European Respiratory Society
Annual Congress 2012

Abstract Number: 5023

Publication Number: 1857

Abstract Group: 8.2. Transplantation

Keyword 1: Bronchoalveolar lavage **Keyword 2:** Lung injury **Keyword 3:** Transplantation

Title: Mechanistical differences of chronic lung allograft dysfunction phenotypes in lung transplantation

Ms. Monika I. 18467 Suwara m.i.suwara@ncl.ac.uk [1], Dr. Bart M. 18468 Vanaudenaerde Bart.Vanaudenaerde@med.kuleuven.be [1,2], Dr. Stijn E. 18489 Verleden Stijn.verleden@med.kuleuven.be [2], Dr. Lee A. 18509 Borthwick lee.borthwick@newcastle.ac.uk [1], Dr. Robin 18510 Vos Robin.vos@uzleuven.be [2], Dr. Nicola J. 18511 Green n.green@newcastle.ac.uk MD [1], Dr. Chris 18517 Ward chris.ward@newcastle.ac.uk [1], Dr. Dirk E. 18518 Van Raemdonck Dirk.vanraemdonck@uzleuven.be [2], Prof. Paul A. 18521 Corris paul.corris@newcastle.ac.uk MD [1], Prof. Derek A. 18532 Mann derek.mann@newcastle.ac.uk [3], Prof. Geert M. 18543 Verleden Geert.verlden@uzleuven.be [2] and Prof. Andrew J. 18556 Fisher a.j.fisher@newcastle.ac.uk MD [1,3]. [1] Lung Immunology Group, Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, United Kingdom, NE2 4HH ; [2] Leuven Lung Transplantation Unit, Katholieke Universiteit Leuven and University Hospital Gasthuisberg, Leuven, Belgium and [3] Fibrosis Research Group, Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, United Kingdom, NE2 4HH .

Body: Purpose: The neomacrolide azithromycin, is now widely used in the treatment of Bronchiolitis Oblierans Syndrome after lung transplantation. However, only a proportion of patients respond by improving their lung function. This study aimed to evaluate differences in airway microenvironment between azithromycin responsive (>10% improvement in FEV_1) and azithromycin resistant BOS patients. Methods: Bronchoalveolar lavage (BAL) from recipients identified as stable n=10 (control), azithromycin responsive n=10 and azithromycin resistant n=10 were evaluated for cell differential, IL-1α, IL-1β, IL-6, IL-8, TNF-α proteins. BAL was then added to primary bronchial epithelial cells (PBEC) and tested for viability by XTT assay. Results: BAL neutrophilia (%) was increased in responders (56% p<0.0001) and non-responders (52.9% p<0.0001) compared to the control (0.8%). IL-1α, IL-1β, IL-6, IL-8, TNF-α were increased in both groups (all proteins <0.05) compared to the control. The levels of IL-1α, IL-1b and TNFa showed increasing trend in responders compared to non-responders. PBEC viability in response to BAL was reduced in non-responders (p=0.012) but not in the responders group (p=0.64). Moreover, there was a negative correlation between PBEC viability and IL-1α (p=0.042), IL-8 (p=0.0017), TNFα (p=0.039), IL-1β (p=0.045) and IL-6 (p=0.0453) concentrations. Conclusions: Unlike in responders, where azithromycin blocks IL-17 T cell mediated neutrophilia, azithromycin resistant phenotype is associated with epithelial damage, inducing IL-1α, TNFα and IL-1β release. This suggests anti-IL-1/TNFα therapies could be considered for BOS patients who develop an azithromycin resistant phenotype.