## Supplementary Table 1 Unconditional univariate logistic analysis of factors associated with FOLFOXIRI in first-line chemotherapy

	Patients	Patients treated			
Characteristics	<i>(n)</i>	with	OR (95%	CI)	P value
		FOLFOXIRI (n)			
Demographic parameters					
Age, years	288	165	1.014	(0.991-	0.236
			1.039)		
Missing	1	0			
Gender					
Male	170	97	1.00 (Ref	erence)	
Female	119	68	1.003	(0.625-	0.989
			1.611)		
Familial history of cancer					
No	121	89	1.00 (Ref	erence)	
Yes	114	75	0.691	(0.395-	0.196
			1.210)		
Missing	54	1			
Personal history of cancer					
No	249	139	1.00 (Ref	erence)	
Yes	36	24	1.583	(0.758-	0.222
			3.306)		
Missing	4	2			
Pathological parameters					
Stage at diagnosis					
Localized	33	13	1.00 (Ref	erence)	
Locally advanced	78	60	5.128	(2.139-	
			12.298)		
Metastatic	178	92	1.646	(0.772-	< 0.001
			3.511)		
Primary tumor site					
Head	146	93	1.00 (Ref	erence)	
Body and/or tail	141	71	0.578	(0.361-	0.023
			0.927)		
Missing	2	1			
Histological grade					

Well or Moderately differentiated  Poorly differentiated or  Undifferentiated	84 32	39 23	1.00 (Reference) 2.949 (1.221- 0.016 7.122)
Missing	173	10	1.122)
Tumor extension			
Stage at chemotherapy initiation			
Locally advanced	74	60	1.00 (Reference)
Metastatic	215	105	0.223 (0.117- < 0.001
			0.423)
Number of metastatic sites			
0	74	60	1.00 (Reference)
1	143	74	0.250 (0.128-
			1.488)
≥ 2	72	31	0.176 (0.084- < 0.001
			0.372)
Lymph node metastases			
No	248	153	1.00 (Reference)
Yes	41	12	0.257 (0.125- < 0.001
			0.528)
Liver metastases			
No	121	84	1.00 (Reference)
Yes	168	81	0.410 (0.251- < 0.001
			0.670)
Peritoneal metastases			
No	243	134	1.00 (Reference)
Yes	46	31	1.681 (0.863- 0.127
			3.273)
Lung metastases			
No	248	146	1.00 (Reference)
Yes	41	19	0.603 (0.311- 0.136
			1.172)
Other metastases			
No	278	162	1.00 (Reference)
Yes	11	3	0.269 (0.070- 0.056
			1.034)

Performance status (WHO)			
0	96	54	1.00 (Reference)
1	169	103	1.214 (0.730-
			2.017)
≥2	20	8	0.519 (0.194- 0.195
			1.383)
Missing	4	0	
Body mass index, kg/m <sup>2</sup>	280	165	0.967 (0.920- 0.182
			1.016)
Missing	9	0	
Pain			
No	173	83	1.00 (Reference)
Yes	112	80	2.711 (1.633- < 0.001
			4.501)
Missing	4	2	
Jaundice			
No	262	148	1.00 (Reference)
Yes	25	17	1.637 (0.682- 0.270
			3.927)
Missing	2	0	
Ascites			
No	274	157	1.00 (Reference)
Yes	11	6	0.894 (0.266- 0.856
			2.999)
Missing	4	2	
Biological parameters			
Albumin, g/L	161	85	0.881 (0.832- < 0.001
			0.933)
Missing	128	80	
Lymphocytes, mm <sup>3</sup>			
< 1000	22	10	1.462 (0.592- 0.410
			3.613)
≥ 1000	146	53	1.00 (Reference)
Missing	121	102	
Neutrophil-to-lymphocyte ratio			
< 5	124	42	1.00 (Reference)

≥ 5	44	21	`	0.886- 0.105
			3.585)	
Missing	121	102		
CA19-9, UI/mL	252	131	1.000 (	1.000- 0.452
			1.000)	
Missing	37	34		
Previous treatment				
Primary tumor resection				
Yes	35	17	1.00 (Refere	ence)
No	254	148	1.478 (	0.728- 0.279
			3.002)	
Adjuvant chemotherapy				
Yes	27	15	1.00 (Refere	ence)
No	262	150	1.072 (	0.483- 0.865
			2.379)	

Logistic regression models used to estimate association of the parameters with FOLFOXIRI regimen. Values of P < 0.05 were considered statistically significant and all tests were two-sided. OR: Odds ratio; CI: Confidence interval; WHO: World Health Organization; CA19-9: Carbohydrate antigen 19-9.

Supplementary Table 2 Unconditional multivariate logistic analysis of factors associated with FOLFOXIRI in first-line chemotherapy for the construction of the propensity score (n = 283)

	Patients	Patients treated			
Characteristics	<i>(n)</i>	with	OR (95%	CI)	P value
		FOLFOXIRI (n)			
Primary tumor site					
Head	143	91	1.00 (Ref	ference)	
Body and/or tail	140	71	0.669	(0.383-	0.159
			1.170)		
Stage at diagnosis					
Localized	32	13	1.00 (Ref	ference)	
Locally advanced	75	57	0.663	(0.113-	
			3.869)		
Metastatic	176	92	2.120	(0.891-	0.143
			5.047)		
Stage at chemotherapy initiation					
Locally advanced	71	57	1.00 (Ref	ference)	
Metastatic	212	105	0.179	(0.025-	0.084
			1.262)		
Number of metastatic sites					
0	71	57	1.00 (Ref	ference)	
1	142	74	0.944	(0.460-	
			1.937)		
≥ 2	70	31	NA		0.876
Lymph node metastases					
No	244	150	1.00 (Ref	ference)	
Yes	39	12	0.325	(0.132-	0.014
			0.799)		
Liver metastases					
No	117	81	1.00 (Ref	ference)	
Yes	166	81	0.639	(0.304-	0.239
			1.345)		
Pain					
No	172	83	1.00 (Ref	ference)	

Yes 111 79 2.937 (1.695- < 0.001 5.089)

Logistic regression models used to estimate association of the parameters with FOLFOXIRI regimen. Values of P<0.05 were considered statistically significant and all tests were two-sided. OR: Odds ratio; CI: Confidence interval.

