(n=6 healthy, 6 asthmatic): Compared to control, healthy ALI suppressed constitutive HLMC histamine release by 39±5% (p=0.01), but asthmatic ALI did not (mean 19±11% suppression, p=0.07). There was a significant difference between healthy compared to asthmatic ALI (p=0.01). Healthy and asthmatic ALI suppressed IgE-dependent histamine release by 55±4%, p=0.001 and 48±1%, p=0.001, respectively.

Conclusions BEAS-2B and healthy airway epithelial cells suppress constitutive and IgE-dependent HLMC histamine secretion when separated by Transwell membranes. Asthmatic ALI cultures do not suppress constitutive HLMC histamine secretion, but do suppress IgE-dependent secretion. These results suggest that the normal regulation of this process is by a secreted, probably labile factor(s), which may be partially deficient in asthma. Isolation and manipulation of this factor may have interesting therapeutic potential.

S34 EFFECTS OF THE CYCLIN-DEPENDENT KINASE INHIBITOR R-ROSCOVITINE ON EOSINOPHIL SURVIVAL AND CLEARANCE

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Background Eosinophils are pro-inflammatory cells implicated in the pathogenesis of asthma and atopy. Apoptosis has been proposed as a potential mechanism underlying the resolution of eosinophilic inflammation and studies have indicated the ability of interventions that induce human eosinophil apoptosis to promote the resolution of eosinophilic inflammation. Recently, the cyclin-dependent kinase (CDK) inhibitor R-roscovitine was shown to enhance neutrophil apoptosis and promote the resolution of neutrophilic inflammation.

Aim The purpose of this study was to examine the expression of CDKs in human blood eosinophils, the effects of R-roscovitine on eosinophil survival and phagocytosis *in vitro* and determine whether R-roscovitine could influence eosinophilic lung inflammation *in vivo*.

Methods Eosinophils were isolated from human peripheral blood and the effects of R-roscovitine on apoptosis, degranulation and phagocytic uptake examined *in vitro*. The effects of R-roscovitine on eosinophilic lung inflammation *in vivo* were also assessed using an ovalbumin mouse model.

Results Our data demonstrate that human eosinophils express five targets for R-roscovitine: CDK1, −2, −5, −7 and −9. R-roscovitine induced eosinophil apoptosis in a time- and concentration-dependent manner but also accelerated transition to secondary necrosis as assessed by light and electron microscopy, flow cytometry and caspase activation. In addition, we report that the pro-apoptotic effect of R-roscovitine is associated with suppression of Mcl-1L expression and that the apoptotic eosinophils are phagocytosed by human monocyte derived macrophages. R-roscovitine also induced apoptosis in mouse eosinophils purified from the bone-marrow, spleen and peripheral blood. Despite this, R-roscovitine did not modulate the tissue and lumen eosinophilia characteristic of the ovalbumin mouse model of airway eosinophilia.

Conclusions These data demonstrate that R-roscovitine is capable of inducing rapid apoptosis and secondary necrosis in human eosinophils but does not affect the onset or resolution of eosinophilic airway inflammation *in vivo*.

How should we be investigating suspected lung cancer?

S35 A RANDOMISED CONTROLLED TRIAL COMPARING COMBINED EBUS/EUS FOLLOWED BY SURGICAL STAGING VERSUS SURGICAL STAGING ALONE IN NON-SMALL CELL LUNG CANCER: THE ASTER STUDY

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Background For many years the standard approach to staging of the mediastinum in non-small cell lung cancer (NSCLC) has been surgical using cervical mediastinoscopy, left anterior mediastinotomy or video assisted thoracoscopic surgery (VATS). More recently endobronchial ultrasound (EBUS) and endoscopic ultrasound (EUS) have been reported. We conducted a randomised phase III trial to compare surgical staging versus endoscopic staging. The primary endpoint was detection of mediastinal nodal metastasis (N2/3); secondary endpoints were complication and futile thoracotomy rates.

Methods Consecutive patients with potentially resectable (suspected) NSCLC in whom invasive mediastinal staging was indicated based on CT or PET-CT findings were randomly assigned to either Arm A, surgical staging or Arm B, combined EBUS/EUS (followed by surgical staging if endoscopic findings were negative for malignancy). Surgical staging involved mediastinoscopy and/or mediastinotomy and/or VATS. Subsequently, in the absence of mediastinal disease, thoracotomy with systematic lymph node sampling was performed. 240 pts were required to show a 20% increase in sensitivity (power 80% and α=0.05) to detect mediastinal nodal disease with a prevalence of 50%.

Results 118 patients were randomised to Arm A and 123 to Arm B. The sensitivity for detection of mediastinal metastases by surgical staging in Arm A was 80% (95% CI, 68 to 89) vs 94% (95% CI, 85 to 98) for endoscopic (± surgical) staging in Arm B (p=0.04). Nodal metastases were found in 41 (35%) of surgically staged patients in Arm A and 62 patients (50%) (56 by EBUS/EUS + 6 by subsequent surgical staging) in Arm B (p=0.019). Overall, the prevalence of mediastinal disease in each arm was similar (p=0.24). Thoracotomy was considered futile in 21 (18%) in those staged in Arm A vs 8 patients (7%) in Arm B (p=0.009). Complication rate was similar in both arms (6 vs 7 patients, p=0.8); however, 12 of 13 complications were due to surgical staging procedures.

Conclusions Mediastinal staging for NSCLC should commence with combined EBUS/EUS (followed by surgical staging if endoscopic findings are negative for malignancy) as this improves the detection of nodal metastases and reduces futile thoracotomies compared to surgical staging alone.

S36 CHECK NOVEL *IN VIVO* REAL TIME IMAGING OF THE BRONCHIAL MUCOSA USING AN ENDO-CYTOSCOPY

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Objectives We investigated the capabilities of an Endo-Cytoscopy system (ECS) that enables microscopic imaging of the