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

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## Aim

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.

## Eligibility Criteria

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

## Primary Endpoints

Week 12 SVR by ITT and by modified ITT (m-ITT), excluding patients who discontinued therapy for reasons other than adverse events (AEs)

# Flow chart

21,157 patients with HCV infection  
initiated DAA-based Rx in Madrid  
from Nov 2014 to Jul 2018

1,620 patients met inclusion criteria

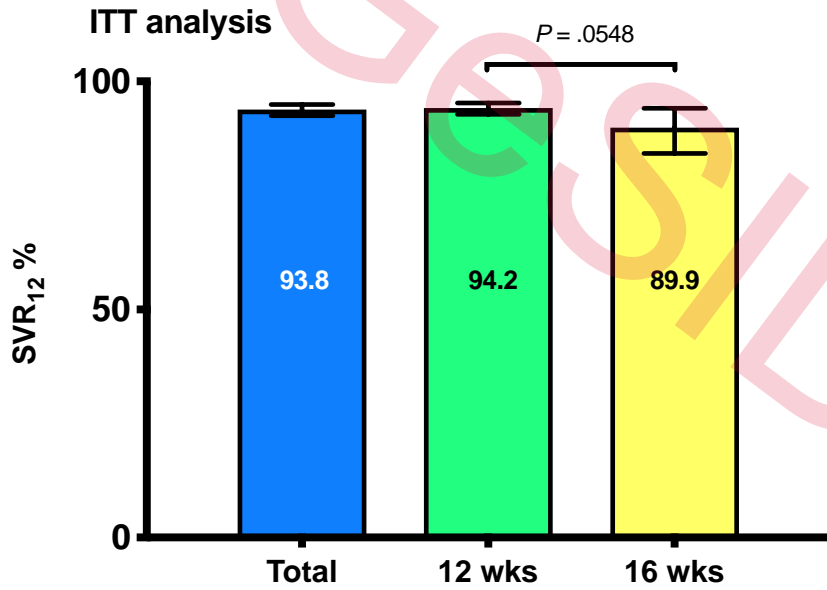
1,486 HCV-monoinfected patients (**MoP**)  
134 HIV/HCV-coinfected patients (**CoP**)

# Characteristics of the study population

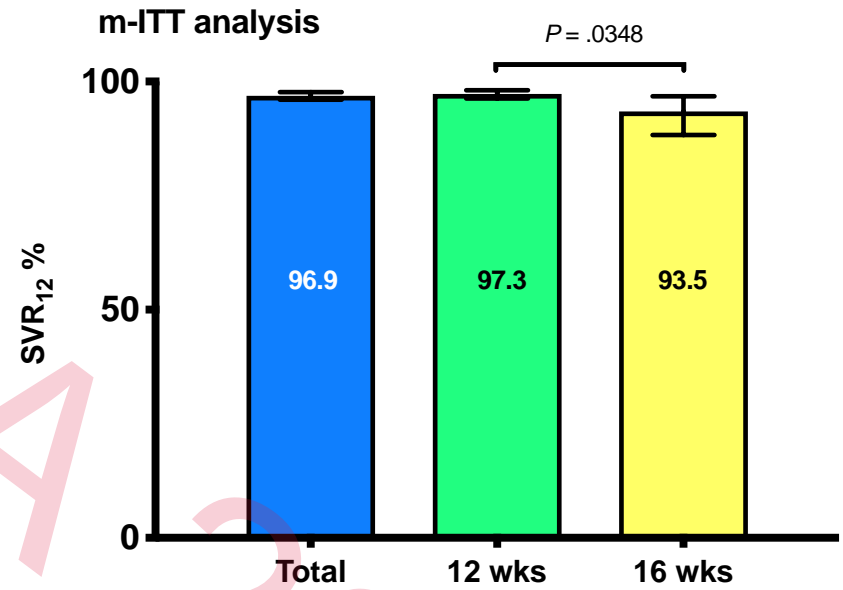
	MoP	CoP	P	Total
<b>Variables</b>	N=1,486	N=134		N=1,620
<b>Age – median (IQR)</b>	59 (52-69)	51 (44-54)	<0.001	58 (51-69)
<b>Male sex – n (%)</b>	733 (49.3)	118 (88.1)	<0.001	851 (52.5)
<b>Prior anti-HCV therapy – n (%)</b>	345 (23.2)	35 (26.1)	0.45	380 (23.5)
<b>Genotype – n (%)</b>			<0.001	
<b>1a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

