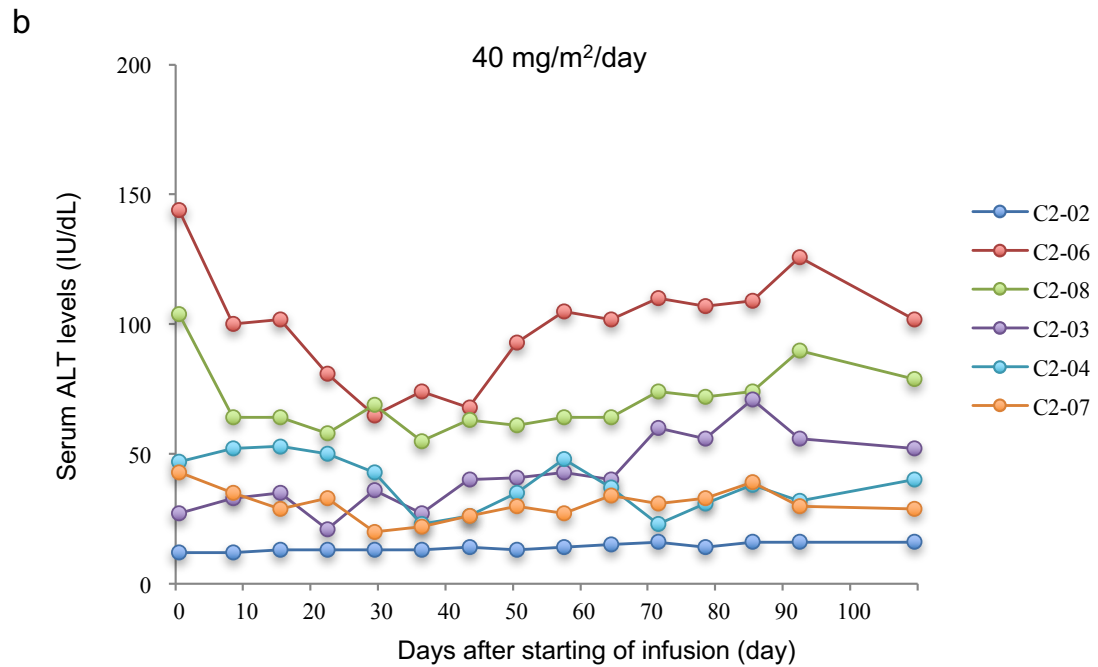
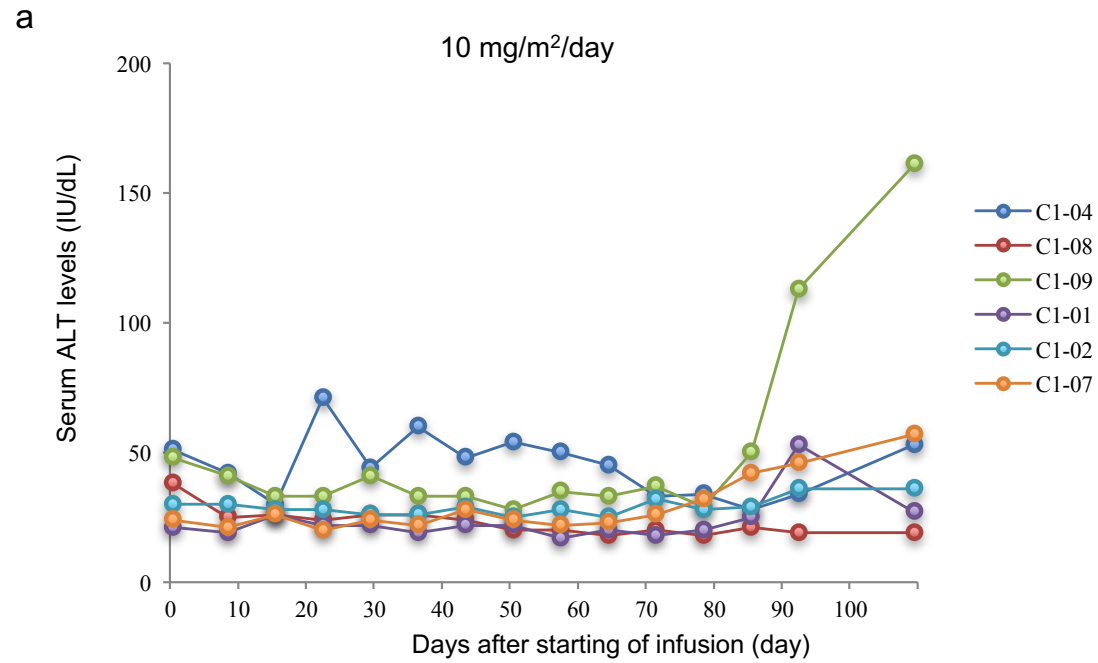
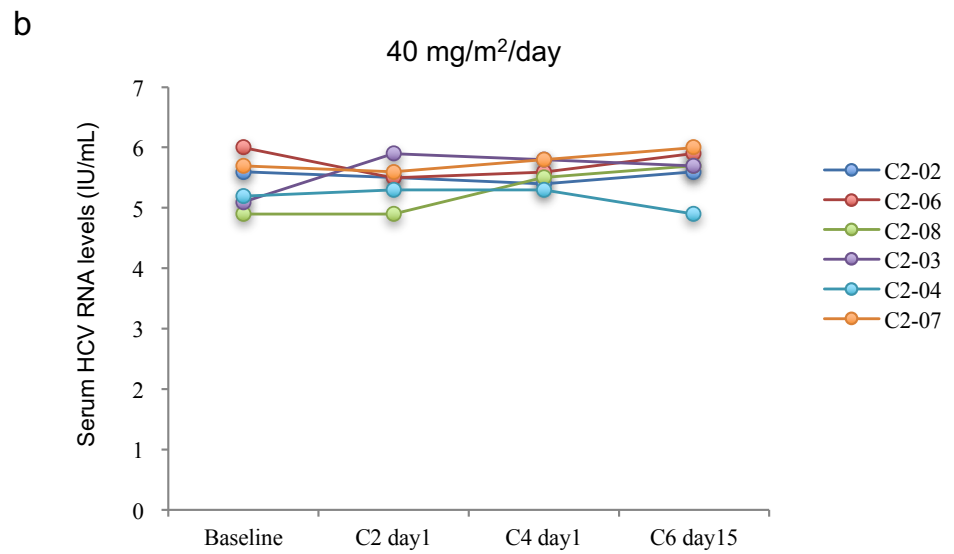
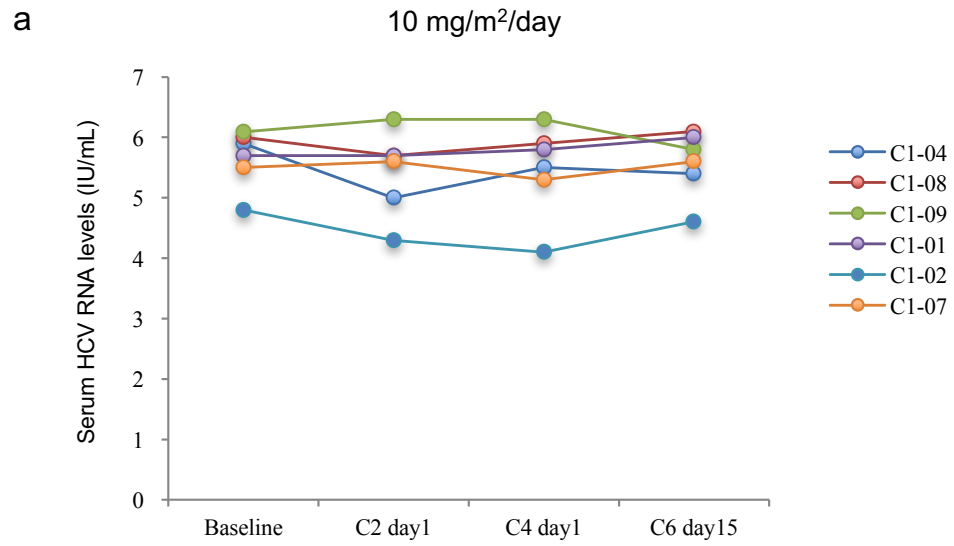


## **Supplemental Data**



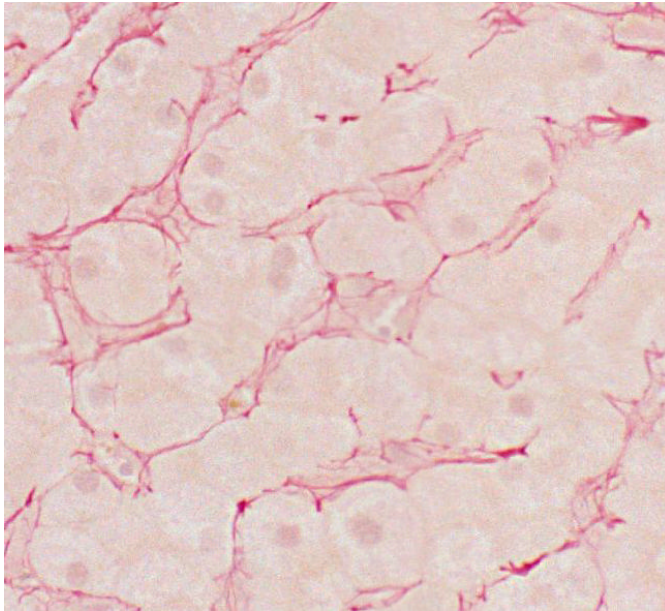
Supplementary Figure 1. Change in serum ALT level after PRI-724 infusion  
 Serum ALT levels of individual patients dosed with 10 mg/m<sup>2</sup>/day PRI-724 (A) and 40 mg/m<sup>2</sup>/day PRI-724 (B) throughout the entire study period.



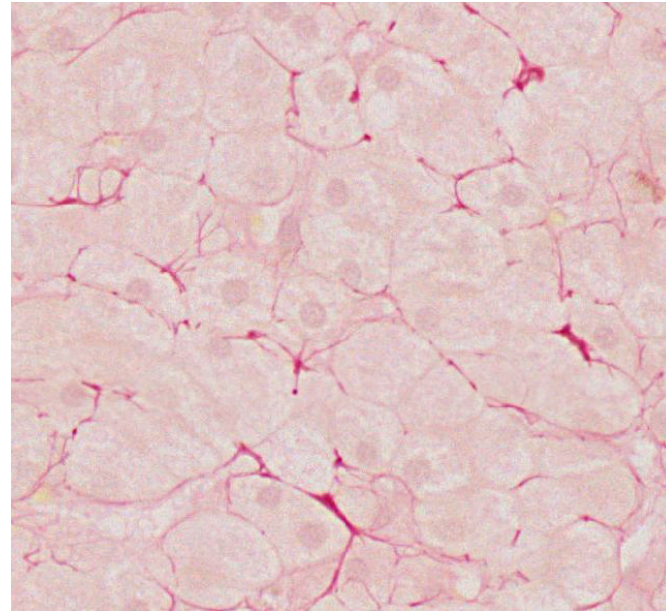
Supplementary Figure 2. Change in serum HCV RNA levels after PRI-724 infusion  
 Serum HCV RNA levels of individual patients dosed with 10 mg/m<sup>2</sup>/day PRI-724 (A) and 40 mg/m<sup>2</sup>/day PRI-724 (B) throughout the entire study period.

C2-03

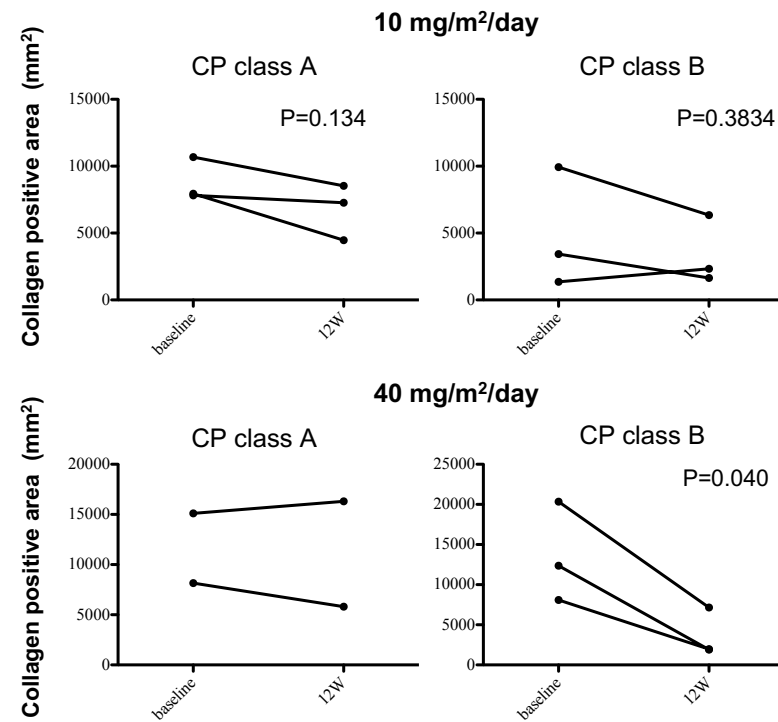
Baseline



12 W



Supplementary Figure 3. Histopathology of hepatic lobules stained with Sirius red (X40)  
Liver biopsy sample from patient C2-03 patient (40 mg/m<sup>2</sup>/day PRI-724 in CP class B cohort).



Supplementary Figure 4. Evaluation of anti-fibrotic effect in hepatic lobules of patients with CP class after PRI-724 infusion. The average of the measured collagen positive areas was compared between baseline and 12 weeks after PRI-724 infusion. Statistical analyses were performed on data from each CP class, using the paired T test.

Cohort	CP class	Pt	time	Histological activity index					HAI score
				Interface hepatitis	Confluent necrosis	Lobular inflammation	Portal inflammation	Stage	
10 mg/m <sup>2</sup> /day	A	C1-04	Baseline	3	0	3	3	5	14
			C6 day15	1	0	1	2	5	9
		C1-08	Baseline	2	0	2	1	3	8
			C6 day15	2	0	2	2	4	10
		C1-09	Baseline	4	0	2	2	5	13
			C6 day15	4	0	2	3	6	15
	B	C1-01	Baseline	3	0	1	3	6	13
			C6 day15	3	0	2	2	5	12
		C1-02	Baseline	4	0	4	3	6	17
			C6 day15	4	0	4	3	6	17
		C1-07	Baseline	4	0	2	4	6	16
			C6 day15	3	0	2	2	6	13
40 mg/m <sup>2</sup> /day	A	C2-02	Baseline	1	0	1	2	6	10
			C6 day15	1	0	1	1	6	9
		C2-06	Baseline	2	0	3	3	5	13
			C6 day15	1	0	3	3	5	12
		C2-08	Baseline	3	0	2	3	6	14
			C6 day15	3	0	2	3	6	14
	B	C2-03	Baseline	3	0	2	2	6	13
			C6 day15	2	0	2	2	6	12
		C2-04	Baseline	2	0	2	2	6	12
			C6 day15	2	0	2	2	5	11
		C2-07	Baseline	3	0	3	3	6	15
			C6 day15	3	0	2	3	5	13
160 mg/m <sup>2</sup> /day	B	C3-01	Baseline	3	0	3	3	6	15
			C6 day15	-	-	-	-	-	-
		C3-03	Baseline	4	0	4	4	6	18
			C6 day15	-	-	-	-	-	-

Supplementary Table 1. Changes in HAI score after PRI-724 infusion

Cohort	CP class	Pt	time	Pericellular collagen positive area (mm <sup>2</sup> )			
				MEAN	SD	MIN	MAX
10 mg/m <sup>2</sup> /day	A	C1-04	Baseline	7941.04	5055.83	4349.36	17861.64
			C6 day15	4474.88	1671.73	2238.97	6567.69
		C1-08	Baseline	10687.26	3881.57	7616.99	17962.5
			C6 day15	8535.7	3073.07	2592.28	11434.33
	C1-09	Baseline	7823.31	2066.57	4607.71	11084.56	
		C6 day15	7264.51	3257.7	924.84	9537.45	
	B	C1-01	Baseline	1356.24	842.75	399.31	2563.96
			C6 day15	2326.27	582.7	828.11	4420.73
		C1-02	Baseline	9929.68	5756.04	3207.46	19999.75
			C6 day15	6345.68	2173.2	3497.66	9278.52
C1-07		Baseline	3432.54	868.73	1955.86	4380.62	
		C6 day15	1645.73	789.16	349.18	2565.73	
40 mg/m <sup>2</sup> /day	A	C2-02	Baseline	15108.34	2900.79	9914.35	18880.27
			C6 day15	16303.44	1956.97	14158.73	19964.95
		C2-06	Baseline	8151.49	1311.46	6553.53	10014.03
			C6 day15	5807.05	2228.55	1623.79	7766.8
	C2-08	Baseline	1583.44	855.48	169.87	2597	
		C6 day15	-	-	-	-	
	B	C2-03	Baseline	20334.77	789.73	19376.31	21550.99
			C6 day15	7162.12	534.41	6279.27	7889.49
		C2-04	Baseline	12359.76	1947.24	10285.35	15754.79
			C6 day15	1913.51	1974.47	447.68	5790.3
C2-07	Baseline	8096.4	2984.35	4617.14	12488.34		
	C6 day15	1974.02	1353.24	523.17	3866.89		
160 mg/m <sup>2</sup> /day	B	C3-01	Baseline	2907.83	1627.01	1941.7	5924.78
			C6 day15	-	-	-	-
	C3-03	Baseline	27093.33	15791.98	10353.18	53842.08	
		C6 day15	-	-	-	-	

Supplementary Table 2. Changes of pericellular collagen positive areas in the hepatic lobules after PRI-724 infusion

Cohort	CP class	Pt	time	Child-Pugh score					C-P score
				Coma	Ascites	Total Bilirubin	Albumin	Prothrombin Time	
10 mg/m <sup>2</sup> /day	A	C1-04	Baseline	1	1	1	1	1	5
			C6 day15	1	1	1	1	2	6
		C1-08	Baseline	1	1	1	1	1	5
			C6 day15	1	1	1	1	1	5
		C1-09	Baseline	1	1	1	1	1	5
	C6 day15		1	1	1	1	1	5	
	B	C1-01	Baseline	1	1	1	2	2	7
			C6 day15	1	1	1	2	2	7
		C1-02	Baseline	1	2	1	3	2	9
			C6 day15	1	2	2	3	2	10
C1-07		Baseline	1	1	1	2	2	7	
	C6 day15	1	1	1	2	2	7		
40 mg/m <sup>2</sup> /day	A	C2-02	Baseline	1	1	1	1	2	6
			C6 day15	1	1	1	1	1	5
		C2-06	Baseline	1	1	1	1	1	5
			C6 day15	1	1	1	1	1	5
		C2-08	Baseline	1	1	1	2	1	6
			C6 day15	1	1	1	1	1	5
	B	C2-03	Baseline	1	1	1	2	2	7
			C6 day15	1	1	1	2	2	7
		C2-04	Baseline	1	1	1	2	2	7
			C6 day15	1	1	1	2	2	7
		C2-07	Baseline	1	2	1	3	1	8
			C6 day15	1	1	1	2	1	6
160 mg/m <sup>2</sup> /day	B	C3-01	Baseline	1	2	2	2	2	9
			C4 day1*	1	1	1	2	1	6
		C3-03	Baseline	1	1	2	2	2	8
			C6 day15	-	-	-	-	-	-

\* C3-01 shows the data of C4 day1.

