European Respiratory Society
Annual Congress 2012

Abstract Number: 1232

Publication Number: P1784

Abstract Group: 5.1. Airway Pharmacology and Treatment

Keyword 1: Anti-inflammatory **Keyword 2:** Bronchoalveolar lavage **Keyword 3:** Asthma - mechanism

Title: Effect of corticosteroids on lymphocytes from severe asthma patients

Dr. Manminder 9062 Kaur manminder.kaur@manchester.ac.uk [1], Dr. Sophie 9063 Reynolds sophie.reynolds@manchester.ac.uk [1], Dr. Lucy 9064 Smyth l.smyth@salford.ac.uk [1], Dr. Simon 9065 Hall simon.r.hall@gsk.com [2], Dr. Karen 9066 Simpson karen.d.simpson@gsk.com [2], Mr. Steven 9067 Fox steven.m.fox@gsk.com [3] and Prof. Dave 9068 Singh dsingh@meu.org.uk [1]. [1] NIHR Translational Research Facility, University of Manchester, United Kingdom, M23 9LT ; [2] Refractory Respiratory Inflammation DPU, Respiratory TAU, GSK Medicine Research Centre, Stevenage, United Kingdom and [3] Statistical Consulting, GSK Medicine Research Centre, Stevenage, United Kingdom .

Body: Patients with severe asthma have persistent airway inflammation that responds poorly to corticosteroids. Lymphocytes play a central role in disease pathogenesis; we hypothesized that lung lymphocytes from patients with severe asthma are insensitive to the effects of corticosteroids. We investigated suppression of lung lymphocyte cytokine production by corticosteroids in healthy non smokers (HNS) and patients with mild asthma (MA) and severe asthma (SA). Patients with MA (n=11), SA (n=11) and HNS controls (n=7) underwent bronchoscopy. Cells obtained by lavage were treated with and without dexamethasone (0.01, 0.1 & 1μM) for 1 h prior to lymphocyte stimulation with CD 2/3/28 activation beads for 24 h. Supernatants were assayed for IL-2 and IFN-γ by ELISA and IL-13 and IL-17 by luminex. Mean maximal inhibition data are shown in table 1. Cytokine release was inhibited by dexamethasone in a dose dependent manner. Dexamethasone had a reduced effect on all cytokines in SA compared to HNS or MA. Dexamethasone had the greatest effect on the Th2 cytokine IL-13, but had a lower effect on Th1 and Th17 cytokines

Cytokine	maximum % inhibition		
	HNS	MA	SA
IL-17	54.5	58.0*	49.1
IL-13	90.9***	92.4***	70.4
IL-2	63.1**	66.3***	51.9
INFγ	63.0	65.8*	56.7

Maximal cytokine inhibition achieved by dexamethasone * denotes significantly higher inhibition compared to severe asthma patients. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Cytokine production from SA BAL lymphocytes show corticosteroid insensitivity compared to cells from controls. This phenomenon may be important in the poor clinical response often observed with corticosteroids. Furthermore, corticosteroids have a reduced effect on Th1 and Th17 cytokines, which may predominate in SA.