Supplementary Material

Sofosbuvir/velpatasvir for hepatitis C virus infection: real-world effectiveness and safety from a nationwide registry in Taiwan

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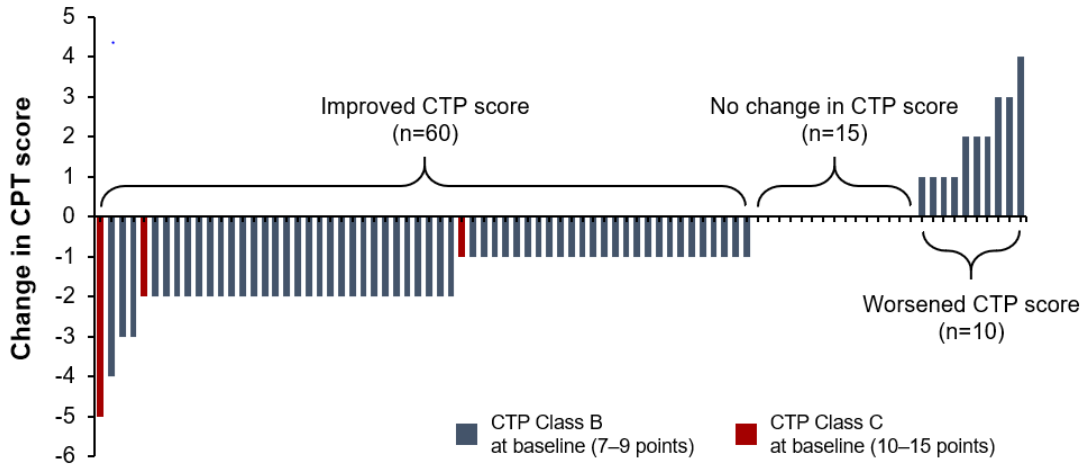

Figure S1. Change in CTP score in individual patients from baseline to end of follow-up.

Changes in CTP score from before treatment initiation with SOF/VEL to end of follow-up. Individual patient data from 85 patients with baseline and end-of-follow-up CTP scores available. All patients that showed no change in CTP score were classified as CTP Class B at baseline.

CTP: Child–Turcotte–Pugh.

