PEGINTERFERON ALFA-2A PLUS RIBAVIRIN VS PEGINTERFERON ALFA-2B PLUS RIBAVIRIN FOR CHRONIC HEPATITIS C VIRUS INFECTION IN HIV-INFECTED PATIENTS

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Background

- The most effective therapy for CHC in HIV+ patients is peg-IFN plus RBV[1–4].
- There are two approved brands of peg-IFN: peg-IFN α-2a (PEG2A) with a molecular weight of 40 kDa and peg-IFN α-2b (PEG2B) with a molecular weight of 12 kDa.
  - PEG2B has a larger Vd and higher renal clearance than PEG2A.
  - PEG2A is administered as a flat dose whereas PEG2B is administered according to body weight.
- It is unknown how these differences affect to sustained viral response (SVR) to therapy.

Objective

The purpose of our study is to compare the efficacy/safety of PEG2A with PEG2B both with RBV against chronic HCV infection in HIV-infected patients.

Methods

Design

- Cohort study

GESIDA 3603 Study Cohort

- Established to follow HIV/HCV+ patients who started IFN-RBV RX between Jan 2000 and Dec 2005 and with active follow-up every 6 mo.
- Primary objective: to determine the effect of achieving a SVR on long-term clinical outcomes including liver-related complications, and liver-related mortality.
- Secondary objetive: to assess the efficacy/safety of different IFN-RBV strategies

Setting

- 11 clinical centers in Spain

Patients

- For the purpose of this study we analyzed patients naïve for IFN who were treated with either PEG2A-RBV (N = 315) or PEG2B-RBV (N = 242).

Assessment

- **End of treatment response (ETR):** Undetectable HCV-RNA at the end of therapy with IFN-RBV
- **SVR:** Undetectable HCV-RNA 24 wk after the end of therapy with IFN-RBV
- **Safety:** Assessed by lab tests and evaluation of AE at least monthly during IFN-RBV therapy

Statistics

- Differences between groups: Chi square, Student's T or Mann Whitney-U as appropriate.
- Analyses were done on an ITT and OT basis
- Logistic-regression models were used to explore base-line factors predicting a SVR and discontinuation of RX due to AE.

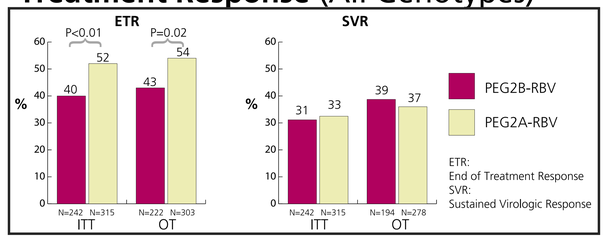
Characteristics

Characteristics	PEG 2b + RBV N=242	PEG 2a + RBV N=315	P
Sex- nº (%)			0.71
Male	181 (75)	229 (73)	0.78
Female	61 (25)	83 (26)	0.78
Age- yr, median (IQR)	39 (35.9; 42.7)	40 (36.7; 43.1)	0.13
Weight- kg, median (IQR)	67 (60; 75)	68 (59; 75)	0.37
Mode of Infection - nº (5)			0.05
Injection-drug use	206 (85)	239 (76)	0.01
Sexual Exposure	24 (10)	36 (11)	0.66
Transfusion	6 (2)	21 (7)	0.04
Unknown or other	5 (2)	16 (5)	0.68
CDC disease state - nº (%)			0.97
A	118 (49)	158 (50)	0.22
B	67 (28)	87 (28)	0.37
C	52 (21)	66 (21)	0.96
CD4 + cells baseline - nº/mm³	492 (363; 740)	563 (411; 749)	0.91
CD4 + cells nadir - nº/mm³	208 (110; 331)	204 (100.5; 324)	0.22
HIV-RNA < 50 copies/mL - nº (%)	135 (56)	184 (58)	0.59
Duration of HCV infection, median (IQR)	17 (12; 21)	18 (13; 22)	0.27
Serum ALT, median (IQR)	98 (62; 151)	93 (63; 138)	0.51
HCV genotype - nº (%)			0.32
1	127 (52)	156 (50)	0.40
2	9 (4)	8 (3)	0.55
3	76 (31)	99 (31)	0.96
4	19 (8)	37 (12)	0.19
Unknown	5 (2)	13 (4)	0.28
HCV-RNA ≥ 500,000 IU/mL - nº (%)	151/222 (68)	188/273 (69)	0.92
Liver biopsy - nº (%)	204 (84)	253 (80)	0.27
Fibrosis stage 0	28 (14)	14 (6)	< 0.01
Fibrosis stage 1	49 (24)	69 (27)	0.47
Fibrosis stage 2	41 (20)	87 (34)	< 0.01
Fibrosis stage 3	63 (31)	51 (20)	0.01
Fibrosis stage 4	23 (11)	32 (13)	0.74
Fibrosis F3-F4 - nº (%)	86 (42)	83 (33)	0.04
HBsAg positive	6 (2)	7 (2)	0.86
Intake of > EtOH daily - nº (%)	10 (4)	9 (3)	0.90
Methadone use - nº (%)	24 (10)	43 (15)	0.14

