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Virological responses during treatment for recent hepatitis C virus: Potential benefit for ribavirin use in HCV/HIV co-infection

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Introduction

A rise in the incidence of hepatitis C virus (HCV) infection among men who have sex with men (MSM) has been reported [1-6]. In HIV negative individuals with recent HCV, sustained virological response (SVR) ranges from 57-88% with pegylated interferon (PEG-IFN) mono-therapy (12-24 weeks), [7-14] with no evidence of additional benefit for ribavirin (RBV). In those with HIV/HCV, treatment recommendations are less clear [15]. In chronic HCV, PEG-IFN/RBV responses are lower in HIV positive patients (SVR of 27-40% vs. 54-56%) [16-20]. Thus, clinicians use more conservative regimens (e.g. PEG/RBV) to treat recent HCV in HIV positive individuals.

It is unclear whether ribavirin provides additional benefit in treatment for recent HCV in those with HIV/HCV. Although data from two small studies suggest that PEG-IFN for the treatment of acute HCV in HCV/HIV co-infection may be ineffective [21, 22], another study showed no difference in those receiving PEG-IFN with and without RBV [23]. Given increased response rates with direct acting antivirals, a randomized controlled trial comparing PEG-IFN with and without ribavirin during recent HCV is unlikely. Data informing guidelines for treatment of recent HCV within this population are required.

The Australian Trial in Acute Hepatitis C (ATAHC) investigated treatment for recent HCV (HIV positive and negative). This study evaluated virological decline (and impact of ribavirin) during treatment for recent HCV, based on a non-randomised comparison of HCV infected individuals receiving PEG-IFN monotherapy and HCV/HIV infected individuals receiving therapy with PEG-IFN/ribavirin. Predictors of rapid virological response (RVR) were also evaluated.

Methods

Study design

ATAHC was a multicenter, prospective cohort study of the natural history and treatment of recent HCV, as described elsewhere [14]. Recruitment was from June 2004 through November 2007. Recent infection with either acute or early chronic HCV infection was diagnosed with the following eligibility criteria:

First positive anti-HCV antibody within 6 months of enrolment; *and either*

- a. *Acute clinical hepatitis C infection*, defined as symptomatic seroconversion illness or alanine aminotransferase (ALT) level greater than 10 times the upper limit of normal (>400 IU/L) with exclusion of other causes of acute hepatitis, at most 12 months before the initial positive anti-HCV antibody; *or*
- b. *Asymptomatic hepatitis C infection with seroconversion*, defined by a negative anti-HCV antibody in the two years prior to the initial positive anti-HCV antibody.

All participants with HCV RNA during the screening period (maximum 12 weeks) were assessed for HCV treatment eligibility. All study participants provided written informed consent. The study protocol was approved by St Vincent's Hospital Human Research Ethics Committee and local ethics committees at sites.

HCV treatment

Participants initiating treatment received PEG-IFN- α -2a (PEG-IFN) 180 micrograms weekly for 24 weeks. Due to non-response at week 12 in the initial two participants with HCV/HIV co-infection, the study protocol was amended to provide PEG-IFN and ribavirin (1000-1200 mg in genotype 1 and 800 mg in genotypes 2/3) therapy for 24 weeks in HIV positive individuals.

Detection and quantification of HCV RNA

HCV RNA assessment was performed at screening, baseline, weeks 4, 8, 12, 24, 36, 48 and 12 weekly following SVR. HCV RNA assessment was performed initially with a qualitative HCV-RNA assay (TMA assay, Versant, Bayer, Australia, lower limit of detection 10 IU/mL) and if detectable repeated on a quantitative assay (Versant HCV RNA 3.0 Bayer, Australia lower limit of detection 615 IU/mL). Samples that were nonreactive by quantitative assays but reactive by qualitative assays were assigned an HCV RNA level of 300 IU/mL, whereas samples testing negative for HCV by both assays were assigned an HCV RNA level of 5 IU/mL. HCV RNA values were log-transformed. HCV genotype (Versant LiPa2, Bayer, Australia) was performed on those with detectable HCV RNA at screening.

