

# EFFICACY OF PEGYLATED INTERFERON PLUS RIBAVIRIN IN HIV/HCV CO-INFECTION OUTSIDE OF WELL CIRCUMSCRIBED CLINICAL TRIALS: THE ANDALUSIAN MULTICENTER STUDY

JA Mira<sup>1</sup>, J Torre-Cisneros<sup>2</sup>, D Merino<sup>3</sup>, MJ Ríos<sup>4</sup>, A Collado<sup>5</sup>, S Vergara<sup>1</sup>, A Rivero<sup>2</sup>, JM Lomas-Cabeza<sup>3</sup>, J Macías<sup>1</sup>, JA Pineda<sup>1</sup>

<sup>1</sup>Hospital Universitario de Valme, Seville, Spain. <sup>2</sup> Hospital Universitario Reina Sofía, Córdoba, Spain. <sup>3</sup> Hospital Juan Ramón Jiménez, Huelva, Spain. <sup>4</sup> Hospital Universitario Virgen Macarena, Seville, Spain. <sup>5</sup>Hospital Torrecárdenas, Almería, Spain. Grupo Andaluz para el Estudio de las Enfermedades Infecciosas (GAEI)

Correspondence to: Dr. Juan A. Pineda  
Unidad de Enfermedades Infecciosas  
Hospital Univ. de Valme  
Cra de Cádiz s/n 41014  
Seville, SPAIN  
Tel: +34-955015887  
FAX: +34-955015747  
E-mail: japineda@nacom.es

POSTER  
133  
CROI 2006

## ABSTRACT

**BACKGROUND:** Recently, four randomized controlled trials have been published comparing the efficacy of pegylated interferon (PEG-IFN) plus ribavirin (RBV) with that of standard interferon (IFN) plus RBV in the treatment of chronic hepatitis C in HIV-coinfected patients. In these trials, the new regimen was superior to the combination of standard IFN plus RBV. Thus, the overall sustained virologic response (SVR) rate with the PEG-IFN/RBV combination ranged from 27-44% in these clinical trials. To date, however, there is little information about the efficacy of the PEG-IFN/RBV combination used in real conditions in subjects with HIV and HCV infections. Likewise, the factors associated to SVR in these individuals in such conditions are not known.

**OBJECTIVES:** To assess the efficacy of pegylated interferon plus ribavirin in a clinical cohort of HIV-infected patients with chronic hepatitis C and the factors predictive of an SVR.

**PATIENTS AND METHODS:** All HIV/HCV-coinfected patients who received at least one dose of the PEG-IFN/RBV combination between June 2000 to December 2005 at eight hospitals in Spain were included in the study. Patients were treated with PEG-IFN alpha-2a (180µg weekly) or PEG-IFN alpha-2b (1.5µg/Kg weekly) plus RBV (500-1500 mg/day) for 24 or 48 weeks. Patients discontinued the therapy at week 12 in the absence of an early virologic response (EVR). The primary endpoint was the rate of SVR, defined as undetectable HCV RNA in serum at 24 weeks after cessation of the therapy. Secondary endpoints were rates of non-response, viral response at end of treatment, relapses and percentage of premature discontinuation of the therapy. Viral response was measured on an intention-to-treat basis. A multiple logistic regression analysis was performed to identify factors predictive of an SVR.

**RESULTS:** Two hundred and seven patients were included in this study. Viral response at the end of treatment and SVR were observed in 100 (48%) and 73 (35%) individuals, respectively. Among the 123 subjects with genotype 1 or 4, 25 (20%) achieved SVR, whereas 48 (58%) out of 83 individuals carrying genotypes 2 or 3 did it. Forty-eight (39%) subjects with genotypes 1 or 4 and 3 (4%) with genotypes 2 or 3 did not reach EVR. Twenty-seven (13%) patients relapsed after end of treatment. Twenty-nine (14%) individuals discontinued the therapy due to adverse events and 20 (10%) patients were lost to follow-up or refused to continue the therapy. HCV genotype 2-3 (adjusted odds ratio [AOR] 5.2, 95% CI 2.8-9.9), adherence to therapy >80% (3.3, 95% CI 1.1-11.9), baseline HCV RNA ≤600,000 copies/mL (AOR 2.2, 95% CI 1.1-4.2) and baseline CD4+ cell counts > 300 cells/mm<sup>3</sup> (AOR 4.3, 95% CI 1.2-15) were associated with an SVR.