## Supplementary Table 3 Patient characteristics of the entire metastatic population according to first-line chemotherapy, n (%)

Characteristics	FOLFIRINOX $(n = 110)$	FOLFOXIRI (n = 105)	P value
Demographic parameters			
Age, median [IQR], yr	60.0 [53.0-65.2]	62.0 [53.4-67.0]	0.147
Missing	1	0	
Gender			0.386
Male	66 (60.0)	69 (65.7)	
Female	44 (40.0)	36 (34.3)	
Familial history of cancer			0.131
No	26 (42.6)	57 (54.8)	
Yes	35 (57.4)	47 (45.2)	
Missing	49	1	
Personal history of cancer			0.056
No	98 (90.7)	85 (81.7)	
Yes	10 (9.3)	19 (18.3)	
Missing	2	1	
Pathological parameters			
Stage at diagnosis			0.406
Localized	18 (16.4)	13 (12.4)	
Advanced	92 (83.6)	92 (87.6)	
Primary tumor site			0.520
Head	42 (38.5)	45 (42.9)	
Body and/or tail	67 (61.5)	60 (57.1)	
Missing	1	0	
Histological grade			0.014
Well or Moderately differentiated	40 (81.6)	27 (58.7)	
Poorly differentiated or	9 (18.4)	19 (41.3)	
Undifferentiated			
Missing	61	59	
Tumor extension			
Number of metastatic sites			0.229
1	69 (62.7)	74 (70.5)	
≥ 2	41 (37.3)	31 (29.5)	
Lymph node metastases			0.005
No	81 (73.6)	93 (88.6)	

Yes	29 (26.4)	12 (11.4)	
Liver metastases			0.730
No	23 (20.9)	24 (22.9)	
Yes	87 (79.1)	81 (77.1)	
Peritoneal metastases			0.005
No	95 (86.4)	74 (70.5)	
Yes	15 (13.6)	31 (29.5)	
Lung metastases			0.722
No	88 (80.0)	86 (81.9)	
Yes	22 (20.0)	19 (18.1)	
Other metastases			0.142
No	102 (92.7)	102 (97.1)	
Yes	8 (7.3)	3 (2.9)	
Clinical parameters			
Performance status (WHO)			0.086
0	36 (34.0)	30 (28.6)	
1	59 (55.7)	71 (67.6)	
≥ 2	11 (10.4)	4 (3.8)	
Missing	4	0	
Body mass index, kg/m <sup>2</sup>	23.9 [21.2-27.8]	23.1 [20.8-26.1]	0.167
Missing	9	0	
Pain			0.005
ı allı			
No	77 (71.3)	55 (52.4)	
	77 (71.3) 31 (28.7)	55 (52.4) 50 (47.6)	
No		, ,	
No Yes	31 (28.7)	50 (47.6)	0.272
No Yes Missing	31 (28.7)	50 (47.6)	
No Yes Missing Jaundice	31 (28.7)	50 (47.6) 0	
No Yes Missing Jaundice No	31 (28.7) 2 102 (94.4)	50 (47.6) 0 95 (90.5)	
No Yes Missing Jaundice No Yes	31 (28.7) 2 102 (94.4) 6 (5.6)	50 (47.6) 0 95 (90.5) 10 (9.5)	
No Yes Missing Jaundice No Yes Missing	31 (28.7) 2 102 (94.4) 6 (5.6)	50 (47.6) 0 95 (90.5) 10 (9.5)	0.272
No Yes Missing Jaundice No Yes Missing Ascites	31 (28.7) 2 102 (94.4) 6 (5.6) 2	50 (47.6) 0 95 (90.5) 10 (9.5) 0	0.272
No Yes Missing Jaundice No Yes Missing Ascites No	31 (28.7) 2 102 (94.4) 6 (5.6) 2 103 (95.4)	50 (47.6) 0 95 (90.5) 10 (9.5) 0 99 (94.3)	0.272
No Yes Missing Jaundice No Yes Missing Ascites No Yes	31 (28.7) 2 102 (94.4) 6 (5.6) 2 103 (95.4) 5 (4.6)	50 (47.6) 0 95 (90.5) 10 (9.5) 0 99 (94.3) 6 (5.7)	0.272
No Yes Missing Jaundice No Yes Missing Ascites No Yes Missing	31 (28.7) 2 102 (94.4) 6 (5.6) 2 103 (95.4) 5 (4.6)	50 (47.6) 0 95 (90.5) 10 (9.5) 0 99 (94.3) 6 (5.7)	0.272

Lymphocytes, median [IQR], mm <sup>3</sup>			0.066
< 1000	10 (10.7)	9 (23.1)	
≥ 1000	83 (89.3)	30 (76.9)	
Missing	17	66	
Neutrophil-to-lymphocyte ratio,			0.010
median [IQR]			
< 5	71 (76.3)	21 (53.9)	
≥ 5	22 (23.7)	18 (46.1)	
Missing	17	66	
CA19-9, median [IQR], UI/mL	1077.0 [76.7-7400.0]	1333.0 [208.7	- 0.184
		12956.0]	
Missing	3	23	
Previous treatment			
Primary tumor resection			0.642
Yes	16 (14.5)	13 (12.4)	
No	94 (85.5	92 (87.6)	
Adjuvant chemotherapy			0.904
Yes	12 (10.9)	12 (11.4)	
No	98 (89.1)	93 (88.6)	

 $<sup>\</sup>chi^2$  tests or Fisher's exact tests used to compare proportions, and Wilcoxon tests used to compare continuous variables between FOLFIRINOX and FOLFOXIRI groups. All statistical tests were two-sided. CA19-9: Carbohydrate antigen 19-9; IQR: Interquartile range; WHO: World Health Organization.

## Supplementary Table 4 Outcomes of the entire metastatic population according to first-line chemotherapy, n (%)

0.1	FOLFIRINOX	FOLFOXIRI	P
Outcomes	(n = 110)	(n = 105)	value
Number of cycles, median [IQR]	11.0 [6.0-13.0]	7.0 [4.0-14.0]	0.110
Missing	1	0	
RECIST best response			0.096
Complete or partial response	47 (48.0)	31 (38.3)	
Stability	26 (26.5)	17 (21.0)	
Progression	25 (25.5)	33 (40.7)	
Missing	12	24	
Toxicity of grade 3 or 4			0.201
No	83 (79.1)	75 (71.4)	
Yes	22 (20.9)	30 (28.6)	
Digestive	5 (4.8)	10 (9.5)	
Hematology	1 (0.9)	5 (4.8)	
Neurology	9 (8.5)	10 (9.5)	
Other	7 (6.7)	5 (4.8)	
Missing	5	0	
Reason for discontinuation			0.731
Progression	78 (71.6)	80 (76.2)	
Toxicity	8 (7.3)	7 (6.7)	
Other	23 (21.1)	18 (17.1)	
Missing	1	0	
Maintenance			0.055
Yes	53 (48.2)	37 (35.2)	
No	57 (51.8)	68 (64.8)	
Second-line chemotherapy			0.504
administration			
Yes	82 (74.6)	74 (70.5)	
No	28 (25.4)	31 (29.5)	

 $<sup>\</sup>chi^2$  tests or Fisher's exact tests used to compare proportions, and Wilcoxon tests used to compare continuous variables between FOLFIRINOX and FOLFOXIRI groups. All statistical tests were two-sided. IQR: Interquartile range.

