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Abstract # 1348

Real-world data on elbasvir/grazoprevir for HCV infection in HIV/non-HIV patients

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Background and Aim

- Elbasvir/Grazoprevir (EBV/GZR) is a two-drug fixed-dose combination containing 50 mg of EBV and 100 mg of GZR in a single tablet.
- EBV/GZR is approved for treatment of chronic hepatitis C infection in patients with or without compensated cirrhosis infected with HCV genotypes 1a, 1b, and 4.
- There are few real-world data on the effectiveness EBV/GZR for treatment of chronic hepatitis C.
- We assessed the effectiveness and safety of EBV/GZR in the Madrid Registry of Use of DAA for HCV (Madrid RUA-VHC), a large prospective registry of individuals receiving direct-acting antivirals (DAAs) for the treatment of 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
  - Madrid-CoRe (Madrid Coinfection Registry)
  - Madrid-MoRe (Madrid Monoinfection Registry)
- Compulsory for all hospitals from the Madrid Regional Health Service (SERMAS)
- 21,157 patients registered between Nov 2014 and Jul 2018

Key inclusion criteria

- Treatment with EBV/GZR
- Scheduled to finish treatment on or before March 1, 2018
- Retreatment after all-oral DAAs were excluded

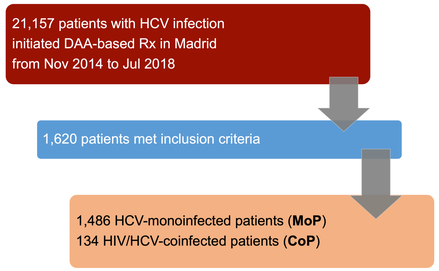
Primary endpoint

- 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



Characteristics of the study population

	MoP	CoP	*P*	Total
Variables	N=1,486	N=134		N=1,620
Age – median (IQR)	59 (52-69)	51 (44-54)	<0.001	58 (51-69)
Male sex – n (%)	733 (49.3)	118 (88.1)	<0.001	851 (52.5)
Prior anti-HCV therapy – n (%)	345 (23.2)	35 (26.1)	0.45	380 (23.5)
Genotype – n (%)			<0.001	
1a	224 (15.1)	50 (37.3)		274 (16.9)
1b	1107 (74.5)	25 (18.7)		1132 (69.9)
1 not subtyped	14 (0.9)	2 (1.5)		16 (1.0)
4	141 (9.5)	57 (42.5)		198 (12.2)
HCV RNA Log IU/mL – Median (IQR)	6.3 (5.7-6.7)	6.1 (5.6-6.7)	0.34	6.3 (5.7-6.7)
HCV RNA > 800.000 IU/mL – n (%)	990 (66.6)	88 (65.7)	0.82	1078 (66.5)
Cirrhosis – n (%)	226 (15.2)	20 (14.9)	0.13	246 (15.2)
Transient elastography – n (%)				
No	58 (3.9)	4 (3.0)		62 (3.8)
Yes	1428 (96.1)	130 (97.0)		1558 (96.2)
Stiffness kPa – Median (IQR)	6.3 (4.9-9.3)	6.9 (5.1-9.0)	0.47	6.3 (4.9-9.3)
Duration of therapy			<0.001	
8 wk	2	0		2 (0.1)
12 wk	1,351 (90.9)	108 (80.6)		1,459 (90.1)
16 wk	133 (9.0)	26 (19.4)		159 (9.8)
Use of ribavirin	111 (7.5)	20 (14.9)	0.002	131 (8.1)

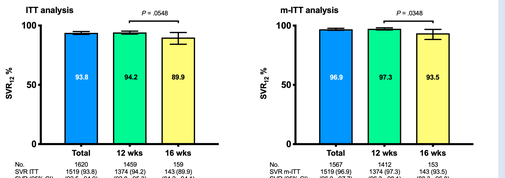
MoP = HCV monoinfected patients. **CoP** = HIV/HCV coinfected patients

HIV-related variables in HIV/HCV coinfected patients

	Total
Variables	N=134
HIV risk factor – n (%)	
Injection drug use	78 (58.2)
Men who have sex with men	42 (31.3)
Heterosexual relations	3 (2.2)
Other/unknown	11 (8.2)
CDC clinical category – n (%)	
A	62 (46.3)
B	14 (10.4)
C	37 (27.6)
Unknown	21 (15.7)
Baseline CD4+/mm³ – n (%)	
Unknown	74 (55.2)
Known	60 (44.8)
Median (IQR)	685 (472-868)
HIV-RNA – n (%)	
Unknown	12 (9.0)
Known	122 (91.0)
Detectable	5 (4.1)
Undetectable	117 (95.9)

	Total
Variables	N=134
ART – n (%)	
No	7 (5.2)
Yes	127 (94.8)
ART regimen before DAA – n (%)	
2nRTI+1PI	0
2nRTI+1 INSTI	97 (76.4)
2nRTI+1nnRTI	21 (16.5)
PI monotherapy	1 (0.8)
Other	8 (6.3)
ART change prior to DAA Rx – n (%)	
No	75 (59.1)
Yes	47 (37.0)
Unknown	5 (3.9)

