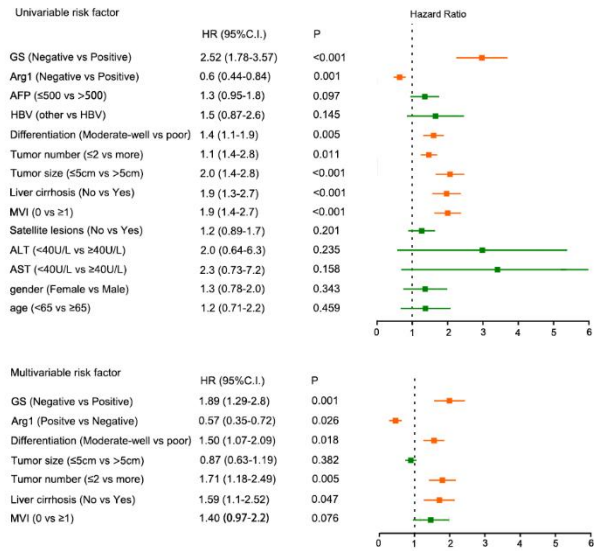
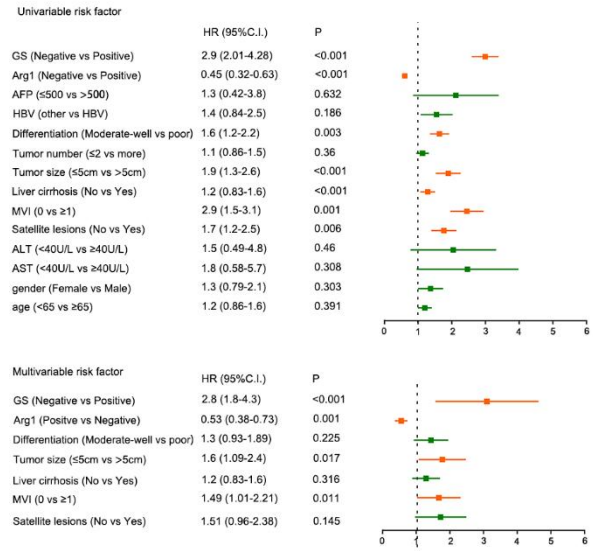


**Supplementary Figure 1.** Kaplan-Meier curves showing the RFS (A) and OS (B) of 251 patients who received only hepatectomy. GS: Glutamine synthetase; Arg1: Arginase 1; RFS: Recurrence-free survival; OS: Overall survival.

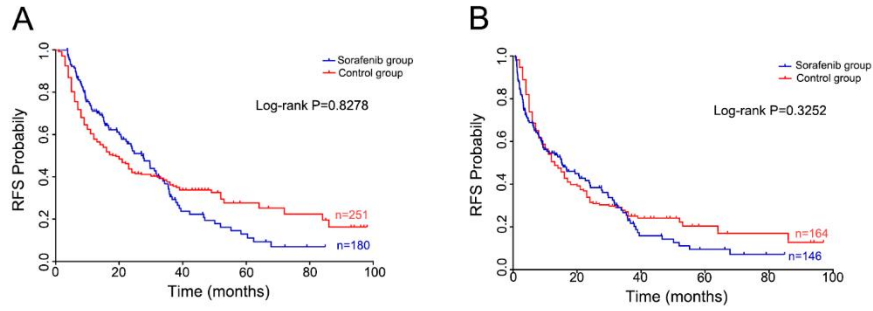
**A**



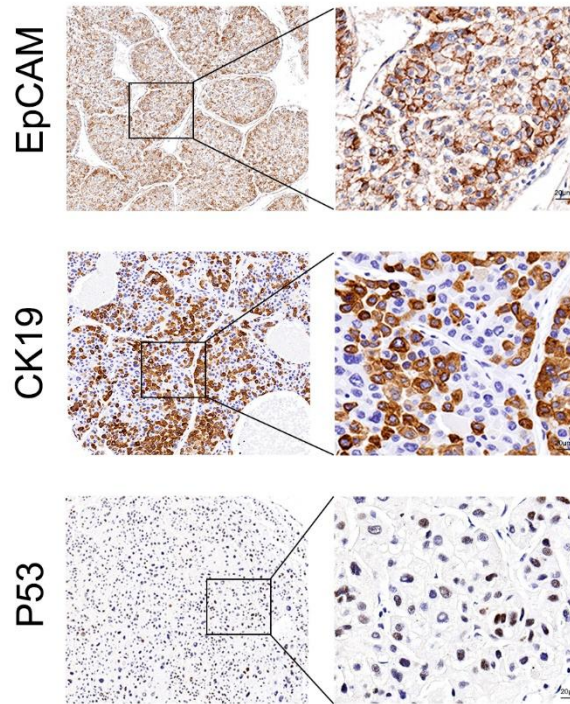
**B**



**Supplementary Figure 2.** Univariate and multivariate analyses of factors related to RFS (A) and OS (B). RFS: Recurrence-free survival; OS: Overall survival.



