Sustained Virological Response to Interferon plus Ribavirin Reduces Liver-Related Complications and Mortality in HIV/HCV-Coinfected Patients

Juan Berenguer,[1] Julio Álvarez-Pellicer,[2] José López-Aldeguer,[3] Miguel Angel Von-Wichman,[4] Carmen Quereda,[5] Josep Mallolas,[6] José Sanz,[7] Cristina Tural,[8] José María Bellón,[1] Juan González,[2] and The GESIDA 3603 Study Group

[1]Hosp Gregorio Marañón, Madrid; [2]Hosp La Paz, Madrid; [3]Hosp La Fé, Valencia; [4]Hosp Donostia, San Sebastian; [5]Hosp Ramón y Cajal, Madrid; [6]Hosp Clinic, Barcelona; [7]Hosp Príncipe de Asturias, Alcalá de Henares; [8]Hosp Germans Trias i Pujol, Badalona.

Funding sources:
Fundación para la Investigación y la Prevención del SIDA en España (FIPSE) (Refs. 36443/03 and 36702/07)

Background

- Response to antiviral therapy, and particularly sustained virological response (SVR), appears to reduce liver complications in chronic hepatitis C*
- Little is known about the clinical consequences of achieving a SVR following interferon plus ribavirin (IFN-RBV) therapy in HIV/HCV+ patients

*Coverdale SA, et al. Am J Gastroenterol 2004;99(4):636-44

Objective

- To determine the effect of achieving an SVR on clinical outcomes including mortality, liver-related complications, and HIV progression in HIV/HCV+ patients

Study Design
GESIDA 3603 Study Cohort

Setting	11 clinical centers in Spain
Patients	HIV/HCV+ patients who started IFN-RBV between Jan 2000 - Dec 2005
Data Retrieval	Data were entered into a common database at each institution by means of an ad hoc online application
Follow-Up	Clinical and laboratory parameters every 6 mo: survival, liver decompensation, HIV-related diseases, ART, CD4 cell count, HIV viral load, HCV RNA, liver biopsy, and anti HCV therapy. Alpha-fetoprotein (AFP) and ultrasound (US) scan in cirrhotic patients
Length of the study	Was calculated from the date SVR or non-SVR was confirmed and ended at death or at the last follow-up visit.