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

# Treatment outcomes at 12 vs 16 weeks\*



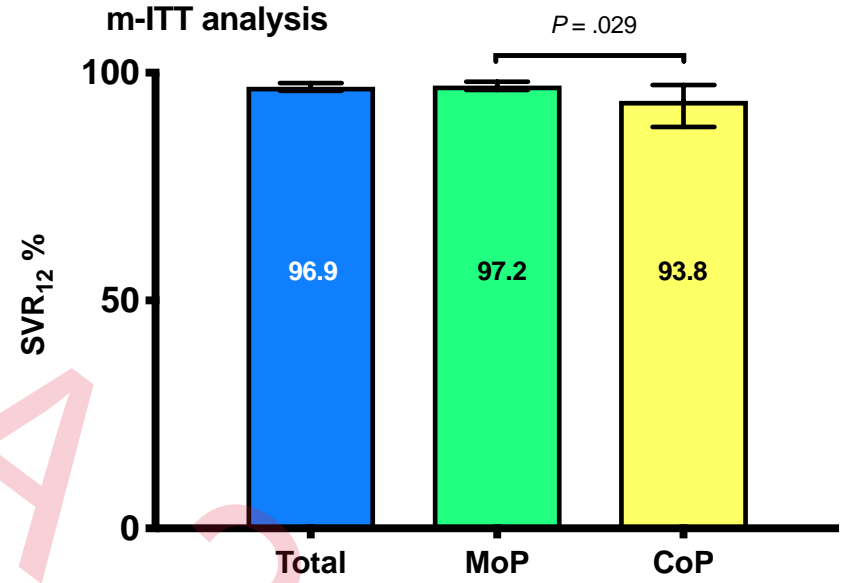
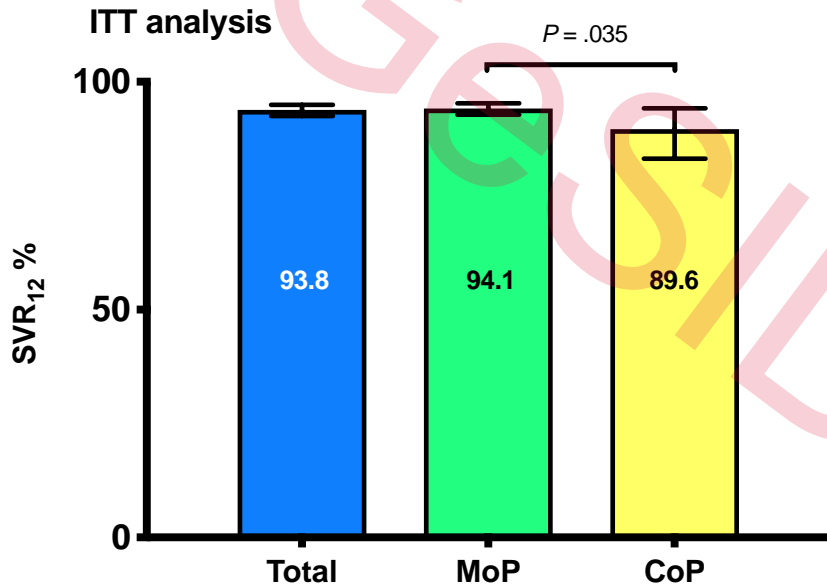
	Total	12 wks	16 wks
No.	1620	1459	159
SVR ITT	1519 (93.8)	1374 (94.2)	143 (89.9)
SVR (95% CI)	(92.5 - 94.9)	(92.8 - 95.3)	(84.2 - 94.1)
Relapse	35 (2.2)	27 (1.8)	8 (5.0)
Breakthrough	4 (0.2)	4 (0.3)	0
DC due to AE	6 (0.4)	5 (0.3)	1 (0.6)
DC other	53 (3.3)	47 (3.2)	6 (3.8)
Death	3 (0.2)	2 (0.1)	1 (0.6)



