**Supplementary Table S5. Phase I patient demographics and baseline disease characteristics.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **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* | 4 | 3 | 3 | 10 |  | 3 | 7 | 3 | 16 | 29 |
| Median age, y (range) | 48.0 (24–58) | 57.0 (51–59) | 50.0 (40–53) | 50.5 (24–59) |  | 70.0 (47–76) | 66.0 (47–77) | 70.0 (58–78) | 58.5 (32–74) | 61.0 (32–78) |
| Gender, *n* (%) |  |  |  |  |  |  |  |  |  |  |
|  Male | 4 (100) | 3 (100) | 3 (100) | 10 (100) |  | 3 (100) | 7 (100) | 2 (66.7) | 13 (81.3) | 25 (86.2) |
|  Female | 0 | 0 | 0 | 0 |  | 0 | 0 | 1 (33.3) | 3 (18.8) | 4 (13.8) |
| Race, *n* (%) |  |  |  |  |  |  |  |  |  |  |
|  Taiwanese | 4 (100) | 3 (100) | 3 (100) | 10 (100) |  | 3 (100) | 7 (100) | 3 (100) | 15 (93.8)a | 28 (96.6) |
| Median time since diagnosis, mo (range) | 14.1 (0.7–54.0) | 34.7 (0.7–38.9) | 5.2 (0.5–78.3) | 14.1 (0.5–78.3) |  | 1.2 (0.3–5.9) | 3.8 (1.5–22.4) | 20.7 (5.8–62.6) | 5.0 (0.4–136.0) | 5.3 (0.3–136.0) |
| ECOG PS, *n* (%) |  |  |  |  |  |  |  |  |  |  |
|  0 | 1 (25.0) | 2 (66.7) | 3 (100) | 6 (60.0) |  | 2 (66.7) | 4 (57.1) | 3 (100) | 12 (75.0) | 21 (72.4) |
|  1 | 3 (75.0) | 0 | 0 | 3 (30.0) |  | 1 (33.3) | 3 (42.9) | 0 | 4 (25.0) | 8 (27.6) |
|  2 | 0 | 1 (33.3) | 0 | 1 (10.0) |  | 0 | 0 | 0 | 0 | 0 |
| Child-Pugh score, *n* (%) |  |  |  |  |  |  |  |  |  |  |
|  5 | 4 (100) | 3 (100) | 3 (100) | 10 (100) |  | 3 (100) | 4 (57.1) | 2 (66.7) | 8 (50.0) | 17 (58.6) |
|  6 | 0 | 0 | 0 | 0 |  | 0 | 1 (14.3) | 1 (33.3) | 5 (31.3) | 7 (24.1) |
|  7 | 0 | 0 | 0 | 0 |  | 0 | 2 (28.6) | 0 | 3 (18.8) | 5 (17.2) |
| BCLC stage, *n* (%) |  |  |  |  |  |  |  |  |  |  |
|  0 | 0 | 0 | 0 | 0 |  | 0 | 0 | 0 | 0 | 0 |
|  A | 0 | 0 | 0 | 0 |  | 0 | 0 | 0 | 0 | 0 |
|  B | 0 | 0 | 0 | 0 |  | 0 | 0 | 0 | 4 (25.0) | 4 (13.8) |
|  C | 4 (100) | 3 (100) | 3 (100) | 10 (100) |  | 3 (100) | 7 (100) | 3 (100) | 12 (75.0) | 25 (86.2) |
|  D | 0 | 0 | 0 | 0 |  | 0 | 0 | 0 | 0 | 0 |
| MVI present, *n* (%) | 1 (25.0) | 2 (66.7) | 0 | 3 (30.0) |  | 3 (100) | 3 (42.9) | 0 | 8 (50.0) | 14 (48.3) |
| EHS present, *n* (%) | 4 (100) | 3 (100) | 3 (100) | 10 (100) |  | 3 (100) | 4 (57.1) | 2 (66.7) | 12 (75.0) | 21 (72.4) |
