SUPPLEMENTAL MATERIAL

Plain Language Summary

We investigated the survival of patients receiving their first treatment for a type of advanced cancer called metastatic pancreatic ductal carcinoma (or "mPDAC"). NALIRIFOX and FOLIFIRINOX are combinations of chemotherapy drugs used to treat mPDAC. Both combinations include four drugs: irinotecan, oxaliplatin, leucovorin and fluorouracil. The difference between them is that irinotecan in the NALIRIFOX combination is enclosed in a tiny, protective bubble called a liposome that helps it stay in the body for longer, giving it more time to work. The benefit of NALIRIFOX and FOLFIRINOX has not been compared in a head-to-head trial yet. To investigate this, we compared survival for patients who received their first mPDAC treatment as NALIRIFOX in a clinical trial called NAPOLI 3 (which compared NALIRIFOX versus another mPDAC treatment combination, nab-paclitaxel plus gemcitabine) with survival for patients receiving FOLFIRINOX in everyday clinical practice in the USA. To reduce possible differences between the treatment groups we only included patients treated with FOLFIRINOX who would have met important criteria for inclusion in NAPOLI 3. We also used statistical adjustments to minimize any remaining differences. Our study included 383 patients treated with NALIRIFOX, 219 patients treated with FOLFIRINOX, and 154 patients treated with a lower dose of FOLFIRINOX. On average, patients treated with NALIRIFOX lived approximately 3 months longer than patients treated with FOLFIRINOX or lower dose FOLFIRINOX. Although we did not compare NALIRIFOX and FOLFIRINOX directly in a clinical trial, our findings support the use of NALIRIFOX as a first treatment for patients with mPDAC.

Table S1. Comparison of Inclusion and Exclusion Criteria from NAPOLI 3 and the External Control Cohort

NAPOLI 3 Trial Population	External Control Cohort (Patients Treated With 1L FOLFIRINOX for mPDAC)
Inclusion criteria	
—	Patients who initiated 1L FOLFIRINOX between January 1, 2020, and July 31, 2022
Male or nonpregnant and nonlactating female and aged ≥ 18 years	Male or female aged ≥ 18 years on the index date
ECOG performance status of 0 or 1 at screening and within 7 days prior to randomization	ECOG performance status of 0 or 1 for the assessment closest to the index date within 7 days prior to or on the index date
Histological or cytologically confirmed PDAC that has not been previously treated in the metastatic setting	Histologically or cytologically confirmed diagnosis with stage 4 PDAC or diagnosis of early-stage PDAC and subsequent development of advanced disease, defined as: a) Diagnosis of pancreatic cancer (ICD-9 157.x or ICD-10 C25.x) and at least two documented clinical visits on or after January 1, 2014 b) Pathology consistent with adenocarcinoma of the pancreas c) Diagnosed with stage 4 disease on or after January 1, 2014, or diagnosed with earlier-stage pancreatic cancer and subsequently developed recurrent or progressive disease on or after January 1, 2014
Adequate renal function with CL_{CR} > 30 mL/min Actual body weight should be used for calculating CL_{CR} using the Cockcroft-Gault Equation: CL_{CR} (mL/min) = (140–age [years]) × (weight [kg]/serum creatinine [mg/dL] × 72) Multiply the result by 0.85 if the patient is female. For patients with a BMI > 30 kg/m^2, adjusted body weight should be used instead	Patients who have had adequate renal function for the laboratory assessment closest to the index date within 30 days prior to the index date or on the index date, defined as CL_{CR} > 30 mL/min Actual body weight was used for calculating CL_{CR} using the Cockcroft-Gault Equation: CL_{CR} (mL/min) = (140–age [years]) × (weight [kg]/serum creatinine [mg/dL] × 72) Multiply the result by 0.85 if the patient is female. For patients with a BMI > 30 kg/m^2, adjusted body weight should be used instead
Patient has adequate biological parameters as demonstrated by the following blood counts: a) ANC ≥ 2000/mm^3 without the use of hemopoietic growth factors within the last 7 days prior to randomization b) Platelet count ≥ 100 000/mm^3 c) Hemoglobin ≥ 9 g/dL obtained ≤ 14 days prior to randomization.	Patients who had adequate biological parameters for the laboratory assessment closest to the index date within 30 days prior to the index date or on the index date, defined as: a) ANC ≥ 2000/mm^3 without the use of hematopoietic growth factors within 30 days prior to the ANC test date, including: • G-CSF, filgrastim • Pegfilgrastim

	• Yeast-derived GM-CSF (sargramostim) b) Platelet count ≥ 100 000/mm^3 c) Hemoglobin ≥ 9 g/dL
Adequate hepatic function as evidenced by: a) Serum total bilirubin ≤ 1.5 × ULN (biliary drainage is allowed for biliary obstruction), and b) AST and ALT ≤ 2.5 × ULN (≤ 5 × ULN is acceptable if liver metastases are present)	Patients who had adequate hepatic function for the laboratory assessment closest to the index date within 30 days prior to the index date or on the index date, defined as: a) Serum total bilirubin ≤ 1.5 × ULN b) AST and ALT ≤ 2.5 × ULN
Patients with HIV infection are eligible if they meet all the following criteria: a) CD4 count is ≥ 350 cells/uL, viral load is undetectable, and not taking prohibited CYP-interacting medications b) Probable long-term survival with HIV if cancer were not present c) Stable on a HAART regimen for ≥ 4 weeks and willing to adhere to their HAART regimen with minimal overlapping toxicity and drug-drug interactions with the experimental agents in this study d) HIV is not multidrug resistant Taking medication and/or receiving antiretroviral therapy that does not interact or have overlapping toxicities with the study medication	Patients without a history of HIV at any time on or prior to the index date
Initial diagnosis of metastatic disease must have occurred ≤ 6 weeks prior to screening	—
Patient has one or more metastatic tumors measurable by CT scan (or magnetic resonance imaging, if the patient is allergic to CT contrast media) according to RECIST v1.1 criteria	—
Electrocardiogram without any clinically significant findings (QT interval corrected by Fridericia's formula (QTcF) < 450 msec and no known arrhythmias) and per the investigator's assessment	—
Adequate coagulation studies (obtained ≤ 14 days prior to randomization) as demonstrated by prothrombin time and partial thromboplastin time within normal limits (≤ 1.5 × ULN). (Patients on warfarin or other vitamin K antagonists should be discussed with the sponsor)	—
Patient has no clinically significant abnormalities in urinalysis results (obtained within the last 7 days prior to randomization), per the investigator's assessment	—