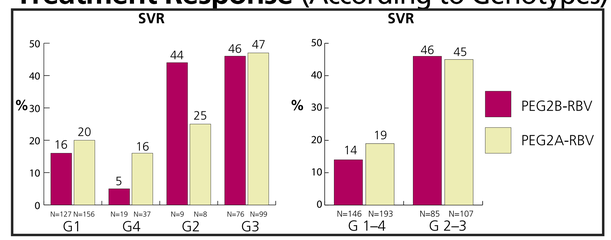
Treatment Details

	PEG 2b + RBV N=242	PEG 2a + RBV N=315	P
peg-IFN dose (given once weekly	1.5 ug/Kg	180 µg	
RBV dose . mg/kg, median (IQR)	13.3 (12.3; 14.7)	14 (11.8; 15.7)	0.09
Antiretroviral therapy - nº (%)			
None	43 (18)	52 (17)	0.78
Any	199 (82)	263 (83)	0.78
3 NRTI	32 (13)	34 (11)	0.46
2 NRTI + PI	45 (19)	98 (31)	0.01
2 NRTI + NNRTI	101 (42)	110 (35)	0.12
2 NRTI + NNRTI + PI	8 (3)	20 (6)	0.15
Other/Unknown	13 (5)	1 (<1)	< 0.01

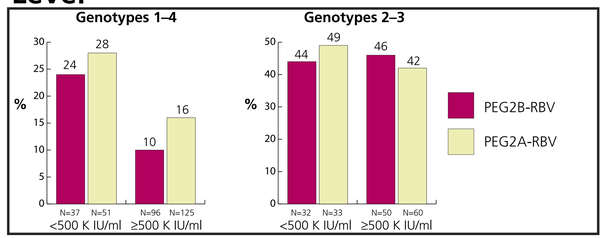
Treatment Response (All Genotypes)



Treatment Response (According to Genotypes)



Sustained Virologic Response according to HCV Genotype and Baseline HCV RNA Level



Independent Factors Associated with a SVR by Multiple Logistic-Regression Analysis

	OR	CI 95%	p
IFN PEG 2a + RBV	1.35	(0.81; 2.26)	0.250
CDC disease state (A/B vs C)	2.45	(1.16;5.21)	0.019
CD4 + cells nadir	1	(1; 1)	0.099
Intake of > 50 EtOH daily (currently)	1.87	(0.39;8.96)	0.432
Fibrosis F3-F4	1.19	(0.63; 2.22)	0.595
HCV genotype 2-3	3.77	(2.23; 6.36)	<0.001
HCV-RNA ≥ 500 K IU/ml	1.27	(0.74; 2.17)	0.390

OR: Odds ratio. CI 95%: 95% Confidence Interval

Reason for interruption of Peg-IFN/RBV therapy

Reason, N° (%)	PEG 2b + RBV N=242	PEG 2a + RBV N=315
Abandon	12 (5)	18 (6)
Withdrawn due to AE	33 (14)	47 (15)
Lack of efficacy	60 (25)	61 (19)
Treatment completion	116 (48)	175 (56)
Unknown - Lost to FU	21 (9)	14 (4)

Dose Reductions and Discontinuation of Peg-IFN/RBV During Treatment

Characteristic	PEG 2b + RBV N=242	PEG 2a + RBV N=315	
Peg IFN/RBV-related to serious AE	54 (22.5)	54 (17.1)	0.16
Premature discontinuation due to AE	43 (17.9)	58 (18.4)	0.93
Reduction od IFN due to AE	34 (14.3)	48 (15.3)	0.79
Reduction of RBV due to AE	37 (15.5)	46 (14.7)	0.92

ART Adverse Events During Treatment

	PEG 2b + RBV N=242	PEG 2a + RBV N=315	
Change in ART during treatment	70 (29.8)	109 (34.7)	0.22
Adverse event	28 (35.4)	32 (26.4)	0.23
Virological failure	5 (6.3)	3 (2.5)	0.32
Simplification	7 (8.9)	21 (17.4)	0.14
Other	25 (31.6)	43 (35.5)	0.68
Unknown	14 (17.7)	22 (18.2)	0.92

Deaths, HIV Disease Progression, Liver Decompensation

Characteristic - nº (%)	PEG 2b + RBV N=242	PEG 2a + RBV N=315	
Death	4 (1.7)	2 (0.6)	0.46
Liver-related	2 (50)	1 (50)	0.82
Other	2 (50)	1 (50)	0.82
Treatment related	0	0	
AIDS-defining event	1 (0.4)	3 (1)	0.81
Esophagal candidiasis	1 (100)	1 (33.3)	0.60
PML	0 (0)	1 (33.3)	0.60
Other	0 (0)	1 (33.3)	0.60
Hepatic decompensation	4 (1.7)	7 (2.2)	0.86

Conclusions

No significant differences were found in efficacy/safety between PEG2A-RBV and PEG2B-RBV for the treatment of chronic HCV infection in HIV-infected patients.

1. Torriani FJ, et al . N Engl J Med 2004; 351 (5): 438–50. 2. Chung RT, et al. N Engl J Med 2004; 351 (5): 451–9. 3. Carrat F, et al. JAMA 2004; 292 (23): 2839–48. 4. Laguno M, et al. AIDS 2004;18 (13): F27–36.