SUPPLEMENTARY MATERIAL

Daclatasvir Plus Sofosbuvir, With or Without Ribavirin, Achieved High Sustained Virologic Response Rates in Patients With HCV Infection and Advanced Liver Disease in a Real-World Cohort

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Supplementary Table 1. Characteristics of Patients Excluded From the mITT Population

Patient	Age/ Gender	Reason for Exclusion	Baseline Characteristics								Regimen	Last HCV RNA Available (IU/mL)	Last HCV RNA Available (Visit Week)
			HCV GT	Prior HCV Therapy	HCV RNA $\log_{10}$ IU/mL	Cirrhosis Status	Child-Pugh Class	MELD Score	LT	HIV			
1	62 / M	Lost to follow-up	1a	Experienced	5.87	Cirrhosis	A	12			D+S+R	< 15	Week 12 (O-T)
2	63 / F	Undocumented reason for D/C	1 UNK	Experienced	4.19	Cirrhosis	A	13	Yes		D+S+R	< 15	Week 12 (O-T)
3	58 / M	Lost to follow-up	3	Naive	5.94	Cirrhosis	B	17			D+S+R	0	Week 24 (EOT)
4	55 / F	Lost to follow-up	3	Experienced	6.11	Cirrhosis	A	8			D+S+R	0	Week 24 (EOT)
5	54 / M	Consent withdrawal	1b	Experienced	5.43	Cirrhosis	A	7			D+S+R	Only baseline data reported	
6	61 / F	Undocumented reasons for D/C	3	Naive	6.76	Cirrhosis	A	7			D+S+R	Only baseline data reported	
7	43 / F	Consent withdrawal	1 UNK	Naive	6.46	Cirrhosis	B	13			D+S+R	Only baseline data reported	
8	65 / M	Consent withdrawal	1b	Naïve	2.96	Cirrhosis	C	23			D+S	Only baseline data reported	
9	55 / F	Lost to follow-up	1b	Experienced	5.69	Cirrhosis	B	14			D+S	< 12	Week 12 (O-T)
10	54 / F	Undocumented reason for D/C	1b	Naïve	6.36	Cirrhosis	A	10			D+S	0	Week 24 (EOT)
11	42 / M	Lost to follow-up	3	Experienced	5.65	Cirrhosis	B	14			D+S	0	Week 12 (O-T)
12	43 / M	Undocumented reason for D/C	1b	Experienced	6.36	Cirrhosis	B	6			D+S	0	Pre-PT Week 12
13	69 / M	Undocumented reason for D/C	1b	Experienced	6.00	Cirrhosis	A	10			D+S	0	Week 24 (EOT)
14	60 / M	Undocumented reason for D/C	1a	Experienced	6.05	Cirrhosis	A	11		NR	D+S	0	Pre-PT Week 12
15	51 / M	Lost to follow-up	3	Experienced	6.00	Cirrhosis	NR	10		Yes	D+S	0	Week 12 (O-T)
16	73 / F	Consent withdrawal	1a	Experienced	6.20	Cirrhosis	A	7			D+S	0	Week 24 (EOT)
17	64 / F	Lost to follow-up	1a	Experienced	5.98	Cirrhosis	B	15			D+S	0	Week 12 (O-T)
18	52 / M	Lost to follow-up	3	Naïve	5.28	No	NR	NR			D+S	< 15	Week 12 (O-T)
19	44 / F	Lost to follow-up	3	Naïve	5.41	Cirrhosis	B	16			D+S	0	Week 12 (O-T)
20	61 / F	Lost to follow-up	3	Experienced	5.47	Cirrhosis	A	13			D+S	0	Week 24 (EOT)
21	55 / F	Undocumented reason for D/C	3	Naïve	6.25	Cirrhosis	B	6		Yes	D+S	0	Pre-PT Week 12
22	55 / F	Lost to follow-up	1a	Experienced	4.31	No	NR	NR		NR	D+S	0	Week 24 (EOT)
23	52 / M	Undocumented reason for D/C	1a	Naïve	6.43	Cirrhosis	B	11		Yes	D+S	0	Week 24 (EOT)
24	40 / M	Lost to follow-up	1 UNK	Experienced	7.23	Indeterminate	NR	NR	Yes		D+S	0	Week 24 (EOT)
25	53 / M	Undocumented reason for D/C	1b	Experienced	5.76	NR	NR	NR			D+S	< 15	Week 24 (EOT)

D+S, daclatasvir + sofosbuvir; D+S+R, daclatasvir + sofosbuvir + ribavirin; D/C, discontinuation; EOT, end of treatment; HIV, HIV/HCV coinfection present; LT, liver transplant; NR, not reported; O-T, on-treatment; Pre-PT week 12: patients with a follow-up visit after EOT but before posttreatment week 12 with no additional data available; UNK, unknown.

Supplementary Table 2. Characteristics of Patients Not Achieving SVR12

2A. Virologic Failures

Patient	Age/Sex	Regimen	Days of Therapy	Prior HCV Therapy	HCV GT	HCV RNA log10	Fibrosis Stage / Cirrhosis Status	Child-Pugh Class	MELD Score	HCC	LT Recipient	HIV/HCV Coinfection	Ribavirin Reduced/Discontinued
Virologic breakthrough													
1[a]	47/M	D+S	176	Experienced	3	5.8	Cirrhosis	B	12				
Relapse													
2	48/M	D+S	169	Experienced	3	5.2	F3						
3	56/M	D+S	169	Experienced	3	5.6	NR						
4	61/F	D+S	180	Experienced	3	5.4	Cirrhosis	B	11				
5	55/M	D+S	169	Experienced	1a	6.0	Cirrhosis	A	7				
6	68/M	D+S	171	Naive	1b	6.7	Cirrhosis	A	6				
7	62/M	D+S	163	Experienced	1b	5.3	Cirrhosis	B	17			Yes[b]	
8	73/M	D+S	169	Experienced	1b	6.4	Cirrhosis	A	8				
9	37/M	D+S	167	Naive	1a	5.2	Cirrhosis	B	11				
10	68/F	D+S	171	Experienced	1b	6.0	Cirrhosis	A	9				
11	59/M	D+S+R	170	Experienced	3	NR	Cirrhosis	A	9	Yes			Reduced from 1000mg to 800mg on Day 85
12	60/F	D+S+R	51	Experienced	3	6.0	Cirrhosis	A	13				
13	64/F	D+S+R	19	Experienced	1b	4.8	Cirrhosis	B	20				
14	50/M	D+S+R	169	Experienced	3	6.6	Cirrhosis	B	11				Discontinued on Day 80-

D, daclatasvir;GT, genotype; HCC, hepatocellular carcinoma; LT, liver transplant; NR, not reported; R, ribavirin; S, sofosbuvir.