Exclusion criteria	
Documented serum albumin < 3 g/dL within 7 days prior to randomization	Serum albumin < 3 g/dL for the laboratory assessment closest to the index date within 7 days prior to the index date or on the index date
History of systemic connective tissue disorders (eg, lupus, scleroderma, arteritis nodosa)	History of systemic connective tissue disorders at any time on or prior to the index date
History of interstitial lung disease, history of slowly progressive dyspnea and unproductive cough, sarcoidosis, silicosis, idiopathic pulmonary fibrosis, pulmonary hypersensitivity pneumonitis or multiple allergies	History of interstitial lung disease, dyspnea, unproductive cough, pulmonary hypersensitivity pneumonitis, sarcoidosis, or multiple allergies at any time on or prior to the index date
History of peripheral artery disease (eg, claudication, Leo Buerger's disease)	History of peripheral artery disease at any time on or prior to the index date
Neuroendocrine (carcinoid, islet cell) or acinar pancreatic carcinoma	History of pancreatic neuroendocrine or acinar tumor as primary pancreatic tumor at any time on or prior to the index date
Use of strong inhibitors or inducers of CYP3A, CYP2C8 and UGT1A1. Patients are ineligible if: a) They are unable to discontinue the use of strong inhibitors of CYP3A, CYP2C8 and UGT1A1 at least 1 week prior to randomization b) They are unable to discontinue the use of strong CYP3A and CYP2C8 inducers at least 2 weeks prior to randomization	Use of strong inhibitors of CYP3A, CYP2C8 and UGT1A1 within 1 week prior to index date; use of strong CYP3A and CYP2C8 inducers within 2 weeks prior to index date
Major surgery, other than diagnostic surgery, within 4 weeks prior to randomization	Surgery for treatment of pancreatic cancer in the metastatic setting at any time on or prior to the index date
Prior treatment of pancreatic cancer in the metastatic setting with surgery, radiotherapy, chemotherapy, or investigational therapy: a) Palliative radiotherapy is permitted b) Placement of biliary stent/tube is permitted	
Clinically significant gastrointestinal disorder, including hepatic disorders, bleeding, inflammation, occlusion, diarrhea > Grade 1, malabsorption syndrome, ulcerative colitis, inflammatory bowel disease, or partial bowel obstruction	History of gastrointestinal disorders (ie, hepatic disorders, bleeding, inflammation, occlusion [including partial bowel obstruction], diarrhea, malabsorption syndrome, Crohn's disease, ulcerative colitis) during baseline
Prior treatment of PDAC with chemotherapy in the adjuvant setting, except those where at least 12 months have elapsed since completion of the last dose and no persistent treatment-related toxicities are present	Treatment with chemotherapy in the adjuvant setting (ie, chemotherapy treatment initiated within 3 months of surgery for PDAC[a]) for PDAC within 1 year prior to or on the index date
History of any second malignancy in the last 2 years; patients with prior history of in situ cancer or basal or squamous cell skin cancer are eligible. Patients with a history of other malignancies are eligible if they have been continuously disease free for at least 2 years prior to screening. Patients who have a concurrent malignancy that is clinically stable and does not require tumor-directed treatment are eligible	History of second malignancy requiring antineoplastic treatment within 2 years prior to index date

Concurrent illnesses that would be a relative contraindication to trial participation, such as active cardiac or liver disease, including: a) Severe arterial thromboembolic events (myocardial infarction, unstable angina pectoris, stroke) < 6 months before screening b) High cardiovascular risk, including, but not limited to, recent coronary stenting or myocardial infarction in the past year prior to screening c) New York Heart Association Class III or IV congestive heart failure, ventricular arrhythmias or uncontrolled blood pressure d) Known historical or active infection with hepatitis B, or active infection with hepatitis C (note that patients with hepatitis C who have been clinically cured, defined as persistent absence of hepatitis C ribonucleic acid detected by PCR test in serum 12 weeks after completing antiviral treatment, are eligible for this study)	History of myocardial infarction, ventricular arrhythmia, stroke, or congestive heart failure during baseline, or history of hepatitis B or hepatitis C at any time on or prior to the index date
Patient has only localized advanced disease	Diagnosis with non-stage IV PDAC during baseline
Known history of CNS metastases. (Patients on a stable or decreasing dose of steroids and deemed clinically stable as per the investigator's assessment are eligible)	—
Known hypersensitivity to any of the components of irinotecan liposome injection, other liposomal products, or any components of 5-FU, LV or oxaliplatin	—
Known hypersensitivity to any of the components of nab-paclitaxel or gemcitabine	—
Active infection or an unexplained fever > 38.5°C during screening visits or on the first scheduled day of dosing (at the discretion of the investigator, patients with tumor fever may be enrolled), which in the investigator's opinion might compromise the patient's participation in the study or affect the study outcome	—
There is presence of any contraindications outlined in the Contraindications or Warnings and Precautions sections of the investigator brochure for irinotecan liposome injection, or in the prescribing information for 5-FU, LV or oxaliplatin	—
There is presence of any contraindications outlined in the Contraindications or Special Warnings and Precautions sections of the product prescribing information for nab-paclitaxel or gemcitabine	—

Patients who, in the opinion of the investigator, have symptoms or signs suggestive of clinically unacceptable deterioration of the primary disease at the time of screening	—
Patients who have received a live vaccine within 4 weeks prior to randomization	—
Known low or absent DPD activity. Where required by local regulations, testing for DPD deficiency must be performed using a validated method which is recommended by local health authorities	—

Abbreviations: 1L, first-line; 5-FU, 5-fluorouracil/leucovorin; ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; BMI, body mass index; CL_{CR}, creatine clearance; CNS, central nervous system; CT, computed tomography; CYP, cytochrome; DPD, dihydropyrimidine dehydrogenase; ECOG, Eastern Cooperative Oncology Group; FOLFIRINOX, oxaliplatin + 5-fluorouracil/leucovorin + irinotecan; G-CSF, granulocyte colony-stimulating factor; GM-CSF, granulocyte-macrophage colony-stimulating factor; HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; ICD-9, International Classification of Diseases, 9th Revision; ICD-10, International Classification of Diseases, 10th Revision; LV, leucovorin; PCR, polymerase chain reaction; PDAC, pancreatic ductal adenocarcinoma; RECIST, Response Evaluation Criteria in Solid Tumors; ULN, upper limit of normal.