IL28B genotyping

A single nucleotide polymorphism (SNP) in the *IL28A/B* gene region, rs12979860, was genotyped for all participants in whom DNA extracted from cell pellets was available [24]. For remaining patients, DNA was extracted from 200 μ L serum with the QIAamp UltraSens Virus Kit (Qiagen, Hilden, Germany) and rs12979860 genotyped by TaqMan® Pre-Designed SNP Genotyping Assay (Applied Biosystems, Foster City, United States) according to the manufacturer's instructions.

Study assessments

Study visits occurred every two weeks from baseline to week 8 and every four weeks from week 8 until the end of treatment. A questionnaire was administered at screening and every 12 weeks, to obtain information on injection of illicit drugs and social functioning [25].

Study definitions

The presentation of recent HCV at the time of diagnosis was classified as either acute clinical or asymptomatic infection. Acute clinical infection included those with either a documented clinical history of symptomatic seroconversion illness and those without clinical symptoms but with a documented peak ALT above 400 IU/ml at or prior to the time of diagnosis. Participants with asymptomatic infection included participants with anti-HCV antibody seroconversion but no acute clinical symptoms or documented peak ALT above 400 IU/ml. The estimated date of infection was calculated as previously described [14]. Adherence was defined as the receipt of at least 80% of scheduled PEG-IFN alfa-2a doses and therapy for 80% of the scheduled treatment period. For participants in whom therapy was terminated at 12 weeks due to virological non-response, the scheduled treatment period was defined as 12 weeks.

Study outcomes

The primary study outcome was HCV RNA decline over the first 12 weeks of therapy. These analyses were restricted to those 80% adherent to PEG-IFN. Secondary endpoints included the proportion of participants with undetectable HCV RNA (<10 IU/mL) at weeks 4 (RVR), 12 (early virological response, EVR), 24 (end-of-treatment response, ETR) and 48 (SVR). If HCV RNA had not been assessed at week 48, the result of next available HCV RNA was used for SVR.

Statistical analyses

Baseline characteristics were compared between groups using the Student's t-test and Fisher exact test (or χ^2 test), as appropriate. The proportion with RVR was assessed in the adherent population and stratified by HIV.

Logistic regression analyses were used to estimate crude and adjusted odds ratios (OR) and 95% confidence intervals (95% CI) to identify predictors of RVR. In unadjusted analyses, potential predictors were determined *a priori* and included sex, injecting drug use in the past month at baseline, social functioning score (stratified by median), *IL28B* genotype (rs12979860), HCV RNA levels at baseline, HCV genotype (1 vs. 2/3), receipt of ribavirin (only HIV infected individuals received ribavirin), duration of HCV and acute presentation. Social functioning was calculated using a validated scale from the Opiate Treatment Index [25] addressing employment, residential stability, inter-personal conflict and social support. A higher score reflects poorer social functioning. HCV RNA levels were stratified by log transformed values of the median (400,000 IU/mL=5.6 log₁₀ IU/L). All variables with P<0.20 in bivariate analysis were considered in multiple logistic regression models using a backwards stepwise approach sequentially eliminated subject to the result of a likelihood ratio test.

To assess the impact of ribavirin on early virological decline during treatment for recent HCV, changes in mean HCV RNA (log₁₀ IU/L) were compared among adherent HCV individuals receiving PEG-IFN and HCV/HIV individuals receiving PEG-IFN/ribavirin (including corresponding 95% CI). All HCV RNA comparisons between groups were performed using Student's t-test. Additional stratified analysis were performed according to

estimated duration of infection (<26 vs. ≥26 weeks) and IL28B genotype (favorable rs12979860 CC; or unfavorable rs12979860 CT/TT).

Among adherent participants, EVR, ETR, SVR and viral relapse, stratified by HIV status, were assessed. Logistic regression analyses were performed to assess whether RVR was associated with SVR. The PPV and NPV of RVR and EVR for predicting SVR was also assessed. Statistically significant differences were assessed at $p < 0.05$; p-values are two-sided. All analyses were performed using Stata v12.0 (College Station, TX, United States).

Results

Patient Population

Overall, 163 participants were enrolled. Among the final treated analysis population ($n=109$), 74 HCV participants received PEG-IFN monotherapy and 35 HCV/HIV participants received PEG-IFN/ribavirin. Baseline characteristics from the ATACH study have been published previously [14], the intent-to-treat ETR and SVR were 69% and 55% in those with HCV infection and 80% and 74% in those with HCV/HIV co-infection [14].

