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Abstract # 607

HIV Predicts Failure of LDV/SOF in HCV G1 Treatment-Naïve Non-Cirrhotic Patients

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Background and Aim

- The efficacy of licensed DAA regimens is assumed to be the same for HCV-monoinfected patients (MoP) and HIV/HCV-coinfected patients (CoP) [1,2].
- However, the high SVR rates of DAA regimens and the relatively small number of patients included in registration trials have made it difficult to identify predictors of treatment failure, including the presence of HIV.
- We compared treatment outcomes for LDV/SOF against HCV G1 in treatment-naïve MoP and CoP without cirrhosis within the Madrid Registry of use of DAA for HCV (Madrid RUA-VHC)

1. Karageorgopoulos DE, et al. World J Hepatol 2015;7:1936-1952.
2. Montes ML, et al. AIDS 2017;31:1253-1260.

Eligibility criteria and study design

Key inclusion criteria
- HCV genotype 1 infection
- Absence of liver cirrhosis
- Previously untreated
- Treatment with LDV/SOF without ribavirin for 8 or 12 wk.
- Scheduled to finish treatment on or before May 31, 2017

Primary endpoint
- Week 12 sustained viral response (SVR_{12}) by intention-to-treat analysis (ITT) and by modified ITT (m-ITT), excluding patients that discontinued therapy for reasons other than adverse events (AEs)

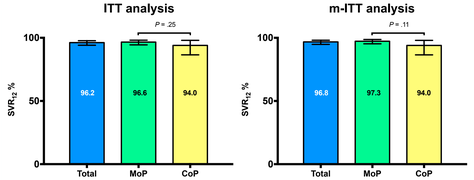
Secondary endpoints
- Viral relapse
- Viral breakthrough
- Discontinuation of treatment due to AEs
- Discontinuation of treatment for reasons other than AEs

Baseline characteristics of study population

	8 Weeks				12 weeks				TOTAL
	Total	MoP	CoP	P	Total	MoP	CoP	P	MoP + CoP
VARIABLES	N=498	N=415	N=83		N=909	N=687	N=222		N=1,407
Age #	56 (49-66)	58 (49-68)	50 (46-54)	<.001	56 (50-67)	60 (52-70)	51 (47-54)	<.001	56 (50-67)
Male sex ‡	259 (52.0)	193 (46.5)	66 (79.5)	<.001	515 (56.7)	348 (50.7)	167 (75.2)	<.001	774 (55.0)
Genotype ‡				<.001				<.001	
1a	160 (32.1)	95 (22.9)	65 (78.3)		408 (44.9)	235 (34.2)	173 (77.9)		568 (40.4)
1b	323 (64.9)	312 (75.2)	11 (13.2)		468 (51.5)	432 (62.9)	36 (16.2)		791 (56.2)
1 non-subtyped	15 (3.0)	8 (1.9)	7 (8.4)		33 (3.6)	20 (2.9)	13 (5.9)		48 (3.4)
HCV RNA									
Log IU/mL #	5.9 (5.4-6.4)	5.9 (5.4-6.3)	6.1 (5.6-6.5)	.03	6.4 (6.0-6.8)	6.4 (5.9-6.8)	6.5 (6.0-6.8)	.05	6.2 (5.7 – 6.7)
> 6x10e6 IU/mL ‡	18 (3.6)	12 (2.9)	6 (7.2)	.05	224 (24.6)	161 (23.4)	63 (28.4)	.14	242 (17.2)
TE									
No ‡	8 (1.6)	8 (1.9)	0		35 (3.8)	35 (5.1)	0		43 (3.1)
Yes ‡	490 (98.4)	407 (98.1)	83 (100.0)		874 (96.1)	652 (94.9)	222 (100.0)		1,364 (96.9)
kPa #	8.6 (7.9-9.4)	8.6 (7.9-9.3)	8.6 (7.8-10.0)	.61	9.1 (8.1-10.4)	9.2 (8.1-10.5)	9.0 (8.1-10.3)	.31	8.8 (8.0 – 10.2)
≥ 9.5 kPa ‡	122 (24.9)	95 (23.3)	27 (32.5)	.08	402 (46.0)	312 (47.8)	90 (40.5)	.06	524 (38.4)

= median (IQR)
‡ = n (%)
MoP = HCV monoinfected patients
CoP = HIV/HCV coinfected patients
TE = transient elastography

Treatment outcomes of LDV/SOF 8 weeks



		ITT			m-ITT		
No.		498	415	83	495	412	83
SVR ITT		479 (96.2)	401 (96.6)	78 (94.0)	479 (96.8)	401 (97.3)	78 (94.0)
SVR (95% CI)		(94.1 - 97.7)	(94.4 - 98.1)	(86.5 - 98.0)	(94.8 - 98.1)	(95.3 - 98.7)	(86.5 - 98.0)
Relapse		15 (3.0)	10 (2.4)	5 (6.0)	15 (3.0)	10 (2.4)	5 (6.0)
Breakthrough		0	0	0	0	0	0
DC due to AE		1 (0.2)	1 (0.2)	0	1 (0.2)	1 (0.2)	0
DC other		3 (0.6)	3 (0.7)	0			
Death		0	0	0			

MoP = HCV monoinfected patients
CoP = HIV/HCV coinfected patients

Factors associated with treatment failure by logistic regression analysis (N = 1,407)