**Supplementary Figure 3.** Kaplan-Meier curves comparing the RFS between the sorafenib group and the control group in all HCC patients (A). Kaplan-Meier curves comparing the RFS between the sorafenib group and the control group in HCC patients with a high risk of recurrence (B). RFS: Recurrence-free survival; HCC: Hepatocellular carcinoma.



**Supplementary Figure 4.** Representative immunostaining of EpCAM, CK19, and mutant TP53 in HCC samples. HCC: Hepatocellular carcinoma.

**Supplementary Table 1.** Demographics of the HCC patient cohort who only received hepatectomy ( $n=251$ ).

Characteristics	Total
Age, years (mean, min–max)	51 (23–83)
Sex, $n$ (%)	
Female	36 (14.34)
Male	215 (85.65)
PLT ( $10^9/L$ )	158.8 (38–476)
TBIL ( $\mu\text{mol/L}$ )	17.31 (0–391)
ALT (U/L)	48.4 (8–279)
AST (U/L)	51 (13–345)
Neutrophil ( $10^9/L$ )	3.56 (0.086–40.000)
Lymphocyte ( $10^9/L$ )	1.59 (0.3–7.0)
TP (g/L)	70.60 (26–87)
ALB (g/L)	41.79 (20.4–77.0)
GGT (U/L)	104.93 (9–625)
Satellite lesions	43 (17.13)
Serum AFP, $n$ (%)	
Low (serum AFP $\leq 500$ )	158 (62.95)
High (serum AFP $> 500$ )	93 (37.05)
Differentiation, $n$ (%)	
Poor	132 (52.59)
Moderate-well	119 (47.41)
Etiology, $n$ (%)	
Hepatitis B virus	220 (87.65)
Other	31 (12.35)
Cirrhosis, $n$ (%)	
Yes	150 (59.76)
No	101 (40.24)
Tumor size, $n$ (%)	
Small (size $\leq 3$ cm)	34 (13.55)
Medium ( $3 < \text{size} \leq 5$ cm)	53 (21.11)
Large (size $> 5$ cm)	164 (65.34)
Tumor number, $n$ (%)	
One	204 (81.27)
Two	38 (15.14)
More	9 (3.59)
MVI	104 (41.43)
Child-Pugh class, $n$ (%)	
A	244 (97.21)
B	7 (2.79)
BCLC stage, $n$ (%)	
A	87 (34.66)
B	134 (53.39)

C	30 (11.95)
Recurrence, <i>n</i> (%)	
Yes	154 (61.35)
No	97 (38.65)
Alive, <i>n</i> (%)	
Yes	119 (40.41)
No	132 (52.59)

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AFP: Alpha-fetoprotein; BCLC: Barcelona Clinic Liver Cancer; MVI: Microvascular invasion.

