Real-world Outcomes With New HCV Antivirals in HIV/HCV-coinfected Subjects: Madrid Coinfection Registry (Madrid-CoRE) Findings

Ángela Gil-Martin[1], Juan J. Gonzalez-García[2], Encarnación Cruz-Martos[1], Ana Moreno[3], Lourdes Dominguez[4], Marisa Montes[2], Teresa Aldámiz-Echevarría[5], María J. Téllez[6], Ignacio Santos[7], Laura Benitez[15], José Sanz[9], Pablo Ryan[10], Gabriel Gaspar[11], Miguel Gorgolas[17], Juan E. Losa[12], Rafael Torres-Perea[13], Carlos Barros[14], Juan V. San Martin[16], Sari Arponen[18], María José Calvo[1], Marta Alcaráz[1], Inmaculada Jarrin[8], Juan Berenguer[5]

[1]Subdirección General de Farmacia y Productos Sanitarios, SERMAS, Madrid, Spain. [2]Hospital La Paz/IdiPaz, Madrid, Spain. [3]Hospital Universitario Ramón y Cajal, Madrid, Spain. [4]Hospital Universitario 12 de Octubre/imas12 , Madrid, Spain. [5]Hospital General Universitario Gregorio Marañon/IiSGM, Madrid, Spain. [6]Hospital Universitario Clínico San Carlos, Madrid, Spain. [7]Hospital de la Princesa, Madrid, Spain. [8]Instituto de Salud Carlos III, Madrid, Spain. [9]Hospital Príncipe de Asturias, Alcalá de Henares, Spain. [10]Hospital Infanta Leonor, Madrid, Spain. [11]Hospital de Getafe, Getafe, Spain. [12]Fundación Hospital de Alcorcón, Alcorcón, Spain. [13]Hospital Universitario Severo Ochoa, Leganés, Spain. [14]Hospital Universitario de Móstoles, Móstoles, Spain. [15]Hospital Puerta de Hierro, Majadahonda, Spain. [16]Hospital Universitario de Fuenlabrada, Fuenlabrada, Spain. [17]Fundación Jiménez Díaz, Madrid, Spain.[18]Hospital de Torrejón, Madrid, Spain.

Disclosure

Juan González-García

- Consulting fees and honoraria
  - AbbVie, BMS, Gilead, Janssen, MSD
- Grant support
  - Gilead, MSD

Juan Berenguer

- Consulting fees and honoraria
  - AbbVie, BMS, Gilead, Janssen, MSD, ViiV Healthcare
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Juan González-García and Juan Berenguer are the senior authors of this presentation

Background and Aim

- Current guidelines emphasize that HIV/HCV-coinfected persons should be treated and retreated the same as non–HIV-infected persons, after identification and management of interactions between direct-acting antivirals (DAAs) used to treat HCV infection and antiretroviral medications

- Currently licensed DAA regimens have been assessed in HIV/HCV-coinfected persons in clinical trials; however, more data are needed, especially subgroup analyses, to fully appreciate their effectiveness and safety under real-life conditions

- Our aims were to assess treatment outcomes in a large prospective registry of HIV/HCV-coinfected persons receiving DAA-based HCV therapy and to analyze factors associated with response to treatment

Madrid-CoRe

Madrid-CoRe (Madrid Coinfection Registry)

- Prospective registry of HIV/HCV-coinfected adults (≥18 years) undergoing therapy with DAAs for HCV infection in the region of Madrid
- Compulsory for all hospitals from the Madrid Regional Health Service (SERMAS)

Patients registered in MADRID-CoRe

- 2,402 patients registered between Nov 2014 and May 2016

Eligibility criteria and study design

Key inclusion criteria

- HIV/HCV coinfection
- Treatment with DAAs for HCV
- Scheduled to finish treatment on May 31, 2016