Treatment outcomes at 12 vs 16 weeks*

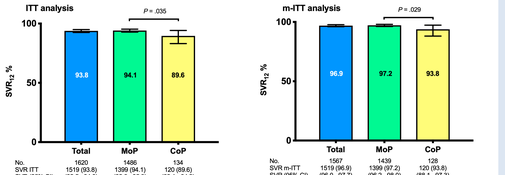


	Total	12 wks	16 wks
No.	1620	1459	159
SVR ITT	1519 (93.8)	1374 (94.2)	143 (89.9)
SVR (95% CI)	(92.5 - 94.9)	(92.8 - 95.3)	(84.2 - 94.1)
Relapse	35 (2.2)	27 (1.8)	8 (5.0)
Breakthrough	4 (0.2)	4 (0.3)	0
DC due to AE	6 (0.4)	5 (0.3)	1 (0.6)
DC other	53 (3.3)	47 (3.2)	6 (3.8)
Death	3 (0.2)	2 (0.1)	1 (0.6)

	Total	12 wks	16 wks
No.	1567	1412	153
SVR m-ITT	1519 (96.9)	1374 (97.3)	143 (93.5)
SVR (95% CI)	(96.0 - 97.7)	(96.3 - 98.1)	(88.3 - 96.8)
Relapse	35 (2.2)	27 (1.9)	8 (5.2)
Breakthrough	4 (0.3)	4 (0.3)	0
DC due to AE	6 (0.4)	5 (0.4)	1 (0.7)
Death	3 (0.2)	2 (0.1)	1 (0.7)

*2 patients treated for 8 weeks not included; both achieved SVR

Treatment outcomes: MoP vs CoP

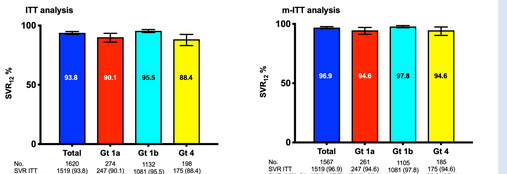


	Total	MoP	CoP
No.	1620	1486	134
SVR ITT	1519 (93.8)	1399 (94.1)	120 (89.6)
SVR (95% CI)	(92.5 - 94.9)	(92.8 - 95.3)	(83.1 - 94.2)
Relapse	35 (2.2)	29 (1.9)	6 (4.5)
Breakthrough	4 (0.2)	3 (0.2)	1 (0.7)
DC due to AE	6 (0.4)	5 (0.3)	1 (0.7)
DC other	53 (3.3)	47 (3.2)	6 (4.5)
Death	3 (0.2)	3 (0.2)	0

	Total	MoP	CoP
No.	1567	1439	128
SVR m-ITT	1519 (96.9)	1399 (97.2)	120 (93.8)
SVR (95% CI)	(96.0 - 97.7)	(96.2 - 98.0)	(88.1 - 97.3)
Relapse	35 (2.2)	29 (2.0)	6 (4.7)
Breakthrough	4 (0.3)	3 (0.2)	1 (0.8)
DC due to AE	6 (0.4)	5 (0.3)	1 (0.8)
Death	3 (0.2)	3 (0.2)	0

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

Treatment outcomes by HCV Genotype*



	Total	Gt 1a	Gt 1b	Gt 4
No.	1620	274	1132	198
SVR ITT	1519 (93.8)	247 (90.1)	1081 (95.5)	175 (88.4)
SVR (95% CI)	(92.5 - 94.9)	(86.0 - 93.4)	(94.1 - 96.6)	(83.1 - 92.5)
Relapse	35 (2.2)	17 (6.0)	16 (1.4)	8 (4.0)
Breakthrough	4 (0.2)	0	3 (0.3)	1 (0.5)
DC due to AE	6 (0.4)	2 (0.7)	3 (0.3)	1 (0.5)
DC other	53 (3.3)	13 (4.7)	27 (2.4)	13 (6.6)
Death	3 (0.2)	1 (0.4)	2 (0.2)	0

	Total	Gt 1a	Gt 1b	Gt 4
No.	1567	261	1105	185
SVR m-ITT	1519 (96.9)	247 (94.6)	1081 (97.8)	175 (94.6)
SVR (95% CI)	(96.0 - 97.7)	(91.2 - 97.0)	(96.8 - 98.6)	(90.3 - 97.4)
Relapse	35 (2.2)	11 (4.0)	16 (1.4)	8 (4.3)
Breakthrough	4 (0.3)	0	3 (0.3)	1 (0.5)
DC due to AE	6 (0.4)	2 (0.8)	3 (0.3)	1 (0.5)
Death	3 (0.2)	1 (0.4)	2 (0.2)	0