[a] Ma SJ, Oladeru OT, Miccio JA, Iovoli AJ, Hermann GM, Singh AK. Association of timing of adjuvant therapy with survival in patients with resected stage I to II pancreatic cancer. *JAMA Netw Open*. 2019;2(8):e199126. doi:10.1001/jamanetworkopen.2019.9126

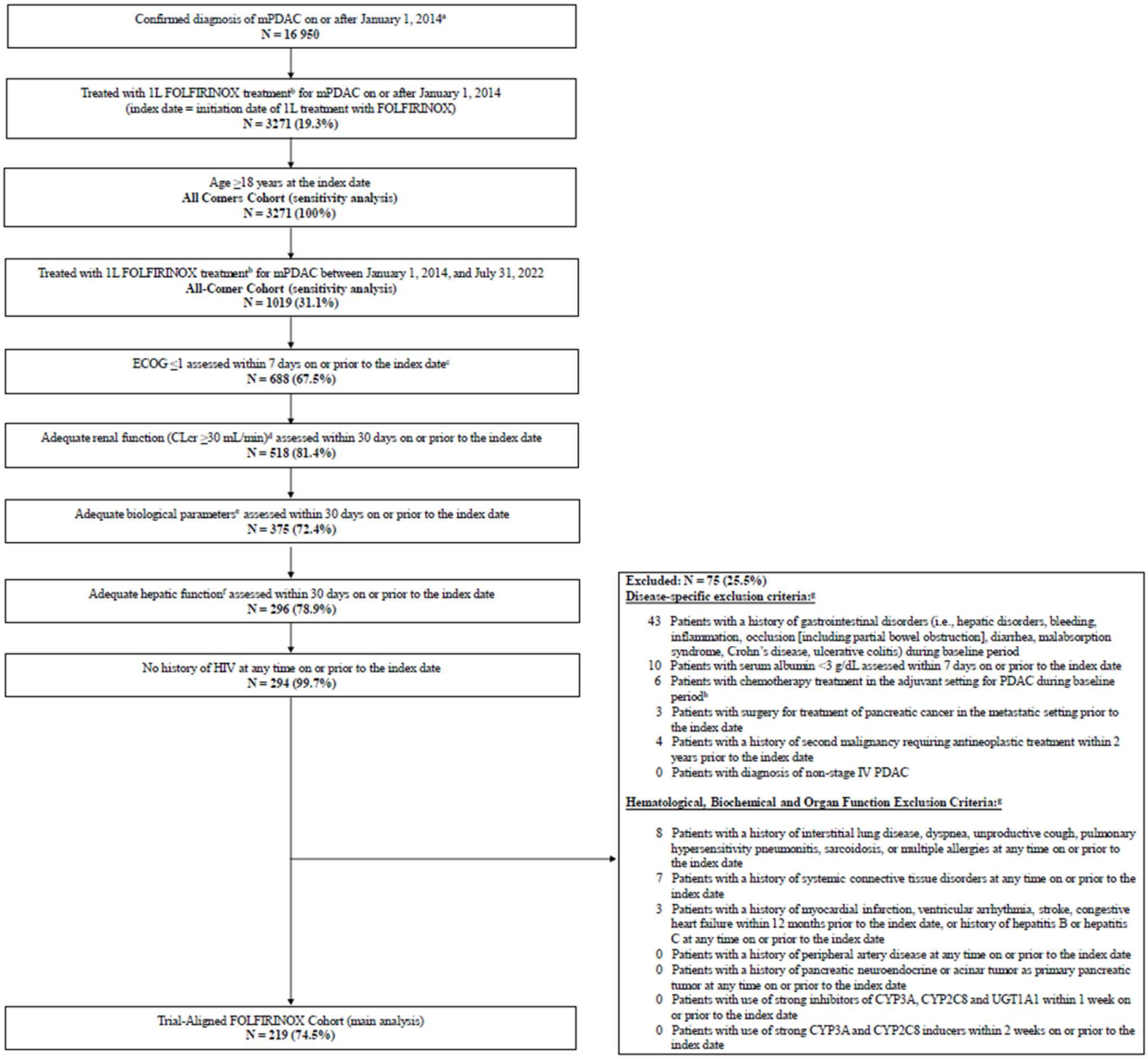
Table S2. Dosing Regimens Categorized as FOLFIRINOX and mFOLFIRINOX for the External Control Arm

No.	Irinotecan (mg/m²)	5-FU (bolus + infusion) (mg/m²)	Oxaliplatin (mg/m²)	Leucovorin (mg/m²)	Count (%) (N = 219)
FOLFIRINOX regimen					
1	> 150	> 2720	> 75	> 400	31 (14.2)
2	> 150	> 2720	> 75	≤ 400	23 (10.5)
3	> 150	> 2720	≤ 75	≤ 400	6 (2.7)
4	> 150	> 2720	≤ 75	> 400	3 (1.4)
5	> 150	> 2720	> 75	–	2 (0.9)
mFOLFIRINOX regimen[a]					
6	> 150	≤ 2720	> 75	> 400	36 (16.4)
7	≤ 150	≤ 2720	> 75	≤ 400	32 (14.6)
8	≤ 150	≤ 2720	≤ 75	≤ 400	19 (8.7)
9	> 150	≤ 2720	> 75	≤ 400	17 (7.8)
10	≤ 150	≤ 2720	≤ 75	> 400	12 (5.5)
11	≤ 150	≤ 2720	> 75	> 400	8 (3.7)
12	> 150	≤ 2720	≤ 75	≤ 400	8 (3.7)
13	> 150	≤ 2720	> 75	–	6 (2.7)
14	> 150	≤ 2720	≤ 75	> 400	5 (2.3)
15	≤ 150	≤ 2720	> 75	–	3 (1.4)
16	≤ 150	≤ 2720	≤ 75	–	2 (0.9)
17	≤ 150	> 2720	≤ 75	≤ 400	2 (0.9)
18	≤ 150	> 2720	≤ 75	> 400	2 (0.9)
19	≤ 150	> 2720	> 75	≤ 400	1 (0.5)
20	≤ 150	> 2720	> 75	> 400	1 (0.5)

Abbreviations: 5-FU, 5-fluorouracil; FOLFIRINOX, oxaliplatin + 5-fluorouracil/leucovorin + irinotecan; mFOLFIRINOX, modified FOLFIRINOX.

[a]Modified FOLFIRINOX regimen was defined as an initial dose of irinotecan ≤ 150 mg/m^2 or initial cumulative dose (bolus + infusion) of 5-FU of ≤ 2720 mg/m^2 during the first cycle (within 30 days of the index date).

Figure S1. Patient Selection Flowchart: Trial-Aligned Patients With Stage IV mPDAC Treated With 1L FOLFIRINOX[1]



Abbreviations: 1L, first line; ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; BMI, body mass index; CL_{CR}, creatinine clearance; CYP, cytochrome; ECOG, Eastern Cooperative Oncology Group; G-CSF, granulocyte colony-stimulating factor; GM-CSF, granulocyte-macrophage colony-stimulating factor; HIV, human immunodeficiency virus; ICD-9, International Classification of Diseases, 9th Revision; ICD-10, International Classification of Diseases, 10th Revision; mPDAC, metastatic pancreatic ductal adenocarcinoma; PDAC, pancreatic ductal adenocarcinoma; ULN, upper limit of normal.

[a]Confirmed diagnosis of mPDAC based on a) diagnosis for pancreatic cancer (ICD-9 157.x or ICD-10 C25.x) and at least two documented clinical visits on or after January 1, 2014; b) pathology consistent with PDAC; and c) diagnosis with stage IV disease on or after January 1, 2014 or diagnosed with earlier-stage pancreatic cancer and subsequently developed recurrent or progressive disease on or after January 1, 2014.