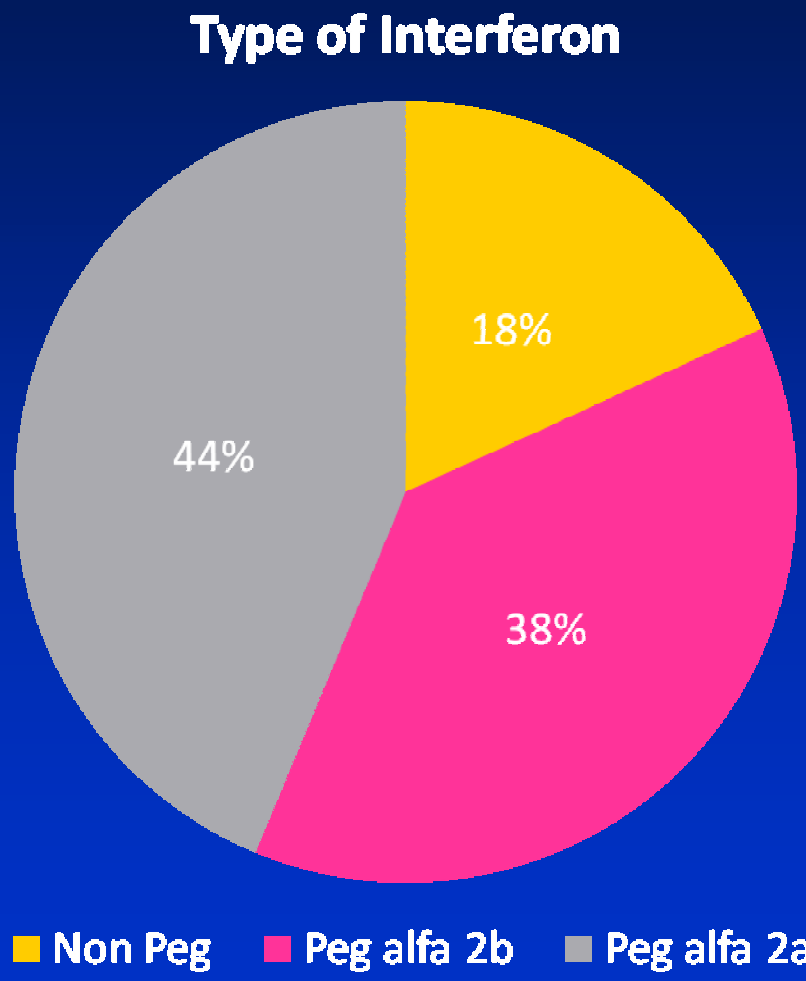
Endpoints

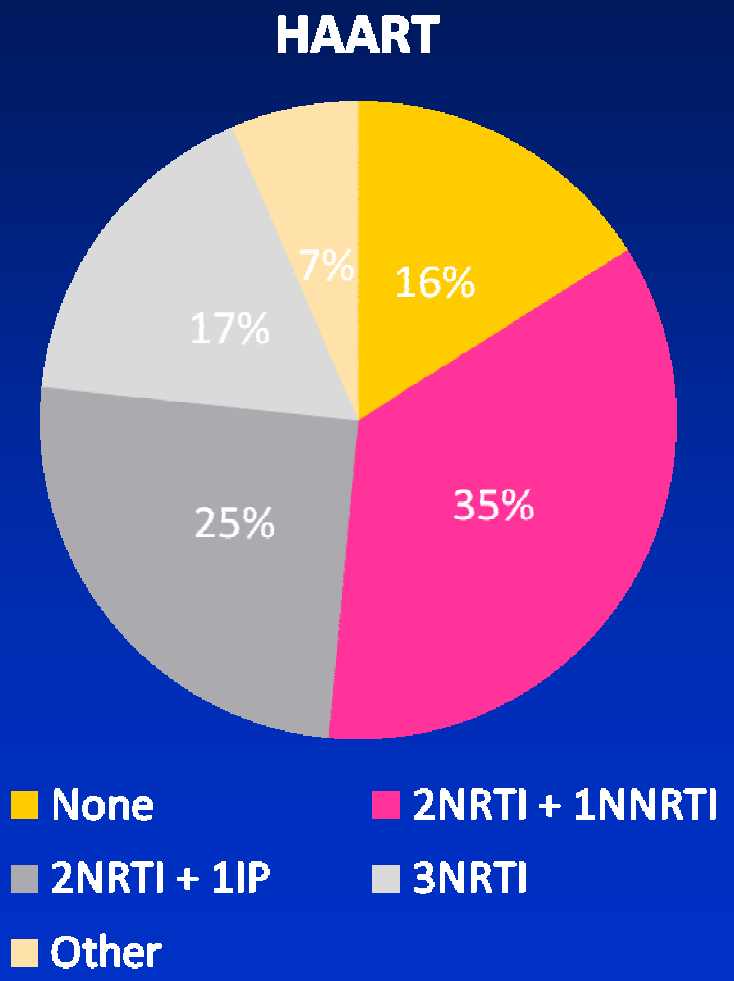
- Liver-related complications
  - Liver decompensation
    - Ascites, Porto-systemic encephalopathy (PSE), Upper GI bleeding
  - Hepatocellular carcinoma (HCC)
    - Histologically or clinically confirmed (high AFP values and evidence of focal liver lesion at imaging techniques.
  - Liver transplantation
- HIV progression
  - CDC criteria
- Mortality
  - Overall mortality
  - Liver-related mortality

