Supplementary

Table S1 Patients distribution

	Sun Yat-Sen University Cancer Center (SYSUCC)	Guangdong Provincial People's Hospital (GPPH)	Southern Medical University Nanfang Hospital (SMUNH)
Sorafenib	69	18	2
TACE	236	21	16
TAI	95	0	0

Table S2 OS rate and PFS rate of overall patients

	PFS rate			OS rate		
	TAI	TACE	Sorafenib	TAI	TACE	Sorafenib
3-mo	83.7%	46.7%	52.6%	97.9%	86.1%	81.1%
6-mo	56.4%	22.9%	31.3%	85.7%	59.3%	59.4%
9-mo	35.6%	14.7%	22.4%	76.0%	38.2%	42.2%
12-mo	31.9%	11.4%	17.9%	70.6%	33.8%	33.5%

Table S3 PPS analysis in matched sorafenib and TAI groups

Progression patterns	Sorafenib			TAI			P value
	Median	95% CI	n	Median	95% CI	n	
Overall	4.1	2.5–5.8	33	Unreached	–	32	0.013
Intrahepatic lesion	6.2	2.5–9.8	22	Unreached	–	18	0.148
Vascular invasion	5.0	3.7–6.4	11	5.0	3.6–6.4	3	0.681
Extrahepatic lesion	3.7	0.0–9.5	10	6.1	–	18	0.132

Table S4 PPS rates in matched sorafenib and TAI groups

Progression patterns	sorafenib (%)				TAI (%)				P value
	2 mo	4 mo	6 mo	8 mo	2 mo	4 mo	6 mo	8 mo	
Overall	79.7	54.7	36.3	27.2	100.0	79.0	67.1	62.6	0.013
Intrahepatic lesion	90.2	69.8	61.0	40.7	100.0	94.1	73.9	67.2	0.148
Vascular invasion	88.9	74.1	27.8	27.8	100.0	100.0	33.3	33.3	0.681
Extrahepatic lesion	55.6	44.4	22.2	22.2	100.0	65.7	57.5	46.0	0.132

Table S5 Univariate and multivariate Cox regression analysis for OS in matched sorafenib and TAI groups