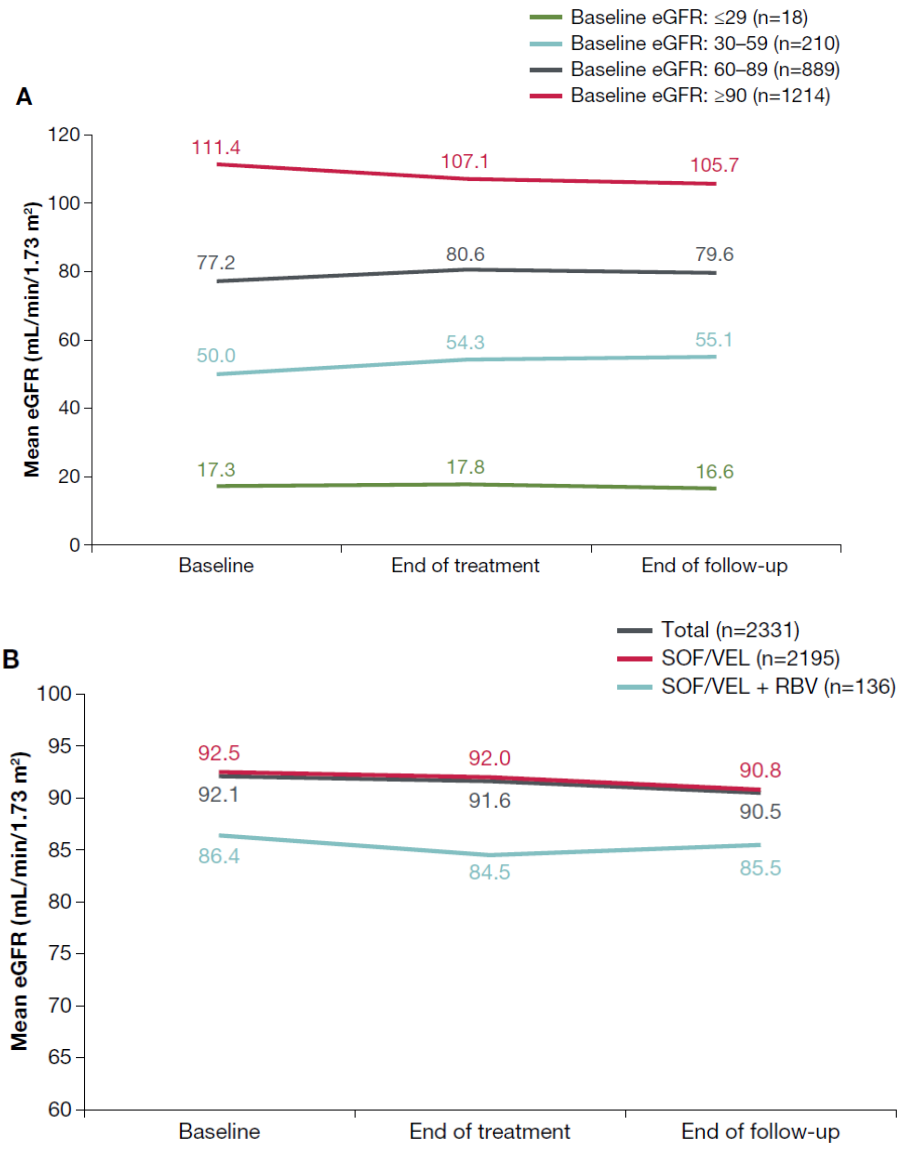

Fig. S2. eGFR at baseline, end of treatment and end of follow-up.

Mean eGFR (mL/min/1.73 m^2) at baseline, end of treatment and end of follow-up following SOF/VEL therapy stratified by (A) baseline eGFR levels and (B) treatment regimen; SOF/VEL or SOF/VEL + ribavirin

eGFR: estimated glomerular filtration rate; RBV: ribavirin.

Table S1. Baseline demographics

Variables	N	N (%)
Hypertension	3480	
No		2499 (71.8)
Yes		981 (28.2)
Hyperlipidemia	3480	
No		3104 (89.2)
Yes		376 (10.8)
Coronary artery disease	3480	
No		3184 (91.5)
Yes		296 (8.5)
Major Thalassemia	3480	
No		3474 (99.8)
Yes		6 (0.2)
Hemophilia	3480	
No		3475 (99.9)
Yes		5 (0.1)
Baseline RAS	3480	
No Mutant		178 (5.1)
Mutant		11 (0.3)
Unknown		3291 (94.6)

RAS: resistance-associated substitution

Table S2. Treatment efficacy of SOF/VEL stratified by genotype and compensated and decompensated cirrhosis

HCV genotype	Compensated cirrhosis (N=426)	Decompensated (N=114)
Total (n=540)	424/426 (99.5)	114/114 (100)
GT 1 (n=209)	154/155 (99.4)	54/54 (100)
GT 2 (n=262)	213/213 (100)	49/49 (100)
GT 1+2 (n=9)	7/7 (100)	2/2 (100)
GT 3 (n=20)	16/17 (94.1)	3/3 (100)
GT 4 (n=1)	1/1 (100)	0/0 (100)
GT 6 (n=36)	30/30 (100)	6/6 (100)
Undetermined (n=3)	3/3 (100)	0/0 (100)

GT: genotype

Table S3. Treatment efficacy of SOF/VEL therapy with on-label use and off-label use for HCV patients in Taiwan

Population	Treatment regimen	SVR, n/N (%)
Label use		
Total		3,331/3,348 (99.5)
HCV GT 1–6 with/without compensated cirrhosis	SOF/VEL 12 weeks	3,256/3,273 (99.5)
HCV GT 1–6 with decompensated cirrhosis	SOF/VEL + ribavirin 12 weeks	72/72 (100)
HCV GT 1–6 previously failed NS5A based therapy	SOF/VEL + ribavirin 24 weeks	3/3 (100)
Off-label use		
Total		128/132 (97.0)
HCV GT 1–6 with cirrhosis, without information of decompensated or compensated liver function	SOF/VEL 12 weeks	60/63 (95.2)
HCV GT 1–6 with/without compensated cirrhosis	SOF/VEL 8 weeks	10/10 (100)
HCV GT 1–6 with/without compensated cirrhosis	SOF/VEL 13 weeks	1/1 (100)
HCV GT 1–6 with/without compensated cirrhosis	SOF/VEL 14 weeks	2/2 (100)
HCV GT 1–6 with/without compensated cirrhosis	SOF/VEL 16 weeks	3/3 (100)
HCV GT 1–6 with/without compensated cirrhosis	SOF/VEL 24 weeks	10/11 (90.9)
HCV GT 1–6 with decompensated cirrhosis	SOF/VEL 12 weeks	39/39 (100)
HCV GT 1–6 with decompensated cirrhosis	SOF/VEL + ribavirin 16 weeks	1/1 (100)
HCV GT 1–6 with decompensated cirrhosis	SOF/VEL + ribavirin 24 weeks	2/2 (100)