[a] HCV RNA increased ≥1 $\log_{10}$ IU/mL from nadir (30 IU/mL) at EOT week 24 (437 IU/mL).

[b] Patient under treatment with tenofovir/emtricitabine + ritonavir-boosted fosamprenavir who received DCV 30 mg

2B. non-Virologic Failures

Patient	Age/Sex	Regimen	Days of Therapy	Prior HCV Therapy	HCV GT	HCV RNA log10	Fibrosis Stage / Cirrhosis Status	Child-Pugh Class	MELD Score	HCC	LT Recipient	HIV/HCV Coinfection	Primary Cause of Death
Discontinuation due to AE													
15	39/M	D+S+R	58	Experienced	UNK	0	Cirrhosis	A	18		Yes		
16	62/F	D+S+R	37	Experienced	3	5.5	Cirrhosis	B	NR				
17	55/M	D+S+R	156	Experienced	1b	6.6	Cirrhosis	A	6	Yes			
Death on-treatment													
18	52/F	D+S	1	Experienced	1b	6.1	Cirrhosis	B	29		Yes		Sepsis
19	85/M	D+S	28	Naive	1b	6.9	Cirrhosis	B	9				Septic multi-organ failure
20	56/F	D+S	85	Experienced	1	5.3	Cirrhosis	B	14				Multi-organ failure after planned pancreas surgery
21	69/M	D+S	81	Experienced	1b	6.6	Non-cirrhotic						Multi-organ failure after surgery for cholangiocarcinoma
22	53/M	D+S	21	Experienced	1a	NR	Cirrhosis	B	16				Oesophageal varices bleeding
23	43/M	D+S	51	Experienced	3	6.1	Cirrhosis	C	15				Liver-related (non-HCC) – liver failure
24	66/M	D+S	35	Experienced	1b	6.0	Cirrhosis	C	13				Hepatic encephalopathy/sepsis
25	60/M	D+S	13	Experienced	1b	3.7	Cirrhosis	B	18	Yes			HCC
26	76/F	D+S+R	117	Naive	1b	5.6	Cirrhosis	B	8				Liver-related (non-HCC) – hepatic decompensation
27	56/M	D+S+R	54	Experienced	Mixed	6.5	Cirrhosis	C	28			Yes	Myocardial infarction, asphyxia
Death during follow-up													
28	63/M	D+S	169	Naive	1b	6.6	Cirrhosis	A	8	Yes			Liver transplant complications
29	61/F	D+S	128	Experienced	1a	5.1	Cirrhosis	C	17		Yes		Sepsis due to *C Clabrata*
30	61/M	D+S	178	Naive	1b	5.8	Cirrhosis	A	12				Liver-related (non-HCC)
31	45/M	D+S	153	Naive	3	5.4	Cirrhosis	C	10			Yes	Multi-organ failure
32	61/M	D+S	170	Experienced	1b	5.8	Cirrhosis	B	14				Multi-organ failure/necrotic peritonitis
33	55/M	D+S	84	Experienced	1b	4.7	Cirrhosis	A	7				Myelodysplastic syndrome, myelofibrosis, leukemia
34	55/M	D+S	141	Experienced	1a	6.6	Cirrhosis	B	7			Yes	Extensive alcohol consumption
35	80/F	D+S	169	Experienced	1b	5.5	Cirrhosis	B	17				Liver-related (non-HCC)
36	60/F	D+S	162	Naive	3	4.5	Cirrhosis	B	17				Liver-related (non-HCC)
37	71/M	D+S	169	Naive	1b	5.7	Cirrhosis	B	8		Yes/FCH		Liver-related (non-HCC)
38	54/F	D+S+R	150	Experienced	1	5.7	Cirrhosis	B	11		Yes		Liver-related (non-HCC) – hepatic decompensation

39	73/M	D+S+R	56	Experienced	1b	6.5	Cirrhosis	A	18				Multi-organ failure due to haemorrhagic shock
40	61/M	D+S+R	169	Naive	1a	3.5	Cirrhosis	A	9				Liver-related (non-HCC)
41	65/F	D+S+R	8	Experienced	Mixed	4.4	NR						Liver-related (non-HCC) – hepatic decompensation

D, daclatasvir; FCH, fibrosing cholestatic hepatitis; GT, genotype; HCC, hepatocellular carcinoma; LT, liver transplant; NR, not reported; R, ribavirin; S, sofosbuvir; UNK, unknown.

On-treatment includes treatment period and the first 7 days after stopping treatment.

None of the deaths during or after treatment were considered related to programme therapy by the treating physician.

Supplementary Table 3. Inverse Probability Weighted (IPW) Analysis Using Propensity Scores

Propensity scores (PS) represented the estimated probability of patients receiving DCV+SOF versus DCV+SOF+RBV as a function of the covariates in the propensity model (observed disease and treatment parameters in Table 3 A and B). After inverse probability weighting using PS, the standardized differences in those covariates were substantially reduced, suggesting two comparable pseudo treatment groups that have similar distributions for those covariates as the overall population.

