

pathogenesis of HCV-related HCC in relation to tumour progression and angiogenesis.

**Method** 30 patients with HCV-related cirrhosis (15 patients with histologically-proven HCC and 15 patients without HCC) and 15 healthy subjects were enrolled in the study. The severity of liver disease was assessed according to Child-Pugh classification and the Model for End Stage Liver Disease (MELD) score. The tumour stage was classified using the Cancer of the Liver Italian Program (CLIP) scoring system. Histological tumour grading was performed according to the Edmondson and Steiner's criteria and the surrounding liver tissue was examined for assessing the modified histological activity index (HAI), presence of cirrhosis and the grade of steatosis. Expressions of MIP-1 $\alpha$ /CCL3, CD68 [a marker for tumour-associated macrophages (TAM)] and CD105 (Endoglin) [for tumour angiogenesis and determination of microvessel density (MVD)] were studied in HCC and adjacent non-neoplastic liver tissues by immunohistochemistry. Serum MIP-1 $\alpha$ /CCL3 levels were measured using solid phase sandwich enzyme linked immunosorbant assay kit. The sensitivity and specificity of serum levels of MIP-1 $\alpha$ /CCL3 as markers for diagnosis of HCC have been assessed by plotting a receiver-operating characteristic (ROC) curve.

**Results** Patients with HCV-related HCCs showed significant increases in MIP-1 $\alpha$ /CCL3 expression, CD68 $^+$  TAM count and CD105 $^+$  MVD in tumour tissues compared with adjacent non-neoplastic liver tissues ( $p=0.0004$ ,  $p<0.001$  and  $p<0.001$  respectively). Serum MIP-1 $\alpha$ /CCL3 levels were significantly higher in patients with and without HCC than in healthy subjects and in HCC patients than in patients without HCC ( $p<0.001$ ). By plotting a ROC curve, the sensitivity and specificity of serum MIP-1 $\alpha$ /CCL3 in discriminating cirrhotic patients with and without HCC were found to be 100% and 93.3% respectively at a cut-off value of 17.5 pg/ml. The MIP-1 $\alpha$ /CCL3 expression in HCC tissues showed positive correlations with serum MIP-1 $\alpha$ /CCL3 levels; tumour size, stage, histopathological grade; serum  $\alpha$ -fetoprotein levels and CD68 $^+$  TAM count and CD105 $^+$  MVD in HCCs ( $p<0.05$ ). Also, CD68 $^+$  TAM count and CD105 $^+$  MVD in HCC tissues were positively correlated ( $p<0.001$ ). On the other hand, no correlations were found between MIP-1 $\alpha$ /CCL3 expression, CD68 $^+$  TAM count and CD105 $^+$  MVD in HCCs on one hand and serum levels of aminotransferases, Child-Pugh score, MELD score and HAI and steatosis grade in the surrounding liver tissue ( $p>0.05$ ).

**Conclusion** The CC chemokine, MIP-1 $\alpha$ /CCL3, may play an important role in the pathogenesis and progression of HCC in HCV-related liver disease, possibly, through migration of macrophages to tumour microenvironment and enhancement of angiogenesis. MIP-1 $\alpha$ /CCL3 may also serve as a potential serum biological marker and a useful therapeutic target for HCC.

P53

### THE COST-EFFECTIVENESS OF HCV ANTIVIRAL TREATMENT FOR INJECTING DRUG USER POPULATIONS

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**Introduction** Injecting drug use is the main risk of HCV transmission in most developed countries. Hepatitis C virus antiviral treatment (peginterferon + ribavirin) is cost-effective for patients with no reinfection risk. Concerns about reinfection and non-compliance may discourage clinicians from treating injecting drug users (IDUs), despite the potential use of treatment as prevention in this population.

**Aim** Using a cost-utility analysis, we examined the cost-effectiveness of providing antiviral treatment for IDUs as compared to treating ex/non-IDUs or no treatment.

**Method** A dynamic model of hepatitis C transmission and disease progression among IDUs and ex-/non-IDUs was developed, incorporating: a fixed number of antiviral treatments allocated at the mild HCV stage over 10 years, no retreatment after initial treatment failure, and potential re-infection for cured IDUs. We performed a probabilistic cost-utility analysis estimating long-term costs and outcomes (measured in QALYs) and calculating the incremental cost-effectiveness ratio (ICER) to determine the cost-effectiveness of treating IDUs as compared to treating ex/non-IDUs or no treatment for three baseline IDU HCV prevalence scenarios (20%, 40%, and 60%).