The overall proportion with 80/80 PEG-IFN adherence was 82% (89 of 109) [26]. HCV/HIV participants ($n=35$) demonstrated a higher PEG-IFN 80/80 adherence than mono-infected participants (91% vs. 77%, $P=0.070$). Sustained virological response (SVR) was higher among those with 80/80 PEG-IFN adherence (67% vs. 35%, $P=0.007$). Given the strong relationship between adherence and response to therapy, further analysis of rapid and early virological response in ATACH were limited to the population with 80/80 adherence.

Baseline characteristics of adherent participants with recent HCV ($n=89$), stratified by HIV infection, are shown in Table 1. Diagnosis of recent HCV was made on the basis of acute clinical hepatitis in 62% (55 of 89) and on anti-HCV antibody seroconversion in 38% (34 of 89). The estimated duration of infection at treatment initiation was ≥26 weeks in 75% (67 of 89).

Among adherent treated participants (Table 1), those with HCV/HIV were older, more often male (100% vs. 61%), more often have tertiary education (72% vs. 42%), have full-time/part-time employment (69% vs. 37%), less often had injected drugs ever (56% vs. 84%), had likely acquired HCV through sexual contact (59% vs. 7%), less often had a duration of infection ≥26 weeks (66% vs. 81%) and had better social functioning (78% vs. 47%).

Among HIV positive individuals, 63% were receiving HAART at the commencement of HCV treatment. All participants receiving HAART at treatment commencement had HIV RNA suppression <400 copies/mL (20 of 20).

Rapid virological response and associated factors

Among adherent participants ($n=89$), four participants did not have a week 4 HCV RNA test. In the remaining 85 participants, RVR was achieved in 51% (43 of 85). RVR was not statistically different between HCV mono-infected (55%, 30 of 55) participants receiving

PEG-IFN and HCV/HIV co-infected participants (43%, 13 of 30, $P=0.323$) receiving PEG-IFN/ribavirin.

In unadjusted analysis (Table 2), RVR occurred less often in those with baseline HCV RNA $>5.6 \log_{10}$ IU/mL [odds ratio (OR) 0.11, 95% confidence interval (95% CI) 0.04, 0.30; $P<0.001$], but more often in those with HCV genotypes 2/3 (compared to genotype 1; OR 2.44, 95% CI 1.00, 5.98, $P=0.050$). In adjusted analysis (Table 2), controlling for HIV infection (and thus, receipt of ribavirin), RVR occurred less often in those with a duration of infection >26 weeks [adjusted OR (AOR) 0.23, 95% CI 0.06, 0.87; $P=0.031$], baseline HCV RNA $>5.6 \log_{10}$ IU/mL (AOR 0.09, 95% CI 0.03, 0.30; $P<0.001$), but more often in those with HCV genotypes 2/3 (compared to genotype 1; AOR 3.31, 95% CI 1.11, 9.90, $P=0.032$). There was no significant change in the estimates of the model when HIV (receipt of ribavirin) was excluded (data not shown).

Impact of ribavirin on early virological response

Early virological responses over the first 12 weeks of therapy among adherent HCV participants receiving PEG-IFN monotherapy ($n=57$) and HCV/HIV participants receiving PEG-IFN/RBV ($n=32$) are shown in Figure 1 and Table 3. Mean baseline HCV RNA levels were not statistically different between HCV ($4.91 \log_{10}$ IU/mL) and HCV/HIV individuals ($5.23 \log_{10}$ IU/mL, $P=0.255$, Table 3). Between baseline and week 4, the mean decline in HCV RNA was similar in those with HCV/HIV receiving PEG-IFN/ribavirin and those with HCV receiving PEG-IFN alone (3.19 vs. $2.76 \log_{10}$ IU/mL, $P=0.247$, Table 3). However, between baseline and week 12, the mean decline in HCV RNA was greater in HCV/HIV participants receiving PEG-IFN/ribavirin as compared to those receiving PEG-IFN alone (4.19 vs. $3.32 \log_{10}$ IU/mL, $P=0.029$, Table 3).

