Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Feld JJ, Jacobson IM, Hézode C, et al. Sofosbuvir and velpatasvir for HCV genotype 1, 2, 4, 5, and 6 infection. N Engl J Med. DOI: 10.1056/NEJMoa1512610

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Table S1. Reasons for screen failure

Screened Patients	847
Screen Failure Patients	106/847 (13%)
Screen Failure Patients Who Did Not Meet Eligibility Criteria	99/106 (93%)
Exclusion Criterion 3: Screening laboratory values not within acceptable ranges	51/99 (52%)
Exclusion Criterion 1: History of clinically-significant illness or any other major medical disorder	10/99 (10%)
Inclusion Criterion 3: HCV RNA $\geq 10^4$ IU/mL at Screening	9/99 (9%)
Exclusion Criterion 7: Infection with HBV or HIV	6/99 (6%)
Exclusion Criterion 2: Screening ECG with clinically significant abnormalities	5/99 (5%)
Exclusion Criterion 8: Clinically-relevant alcohol or drug abuse within 12 months of screening	5/99 (5%)
Inclusion Criterion 1: Willing and able to provide written informed consent	5/99 (5%)
Inclusion Criterion 7: Cirrhosis Determination	5/99 (5%)
Inclusion Criterion 13: Subject must be able to comply with the dosing instructions	4/99 (4%)
Inclusion Criterion 4: HCV genotype 1, 2, 4, 5, 6, or indeterminate	4/99 (4%)
Inclusion Criterion 6: Classification as treatment naive or treatment experienced	3/99 (3%)
Exclusion Criterion 5: Pregnant or nursing female or male with pregnant female partner	2/99 (2%)
Inclusion Criterion 8: Liver imaging within 6 months of Baseline/Day 1	2/99 (2%)
Inclusion Criterion 9: Negative pregnancy tests for females of childbearing potential	2/99 (2%)
Exclusion Criterion 4: Prior exposure to SOF or any other NS5B or NS5A inhibitor	1/99 (1%)
Inclusion Criterion 12: Subject must be of generally good health	1/99 (1%)
Screen Failure Patients Who Met Eligibility Criteria	
Reasons for Non-Enrollment of Patients Who Met Eligibility Criterion	
Withdrew Consent	4/7 (57%)
Lost to Follow-Up	2/7 (29%)
Other	1/7 (14%)

