were significantly higher during therapy than when compared to both before therapy ($p<0.00001$) and after therapy ($p=0.0002$) but levels before therapy were not significantly different from post therapy. Elevated scores on therapy were attributable to an increase in mean HA ($p<0.0002$) and P3NP ($p<0.01$) levels on therapy, whereas a significant change in mean TIMP-1 during therapy was not seen. These elevations were seen in all patients regardless of changes in histological fibrosis after therapy ($n=20$ decrease, $n=25$ no change, $n=35$ increase in Ishak stage). However, individual changes in TIMP1 ($r=0.239$, $p=0.04$) and changes in ELF ($r=0.315$, $p=0.004$) from pre- to post-therapy levels were found to correlate with the change of Ishak fibrosis stage before and during treatment.

Conclusion During interferon-based therapy, levels of HA and P3NP and the ELF score rise globally and subsequently fall to values similar to those seen prior to therapy regardless of fibrosis evolution, while TIMP1 levels remained unaffected. However, ELF scores pre and post therapy did accurately reflect changes in histology. This suggests that ELF scores and non-invasive panels incorporating HA and P3NP should be interpreted with caution during interferon-based therapy.

Abstract PMO-172 Figure 1 Fibrosis evolution compared to changes in mean ELF score during interferon therapy.

Competing interests None declared.

PMO-173 DISTRICT GENERAL HOSPITAL NETWORKS CAN PROVIDE SAFE AND EFFECTIVE HEPATITIS C TREATMENT: RESULTS OF A 4-YEAR AUDIT

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Introduction Chronic Hepatitis C (CHC) treatment is well described in the context of Randomised Controlled Trials (RCTs).¹ Whether these findings can be extrapolated to treatment programmes delivered by nurse specialists working in District General Hospitals (DGHs) is unclear.

Methods The Dorset Viral Hepatitis Network has a catchment area of 750 000 people. Patients are assessed and treated in three DGHs by a team of nurse specialists working under the supervision of four lead clinicians. Between January 2007 and January 2011 standard of care for CHC treatment was Ribavirin and Pegylated Interferon α 2a given for 24 weeks (G2/3 patients) to 48 weeks (G1/4). A retrospective analysis of the network's reference database was undertaken focusing on treatment naïve patients.

Results In total 207 treatment naïve patients received antiviral therapy. Mean age at time of treatment was 43 years (20–66); 74% (154) were male and 67% (139) acquired CHC through injection drug use. G1 patients represented 49% (102) of the cohort; 3% (6) were Hepatitis B/HIV co-infected and 95% (196) were Caucasian. A clinical or histological diagnosis of cirrhosis was present in 8% (16). In total 12% (24) moved out of area or were lost to follow-up within 24 weeks of completing treatment. Based on intention to treat, Sustained Virological Response rates (undetectable HCV RNA in serum 24 weeks post treatment) were comparable to those derived from RCT¹ data (Abstract PMO-173 table 1). Non-response was observed in 11% (11/102), 5% (5/98) and 14% (1/7) of G1, G2/3 and G4 patients respectively. Breakthrough or relapse was observed in 18% (18/102), 13% (13/98) and 14% (1/7) of G1, G2/3 and G4 patients respectively. Overall 1% (3) of patients discontinued treatment as a result of a laboratory abnormality and 12% (24) because of other medical complications or side effect intolerance. These proportions are comparable to those observed in RCTs ($p=0.735$, $p=0.146$).

Abstract PMO-173 Table 1 Comparison of SVR rates between centres

Genotype	SVR in DGH practice	SVR in RCT ¹ *	p Value†
Genotype 1	46% (47/102)	41% (241/583)	0.37
Genotype 2/3	60% (59/98)	68% (194/285)	0.16
Genotype 4	57% (4/7)	58% (14/24)	0.96

*51% Received Peg IFN α 2a.

†Derived from χ^2 test.