**CONCLUSIONS:** The efficacy of pegylated interferon plus ribavirin in HIV/HCV-coinfected patients outside of well-circumscribed trials is in the range of that has been reported in clinical trials. HCV genotype 2 or 3, optimum adherence, low baseline HCV RNA level and a high baseline CD4+ cell count are predictors of SVR in these subjects.

## BACKGROUND

The combination of pegylated interferon (PEG-IFN) plus ribavirin (RBV) is currently the treatment of choice for HCV infection. Results from recent clinical trials in HIV/HCV-coinfected patients have shown an improved sustained virological response (SVR) rates using PEG-IFN plus RBV when compared to standard interferon plus RBV.

	APRICOT <sup>1</sup>	RIBAVIC <sup>2</sup>	ACTG <sup>3</sup>	CLINIVC <sup>4</sup>
Type of PEG-IFN	α-2a	α-2b	α-2a	α-2b
Patients with PEG-IFN, n	289	205	66	52
Overall SVR, %	40	27	27	44
SVR-genotype 1-4, %	29	17	14	38
SVR-genotype 2-3, %	62	44	73	53

<sup>1</sup> Tortiani FJ, et al. N Engl J Med 2004; <sup>2</sup> Carrat F, et al. JAMA 2004; <sup>3</sup> Chung RT, et al. N Engl J Med 2004; <sup>4</sup> Laguno M, et al. AIDS 2004.

Nevertheless, there is little data reported regarding the efficacy of PEG-IFN plus RBV in these individuals outside of well-circumscribed trials. Likewise, it is not known whether the factors associated to SVR are similar to those found in clinical trials.

## OBJECTIVES

- ❖ To determine the efficacy of pegylated interferon plus ribavirin combination in a cohort of HIV/HCV-coinfected patients.
- ❖ To assess the factors associated with a sustained virologic response in these subjects.

## PATIENTS AND METHODS

### Patients

❖ Patients were treatment-naïve adults (aged ≥ 18 years) with quantifiable serum HCV RNA levels (> 600 IU/mL) followed in eight hospitals in southern Spain.

### Study design

❖ This was a retrospective multicenter study of the patients who were treated with PEG-IFN alpha-2a (180µg/week) or alpha-2b (1.5 µg/Kg/week) plus RBV (500-1500 mg/day) in the participant hospitals. All individuals received therapy for 24 or 48 weeks. The study period lasted from June 2000 to December 2005. Patients discontinued the therapy at week 12 in the absence of an early virologic response (EVR).

❖ The primary efficacy end-point was SVR, defined as viral response (undetectable serum HCV RNA by PCR) at 24 weeks after the end of therapy.

❖ The secondary endpoints were:

- Viral response at the end of treatment.
- Non-response: patients who did not reach EVR, defined as a 2-log reduction in HCV RNA levels at 12 week or a viral response at 24 week.
- Virological breakthrough (VB): patients who did reach a viral response during therapy but afterwards the subjects showed detectable serum HCV RNA before the treatment was ended.
- Relapse: Detectable serum HCV RNA after reaching a viral response at the end of treatment.
- Discontinuation of the therapy due to adverse events or patient decision.

### Statistical analysis

- ❖ The analysis was conducted according to the intention-to-treat principle.
- ❖ Univariate and multiple logistic regression analysis were performed to identify factors predictive of an SVR. The variables included were sex, age, body-mass index, intravenous drug users, AIDS, alcohol intake, duration of HCV infection, baseline HCV RNA level, ALT level, cirrhosis, HCV genotype, type of PEG-IFN, adherence to therapy, RBV by weight, participant hospitals, CD4+ cell count and undetectable HIV RNA at baseline, antiretroviral therapy, use of protease inhibitors (PI), didanosine (ddI), stavudine (d4T) and growth factors.