Supplementary Table 5 Unconditional univariate logistic analysis of factors associated with FOLFOXIRI in first-line chemotherapy in patients with metastatic disease

	Patients	Patients treated		
Characteristics	<i>(n)</i>	with FOLFOXIRI	OR (95%CI)	P value
		(n)		
Demographical parameters				
Age, years	214	105	1.020 (0.992-	0.159
			1.049)	
Missing	1	0		
Gender				
Male	135	69	1.00 (Reference)	
Female	80	36	0.783 (0.449-	0.387
			1.363)	
Familial history of cancer				
No	83	57	1.00 (Reference)	
Yes	82	47	0.613 (0.324-	0.132
			1.159)	
Missing	50	1		
Personal history of cancer				
No	183	85	1.00 (Reference)	
Yes	29	19	2.190 (0.966-	0.061
			4.968)	
Missing	3	1		
Pathological parameters				
Stage at diagnosis				
Localized	31	13	1.00 (Reference)	
Advanced	184	92	1.385 (0.641-	0.407
			2.990)	
Primary tumor site				
Head	87	45	1.00 (Reference)	
Body and/or tail	127	60	0.836 (0.484-	0.520
			1.443)	
Missing	1	0		
Histological grade				
Well or Moderately differentiated	67	27	1.00 (Reference)	

Poorly Undifferenti	differentiated ated	or	28	19	3.127 7.936)	(1.232-	0.016
Missing			120	59	,		
Tumor exte	nsion						
Number of r	metastatic sites						
1			143	74	1.00 (Refe	rence)	
≥ 2			72	31	0.705	(0.399-	0.230
					1.247)		
Lymph node	e metastases						
No			174	93	1.00 (Refe	rence)	
Yes			41	12	0.360	(0.173-	0.007
					0.752)		
Liver metas	tases						
No			47	24	1.00 (Refe	rence)	
Yes			168	81	0.892	(0.467-	0.730
					1.704)		
Peritoneal n	netastases						
No			169	74	1.00 (Refe	rence)	
Yes			46	31	2.653	(1.334-	0.005
					5.274)		
Lung metas	tases						
No			174	86	1.00 (Refe	rence)	
Yes			41	19	0.884	(0.447-	0.723
					1.748)		
Other metas	stases						
No			204	102	1.00 (Refe		
Yes			11	3	0.375	(0.097-	0.156
					1.454)		
Clinical para							
Performanc	e status (WHO)						
0			66	30	1.00 (Refe	•	
1			130	71	1.444	(0.797-	
					2.618)		
≥ 2			15	4	0.436	(0.126-	0.098
					1.512)		
Missing			4	0			

Body mass index, kg/m <sup>2</sup>	206	105	0.967 1.022)	(0.915-	0.239
Missing	9	0			
Pain					
No	132	55	1.00 (Refe	rence)	
Yes	81	50	2.258	(1.282-	0.005
			3.977)		
Missing	2	0			
Jaundice					
No	197	95	1.00 (Refe	rence)	
Yes	16	10	1.789	(0.626-	0.277
			5.114)		
Missing	2	0			
Ascites					
No	202	99	1.00 (Refe	rence)	
Yes	11	6	1.248	(0.369-	0.722
			4.220)		
Missing	2	0			
Clinical parameters					
Albumin, g/L	122	53	0.891	(0.838-	<0.001
			0.948)		
Missing	93	52			
Lymphocytes, mm <sup>3</sup>					
< 1000	19	9	2.490	(0.923-	
			6.719)		
≥ 1000	113	30	1.00 (Refe	rence)	0.072
Missing	83	66			
Neutrophil-to-lymphocyte ratio					
< 5	92	21	1.00 (Refe	rence)	
≥ 5	40	18	2.766	(1.255-	0.012
			6.099)		
Missing	83	66			
CA19-9, UI/mL	189	82	1.000	(1.000-	0.155
			1.000)		
Missing	26	23			
Previous treatment					

Primary tumor resection			
Yes	29	13	1.00 (Reference)
No	186	92	1.205 (0.549- 0.643
			2.644)
Adjuvant chemotherapy			
Yes	24	12	1.00 (Reference)
No	191	93	0.949 (0.406- 0.904
			2.218)

Logistic regression models used to estimate association of the parameters with FOLFOXIRI regimen. Values of P<0.05 were considered statistically significant and all tests were two-sided. OR: Odds ratio; CI: Confidence interval; WHO: World Health Organization; CA19-9: Carbohydrate antigen 19-9.

Supplementary Table 6 Unconditional multivariate logistic analysis of factors associated with FOLFOXIRI in first-line chemotherapy for the construction of the propensity score in patients with metastatic disease (n = 122).

	Patients	Patients treated		P
Characteristics	<i>(n)</i>	with	OR (95%CI)	
		FOLFOXIRI (n)		value
Lymph node metastases				
No	94	49	1.00 (Reference)	
Yes	28	4	0.165 (0.049-0.562)	0.004
Peritoneal metastases				
No	96	38	1.00 (Reference)	
Yes	26	15	2.243 (0.793-6.344)	0.128
Pain†				
No	75	24	1.00 (Reference)	
Yes	47	29	3.124 (1.321-7.390)	0.010
Albumin, g/L	122	53	0.896 (0.839-0.956)	0.001

A propensity score was performed by an unconditional multivariable logistic regression model including lymph node and peritoneal metastases, pain and albumin level. Neutrophil-to-lymphocyte ratio was not selected in the propensity score process due to a high rate of missing data. Logistic regression models used to estimate association of the parameters with FOLFOXIRI regimen. Values of P < 0.05 were considered statistically significant and all tests were two-sided. OR: Odds ratio; CI: Confidence interval.

