reported in our paper where exposures (AUC_{tau}) of GS-007 were 1,719% higher than in patients with normal renal function.[2] It is reassuring that in the paper by Huang no treatment attributed adverse events were found, similar to our previously published report. More recently, Taneji *et al.* also demonstrated the safety and efficacy of sofosbuvir/velpatasvir in 51 patients with ESRD on maintenance hemodialysis.[3]

These findings provide reassurance that the increases in GS-331007 exposure are not clinically relevant and indeed renal impairment, including dialysis, is no longer a contraindication for use of sofosbuvir/velpatasvir as reflected in the product monograph.

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Characterizing bacterial infections in acute-on-chronic liver failure among patients with cirrhosis from nonalcoholic steatohepatitis

To the Editor:

I read with great interest the study by Wong and Piano *et al.*[1] In the United States, non-alcoholic fatty liver disease (NAFLD)-related acute-on-chronic liver failure (ACLF) is the second leading cause of transplant listing, while listings for NAFLD-ACLF are outpacing listings for NAFLD without ACLF.[2] This is particularly noteworthy, since unlike other etiologies of liver disease associated with ACLF, namely alcohol-related liver disease and HBV infection, NAFLD is a disease process without an inherent precipitant such as alcohol use or flare of hepatitis B. Though obesity may pose a risk for ACLF development in the NAFLD population,[3] the specific reason for ACLF occurrence in this group is likely from an extrahepatic insult, such as bacterial infection.

In the current paper by Wong, Piano, and colleagues, the authors analyzed a large multi-national cohort of patients with decompensated cirrhosis, of whom 563 were diagnosed with ACLF either at the time of infection or after infection. A particular strength of this study was the ability to evaluate patients across Europe, North America, South American and India. Among the 563 patients with ACLF, 62 (11%) had a diagnosis of NAFLD. I am therefore hoping the authors can provide a subgroup analysis of bacterial infections associated with NAFLD-related ACLF, including the organism and infection site, categorized according to whether ACLF occurred at the time of infection or developed after the initial infection. Given the epidemic of NAFLD globally, an analysis of this nature would be of significant use in tailoring strategies for antibiotic prophylaxis.

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Bacterial infection-related acute-on-chronic liver failure: The standpoint matters!

To the Editor:

We read with great interest the article by Wong and Piano *et al.*[1] regarding the differences among the geographic areas in the development and outcomes of bacterial infection triggered acute-on-chronic liver failure (ACLF). The study highlighted a higher rate and severity of bacterial infection-triggered ACLF in the Indian subcontinent than in Europe and America. The authors also demonstrated a higher incidence of multidrug-resistant (MDR) bacterial infection-related ACLF, leading to a worse outcome in the Asian population. Given the increased mortality associated with ACLF, it is crucial to know the local epidemiology of bacterial infections. Although it is a global study, centers in Eastern Europe were not represented.

We recently performed a prospective observational study (data not published), including 76 patients (70% men, 70% alcohol-induced liver disease) admitted to the intensive care unit (ICU) in a Romanian tertiary hospital for acutely decompensated cirrhosis. Patients were admitted directly to ICU (60%) or transferred to ICU after a mean stay of 14±9.5 days in a regular ward. The main reason for admission to ICU was the need for mechanical ventilation, either for respiratory failure (n = 5), for respiratory failure and airway protection in overt hepatic encephalopathy (n = 15), or airway protection in severe hepatic encephalopathy (n = 24).

A complete infectious evaluation was performed at admission to ICU. Infection diagnosis was established according to conventional criteria.[2,3] The diagnosis and grading of ACLF were made according to the CANONIC study criteria.[4]

Patients had a mean Child-Pugh score of 12±2 and a mean model for end-stage liver disease score of 28±8. The clinical decompensation events were ascites (n = 67/76, 88%), hepatic encephalopathy (n = 47/76, 61.8%), variceal bleeding (n = 24/76, 31.65%) and jaundice (n = 43/76, 56.5%), respectively.

Fifty-one patients (67%) had bacterial infections at admission, and among them, 18 (35%) had a nosocomial infection. Nineteen patients had multiple infections. Pneumonia (44%) was the most frequent type, followed by urinary tract infection (18%) and spontaneous bacterial peritonitis (15%).

Most of the bacterial infections were of Gram-negative etiology. There were 18 infections with multidrug-resistant germs (30%); 80% were nosocomial, and carbapenemase-producing Enterobacteriaceae and *Acinetobacter baumannii* were the most frequent (55%).

The majority (36 cases, 70%) of the infected patients had a quick sequential organ failure assessment score ≥2, and among them, almost all (97%) met the criteria for sepsis. In patients with a bacterial infection, 43 (74%) had ACLF: 34.9% ACLF grade 2 and 62.8% ACLF grade 3. Only 1 patient had ACLF grade 1. Respiratory (30/43) and cerebral failure (31/43) with the need for mechanical ventilation were the most frequent organ failures in our study, being present in almost 70% of cases, followed by coagulation (21/43), renal (21/43), circulation (19/43) and liver (12/43) failure, respectively.

All MDR bacterial infections were associated with ACLF and half of them with ACLF grade 3. Patients had a mean ICU stay of 9.8±11.9 days. During follow-up 63 patients worsened (defined as the occurrence of a new organ failure or the diagnosis of a second infection). In most cases (47/63), circulatory failure was the new organ failure. Moreover, 30 patients presented a second infection. Thus, during admission to ICU, we registered 3 more cases of bacterial infection-related ACLF, and at the time of worsening, the majority of patients reached grade 3 ACLF (90%).

MDR bacteria were responsible for the etiology of 60% of the bacterial infections when worsening. We registered 4 extensively drug-resistant (XDR) bacterial infections too.

The overall mortality at 28 days was 68%. When we considered only the infected patients, the registered mortality at 28 days was higher: 76%. The increased mortality rate observed in

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