

Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Baseline Demographic and Clinical Characteristics in the Intention-to-Treat Population.

Characteristic, n (%)	mFOLFIRINOX (N = 247)	Gemcitabine (N = 246)
Age, years, median (range)	63 (30–79)	64 (30–81)
≥70 years	47 (19.0)	54 (21.9)
Male sex	142 (57.5)	135 (54.9)
WHO performance status ^a		
0	122 (49.8)	128 (52.2)
1	123 (50.2)	117 (47.8)
Status of surgical margins		
R0	148 (59.9)	134 (54.5)
R1	99 (40.1)	112 (45.5)
Tumor histology ^b		
Ductal adenocarcinoma	244 (98.8)	242 (98.4)
Non-ductal carcinoma	3 (1.2)	3 (1.2)
Tumor stage		
I	12 (4.9)	14 (5.7)
IIA	43 (17.4)	47 (19.1)
IIB	183 (74.1)	179 (72.8)
III	1 (0.4)	1 (0.4)
IV	8 (3.2)	5 (2.0)
Tumor stage		
pT1–2 / pT3–4	31 (12.6) / 216 (87.4)	25 (10.2) / 221 (89.8)
pN0 / pN1	55 (22.3) / 192 (77.7)	61 (24.8) / 185 (75.2)
Lymphovascular invasion ^{c*}	154 (73.7)	135 (63.1)
Perineural invasion ^d	205 (92.8)	207 (89.6)
Surgery		
Venous resection ^e	53 (21.6)	69 (28.2)
Portal resection	32 (13.0)	42 (17.1)
SMV resection	19 (7.7)	25 (10.2)
Arterial resection ^f	8 (3.2)	7 (2.8)
Lymph node ratio ^g		
0	57 (23.1)	61 (24.9)
0–0.20	118 (47.8)	102 (41.6)
0.20–0.40	53 (21.5)	57 (23.3)
>0.40	19 (7.7)	25 (10.2)

Note: no statistical difference between groups unless otherwise specified. *P=0.02.

Data missing for: ^a2/1 patients; ^b0/1 patients; ^c38/32 patients; ^d26/15 patients; ^e2/1 patients; ^f0/1 patients; and ^g0/1 patients in the mFOLFIRINOX/gemcitabine groups, respectively.

mFOLFIRINOX, modified 5-fluorouracil, leucovorin, irinotecan, and oxaliplatin; SMV, superior mesenteric vein; WHO, World Health Organization.

eTable 2. Disease-free survival events and sites of first metastases recurrences

	mFOLFIRINOX (N = 247)	Gemcitabine (N = 246)
Cause of first event, n (%)		
Any event	173 (70.0)	194 (78.9)
Metastases	94/173 (54.3)	91/194 (46.9)
Locoregional recurrence	37/173 (21.4)	44/194 (22.7)
Locoregional recurrence + metastases	29/173 (16.8)	47/194 (24.2)
Second cancer	5/173 (2.9)	8/194 (4.1)
Death without recurrence	8/173 (4.6)	4/194 (2.1)
Metastases as first event	123	138
Number of metastasis sites		
One site	104/123 (84.6)	114/137 (83.2)
Liver-only	32/104 (30.8)	46/114 (40.3)
Lung-only	41/104 (39.4)	28/114 (24.6)
Peritoneum-only	17/104 (16.3)	30/114 (26.3)
Other-only	14/104 (13.5)	10/114 (8.8)
2 sites	19/123 (15.4)	22/137 (16.1)
3 sites	0	1/137 (0.7)
Missing	0	1

eTable 3. Median overall survival from date of metastasis recurrence (OSr) according to the site of first recurrence (N=260)

First metastases recurrences sites	N Event / N total	Median OSr (Months) [CI 95%]^a
Polymetastasis	39/42	10.3 [8.5-12.5]
Liver-only	69/78	14.7 [11.5-18.9]
Lung-only	45/69	26.0 [16.8-30.3]
Peritoneum-only	43/47	8.0 [5.1-11.2]
Other-only	21/24	11.6 [9.5-24.0]

eTable 4. Treatments administered at relapse			
First relapse treatment, n (%)	mFOLFIRINOX (N = 160)^a	Gemcitabine (N = 182)^a	p-value
Chemotherapy	107 (66.9)	151 (83.0)	
FOLFIRINOX ^a	22 (20.6)	112 (74.2)	
Gemcitabine-based ^a	72 (67.3)	14 (9.3)	
Other ^b	13 (12.1)	25 (16.6)	
Chemoradiotherapy	5 (3.1)	3 (1.7)	
Radiotherapy	14 (8.8)	7 (3.9)	
Surgery	10 (6.3)	8 (4.4)	
None	15 (9.4)	7 (3.9)	
Any relapse treatment, n (%)	mFOLFIRINOX (N = 160)^a	Gemcitabine (N = 182)^a	
At least one treatment ^b			0.032
No	15 (9.9)	7 (4.0)	
Yes	136 (90.1)	169 (96.0)	
Chemotherapy	126 (83.4)	163 (92.6)	0.010
Radiotherapy and/or surgery	41 (27.2)	29 (16.5)	0.019
Radiotherapy	30 (19.9)	18 (10.2)	0.014
Surgery	13 (8.6)	13 (7.4)	0.684

^a Percentage of patients receiving chemotherapy as first relapse treatment.

mFOLFIRINOX, modified 5-fluorouracil, leucovorin, irinotecan, and oxaliplatin.

^b Data missing for 9 and 6 patients in the mFOLFIRINOX and gemcitabine groups, respectively.

eTable 5. Univariate analysis of prognostic factors present at study inclusion for overall survival.

Factor	N Event/ N total	5-year OS (%)	HR (95% CI)	P value
Adjuvant therapy ^a				
Gemcitabine	168/246	31.4	1	<0.001
mFOLFIRINOX	136/247	43.2	0.68 (0.54–0.85)	
Center				
Inclusion of ≥10 patients	125/220	42.7	0.80 (0.64–1.00)	0.051
Inclusion of <10 patients	179/273	32.7	1	
Sex				
Male	171/277	36.7	1	0.69
Female	133/216	37.6	0.96 (0.76–1.20)	
Age				
<70 years	236/392	38.9	0.80 (0.61–1.05)	0.11
≥70 years	68/101	30.0	1	
WHO performance status				
0	148/250	39.4	0.88 (0.70–1.10)	0.25
1	155/240	34.7	1	
Diabetes				
No	211/361	40.0	0.83 (0.65–1.06)	0.14
Yes	89/127	30.3	1	
Tumor location ^b				
Head/Uncinate	242/380	34.7	1	0.017
Other	62/113	44.9	0.72 (0.54–0.95)	
Head	237/372	34.8	1	0.06
Uncinate	5/8	33.3	1.05 (0.43–2.54)	
Other	62/113	44.9	0.72 (0.54–0.95)	
Histotype ^b				
Pancreatic ductal adenocarcinoma	301/486	36.9	1	0.23
Other	2/6	60.0	0.48 (0.12–1.91)	
Tumor grading ^b				
Well differentiated	88/149	41.6	0.70 (0.48–1.01)	0.076
Moderately differentiated	162/249	33.7	0.90 (0.64–1.26)	
Poorly differentiated/Un-differentiated	42/64	29.5	1	
Well differentiated	88/149	41.6	0.76 (0.59–0.98)	0.03
Moderately/Poorly/Un-differentiated	204/313	32.9	1	
pT ^b				
pT1–pT2	28/56	50.4	0.64 (0.44–0.95)	0.019
pT3–pT4	276/437	35.3	1	
pN ^b				
pN0	56/116	51.5	0.59 (0.44–0.79)	<0.001
pN1	248/377	32.6	1	
Tumor staging ^b				