	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

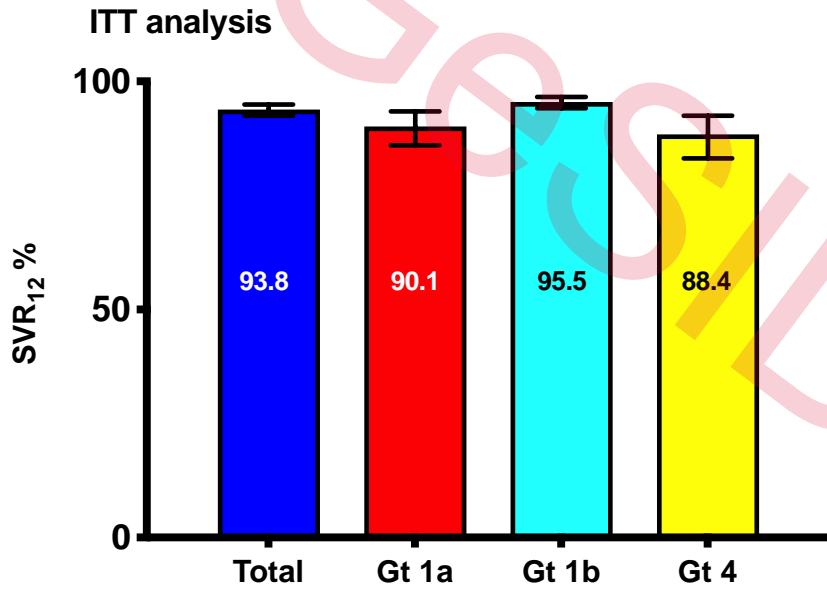


	Total	MoP	CoP
No.	1620	1486	134
SVR ITT	1519 (93.8)	1399 (94.1)	120 (89.6)
SVR (95% CI)	(92.5 - 94.9)	(92.8 - 95.3)	(83.1 - 94.2)
Relapse	35 (2.2)	29 (1.9)	6 (4.5)
Breakthrough	4 (0.2)	3 (0.2)	1 (0.7)
DC due to AE	6 (0.4)	5 (0.3)	1 (0.7)
DC other	53 (3.3)	47 (3.2)	6 (4.5)
Death	3 (0.2)	3 (0.2)	0

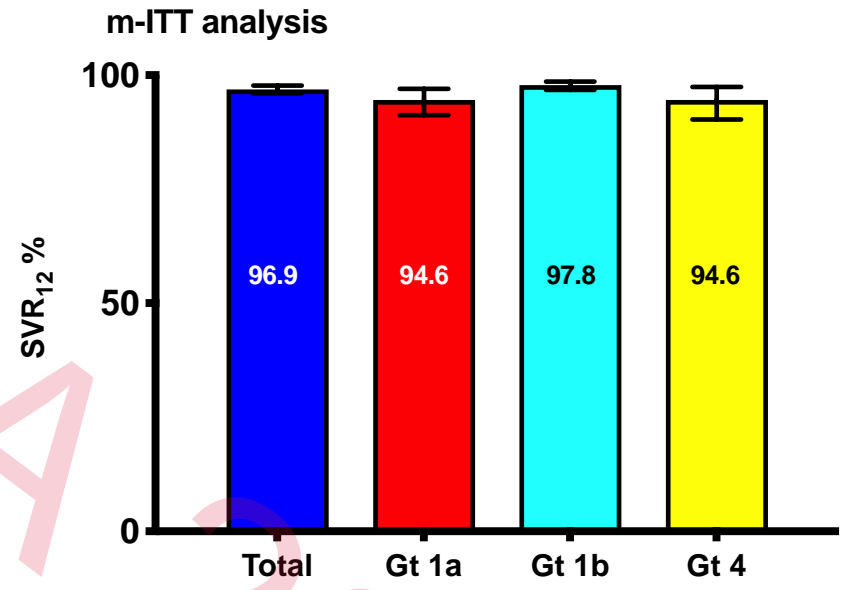
	Total	MoP	CoP
No.	1567	1439	128
SVR m-ITT	1519 (96.9)	1399 (97.2)	120 (93.8)
SVR (95% CI)	(96.0 - 97.7)	(96.2 - 98.0)	(88.1 - 97.3)
Relapse	35 (2.2)	29 (2.0)	6 (4.7)
Breakthrough	4 (0.3)	3 (0.2)	1 (0.8)
DC due to AE	6 (0.4)	5 (0.3)	1 (0.8)
Death	3 (0.2)	3 (0.2)	0

