

Kinetically Guided Peginterferon alfa-2a and Ribavirin Therapy for HIV-Infected Adults with Acute HCV Infection

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Introduction

Acute HCV infection is increasingly being recognized among persons infected with HIV

Treatment during acute HCV infection can lead to shorter duration of treatment with high success rates

Regimens individualized based on virologic kinetic response may be developed to optimize treatment outcomes in HIV-infected individuals

Study Population

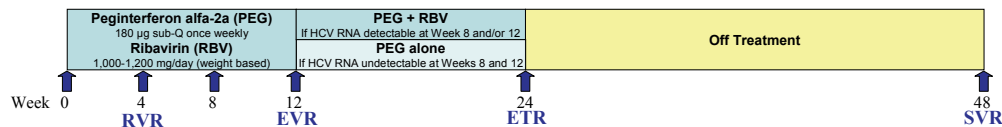
HIV infected individuals with acute HCV infection of <6 months duration, defined by a known or suspected exposure to HCV, detectable HCV RNA, plus any one of the following:

- (1) HCV Ab negative with detectable HCV RNA; **OR**
- (2) Current positive HCV Ab test with negative HCV Ab test <6 months prior; **OR**
- (3) ALL of the following:
 - (a) ALT > 5x upper limits of normal, with normal levels within the prior year; **AND**
 - (b) Current positive HCV Ab test with most recent HCV Ab test negative at any time in the past; **AND**
 - (c) Other causes of acute hepatitis excluded

Results

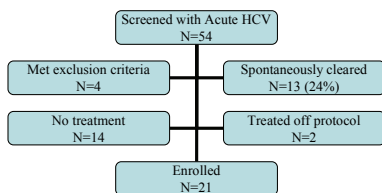
Between May 2006 and August 2009, 54 HIV-positive men with acute HCV were identified (38 in SF; 16 in NY)

Treatment Regimen



Results (cont)

Risk factors for HCV acquisition included men having sex with men (MSM) in 44; injection drug use (IDU) in 3; intranasal (IN) drug use in 1; and both MSM and IDU or IN in 6



Demographics of enrolled subjects (N=21):

- All MSM (one also IDU)
- Median age 42 years (range 26–59)
- 13 Caucasian, 4 Latino, 4 Asian/Pacific Islander
- Median weight = 74.7 kg (range 62.3–103.6)

HCV parameters:

- HCV Genotype: 20 Geno 1 (11 Geno 1a; 3 Geno 1b; 6 subtype unknown); 1 Geno 2b
- Median entry HCV RNA > 6.30 log IU/mL (range 2.47–7.46)
- Median ALT (peak) = 489 U/L (range 176–2715)
- Median ALT (entry) = 161 U/L (range 21–734)

HIV parameters:

- On ART at entry = 19 (15 had undetectable HIV RNA)
- Median CD4 = 451 cells/mm³ (range 147–1332)
- Median days from diagnosis to entry = 87 (range 40–163)

Overall HCV RNA Response

Week	4 (RVR)	8	12 (cEVR)	24 (ETR)	48 (SVR)
Undetectable HCV RNA	12 of 21 (57%)	13 of 21 (62%)	14 of 21 (67%)	16 of 21 (76%)	7* of 15** (47%)

* Response in subjects who did not achieve SVR: 3 Relapse, 1 Rebound, 4 No Response

** 6 Subjects have completed treatment but have not reached SVR determination

Results (cont)

RVR correlated perfectly with ETR and SVR; no subject without RVR achieved SVR to date

In univariate analysis, RVR was negatively associated with entry HCV RNA ($P < 0.01$) and positively associated with entry ALT ($P < 0.01$) and entry CD4 ($P = 0.03$)

13 Subjects stopped RBV at week 12 per protocol; none rebounded through ETR

2 Non-completers (1 SVR; 1 non-responder)

Epoetin used in 4 subjects; G-CSF used in 8; RBV dose reduced in 3 subjects; PEG dose reduced in 5

Conclusions

MSM was the most common risk factor observed for acute HCV infection

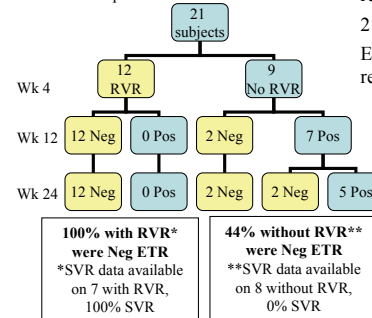
24% of men identified with acute HCV infection spontaneously cleared HCV

Overall ETR and SVR rates are high using this kinetically-guided, 24-week treatment approach when compared to chronic infection

To date, all subjects with SVR had RVR, and RVR was 100% predictive of SVR

In patients with slow HCV clearance, longer therapy may be of benefit and requires further study

HCV RNA Response



Demographics of enrolled subjects (N=21):	
HCV Risk Factor	All MSM (one also IDU)
Race	13 Caucasian, 4 Latino, 4 Asian/Pacific Islander
Age, years - median (range)	42 (26 – 59)
Weight, kg - median (range)	74.7 (62.3 – 103.6)
Days from diagnosis to entry - median (range)	87 (40 – 163)
HCV parameters:	
HCV Genotype	20 Geno 1; 1 Geno 2b (11 Geno 1a; 3 Geno 1b; 3 subtype unknown)
Entry HCV RNA, log iU/mL - median (range)	> 6.30 (2.47 – 7.46)
Peak ALT, U/L - median (range)	489 (176 – 2715)
Entry ALT, U/L - median (range)	161 (21 – 734)
HIV parameters:	
On ART at entry	19 (15 had undetectable HIV RNA)
CD4, cells/mm3 - median (range)	451 (147 – 1,332)