## Supplementary Table 7 Patient characteristics of the propensity score - matched metastatic population according to first-line chemotherapy, n (%)

Characteristics         32)         value           Demographic parameters         Age, median [IQR], years         5 9.8 [54.5-67.9]         60.4 [51.7-66.3]         0.669           Missing         0	Characteristics		FOLFIRINOX (n =	FOLFOXIRI $(n = 32)$	P
Age, median [QR], years       59.8 [54.5-67.9]       60.4 [51.7-66.3]       0.699         Missing       0       0       0         Gender       20 (62.5)       22 (68.8)       0         Female       12 (37.5)       10 (31.2)       1.000         No       9 (56.3)       18 (56.3)       1.000         No       9 (56.3)       18 (56.3)       1.000         Missing       16       0       1.000         No       27 (87.1)       27 (84.4)       1.000         No       27 (87.1)       27 (84.4)       1.000         No       4 (12.9)       5 (15.6)       1.000         Missing       1       0       1.000         Pathologic parameters       1       0       1.000         Stage at diagnosis       5 (15.6)       4 (12.5)       1.000         Localized       5 (15.6)       4 (12.5)       1.000         Advanced       27 (84.4)       28 (87.5)       1.000         Head       14 (45.2)       16 (50.0)       1.000         Well or Moderately differentiated       11 (68.8)       8 (66.7)         Poorly       differentiated       11 (68.8)       8 (66.7)         Poorly <t< th=""><th>Characteristics</th><th></th><th>32)</th><th></th><th>value</th></t<>	Characteristics		32)		value
Missing       0       0         Gender       0.599         Male       20 (62.5)       22 (68.8)         Female       12 (37.5)       10 (31.2)         Familial history of cancer       1.000         No       9 (56.3)       18 (56.3)         Yes       7 (43.7)       14 (43.7)         Missing       16       0         Personal history of cancer       1.000         No       27 (87.1)       27 (84.4)         Yes       4 (12.9)       5 (15.6)         Missing       1       0         Pathologic parameters       1.000         Stage at diagnosis       1       0         Localized       5 (15.6)       4 (12.5)         Advanced       27 (84.4)       28 (87.5)         Primary tumor site       0.701         Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       11 (68.8)       8 (66.7)         Poorly       differentiated       11 (68.8)       8 (66.7)         Poorly       differentiated       1 (65.6)       20         Tumor extension       21 (65.6)       26 (81.3)	Demographic parameters				
Gender       20 (62.5)       22 (68.8)         Female       12 (37.5)       10 (31.2)         Familial history of cancer       1.000         No       9 (56.3)       18 (56.3)         Yes       7 (43.7)       14 (43.7)         Missing       16       0         Personal history of cancer       1.000         No       27 (87.1)       27 (84.4)         Yes       4 (12.9)       5 (15.6)         Missing       1       0         Pathologic parameters       1.000         Stage at diagnosis       1       0         Localized       5 (15.6)       4 (12.5)         Advanced       27 (84.4)       28 (87.5)         Primary tumor site       0.701         Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       11 (68.8)       8 (66.7)         Poorly       differentiated       11 (68.8)       8 (66.7)         Poorly       differentiated       1 (65.8)       8 (66.7)         Promise tension       20       1         Number of metastatic sites       0.157         1       21 (65.6)       26 (81	Age, median [IQR], years		59.8 [54.5-67.9]	60.4 [51.7-66.3]	0.669
Male       20 (62.5)       22 (68.8)         Female       12 (37.5)       10 (31.2)         Familial history of cancer       1.000         No       9 (56.3)       18 (56.3)         Yes       7 (43.7)       14 (43.7)         Missing       16       0         Personal history of cancer       1.000         No       27 (87.1)       27 (84.4)         Yes       4 (12.9)       5 (15.6)         Missing       1       0         Pathologic parameters       1.000         Stage at diagnosis       1       0         Localized       5 (15.6)       4 (12.5)         Advanced       27 (84.4)       28 (87.5)         Primary tumor site       0.701         Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       11 (68.8)       8 (66.7)         Poorly       differentiated       11 (68.8)       8 (66.7)         Poorly       differentiated       1 (65.0)       4 (33.3)         Undifferentiated       1 (65.6)       26 (81.3)         Number of metastatic sites       0.157         1       21 (65.6)	Missing		0	0	
Female       12 (37.5)       10 (31.2)         Familial history of cancer       1.000         No       9 (56.3)       18 (56.3)         Yes       7 (43.7)       14 (43.7)         Missing       16       0         Personal history of cancer       1.000         No       27 (87.1)       27 (84.4)         Yes       4 (12.9)       5 (15.6)         Missing       1       0         Pathologic parameters       1.000         Stage at diagnosis       1.000         Localized       5 (15.6)       4 (12.5)         Advanced       27 (84.4)       28 (87.5)         Primary tumor site       0.701         Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       11 (68.8)       8 (66.7)         Poorly       differentiated       11 (68.8)       8 (66.7)         Poorly       differentiated       1 (65.8)       26 (81.3)         Undifferentiated       1 (65.6)       26 (81.3)         Number of metastatic sites       0.157         1       21 (65.6)       26 (81.3)         22       11 (34.4)       6 (18.7	Gender				0.599
Familial history of cancer       1.000         No       9 (56.3)       18 (56.3)         Yes       7 (43.7)       14 (43.7)         Missing       16       0         Personal history of cancer       1.000         No       27 (87.1)       27 (84.4)         Yes       4 (12.9)       5 (15.6)         Missing       1       0         Pathologic parameters       5 (15.6)       4 (12.5)         Stage at diagnosis       1.000       1.000         Localized       5 (15.6)       4 (12.5)         Advanced       27 (84.4)       28 (87.5)         Primary tumor site       0.701         Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       1.000         Well or Moderately differentiated       11 (68.8)       8 (66.7)         Poorly       differentiated       or 5 (31.2)       4 (33.3)         Undifferentiated       16       20         Tumor extension       10.157         Number of metastatic sites       26 (81.3)         ≥ 2       11 (34.4)       6 (18.7)         Lymph node metastases       1.000	Male		20 (62.5)	22 (68.8)	
No       9 (56.3)       18 (56.3)         Yes       7 (43.7)       14 (43.7)         Missing       16       0         Personal history of cancer       1.000         No       27 (87.1)       27 (84.4)         Yes       4 (12.9)       5 (15.6)         Missing       1       0         Pathologic parameters       5 (15.6)       4 (12.5)         Stage at diagnosis       5 (15.6)       4 (12.5)         Advanced       27 (84.4)       28 (87.5)         Primary tumor site       5 (15.6)       4 (12.5)         Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       11 (68.8)       8 (66.7)         Poorly       differentiated       or       5 (31.2)       4 (33.3)         Undifferentiated       16       20         Tumor extension       Number of metastatic sites       26 (81.3)       26 (81.3)         ≥ 2       11 (34.4)       6 (18.7)         Lymph node metastases       1.000	Female		12 (37.5)	10 (31.2)	
Yes       7 (43.7)       14 (43.7)         Missing       16       0         Personal history of cancer       1.000         No       27 (87.1)       27 (84.4)         Yes       4 (12.9)       5 (15.6)         Missing       1       0         Pathologic parameters       5       1.000         Stage at diagnosis       1       0         Localized       5 (15.6)       4 (12.5)         Advanced       27 (84.4)       28 (87.5)         Primary tumor site       0.701         Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       1.000         Well or Moderately differentiated       11 (68.8)       8 (66.7)         Poorly       differentiated       10 (33.3)         Undifferentiated       16 (20       10 (33.3)         Undifferentiated       1 (34.4)       20         Tumor extension       1 (34.4)       26 (81.3)         ≥ 2       11 (34.4)       6 (18.7)         Lymph node metastases       1 (30.0)	Familial history of cancer				1.000
Missing       16       0         Personal history of cancer       1.000         No       27 (87.1)       27 (84.4)       27 (84.4)         Yes       4 (12.9)       5 (15.6)       4         Missing       1       0	No		9 (56.3)	18 (56.3)	
No       27 (87.1)       27 (84.4)         Yes       4 (12.9)       5 (15.6)         Missing       1       0         Pathologic parameters       5 (15.6)       4 (12.5)         Stage at diagnosis       1.000         Localized       5 (15.6)       4 (12.5)         Advanced       27 (84.4)       28 (87.5)         Primary tumor site       0.701         Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       11 (68.8)       8 (66.7)         Poorly       differentiated       11 (68.8)       8 (66.7)         Poorly       differentiated       1 (53.2)       4 (33.3)         Undifferentiated       16       20         Tumor extension       10.157         Number of metastatic sites       0.157         1       21 (65.6)       26 (81.3)         ≥ 2       11 (34.4)       6 (18.7)         Lymph node metastases       1.000	Yes		7 (43.7)	14 (43.7)	