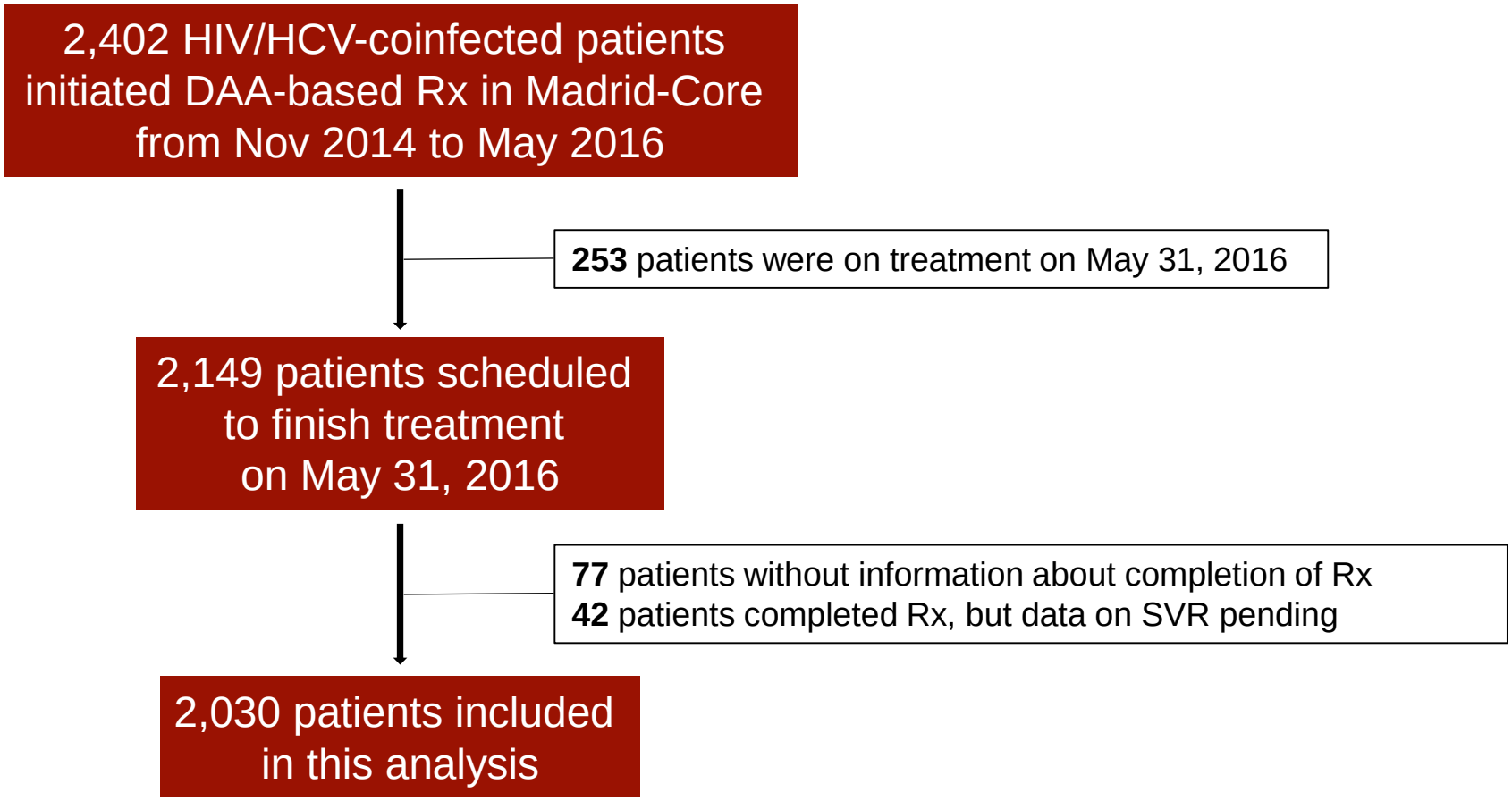
Primary endpoint

- Week 12 sustained viral response (SVR_{12}) by intention-to-treat analysis (ITT)

Secondary endpoints

- Viral relapse
- Viral breakthrough
- Discontinuation of treatment due to adverse events (AEs)
- Discontinuation of treatment for reasons other than AEs