Patient Characteristics

Characteristic	Patients (N = 711)
Male sex – nº (%)	507 (71.5)
Age - yr, median (IQR)	40.9 (37.9; 44.1)
Weight - kg, median (IQR)	67 (59; 75)
Prior Injection-drug use – nº (%)	567 (79.8)
CDC disease category C – nº (%)	148 (21.2)
CD4 + cells baseline – nº/mm3	217 (117; 334)
HIV-RNA < 50 copies/mL baseline – nº(%)	313 (51.7)
Duration of HCV infection, median (IQR)	18 (13; 22)
HCV genotype 1-4 - nº (%)	423 (62.9)
HCV-RNA ≥ 500,000 IU/mL – nº (%)	446 (69.5)
METAVIR fibrosis score 3-4 – nº (%)	237 (38.8)
HBsAg positive	17 (2.4)
Intake of > EtOH daily – nº (%)	34 (5.6)
Methadone use– nº (%)	80 (12.4)

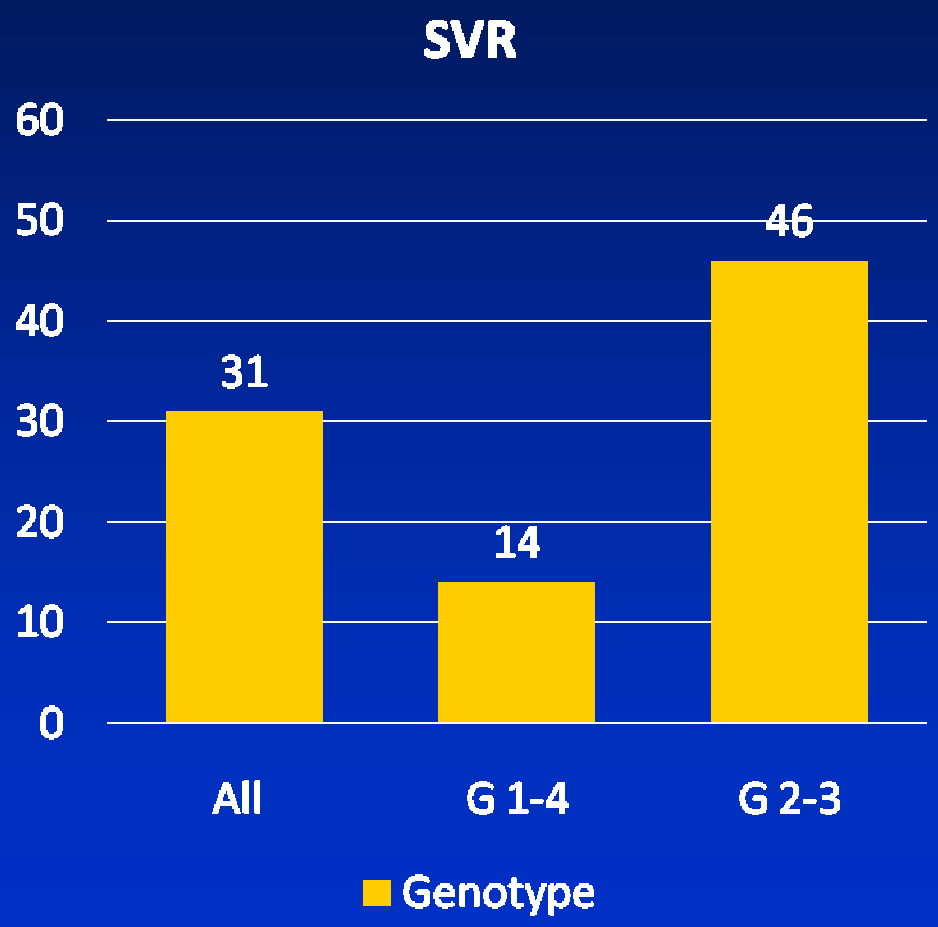
Treatment Details





SVR & Independent Factors Associated with a SVR

by Multiple Logistic-Regression Analysis



	OR	95% CI	P
Type of Interferon			
Non-Peg α2a/α2b	1	-	-
Peg α2b	1.38	(.77; 2.45)	.276
Peg α2a	1.23	(.68; 2.25)	.492
CDC category A/B	1.67	(.94; 2.95)	.078
CD4 + cells	1.00	(1; 1)	.085
HCV genotype 2-3	3.27	(2.12; 5.05)	.000
HCV-RNA < 500 K IU/ml	1.98	(1.27; 3.07)	.002
METAVIR F0-2	1.46	(.93; 2.29)	.098
Intake of > 50 g et-OH	.45	(.15; 1.39)	.167
Nº of ART regimens used	.94	(.86; 1.03)	.216