**Results** Antiviral treatment of IDUs is the most cost-effective option in both the 20% and 40% baseline chronic prevalence settings, with ICERs as compared to no treatment (best supportive care) of £521 and £2539 per QALY saved, respectively. Treatment of ex/non-IDUs is dominated in these scenarios. At 60% baseline prevalence, treatment of ex/non-IDUs or IDUs is roughly equally cost-effective; treating ex/non-IDUs is more likely to be the most cost-effective option (with an ICER as compared to no treatment of £6803), and treating IDUs is dominated due to the high re-infection at this prevalence. A sensitivity analysis indicates that these rankings hold even when IDU SVR rates as compared to ex/non-IDUs are halved.

**Conclusion** Despite the possibility of re-infection, the model projections suggest that providing antiviral treatment to IDUs is the most cost-effective policy option in chronic prevalence scenarios <60%. Further research on how HCV treatment for injectors can be scaled up, and its impact on prevalence is warranted.

P54

### CHASE-B (CHINESE HEPATITIS AWARENESS, SURVEILLANCE AND EDUCATION): A PILOT OF TARGETED CASE FINDING FOR HEPATITIS B VIRUS (HBV) IN THE BRITISH-CHINESE COMMUNITY

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**Introduction** Chronic HBV (cHBV) is a frequent cause of cirrhosis and liver cancer. Many infected individuals are unaware of their condition. Migrants from countries with high prevalence of cHBV, such as China and the Far East (seroprevalence 7–12%), are a high risk group for cHBV. Targeted HBV screening and vaccination is recommended by the AASLD<sup>1</sup> and the European Liver Patients Association (ELPA)<sup>2</sup> in high risk groups including subjects born in endemic areas. However, there are no current UK guidelines.

**Aim** To apply AASLD and ELPA recommendations to British-Chinese community of North East (NE) England.

**Method** Members of the NE Chinese community were invited to attend screening sessions at the Newcastle Chinese Healthy Living Centre [charity registration no. 1125227]. Dry blood spots were obtained by finger prick and tested for HBsAg and HBcAb (Abbott ARCHITECT). HBsAg positive individuals were advised to undergo confirmatory testing and be referred for specialist assessment.

**Results** 575 subjects were screened in 10 sessions (mean age  $49\pm17$  years, 61% female). 53 (9%) were HBsAg positive (48% female) indicating cHBV. 10 of these reported being previously diagnosed with HBV, but were not under follow-up. The prevalence of HBsAg positivity was 7.5% when previously diagnosed individuals

## BASL abstracts

were excluded. 80 (14%) subjects had past infection with HBV (HBsAg negative, HBcAb positive). Individuals with past HBV were significantly older than HBsAg positive and HBsAg, HBcAb negative subjects ( $p < 0.001$ ). The prevalence of HBsAg positivity was highest in subjects born in Vietnam (17.4%, 4/23), followed by China (11.5%, 24/157), Hong Kong (8.3%, 18/288), the UK (6.7%, 5/75) and other (6.2%, 2/32). Only 12% of subjects reported previous vaccination against HBV. To date, 25 of the HBsAg positive individuals have been seen in our clinic. 1 was HBeAg positive (immunotolerant) and 24 were HBeAg negative. Of these, 3 have active disease (including 1 cirrhotic) and have been started on treatment. 14 have inactive cHBV and 7 are undergoing observation to determine disease activity. No cases of co-infection with HCV, HIV or Delta were found.

**Conclusion** 1. Undiagnosed cHBV is common in the British-Chinese community of NE England, including subjects born in the UK. 2. A proportion had active cHBV requiring treatment. 3. If these results were applied to the entire UK British-Chinese population targeted screening should lead to approximately 32 250 newly diagnosed cases of cHBV. 4. These results provide evidence for a UK HBV screening and vaccination program for the British-Chinese community.

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P55

### HCV QUASISPECIES ANALYSIS OF PATIENTS WITH GENOTYPE 3 HCV WHO RELAPSE SUGGEST TWO DIFFERENT MECHANISMS OF RELAPSE

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**Introduction** Patients persistently infected with genotype 3 HCV are more likely to have a sustained viral response (SVR) to interferon and ribavirin therapy than patients infected with genotype 1. However many patients with advanced fibrosis infected with genotype 3 HCV relapse following therapy. The mechanisms underlying relapse are not known.