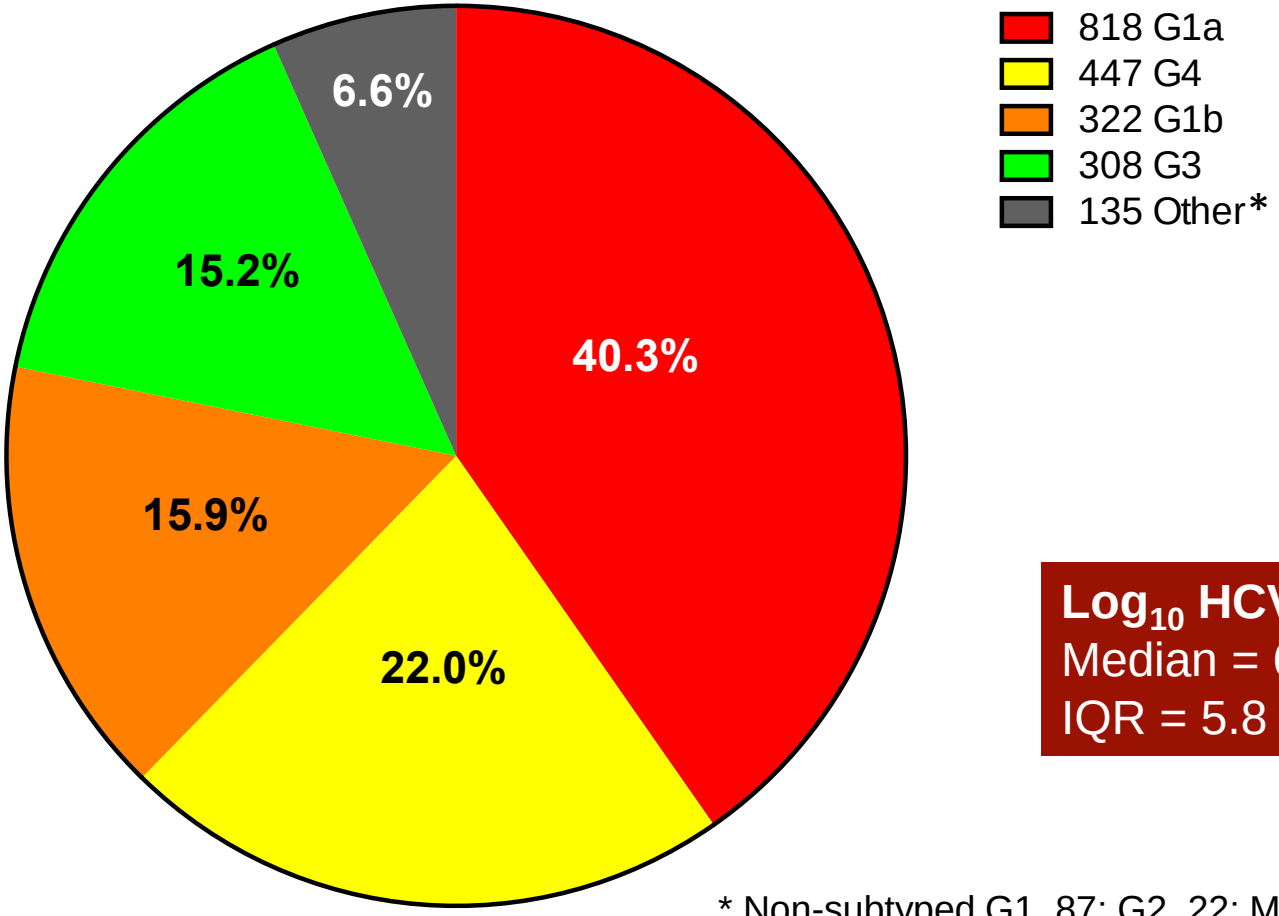
Flow chart


2,402 HIV/HCV-coinfected patients initiated DAA-based Rx in Madrid-Core from Nov 2014 to May 2016
253 patients were on treatment on May 31, 2016
2,149 patients scheduled to finish treatment on May 31, 2016
77 patients without information about completion of Rx
42 patients completed Rx, but data on SVR pending
2,030 patients included in this analysis

