In October 2014, a combination directly acting antiviral (DAA) regimen consisting of ledipasvir (LDV) and sofosbuvir (SOF) was approved by the Food and Drug Administration for the treatment of chronic HCV genotype 1 infection.

On treatment hepatitis C (HCV) RNA levels were early predictors of treatment response and the mainstay of response-guided therapy to previous interferon-containing regimens.

The clinical utility of HCV RNA levels to guide treatment duration and predict treatment outcome with DAA-only therapy needs to be evaluated.

To determine the ability of HCV RNA levels at week 4 (W4) and end of treatment (EOT) to predict treatment outcome in HCV patients with or without HIV co-infection treated with LDV/SOF for 12 weeks.

**METHODS**

**Study Design**

67 HCV genotype 1 patients without cirrhosis or prior treatment experience were enrolled in two NAIAID phase 2 trials and treated with a single pill regimen of LDV/SOF (90/400 mg) once daily for 12 weeks: SYNERGY™: HCV mono-infected participants without cirrhosis (n=17); ERADICATE: HIV/HCV co-infected participants without cirrhosis – on combination antiretroviral (ARV) therapy (n=37) or ARV naive (n=13).

**Primary outcome measurement was sustained virologic response (SVR12), defined as HCV RNA below lower limit of quantification (LLOQ) 12 weeks post-treatment.**

**HCV RNA Measurements**

Serial measurements of HCV RNA levels were taken.

**Calculations**

- Negative predictive value (NPV) and positive predictive value (PPV) of HCV RNA at W4 and EOT:
  - NPV = # patients with HCV RNA LLOQ or TD < LLOQ who do not achieve SVR12
  - PPV = # patients with HCV RNA TD < LLOQ who achieve SVR12

- PPV = # patients with HCV RNA TD < LLOQ who achieve SVR12
- # patients with HCV RNA TD < LLOQ

**RESULTS**

- Table 1: Baseline Demographics and Clinical Characteristics of Study Participants

**CONCLUSIONS**

- Low negative predictive values of HCV RNA at week 4 underscore the importance of continued therapy for patients who fail to achieve undetectable levels of HCV RNA early on during treatment because the likelihood of achieving SVR12 is still high.

- Contrary to past experience with interferon-containing treatments, the presence of detectable HCV RNA at EOT is not predictive of relapse in these studies.

- The majority of patients with HCV RNA LLOQ or HCV RNA TD < LLOQ at week 4 achieved SVR12 (NPV <1%).

- 5 patients on SYNERGY and 7 patients on ERADICATE had HCV RNA TD < LLOQ at EOT by the Abbott assay. All 12 patients achieved SVR12.

- The majority of patients with HCV RNA LLOQ achieved SVR12 (NPV <1%). All patients had HCV RNA TD < LLOQ at EOT.