Variables	Univariate Cox regression analysis for OS			Multivariate Cox regression analysis for OS		
	HR	95% CI	P value	HR	95% CI	P value
Male	1.048	0.371–2.965	0.929			
Age ≤50 yr	1.739	0.957–3.159	0.069			
Previous treatment present	1.268	0.698–2.304	0.436			
Previous radical treatment absent	2.372	0.573–9.823	0.234			
Sorafenib group	2.190	1.195–4.014	0.011	2.209	0.671–7.270	0.192
AFP >400 ng/mL before treatment	1.652	0.895–3.049	0.108			
WBC <4.0×10^9/L before treatment	4.273	1.216–15.013	0.024	1.500	0.209–10.745	0.686
NE <2.0×10^9/L before treatment	1.892	0.251–14.274	0.536			
Hgb <120 g/L before treatment	1.453	0.694–3.042	0.322			
PLT <100×10^9/L before treatment	1.055	0.415–2.681	0.911		–	
ALT >40 U/L before treatment	1.047	0.560–1.959	0.885			
ALB <40 g/L before treatment	1.489	0.815–2.720	0.196			
TBil >20.5 umol/L before treatment	1.864	0.939–3.700	0.075			
PT >13.5 s before treatment	1.221	0.476–3.129	0.678			
CRE >100 umol/L before treatment	2.011	0.784–5.162	0.146			
Child-Pugh score B before treatment	4.652	1.784–12.134	0.002	5.841	0.828–41.220	0.077
Maximum diameter >10 cm	1.231	0.674–2.246	0.499			
Single lesion	1.289	0.637–2.619	0.480			
Uni-lobe involved	1.431	0.790–2.592	0.237			
Macrovascular invasion absent	1.052	0.374–2.957	0.923			
Vp4	2.069	1.095–3.908	0.025	2.980	1.017–8.729	0.046
Distant metastasis present	3.199	1.692–6.049	0.000	17.494	4.008–76.352	0.000
Tumor response evaluation as PD	2.080	1.102–3.924	0.024	4.314	0.847–21.974	0.078
Intrahepatic lesion was PD when target treatment discontinued	1.225	0.595–2.521	0.582			
Macrovascular invasion was PD when target treatment discontinued	2.807	1.064–7.402	0.037	3.240	0.560–18.747	0.189
Extrahepatic lesion was PD when target treatment discontinued	2.120	1.022–4.398	0.044	0.329	0.051–2.142	0.245
AFP >400 ng/mL after treatment	1.891	1.008–3.549	0.047	4.589	1.606–13.114	0.004
AFP level not decrease after treatment	2.180	1.149–4.134	0.017	1.392	0.462–4.198	0.557
WBC <4.0×10^9/L after treatment	1.295	0.541–3.096	0.561			
NE ≥2.0×10^9/L after treatment	1.176	0.461–3.005	0.734			
Hgb <120 g/L after treatment	3.685	1.881–7.220	0.000	1.034	0.246–4.343	0.964
PLT ≥100×10^9/L after treatment	1.505	0.535–4.233	0.438			
ALT >40 U/L after treatment	1.512	0.804–2.845	0.200			
ALB <40 g/L after treatment	2.281	1.219–4.269	0.010	2.268	0.821–6.261	0.114
TBil >20.5 umol/L after treatment	2.296	1.188–4.440	0.013	3.062	0.774–12.119	0.111
PT >13.5 s after treatment	5.784	2.648–12.631	0.000	4.039	0.917–17.788	0.065
CRE >100 umol/L after treatment	1.871	0.450–7.786	0.389			
Child-Pugh score was B or C after treatment	7.346	3.553–15.188	0.000	1.407	0.267–7.413	0.687
Follow-up treatment absent	4.268	2.002–9.099	0.000	4.120	0.914–18.567	0.065
Follow-up potential radical treatment absent	2.907	1.136–7.439	0.026	9.463	1.239–72.250	0.030
Follow-up surgery absent	2.793	0.992–7.861	0.052			
Intrahepatic lesion was not PD when initial progression observed	2.074	1.096–3.925	0.025	3.251	0.883–11.962	0.076
Macrovascular invasion was PD when initial progression observed	1.028	0.433–2.441	0.950			
Extrahepatic lesion was PD when initial progression observed	1.097	0.572–2.102	0.780			

Table S6 Univariate and multivariate Cox regression analysis for PFS in matched sorafenib and TAI groups

Variables	Univariate Cox regression analysis for PFS			Multivariate Cox regression analysis for PFS		
	HR	95% CI	P value	HR	95% CI	P value
Female	1.042	0.448–2.426	0.924			
Age ≤50 yr	1.952	1.188–3.207	0.008	1.571	0.854–2.887	0.146
Previous treatment present	1.080	0.657–1.776	0.761			
Previous radical treatment absent	5.370	1.309–22.025	0.020	4.268	0.900–20.243	0.068
Sorafenib group	1.365	0.829–2.248	0.222			
AFP >400 ng/mL before treatment	1.995	1.191–3.343	0.009	0.713	0.257–1.978	0.516
WBC <4.0×10^9/L before treatment	2.593	0.999–6.731	0.050			
NE <2.0×10^9/L before treatment	3.027	0.921–9.948	0.068			
Hgb <120 g/L before treatment	1.239	0.659–2.331	0.506			
PLT <100×10^9/L before treatment	1.345	0.638–2.835	0.436		–	
ALT >40 U/L before treatment	1.537	0.935–2.528	0.090			
ALB <40 g/L before treatment	1.331	0.799–2.219	0.272			
TBil >20.5 umol/L before treatment	1.859	0.976–3.539	0.059			
PT >13.5 s before treatment	1.418	0.693–2.901	0.339			
CRE >100 umol/L before treatment	1.419	0.561–3.590	0.460			
Child-Pugh score B before treatment	1.974	0.609–6.402	0.257			
Maximum diameter >10 cm	1.410	0.846–2.348	0.187			
Multiple lesion	1.864	0.911–3.814	0.088			
Uni-lobe involved	1.008	0.616–1.649	0.975			
Macrovascular invasion absent	1.286	0.581–2.844	0.535			
Vp4	1.075	0.578–1.998	0.820			
Distant metastasis present	2.025	1.131–3.626	0.018	2.926	1.425–6.007	0.003
Tumor non-response	2.063	1.071–3.973	0.030	1.347	0.601–3.019	0.469
AFP >400 ng/mL after treatment	2.798	1.648–4.749	0.000	3.309	1.204–9.090	0.020
AFP level not decrease after treatment	2.463	1.454–4.170	0.001	1.770	0.897–3.493	0.100
WBC <4.0×10^9/L after treatment	1.549	0.749–3.203	0.237			
NE ≥2.0×10^9/L after treatment	1.886	0.961–3.699	0.065			
Hgb <120 g/L after treatment	1.458	0.741–2.869	0.275			
PLT ≥100×10^9/L after treatment	1.021	0.501–2.080	0.955			
ALT >40 U/L after treatment	1.228	0.712–2.116	0.460			
ALB <40 g/L after treatment	1.879	1.103–3.199	0.020	1.816	0.876–3.766	0.109
TBil >20.5 umol/L after treatment	2.232	1.225–4.067	0.009	1.153	0.510–2.606	0.732
PT >13.5 s after treatment	3.657	1.785–7.494	0.000	2.557	1.007–6.495	0.048
CRE >100 umol/L after treatment	1.677	0.397–7.081	0.482			
Child-Pugh score was B or C after treatment	3.351	1.442–7.785	0.005	1.187	0.390–3.612	0.763
Follow-up treatment absent	1.641	0.983–2.738	0.058			
Follow-up potential radical treatment absent	1.652	0.903–3.023	0.103			
Follow-up surgery absent	1.589	0.823–3.068	0.168			

Table S7 Treatment related adverse events (AEs) in matched sorafenib and TAI groups

AEs and grade	Sorafenib	TAI	P value
Overall			0.229
0	5	2	
1	11	17	
2	26	19	
3	2	8	
4	3	1	
HFSR			0.000
0	36	47	
1	4	0	
2	7	0	
Diarrhea			0.021
0	38	46	
1	3	1	
2	6		
Anorexia			0.046
0	42	34	
1	4	10	
2	1	3	
Anemia			0.770
0	36	36	
1	9	9	
2	1	0	
3	1	1	
4	0	1	
ALT level elevated			0.100
0	36	43	
1	10	3	
3	1	1	
Neutropenia			0.032
0	45	36	
1	1	6	
2	0	4	
3	1	1	
Thrombocytopenia			1.000
0	40	41	
1	3	2	
2	4	3	
3	0	1	
Hypoalbuminemia			0.242
0	24	27	
1	18	19	
2	5	1	
Hypercreatinemia			0.736
0	46	45	
1	0	1	
2	1	1	
Hyperbilirubinemia			0.002
0	29	42	
1	8	3	
2	7	2	
3	1	0	
4	2	0	
Insomnia			0.653
0	46	46	
1	1	0	
2	0	1	
PT prolonged			0.019
0	36	44	
1	10	3	
3	1	0	
Pain			0.006
0	37	21	
1	3	15	
2	7	7	
3	0	4	
Cough			0.653
0	46	46	
1	0	1	
2	1	0	
Erythra			0.079
0	41	45	
1	3	2	
2	3	0	
Gastrointestinal hemorrhage			1.000
0	46	46	
4	1	1	
Vomiting			0.000
0	46	20	
1	0	16	
2	1	10	
3	0	1	
Fever			0.099
0	44	47	
1	2	0	
2	1	0	
Hypertension			1.000
0	46	46	
1	1	1	
Leukocytopenia			0.012
0	45	35	
1	1	9	
2	1	3	
Hiccup			0.241
0	47	44	
1	0	3	
Dysuria			1.000
0	47	46	
2	0	1	
Constipation			1.000
0	47	46	
1	0	1	
Peripheral neuropathy			1.000
0	47	46	
1	0	1	

Table S8 PPS analysis in matched TAI and TACE groups

Progression pattern	TAI			TACE			P value
	Median	95% CI	n	Median	95% CI	n	
Overall	13.9	9.7–18.1	48	4.0	3.6–4.3	55	0.000
Intrahepatic lesion	12.5	–	24	4.0	3.6–4.3	33	0.003
Macrovascular invasion	6.9	3.9–9.8	6	3.4	2.7–4.1	23	0.027
Extrahepatic lesion	13.9	1.7–26.1	27	4.4	3.6–5.2	29	0.073

Table S9 PPS rates in matched TAI and TACE groups

Progression pattern	TAI				TACE				P value
	2 mo	4 mo	6 mo	8 mo	2 mo	4 mo	6 mo	8 mo	
Overall	97.8	78.7	71.1	65.6	79.5	47.9	29.2	26.6	0.000
Intrahepatic lesion	100.0	85.0	69.1	63.8	79.3	50.0	30.8	30.8	0.003
Macrovascular invasion	100.0	100.0	66.7	50.0	76.5	33.5	11.2	11.2	0.027
Extrahepatic lesion	96.0	70.0	65.3	59.9	76.6	57.4	31.9	25.5	0.073

Table S10 Univariate and multivariate Cox regression analysis for OS in matched TAI and TACE groups

Variables	Univariate Cox regression analysis for OS			Multivariate Cox regression analysis for OS		
	HR	95% CI	P value	HR	95% CI	P value
Male	1.552	0.711–3.386	0.270			
Age >50 yr	1.051	0.679–1.627	0.823			
Previous anti-tumor treatment absent	1.104	0.508–2.401	0.802			
Previous radical treatment present	1.022	0.412–2.530	0.963			
TACE group	2.723	1.733–4.279	0.000	1.017	0.419–2.471	0.970
AFP >400 ng/mL before treatment	1.728	0.969–3.080	0.064			
WBC <4.0×10^9/L before treatment	1.331	0.486–3.649	0.578			
NE <2.0×10^9/L before treatment	2.079	0.654–6.611	0.215			
Hgb <120 g/L before treatment	1.443	0.781–2.666	0.242			
PLT <100×10^9/L before treatment	1.033	0.377–2.831	0.950		–	
ALT >40 U/L before treatment	1.142	0.736–1.770	0.554			
ALB <40 g/L before treatment	1.487	0.956–2.313	0.078			
TBil >20.5 μmol/L before treatment	1.740	1.053–2.876	0.031	0.625	0.194–2.015	0.431
PT >13.5 s before treatment	1.398	0.768–2.545	0.272			
CRE >100 μmol/L before treatment	3.220	1.527–6.790	0.002	4.202	1.380–12.793	0.012
Child-Pugh score was B before treatment	4.191	1.514–11.601	0.006	4.215	0.719–24.716	0.111
Maximum diameter >10 cm	1.434	0.918–2.240	0.113			
Multiple lesion	1.064	0.683–1.657	0.784			