Early virological decline among adherent participants with recent HCV (PEG-IFN) or HCV/HIV (PEG-IFN/ribavirin) was also assessed in those with a duration of infection >26 weeks and by IL28B genotype (Figure 2, Supplemental Tables 1 and 2). As shown in Figure 2, when compared to those with HCV receiving PEG-IFN alone, HCV/HIV participants receiving PEG-IFN/ribavirin had greater decline in mean HCV RNA among those with a duration of infection >26 weeks (4.39 vs. $3.21 \log_{10}$ IU/mL, $P=0.010$, Figure 2B, Supplemental Table 1) and those with unfavourable CT/TT IL28B genotype (4.54 vs. $3.11 \log_{10}$ IU/mL, $P=0.014$, Figure 2C, Supplemental Table 2). In HCV/HIV participants (PEG-IFN/ribavirin) compared to those with HCV (PEG-IFN), respectively, there was no difference in mean HCV RNA decline from baseline to week 12 in those with duration of infection <26 weeks (3.83 vs. $3.79 \log_{10}$ IU/mL, $P=0.962$) or in those with favourable CC IL28B genotype (4.07 vs. $3.64 \log_{10}$ IU/mL, $P=0.458$).

EVR at week 12 was higher among HCV/HIV participants receiving PEG-IFN/ribavirin compared to those with HCV receiving PEG-IFN (90% vs. 76%, $P=0.102$), but this was not statistically significant. However, in those with unfavourable IL28B genotypes, EVR was significantly higher in HCV/HIV than HCV participants (100% vs. 67%, $P=0.017$). EVR was not significantly different in HCV and HCV/HIV participants with a duration of infection >26 weeks (90% vs. 77%, $P=0.212$).

End of treatment and sustained virological response

Among adherent HIV negative and positive participants, ETR was 82% and 81% ($P=0.887$), while SVR was 63% and 75% ($P=0.253$), respectively. Relapse was not statistically different between HCV and HCV/HIV participants ($n=4$, 9% vs. $n=2$, 8%; $P=0.903$).

In unadjusted analysis, SVR was associated with RVR (OR 3.61, 95% CI 1.36, 9.62), but not duration of infection ≥ 26 weeks (OR 1.63, 95% CI 0.60, 4.41), baseline HCV RNA ≥ 5.6 log₁₀ IU/mL (OR 0.77, 95% CI 0.31, 1.88), HCV genotypes 2/3 infection (compared to genotype 1; OR 1.71, 95% CI 0.68, 4.31) or HIV infection (OR 1.75, 95% CI 0.67, 4.59). In adjusted analysis controlling for HIV infection (and thus, receipt of ribavirin, AOR 2.35, 95% CI 0.80, 6.85; $P=0.119$), SVR remained associated with RVR (AOR 4.09, 95% CI 1.49, 11.25; $P=0.006$). The positive predictive value (PPV) of RVR for predicting SVR was 81%, 77% and 92% for the overall, HCV and HCV/HIV populations. The PPV of EVR for predicting SVR was 78%, 76% and 82% for the overall, HCV and HCV/HIV populations.

Discussion

This study is one of the first to provide a detailed analysis of early virological responses in the setting of treatment of recent HCV, and is unique in its ability to compare HIV negative and positive individuals and thus the potential role of ribavirin.

In ATAHC, RVR was 51% among adherent participants with recent HCV, with no significant difference observed between HIV negative and HIV positive individuals. This RVR is lower than in other studies of treatment of acute HCV (86% to 90%) [10, 27], likely due to a higher proportion with early chronic HCV in ATAHC (75% with duration of infection ≥ 26 weeks). In ATAHC, RVR was associated with a shorter estimated duration of HCV infection lower HCV RNA levels at baseline and HCV genotypes 2/3. This analysis of factors associated with RVR is novel and suggests that even in the setting of recent infection similar factors drive rapid viral responses as in chronic HCV.