| Location of EHS, *n* (%) |  |  |  |  |  |  |  |  |  |  |
|  Bone | 0 | 1 (33.3) | 0 | 1 (10.0) |  | 0 | 1 (14.3) | 1 (33.3) | 2 (12.5) | 4 (13.8) |
|  Lung | 2 (50.0) | 1 (33.3) | 1 (33.3) | 4 (40.0) |  | 1 (33.3) | 0 | 1 (33.3) | 6 (37.5) | 8 (27.6) |
|  Lymph | 3 (75.0) | 2 (66.7) | 2 (66.7) | 7 (70.0) |  | 2 (66.7) | 2 (28.6) | 1 (33.3) | 5 (31.3) | 10 (34.5) |
|  Other | 1 (25.0) | 0 | 0 | 1 (10.0) |  | 2 (66.7) | 2 (28.6) | 1 (33.3) | 6 (37.5) | 11 (37.9) |
| Aetiology of parenchymal liver disease, *n* (%) |  |  |  |  |  |  |  |  |  |  |
|  Alcohol  related | 0 | 0 | 0 | 0 |  | 0 | 0 | 0 | 0 | 0 |
|  HBV related | 4 (100) | 2 (66.7) | 3 (100) | 9 (90.0) |  | 2 (66.7) | 4 (57.1) | 1 (33.3) | 9 (56.3) | 16 (55.2) |
|  HCV related | 0 | 0 | 0 | 0 |  | 1 (33.3) | 3 (42.9) | 2 (66.7) | 4 (25.0) | 10 (34.5) |
|  HBV + HCV related | 0 | 1 (33.3) | 0 | 1 (10.0) |  | 0 | 0 | 0 | 2 (12.5) | 2 (6.9) |
|  Unknown | 0 | 0 | 0 | 0 |  | 0 | 0 | 0 | 1 (6.3) | 1 (3.4) |
| Parenchymal liver disease, *n* (%) |  |  |  |  |  |  |  |  |  |  |
|  Chronic  hepatitis | 1 (25.0) | 0 | 2 (66.7) | 3 (30.0) |  | 1 (33.3) | 1 (14.3) | 0 | 3 (18.8) | 5 (17.2) |
|  Steatofibrosis | 0 | 0 | 0 | 0 |  | 0 | 0 | 0 | 0 | 0 |
|  Cirrhosis | 3 (75.0) | 3 (100) | 1 (33.3) | 7 (70.0) |  | 2 (66.7) | 6 (85.7) | 3 (100) | 13 (81.3) | 24 (82.8) |
|  No evidence | 0 | 0 | 0 | 0 |  | 0 | 0 | 0 | 0 | 0 |
|  Unknown | 0 | 0 | 0 | 0 |  | 0 | 0 | 0 | 0 | 0 |
| Prior treatment with sorafenib | 1 (25.0) | 0 | 0 | 1 (10.0) |  | 0 | 1 (14.3) | 0 | 1 (6.3) | 2 (6.9) |
| Type of local therapy, *n* (%) |  |  |  |  |  |  |  |  |  |  |
|  Complete  surgical  resection | 0 | 0 | 0 | 0 |  | 0 | 0 | 1 (33.3) | 1 (6.3) | 2 (6.9) |
|  RFA | 0 | 0 | 0 | 0 |  | 0 | 0 | 0 | 1 (6.3) | 1 (3.4) |
|  PEI | 0 | 0 | 0 | 0 |  | 0 | 0 | 0 | 0 | 0 |
|  TACE | 1 (25.0) | 0 | 0 | 1 (10.0) |  | 0 | 0 | 0 | 5 (31.3) | 5 (17.2) |
|  RT | 0 | 0 | 0 | 0 |  | 0 | 0 | 0 | 0 | 0 |
|  Other | 0 | 0 | 0 | 0 |  | 0 | 2 (28.6) | 2 (66.7) | 4 (25.0) | 8 (27.6) |

aOne patient in this group was only specified as being “Asian” on the patient form.

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 chemoembolisation.