Patient characteristics

Variable	N = 2030
Age years – median (IQR)	50 (47 – 54)
Male – n (%)	1591 (78.4)
CD4+ T cells/µL – median (IQR)	570 (356 – 785)
cART – n (%)	1930 (95.1)
Liver disease severity	
No cirrhosis – n (%)	1125 (55.4)
Compensated cirrhosis – n (%)	754 (37.1)
Decompensated cirrhosis – n (%)	146 (7.2)
Unknown – n (%)	5 (0.3)
History of hepatocellular carcinoma – n (%)	15 (0.7)
Liver transplantation – n (%)	17 (0.8)
Liver transplantation waiting list – n (%)	7 (0.3)
Severe extrahepatic manifestations – n (%)	143 (7.0)
Anti-HCV – naïve – n (%)	1256 (61.9)
Liver stiffness kPa – median (IQR)	11.4 (8.1 – 20.2)

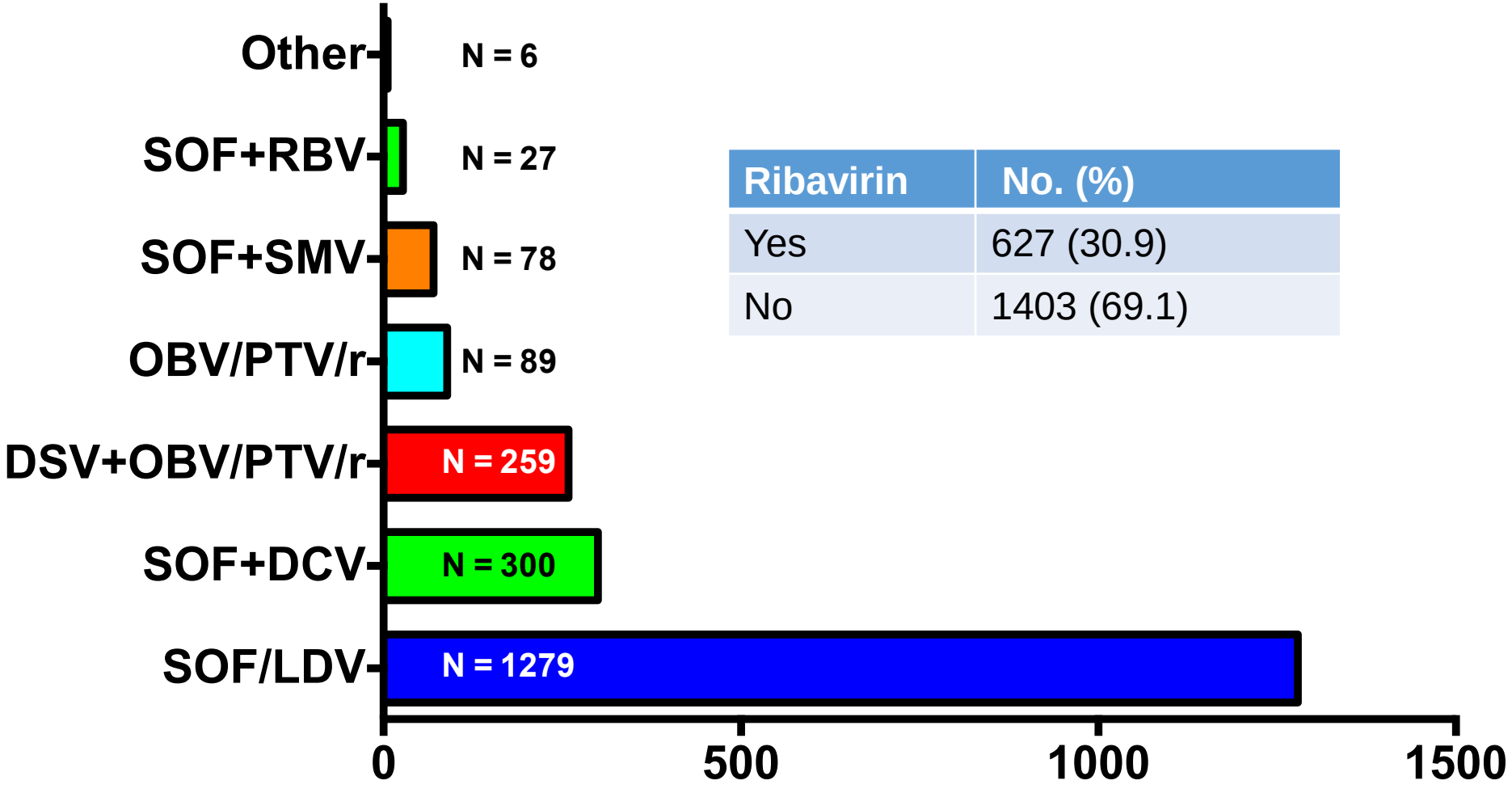
Genotypes and HCV-RNA



Log_{10} HCV-RNA
Median = 6.3
IQR = 5.8 – 6.7

* Non-subtyped G1, 87; G2, 22; Mixed, 23; Undetermined, 3

DAA-based regimens



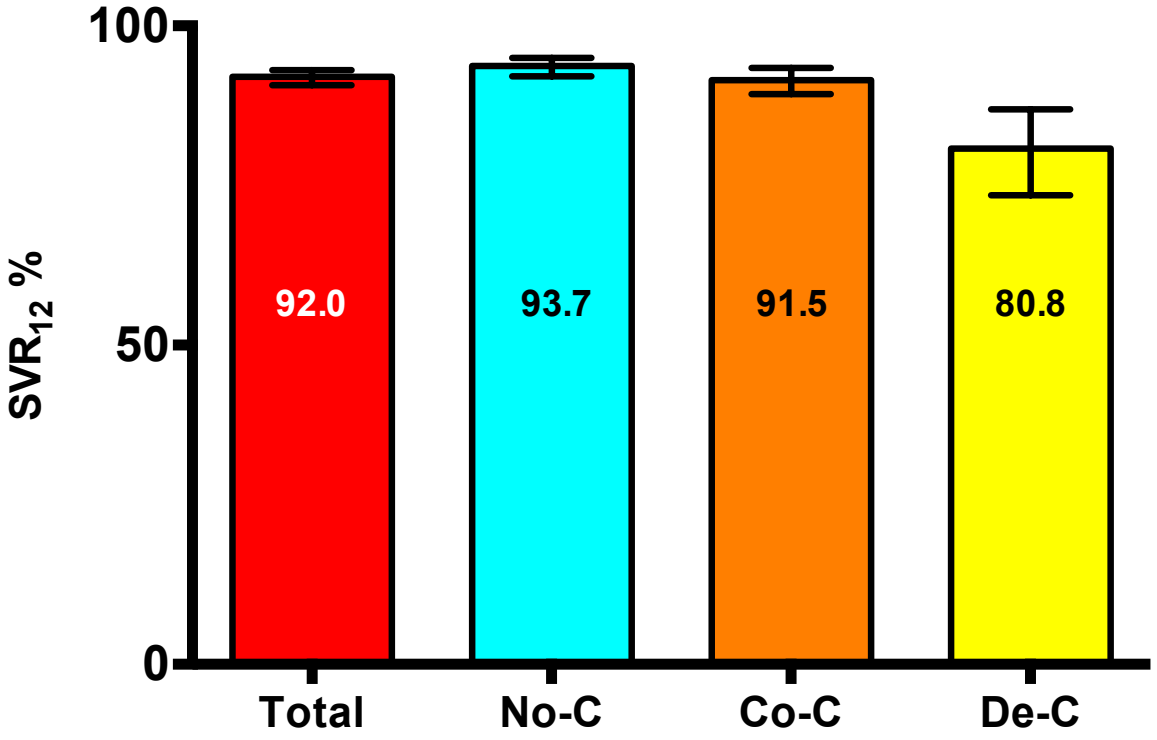
Ribavirin	No. (%)
Yes	627 (30.9)
No	1403 (69.1)

DAA regimens by HCV genotype

Regimen	G1a	G1b	G3	G4	Other [1]
SOF/LDV	604	185	82	325	83
SOF+DCV	38	12	219	18	13
DSV+OBV/PTV/r	141	105	0	0	13
OBV/PTV/r	1	0	0	88	0
SOF+SMV	29	18	0	15	8
Other [2]	5	2	7	1	18

[1] Non-subtyped G1, 87; G2, 22; Mixed, 23; Undetermined, 3
[2] SOF+RBV, 27; SMV+DCV, 4; SOF+SMV+DCV, 2

