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.

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**Abstract 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 3) 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 (31.9%, 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.

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**Abstract 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 versus entecavir 0.5 mg/d (ETV) versus 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, 25%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 5, 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 >log10 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 log10 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
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 TDF group, including those with VB, NR or SR, in contrast 1 ADV patient with NR 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 HBeAg 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.

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**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 rs12979860 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, 53% of CT, 46% of TT) with 48 weeks of therapy.

**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; and 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.