

Supplemental tables:

Supplemental Table 1. Baseline clinical data of 52 patients with advanced HCC.

Presentation	Case (%)
Median age, yr (range)	51 (24-74)
Gender, male (%)	47 (88.46%)
Aetiology (%)	
HBV positive	44 (84.61%)
HCV positive	8 (15.39%)
ECOG PS (%)	
0	16 (30.76%)
1	28 (53.84%)
2	6 (15.40%)
AFP (%)	
Normal	12 (23.10%)
Elevated	40 (76.90%)
extrahepatic metastasis (%)	34 (65.38%)
LN metastasis (%)	23 (44.23%)
Portal vein invasion (%)	36 (69.23%)
Chilg-Pugh (%)	
A	8 (15.38%)
B	32 (61.53%)
C	12 (23.09%)
Median size of index tumor, cm (range)	4.2 (1-13.3)
Median number of index tumors	3 (1-5)
Prior local therapy (%)	None

Supplemental Table 2. qPCR Primers.

Target gene	Primers
PXR	Forward primer: 5'-AGAGCGGCATGAAGAAGGAGATG-3' Reverse primer: 5'-GAAATGGGAGAAGGTAGTGTCAAAGG-3'
CYP3A4	Forward primer: 5'-CTAGCACATCATTGGACTG-3' Reverse primer: 5'-ACAGAGCTTTGTGGGACT-3'
P-gp (MDR-1)	Forward primer: 5'-CCATAGCTCGCGCCCTTGTTAGA-3' Reverse primer: 5'-CGGTGAGCAATCACAATGCAG-3'
miR-148a	Forward primer: 5'- ACAGAACTTTGTGTCGTATCCAGT-3' Reverse primer: 5'- CAGTGCGTGTCGTGGAGTC-3'
Sirt1	Forward primer: 5'-TAGACACGCTGGAACAGGTTGC-3' Reverse primer: 5'-CTCCTCGTACAGCTTCACAGTC-3'
β -Actin	Forward primer: 5'-CTCCATCCTGGCCTCGCTGT-3' Reverse primer: 5'-GCTGTCACCTTCACCGTTCC-3'

Supplemental Table 3. ChIP Primers.

Target region	Primers
PXRE (-362/+52)	Forward primer: 5'-AGATCTGTAGGTGTGGCTTGTTGG-3'
/ <i>cyp3a4</i> promoter	Reverse primer: 5'-TGTTGCTCTTTGCTGGGCTATGTGC-3'
miR-148a promoter	Forward primer: 5'-CCACTCTGTCCCCCATCCTA-3'
	Reverse primer: 5'-ACCTGCTGACTTGACACGAG-3'
Input	Forward primer: 5'-AACCTATTAAC TCACCCTTGT-3'
	Reverse primer: 5'-
	CCTCCATTCAAAAGATCTTATTATTTAGCATCTCCT-3'

Supplemental Table 4 Rhamnetin decelerated the metabolism or clearance of Sorafenib in cultured
HCC cell lines

Groups	MHCC97-H	HepG2
	The half-life ($T_{1/2}$) of Sorafenib	
Solvent control	10.53±7.74	11.84±1.80
Rhamnetin	23.54±8.62	25.61±5.11
Rhamnetin + miR-148a inhibitor	11.69±3.12	12.87±2.66
Rhamnetin + PXR ^{Mut}	16.87±2.63	13.08±3.87

Supplemental Table 5 Rhamnetin decelerated the metabolism or clearance of Sorafenib in
subcutaneous tumor tissues formed by HCC cells

Groups	MHCC97-H	HepG2
	The half-life ($T_{1/2}$) of Sorafenib	
Solvent control	15.57±2.44	11.42±4.74
Rhamnetin	40.76±5.74	50.24±6.67
Rhamnetin + PXR ^{Mut}	16.16±5.25	17.04±2.02

Supplemental Table 6 Rhamnetin enhanced the sensitivity of cultured HCC cells to Sorafenib

Groups	MHCC97-H	HepG2
	The IC_{50} values of Sorafenib	
Solvent control	1.18±0.50	1.42±0.34
Rhamnetin	0.15±0.04	0.29±0.11
Rhamnetin + miR-148a inhibitor	1.06±0.17	1.77±0.66
Rhamnetin + PXR ^{Mut}	1.55±0.16	1.95±0.57

Supplemental Table 7 Rhamnetin enhanced the sensitivity of cultured HCC cells to molecular targeting agents

Groups	Regorafenib	Lenvatinib	Anlotinib	Apatinib
	The IC_{50} values			
Solvent control	0.93±0.09	14.784131	15.628699	16.378337
Rhamnetin	0.33±0.08	14.700715	15.219668	16.647477
Rhamnetin + miR-148a inhibitor	1.01±0.22	14.939194	15.185712	16.443774
Rhamnetin + PXR ^{Mut}	1.38±0.57	14.031827	15.081336	16.082543

Supplemental Table 8 Rhamnetin enhanced antitumor effect of Sorafenib on tumor volumes of subcutaneous tumor tissues formed by HCC cells

Groups	MHCC97-H	HepG2
	The IC_{50} values of Sorafenib	
Solvent control	1.80±0.56	1.94±0.40
Rhamnetin	0.48±0.21	0.50±0.19
Rhamnetin + PXR ^{Mut}	2.14±0.86	2.03±0.42

Supplemental Table 9 Rhamnetin enhanced antitumor effect of Sorafenib on tumor weights of subcutaneous tumor tissues formed by HCC cells

Groups	MHCC97-H	HepG2
	The IC_{50} values of Sorafenib	
Solvent control	1.81±1.93	1.99±0.27
Rhamnetin	0.78±0.10	0.69±0.34
Rhamnetin + PXR ^{Mut}	1.95±0.66	1.85±0.48