Results Natural killer cell cytotoxicity, in the absence of IL-2 stimulation, was no different between the groups. With IL-2 stimulation, EU demonstrated significantly higher cytotoxicity compared to cHCV (32.8±4.4% vs 17.6±3.2%, p=0.023), with similar levels to SR (27.7±9.9%, p=0.50). The proportion of NK cells in PBMC was not significantly different between the groups.
Conclusion The current findings point to enhanced NK cytotoxicity in EU cases compared to those with chronic infection and suggests a role for NK cells in early viral clearance and resistance to HCV infection.

P46 THE PREDICTION OF LIVER RELATED OUTCOMES USING HISTOLOGICAL TOOLS AS AN ENDPOINT FOR STUDIES EVALUATING ANTI-FIBROTIC THERAPIES

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Introduction Liver related outcomes (LRO) represent a meaningful end-point for future anti-fibrotic therapies. Staging of liver fibrosis on histology is a surrogate for these outcomes but may not be an ideal tool.
Aim Our initial aim was to determine liver related outcomes and survival from the individual stages of significant fibrosis. Our second aim was to assess the value of morphometric collagen quantification within cirrhosis to predict clinical outcomes.
Method The study cohort was selected from a single centre within the Trent HCV study, a prospective cohort which began in 1991 to address the natural history of chronic hepatitis C. Inclusion criteria for this study were the presence of significant fibrosis (at least Ishak Stage (IS) three on biopsy) and at least 3-year follow-up post biopsy. LRO was defined as decompensation (variceal bleeding, ascites, encephalopathy), HCC, liver transplant and liver-related death. Automated morphometry was performed to measure the Collagen Area Fraction (CAF). Survival at 3, 5 and 7 years respectively was evaluated.
Results The study cohort comprised 155 patients (70% male; mean age 49 years). The median follow-up time was 78 months. A LRO occurred in 48 patients (31.0%, estimated annual incidence 5.2%). HCC developed in 16 patients (10.6%, estimated annual incidence 1.6%) liver-related death occurred in 34 patients (21.9%, estimated annual incidence 3.3%); clinical decompensation developed in 20 patients (13.3%, estimated annual incidence 2.1%). See Abstract P46 table 1. CAF was measured in a subgroup of 89 patients. The median CAF was calculated for each Ishak stage and increased progressively towards the more advanced stages. (IS 3: median CAF 3.7%, IQR 1.5–5.1; IS 4: median CAF 5.2%, IQR 2.8–7.4; IS 5: median CAF 6.8%, IQR 3.4–9.5; IS 6: median CAF 9.9%, IQR 6.2–15.7). Within Ishak stage 6 the median CAF scores predicting LRO were higher (13.89, 12.48 and 12.69%) compared to median CAF scores in patients with no outcomes (8.59, 8.32 and 8.10%) at years 3, 5 and 7 respectively.
Conclusion Clinical outcomes represent realistic and meaningful end-points for future trials evaluating anti-fibrotic agents once advanced fibrosis has developed. Further development and validation of morphometry within advanced fibrosis could enable better identification of patients at risk of more rapid progression of liver disease than Ishak stage alone.

P47 DE-NOVO ANTIVIRAL THERAPY WITH NUCLEOS(T)IDE ANALOGUES IN 'REAL-LIFE' PATIENTS WITH CHRONIC HEPATITIS B INFECTION: COMPARISON OF VIROLOGICAL RESPONSES BETWEEN LAMIVUDINE + ADEFOVIR VS ENTECAVIR VS TENOFOVIR THERAPY

