operative room. Combination therapy was continued for 7 days after transplant (total of 8 doses). HCV RNA was monitored up to 24 weeks post-transplant, and patients followed for 1 year to determine graft and patient survivals.
Results: 38 patients (32 kidney tx, 2 kidney/pancreas tx, 3 heart tx, 1 heart/kidney tx) have been enrolled to date. All patients completed treatment. Median age for patients was 60 years and 63% were males. Median time from list for HCV viremic grafts to tx was 32, 52, 71, and 151 days for heart, heart/kidney, kidney, and kidney/pancreas tx recipients respectively. Median donor age was 35 years. All donors had confirmed viremia. Transient viremia during the first 2 weeks post tx was detected in 28/38 (74%) patients (HCV RNA range 16–6870 IU/ml), and 12 patients had detectable viremia on post tx day 7 when treatment was completed (HCV RNA range of detectable but not measurable RNA-110 IU/ml). Four (4/38) patients continued to have detectable HCV RNA at week 2 post tx, and one of those patients remained detectable week 3 post tx. All patients achieved undetectable HCV RNA by week 4 post tx and all patients stayed negative 13 weeks post tx (SVR 12 of 100%) (Fig. 1). The cost of this preemptive approach was significantly lower when compared to the standard of care reactive treatment approach. Treatment was well tolerated, and all patients completed 8 days of combination therapy. One kidney transplant recipient died 65 days post-tx with acute subdural hematoma. This patient completed treatment per protocol and achieved viral clearance (undetectable HCV RNA at post tx week 8).
Conclusion: In the largest multicenter U.S. experience to date, G/P combined with ezetimibe was highly effective in preventing HCV infection in 100% of non-liver solid organ transplant recipients of HCV viremic grafts. Short-term graft and patient survivals are excellent. This approach appears to be cost effective and will potentially eliminate the risk of post-transplant complications from HCV transmission and enhance the use of HCV viremic grafts.

OS003
Effectiveness of voxilaprevir/velpatasvir/sofosbuvir in hepatitis C patients previously treated with direct-acting antiviral agents (DAA)

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Background and aims: Voxilaprevir/velpatasvir/sofosbuvir (VOX/VEL/SOF) is approved for HCV retreatment of direct-acting antiviral agents (DAA)-experienced patients. However, real-life data are still limited. The aim of the study was to analyse the effectiveness of VOX/VEL/SOF in a real-world setting.
Method: All consecutive patients with HCV retreated with VOX/VEL/SOF after DAA failure were enrolled in 153 centers in Germany, Austria, Switzerland and Belgium between May 2015 and November 2020. Sustained virological response (SVR) was defined as undetectable HCV RNA 4 (SVR 4) or 12 (SVR12) weeks after the end-of-treatment.
Results: A total of 416 patients were included: median age was 55 (21–84) years, 79% were male, median HCV RNA was 383, 000 (10–58, 300, 000) IU/ml. HCV genotype (GT) was 1 in 54% (1a in 26%, 1b in 28%), 2 in 1%, 3 in 39% and 4 in 6%. Patients received VOX/VEL/SOF for 12 weeks, ribavirin was added in 4% of treatment schedules. Overall, 365/416 (87.7%) patients by intention to treat analysis and 401/416 (96.4%) by per protocol analysis achieved SVR12, respectively. Genotype 3a ($p = 0.008$) and hepatocellular carcinoma ($p = 0.0034$) were the only predictors of a treatment failure. Treatment effectiveness was not significantly affected by the type of previous DAA regimen, by liver cirrhosis, HCV GT 1a and baseline HCV-RNA viral load. Virologic relapse was observed in 20 patients (10% GT1a, 15% GT1b, 75% in GT3a). The presence of resistance-associated substitutions within NS3, NS5A, and NS5B genes did not impact SVR12 ($p = 0.06$).
Conclusion: VOX/VEL/SOF is an effective retreatment for patients with HCV who have failed on a previous DAA course in a real-life setting. We identified HCV GT 3a and HCC as the main predictors of VOX/VEL/SOF failure.

OS004
Glecaprevir/pibrentasvir and sofosbuvir for 16 weeks without ribavirin is safe and highly effective retreatment for patients who have failed an NS5A inhibitor containing antiviral regimen