[b]Patients who received FOLFIRINOX regimen delivered via intravenous infusion were included.

[c]ECOG performance status on the index date was reported. If the assessment on the index date was unavailable, the assessment closest to the index date within 7 days on or prior to index date was reported.

[d]If creatinine clearance was not directly available in patients' lab data, it was calculated based on serum creatinine using the Cockcroft-Gault Formula: CL_{CR} (mL/min) = (140 − age [years]) × weight (kg) / (72 × serum creatinine [mg/dL]) × 0.85 if female; (140 − age [years]) × weight (kg) / (72 × serum creatinine [mg/dL]) if male. For patients with a BMI >30 kg/m^2, adjusted body weight was used instead.

[e]Adequate biological parameters are defined as: a) ANC ≥ 2000/mm^3 without the use of hematopoietic growth factors (G-CSF, filgrastim), pegfilgrastim, yeast-derived GM-CSF, sargramostim) within 30 days prior to the ANC test date; b) platelet count ≥ 100 000/mm^3; and c) hemoglobin ≥ 9 g/dL.

[f]Adequate hepatic function is defined as a) serum total bilirubin ≤ 1.5 × ULN; and b) AST and ALT ≤ 2.5 × ULN.

[g]Exclusion criteria were not mutually exclusive.

[h]Adjuvant chemotherapy was defined as chemotherapy treatment initiated within 3 months of surgery for PDAC during the baseline period.

Table S3. Baseline Characteristics for the NAPOLI 3 Trial NALIRIFOX Cohort vs the Trial-Aligned Modified FOLFIRINOX Cohort, Before and After Weighting

	Unweighted			**Weighted**		
	NAPOLI 3 Trial NALIRIFOX Cohort (N = 383)	**Trial-Aligned Modified FOLFIRINOX Cohort (N = 154)**	**Std. Diff. (%)**	**NAPOLI 3 Trial NALIRIFOX Cohort (N = 366)**	**Trial-Aligned Modified FOLFIRINOX Cohort (N = 153)**	**Std. Diff. (%)**
Age at index ≥ 65 years, n (%)	190 (49.6)	82 (53.2)	7.3	182 (49.8)	71 (46.8)	6.1
Female, n (%)	179 (46.7)	68 (44.2)	5.2	170 (46.7)	71 (46.6)	0.3
Race, n (%)						
White	315 (82.2)	100 (64.9)	40.1[a]	294 (80.4)	118 (77.2)	7.7
Non-White	68 (17.8)	36 (23.4)	13.9[a]	72 (19.6)	30 (19.4)	0.6
Unknown	0 (0.0)	18 (11.7)	51.5[a]	0 (0.0)	5 (3.4)	26.4[a]
Year of mPDAC diagnosis date, n (%)						
2019	107 (27.9)	4 (2.6)	75.3[a]	110 (29.9)	4 (2.5)	80.3[a]
2020	276 (72.1)	45 (29.2)	94.8[a]	257 (70.1)	36 (23.8)	104.7[a]
2021	0 (0.0)	66 (42.9)	122.0[a]	0 (0.0)	60 (39.2)	114.0[a]
2022	0 (0.0)	39 (25.3)	82.4[a]	0 (0.0)	53 (34.6)	103.0[a]
Year of index, n (%)						
2020	383 (100.0)	45 (29.2)	220.1[a]	366 (100.0)	39 (25.3)	243.0[a]
2021	0 (0.0)	62 (40.3)	116.0[a]	0 (0.0)	57 (37.5)	110.0[a]
2022	0 (0.0)	47 (30.5)	93.7[a]	0 (0.0)	57 (37.2)	109.0[a]
ECOG performance status,[b] n (%)						
0	160 (41.8)	77 (50.0)	16.6[a]	161 (43.9)	73 (47.7)	7.8
1	223 (58.2)	77 (50.0)	16.6[a]	206 (56.1)	80 (52.3)	7.8

Stage at initial diagnosis of PDAC, n (%)						
Patients with known cancer stage	383 (100.0)	149 (96.8)	25.9[a]	366 (100.0)	150 (98.2)	19.2[a]
Resectable	19 (5.0)	12 (7.8)	11.6[a]	23 (6.3)	9 (5.7)	2.4
Borderline resectable	3 (0.8)	8 (5.2)	26.1[a]	3 (0.8)	3 (1.9)	9.9
Locally advanced	17 (4.4)	2 (1.3)	18.9[a]	16 (4.4)	1 (0.5)	25.9[a]
Metastatic	344 (89.8)	127 (82.5)	21.4[a]	324 (88.5)	138 (90.0)	5.1
Unknown	0 (0.0)	5 (3.2)	25.9[a]	0 (0.0)	3 (1.8)	19.2[a]
Site of primary disease, n (%)						
Head	147 (38.4)	67 (43.5)	10.4[a]	147 (40.1)	57 (37.0)	6.6
Body	116 (30.3)	37 (24.0)	14.1[a]	105 (28.7)	41 (27.1)	3.5
Other sites (ie, tail, overlapping sites, pancreas NOS)	120 (31.3)	50 (32.5)	2.4	114 (31.2)	55 (35.9)	10.0
Time from metastatic diagnosis to index date, weeks						
mean ± SD	3.6 ± 1.8	4.8 ± 9.6	17.9[a]	3.7 ± 1.8	3.9 ± 5.9	6.2
median (IQR)	3.0 (2.1, 4.7)	3.0 (2.0, 4.4)		3.1 (2.3, 5.0)	3.0 (2.0, 4.1)	
Prior surgery for PDAC, n (%)	18 (4.7)	15 (9.7)	19.6[a]	22 (5.9)	10 (6.2)	1.3
Time from surgery to metastatic disease diagnosis, months						
mean ± SD	29.1 ± 33.5	15.4 ± 13.7	53.6[a]	30.8 ± 32.4	12.4 ± 9.9	76.5[a]
median (IQR)	23.6 (12.5, 36.9)	11.0 (2.9, 22.8)		24.6 (18.7, 36.9)	9.2 (2.2, 18.3)	
Prior chemotherapy for PDAC, n (%)	14 (3.7)	19 (12.3)	32.4[a]	21 (5.8)	9 (5.9)	0.8
Time from last chemotherapy to index, months						
mean ± SD	32.0 ± 34.4	12.8 ± 12.8	73.9[a]	29.5 ± 35.3	11.9 ± 8.2	68.6[a]
median (IQR)	20.6 (13.2, 35.7)	7.6 (2.6, 20.8)		20.7 (13.2, 35.7)	7.6 (2.6, 15.9)	
Comorbidities,[c] n (%)						
Hypertension	187 (48.8)	31 (20.1)	63.3[a]	153 (41.8)	64 (42.1)	0.7
Thrombosis	19 (5.0)	5 (3.2)	8.7	17 (4.7)	7 (4.8)	0.2
Ascites	3 (0.8)	4 (2.6)	14.1[a]	4 (1.1)	2 (1.2)	0.8
Laboratory measures[d]						

