Real-world Data on HIV-Positive Patients with HCV Treated with Sofosbuvir and/or Simeprevir

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Background

- Regimens containing simeprevir (SMV) and sofosbuvir (SOF) have been highly effective in clinical trials.
- The COSMOS trial showed a greater than 93% sustained virological response (SVR) rate 12 weeks after completion of therapy with SMV/SOF with or without ribavirin (RBV) for hepatitis C (HCV) mono-infected genotype 1 patients.
- ***Data for SMV/SOF in HIV-positive patients are lacking.***
- The PHOTON trial placed co-infected patients on courses of SOF/RBV ranging from 12-24 weeks depending on genotype. SVR 12 rates were 76%, 90%, and 75% for genotypes 1, 2 and 3, respectively.
- ***SMV- and SOF-containing regimens in co-infected patients need investigation in real-world clinical practice.***

Methods

- Since December, 2013, data have been collected on patients at Mount Sinai Hospital with chronic HCV prescribed SMV and/or SOF.
- Records of 594 HCV-positive patients have been reviewed.
- Data have been collected on 78 HIV-positive patients with chronic genotype 1, 2 or 3 HCV infection who initiated:
  SMV/SOF with or without RBV
  SOF/RBV
- In this study, advanced fibrosis/cirrhosis was defined by biopsy and/or a FibroScan score ≥ 13.5 kPa and/or a FIB-4 score ≥ 3.25.
- Week 2 on-treatment responses were analyzed.
- Week 4 and week 12 post end-of-treatment (EOT) responses were analyzed to determine the SVR4 and SVR12 on a per-protocol basis.
- Week 2, SVR4 and SVR12 rates among the co-infected patients were compared to those HCV mono-infected patients placed on SMV- and/or SOF-containing regimens during the same period.

Regimens by Genotype

Genotype 1
- **SMV/SOF +/- RBV for 12 weeks for 34 patients (44%)**
- **SOF/RBV for 24 weeks for 31 patients (40%)**

Genotype 2
- **SOF/RBV for 12-24 weeks for 7 patients (9%)**

Genotype 3
- **SOF/RBV for 24 weeks for 6 patients (8%)**

General Patient Demographics

	Categorical: n=78 (%) Continuous: median (IQR)
Gender, male	65 (83%)
Age, years	57 (52-61)
Race, black	20 (26%)
Ethnicity, Hispanic	29 (37%)
BMI > 25	47 (60%)
History of diabetes	13 (17%)
History of hypertension	39 (50%)
History of depression	29 (37%)

Baseline HCV Characteristics

	Categorical: n (%) Continuous: median (IQR)
HCV VL, log IU/mL	6.31 (5.9-6.7)
Genotype 1	65/78 (83%)
Genotype 1a	50/65 (77%)
Genotype 2	7/78 (9%)
Genotype 3	6/78 (8%)
IL28B non-CC genotype	17/22 (77%)
Q80K mutation	2/4 (50%)
Treatment experienced	44/78 (56%)
PEG/RBV	36/44 (82%)
Non-responder	10/36 (28%)
Partial responder	12/36 (33%)
Relapser	9/36 (25%)
Unknown response	5/36 (14%)
Anti-HCV PI + PEG/RBV	7/44 (16%)
FIB-4 score ≥ 3.25	41/78 (52%)
History of HCC	5/78 (6%)
History of liver transplant	2/78 (3%)

Baseline HIV Characteristics

CD4 Count
- 65 patients had data on baseline CD4 counts
- Median CD4 count: 490, IQR: 326-629
- 5 patients had CD4 count < 200; only 3 were on HAART

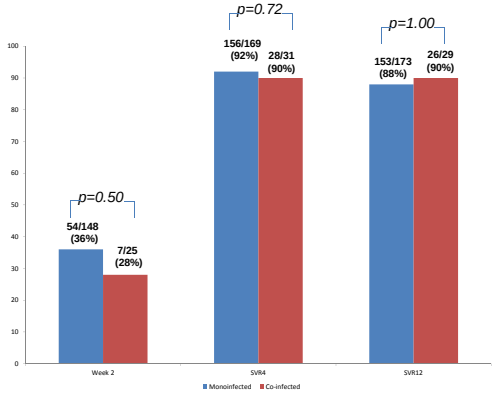
HIV Viral Load
- 49/65 (75%) Undetectable at baseline
- 7/65 (11%) Detectable, but < 20 copies/mL
- 9/65 (14%) Detectable