Conclusion Specialist nurses supported by a network of DGHs can deliver a high quality Hepatitis C service across a broad geographical area. These findings are encouraging when considering a move towards community based CHC management.

Competing interests None declared.

REFERENCE

1. Fried MW, Shiffman ML, Reddy KR, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. *New Engl J Med* 2002; **347**:975–82.

PMO-174 INTRAHEPATIC NATURAL KILLER CELL PHENOTYPING AND FUNCTIONAL ANALYSIS BY FINE NEEDLE ASPIRATION IN CHRONIC HCV INFECTION

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Introduction Hepatitis C virus (HCV) infection results in chronic infection in the majority of subjects, indicating viral immune-evasion strategies. Treatment with interferon alpha (IFN α) stimulates the immune system but the role of NK cells remains unclear.

Methods Intra-hepatic NK cells were obtained from 20 HCV infected donors prior to treatment and 16 non-viral chronic liver disease (CLD) patients along with paired peripheral blood samples. NK phenotype (CD16, NKp30, NKp46, NKG2D and NKG2A) and functional profile (Ki67, CD107a, IFN- γ and Granzyme B) was assessed by flow cytometry. In a separate cohort of 8 HCV patients, who had completed treatment, rate of viral clearance was calculated and pre-treatment peripheral blood NK phenotype and CD107a expression in response to increasing stimulation was measured. At low-level stimulation peripheral blood mononuclear cells (PBMCs) were incubated overnight with 50 u/ml IFN α and exposed to Huh7. Five target cells and at maximal stimulation PBMCs were incubated with 1000 u/ml IFN α and K562 target cells.

Results Intrahepatic vs peripheral blood NK cells demonstrated significantly less expression of CD16 (p NKG2D and NKp30 expression was increased in PBMCs of HCV patients with a more striking down regulation of NKG2D in the liver (p). There was no difference in NKp46 or NKG2A expression between the intrahepatic and peripheral NK cells in either cohort. However, the necroinflammatory score of HCV subjects correlated with NKp46 expression (p=0.003), CD107a expression (p=0.05) and IFN- γ (p=0.05). In the treated cohort, an increased rate of viral clearance correlated with an increased ability of the NK cells to upregulate CD107a ($r^2=0.5$ p<0.05) to increasing stimulation, which was inversely correlated with expression of NKp46 ($r^2=0.85$ p=0.001) at baseline.

Conclusion Intrahepatic NK cells acquire a distinct phenotype and functional profile. NK phenotype and function correlates with necroinflammatory score in HCV infection. The NK cells ability to be activated with IFN α is associated with rapid control of the virus.

Competing interests None declared.

PMO-175 CAN A 3-MONTH "STOPPING RULE" FOR PEGYLATED-INTERFERON- α BE APPLIED TO A UK POPULATION OF CHRONIC HEPATITIS B INFECTED PATIENTS OF MIXED GENOTYPE?

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Introduction Stopping rules have been proposed for the early discontinuation of Pegylated-Interferon- α (PEG-IFN- α) therapy in those patients who are considered unlikely to respond. Recent studies have shown that no reduction in quantitative HBsAg and the absence of >2 log decline in HBV DNA at 12 weeks therapy can predict non-response. However, these data are almost exclusively from genotype A and D cohorts. Here we test how robust this strategy would be in clinical practice and whether this rule could be applied to a UK population of diverse HBV genotypes.

Methods 49 patients (male=35) were treated with PEG-IFN α for CHB over the course of the study. Ten patients remain on therapy and eight patients discontinued due to poor compliance or intolerance. 31 patients (male=20), HBeAg positive (n=24), median age 31 (range 18–55) completed 48 weeks PEG-IFN α and were included in the analysis. HBV genotype was recorded for all patients (A=6, B=5, C=10, D=9, E=1). ALT, HBV DNA and HBsAg was quantified at baseline and longitudinally at 12-week intervals.