**MoP** = HCV monoinfected patients  
**CoP** = HIV/HCV coinfecting 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)	11 (4.0)	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 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

Variable	Univariable		Multivariable model 1 <sup>†</sup>		Multivariable model 2 <sup>‡</sup>	
	OR (95% CI)	P			OR (95% CI)	P
<b>Age</b>						
- <50	1.00		1.00			
- ≥50	0.65 (0.42 – 1.02)	0.062	0.79 (0.49 – 1.28)	0.346		
<b>Sex</b>						
- Male	1.00		1.00			
- Female	0.68 (0.45 – 1.03)	0.067	0.87 (0.56 – 1.36)	0.547		
<b>Cirrhosis</b>						
- 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
<b>HCV genotype</b>						
- 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
<b>HCV RNA IU/mL</b>						
- < 800,000	1.00		1.00			
- ≥ 800,000	1.27 (0.81 – 1.97)	0.298	1.54 (0.95 – 2.50)	0.080		
<b>HIV infection</b>						
- No	1.00		1.00			
- Yes	1.88 (1.04 – 3.40)	0.038	1.04 (0.54 – 2.02)	0.905		
<b>Treatment duration</b>						
- 12 weeks	1.00		1.00			
- 16 weeks	1.81 (1.03 – 3.17)	0.038	0.58 (0.18 – 1.92)	0.375		
<b>Ribavirin</b>						
- No	1.00		1.00			
- Yes	1.93 (1.06 – 3.50)	0.031	1.44 (0.43 – 4.87)	0.554		

<sup>†</sup> Multivariable model 1 is a fully adjusted one, including every variable detailed in the first column.

<sup>‡</sup> 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

Variable	Univariable		Multivariable model 1 <sup>†</sup>		Multivariable model 2 <sup>‡</sup>	
	OR (95% CI)	P			OR (95% CI)	P
<b>Age</b>						
– <50	1.00		1.00			
– ≥50	1.14 (0.55 – 2.37)	0.730	1.39 (0.64 – 3.04)	0.404		
<b>Sex</b>						
– Male	1.00		1.00			
– Female	0.99 (0.56 – 1.77)	0.985	1.39 (0.74 – 2.61)	0.302		
<b>Cirrhosis</b>						
– 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		
<b>HCV genotype</b>						
– 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
<b>HCV RNA IU/mL</b>						
– < 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
<b>HIV-infection</b>						
– No	1.00		1.00			
– Yes	2.33 (1.07 – 5.09)	0.034	1.75 (0.71 – 4.30)	0.225		
<b>Treatment duration</b>						
– 12 weeks	1.00		1.00			
– 16 weeks	2.53 (1.23 – 5.18)	0.011	0.44 (0.08 – 2.38)	0.339		
<b>Ribavirin</b>						
– No	1.00		1.00			
– Yes	3.15 (1.53 – 6.49)	0.002	3.02 (0.57 – 16.01)	0.194		

<sup>†</sup> Multivariable model 1 is a fully adjusted one, including every variable detailed in the first column.

<sup>‡</sup> Multivariable model 2 includes variables with a *P*-value <0.05 in the multivariable analysis.

# Conclusions

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- 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  $\geq 800\text{K IU/mL}$  by m-ITT analysis.
- 3) HIV-infection was not associated with response to treatment

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