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Abstract # 0572

Real-world effectiveness of Sofosbuvir/Velpatasvir for Hepatitis C Virus Infection

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Background and Aim

- Sofosbuvir and Velpatasvir (SOF/VEL) are direct-acting antiviral agents (DAAs) against hepatitis C virus (HCV) with pan-genotypic activity and a high barrier to resistance.
- Little is known about the real-world effectiveness of sofosbuvir and velpatasvir (SOF/VEL) for treatment of chronic hepatitis C.
- We evaluated the effectiveness and safety of SOF/VEL in a large prospective registry HCV-infected individuals with/without coinfection by HIV and receiving DAAs for HCV infection.

Methods

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 (*Hepatology 2018; 68: 32; Open Forum Infect Dis 2019; 6: ofz214.)*
  - Madrid-CoRe (Madrid Coinfection Registry)
  - Madrid-MoRe (Madrid Monoinfection Registry)
- Compulsory for all hospitals from the Madrid Regional Health Service (SERMAS)

Key inclusion and exclusion criteria

- Once-daily treatment with 1 tablet of the combination of SOF/VEL (total dose: 400 mg/100 mg) for HCV
- Scheduled to finish Rx on or before February 1, 2019
- Retreatment after all-oral DAAs were excluded

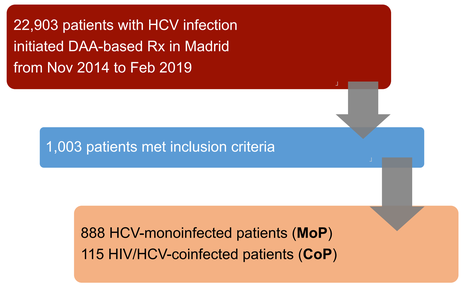
Primary endpoint

- Week 12 sustained viral response (SVR_{12}) by intention-to-treat analysis (ITT) and by modified ITT (m-ITT), excluding patients who 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

Flow chart

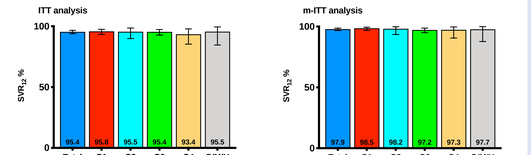


HIV-related variables in HIV/HCV coinfected patients

Variables	Total N=115
HIV risk factor – n (%)	
Injection drug use	83 (72.2)
Men who have sex with men	10 (8.7)
Heterosexual relations	8 (7.0)
Other/unknown	14 (12.1)
CDC clinical category – n (%)	
A	34 (29.6)
B	13 (11.3)
C	42 (36.5)
Unknown	26 (22.6)
Baseline CD4+/mm^3 – n (%)	
Unknown	38 (33.0)
Known	77 (67.0)
Median (IQR)	513 (333-756)
HIV-RNA – n (%)	
Unknown	16 (13.9)
Known	99 (86.1)
Detectable	12 (12.1)
Undetectable	87 (87.9)

Variables	Total N=115
ART – n (%)	
No	5 (4.3)
Yes	110 (95.7)
ART regimen before DAA – n (%)	
2nRTI+1PI	29 (26.4)
2nRTI+1 INSTI	47 (42.7)
2nRTI+1nnRTI	14 (12.7)
PI-based dual therapy	8 (7.3)
PI monotherapy	1 (0.9)
Other	11 (10.0)
ART change prior to DAA Rx – n (%)	
No	78 (70.9)
Yes	30 (27.3)
Unknown	2 (1.8)

Treatment outcomes of SOF/VEL (400 mg/100 mg) for 12 weeks by HCV Genotype



	Total	G1	G2	G3	G4	O/M/U
No.	1,003	401	102	370	76	44
SVR ITT	957 (95.4)	384 (95.8)	107 (95.5)	353 (95.4)	71 (93.4)	42 (95.5)
SVR (95% CI)	93.9-96.6	93.3-97.5	89.9-98.5	92.7-97.2	85.3-97.8	84.5-99.4
Relapse	17 (1.7)	3 (0.7)	2 (1.8)	9 (2.4)	2 (2.6)	1 (2.3)
DC due to AE	2 (0.2)	1 (0.2)	0	1 (0.3)	0	0
DC other	25 (2.5)	11 (2.7)	3 (2.7)	7 (1.9)	3 (3.9)	1 (2.3)
Death	2 (0.2)	2 (0.5)	0	0	0	0

	Total	G1	G2	G3	G4	O/M/U
No.	978	390	100	363	73	43
SVR ITT	957 (97.9)	384 (98.5)	107 (98.2)	353 (97.2)	71 (97.3)	42 (97.7)
SVR (95% CI)	96.7-98.7	96.7-99.4	93.5-99.8	95.0-98.7	90.5-99.7	87.7-99.9
Relapse	17 (1.7)	3 (0.8)	2 (1.8)	9 (2.5)	2 (2.7)	1 (2.3)
DC due to AE	2 (0.2)	1 (0.3)	0	1 (0.3)	0	0
DC other	2 (0.2)	2 (0.5)	0	0	0	0
Death	2 (0.2)	2 (0.5)	0	0	0	0

O/M/U = Other/mixed/unknown

m-ITT analysis = exclusion of patients with DC for reasons other than AE

Conclusions

1) In this large cohort of patients with hepatitis C, treatment with SOF/VEL for 12 weeks led to SVR rates > 95% by ITT analysis and almost 98% by m-ITT analysis.

