S36 COIL TREATMENT FOR PATIENTS WITH SEVERE EMPHYSEMA AND BILATERALLY INCOMPLETE FISSURES; EFFECTIVENESS AND COMPLICATIONS AFTER ONE-YEAR FOLLOW-UP. A SINGLE-CENTRE EXPERIENCE

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Background The aim of this retrospective analysis, was to evaluate the safety and efficacy of Lung Volume Reduction with coils (LVR-Coil) treatment in a single-centre setting in patients with severe heterogeneous emphysema and bilaterally incomplete fissures

Methods In this retrospective analysis 86 patients with severe COPD (\mathcal{O}/\mathbb{Q} :40/46, age: 64 ± 7 years) and bilateral incomplete fissures were included. A total of 10 coils were unilaterally implanted in a single lobe. 28 patients received additional treatment of a contralateral lobe. At 90, 180 and 365 days' follow-up changes in pulmonary function tests, 6-Minute-Walk-Test (6MWT) and modified Medical Research Council (mMRC) dyspnea scale, as well as possible complications were recorded.

Results FEV₁ improved significantly at the 90-day follow up (p:0.001) but the improvement was not sustained at 180 and 365 days (0.71 \pm 0.21 L vs 0.76 \pm 0.23 L vs 0.73 \pm 0.22 L vs 0.69 ± 0.18 L). FEV₁ improved more than 12% (minimal clinically significant change, MCID) in 30 patients (38%). Vital Capacity improved significantly at the 90- (p < 0.001) and 180day (p:0:13) follow up but improvement was lost after 365 days. RV improved significantly at 90 days (6.1 \pm 1.4 L vs 5.5 \pm 1.3 L, p < 0.0001) and at 180 days (6.1 \pm 1.4 L vs 5.7 \pm 1.2 L, p:0.008), but the improvement was not sustained at 365 days. 6MWT improved at 90 days (247 \pm 90 m vs 278 \pm 81 m, p < 0.0001) and 180 days (247 ± 90 m vs 267 ± 90 m, p:0.02) but the improvement was lost at the 365-day follow up. Fortytwo from 71 (59%) patients improved by more than 26 m (MCID) at 90 days while 21 patients (30%) improved more than 54 m. mMRC improved significantly at 90 and 180 days. In a total of 114 procedures no periprocedural deaths occurred. Four patients died within the first 3 months after the treatment (mortality rate 3.5%). Complications observed within the first 90 days included pneumonia requiring hospital admission (28%), pneumothorax with chest tube insertion (6%), significant, persistent hemoptysis was documented in 4 cases (3.5%) and hypercapnia and hypoxemia in 4.4% and 1.75% respectively.

Conclusions LVR-coil improved PFT, 6MWT and mMRC initially but improvement was lost after 365 days. However, this improvement came at a cost of significant complications and with a 3.5% mortality rate.

S37 THE PERSISTENCE OF EOSINOPHILIC INFLAMMATION IN COPD OVER TIME – AERIS COHORT

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Introduction The importance of eosinophilic inflammation in COPD is in its ability to predict an enhanced response to treatment, such as corticosteroids. However, little is know about the persistence of higher eosinophils, or its associations with infectious aetiology during clinical stability and exacerbation. We investigated the natural history of eosinophilic inflammation over time and studied eosinophil-associated acute exacerbations of COPD and the impact of seasonality in a cohort of COPD patients.

Methods 127 subjects with moderate to very severe COPD were enrolled into the AERIS cohort (NCT01360398) and were reviewed monthly for scheduled visits and during exacerbations. Blood sampling was performed quarterly and at exacerbations. Higher blood eosinophils (BE) were defined as $\geq 2\%$. Based on frequency of higher BE over the study, subjects were divided into predominantly (PE), intermittent (IE) and rarely eosinophilic (RE) groups.

Results Blood eosinophil levels $\geq 2\%$ were prevalent at baseline (68.3%) and at exacerbations (51.1%). Over the study 57.6% of subjects had predominantly, 16.16% intermittently and 26.26% rarely $\geq 2\%$ blood eosinophils. Higher BE at enrolment was strongly associated with a predominantly high BE profile for the year (AUC 0.841 p < 0.001) and with greater odds of $\geq 2\%$ eosinophils at exacerbation (OR 9.60 p < 0.001). The odds of $\geq 2\%$ BE at exacerbation were higher in the PE group compared to the rarely group (OR 12.00, p < 0.001). A larger proportion of exacerbations were eosinophilic in the Summer than Winter (OR 2.57, p = 0.001). The odds of bacterial presence at exacerbation was higher in Winter than Summer among those in the PE group (OR 4.74, CI: 1.43; 15.71, p = 0.011), but not among those in the RE group (OR 1.15, CI: 0.29; 4.56, p = 0.838).

