

Safety and efficacy of daclatasvir-sofosbuvir in HCV genotype 1- mono-infected patients

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Supplementary materials and methods

Propensity score analyses.

Methods

The propensity scores, i.e. the probability of being treated with a ribavirin containing regimen or 24 weeks (vs 12 weeks) given the observed covariates, were calculated by using multivariate logistic regression models.

Propensity to receive a ribavirin containing regimen

We found that being treated with a ribavirin containing regimen was strongly associated with past treatment history (Odds-Ratio for treatment naïve versus treatment experienced (OR)= 0.40, 95%CI 0.22-0.73, P=0.0030). We also included age, gender, treatment duration (24 weeks vs 12 weeks), cirrhosis status, AST (>5ULN vs ≤5ULN), , Prothrombin Time (PT, <70% vs ≥ 70%), anaemia (defined by haemoglobin <12g/dL in women, <13g/dL in men) in the logistic model as some of these covariates were associated with having a ribavirin-containing regimen in the univariate analysis. The propensity score for receiving ribavirin was the predicted probability obtained from the logistic equation given the covariate values. Covariates were adequately balanced in the different strata between patients treated with sofosbuvir+daclatasvir and patients treated with sofosbuvir+daclatasvir+ribavirin (supplementary table 1).

Propensity to receive a 24-week vs 12-week regimen

We found that a 24 weeks regimen was strongly associated with past treatment history (OR for treatment naïve versus treatment experienced= 0.20, 95%CI 0.13-

0.31, $P < 0.0001$), cirrhosis (OR for cirrhosis vs no cirrhosis = 2.18, 95%CI 1.48-3.20, $P < 0.0001$) and with AST level (OR for AST > 5ULN vs \leq 5ULN = 4.26, 95%CI 1.94-9.09, $P = 0.0003$). We also included age, gender, ribavirin containing regimen, PT and anemia in the logistic model. Covariates were adequately balanced in the different strata between patients treated 12 weeks and 24 weeks (supplementary table 2).

We used exact conditional logistic regression model to identify independent predictors of SVR12 stratified on propensity.

Supplementary results

With stratification on the propensity to receive a ribavirin containing regimen

Cirrhosis was the only covariate significantly associated with SVR12 in stratified on propensity score analysis. The multivariate adjusted odds-ratio for cirrhosis vs non cirrhosis was 0.32, 95%CI 0.08-0.96, P=0.0397. Of note, the association between past treatment history and SVR12 did not remain significant (multivariate adjusted odds-ratio for treatment naïve versus treatment experienced, 0.39, 95%CI 0.10-1.47, P=0.1986).

With stratification on the propensity to receive a 24-week vs a 12-week regimen

Albumin was the only covariate significantly associated with SVR12 in stratified on propensity score analysis. The multivariate adjusted odds-ratio for albumin <30g/L vs \geq 30g/L was 0.37, 95%CI 0.15-0.98, P=0.0461. The multivariate adjusted odds-ratio for cirrhosis vs non cirrhosis was 0.31, 95%CI 0.07-1.09, P=0.0725. The association between past treatment history and SVR12 did not remain significant (P=0.5424).

Supplementary Table 1. distribution of the covariates used for propensity score calculations of ribavirin containing regimen among strata defined by quintiles of the propensity score

