Supplementary Table S1. Phase I patient demographics and baseline disease characteristics									
Characteristic	Group I				Group II				
	Nintedanib, 100 mg bid	Nintedanib, 150 mg bid	Nintedanib, 200 mg bid	Total	Nintedanib, 50 mg bid	Nintedanib, 100 mg bid	Nintedanib, 150 mg bid	Nintedanib, 200 mg bid	Total
Number of patients, *n*	6	3	4	13	3	4	4	8	19
Median age, y (range)	72.0 (56–74)	61.0 (60–74)	67.5 (60–74)	70.0 (56–74)	70.0 (62–85)	55.5 (50–64)	60.0 (42–75)	62.0 (38–68)	62.0 (38–85)
Gender, *n* (%)									
Male	5 (83.3)	2 (66.7)	4 (100)	11 (84.6)	3 (100)	4 (100)	3 (75.0)	6 (75.0)	16 (84.2)
Female	1 (16.7)	1 (33.3)	0	2 (15.4)	0	0	1 (25.0)	2 (25.0)	3 (15.8)
Race, *n* (%)									
Black	1 (16.7)	0	0	1 (7.7)	1 (33.3)	1 (25.0)	1 (25.0)	1 (12.5)	4 (21.1)
Caucasian	5 (83.3)	3 (100)	4 (100)	12 (92.3)	2 (66.7)	2 (50.0)	1 (25.0)	7 (87.5)	12 (63.2)
Median time since diagnosis, mo (range)	8.1 (1.0–20.7)	1.5 (1.1–8.5)	7.0 (1.0–15.2)	1.8 (1.0–20.7)	3.0 (0.8–3.6)	6.8 (0.7–12.2)	1.8 (0.5–15.1)	2.4 (0.2–12.0)	2.5 (0.2–15.1)
ECOG PS, *n* (%)									
0	5 (83.3)	3 (100)	3 (75)	11 (84.6)	2 (66.7)	2 (50.0)	0	4 (50.0)	8 (42.1)
1	1 (16.7)	0	1 (25.0)	2 (15.4)	1 (33.3)	2 (50.0)	3 (75.0)	4 (50.0)	10 (52.6)
2	0	0	0	0	0	0	1 (25.0)	0	1 (5.3)
Child-Pugh score, *n* (%)									
5	4 (66.7)	3 (100)	3 (75.0)	10 (76.9)	3 (100)	3 (75.0)	2 (50.0)	2 (25.0)	10 (52.6)
6	2 (33.3)	0	1 (25.0)	3 (23.1)	0	0	1 (25.0)	6 (75.0)	7 (36.8)
7	0	0	0	0	0	1 (25.0)	1 (25.0)	0	2 (10.5)
BCLC stage, *n* (%)									
0	0	0	0	0	0	0	0	0	0
A	0	0	0	0	0	0	0	0	0
B	4 (66.7)	0	1 (25.0)	5 (38.5)	0	1 (25.0)	0	1 (12.5)	2 (10.5)
C	2 (33.3)	3 (100)	3 (75.0)	8 (61.5)	3 (100)	3 (75.0)	4 (100)	7 (87.5)	17 (89.5)
D	0	0	0	0	0	0	0	0	0
MVI present, *n* (%)	2 (33.3)	1 (33.3)	1 (25.0)	4 (30.8)	1 (33.3)	1 (25.0)	2 (50.0)	6 (75.0)	10 (52.6)

EHS present, *n* (%)	3 (50.)	3 (100)	2 (50.0)	8 (61.5)	3 (100)	2 (50.0)	2 (50.0)	2 (25.0)	9 (47.4)
Location of EHS, *n* (%)									
Bone	0	0	1 (25.0)	1 (7.7)	0	1 (25.0)	0	0	1 (5.3)
Lung	1 (16.7)	0	1 (25.0)	2 (15.4)	0	2 (50.0)	2 (50.0)	1 (12.5)	5 (26.3)
Lymph	3 (50.0)	2 (66.7)	1 (25.0)	6 (46.2)	3 (100)	1 (25.0)	0	1 (12.5)	5 (26.3)
Other	0	2 (66.7)	0	2 (15.4)	2 (66.7)	0	1 (25.0)	1 (12.5)	4 (21.1)
Aetiology of parenchymal liver disease, *n* (%)									
Alcohol Related	3 (50.0)	0	2 (50.0)	5 (38.5)	0	0	0	2 (25.0)	2 (10.5)
HBV related	0	0	0	0	2 (66.7)	0	1 (25.0)	1 (12.5)	4 (21.1)
HCV related	1 (16.7)	0	0	1 (7.7)	0	2 (50.0)	2 (50.0)	3 (37.5)	7 (36.8)
HBV + HCV Related	0	0	0	0	0	0	0	0	0
Unknown	2 (33.3)	0	0	2 (15.4)	1 (33.3)	2 (50.0)	0	1 (12.5)	4 (21.1)
Other	0	3 (100)	2 (50.0)	5 (38.5)	0	0	1 (25.0)	1 (12.5)	2 (10.5)
Parenchymal liver disease, *n* (%)									
Chronic hepatitis	0	0	0	0	0	1 (25.0)	0	0	1 (5.3)
Steatofibrosis	1 (16.7)	0	0	1 (7.7)	0	0	0	0	0
Cirrhosis	5 (83.3)	0	2 (50.0)	7 (53.8)	2 (66.7)	2 (50.0)	2 (50.0)	6 (75.0)	12 (63.2)
No evidence	0	3 (100)	1 (25.0)	4 (30.8)	1 (33.3)	1 (25.0)	1 (25.0)	1 (12.5)	4 (21.1)
Unknown	0	0	0	0	0	0	1 (25.0)	0	1 (5.3)
Other	0	0	1 (25.0)	1 (7.7)	0	0	0	1 (12.5)	1 (5.3)
Type of local therapy, *n* (%)									
Complete surgical resection	0	0	0	0	0	0	0	0	0
RFA	0	0	1 (25.0)	1 (7.7)	0	0	0	0	0
PEI	0	0	0	0	0	0	0	0	0
TACE	0	0	0	0	0	0	0	2 (25.0)	2 (10.5)
RT	0	0	0	0	0	0	0	1 (12.5)	1 (5.3)

Other	0	0	0	0	0	0	1 (25.0)	0	1 (5.3)

Abbreviations: BCLC, Barcelona Clinic Liver Cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; EHS, extrahepatic spread; HBV, hepatitis B; HCV, hepatitis C; MVI, macrovascular invasion; PEI, percutaneous ethanol injection; RFA, radiofrequency ablation; RT, radiotherapy; TACE, transarterial chemoembolization.