Uni-lobe involved	1.113	0.697–1.778	0.654			
Macrovascular invasion absent	1.385	0.690–2.779	0.360			
Vp4	1.526	0.942–2.473	0.086			
Distant metastasis present	1.902	1.155–3.134	0.012	1.544	0.680–3.506	0.299
Only 1 cycle of TAI/TACE performed	2.942	1.895–4.566	0.000	1.782	0.728–4.365	0.206
Tumor non-response	5.331	2.549–11.152	0.000	1.619	0.568–4.617	0.367
Intrahepatic lesion was PD when target treatment discontinued	2.024	1.235–3.318	0.005	1.166	0.551–2.466	0.689
Macrovascular invasion was PD when target treatment discontinued	4.161	2.383–7.265	0.000	1.570	0.296–8.322	0.596
Extrahepatic lesion was PD when target treatment discontinued	2.110	1.272–3.499	0.004	1.333	0.579–3.065	0.499
AFP >400 ng/mL after treatment	1.728	0.969–3.080	0.064			
AFP level not decrease after treatment	2.931	1.792–4.795	0.000	1.462	0.641–3.332	0.367
WBC <4.0×10^9/L after treatment	1.054	0.579–1.919	0.863			
NE ≥2.0×10^9/L after treatment	1.095	0.526–2.281	0.809			
Hgb <120 g/L after treatment	1.513	0.924–2.476	0.100			
PLT ≥100×10^9/L after treatment	1.098	0.546–2.206	0.794			
ALT >40 U/L after treatment	1.546	0.955–2.503	0.077			
ALB <40 g/L after treatment	2.301	1.416–3.740	0.001	1.610	0.843–3.074	0.149
TBil >20.5 μmol/L after treatment	2.584	1.556–4.292	0.000	2.306	0.718–7.403	0.160
PT >13.5 s after treatment	2.316	1.161–4.618	0.017	0.872	0.342–2.220	0.773
CRE >100 μmol/L after treatment	4.391	1.740–11.085	0.002	4.734	1.103–20.329	0.036
Child-Pugh score was B or C after treatment	3.184	1.356–7.476	0.008	1.059	0.288–3.890	0.931
Follow-up treatment absent	3.063	1.847–5.081	0.000	0.674	0.268–1.690	0.400
Follow-up potential radical treatment absent	4.568	2.437–8.561	0.000	0.800	0.236–2.711	0.720
Follow-up surgery absent	10.340	3.712–28.802	0.000	5.519	1.448–21.032	0.012
Intrahepatic lesion was not PD when initial progression observed	1.126	0.723–1.756	0.599			
Macrovascular invasion was PD when initial progression observed	2.735	1.660–4.504	0.000	1.359	0.328–5.620	0.672
Extrahepatic lesion was PD when initial progression observed	1.069	0.675–1.692	0.776			

