BACKGROUND

• The development of direct acting antivirals (DAAs) has revolutionized the treatment of hepatitis C virus (HCV); drastically improving sustained virologic response (SVR) rates nearing 100% in most genotype (GT) 1 patients.

• Despite these exceptional cure rates, virologic failures still occur, which has been linked to the emergence of resistance mutations.1,2

• For those patients that failed treatment with an NS5A inhibitor, current guidelines recommend retreatment regimens employing the results of resistance testing, extending length of treatment, and adding ribavirin (RBV) to selected DAA regimen.3

• If NS5A inhibitor resistance associated substitutions (RASs) are detected, and NS3 inhibitor RASs are not, treatment with sofosbuvir (SOF), simeprevir (SIM), and RBV for 24 weeks is recommended.4

• Given the relative newness of these agents, there is a paucity of data to support these current guideline recommendations.

OBJECTIVE

• To evaluate the effectiveness of SOF + SIM + RBV for 24 weeks in retreating patients who previously failed HCV treatment containing an NS5A inhibitor.

METHODS

• Single center, observational cohort review of HCV patients that received retreatment with SOF + SIM + RBV for 24 weeks prescribed by the Vanderbilt University Medical Center (VUMC) Hepatology or Liver Transplant Clinic between January 2015 and December 2016 after failing treatment with an NS5A-containing DAA regimen.

Endpoints:

• Primary endpoint: SVR at minimum of 12 weeks following treatment completion.

• Secondary endpoints: viral responses on therapy, adverse events, and treatment discontinuations.

Study Population:

• Inclusion criteria: diagnosis of GT1 chronic hepatitis C, previously failed treatment with an NS5A inhibitor, subsequently prescribed SOF + SIM + RBV for 24 weeks.

• Exclusion criteria: No patients meeting inclusion criteria were excluded from this study.

RESULTS

BASELINE DEMOGRAPHICS (n=13)

Mean age – yr. [range] 53 [23-65]
Male sex – no. [%] 11 [84.6]
Race – no. [%] White – 10 [76.9] Black – 2 [15.4]
HCV Genotype – no. [%] 1a – 11 [84.6] 1b – 2 [15.4]
Mean HCV RNA – log_{10} IU/mL [range] 3.05x10^6 [2.7x10^4-2.14x10^7]
Previous liver transplantation – no. [%] 2 [15.4]
Cirrhosis – no. [%] 8 [61.5]
Child Turcotte Pugh (CTP) score – no. [%] CTP A – 9 [69.2] CTP B – 4 [30.8] CTP C – 0

Prior HCV DAAAs received – no. [%] NS5A + NS5B* = 11 [84.6] NS5A + NS5B + NS3/4A‡ = 2 [15.4]

SVR12

Mean HCV RNA – log_{10} IU/mL (range) 3.05x10^6 [2.7x10^4-2.14x10^7]
Previous liver transplantation – no. [%] 2 [15.4]
Cirrhosis – no. [%] 8 [61.5]
Child Turcotte Pugh (CTP) score – no. [%] CTP A – 3 [23.1] CTP B – 5 [38.5] CTP C – 0

Previous HCV DAAAs received – no. [%] NS5A + NS5B* = 11 [84.6] NS5A + NS5B + NS3/4A‡ = 2 [15.4]

**NS5A RASs not determined in 2 patients

CONCLUSIONS

• The use of SOF + SIM + RBV for 24 weeks is highly efficacious in patients who previously failed treatment with an NS5A-containing DAA regimen, thus aligning with current guideline recommendations.

• Despite a high prevalence of adverse events, treatment with SOF + SIM + RBV was generally well-tolerated in patients, even those with mildly decompensated cirrhosis (CTP B), reducing the risk of treatment discontinuations.

References:

