SUPPLEMENTARY TABLES AND FIGURES

TABLE S1 Sample size determination based on expected SVR rates

95%, 2-sided CI	**Expected SVR rate (%)**	
Sample size	**90%**	**95%**
N=20	(68.3−98.8)	(75.1−99.9)
N=40	(76.3−97.2)	(83.1−99.4)

CI, confidence interval; SVR, sustained virologic response.

TABLE S2 PK parameters for ledipasvir in Panel 1

Parameter	Panel 1 LDV/SOF 90/400 mg QD + SMV 150 mg QD (Day 28)
n	20
C_{trough}, ng/ml	505 (50.7)
C_{min}, ng/ml	436 (47.7)
C_{max}, ng/ml	731 (43.4)
t_{max}, h	4.02 (2.00–24.00)
AUC_{τ}, ng.h/ml	13468 (44.1)
$C_{ss,avg}$, ng/ml	560 (44.1)

All values are geometric mean (% CV) except median (range) for t_{max}.

AUC_{τ}, area under the curve at steady state; C_{max}, maximum plasma concentration; C_{min}, minimum plasma concentration; $C_{ss,avg}$, the average steady-state plasma concentration; C_{trough}, trough plasma concentration; CV, coefficient of variation; LDV, ledipasvir; PK, pharmacokinetic; QD, once daily; SMV, simeprevir; SOF, sofosbuvir; t_{max}, time to C_{max}.

TABLE S3 PK parameters for simeprevir in Panel 2

Parameter	Panel 2 SMV 150 mg QD + LDV/SOF 90/400 mg QD (Day 28)
n	18[a]
C_{trough}, ng/ml	5266 (72.2)
C_{min}, ng/ml	4889 (68.6)
C_{max}, ng/ml	11267 (45.0)
t_{max}, h	6.00 (4.00–11.98)
AUC_{τ}, ng.h/ml	186822 (55.2)
$C_{ss,avg}$, ng/ml	7774 (55.1)

All values are geometric mean (% CV) except median (range) for t_{max}.; [a]Due to PK profile not taken for 2 patients.

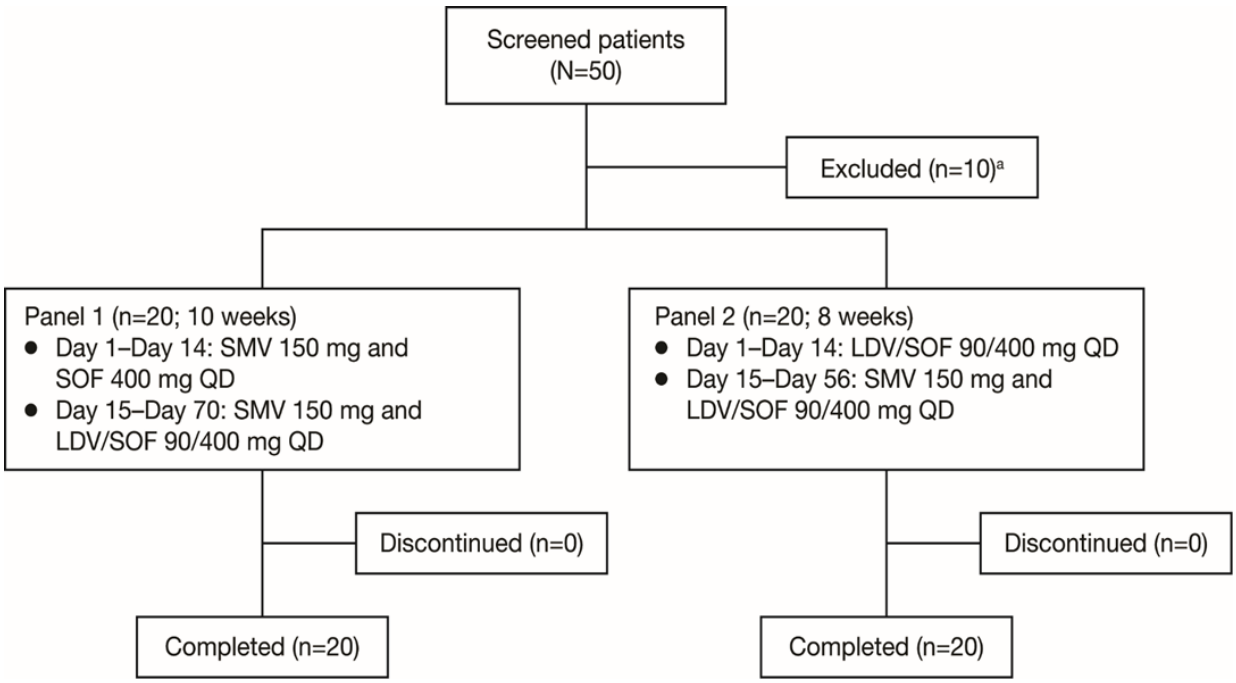
AUC_{τ}, area under the curve at steady state; C_{max}, maximum plasma concentration; C_{min}, minimum plasma concentration; $C_{ss,avg}$, the average steady-state plasma concentration; C_{trough}, trough plasma concentration; CV, coefficient of variation; LDV, ledipasvir; PK, pharmacokinetic; QD, once daily; SMV, simeprevir; SOF, sofosbuvir; t_{max}, time to C_{max}.

TABLE S4 PK parameter ratios for simeprevir and ledipasvir at Day 28 versus Day 14

	PK parameter ratios of SMV, Day 28/14			**PK parameter ratios of LDV, Day 28/14**		
	C_{min} (%)	**C_{max} (%)**	**AUC_{τ} (%)**	**C_{min} (%)**	**C_{max} (%)**	**AUC_{τ} (%)**
N	20	19	19	18	17	17
Mean	619.67	258.48	356.34	182.35	171.17	180.98
SD	422.82	118.46	207.21	55.19	50.24	48.01
Min	108.39	118.13	112.03	97.47	87.78	104.30
Median	584.33	248.94	350.57	179.34	155.93	174.88
Max	1632.39	533.65	903.58	335.29	275.70	284.18
% CV	68.2	45.8	58.2	30.3	29.4	26.5

AUC_{τ}, area under the curve at steady state; C_{max}, maximum plasma concentration; C_{min}, minimum plasma concentration; CV, coefficient of variation; LDV, ledipasvir; PK, pharmacokinetic; SMV, simeprevir.

Fig. S1. Patient disposition (ITT population).



[a]Due to the following reasons: HCV RNA >6,000,000 IU/ml (5/10), HCV RNA >6,000,000 IU/ml and BMI out of range (1/10), BMI was too high (1/10), no suitable veins (1/10), no suitable veins/drug abuse/no stable medication intake (1/10), withdrawal of consent (1/10).

BMI, body mass index; HCV, hepatitis C virus; ITT, intent-to-treat; LDV, ledipasvir; QD, once daily; SMV, simeprevir; SOF, sofosbuvir.