No       27 (87.1)       27 (84.4)         Yes       4 (12.9)       5 (15.6)         Missing       1       0         Pathologic parameters       1.000         Stage at diagnosis       1.000         Localized       5 (15.6)       4 (12.5)         Advanced       27 (84.4)       28 (87.5)         Primary tumor site       0.701         Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       1.000         Well or Moderately differentiated       11 (68.8)       8 (66.7)         Poorly       differentiated       1 (68.8)       8 (66.7)         Poorly       differentiated       1 (68.8)       2 (68.3)         Undifferentiated       1 (68.8)       2 (68.3)       0.157         1       2 (65.6)       2 (68.1.3)       0.157         1       2 (65.6)       2 (68.1.3)       0.157         2       1 (1 (34.4)       6 (18.7)       1.000	Missing		16	0	
Yes       4 (12.9)       5 (15.6)         Missing       1       0         Pathologic parameters       5       1.000         Stage at diagnosis       1.000         Localized       5 (15.6)       4 (12.5)         Advanced       27 (84.4)       28 (87.5)         Primary tumor site       0.701         Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       1.000         Well or Moderately differentiated       11 (68.8)       8 (66.7)         Poorly       differentiated       1 (68.8)       8 (66.7)         Poorly       differentiated       1 (68.8)       20         Tumor extension       1 (69.0)       1 (69.0)       1 (69.0)         Number of metastatic sites       0.157       1 (69.0)       1 (69.0)       1 (69.0)         1       21 (65.6)       26 (81.3)       2 (69.0)       1 (69.0)         2       11 (34.4)       6 (18.7)       1 (69.0)       1 (69.0)         2       1 (10.0)       1 (10.0)       1 (10.0)       1 (10.0)       1 (10.0)       1 (10.0)       1 (10.0)       1 (10.0)       1 (10.0)       1 (10.0)       1 (10.0) <td>Personal history of cancer</td> <td></td> <td></td> <td></td> <td>1.000</td>	Personal history of cancer				1.000
Missing       1       0         Pathologic parameters         Stage at diagnosis       1.000         Localized       5 (15.6)       4 (12.5)         Advanced       27 (84.4)       28 (87.5)         Primary tumor site       0.701         Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       11 (68.8)       8 (66.7)         Well or Moderately differentiated       11 (68.8)       8 (66.7)         Poorly       differentiated       4 (33.3)         Undifferentiated       16       20         Tumor extension       16       20         Number of metastatic sites       0.157         1       21 (65.6)       26 (81.3)         ≥ 2       11 (34.4)       6 (18.7)         Lymph node metastases       1.000	No		27 (87.1)	27 (84.4)	
Pathologic parameters         Stage at diagnosis       1.000         Localized       5 (15.6)       4 (12.5)         Advanced       27 (84.4)       28 (87.5)         Primary tumor site       0.701         Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       1.000         Well or Moderately differentiated       11 (68.8)       8 (66.7)         Poorly differentiated       1 (68.8)       8 (66.7)         Undifferentiated         Missing       16       20         Tumor extension         Number of metastatic sites       0.157         1       21 (65.6)       26 (81.3)         ≥ 2       11 (34.4)       6 (18.7)         Lymph node metastases       1.000	Yes		4 (12.9)	5 (15.6)	
Stage at diagnosis       1.000         Localized       5 (15.6)       4 (12.5)         Advanced       27 (84.4)       28 (87.5)         Primary tumor site       0.701         Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       1.000         Well or Moderately differentiated       11 (68.8)       8 (66.7)         Poorly       differentiated       4 (33.3)         Undifferentiated       16       20         Tumor extension       5 (15.6)       26 (81.3)         Number of metastatic sites       21 (65.6)       26 (81.3)         ≥ 2       11 (34.4)       6 (18.7)         Lymph node metastases       1.000	Missing		1	0	
Localized       5 (15.6)       4 (12.5)         Advanced       27 (84.4)       28 (87.5)         Primary tumor site       0.701         Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       1.000         Well or Moderately differentiated       11 (68.8)       8 (66.7)         Poorly       differentiated       4 (33.3)         Undifferentiated       16       20         Tumor extension       10.157         Number of metastatic sites       0.157         1       21 (65.6)       26 (81.3)         ≥ 2       11 (34.4)       6 (18.7)         Lymph node metastases       1.000	Pathologic parameters				
Advanced       27 (84.4)       28 (87.5)         Primary tumor site       0.701         Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       1.000         Well or Moderately differentiated       11 (68.8)       8 (66.7)         Poorly       differentiated       4 (33.3)         Undifferentiated       16       20         Tumor extension       16       20         Number of metastatic sites       0.157         1       21 (65.6)       26 (81.3)         ≥ 2       11 (34.4)       6 (18.7)         Lymph node metastases       1.000	Stage at diagnosis				1.000
Primary tumor site       0.701         Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       1.000         Well or Moderately differentiated       11 (68.8)       8 (66.7)         Poorly differentiated or 5 (31.2)       4 (33.3)         Undifferentiated         Missing       16       20         Tumor extension         Number of metastatic sites       0.157         1       21 (65.6)       26 (81.3)         ≥ 2       11 (34.4)       6 (18.7)         Lymph node metastases       1.000	Localized		5 (15.6)	4 (12.5)	
Head       14 (45.2)       16 (50.0)         Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       1.000         Well or Moderately differentiated       11 (68.8)       8 (66.7)         Poorly       differentiated       4 (33.3)         Undifferentiated       16       20         Tumor extension       20         Number of metastatic sites       0.157         1       21 (65.6)       26 (81.3)         ≥ 2       11 (34.4)       6 (18.7)         Lymph node metastases       1.000	Advanced		27 (84.4)	28 (87.5)	
Body and/or tail       17 (54.8)       16 (50.0)         Histological grade       1.000         Well or Moderately differentiated       11 (68.8)       8 (66.7)         Poorly differentiated or 5 (31.2)       4 (33.3)         Undifferentiated       4 (33.3)         Missing 16       20         Tumor extension       0.157         Number of metastatic sites       0.157         1 21 (65.6)       26 (81.3)         ≥ 2       11 (34.4)       6 (18.7)         Lymph node metastases       1.000	Primary tumor site				0.701
Histological grade       1.000         Well or Moderately differentiated       11 (68.8)       8 (66.7)         Poorly differentiated       4 (33.3)         Undifferentiated       20         Tumor extension       20         Number of metastatic sites       0.157         1       21 (65.6)       26 (81.3)         ≥ 2       11 (34.4)       6 (18.7)         Lymph node metastases       1.000	Head		14 (45.2)	16 (50.0)	
Well or Moderately differentiated       11 (68.8)       8 (66.7)         Poorly       differentiated       4 (33.3)         Undifferentiated       16       20         Tumor extension       Vumber of metastatic sites       0.157         1       21 (65.6)       26 (81.3)         ≥ 2       11 (34.4)       6 (18.7)         Lymph node metastases       1.000	Body and/or tail		17 (54.8)	16 (50.0)	
Poorlydifferentiatedor $5 (31.2)$ $4 (33.3)$ UndifferentiatedMissing $16$ $20$ Tumor extension $16$ $16$ $16$ Number of metastatic sites $16$ $16$ $16$ 1 $16$ $16$ $16$ $16$ 2 $16$ $16$ $16$ $16$ 2 $16$ $16$ $16$ $16$ 2 $16$ $16$ $16$ $16$ 2 $16$ $16$ $16$ $16$ 2 $16$ $16$ $16$ $16$ 2 $16$ $16$ $16$ $16$ 2 $16$ $16$ $16$ $16$ 2 $16$ $16$ $16$ $16$ 2 $16$ $16$ $16$ $16$ 2 $16$ $16$ $16$ $16$ $16$ 2 $16$ $16$ $16$ $16$ $16$ $16$ 2 $16$ <t< td=""><td>Histological grade</td><td></td><td></td><td></td><td>1.000</td></t<>	Histological grade				1.000
UndifferentiatedMissing1620Tumor extension $$ $$ Number of metastatic sites $$ $$ 121 (65.6)26 (81.3)≥ 211 (34.4)6 (18.7)Lymph node metastases $$ $$	Well or Moderately differentiated		11 (68.8)	8 (66.7)	
Missing       16       20         Tumor extension	Poorly differentiated	or	5 (31.2)	4 (33.3)	
Tumor extension       0.157         Number of metastatic sites       0.157         1       21 (65.6)       26 (81.3)         ≥ 2       11 (34.4)       6 (18.7)         Lymph node metastases       1.000	Undifferentiated				
Number of metastatic sites       0.157         1       21 (65.6)       26 (81.3)         ≥ 2       11 (34.4)       6 (18.7)         Lymph node metastases       1.000	Missing		16	20	
1 21 (65.6) 26 (81.3) ≥ 2 11 (34.4) 6 (18.7)  Lymph node metastases 1.000	Tumor extension				
≥ 2 11 (34.4) 6 (18.7) Lymph node metastases 1.000	Number of metastatic sites				0.157
Lymph node metastases 1.000	1		21 (65.6)	26 (81.3)	
	≥ 2		11 (34.4)	6 (18.7)	
No 28 (87.5) 28 (87.5)	Lymph node metastases				1.000
	No		28 (87.5)	28 (87.5)	