Differences in treatment failure and virologic failure were determined using unweighted (risk-unadjusted) and weighted (IPW, risk-adjusted) analyses. The adjusted risk difference were estimated using generalized linear models (for binomial distribution) with an identity link function, including a single covariate for treatment group and weighting each patient by the inverse of the estimated probability of receiving their observed treatment. The adjusted risk ratios and odds ratios were estimated with similar approaches using log and logit links, respectively. Robust sandwich variance estimates were used to obtain 95% CI.

3A. Patient Characteristics before and after IPW – mITT Population

	Unweighted (Before IPW)				Inverse Weighted (After IPW)			
Baseline Variable	DCV+SOF Mean or %	DCV+SOF +RBV Mean or %	Std Diff (%)	*P* value	DCV+SOF Mean or %	DCV+SOF +RBV Mean or %	Std Diff (%)	*P* value
Age, y	57.38	55.95	14.69	0.341	57.11	57.62	−5.36	0.642
Sex								
Male	0.66	0.71	−9.88	0.358	0.67	0.68	−1.49	0.906
Female	0.34	0.29	9.88	0.358	0.33	0.32	1.49	0.906
Race								
White	0.94	0.92	8.62	0.401	0.94	0.94	−0.13	0.992
Other	0.06	0.08	−8.62	0.401	0.06	0.06	0.13	0.992
Body mass index, kg/m^2	26.30	27.11	−16.84	0.281	26.53	26.25	5.99	0.609
HCV RNA (log_{10} IU/mL)	5.53	5.40	8.05	0.793	5.51	5.52	−0.96	0.935
HCV genotype								
1a	0.38	0.23	32.71	**0.003**	0.34	0.39	−9.70	0.475
1 non-a	0.42	0.34	17.78	0.099	0.40	0.37	7.41	0.546
3	0.16	0.31	−34.88	**0.001**	0.20	0.20	1.54	0.889
Other	0.04	0.13	−32.34	**0.001**	0.06	0.05	2.00	0.838
IL28B genotype								
CC	0.10	0.06	15.14	0.178	0.08	0.10	−5.75	0.738
Non-CC	0.38	0.29	17.84	0.099	0.37	0.37	−0.14	0.991
Not available	0.52	0.65	−25.51	**0.018**	0.55	0.54	3.40	0.790
Cirrhosis status								
No cirrhosis	0.13	0.12	3.45	0.748	0.13	0.16	−7.77	0.564
Child-Pugh A	0.48	0.40	16.21	0.130	0.47	0.46	1.98	0.876
Child-Pugh B	0.26	0.40	−30.10	**0.004**	0.29	0.26	5.17	0.645
Child-Pugh C	0.05	0.03	14.25	0.215	0.04	0.04	0.05	0.997
Indeterminate or Not Reported	0.08	0.06	8.02	0.465	0.07	0.08	−2.17	0.879
MELD score								
<10	0.37	0.29	17.87	0.099	0.35	0.33	3.88	0.763
10–15	0.36	0.47	−21.76	**0.040**	0.39	0.38	2.30	0.851
16–20	0.04	0.05	−4.47	0.667	0.04	0.04	1.34	0.902
≥20	0.02	0.02	0.61	0.955	0.02	0.02	0.62	0.955
Bilirubin level, mg/dL	23.99	28.24	−15.17	**0.048**	24.64	23.45	4.94	0.615
Albumin level, g/L	36.66	35.64	17.76	**0.038**	36.49	36.89	−6.91	0.581
Platelets $\times 10^9$/L	105.42	110.22	−7.10	0.618	107.61	107.17	0.65	0.956
Creatinine clearance, $mL/min/1.73m^2$								
<60	0.14	0.13	0.13	0.990	0.14	0.13	1.91	0.873
60–89	0.61	0.60	2.72	0.798	0.61	0.62	−3.28	0.796
≥90	0.26	0.27	−3.12	0.768	0.25	0.24	2.18	0.868
Liver transplant								
Yes	0.18	0.20	−5.79	0.582	0.19	0.19	−0.60	0.960
No	0.82	0.80	5.79	0.582	0.81	0.81	0.60	0.960
HIV/HCV coinfection								
Yes	0.11	0.13	−8.87	0.392	0.12	0.15	−7.78	0.602
No	0.83	0.82	2.46	0.816	0.82	0.80	5.34	0.701
HCV treatment history								
Experienced	0.70	0.72	−4.80	0.653	0.71	0.70	1.69	0.898
Naive	0.30	0.28	4.80	0.653	0.29	0.30	−1.69	0.898
Started SOF before DCV								
Yes	0.06	0.10	−14.36	0.154	0.07	0.07	0.02	0.999
No	0.94	0.90	14.36	0.154	0.93	0.93	−0.02	0.999

DCV, daclatasvir; HCV, hepatitis C virus; IPW, inverse probability weighted; HIV, human immunodeficiency virus; MELD, model for end-stage liver disease; RBV, ribavirin; SOF, sofosbuvir.

P values <0.05 are shown in bold **red**. The standardized difference (Std Diff) represents the difference in means between the two groups in units of the standard deviation (STD).