HAART Regimen
- 74/78 (95%) were on HAART prior to initiating HCV treatment
  - 18/74 (24%) were on a NNRTI-based regimen
  - 25/74 (34%) were on a PI-based regimen
  - 32/74 (43%) were on a NRTI + integrase inhibitor
  - 4/78 (5%) were not on HAART
- ***15 patients had their HAART regimen changed prior to starting SMV to avoid drug-drug interactions***

FIB-4 score, Treatment Experience, and SVR12 Rate by Genotype and Regimen

	N (%)	FIB-4 ≥3.25, n (%)	Naïve, n (%)	SVR12 Rate
Genotype 1	65/78 (83%)	36/65 (55%)	27/65 (42%)	39/54 (72%)
SMV/SOF ± RBV	34/78 (44%)	19/34 (56%)	16/34 (47%)	26/29 (90%)
SOF/RBV	31/78 (40%)	17/31 (55%)	11/31 (35%)	13/25 (52%)
Genotype 2	7/80 (9%)	2/7 (29%)	2/7 (29%)	3/5 (60%)
Genotype 3	6/80 (8%)	3/6 (50%)	4/6 (66%)	2/5 (40%)

Week 2, SVR4 & SVR12 Results for HCV vs HIV/HCV Patients on SMV/SOF ± RBV



Serious Adverse Events

- **SMV/SOF patients**
  - ***One patient died.***
  - 60-year-old known Child-Pugh Class C cirrhotic who, at baseline, had platelets of 55, a total bilirubin of 3.9, an INR of 2 and an albumin of 1.6
  - He was initially prescribed SMV/SOF
  - He further decompensated 4 weeks into therapy with development of ascites, spontaneous bacterial peritonitis (SBP) and an elevated total bilirubin to 13.2 mg/dL.
  - He was subsequently changed to SOF/RBV
  - 12 weeks after his DAA regimen was changed, he was admitted with fatigue and electrolyte disturbances.
  - Five days after admission, he died of sepsis secondary to an ESBL E. coli. Source was presumably SBP.
- **SOF/RBV patients**
  - No patients died
  - There were 4 early treatment discontinuations due to expected side effects from RBV such as declining hemoglobin values and worsening depression

Patient-reported Adverse Effects

	SMV/SOF (n=19)	SMV/SOF/RBV (n=15)	SOF/RBV (n=44)	Total (n=78)
Rash	5 (26%)	7 (46%)	10 (23%)	22 (28%)
Pruritus	5 (26%)	6 (40%)	5 (11%)	16 (21%)
Fatigue	2 (11%)	7 (46%)	16 (36%)	25 (32%)
Insomnia	3 (16%)	6 (40%)	15 (34%)	24 (31%)
Increased anxiety	3 (16%)	3 (20%)	7 (16%)	13 (17%)
Decreased appetite	1 (5%)	3 (20%)	5 (11%)	9 (12%)
Arthralgia	1 (5%)*	3 (20%)**	5 (11%)	9 (12%)

*Patient clinically suspected of gouty flare given past history and appearance of his ankle joint on physical exam. Also, his uric acid was elevated above 9 mg/dL
**One patient was suspected of a gouty flare

SMV/SOF Treatment Failures

- 45 y.o. male, on HAART, with liver transplant in 2010, on long-standing mycophenolate mofetil and tacrolimus. F3, per liver biopsy, HCV treatment experienced.
- 52 y.o. male, on HAART, suspected cirrhosis, HCV previously treatment naïve
- 49 y.o. female, not on HAART, CD4 count 193, 29%, HIV viral load < 20, detected, suspected cirrhosis, HCV previously treatment experienced

Conclusions

- **Preliminary data indicate that SMV/SOF is a safe and effective option for HIV-positive patients co-infected with genotype 1 HCV who have either (1) fibrosis without cirrhosis or (2) compensated cirrhosis.**
- **Based on past and current data, SMV should not be used in the setting of decompensated cirrhosis.**

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