Figure S1. Patient disposition

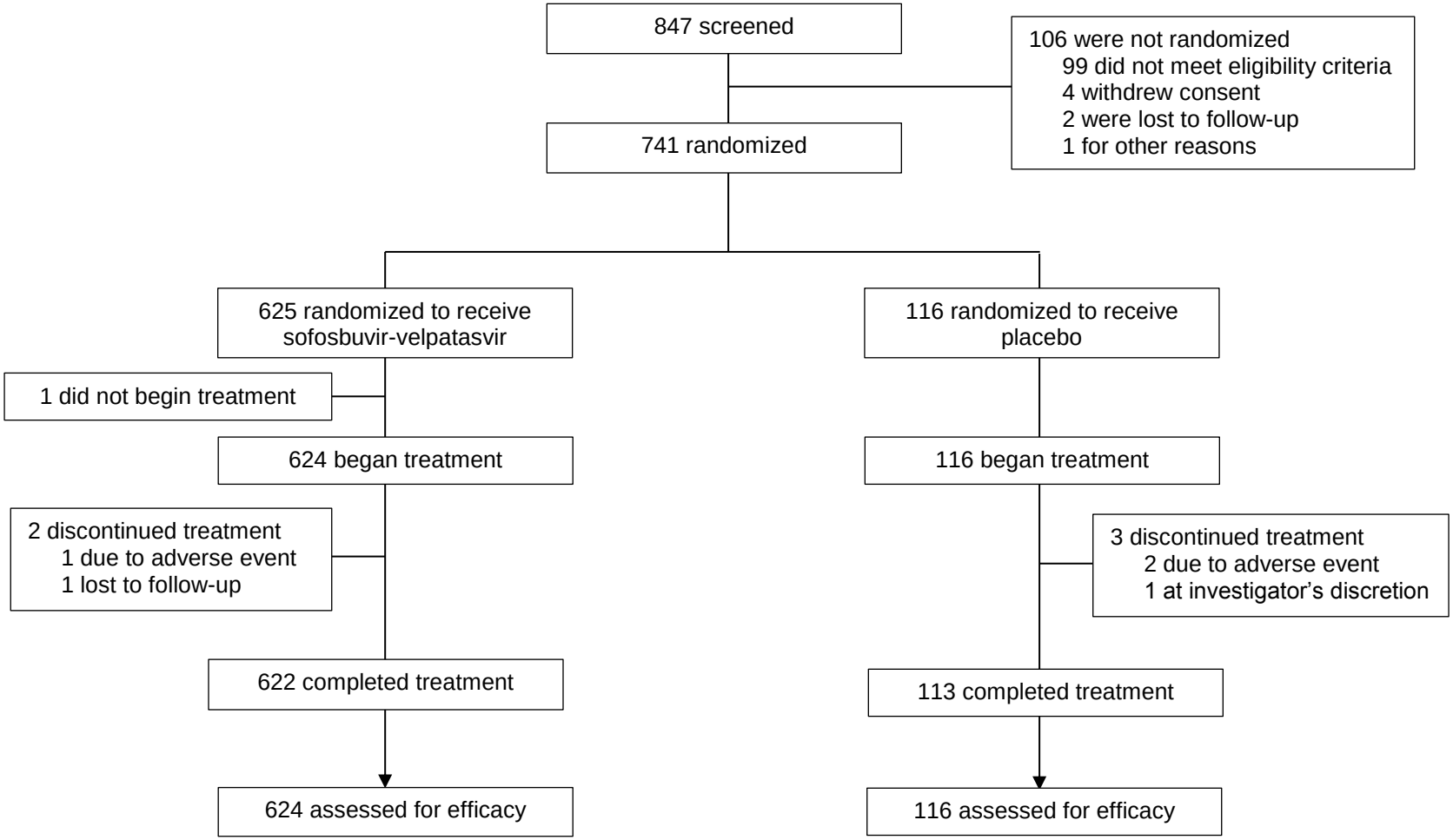

Table S2. Sustained virologic response by subgroups: genotype 1 patients

	SOF/GS-5816 12 Weeks			
	Total (All Genotypes) (N=624)	GT-1a (N=210)	GT-1b (N=118)	GT-1 Total (N=328)
Overall	618/624 (99.0%)	206/210 (98.1%)	117/118 (99.2%)	323/328 (98.5%)
95% CI	97.9% to 99.6%	95.2% to 99.5%	95.4% to 100.0%	96.5% to 99.5%
Age at Baseline (Years)				
< 65	530/536 (98.9%)	187/191 (97.9%)	100/101 (99.0%)	287/292 (98.3%)
95% CI	97.6% to 99.6%	94.7% to 99.4%	94.6% to 100.0%	96.0% to 99.4%
>= 65	88/88 (100.0%)	19/19 (100.0%)	17/17 (100.0%)	36/36 (100.0%)
95% CI	95.9% to 100.0%	82.4% to 100.0%	80.5% to 100.0%	90.3% to 100.0%
Sex at Birth				
Male	369/374 (98.7%)	136/139 (97.8%)	57/58 (98.3%)	193/197 (98.0%)
95% CI	96.9% to 99.6%	93.8% to 99.6%	90.8% to 100.0%	94.9% to 99.4%
Female	249/250 (99.6%)	70/71 (98.6%)	60/60 (100.0%)	130/131 (99.2%)
95% CI	97.8% to 100.0%	92.4% to 100.0%	94.0% to 100.0%	95.8% to 100.0%
Race				
White	488/493 (99.0%)	177/181 (97.8%)	98/98 (100.0%)	275/279 (98.6%)
95% CI	97.6% to 99.7%	94.4% to 99.4%	96.3% to 100.0%	96.4% to 99.6%
Black	51/52 (98.1%)	18/18 (100.0%)	6/7 (85.7%)	24/25 (96.0%)
95% CI	89.7% to 100.0%	81.5% to 100.0%	42.1% to 99.6%	79.6% to 99.9%
Other	76/76 (100.0%)	9/9 (100.0%)	13/13 (100.0%)	22/22 (100.0%)
95% CI	95.3% to 100.0%	66.4% to 100.0%	75.3% to 100.0%	84.6% to 100.0%
Baseline BMI (kg/m2)				
< 30	484/489 (99.0%)	155/158 (98.1%)	99/100 (99.0%)	254/258 (98.4%)
95% CI	97.6% to 99.7%	94.6% to 99.6%	94.6% to 100.0%	96.1% to 99.6%
>= 30	134/135 (99.3%)	51/52 (98.1%)	18/18 (100.0%)	69/70 (98.6%)
95% CI	95.9% to 100.0%	89.7% to 100.0%	81.5% to 100.0%	92.3% to 100.0%
Cirrhosis				
Yes	120/121 (99.2%)	49/49 (100.0%)	23/24 (95.8%)	72/73 (98.6%)
95% CI	95.5% to 100.0%	92.7% to 100.0%	78.9% to 99.9%	92.6% to 100.0%
No	496/501 (99.0%)	157/161 (97.5%)	94/94 (100.0%)	251/255 (98.4%)
95% CI	97.7% to 99.7%	93.8% to 99.3%	96.2% to 100.0%	96.0% to 99.6%

