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 IFNα 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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[1]U S Gill,* [2]L Payaniandy, [2]J Schulz, [3]V Ross, [2]Y Kallis, [2]P Kooner, [2]R Marley, [4]I Ushiro-Lumb, [1]G R Foster, [1]P T F Kennedy. *[1]Department of Hepatology, Blizard Institute of Cell & Molecular Science, Barts and The London School of Medicine & Dentistry, London, UK; [2]Department of Hepatology, Barts and The London NHS Trust, London, UK; [3]Department of Pharmacy, Barts and The London NHS Trust, London, UK; [4]Department of Virology, Barts and The London NHS Trust, London, UK*

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-IFNα 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-IFNα 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-IFNα 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-IFNα 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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[1]U S Gill,* [2]L Payaniandy, [2]D Payaniandy, [2]J Schulz, [3]V Ross, [2]Y Kallis, [2]P Kooner, [2]R Marley, [1]P T F Kennedy, [1]G R Foster. *[1]Department of Hepatology, Blizard Institute of Cell & Molecular Science, Barts and The London School of Medicine & Dentistry, London, UK; [2]Department of Hepatology, Barts and The London NHS Trust, London, UK; [3]Department of Pharmacy, Barts and The London NHS Trust, London, UK*

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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[1]U S Gill,* [1]M Papadaki, [2]D Peppa, [2]L Micco, [1]L Li, [3]I Ushiro-Lumb, [1]G R Foster, [2]M K Maini, [1]P T F Kennedy. *[1]Department of Hepatology, Blizard Institute of Cell &*