Yes	4 (12.5)	4 (12.5)	
Liver metastases			1.000
No	7 (21.9)	7 (21.9)	
Yes	25 (78.1)	25 (78.1)	
Peritoneal metastases			0.756
No	26 (81.3)	25 (78.1)	
Yes	6 (18.7)	7 (21.9)	
Lung metastases			0.740
No	26 (81.3)	27 (84.4)	
Yes	6 (18.7)	5 (15.6)	
Other metastases			0.238
No	29 (90.6)	32 (100.0)	
Yes	3 (9.4)	0 (0.0)	
Clinical parameters			
Performance status (WHO)			0.719
0	9 (29.0)	8 (25.0)	
≥ 1	22 (71.0)	24 (75.0)	
Missing	1	0	
Body mass index, kg/m <sup>2</sup>	24.5 [21.3 -26.6]	23.9 [21.6-26.7]	0.537
Body mass index, kg/m <sup>2</sup> Missing	24.5 [21.3 -26.6] 3	23.9 [21.6-26.7] 0	0.537
	_		0.537
Missing	_		
Missing Pain	3	0	
Missing Pain No	3 20 (62.5)	0 18 (56.3)	
Missing Pain No Yes	3 20 (62.5)	0 18 (56.3)	0.611
Missing Pain No Yes Jaundice	3 20 (62.5) 12 (37.5)	0 18 (56.3) 14 (43.7)	0.611
Missing Pain No Yes Jaundice No	3 20 (62.5) 12 (37.5) 30 (93.8)	0 18 (56.3) 14 (43.7) 27 (84.4)	0.611
Missing Pain No Yes Jaundice No Yes	3 20 (62.5) 12 (37.5) 30 (93.8) 2 (6.2)	0 18 (56.3) 14 (43.7) 27 (84.4) 5 (15.6)	0.611
Missing Pain No Yes Jaundice No Yes Missing	3 20 (62.5) 12 (37.5) 30 (93.8) 2 (6.2)	0 18 (56.3) 14 (43.7) 27 (84.4) 5 (15.6)	0.611
Missing Pain No Yes Jaundice No Yes Missing Ascites	3 20 (62.5) 12 (37.5) 30 (93.8) 2 (6.2) 0	0 18 (56.3) 14 (43.7) 27 (84.4) 5 (15.6) 0	0.611
Missing Pain No Yes Jaundice No Yes Missing Ascites No	3 20 (62.5) 12 (37.5) 30 (93.8) 2 (6.2) 0 32 (100.0)	0 18 (56.3) 14 (43.7) 27 (84.4) 5 (15.6) 0	0.611
Missing Pain No Yes Jaundice No Yes Missing Ascites No Yes	3 20 (62.5) 12 (37.5) 30 (93.8) 2 (6.2) 0 32 (100.0)	0 18 (56.3) 14 (43.7) 27 (84.4) 5 (15.6) 0	0.611
Missing Pain No Yes Jaundice No Yes Missing Ascites No Yes Biological parameters	3 20 (62.5) 12 (37.5) 30 (93.8) 2 (6.2) 0 32 (100.0) 0 (0.0)	0 18 (56.3) 14 (43.7) 27 (84.4) 5 (15.6) 0 28 (87.5) 4 (12.5)	0.611 0.426 0.113
Missing Pain No Yes Jaundice No Yes Missing Ascites No Yes Biological parameters Albumin, median [IQR], g/L	3 20 (62.5) 12 (37.5) 30 (93.8) 2 (6.2) 0 32 (100.0) 0 (0.0)	0 18 (56.3) 14 (43.7) 27 (84.4) 5 (15.6) 0 28 (87.5) 4 (12.5)	0.611 0.426 0.113
Missing Pain No Yes Jaundice No Yes Missing Ascites No Yes Biological parameters Albumin, median [IQR], g/L Lymphocytes, median [IQR], mm³	3 20 (62.5) 12 (37.5) 30 (93.8) 2 (6.2) 0 32 (100.0) 0 (0.0) 38.1 [33.3-41.5]	0 18 (56.3) 14 (43.7) 27 (84.4) 5 (15.6) 0 28 (87.5) 4 (12.5) 38.0 [32.1-42.1]	0.611 0.426 0.113