Variable			Failures	Univariable		Multivariable	
			N (%)	OR (95% CI)	P	OR (95% CI)	P
Age	–	<45	4 (2.9)	1.00			
	–	45-54	23 (4.7)	1.68 (0.57 ; 4.95)	.53		
	–	≥55	29 (3.7)	1.31 (0.45;3.80)			
Sex	–	Female	13 (2.0)	1.00	.001	1.00	.01
	–	Male	43 (5.6)	2.81 (1.49;5.26)		2.37 (1.24;4.52)	
Liver stiffness – kPa	–	< 9.5	28 (3.3)	1.00			
	–	≥ 9.5	27 (5.1)	1.58 (0.92;2.70)	.22		
	–	Unknown	1 (2.3)	0.69 (0.09;5.20)			
HCV Genotype	–	1b	23 (2.9)	1.00			
	–	1a	31 (5.5)	1.93 (1.11;3.34)	.06		
	–	1 nt	2 (4.2)	1.45 (0.33;6.35)			
HCV-RNA IU/mL	–	< 6 M	47 (4.0)	1.00	.82		
	–	≥ 6 M	9 (3.7)	0.92 (0.44;1.90)			
HIV infection	–	No	33 (3.0)	1.00	<.00	1.00	.01
	–	Yes	23 (7.5)	2.64 (1.53;4.57)	1	2.16 (1.23;3.80)	
Treatment duration	–	12 wk	37 (4.1)	1.00	.81		
	–	8 wk	19 (3.8)	0.93 (0.53;1.64)			

Madrid Registry of Use of DAA for HCV

RUA-VHC (Madrid Registry of Use of DAA for HCV)
- Prospective registry of adults (≥18 years) undergoing therapy with DAAs for HCV infection in the region of Madrid
  - Madrid-CoRe (Madrid Coinfection Registry)
  - Madrid-MoRe (Madrid Monoinfection Registry)
- Compulsory for all hospitals from the Madrid Regional Health Service (SERMAS)

Patients registered in RUA
- 17,269 patients registered between Nov 2014 and Sep 2017

Flow chart

17,269 patients with HCV-infection initiated DAA-based Rx in Madrid from Nov 2014 to Sep 2017

↓

1,407 patients met inclusion criteria

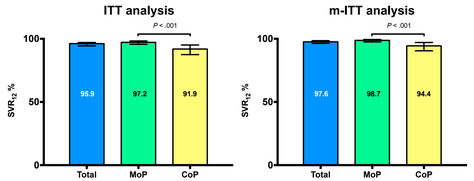
↓

1,102 HCV-Monoinfected patients (**MoP**)
305 HIV/HCV-Coinfected patients (**CoP**)

HIV-related variables among CoP

Variable	8 weeks	12 weeks
	n = 83	n = 222
HIV risk factor – n (%)		
Injection drug use	39 (47.0)	121 (54.5)
Men who have sex with men	8 (9.6)	4 (1.8)
Heterosexual relations	5 (6.0)	8 (3.6)
Transfusions	0	2 (0.9)
Mother to child	0	0
Other/unknown	31 (37.3)	87 (39.2)
CDC clinical category – n (%)		
A	21 (25.3)	38 (17.1)
B	9 (10.8)	39 (17.6)
C	22 (26.5)	60 (27.0)
Unknown	31 (37.3)	85 (38.3)
Nadir CD4+/mm3 – n (%)		
> 500	8 (9.6)	14 (6.3)
200 - 499	17 (20.5)	38 (17.1)
< 200	27 (32.5)	85 (38.3)
Desconocido	31 (37.3)	85 (38.3)
Baseline CD4+/mm³ – n (%)		
Known	33 (39.8)	126 (56.8)
Median (IQR)	632 (474 – 847)	593 (367 – 819)
ART – n (%)		
No	0	3 (1.3)
Yes	83 (100.0)	219 (98.6)
HIV-RNA – n (%)		
Unknown	31 (37.3)	82 (36.9)
Known	52 (62.6)	140 (63.1)
Detectable	8 (5.7)	
Undetectable	47 (90.4)	132 (94.3)

Treatment outcomes of LDV/SOF 12 weeks



		ITT			m-ITT		
No.		909	687	222	893	682	219
SVR ITT		872 (95.9)	668 (97.2)	204 (91.9)	872 (97.6)	668 (98.7)	204 (94.4)
SVR (95% CI)		(94.4 - 97.1)	(95.7 - 98.3)	(87.5 - 95.1)	(96.4 - 98.5)	(97.5 - 99.4)	(90.5 - 97.1)
Relapse		14 (1.5)	7 (1.0)	7 (3.1)	14 (1.6)	7 (1.0)	7 (3.2)
Breakthrough		0	0	0	0	0	0
DC due to AE		5 (0.5)	2 (0.3)	3 (1.3)	5 (0.6)	2 (0.3)	3 (1.4)
DC other		16 (1.8)	10 (1.5)	6 (2.7)	2 (0.2)	0	2 (0.9)
Death		2 (0.2)	0	2 (0.9)			

MoP = HCV monoinfected patients
CoP = HIV/HCV coinfected patients

Conclusions

1) The results of this large prospective real-world study analyzing treatment outcomes for LDV/SOF against HCV G1 in treatment-naïve noncirrhotic patients suggest that HIV infection is a predictor of treatment failure in patients with chronic hepatitis C.

2) Certain characteristics of some CoP, such as low CD4+ count and prior clinical AIDS, that have been associated with treatment failure in this population group[1], may explain these results and require further analysis

1. Berenguer J, et al. Hepatology 2018. In press. DOI 10.1002/hep.29814

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