Table S2. Sustained virologic response by subgroups: genotype 1 patients (continued)

	SOF/GS-5816 12 Weeks			
	Total (All Genotypes) (N=624)	GT-1a (N=210)	GT-1b (N=118)	GT-1 Total (N=328)
IL28B				
CC	185/186 (99.5%)	47/48 (97.9%)	42/42 (100.0%)	89/90 (98.9%)
95% CI	97.0% to 100.0%	88.9% to 99.9%	91.6% to 100.0%	94.0% to 100.0%
Non-CC	428/433 (98.8%)	156/159 (98.1%)	75/76 (98.7%)	231/235 (98.3%)
95% CI	97.3% to 99.6%	94.6% to 99.6%	92.9% to 100.0%	95.7% to 99.5%
CT	336/339 (99.1%)	122/125 (97.6%)	59/59 (100.0%)	181/184 (98.4%)
95% CI	97.4% to 99.8%	93.1% to 99.5%	93.9% to 100.0%	95.3% to 99.7%
TT	92/94 (97.9%)	34/34 (100.0%)	16/17 (94.1%)	50/51 (98.0%)
95% CI	92.5% to 99.7%	89.7% to 100.0%	71.3% to 99.9%	89.6% to 100.0%
Baseline HCV RNA (IU/mL)				
< 800,000	161/163 (98.8%)	41/41 (100.0%)	31/32 (96.9%)	72/73 (98.6%)
95% CI	95.6% to 99.9%	91.4% to 100.0%	83.8% to 99.9%	92.6% to 100.0%
>= 800,000	457/461 (99.1%)	165/169 (97.6%)	86/86 (100.0%)	251/255 (98.4%)
95% CI	97.8% to 99.8%	94.1% to 99.4%	95.8% to 100.0%	96.0% to 99.6%
Prior HCV Treatment Experience				
Treatment-Naive	418/423 (98.8%)	128/132 (97.0%)	86/86 (100.0%)	214/218 (98.2%)
95% CI	97.3% to 99.6%	92.4% to 99.2%	95.8% to 100.0%	95.4% to 99.5%
Treatment-Experienced	200/201 (99.5%)	78/78 (100.0%)	31/32 (96.9%)	109/110 (99.1%)
95% CI	97.3% to 100.0%	95.4% to 100.0%	83.8% to 99.9%	95.0% to 100.0%
Prior HCV Treatment				
DAA+Peg-IFN+RBV	56/56 (100.0%)	37/37 (100.0%)	11/11 (100.0%)	48/48 (100.0%)
95% CI	93.6% to 100.0%	90.5% to 100.0%	71.5% to 100.0%	92.6% to 100.0%
Peg-IFN+RBV	121/122 (99.2%)	37/37 (100.0%)	13/14 (92.9%)	50/51 (98.0%)
95% CI	95.5% to 100.0%	90.5% to 100.0%	66.1% to 99.8%	89.6% to 100.0%
Other	23/23 (100.0%)	4/4 (100.0%)	7/7 (100.0%)	11/11 (100.0%)
95% CI	85.2% to 100.0%	39.8% to 100.0%	59.0% to 100.0%	71.5% to 100.0%

Table S3. Sustained virologic response by subgroups: genotype 2, 4, 5, 6 patients