**Supplementary Table 2.** Baseline patient demographics and disease characteristics in the two groups of patients.

Variable, n (%)	Total (n=431)	Patient only received hepatectomy (n=251)	Patients received sorafenib after hepatectomy (n=180)	P value
Age	51.3 (21.0–83.0)	51 (23.0–83.0)	51.8 (21.0–74.0)	0.166
Female/Male	51/380	36/215	15/165	0.0572
PLT (10 <sup>9</sup> /L)	160.0 (30.0–476.0)	158.8 (38.0–476.0)	136.0 (30.0–458.0)	0.3266
TBIL (μmol/L)	17.73 (0–391.00)	17.31 (0–391.00)	16.58 (3.8.–71.2.)	0.0246
ALT (U/L)	42.06 (8.00–830.00)	48.40 (8.00–279.00)	62.24 (8.00–830.00)	<0.0001
AST (U/L)	53.55 (13.00–1513.00)	51.00 (13.00–345.00)	76.55 (30.00–1513.00)	<0.0001
Neutrophil (10 <sup>9</sup> /L)	4.460 (0.086–58.400)	3.560 (0.086–40.000)	4.030 (1.260–58.400)	0.1426
Lymphocyte (10 <sup>9</sup> /L)	9.97 (0.30–151.00)	1.59 (0.30–7.00)	1.47 (0.30–151.00)	0.3265
TP (g/L)	71.26 (26.00–89.20)	70.60 (26.00–87.00)	69.00 (26.00–89.20)	0.0001
ALB (g/L)	42.89 (5.40–77.00)	41.79 (20.40–77.00)	42.40 (5.40–73.10)	0.144
GGT (u/L)	99.06 (9.00–1319.00)	104.93 (9.00–625.00)	100.6 (12.0–1319.0)	0.0013
Differentiation				
Poor	207 (48.03)	132 (52.59)	75 (41.67)	0.0254
Moderate-well	224 (51.97)	119 (47.41)	105 (58.33)	
Etiology, n (%)				
Hep B	387 (89.79)	220 (87.65)	167 (92.77)	0.0838
Other	44 (10.21)	31 (12.35)	13 (7.23)	
AFP				
Low (serum AFP ≤ 500)	299 (69.37)	158 (62.95)	141 (78.33)	0.0001
High (serum AFP > 500)	132 (30.63)	93 (37.05)	39 (21.67)	
Satellites	148 (34.34)	43 (17.13)	105 (58.33)	<0.0001
Cirrhosis				
Yes	247 (57.31)	150 (59.76)	97 (53.88)	<0.0001
No	204 (42.69)	101 (40.24)	103 (46.12)	
Tumor size				
Small (size ≤ 3 cm)	77 (17.87)	34 (13.55)	43 (23.33)	
Medium (3 < size ≤ 5 cm)	90 (20.88)	53 (21.11)	37 (20.56)	0.286
Large (size > 5 cm)	264 (61.25)	164 (65.34)	100 (55.11)	
Tumor number				
One	373 (86.54)	204 (81.27)	169 (93.88)	0.0005
Two	42 (9.74)	38 (15.14)	4 (2.22)	
More	16 (3.71)	9 (3.59)	7 (3.90)	
MVI (≥ 1)	260 (60.32)	104 (41.43)	156 (86.66)	0.0001
Child-Pugh class, n (%)				
A	420 (97.44)	244 (97.21)	176 (97.78)	0.7682
B	11 (2.56)	7 (2.79)	4 (2.22)	

BCLC stage, n (%)				
A	121 (28.07)	87 (34.66)	34 (18.87)	0.0008
B	260 (60.32)	134 (53.39)	126 (70)	
C	50 (11.61)	30 (11.95)	20 (11.13)	
GS & Arg1 in HCC				
GS-Arg1-	56 (12.99)	30 (11.95)	26 (14.44)	0.1782
GS-Arg1+	63 (14.62)	35 (13.94)	28 (15.56)	
GS+Arg1-	187 (43.39)	120 (47.81)	67 (37.22)	
GS+Arg1+	125 (29.00)	66 (26.30)	59 (32.78)	

AFP: Alpha-fetoprotein; BCLC: Barcelona Clinic Liver Cancer; MVI: Microvascular invasion; GS: Glutamine synthetase;

Arg1: Arginase 1.



**Supplementary Table 3.** The relationship between HCC recurrence and clinical risk factors.

Predictor	Variables	Recurrence		<i>P</i>
		Yes, <i>n</i> (%)	No, <i>n</i> (%)	
Sex	Female	21 (58.33)	15 (41.67)	0.0541
	Male	159 (73.95)	56 (26.05)	
Etiology	Hepatitis B virus	156 (70.91)	64 (29.09)	0.4521
	Other	24 (77.42)	7 (22.58)	
Serum AFP	Low (serum AFP $\leq$ 500)	108 (68.35)	50 (31.65)	0.1235
	High (serum AFP > 500)	72 (77.42)	21 (22.58)	
Tumor number	One	138 (68.32)	64 (31.68)	<b>0.0148</b>
	Two	34 (89.47)	4 (10.53)	
	More	8 (88.89)	1 (11.11)	
Tumor size	Small (size $\leq$ 3 cm)	20 (48.78)	21 (51.22)	<b>&lt;0.0001</b>
	Medium (3 < size $\leq$ 5 cm)	34 (58.62)	24 (41.38)	
	Large (size > 5 cm)	126 (82.89)	26 (17.11)	
Cirrhosis	Yes	73 (72.28)	28 (27.72)	0.8707
	No	107 (71.33)	43 (28.67)	
Differentiation	Poor	88 (66.67)	44 (33.33)	<b>0.0428</b>
	Moderate-well	93 (78.15)	26 (21.85)	
MVI	0	83 (56.46)	64 (43.54)	<b>&lt;0.0001</b>
	$\geq$ 1	97 (93.27)	7 (6.73)	