2) Treatment with SOF/VEL was highly efficacious across all genotypes and in the presence of HIV.

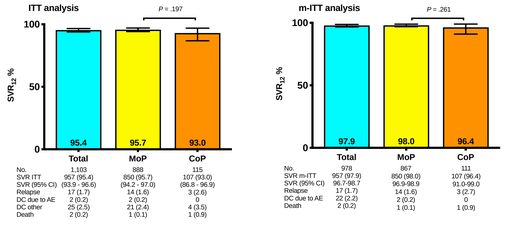
3) Response to treatment was significantly poorer in patients with decompensated cirrhosis than in patients without cirrhosis.

Characteristics of the study population

Variables	MoP N = 888	CoP N = 115	*P*	Total N= 1,003
Age – median (IQR)	55 (49-63)	52 (48-55)	<0.001	55 (49-61)
Male sex – n (%)	518 (58.3)	95 (82.6)	<0.001	613 (61.1)
Prior anti-HCV therapy – n (%)	91 (10.2)	12 (10.4)	0.950	103 (10.3)
Genotype – n (%)			<0.001	
1	376 (42.3)	25 (21.7)		401 (40.0)
2	100 (11.3)	12 (10.4)		112 (11.2)
3	311 (35.0)	59 (51.3)		370 (36.9)
4	61 (6.9)	15 (13.0)		76 (7.6)
Other/mixed/unknown	40 (4.5)	4 (3.5)		44 (4.4)
HCV RNA Log IU/mL – Median (IQR)	6.2 (5.5-6.6)	6.2 (5.6-6.7)	0.487	6.2 (5.6-6.7)
Cirrhosis – n (%)			0.144	
No cirrhosis	669 (75.3)	97 (84.3)		766 (76.4)
Compensated cirrhosis	182 (20.5)	16 (13.9)		198 (19.7)
Decompensated cirrhosis	37 (4.2)	2 (1.7)		39 (3.9)
Transient elastography – n (%)				
Performed	813 (91.5)	109 (94.8)		922 (91.9)
Stiffness kPa – Median (IQR)	6.8 (5.2-11.1)	6.2 (5.1-8.6)	0.107	6.8 (5.2-10.7)

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

Treatment outcomes of SOF/VEL (400 mg/100 mg) for 12 weeks by HIV status



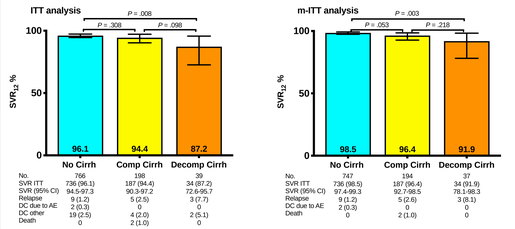
	Total	MoP	CoP
No.	1,103	888	115
SVR ITT	957 (95.4)	850 (95.7)	107 (93.0)
SVR (95% CI)	(93.9 - 96.6)	(94.2 - 97.0)	(86.8 - 96.9)
Relapse	17 (1.7)	14 (1.6)	3 (2.6)
DC due to AE	2 (0.2)	2 (0.2)	0
DC other	25 (2.5)	21 (2.4)	4 (3.5)
Death	2 (0.2)	1 (0.1)	1 (0.9)

	Total	MoP	CoP
No.	978	867	111
SVR m-ITT	957 (97.9)	850 (98.0)	107 (96.4)
SVR (95% CI)	96.7-98.7	96.9-98.9	91.0-99.0
Relapse	17 (1.7)	14 (1.6)	3 (2.7)
DC due to AE	22 (2.2)	2 (0.2)	0
Death	2 (0.2)	1 (0.1)	1 (0.9)

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

m-ITT analysis = exclusion of patients with DC for reasons other than AE

Treatment outcomes of SOF/VEL (400 mg/100 mg) for 12 weeks by severity of liver disease



	No Cirrh	Comp Cirrh	Decomp Cirrh
No.	766	198	39
SVR ITT	736 (96.1)	187 (94.4)	34 (87.2)
SVR (95% CI)	94.5-97.3	90.3-97.2	72.6-95.7
Relapse	9 (1.2)	5 (2.5)	3 (7.7)
DC due to AE	2 (0.3)	0	0
DC other	19 (2.5)	4 (2.0)	2 (5.1)
Death	0	2 (1.0)	0

	No Cirrh	Comp Cirrh	Decomp Cirrh
No.	747	194	37
SVR ITT	736 (98.5)	187 (96.4)	34 (91.9)
SVR (95% CI)	97.4-99.3	92.7-98.5	78.1-98.3
Relapse	9 (1.2)	5 (2.6)	3 (8.1)
DC due to AE	2 (0.3)	0	0
Death	0	2 (1.0)	0

Cirrhosis = liver biopsy, stiffness (TE) >12.5 kPa), or diagnosis based on clinical/biological findings

m-ITT analysis = exclusion of patients with DC for reasons other than AE

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