3B. Patient Characteristics before and after IPW – As-observed Population

	Unweighted (Before IPW)				Inverse Weighted (After IPW)			
Baseline Variable	DCV+SOF Mean or %	DCV+SOF+RBV Mean or %	Std Diff (%)	*P* value	DCV+SOF Mean or %	DCV+SOF+RBV Mean or %	Std Diff (%)	*P* value
Age, y	57.18	55.61	16.36	0.297	56.86	57.52	−7.09	0.571
Sex								
Male	0.66	0.72	−13.33	0.233	0.67	0.66	3.82	0.791
Female	0.34	0.28	13.33	0.233	0.33	0.34	−3.82	0.791
Race								
White	0.94	0.92	8.97	0.398	0.94	0.94	0.32	0.980
Other	0.06	0.08	−8.97	0.398	0.06	0.06	−0.32	0.980
Body mass index, kg/m^2	26.27	27.22	−19.86	0.142	26.51	26.17	7.37	0.556
HCV RNA (log_{10} IU/mL)	5.52	5.44	5.15	0.706	5.51	5.59	−5.53	0.643
HCV genotype								
1a	0.39	0.24	32.87	**0.004**	0.36	0.40	−8.37	0.573
1 non-a	0.41	0.33	16.89	0.131	0.39	0.35	7.53	0.578
3	0.16	0.33	−38.48	**<0.001**	0.21	0.20	0.35	0.977
Other	0.04	0.11	−26.32	**0.008**	0.05	0.05	1.27	0.892
IL28B genotype								
CC	0.10	0.06	17.74	0.132	0.09	0.10	−4.21	0.829
Non-CC	0.39	0.30	18.98	0.091	0.37	0.37	0.74	0.957
Not available	0.51	0.65	−28.06	**0.012**	0.54	0.53	1.76	0.900
Cirrhosis status								
No cirrhosis	0.13	0.13	1.73	0.876	0.14	0.16	−5.08	0.714
Child-Pugh A	0.50	0.40	20.45	0.066	0.48	0.46	3.22	0.817
Child-Pugh B	0.24	0.40	−35.09	**0.001**	0.27	0.25	4.55	0.697
Child-Pugh C	0.04	0.02	14.58	0.228	0.04	0.04	−0.03	0.999
Indeterminate or Not Reported	0.08	0.06	11.44	0.322	0.08	0.10	−6.44	0.716
MELD score								
<10	0.38	0.28	19.80	0.079	0.35	0.33	4.85	0.732
10–15	0.37	0.49	−25.51	**0.020**	0.39	0.39	0.63	0.962
16–20	0.03	0.04	−4.81	0.652	0.03	0.03	2.78	0.792
≥20	0.02	0.01	5.79	0.621	0.01	0.01	5.06	0.613
Bilirubin level, mg/dL	22.95	28.18	−18.56	**0.045**	23.41	22.66	3.40	0.730
Albumin level, g/L	36.89	35.65	21.95	**0.017**	36.68	36.92	−4.14	0.761
Platelets ×10^9/L	106.21	109.90	−5.44	0.869	107.97	103.36	6.83	0.601
Creatinine clearance, mL/min/1.73m^2								
<60	0.13	0.13	1.73	0.876	0.14	0.13	2.53	0.846
60–89	0.61	0.59	3.24	0.769	0.61	0.62	−2.41	0.863
≥90	0.26	0.28	−4.88	0.656	0.26	0.25	0.74	0.960
Liver transplant								
Yes	0.18	0.20	−5.20	0.634	0.19	0.19	−0.67	0.958
No	0.82	0.80	5.20	0.634	0.81	0.81	0.67	0.958
HIV/HCV coinfection								
Yes	0.11	0.14	−9.52	0.374	0.12	0.15	−11.00	0.530
No	0.83	0.82	3.85	0.725	0.83	0.80	7.20	0.651
HCV treatment history								
Experienced	0.70	0.72	−3.39	0.760	0.71	0.71	0.11	0.994
Naive	0.30	0.28	3.39	0.760	0.29	0.29	−0.11	0.994
Started SOF before DCV								
Yes	0.07	0.10	−12.70	0.226	0.07	0.07	1.88	0.864
No	0.94	0.90	12.70	0.226	0.93	0.93	−1.88	0.864
Treatment duration								
<10 weeks	0.02	0.04	−13.12	0.185	0.02	0.02	−1.05	0.920
10-20 weeks	0.06	0.13	−22.39	**0.028**	0.08	0.08	−2.52	0.822
≥20 weeks	0.92	0.84	26.63	**0.009**	0.90	0.89	2.76	0.805

DCV, daclatasvir; HCV, hepatitis C virus; IPW, inverse probability weighted; HIV, human immunodeficiency virus; MELD, model for end-stage liver disease; RBV, ribavirin; SOF, sofosbuvir.

P values <0.05 are shown in bold **red**. The standardized difference (Std Diff) represents the difference in means between the two groups in units of the standard deviation (STD).

3C. Risk Adjusted Analysis

Endpoint	Analysis	Estimated Failure Rate, %		Comparison between DCV+SOF versus DCV+SOF+RBV			
		DCV+SOF	DCV+SOF+RBV	Statistics	Estimate	95% CI	*P* Value
Treatment failure at posttreatment week 12 (mITT population)	Unadjusted	8.21	10.92	Difference DCV+SOF − DCV+SOF+RBV	-2.71	-9.03, 3.60	0.400
				Risk Ratio DCV+SOF / DCV+SOF+RBV	0.75	0.40, 1.40	0.370
				Odds Ratio DCV+SOF vs. DCV+SOF+RBV	0.73	0.36, 1.46	0.373
Treatment failure at posttreatment week 12 (mITT population)	IPW	8.61	10.52	Difference DCV+SOF − DCV+SOF+RBV	-1.91	-8.76, 4.93	0.584
				Risk Ratio DCV+SOF / DCV+SOF+RBV	0.82	0.41, 1.62	0.565
				Odds Ratio DCV+SOF vs. DCV+SOF+RBV	0.80	0.38, 1.71	0.567
Virologic failure at posttreatment week 12 (Observed population)	Unadjusted	3.10	3.64	Difference DCV+SOF − DCV+SOF+RBV	−0.54	−4.52, 3.44	0.790
				Risk Ratio DCV+SOF / DCV+SOF+RBV	0.85	0.27, 2.66	0.782
				Odds Ratio DCV+SOF vs. DCV+SOF+RBV	0.85	0.26, 2.76	0.782
Virologic failure at posttreatment week 12 (Observed population)	IPW	3.41	2.35	Difference DCV+SOF − DCV+SOF+RBV	1.06	−2.22, 4.35	0.527
				Risk Ratio DCV+SOF / DCV+SOF+RBV	1.45	0.42, 4.99	0.553
				Odds Ratio DCV+SOF vs. DCV+SOF+RBV	1.47	0.41, 5.21	0.552

DCV, daclatasvir; IPW, inverse probability weighted; mITT, modified intention-to-treat; RBV, ribavirin; SOF, sofosbuvir.