AFP: Alpha-fetoprotein; BCLC: Barcelona Clinic Liver Cancer; MVI: Microvascular invasion.

**Supplementary Table 4.** Baseline patient demographics and disease characteristics in GS+ or GS- group of the patients

who received only hepatectomy.

Variable, <i>n</i> (%)	Total ( <i>n</i> =251)	GS+ group ( <i>n</i> =186)	GS- group ( <i>n</i> =65)	GS+ vs GS- <i>P</i> value
Age	51 (23–83)	50 (26–82)	52 (24–78)	0.1821
Female/Male	36/215	23/163	13/52	0.1508
PLT ( $10^9/L$ )	158.8 (38.0–476.0)	159.0 (38.0–476.0)	151.0 (42.0–395.0)	0.393
TBIL ( $\mu\text{mol/L}$ )	17.31 (0–391.00)	17.93 (0–391.00)	16.46 (4.20–333.00)	0.3576
ALT (U/L)	48.40 (8.00–279.00)	49.96 (9.00–279.00)	55.34 (8.00–258.00)	0.1011
AST (U/L)	51.00 (13.00–345.00)	50.19 (13–345)	53.09 (17.00–167.00)	0.6154
Neutrophil ( $10^9/L$ )	3.56 (0.086–40.00)	3.08 (0.86–11.48)	2.98 (1.29–7.59)	0.6754
Lymphocyte ( $10^9/L$ )	1.59 (0.30–7.00)	1.58 (0.30–4.88)	1.60 (0.52–7.00)	0.8333
TP (g/L)	70.60 (26.00–87.00)	70.46 (30.60–87.00)	70.98 (26.00–83.90)	0.6175
ALB (g/L)	41.79 (20.40–77.00)	41.56 (20.40–77.00)	42.48 (33.80–73.10)	0.2254
GGT (u/L)	104.93 (9.00–625.00)	100.60 (9.00–625.00)	117.50 (13.00–572.00)	0.2322
Satellite lesions	43 (17.13)	34 (18.28)	9 (13.85)	0.4141
Serum AFP, <i>n</i> (%)				
Low (serum AFP $\leq 500$ )	158 (62.95)	116 (62.37)	42 (64.61)	0.7465
High (serum AFP $> 500$ )	93 (37.05)	70 (37.63)	23 (35.39)	
Differentiation, <i>n</i> (%)				
Poor	132 (52.59)	92 (49.46)	40 (61.54)	0.0933
Moderate-well	119 (47.41)	94 (50.54)	25 (38.46)	
Etiology, <i>n</i> (%)				
Hepatitis B virus	220 (87.65)	167 (89.78)	53 (81.54)	0.0819
Other	31 (12.35)	19 (10.22)	12 (18.46)	
Cirrhosis, <i>n</i> (%)				
Yes	150 (59.76)	111 (59.68)	39 (60)	0.9636
No	101 (40.24)	75 (40.32)	26 (40)	
Tumor size				
Small (size $\leq 3$ cm)	34 (13.55)	26 (13.98)	8 (12.31)	0.1764
Medium ( $3 < \text{size} \leq 5$ cm)	53 (21.11)	34 (18.27)	19 (29.23)	
Large (size $> 5$ cm)	164 (65.34)	126 (67.75)	38 (58.43)	
Tumor number				
One	204 (81.27)	154 (82.80)	50 (76.92)	0.1651
Two	38 (15.14)	24 (12.93)	14 (21.54)	
More	9 (3.59)	8 (4.27)	1 (1.54)	
MVI	104 (41.43)	79 (42.47)	25 (38.46)	0.5719
Child-Pugh class, <i>n</i> (%)				
A	244 (97.21)	181 (97.31)	63 (96.92)	0.84

B	7 (2.79)	5 (2.69)	2 (3.08)	
BCLC stage, <i>n</i> (%)				
A	87 (34.66)	65 (34.95)	22 (33.85)	
B	134 (53.39)	99 (53.23)	35 (53.84)	0.9853
C	30 (11.95)	22 (11.82)	8 (12.31)	

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AFP: Alpha-fetoprotein; BCLC: Barcelona Clinic Liver Cancer; MVI: Microvascular invasion.

