Table SI. Individual patient characteristics and treatment regimens in the triple therapy group (n=15).

| ID | Demographics (sex/age) | Biomarkers (AFP/PIVKA-II) | Liver function (CP/ALBI) | Tumor burden (No./size) | CNLC | Thrombus (PVTT/IVTT) | Regimen details (deidentified) |
|---|---|---|---|---|---|---|---|
| 1 | Male/>50 | ≤400/≤1000 | Class A/Grade 2 | >3/≤10 | IIIa | III/I | 6 cycles of TACE, radiotherapy, systemic therapy: Sorafenib, switched to regorafenib after PD |
| 2 | Female/≤50 | >400/>1000 | Class A/Grade 2 | ≤3/>10 | IIIa | III/II | 1 cycle of TACE, radiotherapy, systemic therapy: Sorafenib, switched to Lenvatinib after PD |
| 3 | Male/>50 | ≤400/>1000 | Class B/Grade 2 | ≤3/≤10 | IIIa | II/II | 3 cycles of TACE, radiotherapy, systemic therapy: Lenvatinib plus PD-1 inhibitor |
| 4 | Male/>50 | >400/>1000 | Class A/Grade 2 | >3/≤10 | IIIa | II/I | 1 cycle of TACE, radiotherapy, systemic therapy: Lenvatinib |
| 5 | Male/>50 | >400/>1000 | Class A/Grade 2 | >3/≤10 | IIIb | 0/I | 5 cycles of TACE, radiotherapy, systemic therapy: Sorafenib + Camrelizumab, sequentially switched to Regorafenib + Camrelizumab, and later to Lenvatinib + Tislelizumab |
| 6 | Male/≤50 | >400/>1000 | Class A/Grade 1 | >3/>10 | IIIb | II/III (RA+) | 1 cycle of TACE, radiotherapy, systemic therapy: Lenvatinib + Camrelizumab |
| 7 | Male/>50 | >400/>1000 | Class A/Grade 1 | >3/>10 | IIIa | II/II | 1 cycle of TACE, radiotherapy, systemic therapy: Donafenib, sequentially switched to Lenvatinib |
| 8 | Male/>50 | >400/>1000 | Class A/Grade 1 | >3/>10 | IIIb | III/I | 1 cycle of TACE, radiotherapy, systemic therapy: Lenvatinib + Camrelizumab, switched to Regorafenib + Camrelizumab after PD |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 9 | Male/>50 | >400/>1000 | Class A/Grade 2 | >3/>10 | IIIa | III/III (RA+) | 2 cycles of TACE, radiotherapy, systemic therapy: Lenvatinib |
| 10 | Male/>50 | ≤400/>1000 | Class B/Grade 1 | ≤3/≤10 | IIIa | I/III (RA+) | 1 cycle of TACE, radiotherapy, systemic therapy: Lenvatinib + Camrelizumab |
| 11 | Female/>50 | >400/>1000 | Class A/Grade 1 | >3/>10 | IIIa | 0/I | 1 cycle of TACE, radiotherapy, systemic therapy: Sorafenib + Camrelizumab, switched to Regorafenib + Camrelizumab after PD |
| 12 | Male/>50 | >400/>1000 | Class B/Grade 2 | >3/>10 | IIIb | III/II | 1 cycle of TACE, radiotherapy, systemic therapy: Lenvatinib |
| 13 | Male/>50 | ≤400/>1000 | Class A/Grade 1 | ≤3/>10 | IIIb | III/I | 1 cycle of TACE, radiotherapy, systemic therapy: Lenvatinib + Camrelizumab |
| 14 | Male/>50 | ≤400/>1000 | Class B/Grade 2 | ≤3/>10 | IIIb | II/III (RA+) | 1 cycle of TACE, radiotherapy, systemic therapy: Lenvatinib |
| 15 | Male/≤50 | >400/>1000 | Class A/Grade 1 | >3/≤10 | IIIb | II/II | 5 cycles of TACE, radiotherapy, systemic therapy: Bevacizumab + Sintilimab, sequentially switched to oral Regorafenib, and finally to Regorafenib + Tislelizumab |

