Poster 692: Effect of HIV Co-infection on Adherence to a 12-week regimen of HCV Therapy with Ledipasvir/Sofosbuvir

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BACKGROUND

- Treatment of hepatitis C virus (HCV) infection has evolved from interferon (IFN) and ribavirin (RBV) to directly acting antiviral agents (DAAs) in HCV mono-infected and HIV/HCV co-infected patients.
- We hypothesized that HIV/HCV co-infected patients on antiretroviral (ARV) therapy with excellent HIV control will have better adherence to study drugs than those who are not on ARVs and those with HCV mono-infection.
- <u>Objective</u>

To compare adherence rates of the DAA regimen of ledipasvir/sofosbuvir (LDV/SOF) among HCV mono-infected and HIV/HCV co-infected patients, with and without concomitant ARV therapy.

METHODS

- Seventy HCV genotype-1, treatment naïve patients were enrolled in two NIAID Phase 2 clinical trials and treated with LDV (90 mg) and SOF (400 mg) in a fixed dose combination once daily for twelve weeks.
  - SYNERGY[1]: HCV mono-infected participants (n=20)
  - ERADICATE[2]: HIV/HCV co-infected participants (ARV untreated n=13, on ARV therapy n=37)
- Adherence was measured using three tools:
  - Medication Event Monitoring System (MEMS) caps
  - Pill Counts
  - Patient Report
- Statistical analysis: nonparametric Wilcoxon rank sum, Chi square tests (GraphPad Prism 6.0) and multivariate logistic regression was performed.

RESULTS

- Baseline characteristics are shown in Table 1.
- Adherence to LDV/SOF was high by all three modalities (Figure 1). In all three groups, adherence as measured by MEMS was significantly less than by patient report.
- Adherence as measured by MEMS decreased from Week 4 to Week 12 in all three treatment groups (Figure 2).
- According to pill counts, 50% of all patients missed no doses (35/70) (Table 2).
- Sixty-nine out of seventy patients (99%) achieved sustained virologic response (SVR) 12 weeks post-treatment.[1,2]
  - The one patient who relapsed kept a pillbox during treatment, making adherence difficult to measure. She returned no pills at the end of treatment.

Table 1: Baseline Characteristics

Baseline Characteristics	HCV Mono-infected *n*=20	HIV/HCV ARV Untreated *n*=13	HIV/HCV ARV Treated *n*=37
	No. (%) & Median (IQR)		
Age	59 (55,61)	59 (54,62)	58 (51,63)
Male	14 (70)	7 (54)	30 (81)
Black	16 (80)	10 (77)	32 (86)
BMI	25 (23,28)	26 (23,29)	26 (22,29)
Advanced Liver Disease	7 (35)	5 (38)⊙	8 (22)⊙
HCV RNA > 800,000 IU/ml	15 (75)	7 (54)	20 (54)
HCV genotype 1a	11 (55)	9 (75)	30 (81)
Patient-Report Baseline Questionnaires *(Some answers may have been left blank)*			
Psychiatric Diagnosis	7 (35)	7 (54)	8 (22)
Alcohol consumption last 30 days (Y)*	1 (5)	7 (54)	22 (59)
Marijuana Last 6 Mo (Y)*	6 (30)	3 (25)	2 (6)
Cocaine Last 6 Mo (Y)	2 (10)	2 (15)	2 (6)
Heroin Last 6 Mo (Y)	0	0	2 (6)
Highest education >12th grade	9 (45)	4 (31)	11 (34)
Work for pay outside the home (Y)	9 (45)	3 (23)	15 (43)

⊙Patients with HIV and Stage 4 liver disease excluded.
*$p<0.05$

Figure 1: High adherence to LDV/SOF for 12 weeks as measured by MEMS, Pill Count and Patient Report.

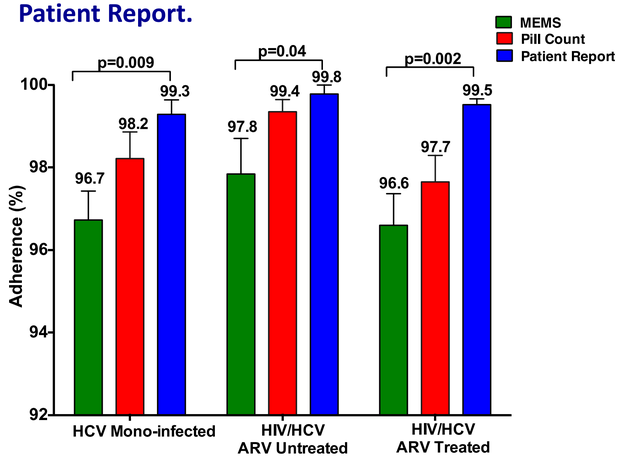
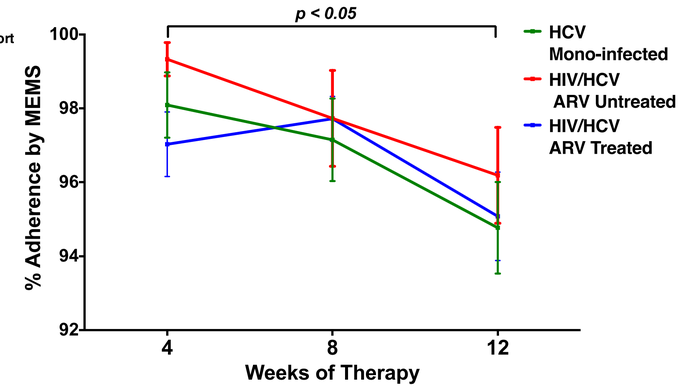


Figure 2: Mean adherence over course of treatment as measured by MEMS



- Adherence to therapy decreased significantly from Week 4 to Week 12 in all three groups. *P = 0.01, 0.02 and 0.01.*

Table 2: Missed Doses by Pill Count

	HCV Mono-infected *n*=20	HIV/HCV ARV Untreated *n*=13	HIV/HCV ARV Treated *n*=37	All Patients *n=50*
	No. (%)			
No missed doses	10 (50)	7 (54)	18 (49)	35 (50)
One to four missed doses (95-99% adherence)	8 (40)	5 (38)	15 (43)	28 (40)
Five to eight missed doses (90-94% adherence)	1 (5)	0	1 (3)	2 (3)
More than eight missed doses (<90% adherence)	1 (5)	1 (8)	3 (8)	5 (7)

CONCLUSIONS

- Adherence to the single daily tablet of LDV/SOF was high in this urban population and did not significantly differ among HCV mono-infected, HIV/HCV co-infected ARV treated, and HIV/HCV co-infected ARV untreated patients.
- Adherence did significantly decline over time in all 3 groups, suggesting pill fatigue, and needs to be evaluated in larger patient population in real-life scenarios.

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2. Osinusi A, et al., "Virologic Response Following Ledipasvir/Sofosbuvir Administration in Patients With HCV Genotype 1 and HIV Coinfections", *JAMA*, (in press).