

A multi-center, randomized trial of 48 versus 72 weeks of Peg Interferon alfa-2b plus Ribavirin in HIV- Hepatitis C Virus co-infected subjects: Longer therapy does not correlate with improved SVR

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Background

Therapy with pegylated interferon (PEG) and ribavirin (RBV) achieves lower sustained viral response (SVR) rates in subjects co-infected with HIV and Hepatitis C Virus (HCV) compared to those with HCV alone. A potential strategy to improve response rates in these individuals may be to extend duration of anti HCV therapy beyond the conventional 48 weeks.

Methods

All patients received PEG alfa -2b 1.5 µg/kg weekly plus weight -based RBV (range 800 mg -1400 mg daily) for 24 weeks. Subjects with undetectable (<600 IU/ml) HCV RNA at week 24 were randomized to standard (Group A, 48 weeks) or extended therapy (Group B, 72 weeks). Growth factors were initiated as per protocol.

SVR was compared between groups using the chi squared test, and predictors of SVR were assessed by multivariate logistic regression.

Results

A total of 206 subjects were enrolled at 21 community and academic sites within the US. 177 subjects received at least one dose of study medications and were included in the analysis. Baseline characteristics of this cohort are summarized in **Table 1**. There was a high number of subjects who did not complete the study per protocol, reasons for failure to complete are detailed in **Figure 1**. At wk 24, 61 subjects with HCV RNA < 600 IU/ml were randomized to either 48 wks (n=30) or 72 wks (n=31) of therapy, however only 29 (47.5%) completed their assigned treatment course.

Viral Response (Intention to treat)	n= 177
EVR	43 % (76/177)
Wk 24 HCV RNA < 600 IU/ml	34.5% (61/177)
Overall SVR	19.8% (35/177)
SVR by HCV genotype	
1	12.8% (18/141)
Non 1	47.2% (17/36)

On univariate analysis, EVR, HCV GT non 1, Caucasian race and use of EPO were significant positive predictors of SVR, on logistic regression only EVR remained significant (p< 0.0001)

Viral response (As randomized)	n= 61
SVR	
Group A	50.0% (15/30)
Group B	54.8% (17/31)

Comparison between groups using chi squared test, p = 0.7

Adverse Events

34 (19%) subjects discontinued treatment prematurely due to AE/SAE's, 28 (82%) stopping before 24 weeks. Haematologic AE/SAE's were responsible for withdrawal of therapy in only 5 cases (14.7%) , which may reflect the liberal use of growth factors.

Conclusions

- Extended treatment duration was not associated with a higher SVR compared to standard of care.
- EVR was a strong predictor of SVR
- Erythropoietin use may have a positive impact on treatment response

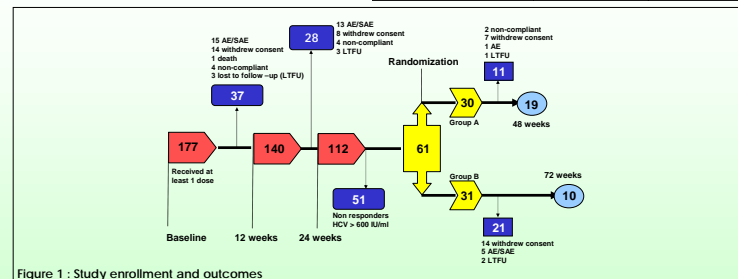
More than 50 % of subjects who achieved an undetectable HCV RNA level on therapy failed to complete their assigned treatment course, thereby precluding definitive hypothesis testing.

These data suggest that longer PEG/RBV therapy may not be feasible for HIV infected subjects.

Table 1: Baseline characteristics of cohort		
		n=177
Age (years) mean	Mean +/- SD	45.38 (8.77)
Gender	Male	123 (69%)
Ethnicity	Caucasian	73 (41%)
	Black	72 (41%)
	Hispanic	29 (16%)
	Asian	2 (1%)
On ARV's		138 (78%)
CD4 > 200 cells/mm3		168 (94%)
HIV RNA < 50 copies/ml		115 (65%)
HCV Genotype		
	1	141 (80%)
	2	16 (9%)
	3	17 (10%)
	Other	3 (1%)
HCV RNA IU/ml (median, IQR)		(500,000 - 1,738,642)
ALT > 40 U/L		134 (76%)
BMI kg/m2 (median, IQR)		26.3 (23.5 - 30.0)
Used EPO		70 (40%)
Used G-CSF		42 (24%)

Aim

To compare SVR rates in a cohort of HIV/HCV co-infected patients treated with PEG/RBV for extended duration (72 weeks) versus standard therapy(48 weeks)



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