Clinical trial results:
A Randomized Phase III Trial Comparing Chemotherapy With Folfirinox to Gemcitabine in Locally Advanced Pancreatic Carcinoma

Summary

EudraCT number	2014-003510-82
Trial protocol	FR
Global end of trial date	08 April 2024

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	UC-0110/1405

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02539537
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UNICANCER
Sponsor organisation address	101 rue de Tolbiac, Paris, France, 75015
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 May 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 April 2024
Global end of trial reached?	Yes
Global end of trial date	08 April 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to compare the progression-free survival (PFS) of the disease in both arms of treatment.

Protection of trial subjects:

This study was conducted in accordance with the French national regulatory requirements and the Declaration of Helsinki (1964) and subsequent amendments, ICH Good Clinical Practice (GCP) Guidelines (CPMP/ICH/135/95), the European Directive (2001/20/CE) and the applicable local regulatory requirements and laws.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 March 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 171
Worldwide total number of subjects	171
EEA total number of subjects	171

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	62
From 65 to 84 years	109

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

From 23-Mar-2015 to 12-Jan-2022, 171 patients were randomized in 1:1 ratio in the NEOPAN study across 30 sites. Thus, 86 patients were allocated in the gemcitabine Arm A and 85 patients in the FOLFIRINOX Arm B.

Pre-assignment

Screening details:

The main criteria for inclusion : patients with locally adenocarcinoma of the pancreas, confirmed through a histologic or cytological examination and inoperable nature confirmed after a multi-discipline discussion involving a surgeon and radiologist.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: Gemcitabine

Arm description:

Gemcitabine was administered at a dose of 1,000 mg/m2, by intravenous infusion (strictly) over 30 minutes. It could be administered on an outpatient basis (day hospital), but not at the patient's home. Gemcitabine administration had to be repeated once a week for 3 consecutive weeks (D1, D8 and D15 of a cycle), followed by a week without injection (1 cycle = 4 weeks) except during the first cycle, which includes an additional infusion of Gemcitabine on D22. Doses were adjusted before each administration of chemotherapy, depending on the patient's weight and individual tolerance to gemcitabine. The dose of gemcitabine was recalculated if the weight change was ≥ 10%.
Gemcitabine treatment was continued for 24 weeks (19 injections and 6 cycles).

Arm type	Active comparator
Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Patients received 1,000 mg/m² on a 30-minute drip for 3 weeks (D1, D8, D15) on each cycle, followed by a week of rest, except for the first cycle which included an additional administration at D22 (19 administrations, 6 cycles, 24 weeks).

Arm title	Arm B: FOLFIRINOX

Arm description:

Treatment started with oxaliplatin 85 mg/m2 as a 2-hour IV infusion, followed by simultaneous administration (via Y-line) of folinic acid 400 mg/m2 (racemic) (or 200 mg/m2 if L-folinic acid) as a 2-hour IV infusion, and then irinotecan 180 mg/m2 as a 90-min IV infusion. The irinotecan infusion was started 30 minutes after the start of the folinic acid infusion.
5-FU (2400 mg/m2/h) was administered as a continuous IV infusion over 46 hours after the end of the folinic acid infusion, i.e. 1200 mg/m2/day for the 2 days.
The next cycle started on D15. Treatment could be given on an outpatient basis (day hospital), but not at the patient's home.
Treatment was continued for 24 weeks (12 cycles).

Arm type	Experimental

Investigational medicinal product name	Folinic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Patients received 400 mg/m² on 2-hour IV drip.

Investigational medicinal product name	Irinotecan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients received 180 mg/m² on D1 for 90 minutes, begin 30 minutes after starting the folinic acid drip.

Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Patients received 85 mg/m² on D1 for 2 hours.

Investigational medicinal product name	5-Fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Patients received 2,400 mg/m² IV in IV drip continuous for 48 hours (1,200 mg/m²/day).

Number of subjects in period 1	Arm A: Gemcitabine	Arm B: FOLFIRINOX
Started	86	85
Completed	51	55
Not completed	35	30
Physician decision	1	-
Patient decision	1	1
Disease progression	19	21
Death	6	1
Adverse event	7	6
Not treated	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Arm A: Gemcitabine

Reporting group description:

Gemcitabine was administered at a dose of 1,000 mg/m2, by intravenous infusion (strictly) over 30 minutes. It could be administered on an outpatient basis (day hospital), but not at the patient's home. Gemcitabine administration had to be repeated once a week for 3 consecutive weeks (D1, D8 and D15 of a cycle), followed by a week without injection (1 cycle = 4 weeks) except during the first cycle, which includes an additional infusion of Gemcitabine on D22. Doses were adjusted before each administration of chemotherapy, depending on the patient's weight and individual tolerance to gemcitabine. The dose of gemcitabine was recalculated if the weight change was ≥ 10%.
Gemcitabine treatment was continued for 24 weeks (19 injections and 6 cycles).

Reporting group title	Arm B: FOLFIRINOX

Reporting group description:

Treatment started with oxaliplatin 85 mg/m2 as a 2-hour IV infusion, followed by simultaneous administration (via Y-line) of folinic acid 400 mg/m2 (racemic) (or 200 mg/m2 if L-folinic acid) as a 2-hour IV infusion, and then irinotecan 180 mg/m2 as a 90-min IV infusion. The irinotecan infusion was started 30 minutes after the start of the folinic acid infusion.
5-FU (2400 mg/m2/h) was administered as a continuous IV infusion over 46 hours after the end of the folinic acid infusion, i.e. 1200 mg/m2/day for the 2 days.
The next cycle started on D15. Treatment could be given on an outpatient basis (day hospital), but not at the patient's home.
Treatment was continued for 24 weeks (12 cycles).

