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TITLE: EXPEDITION-IV: Safety and Efficacy of GLE/PIB in Adults with renal impairment and Chronic Hepatitis C Virus Genotype 1 – 6 Infection
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ABSTRACT BODY:
Abstract Body: BACKGROUND: Combinations of first-generation direct acting antiviral agents (DAAs) have demonstrated high rates of sustained virologic response (SVR) in patients with chronic hepatitis C virus (HCV). However, HCV patients with severe renal impairment have limited treatment options. Glecaprevir (GLE, formerly ABT-493) and pibrentasvir (PIB, formerly ABT-530) are two pangenotypic DAAs that have potent activity against HCV NS3/4A and NS5A, respectively. Neither compound undergoes significant renal excretion which makes them potentially suitable for patients with renal disease. Phase 1 studies demonstrated no clinically relevant increases in the exposure of GLE/PIB in patients with renal disease compared to those with normal renal function. Here we report on the safety and efficacy of GLE/PIB administered for 12 weeks in GT1-GT6 HCV-infected patients with severe renal impairment (GLE was identified by AbbVie and Enanta).
METHODS: Participants had GT1-6 chronic HCV infection and were either treatment-naïve (TN) or treatment-experienced (TE) with interferon- or sofosbuvir-based regimens and either had no cirrhosis or compensated cirrhosis. An eGFR < 30 mL/min/1.73 m² was required at screening. Patients were treated with GLE/PIB 300mg/120mg once daily for 12 weeks. The primary efficacy endpoint was SVR12. Safety is assessed in all patients who received at least 1 dose of the study drugs.
RESULTS: A total of 104 participants (76% male and 62% white) were enrolled in this study, of whom 42% were TE and 19% had compensated cirrhosis. Patients had either GT1 (52%), GT2 (16%), GT3 (11%), GT4 (19%), GT5 (1%) or GT6 (1%) chronic HCV infection and had either CKD stage 4 (13%) or stage 5 (87%); 82% were on dialysis. SVR4 was achieved by 103/104 (99%) patients. The patient not achieving SVR4 prematurely discontinued treatment. Most treatment emergent adverse events (AEs) were mild or moderate in severity. Of the 24% of patients who experienced serious AEs, none were related to study-drug. Four AEs (4%) led to study-drug discontinuation and one patient died after achieving SVR4 due to a serious AE not-related to study drug (intracerebral hemorrhage).
CONCLUSIONS: The fixed dose combination of GLE/PIB administered once daily for 12 weeks was well tolerated in patients with severe renal impairment with 99% of patients achieving SVR4. Serious AEs were considered unrelated to study drugs and associated with the patients’ underlying comorbidities. These results suggest that GLE/PIB is a suitable option for patients with advanced renal disease and support the pangenotypic efficacy of this regimen. Complete SVR12 data will be presented at the conference.
**Financial Conflict of Interest:**

- **Edward Gane:** Yes conflict of interest; AbbVie: Advisory Committees or Review Panels; Janssen: Advisory Committees or Review Panels; AbbVie: Speaking and Teaching; Gilead Sciences: Advisory Committees or Review Panels; Gilead Sciences: Speaking and Teaching; Achillion: Advisory Committees or Review Panels; Merck: Advisory Committees or Review Panels; Merck: Speaking and Teaching; Alnylam: Speaking and Teaching.

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