Among adherent HCV and HCV/HIV participants, SVR was similar (63% vs. 75%, $P=0.253$) and not associated with any of the baseline factors predictive of RVR. This is consistent with data from treatment for acute infection in HCV mono-infected [10] and HCV/HIV co-infected participants [28] demonstrating that baseline factors such as HCV genotype and HCV RNA have less impact on overall treatment response in acute as compared to chronic HCV. The only factor predictive of SVR in this analysis of adherent individuals was RVR. Individuals with an RVR had a four times greater odds of achieving SVR, and RVR had an 81% PPV for SVR. A lower SVR in those without HIV is not surprising, given 81% had a duration of infection ≥ 26 weeks. These data illustrate the importance of maximizing early virological responses during treatment for recent HCV, providing reassurance and encouragement for patients reaching this early milestone.

Despite lower response rates observed in treatment for chronic HCV among those with HCV/HIV as compared to those with HCV alone [16-20], the proportion of HIV/HCV coinfecting participants in ATAHC reaching the important virological milestones of RVR, EVR and SVR were similar to those in HCV mono-infected participants, despite higher

baseline HCV RNA in those with HCV/HIV. This finding is probably related to greater reductions in HCV RNA levels from baseline to week 12 in HIV/HCV co-infected patients receiving PEG-IFN/ribavirin combination therapy compared to HCV patients receiving PEG-IFN alone, especially between weeks 4 and 12 of therapy. It is important to highlight that there was no difference in virological decline among HIV positive and negative individuals with an estimated duration of infection <26 weeks, suggesting that this potential effect of RBV is restricted to those with a longer estimated duration of HCV infection (≥ 26 weeks). A greater effect of RBV was also observed in those with unfavorable IL28B genotypes.

As reviewed elsewhere [29], numerous mechanisms of action have been proposed for ribavirin although none have been convincingly identified. One theory suggests that ribavirin may exert its antiviral activity by potentiating the effect of IFN action on ISG induction, resulting in enhanced antiviral responses [30]. In patients treated with PEG-IFN/RBV, it has been demonstrated that hepatic ISG induction is greater than in those treated with PEG-IFN alone [31]. Irrespective of the mechanism, ribavirin has been shown to improve the second and third phases of HCV RNA decline [32-34]. In this study, the greater HCV RNA decline among HCV/HIV co-infected participants receiving ribavirin in ATAHC over the first 12 weeks of therapy is consistent with this effect of ribavirin on 2nd and 3rd phase viral kinetics.

These data from ATAHC lend support to data suggesting a benefit of ribavirin in treatment of recent HCV in HCV/HIV individuals. In 2010 the NEAT Consensus Guidelines reviewed data from nine studies of 184 HCV/HIV participants treated for acute HCV (25 PEG-IFN, 169 PEG-IFN/ribavirin). Although these studies were small, non-randomised and heterogeneous in nature, overall a significantly higher SVR among participants receiving PEG-IFN/ribavirin was demonstrated as compared to those receiving PEG-IFN alone (60% vs. 48%, $P>0.05$) [15]. Although data from a randomized controlled trial of PEG-IFN and PEG-IFN/ribavirin combination therapy in HCV/HIV participants with acute HCV would be ideal to assess the potential benefit of ribavirin, this is unlikely given the large numbers required and the rapid pace of HCV drug development. As such, data from ATAHC and the available literature suggests that ribavirin should be used in the treatment of HCV/HIV co-infected individuals with recent HCV, particularly those with a longer estimated duration of infection and unfavourable IL28B genotypes.

In HCV mono-infected patients, pilot studies have demonstrated little benefit in terms of response to therapy with the inclusion of ribavirin to PEG-IFN regimens in acute HCV. In one non-randomized prospective study, the SVR in those receiving interferon-based therapy with ribavirin was 93% (n=14) as compared to 67% in those receiving IFN (n=10)/PEG-IFN (n=2) mono-therapy [35]. In another non-randomized prospective study, the SVR was 80% and 85% in those receiving either PEG-IFN (n=20) or PEG-IFN/ribavirin (n=20) [9]. As such, there is insufficient evidence to recommend the use of ribavirin for the treatment of acute HCV mono-infection. However, these ATAHC data raise questions about the potential usefulness of ribavirin in during recent HCV in those with HCV mono-infection, particularly those with an estimated duration of infection ≥ 26 (or an uncertain date of exposure) and unfavorable IL28B genotypes.

