S40 OPTIMISATION OF A HUMAN BCG CHALLENGE MODEL

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Introduction Tuberculosis remains a significant global disease burden with an estimated 9 million new cases and 1.5 million deaths in 2013. BCG continues to be the only licensed TB vaccine, however it is poorly efficacious against adult pulmonary TB disease and there is a desperate need for a better vaccine to provide greater and more consistent protection. Development of such a vaccine has been hampered by the lack of reliable and validated correlates of protection. A human mycobacterial challenge model, using BCG as a surrogate for Mycobacterium tuberculosis challenge would facilitate improved vaccine selection for progression into future field efficacy testing. In this study we evaluate the effect of two BCG strains at two doses to optimise this model.

Methods 40 healthy BCG-naïve adults were assigned to one of four groups to receive intradermal BCG SSI or BCG Tice at standard or high dose. Two weeks following BCG challenge, skin biopsy from the BCG challenge site was performed. Volunteers were followed up for 28 days from challenge to assess reactogenicity and ensure no safety concerns. BCG mycobacterial load was quantified by solid culture and quantitative PCR.

Results BCG, regardless of strain or dose, was tolerated well and reactogenicity was similar between groups. BCG strain did not significantly affect BCG recovery from skin biopsy, however there was significantly greater recovery from the high dose challenge groups compared with the standard dose. Consistent with previous findings there was an inverse correlation between ex-vivo IFN-γ ELISpot responses to PPD and amount of BCG recovered from the skin biopsies.

Conclusions High dose BCG challenge regardless of strain used, significantly improves the sensitivity of this human mycobacterial challenge model. Practical reasons favour the use of BCG SSI over BCG Tice, as BCG SSI is licensed for intradermal administration in the UK and preparation is more straightforward with less product wastage or variability in dose between vials of BCG SSI. Looking ahead we plan to use this optimised BCG SSI challenge model to evaluate novel TB vaccine candidates in order to improve the selection of which vaccines then progress to expensive field efficacy trials.

IPF diagnosis and prognosis and biomarkers

S41 INTERSTITIAL LUNG DISEASE MDT PRESENTATIONS POST VATS LUNG BIOPSY CHANGES THE ORIGINAL HISTOLOGICAL DIAGNOSIS IN 30%

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Introduction NICE recommends MDT presentation of all patients with suspected ILD. Any benefit of representation post VATS biopsy is unknown.

Methods Our hospital (BHH) provides a regional service for thoracic surgery. All VATS lung biopsies for interstitial lung diseases carried out in 2013 were identified. They were presented post surgery at the ILD MDT where their history, physiology, immunology, original CTs and pathology were reviewed by a fully constituted MDT team including ILD specialist histopathologists, radiologists, clinicians and CNS'. The MDT diagnosis was compared with the original specialist pulmonary histopathology report.

Results 71 patients had qualifying VATS biopsies in 2013. In 21 patients (30%) the MDT diagnosis differed significantly from the original histology report. In a further 12 patients the MDT altered a probable to a definite diagnosis. In 3 patients the MDT reduced the confidence of the histological diagnosis. Hypersensitivity pneumonitis was diagnosed much more confidently by the MDT than the histologist alone. The interpretation of necrotising granuloma was a particular problem from the histology alone; the MDT confirming diagnoses of rheumatoid lung, sarcoidosis or no ILD. It was also possible to achieve specific diagnoses in 5 patients whose biopsies were reported as non-specific fibrosis; NSIP (2), UIP (2), HP (1), and in 2 in whom the original report was resolving pneumonia (both HP). In 10/21 patients there was sufficient evidence to classify the UIP as IPF (7), collagen vascular disease UIP (1), chronic HP UIP (1), and drug induced UIP (1). There was often insufficient exposure and immunological data for the MDT to further characterise UIP and NSIP.

Conclusions The post biopsy MDT changed the diagnosis in 30% compared with the histology report alone. An ILD MDT review with the combination of radiology and pathology and an expert team provided significant extra benefit in terms of a precise diagnosis in patients biopsied with interstitial lung disease in whom the referring physician thought that a diagnosis was not possible without a biopsy. This is not surprising as the histologist is limited by sampling, the radiologist by resolution, and both by the lack of physiology, exposure history and immunology.

S42 TRANSBRONCHIAL CRYOBIOPSIES IN THE DIAGNOSIS OF INTERSTITIAL LUNG DISEASES- FIRST UK EXPERIENCE

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Introduction Despite radiological advancements histology is often needed in the diagnosis of Interstitial Lung Disease (ILD). In order to obtain lung biopsies of adequate size and quality patients traditionally undergo a surgical lung biopsy associated with a mean hospital stay of 3.5 days and a complication rate of up to 28%.[1]

We are the first UK centre to have set up a minimally invasive, day case transbronchial cryobiopsy service in the diagnosis of ILDs.

Aims To establish a transbronchial cryobiopsy service for ILDs and assess complication rates and diagnostic yield.

Methods Patients were selected following discussion at the Interstitial Lung Disease Multidisciplinary Team meeting. Only patients in whom significant diagnostic doubt remained after thorough clinic-radiological work up were considered.