Supplementary Table 4. Adverse Events Leading to Treatment Discontinuation

	DCV+SOF N = 359	DCV+SOF+RBV N = 126
Total patients with AE leading to discontinuation	**16**	**12**
Event, n		
General disorders		
Multi-organ failure	4[a]	1
General health deterioration	-	3[b]
Hepatobiliary disorders		
Hepatic cirrhosis	1	1
Hepatic failure	-	2
Acute cholecystitis	1	-
Liver disorder	-	1
Infections and infestations		
Sepsis	2[a]	-
Bacterial peritonitis	-	1
Pneumonia	1	-
Nervous system disorders		
Hepatic encephalopathy	2[a]	1
Somnolence	-	1
Renal and urinary disorders		
Acute kidney injury	-	3
Renal impairment	1	-
Blood and lymphatic system disorders		
Anaemia	-	2
Cardiac disorders		
Cardiopulmonary failure	1	-
Myocardial infarction	-	1[a]
Metabolism and nutrition disorders		
Fluid overload	-	1
Hyponatraemia	-	1
Lactic acidosis	-	1
Neoplasms, benign and malignant		
Cholangiocarcinoma	1	-
Hepatocellular carcinoma	1[a]	-
Respiratory and thoracic disorders		
Asphyxia	-	1[a]
Dyspnoea	-	1
Gastrointestinal disorders		
Oesophageal varices haemorrhage	1[a]	-
Investigations		
Creatinine clearance decreased	1	-
Musculoskeletal and connective tissue disorders		
Arthralgia	1	-
Psychiatric disorders		
Psychotic disorder	1	-
Skin and subcutaneous tissue disorders		
Seborrhoeic dermatitis	1	-
Vascular disorders		
Circulatory collapse	-	1

AE, adverse event; DCV, daclatasvir; RBV, ribavirin; SOF, sofosbuvir.

Some patients experienced >1 event.

[a] Patients with this event died.

[b] 1 patient with this event died.

Supplementary Table 5. On-Treatment Serious Adverse Events

	DCV+SOF N = 359	DCV+SOF +RBV N = 126
Total patients with SAEs	**64**	**30**
Event, n		
Hepatobiliary disorders		
Hepatic failure	2	4
Cholangitis	2	1
Hepatic cirrhosis	1	1
Hyperbilirubinaemia	-	2
Bile duct stone	1	-
Acute cholecystitis	1	-
Jaundice	1	-
Liver disorder	-	1
Portal hypertension	1	-
Portal vein thrombosis	-	1
Nervous system disorders		
Hepatic encephalopathy	9	3
Somnolence	-	2
Cerebral infarction	1	-
Dementia	1	-
Diabetic coma	1	-
Dizziness	1	-
Encephalopathy	1	-
Headache	-	1
Syncope	1	-
Gastrointestinal disorders		
Diarrhoea	1	2
Abdominal pain	1	1
Ascites	2	-
Nausea	2	-
Oesophageal varices haemorrhage	2	-
Alcoholic gastritis	1	-
Haematemesis	1	-
Haemorrhoidal haemorrhage	-	1
Inguinal hernia	1	-
Pancreatitis	1	-
Acute pancreatitis	-	1
Vomiting	1	-
Blood & lymphatic disorders		
Anaemia	2	-
Pancytopenia	1	1
Neutropenia	-	1
Metabolism/nutrition disorders		
Hyponatraemia	-	2
Dehydration	-	1
Fluid overload	-	1
Lactic acidosis	-	1
Renal and urinary disorders		
Acute kidney injury	-	3
Hydronephrosis	2	-
Urinary calculus	-	1
Renal impairment	1	-

Event, n		
Infections and infestations		
Pneumonia	4	-
Infection	1	1
Abdominal abscess	1	-
Cat scratch disease	1	-
C difficile colitis	-	1
Erysipelas	-	1
Gastrointestinal infection	-	1
Bacterial peritonitis	-	1
Pilonidal cyst	1	-
Sepsis	1	-
Streptococcal sepsis	-	1
Urinary tract infection	1	-
Neoplasms		
Hepatocellular carcinoma	6	2
Anal cancer	-	1
Breast cancer	1	-
Cholangiocarcinoma	1	-
General disorders		
General health deterioration	-	4
Multi-organ failure	3	-
Peripheral oedema	1	-
Ulcer haemorrhage	1	-
Cardiac disorders		
Angina pectoris	1	-
Cardiac failure	1	-
Cardiopulmonary failure	1	-
Myocardial infarction		1
Tachycardia	1	-
Vascular disorders		
Circulatory collapse	-	2
Hypertension	-	1
Lymphoedema	-	1
Injury & poisoning		
Femoral neck fracture	1	-
Hand fracture	1	-
Hip fracture	1	-
Wrist fracture	1	-
Overdose	1	-
Immune system disorders		
Immune reconstitution inflammatory syndrome	1	-
Sarcoidosis	1	-
Other disorders		
Asphyxia	-	1
Pleural effusion	1	-
Polyarthritis	1	-
Psychotic disorder	1	-
Hypersensitivity vasculitis	-	1

DCV, daclatasvir; mITT, modified intention-to-treat; RBV, ribavirin; SOF, sofosbuvir.

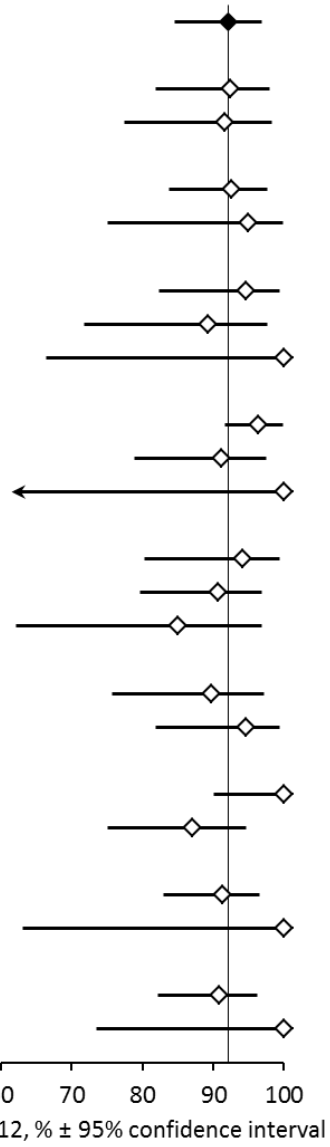
Some patients experienced >1 event.