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Introduction Several nucleos(t)ide analogues (NA) are approved for the treatment of chronic hepatitis B (CH-B); all aim to control HBV replication with minimal risk of drug-resistance and toxicity. Limited comparative data exist assessing differences between viral responses to different de-novo therapeutic regimens in real-life cohorts.
Aim To assess and compare virological and serological responses in 3 real-life CH-B de-novo therapeutic cohorts—lamivudine 100 mg/d + adefovir 10 mg/d (LAM+ADV) combination therapy vs entecavir 0.5 mg/d (ETV) vs tenofovir 245 mg/d (TDF) monotherapies.
Method **Patients:** NA therapy naive 406 CH-B patients treated at a single-centre practice [median 30 months (m), range 3–72] were split into three groups according therapy regimen: LAM+ADV (n=192, 78% males, median age 40 y, 35% HBeAg+, 34% cirrhosis, median duration 36 months), ETV (n=154, 79% males, median age 42 y, 31% HBeAg+, 34% cirrhosis, median duration 28 months) and TDF (n=60, 50% males, median age 40 y, 23%HBeAg+, 25% cirrhosis, median duration 9 months). HBV DNA viral load tested by real-time PCR [log10 IU/ml], serology for HBeAg/HBsAg were compared between baseline, months 3, 6, 9 and 12. Five responses, evaluated by change in serum HBV DNA, were recorded: (1) complete (CR) <12 IU/ml; (2) partial (PR), fall >3log10 but >12 IU/ml; (3) slow (SR), fall 2–3 log10; (4) non-response (NR), fall <1 log10; 5) viral breakthrough (VB), rise >1 log10 from nadir. HBV genotypic resistance was tested pre-treatment and at the time of SR, NR or VB by direct sequencing.
Results Baseline HBV DNA was similar in all cohorts (median $\log_{10}$ 4.6 vs 4.4 vs 4.2 IU/ml), higher proportions achieved CR in TDF cohort than LAM+ADV and ETV (m3: 78%vs 48% and 53%, p<0.01; m6: 82% vs 60% and 65%, p=0.02; m9: 86% vs 62% and 55%, p<0.01), but were similar at m12: 80% vs 73% and 76% and there were no differences in PR, SR and NR in all groups. HBV DNA

Abstract P46 Table 1 LRO and survival by Ishak Stage

Ishak Stage	Annual Incidence of LRO (%)	HR of LRO (95% CI, p value)	3 year survival (%)	5 years survival (%)	7 years survival (%)
3	0.7%	Ref.	97.7 (84.6, 99.7)	97.7 (84.6, 99.7)	94.1 (77.6, 98.5)
4	3.2%	4.76 (0.87 to 26.016, 0.0715)	93.8 (63.2, 99.1)	87.1 (57.3, 96.6)	78.4 (46.0, 92.6)
5	5.1%	6.996 (1.578 to 31.019, 0.0105)	94.4 (79.6, 98.6)	82.8 (65.6, 91.9)	68.2 (48.6, 81.7)
6	11.0%	15.986 (3.816 to 66.961, 0.0001)	68.8 (54.6, 79.3)	53.3 (38.6, 66.0)	41.8 (26.9, 56.0)

decreased in analogous rate in all groups. 2 patients in LAM+ADV and ETV groups developed VB. No viral mutations associated with drug resistance were detected in the LAM + ADV and TDFgroup, including those with VB, NR or SR; in contrast 1 ETV patient with SR at m12 (genotype C) developed mutation rtM204I. HBeAg seroconversion was more frequent in LAM + ADV cohort vs ETV and TDF (21% vs 8% and 7%, p=0.06) and HBsAg seroconversion occurred only in LAM + ADV and ETV patients (2% and 1%).

Conclusion De-novo antiviral therapy with different therapeutic approaches of nucleos(t)ide analogues LAM+ADV, ETV and TDF achieves similar efficacy within 12 months of treatment in real-life patient cohorts with CH-B.

P48 TELAPREVIR SUBSTANTIALLY IMPROVED SVR RATES ACROSS ALL IL28B GENOTYPES IN THE ADVANCE TRIAL

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Aim Single nucleotide polymorphisms (SNPs) near the IL28B gene region have been strongly associated with the likelihood of SVR in genotype 1 HCV patients treated with peginterferon/ribavirin (PR). During the evaluation of an exploratory diagnostic test that characterises genetic polymorphisms near the IL28B gene, the impact of rs1297860 on SVR in telaprevir (T)-based regimens in the ADVANCE trial was evaluated.

Method IL28B genotype testing was performed according to a US FDA guidance governing use of de-identified leftover samples for in vitro diagnostic testing. The guidance requires a strict de-identification procedure that was carried out by an independent third party. Only specimens from the USA were used; and as non-Caucasian patients could not be de-identified in sufficient numbers, they were excluded from the study.

