P89 AMBULATORY OXYGEN ASSESSMENTS IN COPD AND PULMONARY FIBROSIS

doi:10.1136/thoraxjnl-2011-201054c.89

K Heslop, C Stenton, C Irving. *The Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, UK*

Background Between 2006 and 2011, 161 patients were referred for formal ambulatory oxygen assessment at the Newcastle RVI. Their results have been reviewed.

Method The assessments comprised three 6-min walk tests (6MWT) supervised by a trained healthcare professional as per BTS guidelines (2006).

Test 1: On room air (RA)

Test 2: On room air with the oxygen supply switched off

Test 3: On oxygen 4 l/min via nasal cannulae

Minimum SpO_2 during exercise, distance walked and oxygen flow rate required to maintain SpO_2 above 90% were recorded together with the respiratory diagnosis and basic demographic details.

Results 18 patients were excluded as they did not de saturate on walk 1 or were unable to complete the 6MWT. 143 patients' results were analysed. 82 were male with 61 female. The two commonest clinical diagnoses were Interstitial Pulmonary Fibrosis (IPF) and COPD.

IPF patients walked on average 70 m (31%) further than COPD patients on room air. They had the greatest increase in oxygen saturation when exercising on supplemental oxygen (12%) but had the lowest improvement in walking distance (7.3%). There was no relationship between improvement in walk test distance and improvement in oxygenation in any of the subgroups.

Conclusion Further studies may be needed to explore the relative benefits of ambulatory oxygen in non-COPD patients.

P90 CYCLIN-DEPENDENT KINASES 7 AND 9 SPECIFICALLY REGULATE NEUTROPHIL TRANSCRIPTION AND THEIR INHIBITION DRIVES APOPTOSIS TO PROMOTE RESOLUTION OF INFLAMMATION

doi:10.1136/thoraxjnl-2011-201054c.90

A G Rossi, R Duffin, C Haslett, A E Leitch. *University of Edinburgh, Edinburgh, UK*

Introduction and Objectives Terminally-differentiated neutrophils are short-lived but key effector cells of the innate immune response and play a prominent role in the pathogenesis and propagation of many inflammatory diseases including interstitial lung disease. BAL neutrophilia has been correlated with poor outcome in idiopathic pulmonary fibrosis (IPF) and neutrophils are the dominant cell type in acute exacerbations of IPF as well as in diffuse alveolar damage. Non-specific cyclin-dependent kinase inhibitor drugs have previously been shown to resolve neutrophil-dominant inflammation in the murine bleomycin lung injury model an established model of IPF. Here we elucidate the mechanism by which CDK inhibitor drugs mediate neutrophil apoptosis and hence promote resolution of inflammation.

Methods We isolated peripheral blood neutrophils from healthy human donors and performed a variety of experiments including microarray, confocal microscopy and apoptosis assays (flow cytometry, fluorometric assay, DNA ladders and mitochondrial integrity assay and western blotting) to show that specific effects on neutrophil transcriptional capacity are responsible for CDK-inhibitor driven neutrophil apoptosis. Finally we show that specific CDK inhibitors drive resolution of neutrophil-dominant inflammation in the murine bleomycin lung injury model (Histology, BAL analysis).

Results CDK inhibitors drive neutrophil apoptosis. Neutrophil apoptosis is dependent on a critical balance of pro- and anti-apoptotic proteins. Functional transcriptional machinery is present in human peripheral blood neutrophils. CDKs are present in neutrophils and their activity is both demonstrated and modulated with the use of specific CDK inhibitors. Specific CDK inhibition is a successful strategy for the resolution of murine bleomycin lung injury.

Conclusion We highlight a novel mechanism that controls both neutrophil transcription and apoptosis that could be targeted by selective CDK inhibitor drugs to resolve established neutrophil-dominant inflammation.

P91 ARE CASES OF GRANULOMATOUS COMMON VARIABLE IMMUNODEFICIENCY MISDIAGNOSED AS SARCOIDOSIS IN ROUTINE CLINICAL PRACTICE?

doi:10.1136/thoraxjnl-2011-201054c.91

P Oppong, S Banik, D Derry. *Derriford Hospital, Plymouth, UK*

Introduction Common variable immunodeficiency (CVID) is a primary immune disorder characterised by impaired B cell differentiation and hypogammaglobulinaemia. It predisposes to encapsulated bacterial infections, commonly affecting the respiratory tract. 8%–20% of CVID patients have a granulomatous form. Granulomatous CVID may share clinical features with sarcoidosis, namely persistent cough, breathlessness, fatigue, fever, and arthralgia. Non caseating granulomata in lymph node biopsies and elevated angiotensin converting enzyme levels occur in both conditions. Differentiation between the two conditions is essential to allow management with immunoglobulin replacement and avoidance of excessive corticosteroids.

Method Patients with a diagnosis of "sarcoidosis" recorded in chest clinic letters between April 2009 and September 2010 were identified. Clinic letters, blood tests, histology and imaging were reviewed.

Results 175 patients with a diagnosis of sarcoidosis were identified. 80% had lymphadenopathy and 62% pulmonary involvement. Dermatological, ocular, rheumatological and other involvement was found in 19%, 17%, 16% and 9% respectively. 24% had potential features of CVID, such as recurrent chest infections, sinusitis, bronchiectasis or inflammatory bowel disease. Total globulin had been measured in 172/175 (98%) patients. 45/172 (26%) had elevated total globulin; 3/172 (2%)had low total globulin levels. Immunoglobulins had been measured in 106/175 (61%). Immunoglobulins had been measured in: 20/28 (71%) of those with recurrent sinusitis or lower respiratory tract infections; 20/25 (80%) of those with bronchiectasis; and8/8 (100%) of those with both recurrent chest infections and bronchiectasis. Four patients had persistently low IgM, two had persistently low IgA and one had persistently low IgG. No single

Abstract P89 table 1

Diagnosis	Number of patients	Average pre test SpO_2	Average lowest SpO_2 on RA	Average lowest SpO_2 on O2 4 l	Walk 1 (m)	Walk 2 (m)	Walk 3 (m)	% Increase in SpO_2 on oxygen	% Increase in walk distance on oxygen
All Patients	143	91	77	87	242	251	273	11.8	8.7
COPD	61	91	79	88	213	228	252	12.1	10.6
IPF	23	93	76	85	298	299	320	12.2	7.3