Results Of the 31 patients, 10 were considered responders; seven were HBeAg positive and seroconverted on therapy and three were HBeAg negative pre-therapy and considered responders with sustained immune control off treatment. The decline in HBV DNA and qHBsAg by 12 weeks was 3.99 log, 0.17 log (HBeAg positive group) and 2.9 log, 0.5 log (HBeAg negative group) respectively. 16/31 patients were non-genotype A or D. Of the responders from this group there was a decline in HBV DNA and qHBsAg of 4.10 log and 0.58 log respectively by 12 weeks. On sub-group analysis by genotype, there was no statistically significant difference in HBV DNA and qHBsAg decline at 12 weeks across all genotypes, when comparing HBV DNA and qHBsAg between genotype A and D and non A and D patients (p=0.40 and 1.0 respectively). More over adopting the rule of >2 log decline in HBV DNA and no decline in qHBsAg by 12 weeks, reveals we would not exclude those likely to respond; as all responders achieve the outlined viral response by 12 weeks therapy.

Conclusion These data highlight the utility of this stopping rule for PEG-IFN α across all genotypes. The absence of >2 log decline in HBV DNA and reduction in qHBsAg at 12 weeks therapy makes a favourable response unlikely. This rule should be adopted in clinical practice to avoid poorly tolerated side effects and the cost of completing 48 weeks therapy. Furthermore, this 12-week milestone would allow the early switch to an oral antiviral in PEG-IFN α non-responders.

Competing interests None declared.

PMO-176 INDUCTION MAINTENANCE TREATMENT IN CHRONIC HEPATITIS B; STEP-DOWN FROM TENOFOVIR AND LAMIVUDINE TO LAMIVUDINE MONOTHERAPY IS EFFECTIVE

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Introduction Tenofovir Disoproxil Fumarate (TDF) is a potent and effective oral antiviral used to treat Chronic Hepatitis B (CHB), but concerns remain about possible long-term toxicity and the costs of indefinite use. An induction-maintenance treatment strategy may allow the use of combination Lamivudine (LAM) and TDF, to avert the development of resistance, followed by maintenance of viral suppression with LAM. To date, there are no data on such a step-down strategy in HBeAg negative CHB. Here we report on patients in whom we safely discontinued TDF, while maintaining viral suppression and normal liver biochemistry.

Methods We selected patients who were had received combination therapy for a minimum of 18 months. Selection criteria included HBeAg negative disease, fibrosis score of <4/6 on biopsy, undetectable HBV DNA and normal serum ALT for a minimum of 12 consecutive months. Patients meeting these criteria were invited to stop TDF and step-down to maintenance LAM monotherapy. Patients were followed at monthly intervals to determine whether viral suppression and ALT normalisation was maintained in the absence of TDF.

Results 21 patients (13 male), median age 47, (range 39–62) discontinued TDF. Median follow-up was 3 months (range 1–10 months). During monthly follow-up biochemical and serological data have been measured. All patients had undetectable HBV DNA prior to step-down therapy to LAM and this remained undetectable during follow-up. Pre-discontinuation of TDF the median ALT was 27 (range 15–38) and during follow-up, on LAM monotherapy, was 22 (range 15–45), (p=NS). Median HBsAg level pre-discontinuation of TDF was log 3.48 (range 1.55–4.49) and 3.49 (range 1.55–4.55), (p=NS) on LAM monotherapy.

Conclusion We demonstrate no viral breakthroughs or biochemical flares on discontinuing TDF. These data suggest that an induction-maintenance strategy may be pursued in selected CHB patients to avoid long-term exposure to TDF and reduce the burden on healthcare budgets in the context of lifelong oral antiviral therapy.

Competing interests None declared.

PMO-177 MAXIMAL BOOSTING OF INNATE IMMUNITY DURING PEGYLATED INTERFERON- α THERAPY IS REACHED AT 48 WEEKS IN E-ANTIGEN POSITIVE CHRONIC HEPATITIS B

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