**Supplementary Table 5.** Baseline patient demographics and disease characteristics in Arg1+ or Arg1- group of the patients who only received hepatectomy.

Variable, <i>n</i> (%)	Total ( <i>n</i> =251)	Arg1+ group ( <i>n</i> =101)	Arg1- group ( <i>n</i> =150)	Arg1+ vs Arg1- <i>P</i> value
Age	51.00 (23.00–83.00)	51.60 (29.00–78.00)	50.04 (23.00–83.00)	0.2897
Female/Male	36/215	11/90	25/125	0.2704
PLT (10 <sup>9</sup> /L)	158.8 (38.0–476.0)	157.7 (42.0–475.0)	159.5 (38.0–476.0)	0.8651
TBIL (μmol/L)	17.31 (0–391.00)	14.53 (0–344.00)	19.14 (0–391.00)	0.1766
ALT (U/L)	48.40 (8.00–279.00)	44.43 (9.00–235.00)	50.92 (10.00–279.00)	0.2046
AST (U/L)	51 (13–345)	51.27 (13–291)	50.72 (15.00–345.00)	0.9156
Neutrophil (10 <sup>9</sup> /L)	3.560 (0.086–40.000)	3.640 (0.860–40.000)	3.560 (1.200–11.450)	0.2886
Lymphocyte (10 <sup>9</sup> /L)	1.59 (0.30–7.00)	1.63 (0.30–7.00)	1.56 (0.42–4.88)	0.431
TP (g/L)	70.60 (26.00–87.00)	70.97 (26.00–84.40)	70.34 (38.60–87.00)	0.4991
ALB (g/L)	41.79 (20.40–77.00)	42.38 (32.40–73.00)	41.41 (20.40–77.00)	0.152
GGT (u/L)	104.93 (9.00–625.00)	106.10 (13.00–425.00)	104.3 (9.00–425.00)	0.8841
Satellite lesions	43 (17.13)	17 (16.83)	26 (17.33)	0.9176
Serum AFP, <i>n</i> (%)				
Low (serum AFP ≤ 500)	158 (62.95)	67 (66.34)	91 (60.67)	0.3617
High (serum AFP > 500)	93 (37.05)	34 (33.66)	59 (39.33)	
Differentiation, <i>n</i> (%)				
Poor	132 (52.59)	57 (56.44)	75 (50)	0.3167
Moderate-well	119 (47.41)	44 (43.56)	75 (50)	
Etiology, <i>n</i> (%)				
Hepatitis B virus	220 (87.65)	87 (86.14)	133 (88.67)	0.5505
Other	31 (12.35)	14 (13.86)	17 (11.33)	
Cirrhosis, <i>n</i> (%)				
Yes	150 (59.76)	60 (49.41)	90 (60)	0.925
No	101 (40.24)	41 (40.59)	60 (40)	
Tumor size				
Small (size ≤ 3 cm)	34 (13.55)	12 (11.88)	22 (14.67)	
Medium (3 < size ≤ 5 cm)	53 (21.11)	22 (21.78)	31 (20.67)	0.8158
Large (size > 5 cm)	164 (65.34)	67 (66.34)	97 (64.66)	
Tumor number				
One	204 (81.27)	83 (82.18)	121 (80.67)	0.8757
Two	38 (15.14)	14 (13.86)	24 (16)	
More	9 (3.59)	4 (3.96)	5 (3.33)	
MVI	104 (41.43)	43 (42.57)	61 (40.67)	0.7635
Child-Pugh class, <i>n</i> (%)				0.8861

A	244 (97.21)	98 (97.03)	146 (97.33)	
B	7 (2.79)	3 (2.97)	4 (2.67)	
BCLC stage, <i>n</i> (%)				
A	87 (34.66)	29 (28.71)	58 (38.67)	0.1354
B	134 (53.39)	56 (55.45)	78 (52)	
C	30 (11.95)	16 (15.84)	14 (9.33)	

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AFP: Alpha-fetoprotein; BCLC: Barcelona Clinic Liver Cancer; MVI: Icrovascular invasion.