However, we found a significant association between CAT and EXACT-PRO scores (rho 0.46;  $p < 0.01$ ).

**Conclusion** We observed that visual colour score of sputum at exacerbations is related to underlying airway and systemic inflammation but not to symptom scores. The use of a SC combined with other clinical and laboratory biomarkers, as part of a multicomponent diagnostic tool, may further improve its clinical utility to better guide effective exacerbation treatment. Further analysis of the full AERIS cohort will explore this.

## Pulmonary arterial hypertension: scientific advances

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### BMPR-II DEFICIENCY LEADS TO AN INCREASE IN LUNG EGG DEPOSITION, PULMONARY VASCULAR REMODELLING AND AN ABNORMAL LIVER VASCULATURE IN MICE CHRONICALLY INFECTED WITH *S. MANSONI*

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**Rationale and objectives** Schistosomiasis is the world-wide leading cause of pulmonary arterial hypertension (PAH) and is particularly prevalent in developing countries. More than 80% of patients with familial PAH in the western-world have a mutation in bone morphogenetic protein type-II receptor (BMPR-II), which is a member of the transforming growth receptor-beta (TGF- $\beta$ ) superfamily and is important in cell proliferation and differentiation. The aim of the study was to determine if mice with a heterozygous null mutation in BMPR-II are more susceptible to pulmonary vascular remodelling induced by *S. mansoni* infection, compared with wild-type littermates.

**Methods** Wild-type (BMPR-II+/+) and BMPR-II heterozygous (BMPR-II+/-) C57/BL6 mice were infected percutaneously with *S. mansoni*. Seventeen weeks post-infection right ventricular systolic pressure (RVSP), right ventricular hypertrophy (RVH), liver and lung egg counts were measured. Pulmonary vascular remodelling and liver histology were assessed by morphometry, following immunohistochemistry. Lung, liver and serum cytokines were also measured. A macrophage phagocytosis assay and *in vivo* bead assay were also performed.

**Measurements and main results** At 17 weeks post-infection there was a significant increase in pulmonary vascular remodelling associated with a significant increase in egg deposition and cytokines in the lung, in BMPR-II+/- mice. Furthermore, there was a positive correlation between lung egg deposition and pulmonary vascular wall thickness. Additionally, there was a significant dilatation of the central hepatic vein in the BMPR-II+/- infected mice compared with the BMPR-II+/+ infected mice. However, no differences in RVSP, RVH or liver egg deposition were found.

**Conclusions** This study has shown that mice deficient in BMPR-II are more susceptible to pulmonary vascular remodelling induced by *S. mansoni* which is directly correlated to an increase in egg burden in these mice. Additionally, we have shown that BMPR-II+/- mice have an abnormal liver vasculature, which may be responsible for increased egg shunting into the lungs.

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### BMP9 AND BMP10 MEDIATE CONNEXIN EXPRESSION IN ENDOTHELIAL CELLS: IMPLICATIONS FOR PAH AND HHT

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**Background** Germ-line mutations in the bone morphogenetic protein type-II receptor, BMPR-II, underlie 80% of heritable