Interferon-free Hepatitis C treatment increases surrogates of cardiovascular disease risk in black veterans

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INTRODUCTION

- Hepatitis C virus (HCV) usurps hepatic lipoproteins to sustain its life cycle.
- Untreated HCV infection decreases low density lipoprotein (LDL) and total cholesterol (TC) levels. After sustained virologic response (SVR), there is an initial increase in LDL and TC, which may ultimately increase cardiovascular disease (CVD) risk.
- In contrast, SVR with either Interferon (IFN)-based or IFN-free regimens with direct-acting antivirals (DAAs) has been shown to reduce CVD events in majority white populations stratified by ASCVD score.
- Statins are the mainstay of therapy to reduce CVD risk. However, statin use is limited by drug-drug interactions with antiretrovirals and direct-acting antivirals in patients with HIV and HCV.
- The effect of IFN-free therapy on lipid profiles after SVR, as an indirect measure of CVD risk, is unknown in Black patients.

AIM

- Assess demographics and prevalence of advanced liver disease in Veterans treated for HCV.
- Determine if surrogate markers for CVD risk differ based on comorbidities and presence of advanced liver fibrosis.

METHOD

- We evaluated HCV-infected Veterans from the Baltimore VA who were treated with DAAs between 2015-2019.
- We performed a retrospective analysis comparing lipid profile changes following SVR among those with early stage (F0-F2) fibrosis and advanced liver disease (ALD, F3-F4 fibrosis) using two-tailed paired t-tests.
- Independent t-tests were used to assess differences in lipid profiles based on fibrosis stage in patients with HIV and Type II Diabetes Mellitus (DM2).

RESULTS

- Of those treated for HCV (n=1,528), 96% (n=1,474) achieved SVR.
- Most patients were Black males (75%) and a minority (2.7%) received statin therapy during treatment (Table 1).
- Of 1,094 patients for whom data was available, an increase in total cholesterol (TC) and LDL ($p<0.01$ for both) was seen an average of 17 months after SVR, regardless of fibrosis stage (Figure 1).
- A significant decrease in triglyceride levels ($p=0.04$) was also seen in the ALD group after SVR (Figure 1).
- Mean pre-treatment HCV RNA level was comparable between fibrosis groups (F0-F2: 6.35 logs, F3-F4: 6.37 logs, $p=0.46$).
- There were 101 and 436 patients with HIV and DM2, respectively, for whom pre-treatment liver fibrosis data was available. In both groups, there were significant increases in LDL ($p=0.008$ (HIV), $p=0.003$ (DM2)) among patients with ALD following SVR.

Baseline Characteristic	N= 1474
Age, median years (SD)	64.6 (61,69)
Race % (N)	
Black or African American	75 (1110)
White	23 (345)
Other/Unknown/Declined to answer	2 (27)
Sex, % (N) male	97 (1426)
Diabetes, % (N)	35 (500)
Ethnicity, % (N)	
Not Hispanic or Latino	98 (1451)
Other/Unknown/Declined to answer	1.2 (18)
Hispanic or Latino	<1 (5)
HIV, % (N)	7 (101)
Median pre-treatment HCV RNA, IU/L	2,262,252.71 (SD 2,732,164.83)
Fibrosis stage pre-treatment, % (N)	
F0-F2	56 (828)
F3-F4	36 (525)
Treatment regimens, % (N)	
Ledipasvir/Sofosbuvir	75 (1106)
Elbasvir/Grazoprevir	8 (124)
Paritaprevir/Ombitasvir/Dasabuvir/ ritonavir	6 (85)
Sofosbuvir/Velpatasvir	3 (51)
Glecaprevir/Pibrentasvir	3 (40)
Sofosbuvir/Velpatasvir/Voxilaprevir	1 (15)
Other	4 (53)
Statin use during HCV treatment, % (N)	2.7 (40)

Table 1. Baseline characteristics of treated HCV-infected persons who achieved SVR.

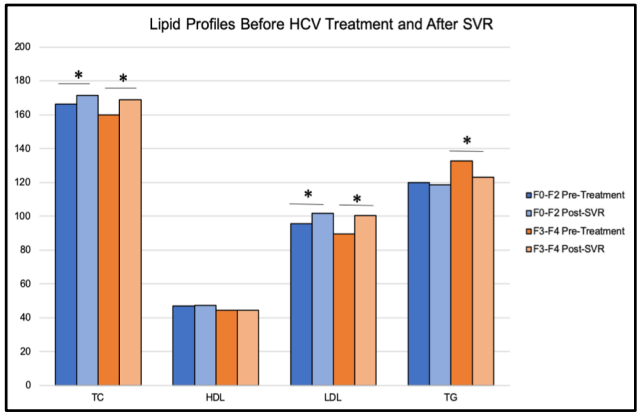

Figure 1. Mean lipid profile parameters before and after HCV treatment for patients who achieved SVR. TC was measured a mean of 8.1 months (228 days, SD 333 days) before treatment and 17.4 months (488 days, SD 196 days) after SVR. LDL was measured a mean of 8 months (224 days, SD 284 days) before treatment and 17.5 months (492 days, SD 201 days) after SVR. *=differences in means using paired t-test were statistically significant with $p<0.05$. HCV= Hepatitis C Virus, SVR= Sustained Virologic Response TC=Total Cholesterol, HDL= High Density Lipoprotein, LDL= Lipoprotein, TG= Triglycerides.

CONCLUSIONS

- In a cohort of mostly Black HCV-infected Veterans, significant increases in TC, driven by increases in LDL, were observed an average of 17 months after SVR regardless of fibrosis stage.
- Patients with ALD and HIV or DM2, who have an inherently higher risk of CVD, had increased LDL levels, suggesting that these patients should be screened and treated for HCV prior to development of ALD.
- Correlates such as the ASCVD score should be considered in the timing of HCV treatment, in order to reduce the long-term risk of CVD.
- Statin therapy in Veterans with HIV and HCV may be underutilized and adjustments in prescribing practices may reduce CVD risk in this population.

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