Conclusion Our data suggests that it is possible to stratify COPD patients by stable state blood eosinophil levels. This measure is easily accessible and provides important insights into the longitudinal inflammatory phenotype of COPD. Persistent higher blood eosinophil levels were associated with risk of bacterial infection at exacerbation, and seasonality of exacerbation. Intervention studies are required to establish clear treatment algorithms utilising this measure to stratify therapy.

Non-Tuberculous Mycobacteria: Passengers or Pathogens?

S38 CLINICAL ISOLATES OF MYCOBACTERIUM AVIUM DRIVE COLLAGENOLYTIC AND ELASTOLYTIC ACTIVITY IN MONONUCLEAR CELLS

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Background Pulmonary non-tuberculous mycobacterial (NTM) infections are increasing rapidly in the UK. The commonest pulmonary NTM infection outside the setting of cystic fibrosis lung disease is with the mycobacterium avium complex (MAC), consisting of *M. avium* and *M. intracellulare*. Patients with pulmonary MAC infection present with cavitatory lung disease or nodular bronchiectasis. Prolonged treatment is required, frequently not tolerated, and often associated with progressive lung destruction. A large body of evidence suggests the tissue damage that occurs in tuberculous lung disease is driven by host derived matrix metalloproteinases (MMPs), in particular MMP-1 and 9. The mechanisms of tissue damage in NTM infection are not understood. We hypothesised that NTM drives MMP secretion and that this drives cavitation and bronchiectasis.

Methods Monocytes isolated from healthy human volunteer blood by density centrifugation were stimulated with *M. avium* clinical isolates for 24 hours. Human monocyte-derived macrophages (MDMs) were generated from monocytes through 5–7 day incubation with GM-CSF before stimulation with four different clinical isolates of *M. avium* for up to 72 hours. mRNA expression was investigated using qRT-PCR. Protein in cell supernatants was quantified using ELISA and Luminex array techniques.

Results Stimulation with *M. avium* does not increase MMP-9 secretion in monocytes or macrophages. *M. avium* significantly increases gene expression of MMP-1 and induces MMP-1 secretion by MDMs (Figure 1). Additionally, *M. avium* drives induction of MMP-7, an elastolytic enzyme (Figure 1), and reduces the secretion of TIMP-1; the major *in vivo* inhibitor of MMP-1.

Conclusions Interestingly, unlike *Mycobacterium tuberculosis* or other chronic pulmonary pathogens such as *Pseudomonas* or *Haemophilus influenzae*, *M. avium* does not drive secretion of MMP-9 by infected mononuclear cells from healthy donors. Instead it drives functionally unopposed MMP-1, which was previously thought to be an *M. tuberculosis*-specific response. Data suggest MMP-1 and -7 may drive the destructive pulmonary pathophysiology that characterises *M. avium* infection. This will be further investigated with patient sputum samples and inflammatory cells.

S39 RISK OF NTM (NON TUBERCULOUS MYCOBACTERIUM) INFECTION IN PATIENTS ON LONG TERM PROPHYLACTIC MACROLIDE ANTIBIOTICS

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Introduction Long term prophylactic macrolide therapy is commonly used in respiratory diseases characterised by persistent airway inflammation and chronic bacterial infection. There is growing evidence that they possess immuno-regulatory and antiinflammatory effects as well as an antimicrobial action. The development of macrolide resistant bacteria, particularly NTM infection, is a concern because macrolide therapy is the primary treatment of NTM. There is little published data investigating this risk.

Methods We identified the cases, retrospectively, of all adult patients who had been given long term continuous prophylactic macrolide therapy attending the respiratory outpatients clinic until January 2016 at Russell Hall Hospital. The clinic letters were reviewed to get a clinical diagnosis and then data regarding sputum culture results were collected from the electronic reporting system. Approximately 75% of cases were reviewed.

Results 226 patient cases were reviewed. 192 (85%) were on long term Clarithromycin. 86 (38%) had a diagnosis of COPD; 133 (59%) of Non CF Bronchiectasis and 100 (44%) of Asthma. The average starting FEV1 was 1.55. The average change in FEV1 was -0.1 (range -3.22 to +1.07). Average time on macrolides was 3 years and 10 months (range 11 months to 8 years and 8 months). Out of all those who had sputum analysed, not one patient demonstrated evidence of NTM infection in their sputum up to 96 months (Figure 1).

Conclusion Our data suggests that the use of long term prophylactic macrolide therapy in the treatment of respiratory disease does not increase the risk of NTM infection and therefore should not be a concern to limit use in clinical practice. However



Abstract S38 Figure 1 MMP-1 (left) and MMP-7 (right) secretion from MDMs at 72 hours post stimulation with 4 different clinical isolates of *M. avium*