Sofosbuvir and Peginterferon Alfa-2a/Ribavirin for Treatment-Naïve Genotype 1–4 HCV-Infected Patients Who Are Coinfected With HIV

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Introduction

- 4–5 million people are infected with HIV and hepatitis C virus (HCV) worldwide[1]
  - ~30% of HIV-infected people are HCV coinfected
  - ~6% of HCV-infected people are HIV coinfected
- Coincident HIV infection increases rates of fibrosis, cirrhosis, hepatocellular carcinoma, and overall mortality in HCV-infected people[2,3]
- Standard-of-care treatment with 48 weeks of pegylated interferon (PEG)/ribavirin (RBV) results in sustained virologic response (SVR) rates of 27%–40%[4,5]
- Sofosbuvir (SOF)—an NS5B nucleoside inhibitor—has demonstrated safety and efficacy in HCV–mono-infected patients[6,7]

Objective

- To assess the safety and efficacy of a 12-week course of SOF + PEGα-2a (Pegasys®, Genentech USA, Inc., South San Francisco, CA)/RBV for the treatment of patients with chronic HCV coinfected with HIV

Methods

- Single-center, open-label, single-arm trial (Study P7977-1910; ClinicalTrials.gov Identifier NCT01565889)
- Patients with HCV genotype (GT) 1–4 received SOF 400 mg/d + subcutaneous PEG 180 µg/wk and weight-based RBV (1000–1200 mg/d) for 12 weeks
- Primary endpoints
  - Efficacy: proportion of patients with SVR 12 weeks after end of treatment (SVR12)
  - Safety and tolerability of treatment, including effects on HIV RNA and CD4 T-cell %
- Assays used:
  - HCV: Roche COBAS® Taqman® HCV Test v2.0 (Roche Molecular Systems Inc., Pleasanton, CA); lower limit of quantitation (LLOQ): 25 IU/mL
  - HIV: COBAS AmpliPrep/COBAS TaqMan HIV-1 Test, v2.0 (Roche Molecular Systems)

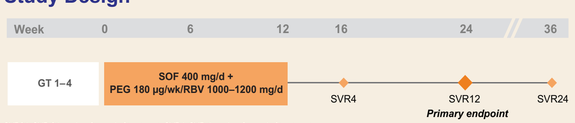
Inclusion Criteria

- HCV treatment naïve
- HCV GT 1–6 (only GT 1–4 enrolled)
- Stable antiretroviral (ARV) regimen for >8 weeks
- CD4 T-cell count >200 cells/mm^3
- No cirrhosis

Allowed ARV Regimens

- Tenofovir/emtricitabine +
  - Efavirenz;
  - Atazanavir/ritonavir;
  - Raltegravir;
  - Darunavir/ritonavir; or
  - Rilpivirine

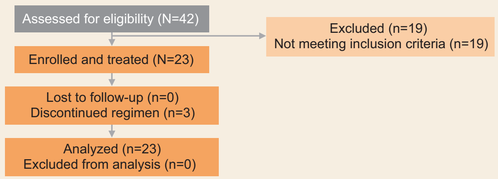
Study Design



SVR24, SVR 24 weeks after end of treatment; SVR4, SVR 4 weeks after end of treatment.

Results

Disposition



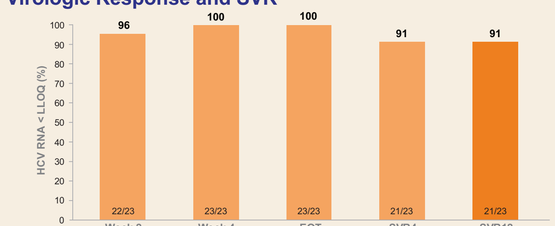
Demographics

Characteristics	SOF + PEG/RBV (N=23)
Host	
Male, n (%)	18 (78)
Black race, n (%)	8 (35)
Mean age, y (range)	47 (29–59)
Mean BMI, kg/m^2 (range)	26.3 (18.0–46.4)
IL28B GT, n (%)	
CC	5 (22)
CT	14 (61)
TT	3 (13)
Missing	1 (4)
Disease	
HCV GT, n (%)	
1a	15 (65)
1b	4 (17)
2b	1 (4)
3a	2 (9)
4a/b/c	1 (4)
Mean HCV-RNA, $\log_{10}$ IU/mL (SD)	6.59 (0.87)
Mean CD4 T-cell count, cells/µL (SD)	562 (302)
Mean CD4 T-cell %, SD	28.8 (9.7)
ARV regimen: tenofovir/emtricitabine +, n (%)	
Efavirenz	7 (30)
Atazanavir/ritonavir	5 (22)
Raltegravir	6 (26)
Darunavir/ritonavir	4 (17)
Rilpivirine	1 (4)

BMI, body mass index; IL28B, interleukin-28B; SD, standard deviation.

