Non-adherence is the most important risk factor for ledipasvir/sofosbuvir HCV treatment failure in the real world.

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Abstract Body Background: Ledipasvir/sofosbuvir (LDV/SOF) fixed-dose combination is approved for treatment of chronic hepatitis C virus (HCV) genotypes 1, 4, 5, and 6. Sustained virologic response (SVR) rates are 94-98% for both treatment naïve and experienced genotype 1 HCV-infected patients with or without cirrhosis in clinical trials and 91-97% in real world practice. As more patients are treated, the population of patients who fail LDV/SOF is growing. Information about risk factors for failure may improve future management.

Objective: To investigate non-adherence and other risk factors for LDV/SOF treatment failure.

Methods: Demographic, virologic and clinical data were collected through post treatment week (PTW) 24 on all adult patients with chronic HCV infection who failed LDV/SOF between November 2014 and March 2016 at Mount Sinai. Adherence was addressed by patient self-report to provider. Non-adherence was defined as missing at least 7 doses of LDV/SOF. Case patients were compared to a convenience sample of (n=101) contemporaneously treated patients who achieved SVR12. Univariable analysis was conducted using chi-squared test to identify factors associated with LDV/SOF failure.

Results: Treatment failed in 39 patients; 85% (n=33) were male, the mean age was 59 years (range 34-80). Nearly all (n=36) had genotype 1 HCV (25 had 1a, ten had 1b, and one had 1l), eleven (28%) had HIV co-infection and 19 (49%) had liver cirrhosis. Intended treatment duration was 12 weeks in 30 (77%), 24 weeks in four (10%), and eight weeks in five (13%). During therapy, 34 (87%) had undetectable HCV viral load, while four never became viral load negative, despite a ≥ 4-log reduction. No patients had HCV breakthrough. Ten patients (26%) missed ≥ 7 doses, due to not taking medication as prescribed (n=4), hospitalization (n=3), loss of medication (n=3), failure to refill medication (n=1), and side effects (n=1). Treatment failure was associated with non-adherence (Odds Ratio (OR) 19.6, 95% Confidence Interval (CI) 3.87-99.28), male sex (OR 4.52, 95% CI 1.87-10.91) and Black race (OR 3.26, 95% CI 1.14-9.30).

Conclusion: LDV/SOF has a high SVR rate, but has failed in a growing number of patients as more HCV infected patients are treated. Missing ≥ 7 doses (non-adherence) was the single most important risk factor for treatment failure in our study. Our findings underscore the need for providers to clearly communicate dosing information and to ensure that patients have access to an uninterrupted supply of medication. Pre-treatment adherence counseling and a pill bottle monitoring system may also improve SVR rates.