Results The diagnostic assay developed provided consistent, unambiguous genotype calls and was considered suitable for research. 454/1088 (42%) patients had IL28B test results available. 150/454 (33%) were CC, 224/454 (49%) CT, and 80/454 (18%) TT. SVR rates for each subgroup by arm are shown in the Abstract P48 table 1. 72%, 54% and 48% of CC, CT and TT telaprevir patients, respectively had undetectable HCV RNA at weeks 4 and 12 (eRVR) compared with 16%, 2% and 0% of PR patients. Among eRVR telaprevir patients, 91% achieved SVR (97% of CC, 88% of CT, 85% of TT) with 24 weeks of therapy whereas 43% of non-eRVR telaprevir patients had SVR (63% of CC, 33% of CT, 46% of TT) with 48 weeks of therapy.

Abstract P48 Table 1 SVR rates

	In patients tested for IL28B allele				In all ADVANCE patients
% (n/N)	CC (N=150)	CT (N=224)	TT (N=80)	Total (N=454)	(N=1088)
T12PR*	90 (45/50)	71 (48/68)	73 (16/22)	78 (109/140)	75 (271/363)
T8PR**	84 (38/45)	57 (43/76)	59 (19/32)	65 (100/153)	69 (250/364)
PR	64 (35/55)	25 (20/80)	23 (6/26)	38 (61/161)	44 (158/361)

*T12PR = T+PR 12 weeks, then PR 12 or 36 weeks depending on eRVR status.
**T8PR = T+PR 8 weeks, then PR 16 or 40 weeks depending on eRVR status.

Conclusion Telaprevir-based therapy improved eRVR and SVR rates across all IL28B genotypes. Specifically, telaprevir-based therapy more than doubled the rates of SVR in CT/TT patients, and substantially increased SVR rates in those with CC genotype, as compared with PR therapy alone. Non-attainment of eRVR was associated with lower SVR rates across all IL28B genotypes, with the largest decrement in CT/TT patients.

P49 TREATING HEPATITIS C IN THE PATIENT'S HOME: A HOSPITAL AND HOMECARE PARTNERSHIP

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Introduction It is long established that the UK has poorer outcomes regarding numbers of patients treated with antivirals for chronic hepatitis C (HCV) than it's European counterparts. Exploring alternative models of care that will facilitate the engagement of those whom regular hospital attendance would be a barrier to treatment is important if one is to reduce the incidence of end stage liver disease among this group of patients. Against this backdrop we initiated a project in Nottingham to deliver care in tandem with a community nursing service.

Aim To treat HCV infected patients with pegylated interferon and ribavirin in the patient's home via a partnership between secondary care and an established homecare company.

Method Patients with stable HCV infection and no evidence of decompensated liver disease are offered this model of care in the hepatitis clinic and referred to the homecare company by the Consultant or Specialist Nurse. The antiviral drugs are delivered directly to the patient's home, and a skilled homecare nurse trained in the management of HCV visits the patient to undertake: teaching how to self inject pegylated interferon and take ribavirin correctly; draw blood samples for monitoring treatment progress and safety, to assess side effects and provide nursing care in managing these; and regularly report back to the referring clinician. Nursing support is available to patients 24 h a day. Once treatment is complete the patient returns to the hepatitis clinic to be reviewed.

Results Since this model's inception in February 2004, approximately 110 patients were offered the option of homecare. 87 patients elected to be treated at home and were referred by the secondary care HCV clinic using an agreed proforma. Investigations during treatment were conducted using the same schedule as the specialist clinic and hospital staff reviewed the results. The specialist team took all decisions on changes to drug treatment. Treatment outcomes and drop out rates are comparable to hospital-managed clinics, but the non-attendance rates are exceptionally low; only two home visits have been missed by patients. No adverse events as a result of receiving treatment and monitoring at home have occurred. Furthermore this model of care is cost effective; drugs are supplied VAT-free by not being routed into the hospital pharmacy, and this offsets the home nursing cost.

Conclusion Our results demonstrate that homecare treatment for HCV infection is feasible, safe and the preferred option of most patients. It is well tolerated by patients with very high compliance rates which we anticipate will lead to improvements in treatment outcomes. We suggest that this innovative homecare model can be an important facet of hospital HCV services, and thus be a major means of facilitating the engagement of more patients into therapy without an additional burden of nursing staff costs.