Molecular Science, Barts and The London School of Medicine & Dentistry, London, UK; [2]Division of Infection & Immunity, UCL, London, UK; [3]Department of Virology, Barts and The London NHS Trust, London, UK

Introduction Stopping-rules now exist for Pegylated Interferon-α (PEG-IFNα) treated Chronic Hepatitis B (CHB) patients. Despite the utility of such strategies, the immunological mechanisms that drive HBV DNA and HBsAg decline remain poorly understood. Recent data have identified changes in a subset of NK cells in HBeAg negative disease, which may determine treatment response. However, HBeAg positive disease responds more favourably to PEG-IFNα; here we report on a longitudinal analysis of changes in the immune profile in this cohort, to define the effects of PEG-IFNα on innate immunity.

Methods PBMCs from a cohort of 17 HBeAg positive patients followed longitudinally at 3 monthly intervals pre, during and post PEG-IFNα therapy were utilised. Phenotypic analysis of NK cells was performed by multicolour flow cytometry. Changes in the immune responses were correlated with simultaneous measurements of ALT, HBV DNA and quantitative HBsAg levels (Abbott ARCHITECT).

Results PEG-IFNα increased $CD56^{bright}$ NK cells by fourfold (mean fold change; MFC 3.7, p=0.0001). This was parallelled by the activation and proliferation of this subset, as marked by HLA-DR and Ki67 expression respectively (MFC 1.5 and 2.3, p=0.009 and p=0.0001 respectively). This increase was more marked at 48 weeks treatment, correlating with a nadir of HBV DNA and HBsAg. The activating (NKG2C and NKp30) and inhibitory (NKG2A) receptors were also analysed in this population. A twofold increase in NKp30 expression (MFC 2.27, p=0.04) was seen which was maximal at 48 weeks, while no significant change was noted for NKG2A and NKG2C. There was a twofold up-regulation of TRAIL expression on $CD56^{bright}$ NK cells, which temporally correlated with ALT levels, (MFC 1.8, p=0.0001), this effect was most dramatic at 24 weeks of therapy and sustained to 48 weeks.

Conclusion PEG-IFNα therapy in this cohort enhances and activates $CD56^{bright}$ NK cells. Similarly, TRAIL and NKp30 expression is augmented and sustained throughout treatment and all these effects are maximal at 48 weeks. The restorative innate immune changes begin early and increase throughout therapy in all patients. Thus, 48 weeks therapy may provide the optimal immunological conditions to introduce an oral-antiviral to achieve disease control in PEG-IFNα non-responders.

Competing interests None declared.

PM0-178 THE SIGNIFICANCE OF VIRAL AND SEROLOGICAL MARKERS IN PREDICTING LIVER DISEASE SEVERITY IN E-AG NEGATIVE HEPATITIS B VIRUS INFECTION

doi:10.1136/gutjnl-2012-302514b.178

V K Audimoolam,* I Carey, M Bruce, M Horner, S Abid, K Agarwal, P Harrison. *Institute of Liver studies, King's College Hospital, London, UK*

Introduction In hepatitis B virus (HBV) infection, seroconversion to HBeAg negative/eAb positive accompanied by low serum HBV-DNA (persistently ≤2000 IU/ml) and low quantitative HBsAg (qHBsAg) signifies transition to an inactive carrier (IC) state. However, in patients with raised serum HBV DNA differentiating those with inactive disease (ID) from eAg negative chronic HBV (eAg-CHB) currently relies on liver biopsy. This study investigated whether serological (qHBsAg) and virological markers (serum HBV DNA) can predict disease severity in patients with eAg negative HBV across a range of HBV genotypes.

Methods Liver biopsy was performed in 364 consecutive eAg negative patients (median age 38 years, 212 males) who had HBV DNA >1000 IU/ml on at least two clinic visits over 6–18 months. ALT [IU/l], qHBsAg [Abbott ARCHTECT®], HBV genotype [direct sequencing] and HBV DNA [real-time TaqMan PCR] were evaluated at the time of liver biopsy.

