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Does the Choice of peg-IFN Formulation Affect Safety or Efficacy in HIV/HCV-Coinfected Patients Receiving Weight-adjusted Ribavirin?

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BACKGROUND

- There is scant information on differences in treatment outcome in HCV/HIV-coinfected patients according to peg-IFN formulation.

METHODS

• Prospective, non-randomized study of 174 consecutive, HBVsAg (-), caucasic, HCV-treatment naive, HIV-infected patients with chronic hepatitis C starting their first cycle of peg-IFN plus weight-adjusted RBV, between January 2001-March 2006.

Objectives

1. To assess, by univariate analyses, potential differences in baseline and evolutive features according the formulation of peg-IFN.

2. To assess, using univariate and multivariate regression analyses, baseline predictors of SVR in the whole population.

RESULTS

Baseline HIV and HCV features (n=174)

Age (years; median, range)	41 (28-63)
Male Sex (%)	78
Prior IVDU (%)	87
Prior AIDS (%)	27
Baseline CD4 count (cells/ml; median, range)	513 (45-1513)
- Nadir CD4 count (cells/ml; median, range)	164 (4-930)
- Prior counts <200 cells/ml (%)	55
Baseline HIV-load ($\log_{10}$ copies/ml; median, range)	1.7 (1.7-5.3)
- VL <1,7$\log_{10}$ copies (%)	67
HAART (%)	82
- PI-based (%)	49
- NNRTI-based (%)	31
- 3-NRTI (%)	18

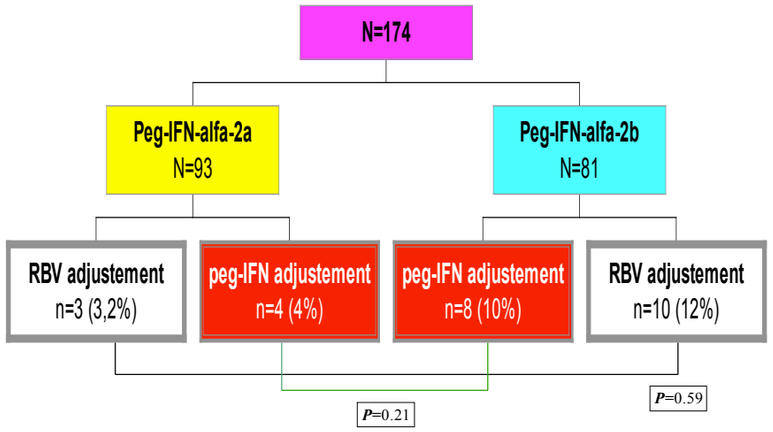
Baseline HIV and HCV features according peg-IFN Formulation

	Peg-IFN! -2a (n=93)	Peg-IFN! -2b (n=81)	*P*
Age (years; mean±SD)	42 ± 5	40 ± 4	0.001*
Male sex (%)	80	76	0.63
Prior IVDU (%)	84	90	0.22
Prior AIDS (%)	30	23	0.32
CD4 counts (cells/ml; mean ± SD)	582 ± 304	553 ± 295	0.58
- prior nadir <200 cells/ml (%)	54	56	0.81
HIV-RNA ($\log_{10}$ copies/ml; mean ± SD)	2,16 ± 0,9	2,05 ± 0,71	0.79
- <50 copies/ml (%)	67	67	
On HAART (%)	82	83	0.86

	Peg-IFN! -2a (n=93)	Peg-IFN! -2b (n=81)	*P*
Time of HCV (years; mean±SD)	21 ± 4,6	20 ± 4,27	0.029*
Genotype 1 or 4 (%)	62	54	0.28
Liver Biopsy (%)	72	61	0.10
- F3/F4 (%)	46	64	0.07
- cirrhosis (%)	31	41	0.29
HCV-RNA ($\log_{10}$ IU/ml; mean ± SD)	5,65 ± 0,81	5,66 ± 0,56	0.58
- >800,000 IU/ml (%)	46	42	0.58
AST (U/l; mean ± SD)	80 ± 74	85 ± 45	0.012*
ALT (U/l; mean ± SD)	102 ± 87	111 ± 74	0.06
GGT (U/l; mean ± SD)	127 ± 105	173 ± 161	0.015*
- ≥100 U/l (%)	46	66	0.008*
RBV dosage (mg/kg/day; mean ± SD)	15,2 ± 2,43	14,17 ± 2,24	0.004*

