Table 1 Baseline patient characteristics

		n = 35	
Age, median (range), years		66	(40–75)
Sex, *n* (%)			
Male		23	(65.7%)
Female		12	(34.3%)
ECOG performance status			
0		27	(77.1%)
1		8	(22.9%)
Location of primary disease, *n* (%)			
Intrahepatic		21	(60.0%)
Hilar		3	(8.6%)
Distal		7	(20.0%)
Gallbladder		2	(5.7%)
Papilla of Vater		2	(5.7%)
Extent of disease, *n* (%)			
Metastatic		21	(60.0%)
Locally advanced		5	(14.3%)
Recurrent		9	(25.7%)
Sites of metastasis, *n* (%)			
Liver		12	(34.3%)
Lung		5	(14.3%)
Lymph node		16	(45.7%)
Peritoneal dissemination		4	(11.4%)
Size of target lesions, median (range), mm		62	(12-176)
CEA, median (range), ng/mL		4.4	(0.5-1457.5)
CA19-9, median (range), IU/mL		113.9	(1.0-103,949)
Biliary drainage, *n* (%)		8	(22.9%)
UGT1A1 polymorphisms, *n* (%)			
Wild type	*1/*1	21	(60.0%)
Heterozygous type	*1/*6	9	(25.7%)
	*1/*28	5	(14.3%)

All values are expressed as *n* (%) or median (range).

ECOG, Eastern Cooperative Oncology Group; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9, UGT1A1, uridine diphosphate glucuronosyltransferase 1A1.

Table 2 Efficacy

	n	PFS, months	OS, months	ORR, %	DCR, %
All cohort	35	7.4 (5.5-7.5)	14.7 (11.8-15.7)	31.4	74.3
Location of primary disease					
Intrahepatic	21	7.7 (6.7-9.2)	17.2 (13.4-24.8)	28.6	85.7
Hilar	3	7.5 (2.2-NR)	15.7 (2.7-NR)	66.7	66.7
Distal	7	3.5 (2.0-7.5)	9.7 (7.8-14.9)	14.3	57.1
Gallbladder	2	1.7 (1.4-NR)	8.7 (6.8-NR)	0.0	0.0
Papilla of Vater	2	6.4 (5.4-NR)	NR	100.0	100.0
Extent of disease					
Metastatic	21	7.4 (6.0-9.1)	14.7 (11.8-24.8)	28.6	76.2
Locally advanced	5	7.5 (2.0-7.9)	15.7 (3.6-18.2)	40.0	80.0
Recurrent	9	5.4 (2.1-7.4)	12.9 (8.4-15.2)	33.3	66.7
Size of target lesions at baseline					
< 60 mm	17	7.3 (3.8-7.4)	14.9 (9.7-15.7)	35.3	70.6
≥ 60 mm	18	7.5 (5.5-9.1)	14.0 (11.8-18.2)	27.8	77.8
CEA level at baseline					
< 5 ng/mL	19	7.5 (7.4-17.3)	15.7 (13.0-24.9)	42.1	78.9
≥ 5 ng/mL	16	4.1 (3.0-6.7)	10.1 (8.4-14.7)	18.8	68.8
CA19-9 level at baseline					
< 37 IU/mL	11	7.4 (5.4-7.9)	14.9 (12.9-18.2)	36.4	81.8
≥ 37 IU/mL	24	7.3 (4.4-7.5)	13.3 (9.7-15.7)	29.2	70.8

PFS and OS are expressed as median (80% confidence interval) and ORR and DCR are expressed in %.

PFS, progression-free survival; OS, overall survival; ORR, objective response rate; DCR, disease control rate; NR, not reached