Results Based on the liver histology findings, 217 had ID (an Ishak fibrosis score of F0-1) and 147 had eAg-CHB (≥F2). HBV genotype-E predominated (50%) followed by D (16%), A (15%), B (10%) and C (9%). Overall qHBsAg levels were higher in ID than eAg-CHB patients (median 3.84 vs 3.7 $\log_{10}$ IU/ml; p=0.02). Assessment by individual genotype demonstrated that qHBsAg levels remained higher in ID than eAg-CHB in genotypes A and E (4.01 vs 3.73 and 3.95 vs 3.8 $\log_{10}$ IU/ml; both p<0.05). However, in genotype B qHBsAg levels correlated with the severity of fibrosis [2.81 in F0-1 vs 3.34 in F≥2; p<0.01]. The qHBsAg levels were similar in ID and eAg-CHB in genotypes C and D. HBV genotype had no impact on the severity of liver fibrosis (p=0.16). Patients with eAg-CHB compared to those with ID had raised ALT [81% vs 65 %; p<0.01], higher HBV DNA (3.99 vs 3.6 $\log_{10}$ IU/ml; p<0.01), older age (39 vs 36 years; p<0.01) and more were males (68% vs 51%; p<0.01).

Conclusion In eAg negative patients with HBV DNA >1000 IU/ml, the relationship between qHBsAg levels and liver fibrosis was genotype specific. Even allowing for HBV genotype, the absolute qHBsAg level was a poor discriminator of clinically significant liver fibrosis.

Competing interests V Audimoolam: None declared, I Carey Grant/Research Support from: Gilead, M Bruce: None declared, M Horner: None declared, S Abid: None declared, K Agarwal: None declared, P Harrison: None declared.

PM0-179 ROLE OF ANTIVIRALS IN ACUTE HEPATITIS B INFECTION; A 5-YEAR EXPERIENCE AT A LIVER TRANSPLANT CENTRE

doi:10.1136/gutjnl-2012-302514b.179

[1]V S Hegade,* [1]N Mohammed, [1]M Aldersley, [2]S Riyaz. *[1]Liver Transplant Unit, St James Hospital, Leeds, UK; [2]Gastroenterology and Hepatology Department, Barnsley Hospitals NHS Foundation Trust, Barnsley, UK*

Introduction Acute hepatitis B in adults is successfully cleared in more than 95% of immunocompetent patients. A small proportion of patients develop fulminant hepatitis. Few controlled trials[1 2] have evaluated the role of antivirals in patients with acute severe hepatitis B (AS-HBV). The aim of this study was to report our experience of AS-HBV management at a tertiary centre.

Methods We retrospectively identified all patients between August 2006 and August 2011, referred to our centre with acute HBV infection (diagnosis based on recent onset of jaundice, detection of serum HBsAg and IgM HBcAb). 1-Year data following the diagnosis was collected using medical and electronic records. We identified all patients meeting at least one of the three criteria for AS-HBV[1] that is, INR ≥1.6, serum bilirubin ≥170 μmol/l and hepatic encephalopathy. Patients with other causes of acute liver injury such as alcohol and drugs were excluded.

Results 98 patients with acute HBV were identified during the study period. Of these, 64 (65.3%) patients had milder episodes. Thirty-four patients (34.7%; mean age 32, 50% females) had evidence of AS-HBV. Out of these, 17 (50%) patients had a bilirubin ≥170 μmol/l and 3 (8.8%) patients had INR ≥1.6 while 14 (41%) patients had both. None of the AS-HBV patients had evidence of encephlopathy. All patients had normal ultrasound scans of the liver and negative non-invasive liver screen, at the time of diagnosis. Of the 34 patients with AS-HBV, 20 (59%) patients received treatment with antiviral drugs, 55% with newer agents (Entecavir or Tenofovir) and 45% with older agents (Lamivudine or Adefovir). None of the patients developed any side effects to antiviral drugs. The remaining 14 (41%) patients with AS- HBV received supportive care