(Continued)	SOF/GS-5816 12 Weeks			
	GT-2 (N=104)	GT-4 (N=116)	GT-5 (N=35)	GT-6 (N=41)
Overall	104/104 (100.0%)	116/116 (100.0%)	34/35 (97.1%)	41/41 (100.0%)
95% CI	96.5% to 100.0%	96.9% to 100.0%	85.1% to 99.9%	91.4% to 100.0%
Age at Baseline (Years)				
< 65	79/79 (100.0%)	105/105 (100.0%)	18/19 (94.7%)	41/41 (100.0%)
95% CI	95.4% to 100.0%	96.5% to 100.0%	74.0% to 99.9%	91.4% to 100.0%
>= 65	25/25 (100.0%)	11/11 (100.0%)	16/16 (100.0%)	0/0
95% CI	86.3% to 100.0%	71.5% to 100.0%	79.4% to 100.0%	
Sex at Birth				
Male	57/57 (100.0%)	86/86 (100.0%)	13/14 (92.9%)	20/20 (100.0%)
95% CI	93.7% to 100.0%	95.8% to 100.0%	66.1% to 99.8%	83.2% to 100.0%
Female	47/47 (100.0%)	30/30 (100.0%)	21/21 (100.0%)	21/21 (100.0%)
95% CI	92.5% to 100.0%	88.4% to 100.0%	83.9% to 100.0%	83.9% to 100.0%
Race				
White	82/82 (100.0%)	96/96 (100.0%)	34/35 (97.1%)	1/1 (100.0%)
95% CI	95.6% to 100.0%	96.2% to 100.0%	85.1% to 99.9%	2.5% to 100.0%
Black	13/13 (100.0%)	14/14 (100.0%)	0/0	0/0
95% CI	75.3% to 100.0%	76.8% to 100.0%		
Other	8/8 (100.0%)	6/6 (100.0%)	0/0	40/40 (100.0%)
95% CI	63.1% to 100.0%	54.1% to 100.0%		91.2% to 100.0%
Baseline BMI (kg/m2)				
< 30	84/84 (100.0%)	80/80 (100.0%)	26/27 (96.3%)	40/40 (100.0%)
95% CI	95.7% to 100.0%	95.5% to 100.0%	81.0% to 99.9%	91.2% to 100.0%
>= 30	20/20 (100.0%)	36/36 (100.0%)	8/8 (100.0%)	1/1 (100.0%)
95% CI	83.2% to 100.0%	90.3% to 100.0%	63.1% to 100.0%	2.5% to 100.0%
Cirrhosis				
Yes	10/10 (100.0%)	27/27 (100.0%)	5/5 (100.0%)	6/6 (100.0%)
95% CI	69.2% to 100.0%	87.2% to 100.0%	47.8% to 100.0%	54.1% to 100.0%
No	93/93 (100.0%)	89/89 (100.0%)	28/29 (96.6%)	35/35 (100.0%)
95% CI	96.1% to 100.0%	95.9% to 100.0%	82.2% to 99.9%	90.0% to 100.0%

Table S3. Sustained virologic response by subgroups: genotype 2, 4, 5, 6 patients (continued)

(Continued)	SOF/GS-5816 12 Weeks GT-2 (N=104)	GT-4 (N=116)	GT-5 (N=35)	GT-6 (N=41)
IL28B				
CC	30/30 (100.0%)	27/27 (100.0%)	11/11 (100.0%)	28/28 (100.0%)
95% CI	88.4% to 100.0%	87.2% to 100.0%	71.5% to 100.0%	87.7% to 100.0%
Non-CC	74/74 (100.0%)	89/89 (100.0%)	23/24 (95.8%)	11/11 (100.0%)
95% CI	95.1% to 100.0%	95.9% to 100.0%	78.9% to 99.9%	71.5% to 100.0%
CT	56/56 (100.0%)	68/68 (100.0%)	21/21 (100.0%)	10/10 (100.0%)
95% CI	93.6% to 100.0%	94.7% to 100.0%	83.9% to 100.0%	69.2% to 100.0%
TT	18/18 (100.0%)	21/21 (100.0%)	2/3 (66.7%)	1/1 (100.0%)
95% CI	81.5% to 100.0%	83.9% to 100.0%	9.4% to 99.2%	2.5% to 100.0%
Baseline HCV RNA (IU/mL)				
< 800,000	29/29 (100.0%)	42/42 (100.0%)	8/9 (88.9%)	10/10 (100.0%)
95% CI	88.1% to 100.0%	91.6% to 100.0%	51.8% to 99.7%	69.2% to 100.0%
>= 800,000	75/75 (100.0%)	74/74 (100.0%)	26/26 (100.0%)	31/31 (100.0%)
95% CI	95.2% to 100.0%	95.1% to 100.0%	86.8% to 100.0%	88.8% to 100.0%
Prior HCV Treatment Experience				
Treatment-Naive	79/79 (100.0%)	64/64 (100.0%)	23/24 (95.8%)	38/38 (100.0%)
95% CI	95.4% to 100.0%	94.4% to 100.0%	78.9% to 99.9%	90.7% to 100.0%
Treatment-Experienced	25/25 (100.0%)	52/52 (100.0%)	11/11 (100.0%)	3/3 (100.0%)
95% CI	86.3% to 100.0%	93.2% to 100.0%	71.5% to 100.0%	29.2% to 100.0%
Prior HCV Treatment				
DAA+Peg-IFN+RBV	0/0	6/6 (100.0%)	2/2 (100.0%)	0/0
95% CI		54.1% to 100.0%	15.8% to 100.0%	
Peg-IFN+RBV	22/22 (100.0%)	39/39 (100.0%)	7/7 (100.0%)	3/3 (100.0%)
95% CI	84.6% to 100.0%	91.0% to 100.0%	59.0% to 100.0%	29.2% to 100.0%
Other	3/3 (100.0%)	7/7 (100.0%)	2/2 (100.0%)	0/0
95% CI	29.2% to 100.0%	59.0% to 100.0%	15.8% to 100.0%	