This study has several limitations. First, this was not a randomized controlled trial designed to evaluate PEG-IFN with and without ribavirin. As such, there are potential unmeasured confounding factors which may have influenced the observed effects of ribavirin in this study. HIV negative patients may have also had characteristics (e.g. higher proportion with asymptomatic infection) leading to a lower virological response. That being said, ribavirin was associated with significant difference in decline in HCV RNA from baseline to week 12, despite these individuals being HIV positive and having higher HCV RNA levels prior to treatment initiation, two major factors known to be associated with reduced response to HCV therapy. Thus, any existing bias is likely to have worked against a potential beneficial effect of ribavirin. Second, the ATACH study was not originally designed to assess HCV viral kinetics. Given this, there are no detailed viral kinetic measurements between baseline to week 4 and weeks 4 to 12. As such, it makes it difficult to speculate on the impact of ribavirin on the first, second and third phase decline.

The findings from this study are important for the management of recent HCV, particularly among HCV/HIV co-infected individuals. These results suggest that ribavirin may be beneficial for HCV/HIV co-infected individuals, particularly those with a longer estimated duration of infection (or uncertain date of exposure) and unfavourable IL28B genotypes. Given data from this study demonstrating that individuals achieving an RVR were four times more likely to achieve an SVR, strategies to enhance early virological response remain important to improve treatment outcomes for patients with recent HCV infection. In the absence of randomized controlled clinical trial data comparing PEG-IFN with and without ribavirin for the treatment of recent HCV, the results of this study will be useful for guiding treatment decisions in early HCV infection among HCV/HIV co-infected individuals.

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Figure 1. Early virological decline among adherent participants with recent HCV (PEG-IFN, n=57, circles and solid line) or HCV/HIV (PEG-IFN/ribavirin, n=32, squares and dotted line). Error bars represent 95% confidence intervals.

Figure 2.

Early virological decline among adherent participants with recent HCV (PEG-IFN, circles and solid line) or HCV/HIV (PEG-IFN/ribavirin, squares and dotted line) in those with an estimated duration of infection <26 weeks (A), an estimated duration of infection ≥26 weeks (B), unfavourable IL28B genotype (rs12979860 CT/TT) (C) and favourable IL28B genotype (rs12979860 CC) (D). Error bars represent 95% confidence intervals.

Table 1
Baseline characteristics among treated HCV and HCV/HIV infected participants with recently acquired HCV infection and adherent to PEG-IFN therapy (n=89)

	Overall (n=89) n (%)	HCV infected (PEG-IFN) (n=57) n (%)	HCV/HIV infected (PEG-IFN/ ribavirin)(n=32) n (%)
Male Sex	67 (75)	35 (61)	32 (100)
Mean age, yrs (SD)	34.8 (10.5)	31.0 (9.2)	41.6 (9.4)
Tertiary education or greater	47 (53)	24 (42)	23 (72)
Full-time or part-time employment	43 (48)	21(37)	22 (69)
Injecting drug use ever	66 (74)	48 (84)	18 (56)
Injection drug use in previous 30 days	26 (30)	22 (39)	4 (13)
Social support			
14	52 (58)	27 (47)	25 (78)
14	28 (31)	23 (40)	5 (16)
Missing	9 (10)	7 (12)	2 (6)
IL28B genotype			
rs8099917			
GG	4 (5)	1 (2)	3 (10)
GT	31 (36)	23 (42)	8 (26)
TT	51 (59)	31 (56)	20 (65)
rs12979860			
CC	42 (48)	24 (43)	18 (58)
CT	36 (41)	27 (48)	9 (29)
TT	9 (10)	5 (9)	4 (13)
Mode of HCV acquisition			
Injecting drug use	60 (67)	48 (84)	12 (38)
Sexual	23 (26)	4 (7)	19 (59)
Other	6 (7)	5 (9)	1 (3)
Estimated duration of HCV infection 26 wks*	67 (75)	46 (81)	21(66)
Presentation of recent HCV ‡			
Acute clinical (symptomatic)	34 (38)	20 (35)	14 (44)
Acute clinical (ALT >400 IU/mL)	21 (24)	11 (19)	10 (31)
Asymptomatic seroconversion	34 (38)	26 (46)	8 (25)
HCV RNA 5.6 log10 IU/mL*	36 (40)	18 (32)	18 (56)
HCV genotype			
Genotype 1	50 (56)	33 (58)	17 (53)
Genotype 2	5 (6)	1 (2)	4 (13)
Genotype 3	33 (37)	22 (39)	11 (34)
Mixed HCV genotype 1/3	1 (1)	1 (2)	0 (0)

* at baseline,

‡ denominator is in total number of people reporting documented illness.

