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Integrated Analysis of Elbasvir/Grazoprevir Clinical Trials in Korean Participants with Hepatitis C Virus Genotype 1b Infection

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Aims: All-oral direct-acting antiviral medications have transformed the treatment of hepatitis C virus (HCV) infection; however, local evidence is limited in some regions, including Korea. We conducted an integrated analysis of the efficacy of elbasvir (EBR)/grazoprevir (GZR) in Korean participants with HCV infection enrolled in EBR/GZR phase 3 clinical studies.

Methods: Participants with HCV GT1b infection enrolled at Korean study centers who received EBR/GZR 50 mg/100 mg for 12 weeks were included. The primary endpoint of all studies was sustained virologic response (HCV RNA <15 IU/mL) 12 weeks after end of therapy (SVR12) in the full analysis set (all participants who received ≥1 dose of study medication).

Results: A total of 74 Korean participants were included. Mean age was 55 years (SD, 11 years), 25 (33.8%) had cirrhosis, and 70 (94.6%) were treatment-naïve. There were no participants with HCV/HIV coinfection. SVR12 was achieved by 73 of 74 (98.6%) participants; and only 1 participant, who withdrew consent, failed to achieve SVR12. Therefore, in the modified full analysis set (excluding participants who discontinued for reasons unrelated to study medication), SVR12 was 100% (73/73). SVR remined high among participants with cirrhosis (25/25, 100%), baseline viral load >2,000,000 IU/mL (34/34 (100%), and age >65 years (16/16, 100%). Baseline NS5A resistance associated substitutions (RASs) were detected in 16 of 73 participants (22%) who had a treatment outcome of SVR or virologic failure; all 16 achieved SVR12. Rates of SVR12 among Korean participants in this analysis (73/74, 98.6%) were similar to those in non-Korean Asian participants with GT1b infection (378/388, 97.4%), and to non-Asian participants with GT1b infection (589/608, 96.9%) enrolled in phase 2/3 EBR/GZR clinical trials.

Conclusions: The combination of EBR/GZR was highly effective in Korean participants with HCV GT1b infection, with high rates of SVR12 across all subgroups examined, including those with NS5A RASs.

Keywords: Hepatitis C, Elbasvir, Grazoprevir

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Rapid Virological Response, as a Predictor of Sustained Virologic Response of Sofosbuvir and Ribavirin in Korean Patients with Genotype 2 Chronic Hepatitis C Virus Infection

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Aims: The aim of this study is to investigate real-world data with sofosbuvir/ribavirin (SOF/RBV) in Korean patients with genotype 2 hepatitis C virus (HCV) infection and to investigate predicting factor of SVR 12.

Methods: 140 patients with genotype 2 chronic HCV infection treated with SOF/RBV were investigated prospectively. 400mg of SOF combined with weight adjusted RBV was administered for 12 weeks in patients without cirrhosis and for 16 weeks with cirrhosis. HCV RNA level was examined in pre-treatment, 4 weeks, end of treatment, and 12 weeks after end of treatment by RT-PCR method (COBAS® TaqMan® Analyzer, low detection limit,15 IU/mL; non-detection and below 15 IU/mL reported separately). The definition of rapid virological response (RVR) was defined as non-detection of HCV RNA at 4 weeks only.

Results: A total of 136 completed the treatment. 55 was male (40.4%) with a mean age of 61.6 ± 11.1 years. 99 (72.8%) were treatment naïve, 6 (4.4%) had a history of HCC, 23 (16.9%) had diabetes, and 33 (24.3%) had cirrhosis, of which had decompensation in 6. RVR was 77.9% (106/136), end of treatment response was 100% (136/136) and SVR12 was 96.0% (122/127). Of 5 with relapse, 4 were received 12 weeks of treatment and three of them did not reach RVR. Clinical factors associated with SVR12 were RVR status in multivariable analysis (P-value = 0.031). Contributing factors of RVR, cirrhosis, estimates glomerular filtration rate, and pre-treatment HCV RNA level were found to be significant. According to treatment duration, in 16 weeks treatment, SVR12 was not significantly different in RVR (-) and RVR (+) (94.7% vs. 100%, P-value = 0.483). However, in 12 weeks treatment, SVR12 was significantly higher in RVR (+) than RVR (-) (98.7% vs. 83.3%, P-value = 0.003). During treatment, 51/136 (37.5%) showed mild to moderate adverse events (urticaria, anemia, fatigue, insomnia, headache). 26 (19.1%) were reduced RBV dose due to anemia.

Conclusions: SOF/RBV treatment in genotype 2 HCV was effective, tolerable and RVR is an important predictor of SVR12. 16 weeks of treatment would be better for patients without RVR.

Keywords: Chronic hepatitis C, Genotype 2, Sofosbuvir, Rapid virologic response