Absolute neutrophil count, 10^9/L						
mean ± SD	6.5 ± 3.3	6.1 ± 2.7	13.4[a]	6.4 ± 3.2	6.4 ± 2.7	1.4
median (IQR)	5.6 (4.5, 7.9)	5.3 (4.3, 7.2)		5.5 (4.5, 7.7)	5.5 (4.5, 7.6)	
ALT, IU/L						
mean ± SD	38.2 ± 40.1	31.2 ± 21.9	21.9[a]	36.2 ± 36.2	34.7 ± 22.6	5.0
Median (IQR)	25.0 (16.0, 46.0)	25.0 (16.0, 40.0)		24.0 (16.0, 43.0)	29.0 (17.0, 44.0)	
AST, IU/L						
mean ± SD	31.9 ± 34.2	30.4 ± 18.7	5.7	30.7 ± 31.6	32.3 ± 19.1	6.2
median (IQR)	24.0 (16.0, 36.0)	24.0 (18.0, 36.0)		23.0 (15.0, 35.0)	27.0 (18.0, 41.0)	
Creatinine clearance,[e] mL/min						
mean ± SD	100.9 ± 32.9	91.6 ± 28.4	30.0[a]	98.7 ± 31.7	98.6 ± 28.5	0.4
median (IQR)	96.8 (78.8, 120.8)	90.0 (70.6, 107.4)		94.8 (77.8, 119.8)	97.2 (75.6, 115.7)	
Hemoglobin, g/L						
mean ± SD	126.4 ± 16.5	124.7 ± 15.3	10.4[a]	126.4 ± 16.0	127.3 ± 15.6	6.0
median (IQR)	128.0 (116.0, 138.0)	125.3 (115.0, 134.0)		128.0 (116.0, 138.0)	127.0 (118.0, 138.0)	
Platelet count, 10^9/L						
mean ± SD	261.3 ± 91.6	244.2 ± 79.9	19.9[a]	256.9 ± 86.9	256.2 ± 79.7	0.9
median (IQR)	249.0 (198.0, 305.0)	226.0 (184.0, 283.0)		244.0 (193.0, 302.0)	240.0 (197.0, 301.0)	
Serum albumin, g/L						
mean ± SD	38.0 ± 4.1	39.0 ± 3.9	23.7[a]	38.3 ± 4.0	38.7 ± 3.8	10.8[a]
median (IQR)	38.0 (36.0, 41.0)	39.0 (36.0, 42.0)		39.0 (36.0, 41.0)	40.0 (36.0, 42.0)	
Serum total bilirubin, μmol/L						
mean ± SD	11.6 ± 7.5	10.5 ± 5.2	17.0[a]	11.4 ± 7.1	10.9 ± 5.8	6.2
median (IQR)	9.4 (6.8, 14.0)	10.3 (6.8, 12.0)		9.2 (6.8, 13.3)	10.3 (6.8, 13.7)	

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CL_{CR}, creatinine clearance; ECOG, Eastern Cooperative Oncology Group; FOLFIRINOX, oxaliplatin + 5-fluorouracil/leucovorin + irinotecan; IQR, interquartile range; mPDAC, metastatic pancreatic ductal adenocarcinoma; NALIRIFOX, irinotecan liposome injection + oxaliplatin + 5-fluorouracil/leucovorin; NOS, not otherwise specified; PDAC, pancreatic ductal adenocarcinoma; SD, standard deviation; std. diff., standardized difference.

[a]Standardized difference ≥ 10%.

[b]For the NALIRIFOX cohort, ECOG performance status on Cycle 1 Day 1 (C1D1) was reported; if the assessment on C1D1 was unavailable, the closest assessment within 7 days prior to randomization was reported. For the trial-aligned modified FOLFIRINOX cohort, the most recent ECOG performance status score within 7 days on or prior to the index date was reported. One patient had an ECOG performance status score of 2 after randomization and continued to receive treatment. For the trial-aligned FOLFIRINOX cohort, the most recent ECOG performance status score within 7 days on or prior to the index date was reported.

[c]Categories are not mutually exclusive and therefore may not sum to 100%.

[d]For the trial-aligned modified FOLFIRINOX cohort, laboratory measures on the index date were reported; if assessment on the index date was unavailable, the assessment closest to the index date during the baseline period was reported. If multiple test results were available on the same date, the average value was used.

[e]For the trial-aligned modified FOLFIRINOX cohort, if creatinine clearance value was not directly available in patients' lab data, it was calculated based on serum creatinine using the Cockcroft-Gault Formula: (140 − age [years]) × weight (kg) / (72 × serum creatinine [mg/dL]) if male; (140 − age [years]) × weight (kg) / (72 × serum creatinine [mg/dL]) × 0.85 if female. For patients with a BMI > 30 kg/m^2, adjusted body weight was used instead.

Table S4. Baseline Characteristics for the NAPOLI 3 Trial NALIRIFOX Cohort vs the All-Comer FOLFIRINOX Cohort, Before and After Weighting

	Unweighted			**Weighted**		
	NAPOLI 3 Trial NALIRIFOX Cohort (N = 383)	**All-Comer FOLFIRINOX Cohort (N = 3271)**	**Std. Diff. (%)**	**NAPOLI 3 Trial NALIRIFOX Cohort (N = 251)**	**All-Comer FOLFIRINOX Cohort (N = 3271)**	**Std. Diff. (%)**
Age at index ≥ 65 years, n (%)	190 (49.6)	1559 (47.7)	3.9	113 (45.1)	1564 (47.8)	5.4
Female, n (%)	179 (46.7)	1377 (42.1)	9.4	109 (43.4)	1391 (42.5)	1.7
Race, n (%)						
White	315 (82.2)	2118 (64.8)	40.4[a]	198 (78.9)	2179 (66.6)	27.7[a]
Non-White	68 (17.8)	742 (22.7)	12.3[a]	53 (21.1)	723 (22.1)	2.4
Unknown	0 (0.0)	411 (12.6)	53.6[a]	0 (0.0)	368 (11.2)	50.4[a]
Year of mPDAC diagnosis date, n (%)						
2014	0 (0.0)	190 (5.8)	35.1[a]	0 (0.0)	186 (5.7)	34.7[a]
2015	0 (0.0)	223 (6.8)	38.3[a]	0 (0.0)	220 (6.7)	38.0[a]
2016	0 (0.0)	248 (7.6)	40.5[a]	0 (0.0)	248 (7.6)	40.5[a]
2017	0 (0.0)	285 (8.7)	43.7[a]	0 (0.0)	285 (8.7)	43.7[a]
2018	0 (0.0)	299 (9.1)	44.9[a]	0 (0.0)	301 (9.2)	45.0[a]
2019	107 (27.9)	382 (11.7)	41.7[a]	81 (32.1)	388 (11.9)	50.4[a]
2020	276 (72.1)	366 (11.2)	157.0[a]	171 (67.9)	366 (11.2)	142.4[a]
2021	0 (0.0)	407 (12.4)	53.3[a]	0 (0.0)	405 (12.4)	53.2[a]
2022	0 (0.0)	419 (12.8)	54.2[a]	0 (0.0)	423 (12.9)	54.5[a]
2023	0 (0.0)	407 (12.4)	53.3[a]	0 (0.0)	402 (12.3)	52.9[a]
2024	0 (0.0)	45 (1.4)	16.7[a]	0 (0.0)	46 (1.4)	16.9[a]
Year of index, n (%)						