	Quintiles of the propensity score									
	1		2		3		4		5	
	SOF+DCV ^a (n=137)	SOF+DCV+RIB (n=16)	SOF+DCV (n=125)	SOF+DCV+RIB (n=29)	SOF+DCV (n=125)	SOF+DCV+RIB (n=29)	SOF+DCV (n=110)	SOF+DCV+RIB (n=44)	SOF+DCV (n=102)	SOF+DCV+RIB (n=51)
Propensity score	0.11 (0.03)	0.12 (0.03)	0.18 (0.01)	0.18 (0.01)	0.22 (0.01)	0.22 (0.01)	0.26 (0.01)	0.26 (0.01)	0.33 (0.05)	0.34 (0.06)
Age (years)	65 (11)	64 (12)	65 (10)	66 (9)	59 (7)	61 (7)	55 (7)	54 (7)	54 (9)	53 (8)
Treatment naïve	41 (30%)	7 (44%)	113 (90%)	26 (90%)	122 (98%)	28 (97%)	109 (99%)	43 (98%)	102 (100%)	51 (100%)
Gender Male	65 (47%)	9 (56%)	46 (37%)	11 (38%)	83 (66%)	20 (69%)	91 (83%)	35 (80%)	88 (86%)	42 (82%)
24 week treatment duration	63 (46%)	10 (63%)	96 (77%)	19 (66%)	91 (73%)	21 (72%)	98 (89%)	41 (93%)	91 (89%)	44 (86%)
Cirrhosis	90 (66%)	13 (81%)	90 (72%)	20 (69%)	84 (67%)	16 (55%)	90 (82%)	36 (82%)	82 (80%)	42 (82%)
AST > 5 ULN	9 (7%)	1 (6%)	8 (6%)	2 (7%)	9 (7%)	4 (14%)	11 (10%)	4 (9%)	27 (26%)	11 (22%)
Prothrombin Time < 70%	13 (9%)	0 (0%)	14 (11%)	5 (17%)	11 (9%)	3 (10%)	12 (11%)	5 (11%)	33 (32%)	16 (31%)
Anaemia	52 (38%)	7 (44%)	26 (21%)	6 (21%)	10 (8%)	4 (14%)	12 (11%)	3 (7%)	8 (8%)	2 (4%)
SVR 12	122 (89%)	16 (100%)	122 (98%)	26 (90%)	120 (96%)	29 (100%)	104 (95%)	44 (100%)	96 (94%)	50 (98%)

^aSOF+DCV= sofosbuvir+daclatasvir regimen; SOF+DCV+RBV=sofosbuvir+daclatasvir+ribavirin regimen. Data are Mean (SD) or number (%)

Supplementary Table 2. distribution of the covariates used for propensity score calculations of 24-week duration of treatment among strata defined by quintiles of the propensity score

	Quintiles of the propensity score									
	1		2		3		4		5	
	12 Weeks (n=73)	24 Weeks (n=80)	12 Weeks (n=54)	24 Weeks (n=100)	12 Weeks (n=24)	24 Weeks (n=130)	12 Weeks (n=26)	24 Weeks (n=128)	12 Weeks (n=17)	24 Weeks (n=136)
Propensity score	0.43 (0.12)	0.53 (0.11)	0.72 (0.04)	0.72 (0.04)	0.8 (0.01)	0.81 (0.01)	0.83 (0.01)	0.83 (0.01)	0.88 (0.04)	0.9 (0.04)
Age (years)	63 (11)	61 (11)	58 (11)	62 (10)	63 (8)	61 (9)	60 (11)	57 (9)	54 (10)	56 (9)
Treatment naïve	10 (14%)	30 (38%)	51 (94%)	98 (98%)	24 (100%)	126 (97%)	26 (100%)	126 (98%)	16 (94%)	135 (99%)
Gender Male	49 (67%)	53 (66%)	35 (65%)	65 (65%)	20 (83%)	100 (77%)	14 (54%)	83 (65%)	8 (47%)	63 (46%)
RBV containing regimen	4 (5%)	9 (11%)	6 (11%)	27 (27%)	6 (25%)	5 (4%)	10 (38%)	46 (36%)	8 (47%)	48 (35%)
Cirrhosis	38 (52%)	37 (46%)	15 (28%)	31 (31%)	23 (96%)	129 (99%)	26 (100%)	127 (99%)	17 (100%)	120 (88%)
AST > 5 ULN	0 (0%)	3 (4%)	3 (6%)	2 (2%)	0 (0%)	4 (3%)	0 (0%)	2 (2%)	5 (29%)	67 (49%)
Prothrombin Time < 70%	8 (11%)	15 (19%)	9 (17%)	6 (6%)	1 (4%)	20 (15%)	6 (23%)	23 (18%)	3 (18%)	21 (15%)
Anaemia	14 (19%)	13 (16%)	4 (7%)	7 (7%)	2 (8%)	6 (5%)	6 (23%)	34 (27%)	5 (29%)	39 (29%)
SVR12	66 (90%)	73 (91%)	53 (98%)	96 (96%)	23 (96%)	123 (95%)	23 (88%)	125 (98%)	14 (82%)	133 (98%)