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EP-125 - TIME TO VIRAL SUPPRESSION DOES NOT IMPACT SVR IN PATIENTS TREATED WITH GLECAPREVIR/PIBRENTASVIR FOR 8 WEEKS

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Objective:

The pangenotypic direct-acting antivirals (DAAs) glecaprevir (developed by AbbVie and Enanta) coformulated with pibrentasvir (G/P) are approved as an 8-week regimen to treat chronic HCV infection for all six major genotypes (GT). Historically, an on-treatment predictor of HCV cure with interferon (IFN)-containing regimens has been viral suppression at treatment week 4. However, the relevance of viral kinetics as predictors of cure in the era of shortened, 8-week DAA regimens is unclear, and concerns remain that failure to suppress HCV RNA quickly may lead to relapse. An integrated analysis of patients treated with G/P for 8 weeks was performed to investigate factors impacting time to viral suppression, and whether lack of viral suppression by treatment week 4 was predictive of relapse.

Methods:

Data were pooled from five phase 2 or 3 clinical studies, and included patients with HCV GT 1–6 infection without cirrhosis who were either treatment naïve or experienced with IFN or pegIFN with or without ribavirin (RBV) or sofosbuvir and RBV with or without pegIFN. G/P (300 mg/120 mg) was orally dosed once-daily for 8 weeks. Patients lost to follow up or with missing SVR12 data (N = 13) were excluded from the analysis since the impact of viral suppression (HCV RNA below lower limit of quantification [LLOQ]) on response cannot be assessed in these patients. Two patients with on-treatment virologic failure were excluded since we sought to determine whether detectable HCV RNA at treatment week 4 was predictive of relapse.

Results:

The analysis included 950 patients; 63 (7%) were black, 171 (18%) had BMI ≥ 30 , and 24% had baseline HCV RNA ≥ 6 million. The majority of patients were white, male, and HCV treatment-naïve. Among 942 patients with data, 906 (96%) had HCV RNA <LLOQ at treatment week 4, and of those, 899/906 (99%; 95% CI 98.4–99.6) achieved SVR12;

There was no common baseline factor more frequently observed among the 7 seven patients who relapsed other than male sex (5/7; 71%). Of the 36 patients with HCV RNA >LLOQ at treatment week 4 (median baseline HCV RNA 6.7 log₁₀ IU/mL; range 5.2–7.6 log₁₀ IU/mL), 100% (95% CI 90.4–100.0) achieved SVR12.

In patients treated with G/P for 8 weeks, failure to suppress HCV RNA by treatment week 4 was not predictive of treatment outcome, suggesting that treatment extension in patients eligible for 8-week regimens based on this milestone is not warranted.