Efficacy

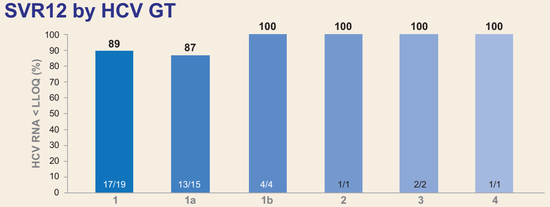
Virologic Response and SVR



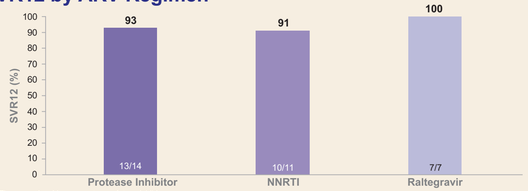
EOT, end of treatment.

- No on-treatment HCV virologic breakthrough
- 2 patients did not achieve SVR12:
  - Patient 1: white Latino man aged 41 years with HCV GT 1a and IL28B TT GT, who discontinued treatment after 6 weeks due to withdrawal of consent
  - Patient 2: white Latino man aged 53 years with HCV GT 1a and IL28B CT GT, who completed study treatment and subsequently relapsed

SVR12 by HCV GT



SVR12 by ARV Regimen



NNRTI, non-nucleoside reverse transcriptase inhibitor.

Safety

Adverse Events (AEs) Summary

AE, n (%)	SOF + PEG/RBV (N=23)
Any AE	16 (70)
Serious AE	0
Grade 3 AE	7 (30)
Grade 4 AE	0
Discontinuation due to AE*	2 (9)

*Anemia at Week 6 (n=1) and altered mood at Week 8 (n=1).

Common AEs in >5% of Patients

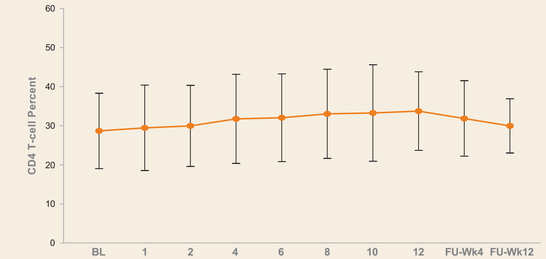
AE, n (%)	SOF + PEG/RBV (N=23)
Anemia	12 (52)
Fatigue	8 (35)
Hyperbilirubinemia	4 (17)
Neutropenia	4 (17)
Thrombocytopenia	4 (17)
Myalgia	3 (13)
Abdominal pain	2 (9)
Vomiting	2 (9)
Herpes zoster	2 (9)
Dizziness	2 (9)
Depression	2 (9)
Leukopenia	2 (9)

Grade 3/4 Laboratory Abnormalities

Abnormalities, n (%)	Grade 3	Grade 4
Any Grade 3/4	3 (13)	4 (17)
Neutropenia	1 (4)	2 (9)
Leukocytopenia	3 (13)	0
Elevated GGT	1 (4)	0
Hyperbilirubinemia*	2 (9)	2 (9)
Hyperglycemia	1 (4)	0

*All patients were taking atazanavir as part of ARV regimen. GGT, γ-glutamyl transpeptidase.

HIV Safety Labs



BL, baseline; FU, follow-up.

- No HIV virologic breakthrough through follow-up Week 4 of the study
- No changes to ARV regimens throughout study

Conclusions

- A 12-week treatment regimen of SOF + PEG/RBV was highly effective in this pilot study of HCV/HIV-coinfected patients
- SVR12 rates were similar to those seen with this regimen in HCV mono-infected patients[7]
- SOF was well-tolerated in patients taking a wide variety of HIV ARV regimens
- Low risk of HIV virologic breakthrough with SOF + PEG/RBV treatment

References

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