Time of HCV infection (years; median, range)	21 (6-32)
HCV genotype (n,%)	
- 1	81 (47%)
- 2	6 (3%)
- 3	65 (37%)
- 4	22 (13%)
Liver biopsy (n,%)	116 (67%)
-HAI (median, range)	6 (2-12)
-Fibrosis scoring (n,%)	
- 0	4 (3%)
- 1	25 (22%)
- 2	23 (20%)
- 3	23 (20%)
- 4	41 (35%)
HCV-RNA ($\log_{10}$ IU/ml; median, range)	5.8 (2.9-7.25)
->800,000 IU/ml	76 (44%)
AST (U/l; median, range)	65 (20-478)
ALT (U/l; median, range)	84 (18-478)
GGT (U/l; median, range)	114 (21-1040)
-GGT>100 U/l	96 (55,5%)
Peg-IFN (n,%)	
-Peg-IFN! -2a	93 (53%)
-Peg-IFN! -2b	81 (47%)
RBV dosage (mg/kg/day; median, range)	14,28 (8-23,07)

Safety



DRUG ADJUSTEMENTS	
Peg-IFN	**12** (7%)
-thrombocytopenia	6 (50%)
-intolerance	5 (42%
-neutropenia	1 (8%)
RBV	**13** (7%)
-all due to anemia*	

Overall Outcomes according peg-IFN Formulation

	Peg-IFN! -2a (n=93)	Peg-IFN! -2b (n=81)	*P*
HCV-RNA ($\log_{10}$IU/ml; mean±SD)			
- Week 4	2,96 ± 2,42	2,83 ± 2,51	0.72
- Week 12	1,80 ± 2,28	2,40 ± 2,6	0.21
- Week 24	1,31 ± 2,20	1,84 ± 2,6	0.27
Negative HCV-RNA (%)			
- Week 4	33	41	0.28
- Week 12	54	48	0.44
- Weeek 24	68	62	0.46
EVR (%)	70	57	0.07
SVR (%)	49,5	41	0.24
Early withdrawals (%)	15	18	0.54

Univariate analysis of factors associated to SVR

	RVS (n=79, 45%)	Non-SVR (n=95, 55%)	*P*
Baseline HCV-RNA $\log_{10}$IU/ml	5.6 (2.9-7.25)	5.95 (3.8-6.9)	0.0001*
-HCV-RNA >800,00 IU/ml (%)	32	54%	0.004*
HCV genotype 1 or 4 (%)	33	80	0.0001*
Fibrosis scoring (median, range)	2 (0-4)	3 (0-4)	0.036*
Baseline CD4 count (cells/ml)	554 (108-1418)	454 (45-1513)	0.035*
GGT ≥ 100 U/l (%)	44	65	0.004*
AST (U/l); (median, range)	62 (20-408)	67 (20-478)	0.09
ALT (U/l); (median, range)	93 (19-439)	73 (18-478)	0.056
Peg-IFN Formulation (%)			0.25
- peg-IFN$^{\alpha}$-2a	58	49,5	
- peg-IFN$^{\alpha}$-2b	42	50,5	

By univariate analysis age, gender, prior IVDU or AIDS diagnosis, prior history of CD4 counts<200cells/ml, F3/F4 or cirrhosis, RBV dosage, or HIV-RNA were not significantly associated to RVS

Multivariate regression analysis of factors associated to SVR

	OR	95% CI	P
HCV genotype 1 or 4	7.59	2.53-22.77	**0.0003***
HCV-RNA $\log_{10}$ IU/ml	3.27	1.55-6.90	**0.0018***
Fibrosis scoring	1.74	1.16-2.60	**0.0066***

CONCLUSIONS

1. In our HIV/HCV-cohort, both peg-IFN formulations plus weight-adjusted RBV showed similar safety and effectiveness profiles.
2. After multivariate analysis, HCV genotypes 1 or 4, and higher HCV-RNA levels or fibrosis scoring were independently associated to treatment failure.