2014	0 (0.0)	170 (5.2)	33.1[a]	0 (0.0)	168 (5.1)	32.9[a]
2015	0 (0.0)	216 (6.6)	37.6[a]	0 (0.0)	213 (6.5)	37.3[a]
2016	0 (0.0)	255 (7.8)	41.1[a]	0 (0.0)	255 (7.8)	41.1[a]
2017	0 (0.0)	283 (8.7)	43.5[a]	0 (0.0)	283 (8.7)	43.5[a]
2018	0 (0.0)	282 (8.6)	43.4[a]	0 (0.0)	285 (8.7)	43.7[a]
2019	0 (0.0)	394 (12.0)	52.3[a]	0 (0.0)	400 (12.2)	52.8[a]
2020	383 (100.0)	358 (10.9)	403.4[a]	251 (100.0)	359 (11.0)	402.9[a]
2021	0 (0.0)	410 (12.5)	53.5[a]	0 (0.0)	409 (12.5)	53.4[a]
2022	0 (0.0)	422 (12.9)	54.4[a]	0 (0.0)	425 (13.0)	54.7[a]
2023	0 (0.0)	414 (12.7)	53.8[a]	0 (0.0)	408 (12.5)	53.4[a]
2024	0 (0.0)	67 (2.0)	20.5[a]	0 (0.0)	68 (2.1)	20.5[a]
ECOG performance status,[b] n (%)						
0	160 (41.8)	1135 (34.7)	14.6[a]	104 (41.2)	1159 (35.4)	11.9[a]
1	223 (58.2)	1576 (48.2)	20.2[a]	148 (58.8)	1611 (49.2)	19.2[a]
Stage at initial diagnosis of PDAC, n (%)						
Patients with known cancer stage	383 (100.0)	3138 (95.9)	29.1[a]	251 (100.0)	3143 (96.1)	28.5[a]
Resectable	19 (5.0)	193 (5.9)	4.2	21 (8.4)	182 (5.6)	11.0[a]
Borderline resectable	3 (0.8)	214 (6.5)	31.0[a]	4 (1.5)	202 (6.2)	24.7[a]
Locally advanced	17 (4.4)	103 (3.1)	6.8	12 (4.8)	98 (3.0)	9.3
Metastatic	344 (89.8)	2628 (80.3)	26.8[a]	215 (85.4)	2661 (81.4)	10.8[a]
Unknown	0 (0.0)	133 (4.1)	29.1[a]	0 (0.0)	128 (3.9)	28.5[a]
Site of primary disease, n (%)						
Head	147 (38.4)	1475 (45.1)	13.6[a]	108 (42.8)	1451 (44.4)	3.1
Body	116 (30.3)	710 (21.7)	19.7[a]	61 (24.3)	739 (22.6)	4.0
Other sites (ie, tail, overlapping sites, pancreas NOS)	120 (31.3)	1086 (33.2)	4.0	83 (32.9)	1080 (33.0)	0.3
Time from metastatic diagnosis to index date, weeks						
mean ± SD	3.6 ± 1.8	4.5 ± 8.4	15.9[a]	3.8 ± 1.6	4.4 ± 8.0	11.8[a]

median (IQR)	3.0 (2.1, 4.7)	3.0 (1.9, 4.7)		3.4 (2.1, 5.0)	3.0 (1.9, 4.6)	
Prior surgery for PDAC, n (%)	18 (4.7)	371 (11.3)	24.6[a]	23 (9.3)	349 (10.7)	4.7
Time from surgery to metastatic disease diagnosis, months						
mean ± SD	29.1 ± 33.5	14.6 ± 14.8	56.1[a]	34.1 ± 40.1	14.6 ± 14.4	64.7[a]
median (IQR)	23.6 (12.5, 36.9)	10.7 (3.8, 19.5)		24.6 (18.7, 36.9)	10.7 (3.7, 19.5)	
Prior chemotherapy for PDAC, n (%)	14 (3.7)	452 (13.8)	36.6[a]	22 (8.9)	417 (12.8)	12.5[a]
Time from last chemotherapy to index, months						
mean ± SD	32.0 ± 34.4	8.3 ± 11.5	92.4[a]	32.3 ± 44.1	8.2 ± 11.0	74.8[a]
median (IQR)	20.6 (13.2, 35.7)	3.9 (1.1, 10.7)		20.6 (13.2, 35.7)	3.8 (1.1, 10.6)	
Comorbidities,[c] n (%)						
Hypertension	187 (48.8)	747 (22.8)	56.3[a]	79 (31.5)	836 (25.6)	13.2[a]
Thrombosis	19 (5.0)	160 (4.9)	0.3	10 (4.1)	162 (5.0)	4.0
Ascites	3 (0.8)	66 (2.0)	10.5[a]	3 (1.2)	62 (1.9)	5.4
Laboratory measures[d]						
Absolute neutrophil count, 10^9/L						
mean ± SD	6.5 ± 3.3	8.0 ± 80.1	2.7	6.6 ± 2.8	7.9 ± 75.9	2.3
median (IQR)	5.6 (4.5, 7.9)	5.5 (4.4, 6.9)		5.6 (4.5, 8.0)	5.5 (4.4, 6.8)	
ALT, IU/L						
mean ± SD	38.2 ± 40.1	46.3 ± 60.7	15.7[a]	44.0 ± 41.4	45.5 ± 59.1	3.0
median (IQR)	25.0 (16.0, 46.0)	29.0 (18.8, 50.0)		27.0 (16.0, 49.0)	29.0 (18.0, 49.0)	
AST, IU/L						
mean ± SD	31.9 ± 34.2	40.2 ± 44.9	20.9[a]	38.4 ± 39.0	39.4 ± 43.3	2.5
median (IQR)	24.0 (16.0, 36.0)	28.0 (20.0, 44.0)		25.0 (16.0, 43.0)	28.0 (20.0, 43.0)	
Creatinine clearance,[e] mL/min						
mean ± SD	100.9 ± 32.9	95.4 ± 30.8	17.1[a]	98.1 ± 25.4	96.0 ± 31.0	7.4
median (IQR)	96.8 (78.8, 120.8)	91.8 (76.1, 109.6)		94.8 (77.8, 118.8)	91.8 (76.4, 110.2)	
Hemoglobin, g/L						