Demographics are presented as sex/age group. Biomarkers are presented as AFP (threshold, 400 ng/ml)/PIVKA-II (threshold: 1,000 mAU/ml) category. Liver function is presented as Child-Pugh class/ALBI grade. Tumor burden is presented as Tumor number/Maximum diameter (threshold, 10 cm) category. Thrombus is presented as PVTT/IVTT stage. AFP, α-fetoprotein; ALBI, albumin-bilirubin; IVTT, inferior vena cava tumor thrombus; PD, progressive disease; PIVKA-II, protein induced by vitamin K absence-II; PVTT, portal vein tumor thrombus; RA, right atrial tumor thrombus extension (Cheng's stage III); TACE, transarterial chemoembolization.

Table SII. Baseline characteristics of hepatocellular carcinoma patients with IVTT, by treatment group.

| | Groups | | | | |
|---|---|---|---|---|---|
| Characteristics | T/R | S | S+T/R | S+T+R | P-value |
| Age, years | 52.50±19.84 | 46.88±12.18 | 56.79±9.61 | 54.13±9.13 | 0.265[a] |
| Sex, n (%) | | | | | |
| Male | 2 (5.9) | 7 (20.6) | 12 (35.3) | 13 (38.2) | 0.371[b] |
| Female | 2 (28.6) | 1 (14.3) | 2 (28.6) | 2 (28.6) | |
| AFP, n (%) | | | | | |
| ≤400 ng/ml | 2 (11.8) | 4 (23.5) | 6 (35.3) | 5 (29.4) | 0.829[c] |
| >400 ng/ml | 2 (8.3) | 4 (16.7) | 8 (33.3) | 10 (41.7) | |
| PIVKA-II, n (%) | | | | | |
| ≤1,000 mAU/ml | 1 (20.0) | 2 (40.0) | 1 (20.0) | 1 (20.0) | 0.353[b] |
| >1,000 mAU/ml | 3 (8.3) | 6 (16.7) | 13 (36.1) | 14 (38.9) | |
| ALT, n (%) | | | | | |
| ≤40 U/l | 2 (11.1) | 3 (16.7) | 6 (33.3) | 7 (38.9) | >0.999[c] |
| >40 U/l | 2 (8.7) | 5 (21.7) | 8 (34.8) | 8 (34.8) | |
| AST, n (%) | | | | | |
| ≤40 U/l | 1 (11.1) | 1 (11.1) | 2 (22.2) | 5 (55.6) | 0.627[c] |
| >40 U/l | 3 (9.4) | 7 (21.9) | 12 (37.5) | 10 (31.3) | |
| TB, μmol/l | 35.20 (20.35, 38.05) | 16.40 (10.98, 36.83) | 32.15 (18.18, 45.88) | 24.50 (15.80, 32.80) | 0.445[d] |
| Ab, g/l | 38.82±2.69 | 36.64±4.67 | 39.64±3.91 | 41.05±5.82 | 0.229[a] |
| ALBI, n (%) | | | | | |
| Grade 1 | 1 (7.1) | 2 (14.3) | 3 (21.4) | 8 (57.1) | 0.298[b] |
| Grade 2 | 3 (11.1) | 6 (22.2) | 11 (40.7) | 7 (25.9) | |
| Chlid-Pugh stage, n (%) | | | | | |
| A | 3 (9.4) | 5 (15.6) | 12 (37.5) | 12 (37.5) | 0.679[b] |
| B | 1 (11.1) | 3 (33.3) | 2 (22.2) | 3 (33.3) | |