Table 3 Factors associated with progression-free survival and overall survival

		n	PFS			p-value	OS			p-value
			HR	80% CI			HR	80% CI		
Age	< 65 years	14	1.40	0.87	~ 2.24	0.36	1.37	0.83	~ 2.28	0.42
	≥ 65 years	21	Ref				Ref			
Sex	Male	23	0.63	0.39	~ 1.03	0.23	0.73	0.43	~ 1.23	0.44
	Female	12	Ref				Ref			
ECOG performance status	0	27	1.05	0.61	~ 1.83	0.90	0.90	0.49	~ 1.63	0.82
	1	8	Ref				Ref			
Location of primary disease	Intrahepatic	21	0.48	0.18	~ 1.28	0.34	0.98	0.26	~ 3.77	0.99
	Hilar	3	0.70	0.21	~ 2.30	0.70	1.16	0.24	~ 5.70	0.90
	Distal	7	0.79	0.27	~ 2.29	0.78	1.96	0.48	~ 7.97	0.54
	Gallbladder	2	24.79	4.06	~ 151.31	0.02	4.18	0.85	~ 20.53	0.25
	Papilla of Vater	2	Ref				Ref			
Extent of disease	Metastatic	21	0.72	0.42	~ 1.24	0.44	0.80	0.45	~ 1.45	0.63
	Locally advanced	5	0.66	0.30	~ 1.45	0.50	0.83	0.37	~ 1.85	0.76
	Recurrent	9	Ref				Ref			
Size of target lesions at baseline	< 60 mm	17	1.21	0.76	~ 1.93	0.60	0.85	0.51	~ 1.42	0.68
	≥ 60 mm	18	Ref				Ref			
CEA level at baseline	< 5 ng/mL	19	0.35	0.22	~ 0.58	<0.01	0.46	0.27	~ 0.78	0.06
	≥ 5 ng/mL	16	Ref				Ref			
CA19-9 level at baseline	< 37 U/mL	11	1.02	0.62	~ 1.67	0.97	0.95	0.55	~ 1.65	0.91
	≥ 37 U/mL	24	Ref				Ref			
Biliary drainage	No	27	0.86	0.49	~ 1.50	0.73	0.64	0.35	~ 1.18	0.35
	Yes	8	Ref				Ref			

ECOG, Eastern Cooperative Oncology Group; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; PFS, progression-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; Ref, reference

Table 4 Adverse events

	Grade 1-4		Grade 3-4	
	n	%	*n*	%
Hematological				
Neutropenia	24	68.6%	19	54.3%
Febrile neutropenia	6	17.1%	6	17.1%
Leukopenia	22	62.9%	12	34.3%
Anemia	18	51.4%	1	2.9%
Thrombocytopenia	16	45.7%	3	8.6%
Non-hematological				
Nausea	22	62.9%	1	2.9%
Diarrhea	19	54.3%	1	2.9%
Anorexia	19	54.3%	1	2.9%
Peripheral sensory neuropathy	19	54.3%	1	2.9%
Constipation	15	42.9%	0	0%
Alopecia	11	31.4%	0	0%
Mucostitis oral	10	28.6%	0	0%
Fatigue	10	28.6%	0	0%
Cholinergic syndrome	6	17.1%	0	0%
Biliary tract infection	6	17.1%	3	8.6%
Hiccups	6	17.1%	0	0%
Hypertension	6	17.1%	2	5.7%
AST increased	15	42.9%	1	2.9%
ALT increased	14	40.0%	0	0%
GGT increased	14	40.0%	7	20.0%
Hypoalbuminaemia	12	34.3%	0	0%
ALP increased	9	25.7%	1	2.9%
Hypertension	6	17.1%	2	5.7%
Proteinurea	6	17.1%	0	0%

Adverse events are listed in which grade 1-4 toxicities occurred in more than 15% of patients.
AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, galactolipid galactosyltransferase; ALP, alkaline phosphatase

Table 5 Previous studies of FOFIRINOX for biliary tract cancer

Author	Year	N	Study design	Setting	Regimen	PFS, months	OS, months	ORR, %	DCR, %
Phelip JM, et al. [18]	2021	92	Randomized phase II	First-line	Modified	6.2	11.7	25.0	66.3
Sharma A, et al. [19]	2021	29*	Prospective	First-line	Modified	8.4	10.3	48.3	79.3
Ulusakarya A, et al. [20]	2020	27	Retrospective	First-line	Modified	8.0	15.1	29.3	75.6
Cui XY, et al. [21]	2021	15*	Retrospective	First-line	Modified	5.0	9.5	16.0	76.0
Zou L, et al. [22]	2021	27	Retrospective	First-line	Modified	9.9	15.7	33.3	77.8
Belkouz A, et al. [23]	2020	30	Prospective	Salvage	Full-dose	6.2	10.7	10.0	66.7
Ye LF, et al. [24]	2021	15*	Retrospective	Salvage	Modified	6.7	13.2	26.7	80.0
Present study	2022	35	Prospective	First-line	Full-dose	7.4	14.7	31.4	74.3

PFS, progression-free survival; OS, overall survival; ORR, objective response rate; DCR, disease control rate;

* indicates gallbladder cancer