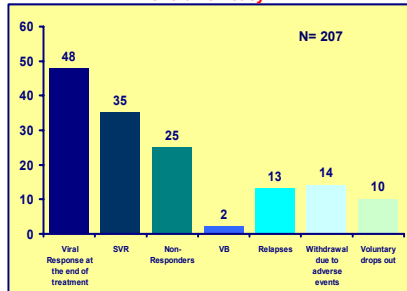
## RESULTS

### Characteristics of the study population

Characteristics	Patients n=207
Age (years)*	39 (36-42)
Male sex, no (%)	180 (87)
Body-mass index (Kg/m <sup>2</sup> )*	23.3 (21.1-25.8)
IDU, no (%)	180 (87)
AIDS, no (%)	58 (28)
Daily alcohol intake > 50 g/day, no (%)	21 (10)
HBsAg positive, no (%)	7 (3)
Duration of HCV infection (years)*	13.8 (12.3-15)
Baseline log HCV viremia (IU/mL)*	5.9 (5.5-6.2)
Baseline ALT level (IU/mL)*	93 (60-140)
Cirrhosis, no (%)†	30 (22)
HCV genotype, no (%)	
1-4	123 (60)
2-3	83 (40)
Pegylated interferon, no (%)	
alpha-2a	159 (77)
alpha-2b	48 (23)
PEG-IFN plus RBV for 24 weeks	24 (11)
RBV > 10.6 mg/Kg/day, no (%)	187 (90)
Adherence > 80% during therapy, no (%)	178 (86)
Baseline CD4+ cell count (cells/mm <sup>3</sup> )*	573 (391-721)
Baseline undetectable HIV RNA, no (%)	142 (69)
Antiretroviral therapy, no (%)	172 (83)

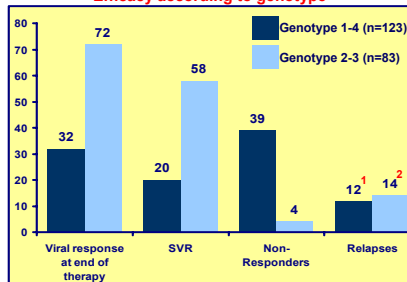
\*median (interquartile range), †available liver biopsy in 139 patients; IDU, intravenous drug users.

### Overall efficacy



VB: virological breakthrough.

### Efficacy according to genotype



Among the patients with viral response at end of therapy, 137% and 20% of individuals presented a relapse.

### Factors associated with sustained virologic response

Variable	SVR [n (%)]	P univariate	Adjusted Odds Ratio (95% CI)	P multivariate
Male sex				
Yes	63 (35)			
No	10 (37)	0.8		NS
AIDS				
Yes	19 (33)			
No	54 (36)	0.7		NS
Body-mass index				
≤ 23 Kg/m <sup>2</sup>	25 (40)			
> 23 Kg/m <sup>2</sup>	48 (33)	0.3		NS
ALT level				
≤ 40 IU/mL	6 (43)			
> 40 IU/mL	67 (35)	0.5		NS
Cirrhosis*				
Yes	10 (33)			
No	32 (30)	0.8		NS
Baseline HCV RNA				
≤ 600,000 copies/mL	37 (47)			
> 600,000 copies/mL	36 (28)	0.007	2.2 (1.1-4.2)	0.014
HCV genotype				
1-4	25 (20)			
2-3	48 (58)	<0.001	5.2 (2.8-9.9)	<0.001
PEG-IFN				
alpha-2a	56 (35)			
alpha-2b	17 (35)	0.9		NS
RBV > 10.6 mg/Kg/day†				
Yes	63 (35)			
No	6 (29)	0.5		NS
Adherence > 80% during therapy				
Yes	70 (37)			
No	3 (15)	0.05	3.3 (1.1-11.9)	0.05
Antiretroviral therapy				
Yes	58 (34)			
No	15 (43)	0.3		NS
Baseline CD4+ cell counts				
≤ 300 cells/mm <sup>3</sup>	3 (12)			
> 300 cells/mm <sup>3</sup>	70 (38)	0.01	4.3 (1.2-15)	0.05
Baseline undetectable HIV RNA				
Yes	49 (34)			
No	24 (37)	0.7		NS

\* Available in 42 patients; † available in 69 patients. NS, non-significant.

- ❖ Among the 97 patients with genotype 1-4 who were treated with PEG-IFN alpha-2a, 21 (22%) achieved SVR, whereas 4 (15%) out of 26 individuals who received PEG-IFN alpha-2b did it (p=0.5).
- ❖ In the group of patients with genotype 2-3, 35 (56%) out of 62 subjects who received PEG-IFN alpha-2a and 13 (62%) out of 21 individuals who were treated with PEG-IFN alpha-2b reached an SVR, respectively (p=0.7).

## CONCLUSIONS

- ❖ The efficacy of pegylated interferon plus ribavirin in HIV/HCV-coinfected patients in daily use conditions is in the range previously found in clinical trials.
- ❖ HCV genotype 2 or 3, optimum adherence, low baseline HCV RNA level and high baseline CD4+ cell counts are predictors of sustained virologic response in these subjects.
- ❖ The efficacy of both pegylated interferons currently available seems to be similar in this population.