mean ± SD	126.4 ± 16.5	122.1 ± 17.1	25.2[a]	125.3 ± 14.0	122.6 ± 17.1	16.9[a]
median (IQR)	128.0 (116.0, 138.0)	123.0 (111.0, 134.0)		128.0 (115.0, 138.0)	123.0 (112.0, 134.0)	
Platelet count, 10^9/L						
mean ± SD	261.3 ± 91.6	256.6 ± 97.0	5.0	263.2 ± 74.8	256.0 ± 95.8	8.4
median (IQR)	249.0 (198.0, 305.0)	241.0 (199.0, 295.0)		253.0 (200.0, 309.0)	241.0 (199.0, 294.0)	
Serum albumin, g/L						
mean ± SD	38.0 ± 4.1	37.6 ± 5.1	9.1	37.9 ± 3.5	37.7 ± 5.1	4.2
median (IQR)	38.0 (36.0, 41.0)	38.0 (35.0, 41.0)		38.0 (35.0, 41.0)	38.0 (35.0, 41.0)	
Serum total bilirubin, μmol/L						
mean ± SD	11.6 ± 7.5	16.9 ± 26.7	27.2[a]	13.0 ± 7.5	16.4 ± 25.5	17.8[a]
median (IQR)	9.4 (6.8, 14.0)	10.3 (6.8, 15.4)		9.7 (7.0, 15.6)	10.3 (6.8, 15.4)	

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CL_{CR}, creatinine clearance; ECOG, Eastern Cooperative Oncology Group; FOLFIRINOX, oxaliplatin + 5-fluorouracil/leucovorin + irinotecan; IQR, interquartile range; mPDAC, metastatic pancreatic ductal adenocarcinoma; NALIRIFOX, irinotecan liposome injection + oxaliplatin + 5-fluorouracil/leucovorin; NOS, not otherwise specified; PDAC, pancreatic ductal adenocarcinoma; SD, standard deviation; std. diff., standardized difference.

[a]Standardized difference ≥ 10%.

[b]For the NALIRIFOX cohort, ECOG performance status on Cycle 1 Day 1 (C1D1) was reported; if the assessment on C1D1 was unavailable, the closest assessment within 7 days prior to randomization was reported. For the all-comer FOLFIRINOX cohort, the most recent ECOG performance status score on or prior to the index date during the baseline period was reported. One patient had an ECOG performance status score of 2 after randomization and continued to receive treatment. For the trial-aligned FOLFIRINOX cohort, the most recent ECOG performance status score within 7 days on or prior to the index date was reported.

[c]Categories are not mutually exclusive and therefore may not sum to 100%.

[d]For the all-comer FOLFIRINOX cohort, laboratory measures on the index date were reported; if assessment on the index date was unavailable, the assessment closest to the index date during the baseline period was reported. If multiple test results were available on the same date, the average value was used.

[e]For the all-comer FOLFIRINOX cohort, if creatinine clearance value was not directly available in patients' lab data, it was calculated based on serum creatinine using the Cockcroft-Gault Formula: (140 − age [years]) × weight (kg) / (72 × serum creatinine [mg/dL]) if male; (140 − age [years]) × weight (kg) / (72 × serum creatinine [mg/dL]) × 0.85 if female. For patients with a BMI > 30 kg/m^2, adjusted body weight was used instead.

Table S5. Baseline Characteristics for the NAPOLI 3 Trial NALIRIFOX Cohort vs the All-Comer Contemporary FOLFIRINOX Cohort, Before and After Weighting

	Unweighted			**Weighted**		
	NAPOLI 3 Trial NALIRIFOX Cohort (N = 383)	**All-Comer Contemporary FOLFIRINOX Cohort (N = 1000)**	**Std. Diff. (%)**	**NAPOLI 3 Trial NALIRIFOX Cohort (N = 288)**	**All-Comer Contemporary FOLFIRINOX Cohort (N = 1001)**	**Std. Diff. (%)**
Age at index ≥ 65 years, n (%)	190 (49.6)	509 (50.9)	2.6	140 (48.6)	502 (50.2)	3.2
Female, n (%)	179 (46.7)	425 (42.5)	8.5	128 (44.3)	438 (43.7)	1.2
Race, n (%)						
White	315 (82.2)	607 (60.7)	49.1[a]	225 (78.1)	670 (66.9)	25.3[a]
Non-White	68 (17.8)	249 (24.9)	17.5[a]	63 (21.9)	227 (22.7)	2.0
Unknown	0 (0.0)	144 (14.4)	58.0[a]	0 (0.0)	104 (10.4)	48.2[a]
Year of mPDAC diagnosis date, n (%)						
2018	0 (0.0)	1 (0.1)	4.5	0 (0.0)	1 (0.1)	3.9
2019	107 (27.9)	25 (2.5)	75.7[a]	90 (31.2)	24 (2.4)	83.4[a]
2020	276 (72.1)	366 (36.6)	76.2[a]	198 (68.8)	363 (36.3)	68.9[a]
2021	0 (0.0)	406 (40.6)	117.0[a]	0 (0.0)	400 (40.0)	115.0[a]
2022	0 (0.0)	202 (20.2)	71.2[a]	0 (0.0)	213 (21.3)	73.5[a]
Year of index, n (%)						
2020	383 (100.0)	358 (35.8)	189.4[a]	288 (100.0)	357 (35.7)	189.7[a]
2021	0 (0.0)	410 (41.0)	118.0[a]	0 (0.0)	404 (40.4)	116.0[a]
2022	0 (0.0)	232 (23.2)	77.7[a]	0 (0.0)	239 (23.9)	79.3[a]
ECOG performance status,[b] n (%)						
0	160 (41.8)	369 (36.9)	10.0	123 (42.7)	381 (38.1)	9.5
1	223 (58.2)	480 (48.0)	20.6[a]	165 (57.3)	511 (51.0)	12.6[a]

