

Table S1 Association between clinicopathologic data and TPH-1 H-Score dichotomized at the median

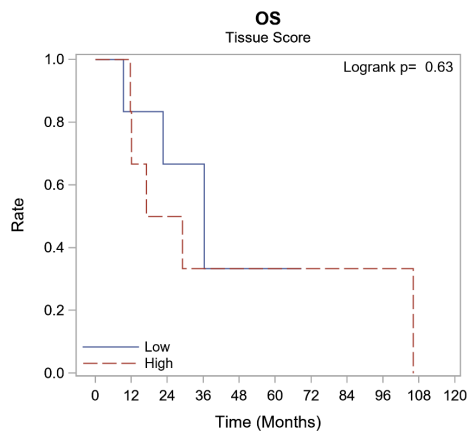
Characteristic	Category	TPH-1 < median	TPH-1 ≥ median	P value
Gender, n (%)	Female	4 (36.4)	6 (54.5)	0.670
	Male	7 (63.6)	5 (45.5)	
Age (years)	Median (min to max)	57 (52 to 78)	59 (38 to 77)	0.511
Race, n (%)	African American	1 (9.1)	1 (9.1)	1.000
	Caucasian	10 (90.9)	10 (90.9)	
Tobacco use, n (%)	Current	4 (36.4)	2 (18.2)	0.437
	Former	2 (18.2)	5 (45.5)	
	Never	5 (45.5)	4 (36.4)	
Alcohol use, n (%)	Unknown	2 (18.2)	0	0.028
	Current	8 (72.7)	4 (36.4)	
	Former	0	1 (9.1)	
	Never	1 (9.1)	6 (54.5)	
Primary tumor site, n (%)	Intrahepatic bile duct	5 (45.5)	9 (81.8)	0.183
	Other	6 (54.5)	2 (18.2)	
Stage at diagnosis, n (%)	IV	6 (54.5)	5 (45.5)	1.000
	I-III	5 (45.5)	6 (54.5)	
Response, n (%)	Non-responder	10 (90.9)	8 (72.7)	0.586
	Responder	1 (9.1)	3 (27.3)	
M stage at diagnosis, n (%)	0	5 (45.5)	5 (50.0)	1.000
	1	6 (54.5)	5 (50.0)	
N stage at diagnosis, n (%)	0	9 (81.8)	7 (77.8)	1.000
	1 or higher	2 (18.2)	2 (22.2)	
T stage at diagnosis, n (%)	1	2 (28.6)	2 (25.0)	0.888
	2	2 (28.6)	4 (50.0)	
	3	2 (28.6)	2 (25.0)	
	4	1 (14.3)	–	
Grade, n (%)	II	2 (18.2)	6 (54.5)	0.119
	III	5 (45.5)	1 (9.1)	
	Not determined	4 (36.4)	4 (36.4)	
Histology, n (%)	Adenocarcinoma	5 (45.5)	3 (27.3)	0.387
	Cholangiocarcinoma	5 (45.5)	8 (72.7)	
	Mixed cholangiocarcinoma/hepatocellular carcinoma	1 (9.1)	–	
5HT H-Score	Median (min/max)	0 (0 to 0.46)	0 (0 to 4.93)	0.834
5HT staining intensity, n (%)	0	8 (72.7)	8 (72.7)	1.000
	1	3 (27.3)	3 (27.3)	

Table S2 Association between clinicopathologic data and 5HT H-Score (0 vs. >0)

Characteristic	Category	Serotonin =0	Serotonin >0	P value
Gender, n (%)	Female	7 (43.8)	3 (50.0)	1.000
	Male	9 (56.3)	3 (50.0)	
Age (years)	Median/min/max	62.00/43.00/78.00	56.00/38.00/71.00	0.605
Race, n (%)	African American	1 (6.3)	1 (16.7)	0.481
	Caucasian	15 (93.8)	5 (83.3)	
Tobacco use, n (%)	Current	5 (31.3)	1 (16.7)	0.487
	Former	6 (37.5)	1 (16.7)	
	Never	5 (31.3)	4 (66.7)	
Alcohol use	Unknown	1 (6.3)	1 (16.7)	0.861
	Current	9 (56.3)	3 (50.0)	
	Former	1 (6.3)	0	
	Never	5 (31.3)	2 (33.3)	
Primary tumor site	Intrahepatic bile duct	10 (62.5)	4 (66.7)	1.000
	Other	6 (37.5)	2 (33.3)	
Stage at diagnosis, n (%)	IV	8 (50.0)	3 (50.0)	1.000
	I-III	8 (50.0)	3 (50.0)	
Response, n (%)	Non-responder	13 (81.3)	5 (83.3)	1.000
	Responder	3 (18.8)	1 (16.7)	
M stage at diagnosis, n (%)	0	7 (46.7)	3 (50.0)	1.000
	1	8 (53.3)	3 (50.0)	
N stage at diagnosis, n (%)	0	12 (80.0)	4 (80.0)	1.000
	1 or higher	3 (20.0)	1 (20.0)	
T stage at diagnosis, n (%)	1	4 (33.3)	–	0.789
	2	4 (33.3)	2 (66.7)	
	3	3 (25.0)	1 (33.3)	
	4	1 (8.3)	–	
Grade	II	5 (31.3)	3 (50.0)	0.842
	III	5 (31.3)	1 (16.7)	
	Not determined	6 (37.5)	2 (33.3)	
Histology	Adenocarcinoma	6 (37.5)	2 (33.3)	1.000
	Cholangiocarcinoma	9 (56.3)	4 (66.7)	
	Mixed cholangiocarcinoma/ hepatocellular carcinoma	1 (6.3)	–	
TPH-1 H-Score	Median/min/max	170.71/100.78/235.11	171.26/130.15/273.88	0.658
TPH-1 staining intensity, n (%)	1	6 (37.5)	2 (33.3)	0.132
	2	10 (62.5)	2 (33.3)	
	3		2 (33.3)	

Table S3 Serum serotonin concentration (in ng/mL)

Serum serotonin concentration	N (%)	Mean/standard deviation/N	Median/min/max
Primary site			
Intrahepatic bile duct	9 (75.0)	111.33/54.94/9	101.00/30.00/189.00
Other	3 (25.0)	92.33/83.39/3	54.00/35.00/188.00
Overall	12 (100.0)	106.58/59.44/12	97.00/30.00/189.00
P value		0.712	
Sex			
Male	8 (66.7)	89.88/64.62/8	68.50/30.00/189.00
Female	4 (33.3)	140.00/31.27/4	141.50/101.00/176.00
Overall	12 (100.0)	106.58/59.44/12	97.00/30.00/189.00
P value		0.203	
Clinical stage			
I-III	5 (50.0)	102.40/52.11/5	93.00/47.00/188.00
IV	5 (50.0)	112.80/76.09/5	134.00/30.00/189.00
Overall	12 (100.0)	107.60/61.73/10	97.00/30.00/189.00
P value		0.917	
Response			
Non-responder	9 (75.0)	108.33/65.43/9	93.00/30.00/189.00
Responder	3 (25.0)	101.33/47.50/3	101.00/54.00/149.00
Overall	12 (100.0)	106.58/59.44/12	97.00/30.00/189.00
P value		1.000	



Serotonin concentration	Median survival (95% CI), ng/mL	Sample	Log rank P value
Total	29.1 (11.7, 106.1)	E=8, C=4, T=12	0.629
Low	36.4 (9.4, NR)	E=3, C=3, T=6	
High	23.0 (11.7, 106.1)	E=5, C=1, T=6	

Figure S1 5HT concentration (ng/mL) and overall survival.