Frequency of Events During Follow-up

in 711 HIV/HCV+ patients stratified according to response to IFN-RBV

	Non-SVR N = 493	SVR N = 218
Follow-up – yr, median (IQR)	22.1 (12.7; 39.1)	18.7 (11.3; 36.9)
Lost to follow-up	25 (5)	13 (6)
Deaths – nº (%)	34 (6.9)	2 (.9) *
Liver-related – nº (%)	18 (3.7)	1 (.5) *
AIDS-related – nº (%)	2 (.4)	0 (0)
Other causes – nº (%)	14 (2.8)	1 (.5) *
New AIDS defining condition – nº (%)	10 (2)	1 (.5)
Liver decompensation – nº (%)	45 (9.1)	1 (.5) *
Hepatocarcinoma – nº (%)	9 (1.8)	0 (0)
Liver transplantation – nº (%)	11 (2.2)	0 (0)

* $P < .05$

Rate of Events During Follow-up

in 711 HIV/HCV+ patients stratified according to response to IFN-RBV

Event	Rate/100 person-years (95% CI)		*P* *
	Non-SVR	SVR	
Overall mortality	3.12 (2.16; 4.37)	.46 (.06; 1.65)	.003
Liver-related mortality	1.65 (.98; 2.61)	.23 (.01; 1.27)	.028
Liver decompensation	4.33 (3.16; 5.8)	.23 (.01; 1.27)	<.001
#epatocellular carcinoma	.83 (.38; 1.58)	0 (0; .84)	.099
Liver transplantation	1.02 (.50; 1.82)	0 (0; .84)	.034
New AIDS conditions	.93 (.44; 1.70)	.23 (.01; 1.27)	.144

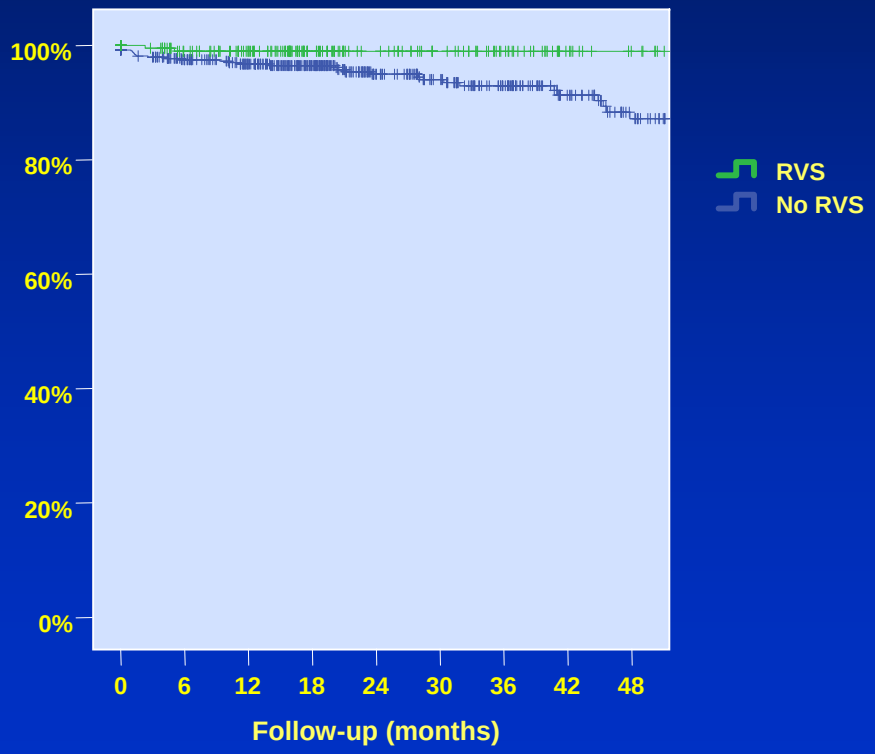
*By log-rank test.