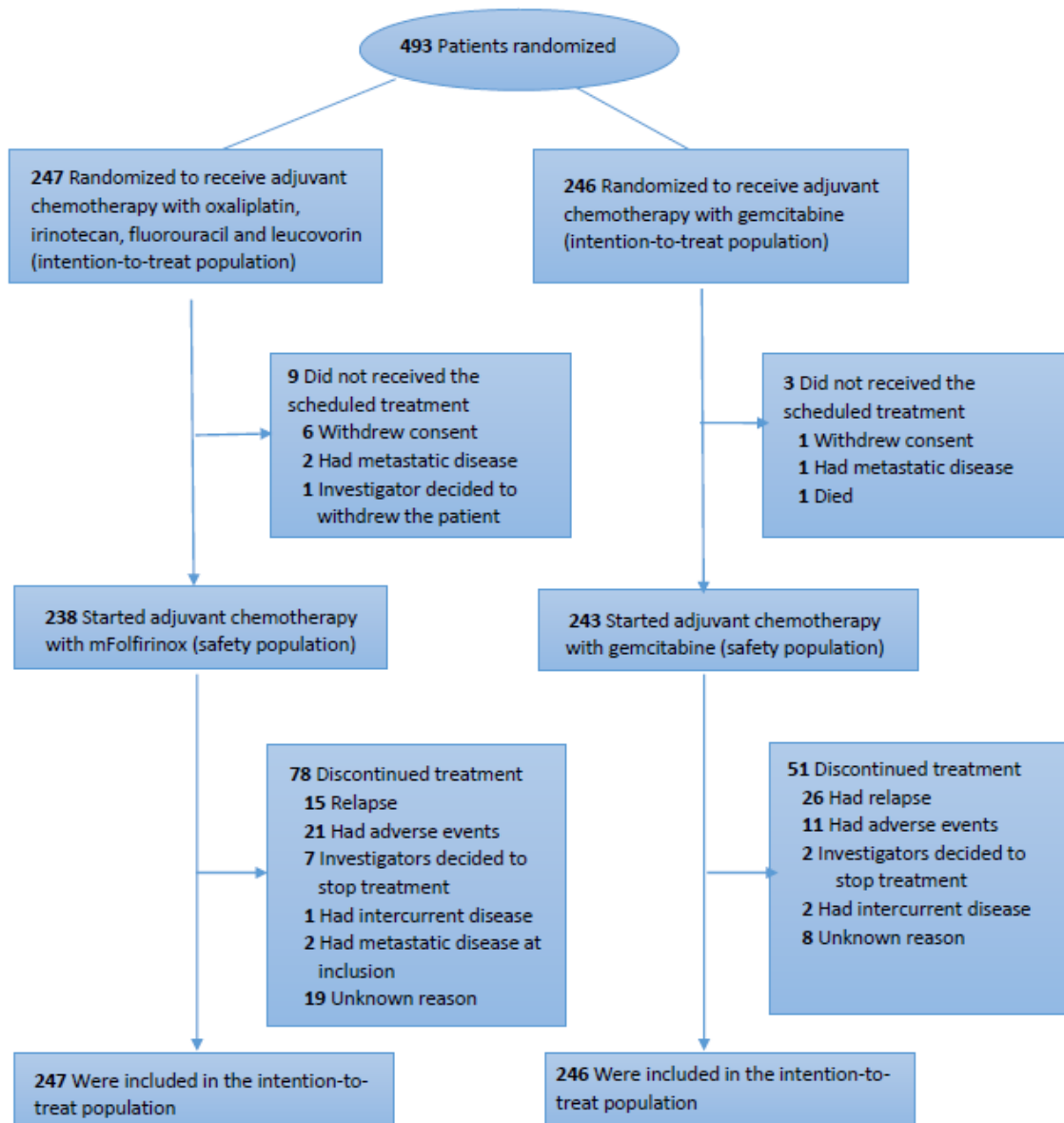
IA/IB	8/26	71.3	0.14 (0.05–0.38)	<0.001
IIA	48/90	45.3	0.32 (0.15–0.68)	
IIB	240/362	33.2	0.46 (0.22–0.92)	
III/IV	8/15	0	1	
Lymph nodes ratio				
0	58/118	51.9	0.37 (0.24–0.56)	<0.001
0–0.20	130/220	40.9	0.48 (0.33–0.71)	
0.20–0.40	81/110	21.0	0.82 (0.55–1.23)	
>0.40	34/44	19.3	1	
Number of lymph nodes retrieved				
<12	62/100	38.4	1	0.77
≥12	241/392	36.8	0.96 (0.73–1.27)	
Excision procedure				
Pancreaticoduodenectomy	248/392	35.5	0.86 (0.54–1.00)	0.11
Distal pancreatectomy	50/92	43.2	0.63 (0.52–2.62)	
Total pancreatectomy	6/9	38.1	1	
Resection status ^b				
R0	150/282	43.4	0.59 (0.47–0.74)	<0.001
R1	154/211	28.8	1	
Venous resection				
No	222/368	39.1	0.73 (0.57–0.94)	0.019
Yes	80/122	30.7	1	
Superior mesenteric vein resection ^b				
No	276/449	38.1	0.63 (0.43–0.93)	0.028
Yes	28/44	25.6	1	
Portal vein resection ^b				
No	251/419	38.7	0.66 (0.49–0.88)	0.008
Yes	53/74	28.3	1	
Sampling paraaortic nodes ^b				
No	225/368	37.3	0.98 (0.75–1.27)	0.86
Yes	74/117	35.8	1	
Lymphovascular invasion ^b				
No	77/134	41.5	0.79 (0.60–1.02)	0.07
Yes	186/289	33.1	1	
Postoperative CA19-9 level				
≤90 U/mL	282/457	37.2	0.86 (0.56–1.33)	0.51
>90 U/mL	22/36	35.3	1	
Time-to adjuvant-treatment				
≤8 weeks	142/211	34.9	1	0.42
>8 weeks	161/270	39.1	0.91 (0.73–1.14)	