Stage at initial diagnosis of PDAC, n (%)						
Patients with known cancer stage	383 (100.0)	960 (96.0)	28.9[a]	288 (100.0)	962 (96.1)	28.5[a]
Resectable	19 (5.0)	59 (5.9)	4.2	23 (8.1)	49 (4.9)	13.1[a]
Borderline resectable	3 (0.8)	43 (4.3)	22.5[a]	4 (1.2)	38 (3.8)	16.5[a]
Locally advanced	17 (4.4)	28 (2.8)	8.8	13 (4.6)	24 (2.4)	11.7[a]
Metastatic	344 (89.8)	830 (83.0)	20.0[a]	248 (86.1)	851 (85.0)	3.2
Unknown	0 (0.0)	40 (4.0)	28.9[a]	0 (0.0)	39 (3.9)	28.5[a]
Site of primary disease, n (%)						
Head	147 (38.4)	434 (43.4)	10.2[a]	119 (41.3)	418 (41.7)	0.8
Body	116 (30.3)	245 (24.5)	13.0[a]	75 (25.9)	260 (26.0)	0.2
Other sites (ie, tail, overlapping sites, pancreas NOS)	120 (31.3)	321 (32.1)	1.7	94 (32.7)	323 (32.3)	1.0
Time from metastatic diagnosis to index date, weeks						
mean ± SD	3.6 ± 1.8	4.4 ± 7.4	14.8[a]	3.7 ± 1.7	4.1 ± 6.5	9.7
median (IQR)	3.0 (2.1, 4.7)	3.0 (2.0, 4.4)		3.3 (2.1, 5.0)	3.0 (2.0, 4.4)	
Prior surgery for PDAC, n (%)	18 (4.7)	95 (9.5)	18.8[a]	25 (8.6)	83 (8.3)	1.1
Time from surgery to metastatic disease diagnosis, months						
mean ± SD	29.1 ± 33.5	14.6 ± 13.7	56.9[a]	32.7 ± 36.6	13.7 ± 12.5	69.8[a]
median (IQR)	23.6 (12.5, 36.9)	11.0 (2.9, 22.8)		24.6 (20.9, 36.9)	10.1 (2.2, 21.4)	
Prior chemotherapy for PDAC, n (%)	14 (3.7)	127 (12.7)	33.5[a]	25 (8.8)	102 (10.2)	4.7
Time from last chemotherapy to index, months						
mean ± SD	32.0 ± 34.4	9.9 ± 12.1	85.7[a]	29.0 ± 41.3	9.7 ± 10.7	63.8[a]
median (IQR)	20.6 (13.2, 35.7)	4.3 (1.6, 14.7)		20.6 (13.2, 29.5)	4.2 (1.6, 14.0)	
Comorbidities,[c] n (%)						
Hypertension	187 (48.8)	249 (24.9)	51.2[a]	103 (35.8)	316 (31.6)	8.8
Thrombosis	19 (5.0)	52 (5.2)	1.1	12 (4.3)	53 (5.3)	4.9
Ascites	3 (0.8)	23 (2.3)	12.3[a]	4 (1.5)	19 (1.9)	2.9
Laboratory measures[d]						

Absolute neutrophil count, 10^9/L						
mean ± SD	6.5 ± 3.3	6.5 ± 4.0	1.1	6.6 ± 3.1	6.4 ± 3.8	7.2
median (IQR)	5.6 (4.5, 7.9)	5.5 (4.5, 7.1)		5.6 (4.5, 8.1)	5.5 (4.5, 7.0)	
ALT, IU/L						
mean ± SD	38.2 ± 40.1	48.9 ± 69.4	18.8[a]	44.2 ± 47.5	46.1 ± 63.8	3.3
Median (IQR)	25.0 (16.0, 46.0)	28.0 (18.0, 49.0)		27.0 (16.0, 48.0)	28.0 (17.0, 47.0)	
AST, IU/L						
mean ± SD	31.9 ± 34.2	42.3 ± 55.0	22.7[a]	39.0 ± 45.4	39.7 ± 49.2	1.6
median (IQR)	24.0 (16.0, 36.0)	29.0 (20.0, 46.0)		25.0 (16.0, 41.0)	29.0 (19.0, 44.0)	
Creatinine clearance,[e] mL/min						
mean ± SD	100.9 ± 32.9	95.0 ± 30.2	18.5[a]	97.8 ± 27.6	96.8 ± 30.9	3.7
median (IQR)	96.8 (78.8, 120.8)	92.4 (75.2, 110.3)		94.8 (77.8, 117.8)	92.4 (76.0, 112.3)	
Hemoglobin, g/L						
mean ± SD	126.4 ± 16.5	122.0 ± 17.6	25.5[a]	124.6 ± 15.2	123.3 ± 17.5	7.9
median (IQR)	128.0 (116.0, 138.0)	122.5 (111.0, 133.0)		128.0 (115.0, 137.0)	123.0 (113.0, 135.0)	
Platelet count, 10^9/L						
mean ± SD	261.3 ± 91.6	258.6 ± 91.4	3.0	262.8 ± 79.6	257.6 ± 89.2	6.1
median (IQR)	249.0 (198.0, 305.0)	246.0 (204.0, 299.0)		253.0 (200.0, 307.0)	246.0 (204.0, 295.0)	
Serum albumin, g/L						
mean ± SD	38.0 ± 4.1	37.7 ± 5.4	7.7	37.8 ± 3.8	37.9 ± 5.3	2.3
median (IQR)	38.0 (36.0, 41.0)	38.0 (35.0, 41.0)		38.0 (35.0, 41.0)	38.0 (36.0, 42.0)	
Serum total bilirubin, μmol/L						
mean ± SD	11.6 ± 7.5	16.8 ± 25.5	27.8[a]	12.9 ± 8.2	15.3 ± 22.3	14.5[a]
median (IQR)	9.4 (6.8, 14.0)	10.3 (6.8, 15.4)		9.7 (7.0, 15.0)	10.3 (6.8, 13.7)	

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CL_{CR}, creatinine clearance; ECOG, Eastern Cooperative Oncology Group; FOLFIRINOX, oxaliplatin + 5-fluorouracil/leucovorin + irinotecan; IQR, interquartile range; mPDAC, metastatic pancreatic ductal adenocarcinoma; NALIRIFOX, irinotecan liposome injection + oxaliplatin + 5-fluorouracil/leucovorin; NOS, not otherwise specified; PDAC, pancreatic ductal adenocarcinoma; SD, standard deviation; std. diff., standardized difference.

[a]Standardized difference ≥ 10%.

[b]For the NALIRIFOX cohort, ECOG performance status on Cycle 1 Day 1 (C1D1) was reported; if the assessment on C1D1 was unavailable, the closest assessment within 7 days prior to randomization was reported. For the all-comer contemporary FOLFIRINOX cohort, the most recent ECOG performance status score on or prior to the index date during the baseline period was reported. One patient had an ECOG performance status score of 2 after randomization and continued to receive treatment. For the trial-aligned FOLFIRINOX cohort, the most recent ECOG performance status score within 7 days on or prior to the index date was reported.

[c]Categories are not mutually exclusive and therefore may not sum to 100%.

[d]For the all-comer contemporary FOLFIRINOX cohort, laboratory measures on the index date were reported; if assessment on the index date was unavailable, the assessment closest to the index date during the baseline period was reported. If multiple test results were available on the same date, the average value was used.

[e]For the all-comer contemporary FOLFIRINOX cohort, if creatinine clearance value was not directly available in patients' lab data, it was calculated based on serum creatinine using the Cockcroft-Gault Formula: (140 − age [years]) × weight (kg) / (72 × serum creatinine [mg/dL]) if male; (140 − age [years]) × weight (kg) / (72 × serum creatinine [mg/dL]) × 0.85 if female. For patients with a BMI > 30 kg/m^2, adjusted body weight was used instead.