*16 patients with non-subtyped Genotype not included; all achieved SVR

Results of logistic regression models to identify independent baseline predictors of treatment failure by ITT analysis

	Univariable		Multivariable model 1[1]		Multivariable model 2[2]	
Variable	OR (95% CI)	P			OR (95% CI)	P
Age						
– <50	1.00		1.00			
– ≥50	0.65 (0.42 – 1.02)	0.062	0.79 (0.49 – 1.28)	0.346		
Sex						
– Male	1.00		1.00			
– Female	0.68 (0.45 – 1.03)	0.067	0.87 (0.56 – 1.36)	0.547		
Cirrhosis						
– No	1.00		1.00		1.00	
– Yes	1.57 (0.95 – 2.59)	0.081	1.76 (1.05 – 2.96)	0.032	1.67 (1.00 – 2.78)	0.050
– Unknown	2.40 (0.91 – 6.30)	0.076	2.47 (0.91 – 6.67)	0.074	2.25 (0.84 – 6.00)	0.105
HCV genotype						
– 1b	1.00		1.00		1.00	
– 4	2.79 (1.66 – 4.67)	<0.001	2.93 (1.61 – 5.36)	<0.001	2.86 (1.70 – 4.82)	<0.001
– 1a	2.32 (1.42 – 3.77)	0.001	2.33 (1.26 – 4.31)	0.007	2.29 (1.41 – 3.73)	0.001
HCV RNA IU/mL						
– < 800,000	1.00		1.00			
– ≥ 800,000	1.27 (0.81 – 1.97)	0.298	1.54 (0.95 – 2.50)	0.080		
HIV infection						
– No	1.00		1.00			
– Yes	1.88 (1.04 – 3.40)	0.038	1.04 (0.54 – 2.02)	0.905		
Treatment duration						
– 12 weeks	1.00		1.00			
– 16 weeks	1.81 (1.03 – 3.17)	0.038	0.58 (0.18 – 1.92)	0.375		
Ribavirin						
– No	1.00		1.00			
– Yes	1.93 (1.06 – 3.50)	0.031	1.44 (0.43 – 4.87)	0.554		

[1] Multivariable model 1 is a fully adjusted one, including every variable detailed in the first column.
[2] Multivariable model 2 includes variables with a *P*-value <0.05 in the multivariable analysis.

Results of logistic regression models to identify independent baseline predictors of treatment failure by m-ITT analysis

	Univariable		Multivariable model 1[1]		Multivariable model 2[2]	
Variable	OR (95% CI)	P			OR (95% CI)	P
Age						
– <50	1.00		1.00			
– ≥50	1.14 (0.55 – 2.37)	0.730	1.39 (0.64 – 3.04)	0.404		
Sex						
– Male	1.00		1.00			
– Female	0.99 (0.56 – 1.77)	0.985	1.39 (0.74 – 2.61)	0.302		
Cirrhosis						
– No	1.00		1.00			
– Yes	1.55 (0.76 – 3.18)	0.227	1.65 (0.79 – 3.44)	0.181		
– Unknown	2.00 (0.46 – 8.63)	0.354	2.26 (0.51 – 10.05)	0.284		
HCV genotype						
– 1b	1.00		1.00		1.00	
– 4	2.57 (1.21 – 5.47)	0.014	2.77 (1.13 – 6.82)	0.026	2.96 (1.38 – 6.37)	0.005
– 1a	2.55 (1.30 – 5.01)	0.006	2.48 (1.00 – 6.15)	0.050	2.59 (1.32 – 5.08)	0.006
HCV RNA IU/mL						
– < 800,000	1.00		1.00		1.00	
– ≥ 800,000	1.94 (0.96 – 3.92)	0.066	2.07 (0.97 – 4.40)	0.059	2.16 (1.06 – 4.42)	0.035
HIV-infection						
– No	1.00		1.00			
– Yes	2.33 (1.07 – 5.09)	0.034	1.75 (0.71 – 4.30)	0.225		
Treatment duration						
– 12 weeks	1.00		1.00			
– 16 weeks	2.53 (1.23 – 5.18)	0.011	0.44 (0.08 – 2.38)	0.339		
Ribavirin						
– No	1.00		1.00			
– Yes	3.15 (1.53 – 6.49)	0.002	3.02 (0.57 – 16.01)	0.194		

[1] Multivariable model 1 is a fully adjusted one, including every variable detailed in the first column.
[2] Multivariable model 2 includes variables with a *P*-value <0.05 in the multivariable analysis.

Conclusions

1) The results of this large prospective real-world study analyzing treatment outcomes for EBV/GZR against HCV in DAA-naïve patients were similar to those found in pivotal clinical trials

2) Factors associated with treatment failure included infection by HCV G1a or G4 and liver cirrhosis by ITT analysis, as well as infection by HCV G1a or G4 and HCV RNA ≥800K IU/mL by m-ITT analysis.

3) HIV-infection was not associated with response to treatment

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