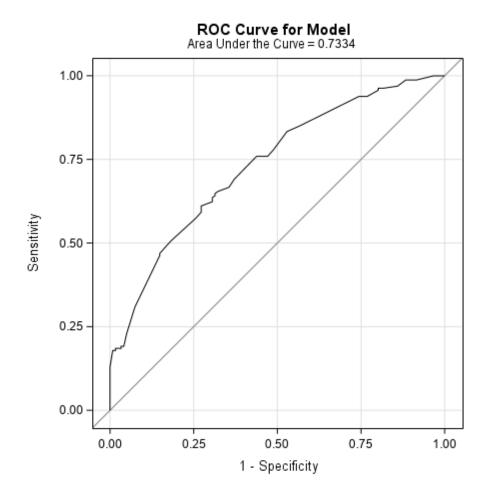
Neutrophil-to-lymphocyte	ratio,			0.393
median [IQR]				
< 5		22 (71.0)	10 (58.8)	
≥ 5		9 (29.0)	7 (41.2)	
Missing		1	15	
CA19-9, median [IQR], UI/mL		150.0 [32.1-8700.0]	1307.0 [108.0-8608.0]	0.439
Missing		0	3	
Previous treatment				
Primary tumor resection				1.000
Yes		3 (9.4)	4 (12.5)	
No		29 (90.6)	28 (87.5)	
Adjuvant chemotherapy				1.000
Yes		3 (9.4)	3 (9.4)	
No		29 (90.6)	29 (90.6)	

After propensity score matching, 32 patients each group (29.0% and 30.5% in the FOLFIRINOX and FOLFOXIRI groups, respectively) have been matched successfully. Baseline characteristics were no statistically different between the two matched groups.  $\chi^2$  tests or Fisher's exact tests used to compare proportions, and Wilcoxon tests used to compare continuous variables between FOLFIRINOX and FOLFOXIRI groups. All statistical tests were two-sided. CA19-9: Carbohydrate antigen 19-9; IQR: Interquartile range; WHO: World Health Organization.

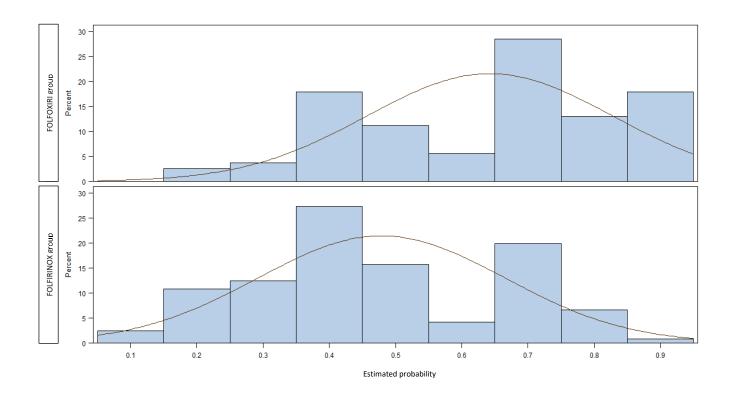
Supplementary Table 8 Outcomes of the propensity score - matched metastatic population according to first-line chemotherapy, n (%)

Outcomes	FOLFIRINOX	FOLFOXIRI (n	P
Outcomes	(n = 32)	= 32)	value
Number of cycles, median [IQR]	10.0 [4.0-12.0]	12.0 [4.0-17.0]	0.213
Missing	0	0	
RECIST best response			0.317
Complete or partial response	11 (40.8)	15 (60.0)	
Stability	10 (37.0)	5 (20.0)	
Progression	6 (22.2)	5 (20.0)	
Missing	5	7	
Toxicity of grade 3 or 4			0.362
No	22 (73.3)	20 (62.5)	
Yes	8 (26.7)	12 (37.5)	
Digestive	4 (1.3)	3 (0.9)	
Hematology	1 (0.3)	1 (0.3)	
Neurology	2 (0.6)	6 (1.8)	
Other	1 (0.3)	3 (0.3)	
Missing	2	0	
Reason for discontinuation			1.000
Progression	20 (62.5)	20 (62.5)	
Toxicity	4 (12.5)	5 (15.6)	
Other	8 (25.0)	7 (21.9)	
Maintenance			1.000
Yes	12 (37.5)	12 (37.5)	
No	20 (62.5)	20 (62.5)	
Second-line chemotherapy			1.000
administration			
Yes	22 (68.8)	22 (68.8)	
No	10 (31.2)	10 (31.2)	