Ascites, upper GI bleeding, hepatic encephalopathy

Cumulative Incidence of Mortality

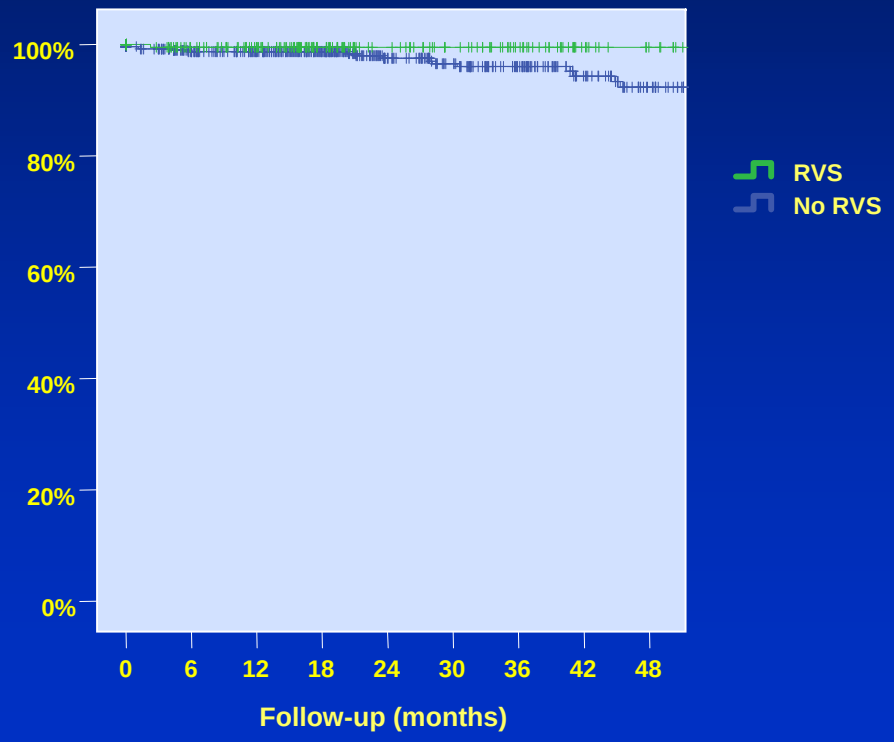
in 711 HIV/HCV+ patients stratified according to response to IFN-RBV