Treatment outcomes by severity of liver-disease



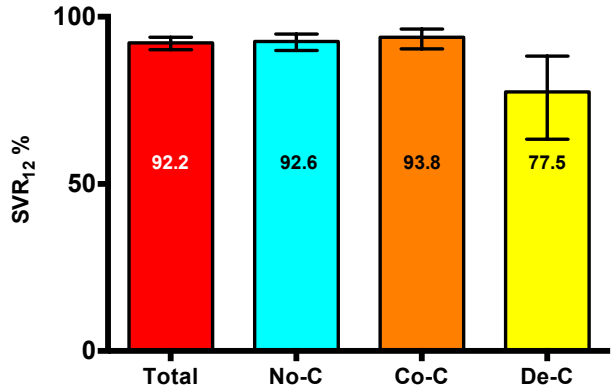
No-C = no cirrhosis
Co-C = compensated cirrhosis
De-C = decompensated cirrhosis

* Severity of liver disease was not evaluated in 5 patients

	Total	No-C	Co-C	De-C
No.	2030	1125	754	146
SVR ITT	1867 (92.0)	1054 (93.7)	690 (91.5)	118 (80.8)
SVR (95% CI)	(90.7 - 93.1)	(92.1 - 95.0)	(89.3 - 93.4)	(73.5 - 86.9)
Relapse	89 (4.4)	36 (3.2)	36 (4.8)	17 (11.6)
Breakthrough	5 (0.2)	3 (0.3)	1 (0.1)	1 (0.7)
DC due to AE	14 (0.7)	7 (0.6)	5 (0.7)	2 (1.4)
DC other	36 (1.8)	23 (2.0)	10 (1.3)	3 (2.0)
Death	19 (0.9)	2 (0.2)	12 (1.6)	5 (3.4)

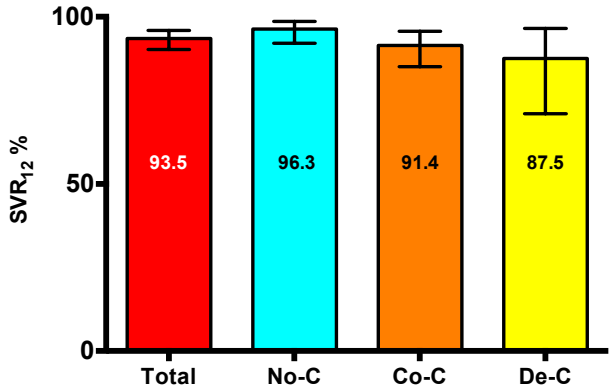
Treatment outcomes by HCV genotype

G1a



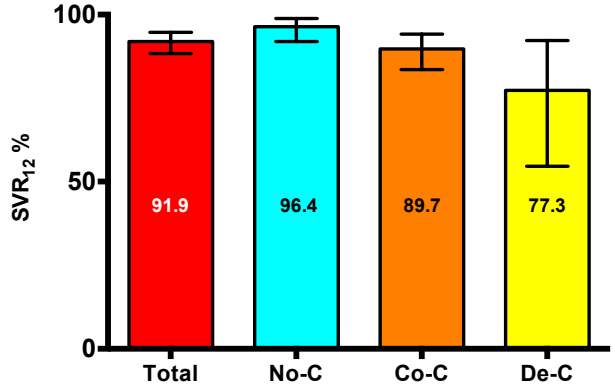
	Total	No-C	Co-C	De-C
No.	818	474	292	49
SVR ITT	754 (92.2)	439 (92.6)	274 (93.8)	38 (77.5)
SVR (95% CI)	(90.1 - 93.9)	(89.9 - 94.8)	(90.4 - 96.3)	(63.4 - 88.2)
Relapse	33 (4.0)	18 (3.8)	9 (3.1)	6 (12.2)
Breakthrough	0	0	0	0
DC due to AE	7 (0.9)	4 (0.8)	1 (0.3)	2 (4.1)
DC other	17 (2.1)	11 (2.3)	4(1.4)	2 (4.1)
Death	7 (0.9)	2 (0.4)	4 (1.4)	1 (2.0)