**Aim** To examine the speed of relapse and compare quasispecies prior to and immediately following relapse.

**Method** 30 chronically infected patients with advanced fibrosis (fibrosis score  $> F3/6$ ) were treated for 24–48 weeks with Peg IFN  $\alpha$  2a and ribavirin. Plasma samples were taken pre-treatment, during treatment and weekly post treatment. The HCV quasispecies in the pre-treatment sample and the first HCV-RNA positive post-treatment samples of the relapsed patients were assessed.

**Results** All of the patients responded with loss of virus on treatment. 18 had a sustained viral response and 12 patients relapsed post-treatment. All of the patients that relapsed did so within 4–6 weeks of treatment cessation.

HCV-RNA was extracted from the pre- and post samples of relapsed patients. 10–15 clones from both samples were successfully prepared and sequenced over the E2 region, including the HVR1, 2 and 3 regions and the PKR-eIF2 $\alpha$  region in five patients. Construction of phylogenetic trees showed that in two patients the quasispecies that emerged post-treatment were similar to those seen pre-treatment but in three patients a dramatic shift in populations occurred.

**Conclusion** Relapse post therapy is very rapid and two distinct patterns of relapse were seen. These data suggest that there may be different mechanisms of relapse following treatment withdrawal in patients with genotype 3 HCV.

P56

### WHAT IS THE BEST METHOD OF CASE FINDING FOR CHRONIC VIRAL HEPATITIS IN MIGRANT COMMUNITIES?

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**Introduction** The prevalence of chronic viral hepatitis in people born in Pakistan living in the UK is 5% (2.7% Hepatitis C Virus (HCV) and 1.8% Hepatitis B Virus (HBV). Studies from the HPA show an increased risk of end stage liver disease from HCV in people from Pakistan living in the UK. Screening migrants from high prevalence regions (>2%) for HBV is cost effective if screening of 35% of a population is achieved. Given that screening for viral hepatitis in migrants will reduce morbidity, mortality and onward transmission of chronic viral hepatitis, the outstanding question is how should this be done?

**Aim** The aim of this observational study was to evaluate community, and general practice (GP) based approaches to screening migrants for viral hepatitis.

**Method** We distributed 5000 testing cards in Mosques, following an awareness campaign, encouraging people from Pakistan to attend their GP surgery for viral hepatitis testing. In primary care practices we studied two approaches targeting registered Pakistani/British Pakistani patients: an opportunistic approach, whereby patients attending the practice were offered screening for HBV and HCV, and an 'opt out' approach, where patients were contacted by letter and invited to opt out of screening. Those who did not 'opt out' were telephoned and asked to attend screening clinics.

**Results** 5000 leaflets were distributed to Mosques but no patients presented to their GP for testing. In the primary care study there were 1163 Pakistani/British Pakistani patients in the 'opportunistic' arm. Of these 17 (1.5%) were screened and all were uninfected. In the 'opt out' arm there were 1134 eligible patients. It was not possible to screen 524 patients (46%) due to inadequate contact details (38%), previous screening (4%) or incorrectly recorded ethnicity (4%). Of those who could be contacted and were eligible for screening, 37% (223/600) have been screened. 75% of those who made a screening appointment were born in Pakistan, and 25% were British Pakistani patients. 1% of those screened were found to be HBsAg positive and 2.4% were HCV antibody positive.

**Conclusion** Community awareness campaigns and leaflets do not directly lead to testing for viral hepatitis in at risk immigrant groups. A direct screening approach is more effective than an opportunistic screening approach in primary care. Inaccurate GP records reduce the efficiency of screening but GP based testing is easy to implement, popular with patients and effective. First generation migrants are more likely to comply with screening which may improve the cost-effectiveness of this approach.

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P57

### THE IL28B GENE SNP RS12979860 CC HAPLOTYPE, PREDICTOR OF RESPONSE TO TREATMENT IN CHRONIC HCV INFECTION, IS ASSOCIATED TO HIGH NUMBERS OF CD56BRIGHT NK CELLS, LOW NUMBERS OF CD3-CD56-CD16 + NK CELLS AND LOW HCV-SPECIFIC IL-10 PRODUCTION

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**Introduction** Single nucleotide polymorphisms (SNPs) rs12979860 and rs8099917 near the IL28B gene predict response to treatment in