Supplementary Table 6. List of Participants

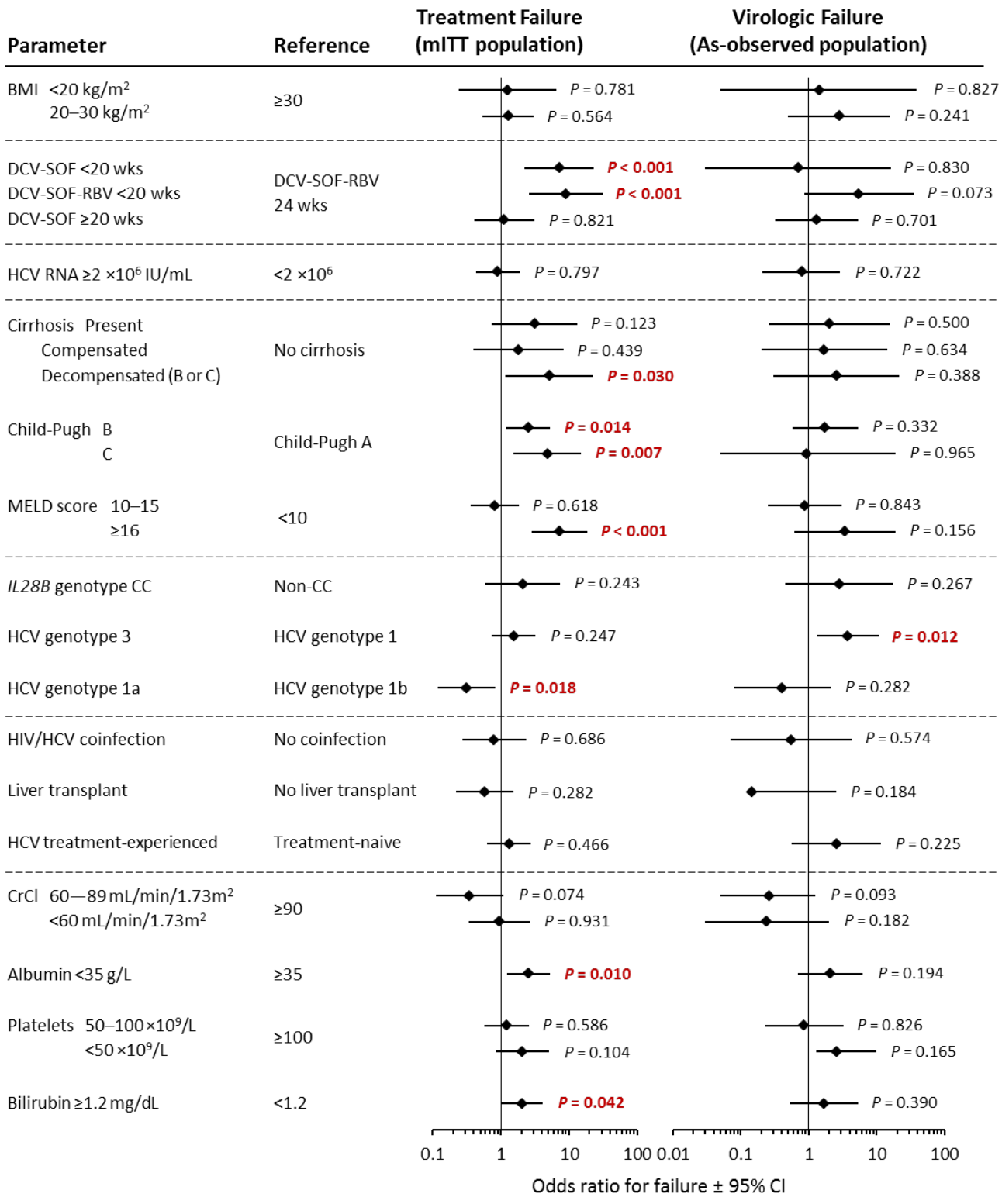
Austria	**Thomas Bamberger** - General Hospital Linz, Linz **Martin Bischof** - Krakenhaus Rudolfstiftung, Vienna **Christian Datz** - Hopital Oberndorf Salsburg, Oberndorf **Peter Ferenci** - Medical University of Vienna, Vienna **Ivo Walter Graziadei** - Hospital Hall Academy Teaching Hospital, Hall **Michael Gschwantler** - Wilhelminenspital, Vienna **Sabine Horist-Kollmann** - A.O. Krankenhaus Oberpullendorf/ A.oe. Landeskrankenhaus, Oberpullendorf **Wolfgang Korak** - Klinikum Klagenfurt Am Worthersee, Carinthia	**Andreas Maieron** - Kh Der Elisabethinen, Linz **Marcin Nowak** - Municipal Hospital Braunau, Braunau/Inn **Markus Peck-Radosavljevic** - Medical University Of Vienna, Vienna **Miriam Stetter** - Krankenhaus Amstetten, Amstetten **Michael Strasser** - Lkh Salzburg, Salzburg **Herbert Vedoveli** - Donauspital Im Smz-Ost Der Stadt Vienna, Vienna **Heinz Zoller** - Med. Universität Innsbruck, Innsbruck **Alexander Zoufaly** - Kaiser-Franz-Josef-Spital, Vienna
Germany	**Christoph Berg** - Universitätsklinikum Tübingen/ Universität Tübingen/nephrologie, Tübingen **Stefan Christensen** – Cim, Münster **Markus Cornberg** - Hannover Medical School, Hannover **Muenevver Demir** - Universitätsklinik Köln, Cologne **Marc Eisold** - Gastro Enterologische Schwerpunkt Praxis, Mössingen **Balazs Fulop** - Leber Und Studienzentrum Am Checkpoint, Berlin **Peter Galle** - Universitätsklinikum Mainz/ Iii. Medizinische Klinik Und Poliklinik/ Schwerpunkt Pneumologie, Mainz **Andreas Geier** - Universitätsklinik Würzburg, Würzburg **Norbert Hubert Gruener** - Klinikum Grosshadern, München **Heinz Hartmann** - Gastro Praxis Herne, Herne **Andreas Herrmann** - Universitätsklinikum Jena/ Klinik Für Innere Medizin Ii/ Abteilung Haematolgie U Intern. Onkologie, Jena **Kerstin Herzer** - Universitätsklinikum Essen, Essen **Gudrun Hilgard** - Universitätsklinikum Essen, Essen **Holger Hinrichsen** - Gastroenterologisch Hepatologisches Zentrum Kiel, Kiel **Wolf Peter Hofmann** - Gastroenterology Bayerischer Platz, Berlin **Stefanie Holm** - Prexis Georgstrasse, Hannover **Patrick Ingiliz** - Zibp Infektiologie Berlin, Berlin **Christine John** - Tätigkeitsschwerpunkt, Berlin **Sabine Jordan** - Universitatsklinikum Hamburg-Eppendorf, Hamburg **Pavel Khaykin** - Main Fach Artz, Frankfurt **Dietmar Klass** - University Hospital ULM Dept of Internal Medizin, Ulm	**Hartwig Klinker** - Universitätsklinik Würzburg, Würzburg **Thomas Lutz** - Infektio Research GmbH & Co. KG, Frankfurt am Main **Pr H. Messman** - Klinikum Augsburg, Augsburg **Anja Meurer** - ZIMI, München **Marion Muche** - Charite - Campus Benjamin Franklin/ Univertätsklinikum Benjamin-franklin, Berlin **Uwe Naumann** - Praxiszentrum Kaiserdamm, Berlin **Jorg Petersen** - ifi-Studien und Projekte GmbH, Hamburg **Nils Postel** - Prinzmed, München **Jürgen Rockstroh** - Universitätsklinikum Bonn/ Med. Klinik Und Poliklinik I, Bonn **Michael Sabranski** - ICH Hamburg, Hamburg **Eckart Schott** - Charite Campus Virchow Klinikum, Berlin **Gernot Sellge** - Universitätsklinikum Aachen/ Medizinische Klinik I, Aachen **Ulrich Spengler** - Universitätsklinikum Bonn, Bonn **Kerstin Stein** - University Hospital Madgeburg, Madgeburg **Luca Stein** - Praxis Jessen, Berlin **Andreas Trein** - Gemeinschaftspraxis Schwabstrasse 57, Stuttgart **Andreas Umgelter** - Klinikum Rechts Der Isar/ Ii. Medizinische Klinik, München **Esther Voigt** - Praxis AM Ebertplatz, Cologne **Andreas Weber** - Klinikum Nürnberg, Bavaria **Johannes Wiegand** - Universitatsklinikum Leipzig Aor/ Zentrum Fur Innere Medizin, Leipzig **Stefan Zeuzem** - Universitatsklinikum Frankfurt, Frankfurt am Main
Netherlands	**Jos Frissen** - Onze Lieve Vrouwe Gasthuis, Amsterdam **Akin Inderson** - Leiden University Medical Center, Leiden **Tatiana Mudrikova** - University Medical Center Utrecht, Utrecht	**Dirk Posthouwer** - Maastricht University, Maastricht **Bart Rijnders** - Erasmus Mc, Rotterdam **Marc Van der Valk** - F4-217 Division of infectious Diseases/ Tropical Medicine and AIDS, Amsterdam
Norway	**Jan Svendsen** - Baerum Hospital, Baerum Postterminal	
Sweden	**Soo Aleman** - Karolinska Universitetssjukhuset, Stockholm **Paringe Bergvist** - Hospital Of Helsingborg, Helsingborg **Astrid Danielsson** - Infectious Clinic, Falun **Hakan Ekvall** - Sundsvall County Hospital, Sundsvall **Elin Folkesson** - Sunderby Hospital, Lulea	**Carl-Johan Fraenkel** - Skane University Hospital, Lund **Mats Haglund** - Kalmar County Hospital, Kalmar **Robert Schwarz** - Karolinska University Hospital, Stockholm **Magdalena Ydreborg** - Sahlgrenska University Hospital, Göteborg