Overall Mortality



P = .003 by log-rank test

Liver-related Mortality

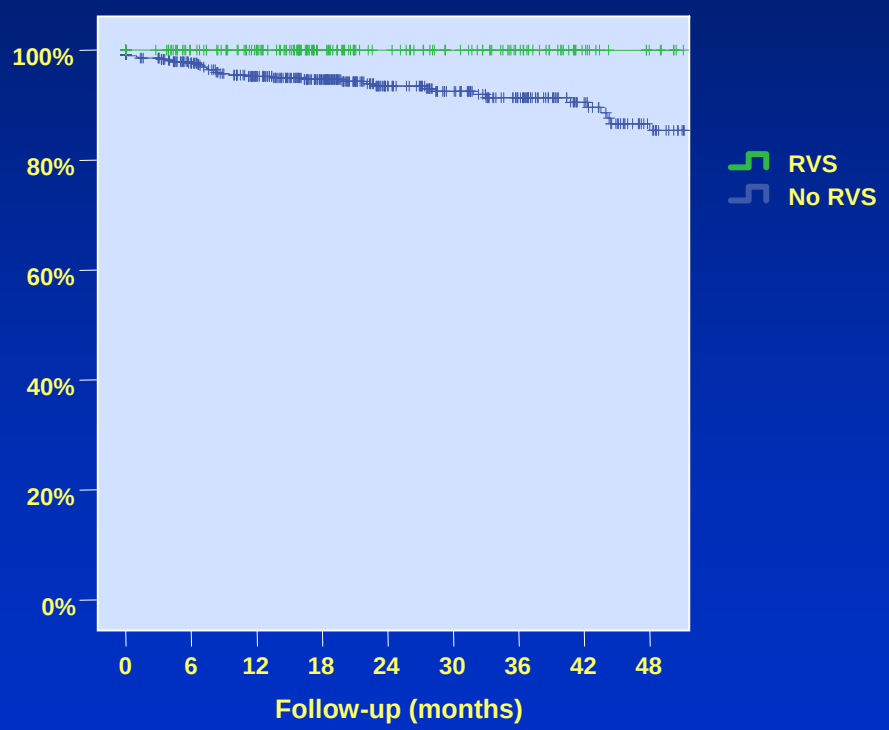


P = .028 by log-rank test

Cumulative Incidence of Decompensation & HCC

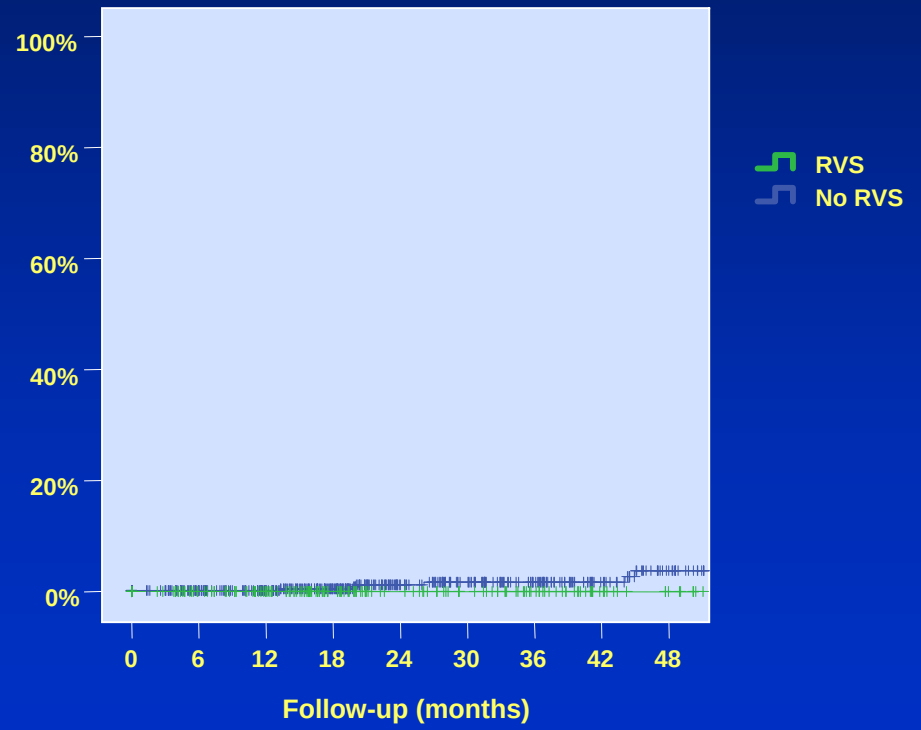
in 711 HIV/HCV+ patients stratified according to response to IFN-RBV