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Background and aims: Oral DAA therapy has been available in New Zealand since mid-2016 for treatment of chronic hepatitis C. Over the last 5 years, more than 10,000 New Zealanders have been treated with NS5A inhibitor- based DAA therapy, of whom more than 300 have had virologic failure. Retreatment of patients with confirmed antiviral resistance requires a triple DAA combination of a polymerase, a protease and an NS5A inhibitor.
Method: In an open-labelled, ethics-approved study, 100 New Zealanders who had failed DAA therapy with confirmed NS5A resistance will be retreated with glecaprevir/pibrentasvir (GLE/PIB) from Feb 2019) plus sofosbuvir for 16 weeks. Patients with decompensated cirrhosis or hepatocellular carcinoma or post-transplant are excluded.
Results: To-date, 57 patients have been enrolled in the study. Median age was 56 years (38–80), 78% were male and 44% had established cirrhosis. Thirty-five patients had previously failed GLE/PIB, 19 failed ombitasvir, paritaprevir, dasabuvir, and ritonavir (PrOD) and 1 each failed grazoprevir/elbasvir (GRZ/ELB), ledipasvir/sofosbuvir (LDV/SOF) and sofosbuvir/velpatasvir (SOF/VEL). Six patients had failed multiple regimens. Most frequently detected NS5A resistance-associated substitutions (RASs) were Y93H (57%), A30 K (26%), Q30 K/H (26%, M28 T/F/V (11%). Multiple NS5A RASs were detected in 39% patients. Resistance profiles were similar in PrOD and GLE/PIB failures.
One patient died from opioid overdose during treatment. There were no other SAEs or AE-related treatment discontinuations. Two other patients stopped treatment within 4 weeks because of psychosocial issues, one of whom has started retreatment.
45 patients have completed therapy and 37 have reached the SVR12 timepoint, of whom 36 (98%) are cured (complete SVR results will be available in early 2022). The only treatment failure to-date was a 53-year-old noncirrhotic female, previously treated with PrOD.

Conclusion: Glecaprevir/pibrentasvir plus sofosbuvir for 16 weeks is a safe and highly effective retreatment regimen for patients who have previously failed GLE/PIB and other DAA regimens regardless or cirrhosis status, or NS5A RAS profile. There is no indication for adding ribavirin.

OS005

Excess mortality risk among hepatitis C patients after being "cured" in the interferon-free era: results from three population-based cohorts

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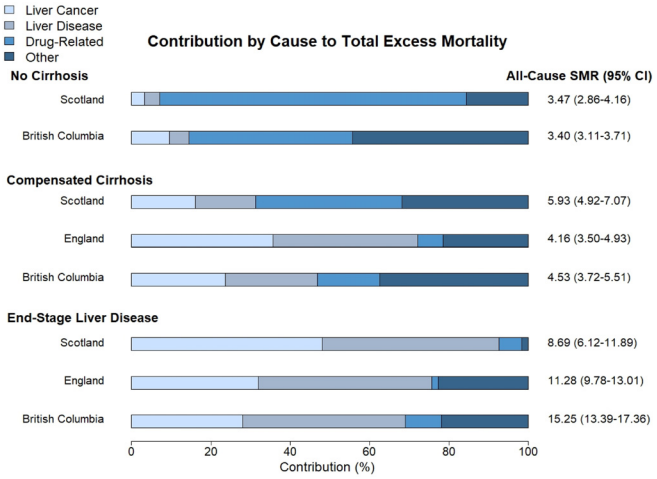
Background and aims: Although the number of people living with a hepatitis C sustained viral response (SVR) has increased dramatically, mortality rates in this patient group remain poorly understood. Here, our goal was to assess excess mortality after SVR achievement in the interferon (IFN)-free era.

Method: We performed data analysis on patients achieving SVR in the IFN-free era (2014–2018/19) from three population-based cohorts in Scotland (SC), England (EN), and British Columbia (BC). Patients were divided into three disease stage groups: no cirrhosis (SC and BC only); compensated cirrhosis; and end stage liver disease (ESLD). Age-standardised mortality rates were calculated to take account of different age/sex structures between cohorts and disease stage groups. Further, we calculated standardised mortality ratios (SMRs) to compare the frequency of mortality in SVR patients to the general population (GP). We also quantified the proportion of excess death attributable to: a) death from liver cancer; b) death from liver disease unrelated to cancer; c) and death from drug-related causes. Finally, Poisson regression was used to identify factors associated with excess mortality.

Results: Our analysis included 20, 031 patients, of which 1, 402 (7%) died during follow-up. Mean follow-up duration was 2.2–3.9 years, and mean age ranged from 46.3 (SC) to 56.7 (BC). Mortality rates varied considerably according to disease stage. For example, the age-standardised mortality rate ranged from 12 to 23, 27–38, and 62–118 deaths per 1000 person-years in non-cirrhosis, compensated cirrhosis and ESLD patients, respectively. SMRs indicated that all-cause mortality was 3.4–3.5 times higher than the GP in non-cirrhosis patients, 4.2–5.9 times higher in compensated cirrhosis patients, and 8.7–15.3 times higher in ESLD patients. For non-cirrhosis patients, drug-related causes were responsible for the greatest proportion of excess death (77% SC; 41% BC). Conversley, for cirrhosis patients, liver-related causes were the key driver, responsible for 30–95% of excess deaths. In the regression analysis, younger age, drug use and comorbidities were associated with greater excess mortality (see Figure).



Conclusion: In the largest study performed to-date, we show that individuals achieving SVR in the interferon-free era have a considerably higher mortality risk than the GP, driven mainly by drug-related mortality (in non-cirrhosis patients) and liver-related causes (in cirrhosis patients).

OS006

Impact of direct-acting antiviral treatment for hepatitis C on cardiovascular diseases and extrahepatic cancers

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Background and aims: The impact of direct-acting antivirals (DAAs) on extrahepatic complications in chronic hepatitis C (CHC) patients remains poorly described. We estimated the association of DAAs with cardiovascular events and extrahepatic cancers.