Supplementary Figure 1. SVR12 (As-observed) by Baseline Factors – Genotype 3

Parameter	n/N	% with SVR12 (95% CI)
All patients	82/89	92 (84.5–96.8)
Treatment group		
DCV+SOF	49/53	92 (81.8–97.9)
DCV+SOF+RBV	33/36	92 (77.5–98.2)
Baseline HCV RNA, IU/mL		
≥ 2,000,000	19/20	95 (75.1–99.9)
< 2,000,000	63/68	93 (83.7–97.6)
Child-Pugh class		
A	36/38	95 (82.3–99.4)
B	25/28	89 (71.8–97.7)
C	9/9	100 (66.4–100)
MELD score category		
<10	27/28	96 (81.7–99.9)
10–15	41/45	91 (78.8–97.5)
16–20	2/2	100 (15.8–100)
Platelets×10^9/L		
<50	17/20	85 (62.1–96.8)
<100	49/54	91 (79.7–96.9)
≥100	32/34	94 (80.3–99.3)
Albumin, g/L		
<35	35/39	90 (75.8–97.1)
≥35	35/37	95 (81.8–99.3)
Prior HCV therapy		
No	35/35	100 (90.0–100)
Yes	47/54	87 (75.1–94.6)
Liver transplant recipient		
No	74/81	91 (83.0–96.5)
Yes	8/8	100 (63.1–100)
HIV/HCV coinfection		
No	70/77	91 (82.2–96.3)
Yes	12/12	100 (73.5–100)



Supplementary Figure 2. Univariate Logistic Regression Analysis – Treatment and Virologic Failure



BMI, body mass index; CrCl, creatinine clearance; DCV, daclatasvir; HCV, hepatitis C virus; HIV, human immunodeficiency virus; MELD, model for end-stage liver disease; RBV, ribavirin; SOF, sofosbuvir.