Table 2
Predictors of rapid virological response among treated HCV and HCV/HIV infected participants with recently acquired HCV infection adherent to therapy (n=85^{*})

	RVR (n=43) n, (%) £	Unadjusted odds ratio (95% CI)	P	P overall	Adjusted odds ratio (95% CI)	P
Male Sex (vs. female sex)	31 (49)	1.24 (0.47, 3.28)	0.667	-	-	-
Injection drug use in previous 30 days (vs. none)	13 (50)	1.00 (0.40, 2.52)	1.000	-	-	-
Social support						
14	23 (46)	1.00	-	-	-	-
>14	17 (65)	2.22 (0.83, 5.91)	0.112	0.161	-	-
Missing	3 (33)	0.59 (0.13, 2.61)	0.484	-	-	-
IL28B genotype						
rs8099917 favorable TT (vs. GT/GG)	27 (55)	1.67 (0.68, 4.06)	0.262	-	-	-
rs12979860 favorable CC (vs. CT/TT)	22 (55)	1.54 (0.65, 3.67)	0.326	-	-	-
Estimated duration of HCV infection of 26 wks at baseline (vs. <26 weeks)	30 (46)	0.46 (0.16, 1.31)	0.145	-	0.23 (0.06, 0.87)	0.031
Presentation of recent HCV						
Acute clinical (symptomatic)	18 (56)	1.00	-	-	-	-
Acute clinical (ALT >400 IU/mL)	7 (35)	0.42 (0.13, 1.33)	0.139	0.288	-	-
Asymptomatic seroconversion	18 (55)	0.93 (0.35, 2.48)	0.890	-	-	-
HCV RNA 5.6 log ₁₀ (IU/mL) at baseline (vs. <5.6 log ₁₀)	7 (21)	0.11 (0.04, 0.30)	<0.001	-	0.09 (0.03, 0.30)	<0.001
HCV genotype						
Genotype 1 [‡]	18 (39)	1.00	-	-	-	-
Genotype 2/3	22 (61)	2.44 (1.00, 5.98)	0.050	-	3.31 (1.11, 9.90)	0.032
Received ribavirin/HIV infection	13 (43)	0.64 (0.26, 1.56)	0.324	-	0.71 (0.23, 2.25)	0.563

^{*} four of the 89 adherent participants did not have evaluable HCV RNA at week 4 and were excluded from this analysis,

[‡] includes one participant with mixed genotype 1/3 infection,

[£] row percentage (e.g. proportion with cRVR). RVR, rapid virological response; CI, confidence interval.

Table 3

Mean HCV RNA levels, mean HCV RNA decline and proportion with undetectable HCV RNA at weeks 4, 8 and 12 among adherent participants with recent HCV (PEG-IFN, n=57) or HCV/HIV (PEG-IFN/ribavirin, n=32).

	N	HCV infected (PEG-IFN) (n=57)	HCV/HIV infected (PEG-IFN/ribavirin) (n=32)	P
Mean HCV RNA log ₁₀ IU/mL (SD)				
Baseline	89	4.91 (1.17)	5.23 (1.42)	0.255
Week 4	85	2.15 (1.95)	1.95 (1.26)	0.607
Week 8	77	1.66 (1.82)	1.25 (1.01)	0.290
Week 12	85	1.59 (1.78)	0.99 (0.95)	0.082
Mean HCV RNA decline log ₁₀ IU/mL (SD)				
Change from baseline to week 4	85	2.76 (1.78)	3.19 (1.30)	0.247
Change from baseline to week 8	77	3.33 (1.90)	4.19 (1.24)	0.038
Change from baseline to week 12	85	3.32 (1.87)	4.19 (1.48)	0.029
HCV RNA undetectable <10 IU/mL, n (%)				
Week 4	85	30 (55%)	13 (43%)	0.323
Week 8	77	37 (74%)	20 (74%)	0.994
Week 12	85	41 (76%)	28 (90%)	0.102