^a Stratified Cox model and log-rank test on lymph node status, resection margins, and post-operative CA19-9 only for arm.

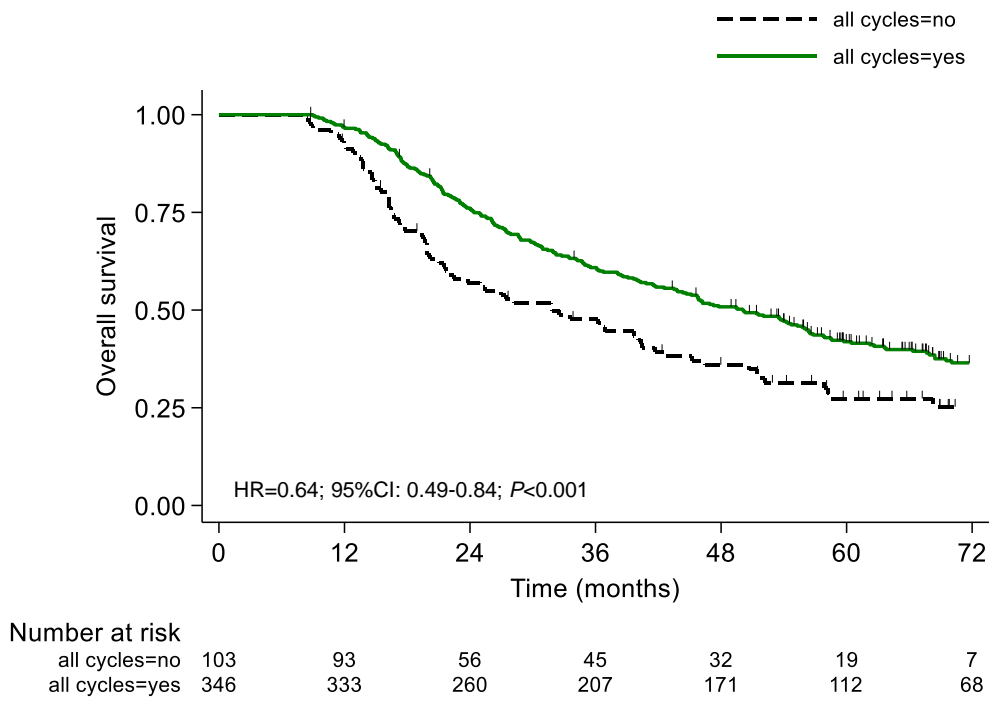
^b Centralized review.

CI, confidence interval; HR, hazard ratio; mFOLFIRINOX, modified 5-fluorouracil, leucovorin, irinotecan, and oxaliplatin; OS, overall survival.

eFigure 1. CONSORT Diagram of Participant Enrollment



eFigure 2. Kaplan-Meier analysis of Overall survival according to chemotherapy completion (Landmark method)



eFigure 3. Kaplan-Meier analysis of Overall survival from relapse according to the time from end of chemotherapy to relapse:

