Poster # 559

Field-based Delivery of HCV therapy with Minimal Monitoring to PWID in Chennai, India

Sunil S Solomon,[1] Amrose Pradeep,[2] Mark Sulkowski,[1] Allison M McFall,[2] Aylur K Srikrishnan,[3] Nandagopal Paneerselvam,[3] Shanmugam Saravanan,[3] Santhanam Anand,[3] Muniratnam S Kumar,[3] David Thomas,[1] Shruti H Mehta[2]

[1]Johns Hopkins University School of Medicine, MD; [2]Johns Hopkins Bloomberg School of Public Health, USA; [3]YR Gaitonde Centre for AIDS Research and Education, India

Correspondence to:
Sunil S Solomon,
1830 E Monument St, Rm 444,
Baltimore, MD 21287
sss@jhmi.edu

The Chennai HIV, Hepatitis C and EERal Study

BACKGROUND

- In 2016, WHO released **elimination** targets for hepatitis C virus (HCV)
- For these targets to be achieved, strategies must reach those **hardest to reach** in **low-and-middle-income countries** (LMICs) such as **people who inject drugs**
- Access in LMICs has improved with availability of **generic antivirals** ($200 USD / 28 days) but monitoring remains costly (cost of HCV RNA is $80 USD and HCV genotype is $90 USD)
- We evaluated the **feasibility** of **field-based directly observed therapy** (DOT) with **minimal molecular monitoring** for HCV therapy in current and former **PWID** in Chennai, **India** where **genotypes 1 and 3** predominate.

METHODS

RANDOMIZATION

- Study participants were recruited from an ongoing cohort of current and former PWID (CHHEERS) from September 2015 to March 2016
- 50 PWID (of 98 screened) were randomized 1:1 to receive Sofosbuvir + Pegylated interferon + Ribavirin (SOF + PR) for 12 weeks (Arm 1) or Sofosbuvir + Ribavirin (SOF + RBV) for 24 weeks (Arm 2)

TREATMENT DELIVERY / MONITORING

- HCV RNA testing was done at baseline and 12 weeks after the end of treatment (EOT) to measure sustained virologic response 12 (SVR, HCV RNA < lower limit of quantification [LLOQ] 12 weeks after EOT)
- Subjects in Arm 1 visited the study clinic once weekly for pegylated interferon injections
- For subjects in both arms, SOF/RBV was delivered daily by outreach workers at subject-selected venues along with a food packet
- Safety labs (complete blood count) were performed every four weeks and liver enzymes were assessed after 12 weeks of treatment for Arm 2
- Study visits occurred every 4 weeks

ELIGIBILITY CRITERIA

- Age ≥18 years and able to provide written informed consent
- Chronic HCV Infection (detectable HCV RNA)
- If HIV co-infected, participants had to be either ART naïve or on tenofovir-containing regimen
- Have the following laboratory parameters: ALT ≤ 10 x ULN; AST ≤ 10 x ULN; hemoglobin ≥ 12 g/dl; INR ≤ 1.5 x ULN (unless known hemophilia or stable on an anticoagulant regimen); albumin ≥ 3 g/dl; direct bilirubin ≤ 1.5 x ULN; Creatinine clearance ≥ 60 ml/min; alpha fetoprotein <50 ng/ml; absolute neutrophil count ≥ 1500 µl; platelet count ≥90,000 µ/l; and thyroid stimulating hormone ≤ ULN
- Female patients who were pregnant/nursing and male patients with pregnant female partners were excluded
- Persons were also excluded if they had evidence of hepatic decompensation, had previously been treated for HCV, were co-infected with hepatitis B (HBsAg) or had a medication that was contraindicated for use with either pegylated interferon or ribavirin

TRIAL OUTCOMES AND STATISTICAL ANALYSIS

- The primary outcome was treatment completion
- Secondary outcomes included 1) SVR; 2) frequency of severe adverse events (SAEs); and 3) change in insulin resistance (HOMA-IR)
- 1 of the 6 persons who did not complete treatment was reached for HCV RNA testing. Other secondary outcomes could not be ascertained in these 6 persons.
- An intention to treat (Missing=Failure) was the primary analytical approach

RESULTS

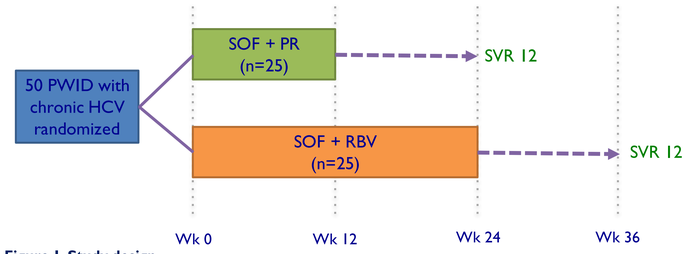

Figure 1. Study design

	Week							
	0	4	8	12	16	20	24	36
HCV RNA	X						X*	X**
HCV genotyping								
CBC	X	X	X	X	X**	X**	X*,**	
LFT				X**			X*,**	X**

Table 1. Schedule of laboratory testing during study
***only in the SOF+PR arm; ** only in the SOF+RBV arm**

	SOF+PR (n=25)	SOF+RBV (n=25)
Median age in years, (IQR)	46 (41 – 50)	46 (44 – 47)
Male, n(%)	25 (100)	25 (100)
Median monthly income, in USD (IQR)	90 (68 – 1290)	90 (72 – 150)
History of substance use in the prior month, n(%)	13 (52)	12 (48)
Liver stiffness category, n(%)		
• *<8 kPa*	15 (60)	12 (48)
• *8-12.3 kPa*	5 (20)	8 (32)
• *>12.3 kPa*	5 (20)	5 (20)
FIB-4 Index, n(%)		
• *Class 1, ≤1.45*	6 (24)	7 (28)
• *Class 2, 1.46 - 3.25*	16 (64)	11 (44)
• *Class 3, >3.25*	3 (12)	7 (28)
CTP Classification, n(%)		
• *Class A*	25 (100)	25 (100)
Median MELD score, (IQR)	7 (6 – 7)	7 (6 – 7)
Median HCV RNA in log_{10} copies/ml, (IQR)	6.5 (6.1 – 6.6)	6.1 (5.5 – 6.7)
HCV Genotype, n(%)		
• *1a*	2 (8)	5 (20)
• *3a*	22 (88)	20 (80)
• *6n*	1 (4)	0
HIV co-infected, n(%)	0	2 (8)
Median HOMA-IR	1.3 (0.7 – 3.4)	2.4 (1.1 – 5.6)

Table 2. Demographic and clinical characteristics of participants at baseline

	SOF+PR (n=25)	SOF/RBV (n=25)	p-value
Primary Outcome			
Treatment Completion, n(%)	22 (88)	22 (88)	1.0
Secondary Outcomes			
Sustained virologic response 12 (SVR12), n(%)	22 (88)	15 (60)	0.05
Median number of SAEs	0	0	-
Median change in insulin resistance (measured using HOMA-IR), IQR	1.2 (-0.1 – 9.1)	0.20 (-1.3 – 6.0)	0.30
Exploratory outcomes			
Percentage completed doses			
• *0-30%*	3 (12)	3 (12)	
• *75 -90%*	3 (12)	2 (8)	0.93
• *>90-95%*	2 (8)	4 (16)	
• *>95%-100%*	17 (68)	16 (64)	
Percentage observed doses received†			
• *70-90%*	0 (0)	3 (12)	
• *>90-95%*	4 (16)	3 (12)	0.31
• *>95-100%*	21 (84)	19 (76)	

Table 2. Trial outcomes

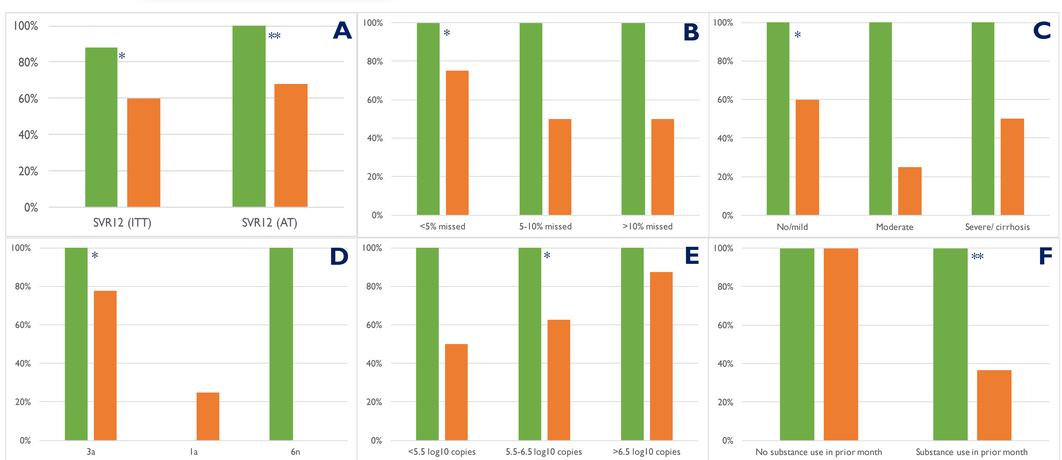

Figure 1. Sustained virologic response 12 (SVR) by treatment arm and factors of interest. Green is SOF + PR and Orange is SOF + RBV. ***Panel A***. SVR 12 for the intention to treat analysis (ITT, n=50) analysis and the As treated analysis (AT, n=44). Other AT comparisons are by: ***Panel B***. Percentage of missed doses; ***Panel C***. Pre-treatment liver stiffness; ***Panel D***. HCV genotype; ***Panel E***. Pre-treatment HCV RNA level; ***Panel F***. Drug or alcohol use in the month prior to treatment. * - p<0.05; ** - p<0.01

CONCLUSIONS

- Field-based DOT of HCV therapy without real-time molecular monitoring was logistically feasible in this population of current and former PWID many of who were still using drugs or alcohol regularly
- However, achieving 100% adherence was challenging even in the context of daily field-based delivery
- SOF+PR appeared superior to SOF/RBV in achieving SVR, especially in those who missed doses
- No discontinuations due to side effects were observed in either arm
- Ongoing substance use appeared to be a barrier to achieving SVR in the those receiving SOF/RBV for 24 weeks but not in those on SOF + PR for 12 weeks
- In settings where injections are perceived more effective than pills and/or adherence may be challenging, there may remain a role for peginterferon in combination with oral direct acting antivirals for short treatment durations

ACKNOWLEDGEMENTS

This research was supported by the National Institutes of Health, US Grant # 1R01DA026727 and facilitated by the Johns Hopkins Center for AIDS Research (1P30AI094189). We thank our study staff and participants, without whom this research would not have been possible. ClinicalTrials.gov identifier: NCT02541409