Table S11 Univariate and multivariate Cox regression analysis for PFS in matched TAI and TACE groups

Variables	Univariate Cox regression analysis for PFS			Multivariate Cox regression analysis for PFS		
	HR	95% CI	P value	HR	95% CI	P value
Male	1.058	0.550–2.037	0.866			
Age ≤50 yr	1.461	0.983–2.171	0.061			
Previous anti-tumor treatment present	1.119	0.582–2.152	0.735			
Previous radical treatment present	1.077	0.471–2.463	0.860			
TACE group	2.371	1.594–3.526	0.000	1.609	0.887–2.918	0.118
AFP >400 ng/mL before treatment	1.670	1.021–2.730	0.041	0.381	0.146–0.994	0.049
WBC <4.0×10^9/L before treatment	1.556	0.680–3.561	0.295			
NE <2.0×10^9/L before treatment	1.403	0.443–4.448	0.565			
Hgb <120 g/L before treatment	1.119	0.612–2.047	0.714			
PLT <100×10^9/L before treatment	1.412	0.615–3.241	0.416		–	
ALT >40 U/L before treatment	1.086	0.735–1.604	0.679			
ALB <40 g/L before treatment	1.460	0.973–2.189	0.067			
TBil >20.5 μmol/L before treatment	1.703	1.064–2.727	0.027	1.334	0.697–2.554	0.384
PT >13.5 s before treatment	1.243	0.716–2.158	0.439			
CRE >100 μmol/L before treatment	1.301	0.525–3.226	0.570			
Child-Pugh score was B before treatment	2.006	0.490–8.204	0.333			
Maximum diameter >10 cm	1.508	1.015–2.242	0.042	1.254	0.753–2.089	0.384
Multiple lesion	1.107	0.748–1.637	0.612			
Bi-lobe involved	1.044	0.685–1.593	0.840			
Macrovascular invasion absent	1.402	0.728–2.701	0.313			
Vp1-3	1.083	0.676–1.738	0.739			
Distant metastasis present	1.805	1.133–2.875	0.013	0.649	0.365–1.156	0.142
AFP >400 ng/mL after treatment	1.670	1.021–2.730	0.041	4.756	1.904–11.881	0.001
AFP level not decrease after treatment	3.489	2.258–5.392	0.000	0.500	0.276–0.905	0.022
WBC <4.0×10^9/L after treatment	1.063	0.641–1.763	0.812			
NE ≥2.0×10^9/L after treatment	1.044	0.581–1.879	0.885			
Hgb <120 g/L after treatment	1.841	1.143–2.967	0.012	1.241	0.664–2.320	0.498
PLT ≥100×10^9/L after treatment	1.592	0.848–2.989	0.148			
ALT >40 U/L after treatment	1.198	0.767–1.872	0.428			
ALB <40 g/L after treatment	1.738	1.154–2.618	0.008	1.660	0.951–2.899	0.075
TBil >20.5 μmol/L after treatment	1.389	0.834–2.313	0.206			
PT >13.5 s after treatment	3.093	1.724–5.550	0.000	3.451	1.730–6.885	0.000
CRE >100 μmol/L after treatment	2.076	0.645–6.681	0.220			
Child-Pugh score was B or C after treatment	1.126	0.411–3.086	0.818			
Follow-up treatment absent	3.196	2.067–4.943	0.000	1.550	0.676–3.555	0.300
Follow-up potential radical treatment absent	4.057	2.519–6.534	0.000	0.734	0.275–1.964	0.538
Follow-up surgery absent	5.521	3.035–10.043	0.000	3.482	1.397–8.682	0.007

Table S12 Treatment related adverse events (AEs) in matched TAI and TACE groups

AEs and grade	TAI	TACE	P value
Overall			0.280
0	4	6	
1	36	31	
2	31	40	
3	11	8	
4	3	0	
Diarrhea			0.180
0	84	79	
1	1	3	
2	0	3	
Cough			0.747
0	84	82	
1	1	1	
2	0	2	
Thrombocytopenia			0.322
0	69	76	
1	9	4	
2	6	3	
3	1	2	
Hypoalbuminemia			0.908
0	42	41	
1	41	43	
2	2	1	
PT prolonged			0.370
0	76	71	
1	9	14	
Hypercreatinemia			1.000
0	81	81	
1	3	3	
2	1	1	
Hiccup			0.277
0	79	83	
1	6	2	
Vomiting			0.217
0	46	57	
1	24	19	
2	13	9	
3	2	0	
Pain			0.968
0	42	45	
1	23	21	
2	14	14	
3	6	5	
Constipation			0.455
0	81	78	
1	4	5	
2	0	2	
ALT level elevated			0.002
0	78	61	
1	7	17	
2	0	5	
3	0	2	
Fever			0.000
0	85	59	
1	0	20	
2	0	5	
3	0	1	
Hyperbilirubinemia			0.063
0	73	67	
1	9	11	
2	1	7	
3	2	0	
Anorexia			0.919
0	65	67	
1	15	14	
2	5	4	
Anemia			0.128
0	68	62	
1	14	18	
2	1	5	
3	2	0	
Leukocytopenia			0.001
0	62	79	
1	18	5	
2	5	1	
Hypertension			1.000
0	84	84	
1	1	1	
Neutropenia			0.000
0	67	84	
1	10	1	
2	6	0	
3	1	0	
4	1	0	
Erythra			0.246
0	82	85	
1	3	0	
Dysuria			0.029
0	79	85	
1	2	0	
2	4	0	
Gastrointestinal hemorrhage			0.477
0	83	85	
4	2	0	
Peripheral neuropathy			1.000
0	84	85	
1	1	0	