Liver Decompensation



P < .001 by log-rank test

Hepatocellular carcinoma

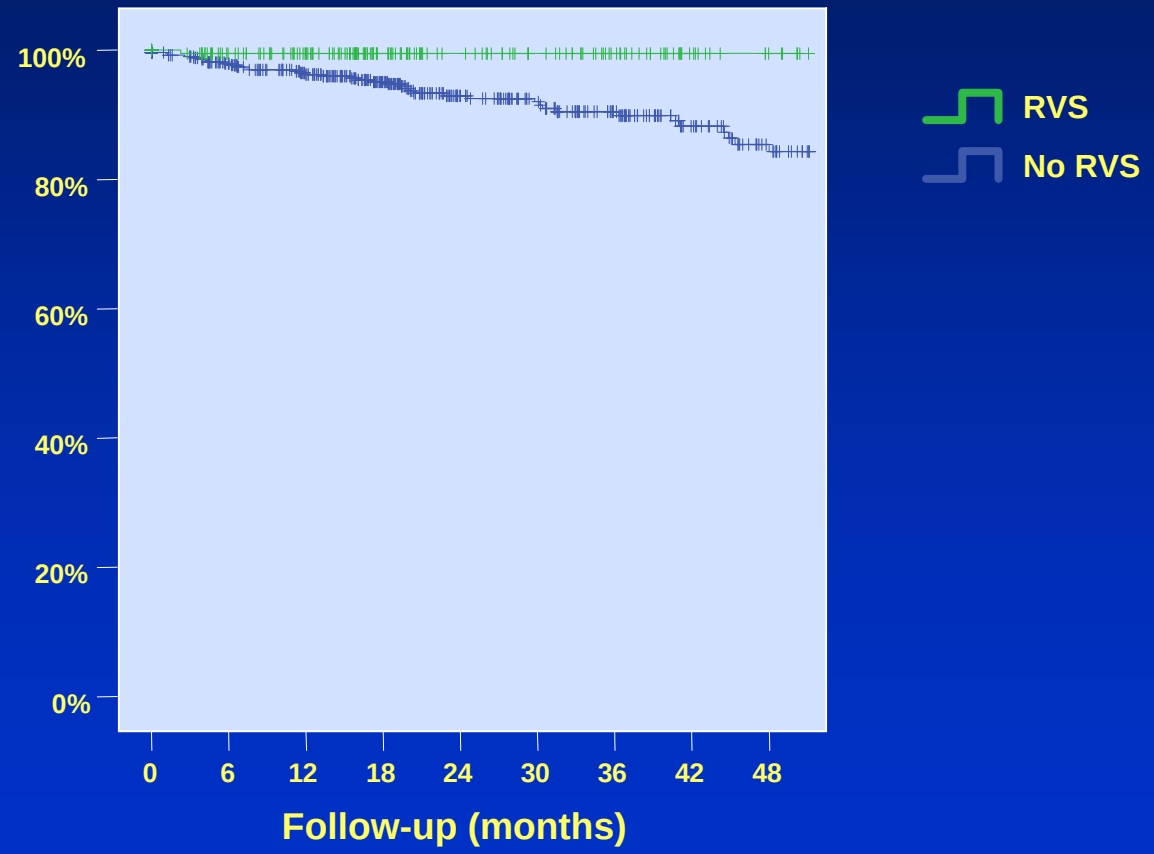


P = .099 by log-rank test

Cumulative Incidence of Liver-related Events*

in 711 HIV/HCV+ patients stratified according to response to IFN-RBV

* Liver-related death, liver decompensation, HCC, and liver transplantatio



P < .001 by log-rank test

Multivariate Analysis of Factors Associated with Liver-related Events* by Cox Regression Analysis

	Adjusted HR	95% CI	P
Non-SVR vs. SVR	10.22	(1.38; 75.46)	.023
F3-4 vs F0-2	3.65	(1.83; 7.31)	.000
Genotype 1-4 vs 2-3	1.48	(.7; 3.13)	.301
CDC Category C vs. A/B	.95	(.49; 1.87)	.892

* Liver-related death, liver decompensation, HCC, and liver transplantation

Conclusions

- Our results suggest that the achievement of an SVR after IFN-RBV therapy in HIV/HCV+ patients reduces liver-related complications and mortality

Acknowledgments

The GESIDA 3603 Team

Hosp. Gregorio Marañón, Madrid
JM Bellón, J Berenguer, J Cosín, I Gutiérrez, JC López, P Miralles, B Padilla, M Ramírez, P Ryan, M Sánchez-Conde,
Hosp. La Paz, Madrid
M Amer, J Alvarez, J R Arribas, J González; ML Montes
Hosp. La Fé, Valencia
S Cuellar, J López-Aldeguer
Hosp. Donostia, San Sebastián
MA Von-Wichmann
Hosp. Ramón y Cajal, Madrid
A Moreno, C Quereda
Hosp. Clinic, Barcelona
P Callau, M Laguno, J Mallolas
Hosp. Príncipe de Asturias, Alcalá Henares
J Sanz
Hosp. Germans Trias i Pujol, Badalona
C Tural
Hosp. General, Valencia
E Ortega
Hosp. 12 de Octubre, Madrid
MA Hernnado, F Pulido, R Rubio
Hosp. La Princesa, Madrid
I Santos, J Sanz
AEC GESIDA, Madrid
E Barquilla, H Esteban, B Mahillo, B Moyano