Supplementary Table 3. Changes in C-P score after PRI-724 infusion



		N	MEAN	SD	MIN	MEDIAN	MAX
10 mg/m <sup>2</sup> /day	Baseline	6	220	163.3	100	175	530
	C4 day1	6	256.7	151.3	110	190	520
	C6 day15	6	240	146	100	185	480
40 mg/m <sup>2</sup> /day	Baseline	6	528.3	261.4	200	535	820
	C4 day1	6	425	237.4	160	370	750
	C6 day15	6	465	247.3	180	480	730
160 mg/m <sup>2</sup> /day	Baseline	2	295	21.2	280	295	310
	C4 day1	1	160	-	160	160	160
	C6 day15	1	260	-	260	260	260

Supplementary Table 4. Changes in serum PTH levels (pg/mL) after PRI-724 infusion

		N	MEAN	SD	MIN	MEDIAN	MAX
10 mg/m <sup>2</sup> /day	Baseline	6	18.55	4.13	11.6	19.6	23
	C4 day1	6	21.32	6.63	10.2	23.2	27.5
	C6 day15	6	22.07	9.01	10.2	23.65	32.1
40 mg/m <sup>2</sup> /day	Baseline	6	20.18	6.18	14.6	17.95	31.7
	C4 day1	6	19.23	4.93	14.2	18.15	27.2
	C6 day15	6	22.8	7.31	17.1	19.7	36.3
160 mg/m <sup>2</sup> /day	Baseline	2	37.45	13.93	27.6	37.45	47.3
	C4 day1	1	38.7	-	38.7	38.7	38.7
	C6 day15	1	40.9	-	40.9	40.9	40.9

Supplementary Table 5. Changes in serum Bone Specific Alkaline Phosphatase (BAP) levels (ug/L) after PRI-724 infusion

		N	MEAN	SD	MIN	MEDIAN	MAX
10 mg/m <sup>2</sup> /day	Baseline	6	6.37	4.01	1.5	7.2	11
	C4 day1	6	9.55	2.5	6.6	10	13
	C6 day15	6	10.15	2.49	7.3	10.5	14
40 mg/m <sup>2</sup> /day	Baseline	6	9.37	4.88	4.3	8.25	16.9
	C4 day1	6	10.95	7.85	4.8	8.9	26
	C6 day15	6	11.1	6.59	5.9	8.8	23.5
160 mg/m <sup>2</sup> /day	Baseline	2	17.45	0.78	16.9	17.45	18
	C4 day1	1	17	-	17	17	17
	C6 day15	1	8.2	-	8.2	8.2	8.2

Supplementary Table 6. Changes in serum osteocalcin levels (ng/mL) after PRI-724 infusion

		N	MEAN	SD	MIN	MEDIAN	MAX
10 mg/m <sup>2</sup> /day	Baseline	6	170.8	78.1	66	160	284
	C4 day1	6	174.8	68.9	67	175	275
	C6 day15	6	184.2	100.9	81	165	370
40 mg/m <sup>2</sup> /day	Baseline	6	154.7	109.9	28	169.5	270
	C4 day1	6	119.2	93.5	12	104	243
	C6 day15	6	171.2	128.1	13	162.5	347
160 mg/m <sup>2</sup> /day	Baseline	2	138	36.8	112	138	164
	C4 day1	1	99	-	99	99	99
	C6 day15	1	35	-	35	35	35

Supplementary Table 7. Changes in urine C-terminal telopeptide of type I collagen degradation products (CTX) levels ( $\mu\text{g}/\text{mmol} \cdot \text{Cr}$ ) after PRI-724 infusion