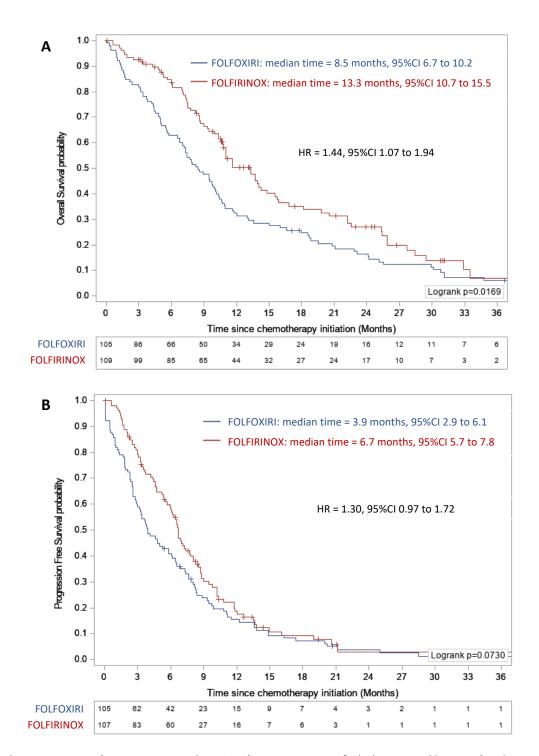
 $<sup>\</sup>chi^2$  tests or Fisher's exact tests used to compare proportions, and Wilcoxon tests used to compare continuous variables between FOLFIRINOX and FOLFOXIRI groups. All statistical tests were two-sided. IQR: Interquartile range.



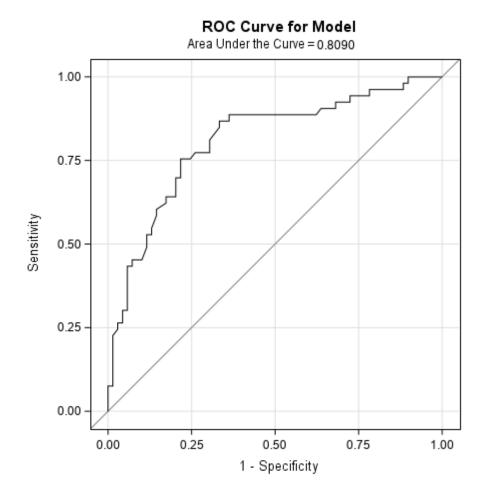
Supplementary Figure 1 Unconditional multivariable logistic regression ROC Curve analysis.



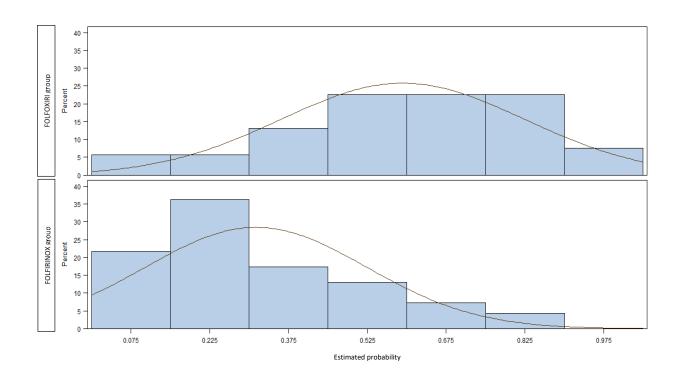
Supplementary Figure 2 Distribution of the probability estimated of the propensity score by the logistic multivariable model in FOLFIRINOX and FOLFOXIRI groups.



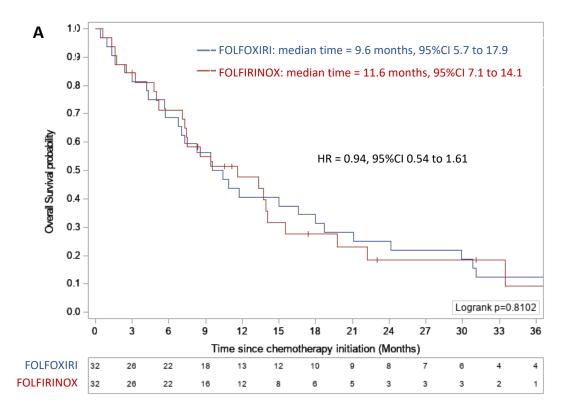
Supplementary Figure 3 Kaplan-Meier curves of (A) overall survival and (B) progression free survival for the FOLFIRINOX and FOLFOXIRI groups in the entire metastatic population. Values of the log-rank test P < 0.05 were considered statistically significant, and all tests were two-sided. CI: confidence interval; HR: hazard ratio.

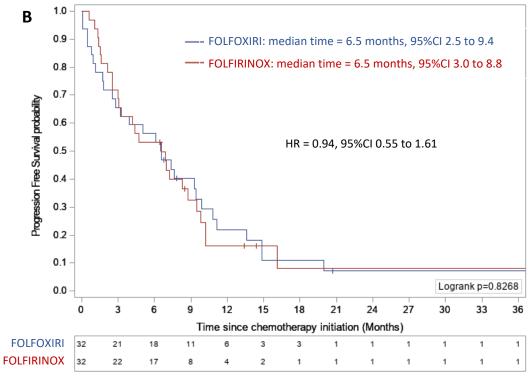


Supplementary Figure 4 Unconditional multivariable logistic regression receiver operating characteristic curve analysis in patients with metastatic disease.



Supplementary Figure 5 Distribution of the probability estimated of the propensity score by the logistic multivariable model in FOLFIRINOX and FOLFOXIRI groups in patients with metastatic disease. After a propensity score value calculated for each patient, patients treated with FOLFOXIRI regimen were matched, with a caliper of 0.10 and ratio of 1:1, with patients in the FOLFIRINOX group.





Supplementary Figure 6 Kaplan-Meier curves of (A) overall survival and (B) progression free survival for the FOLFIRINOX and FOLFOXIRI groups in the propensity score-matched metastatic population. Values of the log-rank test P < 0.05 were considered statistically significant, and all tests were two-sided. CI: confidence interval; HR: hazard ratio.