| | | | | | |
|---|---|---|---|---|---|
| Cirrhosis, n (%) | | | | | |
| No | 0 (0.0) | 1(14.3) | 5(71.4) | 1(14.3) | 0.16[b] |
| Yes | 4 (11.8) | 7(20.6) | 9(26.5) | 14(41.2) | |
| Hepatitis, n (%) | | | | | |
| No | 0 (0.0) | 0 (0.0) | 20 (100.0) | 0 (0.0) | 0.333[b] |
| HBV | 4 (10.3) | 8 (20.5) | 12 (30.8) | 15 (38.5) | |
| Tumor no., n (%) | | | | | |
| ≤3 | 1 (12.5) | 0 (0.0) | 2 (25.0) | 5 (62.5) | 0.264[b] |
| >3 | 3 (9.1) | 8 (24.2) | 12 (36.4) | 10 (30.3) | |
| Tumor diameter, n (%) | | | | | |
| ≤10 cm | 2 (9.1) | 5 (22.7) | 9 (40.9) | 6 (27.3) | 0.553[c] |
| >10 cm | 2 (10.5) | 3 (15.8) | 5 (26.3) | 9 (47.4) | |
| Intrahepatic metastasis, n (%) | | | | | |
| No | 1 (25.0) | 0 (0.0) | 1 (25.0) | 2 (50.0) | 0.552[b] |
| Yes | 3 (8.1) | 8 (21.6) | 13 (35.1) | 13 (35.1) | |
| Lymph metastasis, n (%) | | | | | |
| No | 2 (6.5) | 5 (16.1) | 11 (35.5) | 13 (41.9) | 0.345[b] |
| Yes | 2 (20.0) | 3 (30.0) | 3 (30.0) | 2 (20.0) | |
| Metastasis, n (%) | | | | | |
| No | 1 (4.8) | 5 (23.8) | 7 (33.3) | 8 (38.1) | 0.733[b] |
| Yes | 3 (15.0) | 3 (15.0) | 7 (35.0) | 7 (35.0) | |
| CNLC stage | | | | | |
| IIIa | 1 (4.8) | 5 (23.8) | 7 (33.3) | 8 (38.1) | 0.733[b] |
| IIIb | 3 (15.0) | 3 (15.0) | 7 (35.0) | 7 (35.0) | |
| PVTT, n (%) | | | | | |
| No | 2 (16.7) | 3 (25.0) | 5 (41.7) | 2 (16.7) | 0.226[b] |
| I | 0 (0.0) | 0 (0.0) | 1 (50.0) | 1 (50.0) | |

| | | | | | |
|---|---|---|---|---|---|
| II | 1 (11.1) | 2 (22.2) | 0 (0.0) | 6 (66.7) | |
| III | 1 (6.3) | 2 (12.5) | 7 (43.8) | 6 (37.5) | |
| IV | 0 (0.0) | 1 (50.0) | 1 (50.0) | 0 (0.0) | |
| IVTT, n (%) | | | | | |
| I | 3 (13.6) | 4 (18.2) | 9 (40.9) | 6 (27.3) | 0.645[b] |
| II | 0 (0.0) | 2 (25.0) | 1 (12.5) | 5 (62.5) | |
| III | 1 (9.1) | 2 (18.1) | 4 (36.4) | 4 (46.4) | |
| Pulmonary embolism, n (%) | | | | | |
| No | 4 (10.3) | 7 (17.9) | 13 (33.3) | 15 (38.5) | 0.598[b] |
| Yes | 0 (0.0) | 1 (50.0) | 1 (50.0) | 0 (0.0) | |

P-values were calculated using: [a]One-way ANOVA; [b]Fisher's exact test; [c]Pearson $\chi^2$ test; [d]Kruskal-Wallis test. ALT, alanine aminotransferase; AST, aspartate aminotransferase; AFP, α-fetoprotein; PIVKA-II, protein induced by vitamin K absence II; ALBI, albumin-bilirubin; HBV, hepatic B virus; PVTT, portal vein tumor thrombus; IVTT, inferior vena cava tumor thrombus; RATT, right atrial tumor thrombus; S, systemic therapy; T, TACE (transarterial chemoembolization); R, radiation therapy; S, systemic therapy; TACE, transarterial chemoembolization; SBRT, stereotactic body radiation therapy; T/R, TACE or SBRT; S+T/R, systemic therapy combined with T/R; S+T+R, triple-modality therapy consisting of systemic therapy, TACE, and SBRT.