Table S4. Characteristics of patients with virologic relapse

Age	Sex	Race	BMI	GT	Cirrhosis	IL28B	HCV RNA	Timing of VF	HCV treatment history	Resistance-associated variants			
										NS5A		NS5B	
										BL	FU	BL	FU
56	M	White	22	1a	No	CT	6.5	FU wk 4	Naive	Q30R (2.6%)	Y93N (>99%)	None	None
58	M	Black	27	1b	Yes	TT	6.8	FU wk 4	Prev Peg/RBV	Q30L (1.1%) Q30R (98.7%) L31M (>99%)	Q30R (>99%) L31I (2.8%) L31M (88.4%) L31V (8.6%) Y93H (72.3%)	None	None

BMI denotes body mass index; GT, genotype; VF, virologic failure; BL, baseline; FU, follow-up.

Table S5. Patients Receiving Sofosbuvir-Velpatasvir Who Experienced Serious Adverse Events

Age	Sex	Race	Genotype	Cirrhosis	Serious Adverse Event	Date of Onset	Relevant History
63	M	White	1a	No	Abscess in left foot Cellulitis in left foot Necrosis in left foot	Post-treatment day 4	Type 2 diabetes mellitus with peripheral neuropathy, radiculopathy and bilateral foot pain.
66	F	White	2b	No	Acute myocardial infarction	Post-treatment day 10	Low hypertension with underlying coronary artery disease. Acute STEMI (complete left anterior descending artery occlusion) and ischemic cardiomyopathy (left ventricular ejection fraction 35 to 40%)
59	M	Asian	1b	No	Recurring appendicitis	Treatment day 43	Diverticular disease with ruptured appendix 5 months earlier
50	M	White	4	No	Bronchitis	Post-treatment day 26	Long term smoker (60 pack years) with likely underlying chronic obstructive pulmonary disease
60	F	White	1a	No	Chronic obstructive pulmonary disease Influenza	Post-treatment day 20	Chronic obstructive pulmonary disease, splenectomy with COPD exacerbation due to influenza during the flu season
64	M	White	2b	No	Epileptic seizure	Treatment day 50	Hypertension, aneurysm with epileptic seizure (CT with hypodense left periventricular lesions)
63	M	ND	1a	No	Gastroenteritis	Treatment day 79	None
48	M	Asian	6a/6b	No	Ligament sprain in right arm Rotator cuff syndrome	Treatment day 48	Accidental fall from height
66	F	White	2a/2c	No	Lung cancer	Treatment day 82	Long-term smoker (100 pack years)
45	F	White	1a	No	Mania	Post-treatment day 10	Anxiety and sleep disorder
55	M	White	1a	No	Palpitations	Treatment day 30	Ventricular extrasystoles and sarcoidosis.
65	F	Black	1b	No	Small bowel obstruction	Post-treatment day 12	Obesity, colon adenoma and Roux en Y gastric bypass
55	M	White	5a	No	Sudden death during sleep	Post-treatment day 8	Dyslipidemia on simvastatin and ezetimibe
56	F	White	1b	No	Upper limb fracture	Treatment day 48	Fall while ice skating
69	F	White	5a	No	Vestibular neuronitis	Treatment day 72	History of hypertension, diagnosed with hypertensive crisis and vertigo 9 days earlier

ND denotes not disclosed.