G1b



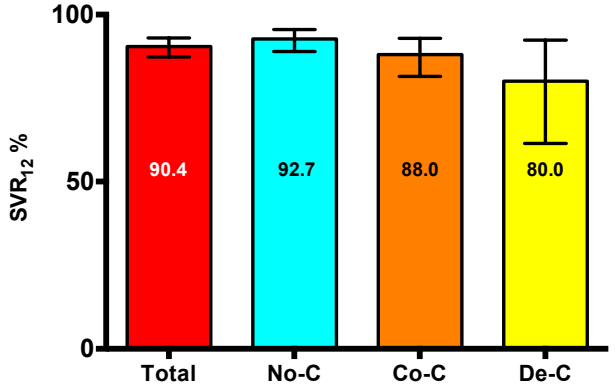
	Total	No-C	Co-C	De-C
No.	322	162	128	32
SVR ITT	301 (93.5)	156 (96.3)	117 (91.4)	28 (87.5)
SVR (95% CI)	(90.2 - 95.9)	(92.1 - 98.6)	(85.1 - 95.6)	(71.0 - 96.5)
Relapse	12 (3.7)	3 (1.8)	5 (3.9)	4 (12.2)
Breakthrough	1 (0.3)	1 (0.6)	0	0
DC due to AE	2 (0.6)	0	2 (1.6)	0
DC other	3 (0.9)	2 (1.2)	1 (0.8)	0
Death	3 (0.9)	0	3 (2.3)	0

G3



	Total	No-C	Co-C	De-C
No.	308	141	145	22
SVR ITT	283 (91.9)	136 (96.4)	130 (89.7)	17 (77.3)
SVR (95% CI)	(88.3 - 94.7)	(91.9 - 98.8)	(83.5 - 94.1)	(54.6 - 92.2)
Relapse	12 (3.9)	3 (2.1)	6 (4.1)	3 (13.6)
Breakthrough	1 (0.3)	0	1 (0.7)	0
DC due to AE	1 (0.3)	0	1 (0.7)	0
DC other	6 (1.9)	2 (1.4)	3 (2.1)	1 (4.5)
Death	5 (1.6)	0	4 (2.8)	1 (4.5)

G4



	Total	No-C	Co-C	De-C
No.	447	274	142	30
SVR ITT	404 (90.4)	254 (92.7)	125 (88.0)	24 (80.0)
SVR (95% CI)	(87.3 - 93.0)	(88.9 - 95.5)	(81.5 - 92.9)	(61.4 - 92.3)
Relapse	25 (5.6)	10 (3.6)	13 (9.1)	2 (6.7)
Breakthrough	2 (0.4)	1 (0.4)	0	1 (3.3)
DC due to AE	3 (0.7)	2 (0.7)	1 (0.7)	0
DC other	9 (2.0)	7 (2.5)	2 (1.4)	0
Death	4 (0.9)	0	1 (0.7)	3 (10.0)

Factors associated with treatment failure by logistic regression analysis

	Univariate analysis			Multivariate analysis		
Variable	**OR**	**95% CI**	**P**	**OR**	**95% CI**	**P**
Female sex	0.66	0.43 – 1.03	0.068	0.67	0.43 - 1.04	0.079
No cirrhosis	Ref.			Ref.		
Comp. cirrhosis	1.37	0.96 – 1.95	0.074	1.26	0.88 – 1.82	0.198
Dec. cirrhosis	3.52	2.18 – 5.67	<0.001	2.29	1.30 – 4.05	0.004
Hep. carcinoma	5.87	1.98 – 17.40	0.001	2.81	0.84 – 9.36	0.091
DSV+OBV/PTV/r	Ref.			Ref.		
SOF/LDV	1.23	0.70 – 2.16	0.469	1.14	0.65 – 2.02	0.634
SOF+DCV	1.54	0.79 – 2.98	0.196	1.31	0.67 – 2.56	0.429
OBV/PTV/r	1.38	0.54 – 3.52	0.490	1.49	0.58 – 3.82	0.396
SOF+SMV	5.21	2.45 – 11.10	<0.001	3.69	1.66 – 8.23	0.001
SOF+RBV	4.64	1.63 – 13.23	0.004	3.54	1.20 – 10.41	0.021
SMV+DCV	16.26	2.14 - 123.62	<0.001	12.06	1.54 – 9.40	0.018