Table SIII. Univariable and multivariable analysis of variables for progression-free survival.

| | Univariable analysis | | Multivariable analysis | |
|---|---|---|---|---|
| Variable | HR (95% CI) | P-value | HR (95% CI) | P-value |
| Age, years | | | | |
| >50 vs. ≤50 | 0.68 (0.34-1.37) | 0.28 | | |
| Sex | | | | |
| Male vs. female | 0.82 (0.33-2.01) | 0.66 | | |
| AFP, ng/ml | | | | |
| >400 vs. ≤400 | 1.02 (0.52-1.97) | 0.96 | | |
| PIVKA-II, mAU/ml | | | | |
| >1000 vs. ≤1000 | 0.66 (0.25-1.72) | 0.39 | | |
| ALT, U/l | | | | |
| >40 vs. ≤40 | 0.87 (0.46-1.67) | 0.68 | | |
| AST, U/l | | | | |
| >40 vs. ≤40 | 1.38 (0.63-3.05) | 0.42 | | |
| ALBI | | | | |
| Grade 2 vs. Grade 1 | 2.48 (1.11-5.55) | 0.03[a] | 1.62 (0.61-4.28) | 0.33 |
| Chlid Pugh stage | | | | |
| B vs. A | 1.12 (0.51-2.50) | 0.77 | | |
| Cirrhosis | | | | |
| Yes vs. no | 1.03 (0.40-2.67) | 0.95 | | |
| Hepatitis | | | | |
| HBV vs. no | 1.67 (0.40-7.05) | 0.49 | | |

| | | | | |
|---|---|---|---|---|
| Tumor number | | | | |
| >3 vs. ≤3 | 1.24 (0.56-2.72) | 0.60 | | |
| Tumor diameter, cm | | | | |
| >10 vs. ≤10 | 1.86 (0.95-3.64) | 0.07 | 3.94 (1.79-8.65) | <0.001[b] |
| Intrahepatic metastasis | | | | |
| Yes vs. no | 0.97 (0.34-2.78) | 0.95 | | |
| Lymph metastasis | | | | |
| Yes vs. no | 1.87 (0.89-3.91) | 0.10 | 2.09 (0.88-4.95) | 0.095 |
| Metastasis | | | | |
| Yes vs. no | 1.72 (0.89-3.34) | 0.11 | | |
| PVTT | | | | |
| I vs. no | 0.42 (0.05-3.31) | 0.41 | | |
| II vs. no | 0.65 (0.26-1.65) | 0.37 | | |
| III vs. no | 1.78 (0.77-4.13) | 0.18 | | |
| IV vs. no | 1.27 (0.28-5.83) | 0.76 | | |
| IVTT | | | | |
| II vs. I | 0.93 (0.40-2.16) | 0.87 | | |
| III vs. I | 1.51 (0.70-3.28) | 0.30 | | |
| RATT | | | | |
| Yes vs. no | 1.54 (0.73-3.24) | 0.25 | | |
| Pulmonary embolism | | | | |
| Yes vs. no | 10.06 (2.00-50.6) | 0.01[a] | | |

| | | | | |
|---|---|---|---|---|
| Treatment | | | | |
| S vs. S+T+R | 2.36 (0.89-6.28) | 0.084 | 2.35 (0.80-6.94) | 0.122 |
| T/R vs. S+T+R | 3.49 (1.08-11.30) | 0.037[a] | 5.89 (1.51-22.94) | 0.011[a] |
| S+T/R vs. S+T+R | 3.01 (1.29-7.04) | 0.011[a] | 4.24 (1.55-11.62) | 0.005[c] |

[a]P<0.05; [b]P<0.001; [c]P<0.01. ALT, alanine aminotransferase; AST, aspartate aminotransferase; AFP, α-fetoprotein; PIVKA-II, protein induced by vitamin K absence II; ALBI, albumin-bilirubin; HBV, hepatic B virus; PVTT, portal vein tumor thrombus; IVTT, inferior vena cava tumor thrombus; RATT, right atrial tumor thrombus; S, systemic therapy; T, TACE (transarterial chemoembolization); R, radiation therapy.