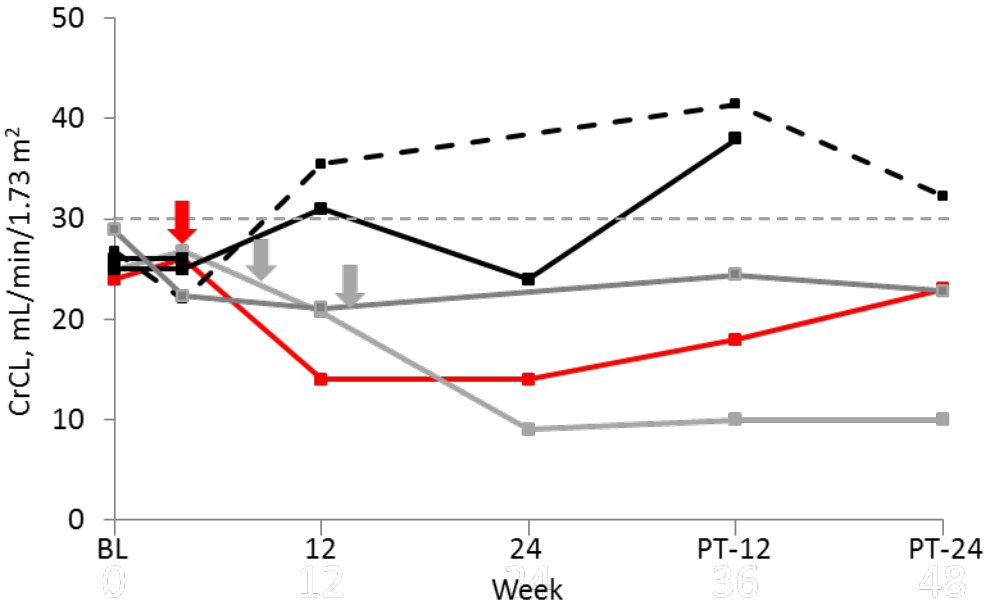
P values < 0.05 are shown in bold **red**.

Relationships between baseline covariates and all treatment failure (mITT population, left) and virologic failure (as-observed population, right) were assessed by logistic regression analysis.

Supplementary Figure 3. Individual Patient Creatinine Clearance in Patients with Reduced Renal Function

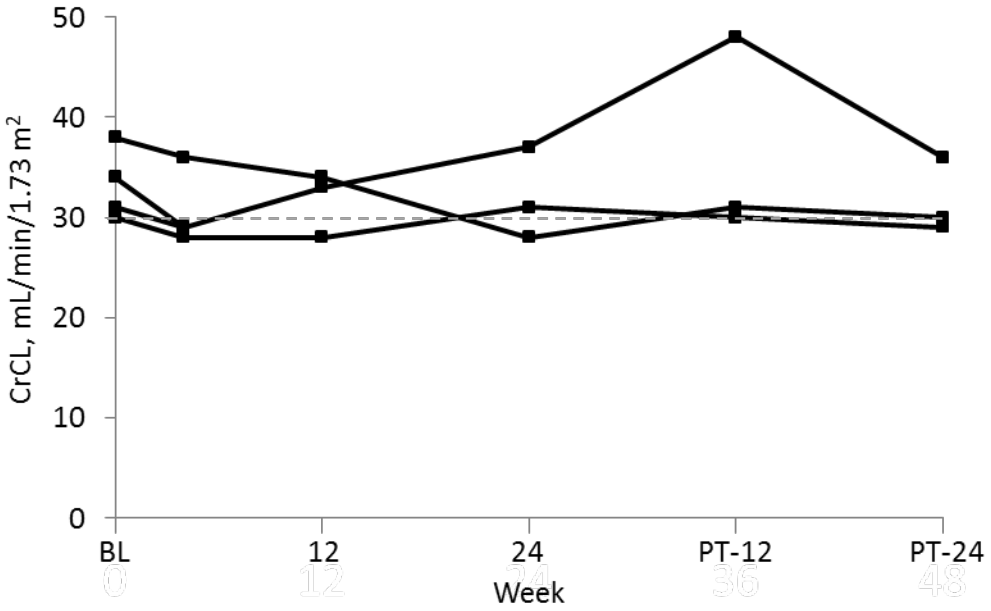
Creatinine clearance in patients with a CrCl <30 mL/min/1.73 m^2 at baseline (A) and in patients with a baseline CrCL of 30–60 mL/min/1.73 m^2 at baseline with a subsequent on-treatment reduction in CrCl<30 mL/min/1.73 m^2 at baseline (B) are presented

3A. Individual Patient Creatinine Clearance in Patients with Baseline CrCL < 30 mL/min/1.73 m^2



Solid lines are data from patients receiving DCV + SOF. Dashed lines are data from a patient who received DCV+SOF+RBV. Grey lines indicate patients with on-treatment SOF dose reductions; arrows show the timing of SOF dose reductions. The line in red depicts CrCL changes in a patient who initiated therapy with SOF 200 mg; arrow shows timing of SOF dose on-treatment increase to 400 mg.

3B. Individual Patient Creatinine Clearance in Patients with Baseline CrCL 30-60 mL/min/1.73 m^2 with a Subsequent On-Treatment Reduction in CrCL < 30 mL/min/1.73 m^2



BL, baseline; CrCl, creatinine clearance; PT, post-treatment