GT: genotype; SOF: sofosbuvir; VEL: velpatasvir; SVR: sustained virological response

Table S4. Baseline characteristics and outcomes of patients who did not achieve SVR12

Characteristics	Non-SVR (n=21), mean (SD or n (%)
Age	58.0±13.6
Male	13 (61.9)
Treatment history	
Naïve	17 (81.0)
Experienced*	4 (19.1)
HCV genotype	
1	7 (33.3)
2	10 (47.6)
3	3 (14.3)
6	1 (4.8)
Liver cirrhosis	5 (23.8)
Compensated cirrhosis	2 (9.5)
Decompensated cirrhosis	0 (0.0)
Unknown	3 (14.3)
Treatment duration	
≤12 weeks	20 (95.2)
HCV RNA, $\log_{10}$ IU/mL	6.5±0.8
FIB-4	2.4±1.8
DAA adherence	
>60%	17 (81.0)
≤60%	4 (19.0)
Virologic failure	
Relapse	15 (71.4)
Non-response	2 (23.8)
Non-virologic failure (DAA adherence <60%)	4 (19.0)

*3 patients had previous experience with IFN and 1 patient had previous experience with SOF/LDV±ribavirin.

DAA: direct-acting antiviral; FIB-4: fibrosis score 4; IFN: interferon; LDV: ledipasvir; SOF: sofosbuvir; SVR: sustained virologic response.

Table S5. Risk factors for not achieving SVR

		Treatment failure (%)	Odds ratio 95% CI	P-value	Adjusted odds ratio 95% CI	P-value
Age, years	<65 yr	13/2282 (0.6)	Ref.	-	-	-
	≥65 yr	8/1198 (0.7)	1.17 (0.48-2.84)	0.723	-	-
Sex	Male	13/1781 (0.7)	Ref.	-	-	-
	Female	8/1699 (0.5)	0.64 (0.27-1.56)	0.328	-	-
BMI	<27	11/1920 (0.6)	Ref.	-	-	-
	≥27	5/605 (0.8)	1.45 (0.50-4.18)	0.496	-	-
Diabetes	No	13/2893 (0.4)	Ref.	-	Ref.	-
	Yes	8/587 (1.4)	3.06 (1.26-7.42)	0.013	1.08 (0.29-4.05)	0.906
Hypertension	No	10/2499 (0.4)	Ref.	-	Ref.	-
	Yes	11/981 (1.1)	2.82 (1.19-6.67)	0.018	1.76 (0.57-5.38)	0.323
Hyperlipidemia	No	17/3104 (0.5)	Ref.	-	-	-
	Yes	4/376 (1.1)	1.95 (0.65-5.83)	0.231	-	-
Coronary artery disease	No	17/3184 (0.5)	Ref.	-	-	-
	Yes	4/296 (1.3)	2.55 (0.85-7.63)	0.094	-	-
PWID	No	19/3088 (0.6)	Ref.	-	-	-
	Yes	2/392 (0.5)	0.83 (0.19-3.57)	0.801	-	-
HBV coinfection	No	18/3229 (0.6)	Ref.	-	-	-
	Yes	3/251 (1.2)	2.16 (0.63-7.38)	0.220	-	-
HIV coinfection	No	16/2887 (0.6)	Ref.	-	Ref.	-
	Yes	2/65 (3.1)	5.70 (1.28-25.3)	0.022	4.97 (0.90-27.39)	0.066
Liver cirrhosis	No	16/2877 (0.6)	Ref.	-	-	-
	Yes	5/603 (0.8)	1.50 (0.55-4.10)	0.434	-	-
HCC	No	16/3273 (0.5)	Ref.	-	Ref.	-
	Inactive HCC	4/139 (2.9)	6.03 (1.99-18.29)	0.002	4.12 (0.92-18.39)	0.064
	Active HCC	1/68 (1.5)	3.04 (0.40-23.2)	0.284	2.80 (0.31-25.49)	0.361
FIB-4	<3.25	15/2582 (0.6)	Ref.	-	-	-
	≥3.25	6/861 (0.7)	1.20 (0.46-3.10)	0.706	-	-
eGFR	<90	11/1713 (0.6)	1.76 (0.65-4.77)	0.266	-	-
	≥90	6/1641 (0.4)	Ref.	-	-	-
Chronic kidney disease	No	15/2925 (0.5)	Ref.	-	-	-
	Yes	6/550 (1.1)	2.14 (0.83-5.54)	0.117	-	-