Conclusions

1) In this large prospective cohort of HIV/HCV-coinfected persons, 45% of whom had liver cirrhosis, the SVR_{12} of DAA-based therapy for HCV infection was >90%

2) <1% of patients discontinued therapy owing to adverse events

3) Decompensated cirrhosis, and therapy with SOF+SMV, SOF+RBV, and SMV+DCV were independently associated with treatment failure

Funding

- Unrestricted grant from the GILEAD Fellowship Programme (Spain) Ref. GLD15/00314-GeSIDA-8916

- Red de Investigación en SIDA (AIDS Research Network) (RIS) Ref RD12/0017

- FibroScan® devices were available at the institutions by a donation from AbbVie Spain to GeSIDA/SEIMC

Madrid-CoRe Team

Hospital Ramon y Cajal: Moreno A, Quereda C, Casado J, Perez MJ, Vivancos MJ, Diaz A, Navas E, Fortún J, Moreno S, Serrano S, García M, Rodríguez MA. **Hospital Doce de Octubre:** Pulido F, Rubio R, Domínguez L, Matarranz M, de Lagarde M, Fernández I, Muñoz R, Martín A, Pinar O. **Hospital La Paz-Carlos III:** González JJ, Montes ML, Martín L, Moreno V, Valencia E, Pérez I, Bernardino I, Jiménez I, Moreno F. **Hospital Gregorio Marañón:** Berenguer J, Aldámiz T, Miralles T, López JC, Parras F, Gijón P, Padilla B, Montilla P, Fernández-Cruz A, Valerio M, Bermúdez E, Catalán P, Giménez A. **Hospital Clínico San Carlos:** Téllez MJ, Estrada V, Vergas J, Cabello N, Saénz M, Santiago A. **Hospital La Princesa:** Santos I, Martínez C. **Hospital Príncipe de Asturias:** Sanz J, De Miguel J, Arranz A, Casas E, Víctor V, Herrero M. **Hospital Infanta Leonor:** Ryan P, Troya J, Cuevas G, Esteban C. **Hospital Clinica Puerta de Hierro:** Benítez L, Arias A, Díaz A, Baños I, Duca A, Menchen B, Santiago M. **Hospital de Getafe:** Gaspar G, Sánchez-Rubio J. **Hospital Fundación Jiménez Díaz:** Górgolas A. Alvarez B, Polo B, Varela A, González A, Cabello A, Calvo R, Porres JC, Bonilla M. **Hospital Severo Ochoa:** Torres R, Cervero M, Jusadado JJ, Díaz E. **Hospital de Móstoles:** Merino F, Barros C, Corrales L. **Hospital Fundación de Alcorcón:** Losa JE, Hervas R, Velasco M, Moreno L, Henríquez C, Pérez M, Polanco M. **Hospital de Fuenlabrada:** San Martín J, Cnalejo E, Hinojosa J, Ruiz JM, Aguilar C, Hernández B. **Hospital de Torrejón:** Arponen S, Gimeno A, Montero MC. **Hospital del Henares:** Serrano R, Sanz P, Egües E, Tovar M. **Hospital del Tajo:** Monsalvo R, Terrancle I, Pedraza LA. **Hospital Infanta Elena:** Vegas A, del Portillo A, Collado V. **Hospital Infanta Cristina:** De Guzman MT, Martínez JA, Pérez JL, Melero JA, Matilla E. **Hospital del Sureste:** García MT, Peñalver R, Capilla C. **Hospital Rey Juan Carlos:** Gotuzzo L, Marcos J, García A. **Hospital Infanta Sofía:** Malmierca E, Suárez I, Portillo L. **Hospital El Escorial:** Belda L, Sanchez S. **Hospital Gómez Ulla:** Menéndez MA. **Subdirección General de Farmacia del SERMAS:** Cruz E, Gil A, Calvo MJ, Alcaraz M. **Instituto de Salud Carlos III:** Jarrín I.