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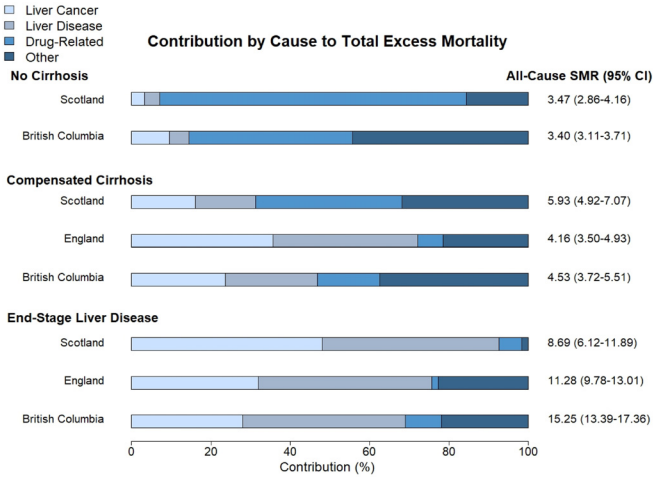
Background and aims: Although the number of people living with a hepatitis C sustained viral response (SVR) has increased dramatically, mortality rates in this patient group remain poorly understood. Here, our goal was to assess excess mortality after SVR achievement in the interferon (IFN)-free era.

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.

Method: The prospective ANRS CO22 HEPATHER cohort was enriched with individual data until December 2018 from the French National Health Insurance Database (SNDS), which contains medical information regarding ambulatory care and hospital admissions. CHC patients were enrolled between August 2012 and December 2015 in 32 French hepatology centers. A total of 8148 CHC adults were selected. Cardiovascular events (stroke, acute coronary syndrome, pulmonary embolism, heart failure, arrhythmias and conduction disorders [ACD], peripheral arterial disease [PAD]) and cancers (colorectal, bladder, prostate, kidney, lung, pancreas, thyroid, head/neck, breast) were derived from the SNDS. Associations between DAAs and extrahepatic events were estimated using marginal structural models, with adjustments for clinical confounders and medications.

Outcomes	Adjusted hazard ratios associated with DAAs (95% Confidence Interval)
Total population (n = 8148)	
Acute stroke	1.30 (0.82, 2.08)
Acute coronary syndrome	1.00 (0.63, 1.60)
Acute pulmonary embolism	2.10 (0.64, 6.85)
Acute heart failure	1.15 (0.74, 1.78)
Arrhythmias and conduction disorders	1.46 (1.04, 2.04)
Peripheral arterial disease	0.54 (0.33, 0.89)
Major cardiovascular events	1.03 (0.81, 1.31)
Any cardiovascular event	1.10 (0.90, 1.36)
Any extrahepatic solid cancer	1.23 (0.50, 3.03)
Patients with advanced fibrosis (n = 3586)	
Acute stroke	0.58 (0.29, 1.18)
Acute coronary syndrome	0.59 (0.29, 1.19)
Acute pulmonary embolism	0.79 (0.16, 3.97)
Acute heart failure	0.47 (0.27, 0.81)
Arrhythmias and conduction disorders	1.02 (0.57, 1.84)
Peripheral arterial disease	0.36 (0.17, 0.73)
Major cardiovascular events	0.50 (0.36, 0.71)
Any cardiovascular events	0.58 (0.42, 0.79)
Any extrahepatic solid cancer[c]	0.39 (0.09, 1.71)

Results: Analyses of 12 905 person-years (PY) of no DAA exposure and 22 326 PY following DAA exposure showed a reduced risk of PAD after DAAs (HR, 0.54; 95% CI, 0.33 to 0.89), a beneficial effect of DAAs on overall cardiovascular outcomes in patients with advanced fibrosis (aHR, 0.58; 95% CI, 0.42 to 0.79), and an increased risk of ACD (hazard ratio [HR], 1.46; 95% CI, 1.04 to 2.04) predominant after the first year following DAA initiation. There was no association between DAAs and extrahepatic cancer (HR, 1.23; 95% CI, 0.50 to 3.03).
Conclusion: DAAs were associated with a decreased risk of cardiovascular outcomes in patients with advanced fibrosis, a decreased risk of PAD regardless of the fibrosis stage, and an increased risk of ACD, supporting long-term cardiac monitoring after DAA therapy. DAAs were not associated with extrahepatic cancer development or reduction.

Cirrhosis and its complications: Other clinical complications except ACLF and critical illness

OS007
Etiological cure prevents further decompensation and mortality in cirrhotic patients with ascites as the single first decompensating event

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Background and aims: Etiologic treatment reduces the risk of decompensation and mortality in compensated cirrhosis. However, in the setting of decompensated cirrhosis the impact of etiologic treatment is less predictable, in particular in patients with ascites, who remain at high risk of developing further decompensating events and death. The aim of the study was to evaluate the impact of etiological treatment in decompensated patients with cirrhosis and ascites as the single index decompensating event. The end points were the occurrence of further decompensation (i.e. refractory ascites, spontaneous bacterial peritonitis [SBP], hepatorenal syndrome [HRS-AKI], variceal bleeding [VB] and hepatic encephalopathy [HE]) and mortality.
Method: Cirrhotic patients with ascites as single first decompensation event at the University Hospital of Padova or the Vienna General Hospital between 2003–2021 were included and followed until death, liver transplantation or September 2021. The etiology was considered as "cured" in case of removal of the primary etiological factor (e.g. HCV: virological cure, HBV: virological suppression, ALD: alcohol abstinence) and as "controlled" in case of partial removal of etiologic factor (e.g. HBV: partial suppression of HBV-DNA, ALD: mostly abstinent but with drinking episodes).
Results: We included 622 patients (mean age: 57 ± 11 years, male 68%, mean MELD 15 ± 6), the most common etiology were ALD (59%) and HCV (23%). Etiology was "cured" in 146 patients (24%), "controlled" in 170 (27%) and uncontrolled in 306 (49%). During a median follow-up of 33months, 350 patients (56%) developed further decompensation (33%refractory ascites, 29% HE, 17% SBP, 13% HRS-AKI, 9% VB). The incidence of further decompensation at 5 years was significantly lower in patients with "cured" vs "controlled" vs uncontrolled etiology (38% vs 64% vs 72%, respectively; $p < 0.001$; Fig. 1A). In multivariable analysis (adjusted for age, varices, etiology, Child Pugh class, creatinine and sodium), "cured" (aHR = 0.52; $p < 0.001$) and "controlled" etiology (aHR = 0.60; $p < 0.001$) were both independently associated with a lower risk of further decompensation. Considering response to etiological treatment as time-dependent covariates, 5-year cumulative incidence of survival was significantly higher in patients with cured vs controlled vs uncontrolled etiology (83% vs 58% vs40%, respectively; $p < 0.001$; Fig. 1B). In multivariable analysis, etiological cure (aHR = 0.35, $p < 0.001$) and controlled etiology (aHR = 0.61, $p = 0.003$) were independently associated with lower mortality.