HCV RNA viral load	≤6,000,000 IU/mL	13/2764 (0.5)	Ref.	-	Ref.	-
	>6,000,000 IU/mL	8/702 (1.1)	2.44 (1.01-5.91)	0.048	3.39 (1.13-10.13)	0.028
HCV genotype	GT3	3/97 (3.1)	5.97 (1.73-20.60)	0.005	11.01 (2.61-46.37)	0.001
	Non-GT 3	18/3383 (0.5)	Ref.	-	Ref.	-
Treatment history	Naïve	17/3285 (0.5)	Ref.	-	Ref.	-
	IFN-experienced	3/179 (1.7)	3.28 (0.95-11.29)	0.060	2.52 (0.52-12.16)	0.251
	DAA-experienced	1/16 (6.3)	12.82 (1.60-102.54)	0.016	6.00 (0.36-101.44)	0.214
Drug adherence	≥60%	17/3471 (0.5)	Ref.	-	Ref.	-
	<60%	4/9 (44.4)	162.54 (40.14-658.13)	<0.001	173.37 (27.09-1109.57)	<0.001
Treatment duration	≤12w	20/3457 (0.6)	Ref.	-	Ref.	-
	>12w	1/23 (4.4)	7.81 (1.00-60.78)	0.050	3.49 (0.23-52.43)	0.366
Ribavirin	No	19/3297 (0.6)	Ref.	-	-	-
	Yes	2/183 (1.1)	1.91 (0.44-8.25)	0.388	-	-
Baseline RAS	No mutant	1/178 (0.6)	Ref.	-	-	-
	Mutant	0/11 (0.0)	-	-	-	-

BMI: body mass index; DAA: direct-acting antiviral; eGFR: estimated glomerular filtration rate; FIB-4: fibrosis stage 4; GT: genotype; HCC: hepatocellular carcinoma; IFN: interferon; RAS: resistance-associated substitution; SVR: sustained virologic response.

Table S6. Renal function from baseline, end of treatment and end of follow-up

	Baseline	End of treatment	End of follow-up
Total (n=2,331)*	92.1±27.5	91.6±27.6	90.5±27.2
	BL vs. EOT: p=0.123	BL vs. EOF: p<0.001	EOT vs. EOF: p<0.001
-RBV (n=2,195)	92.5±26. 9	92.0±27.0	90.8±26.3
	BL vs. EOT: p=0.198	BL vs. EOF: p<0.001	EOT vs. EOF: p<0.001
+RBV (n=136)	86.4±36.2	84.5±34.7	85.5±38.2
	BL vs. EOT: p=0.291	BL vs. EOF: p=0.594	EOT vs. EOF: p=0.573
Baseline eGFR ≤29 (n=18)	17.3±8.8	17.8±10.5	16.6±11.0
	BL vs. EOT: p=0.681	BL vs. EOF: p=0.673	EOT vs. EOF: p=0.252
Baseline eGFR 30–59 (n=210)	50.0±7.8	54.3±16.0	55.1±15.9
	BL vs. EOT: p<0.001	BL vs. EOF: p<0.001	EOT vs. EOF: p=0.267
Baseline eGFR 60–89 (n=889)	77.2±8.0	80.6±15.3	79.6±15.1
	BL vs. EOT: p<0.001	BL vs. EOF: p<0.001	EOT vs. EOF: p=0.018
Baseline eGFR ≥90 (n=1,214)	111.4±21.7	107.1±24.4	105.7±25.3
	BL vs. EOT: p<0.001	BL vs. EOF: p<0.001	EOT vs. EOF: p=0.005
No cirrhosis (n=1,909)	92.8±26.0	92.5±26.5	91.3±26.1
	BL vs. EOT: p=0.359	BL vs. EOF: p<0.001	EOT vs. EOF: p=0.001
Compensated cirrhosis (n=307)†	88.6±31.6	87.2±30.6	86.1±27.4
	BL vs. EOT: p=0.130	BL vs. EOF: p=0.015	EOT vs. EOF: p=0.260
Decompensated cirrhosis (n=89)†	89.4±41.2	87.9±37.6	87.4±42.3
	BL vs. EOT: p=0.540	BL vs. EOF: p=0.404	EOT vs. EOF: p=0.794
Cirrhosis + eGFR < 90 (n=242)	68.9±14.7	71.6±19.8	71.2±19.4
	BL vs. EOT: p=0.004	BL vs. EOF: p=0.009	EOT vs. EOF: p=0.621

*2331 patients excluded: hemodialysis or eGFR information not available.

†26 patients excluded: due missing cirrhosis information. BL: baseline; eGFR: estimated glomerular filtration rate; EOT: end of treatment; EOF: end of follow-up; RBV: ribavirin