Reporting group values	Arm A: Gemcitabine	Arm B: FOLFIRINOX	Total
Number of subjects	86	85	171
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	32	30	62
From 65-84 years	54	55	109
85 years and over	0	0	0
Age continuous Units: years			
median	68	68	
full range (min-max)	43 to 81	42 to 84	-
Gender categorical Units: Subjects			
Female	46	40	86
Male	40	45	85
ECOG performance status Units: Subjects			
ECOG 0	38	37	75
ECOG 1	47	48	95
Missing	1	0	1
Head of pancreas tumor			

Units: Subjects			
No	37	41	78
Yes	49	44	93

End points

End points reporting groups

Reporting group title	Arm A: Gemcitabine

Reporting group description:

Gemcitabine was administered at a dose of 1,000 mg/m2, by intravenous infusion (strictly) over 30 minutes. It could be administered on an outpatient basis (day hospital), but not at the patient's home. Gemcitabine administration had to be repeated once a week for 3 consecutive weeks (D1, D8 and D15 of a cycle), followed by a week without injection (1 cycle = 4 weeks) except during the first cycle, which includes an additional infusion of Gemcitabine on D22. Doses were adjusted before each administration of chemotherapy, depending on the patient's weight and individual tolerance to gemcitabine. The dose of gemcitabine was recalculated if the weight change was ≥ 10%.
Gemcitabine treatment was continued for 24 weeks (19 injections and 6 cycles).

Reporting group title	Arm B: FOLFIRINOX

Reporting group description:

Treatment started with oxaliplatin 85 mg/m2 as a 2-hour IV infusion, followed by simultaneous administration (via Y-line) of folinic acid 400 mg/m2 (racemic) (or 200 mg/m2 if L-folinic acid) as a 2-hour IV infusion, and then irinotecan 180 mg/m2 as a 90-min IV infusion. The irinotecan infusion was started 30 minutes after the start of the folinic acid infusion.
5-FU (2400 mg/m2/h) was administered as a continuous IV infusion over 46 hours after the end of the folinic acid infusion, i.e. 1200 mg/m2/day for the 2 days.
The next cycle started on D15. Treatment could be given on an outpatient basis (day hospital), but not at the patient's home.
Treatment was continued for 24 weeks (12 cycles).

Primary: The progression-free survival (PFS)

End point title	The progression-free survival (PFS)

End point description:

PFS was defined as the time elapsed between the randomization date and the tumor progression date or death (from any cause) or the date of the last study visit (for alive patients that do not present tumor progression).
The progression was defined as follow:
- An increase of at least 20% in the sum of target lesion diameters compared to the smallest sum of target lesions during the trial, including the reference assessment (baseline) with an absolute increase in the sum of at least 5 mm (RECIST 1.1).
- Appearance of new lesions (RECIST 1.1).

End point type	Primary

End point timeframe:

From randomization until disease progression or date of death, assessed up until to 128 weeks.

End point values	Arm A: Gemcitabine	Arm B: FOLFIRINOX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	83		
Units: Months				
median (confidence interval 95%)	7.7 (6.2 to 9.2)	9.7 (7.0 to 11.7)		

Statistical analyses

Statistical analysis title	PFS analysis
Comparison groups	Arm A: Gemcitabine v Arm B: FOLFIRINOX
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0243
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	0.95

Secondary: Overall survival

End point title	Overall survival

End point description:

The OS was defined as the time elapsed between the randomization date and date of death (or the last monitoring visit for alive patients).

End point type	Secondary

End point timeframe:

Until death, assessed up 128 weeks after randomization

End point values	Arm A: Gemcitabine	Arm B: FOLFIRINOX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	84		
Units: Months				
median (confidence interval 95%)	15.4 (11.7 to 18.6)	15.7 (11.9 to 20.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Modality of PFS events

End point title	Modality of PFS events

End point description:

The failure modality were events such as distant progression (metastases) or loco-regional progression or death without progression.

End point type	Secondary

End point timeframe:

Until Disease Progression, assessed uo until 128 weeks after randomization.

End point values	Arm A: Gemcitabine	Arm B: FOLFIRINOX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85[1]	83[2]		
Units: percent				
number (not applicable)				
Local relapse	41.18	48.19		
Metastatic relapse	44.71	43.37		
Death without progression	14.12	8.43		

Notes:

[1] - 85 out of the 86 randomized patients experienced a progression event in arm A.

[2] - 83 out of the 84 randomized patients experienced a progression event in arm B.

Statistical analyses

No statistical analyses for this end point

Secondary: Curative surgery

End point title	Curative surgery

End point description:

Percentage of patients who were undergo excision of their pancreatic tumor, with R0 resection confirmed by an anatomo-pathologist.

End point type	Secondary

End point timeframe:

Until surgery, if applicable, up until 128 weeks after randomization

End point values	Arm A: Gemcitabine	Arm B: FOLFIRINOX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	85		
Units: percent				
number (confidence interval 95%)	4.7 (1.3 to 11.0)	5.9 (1.9 to 13.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Tumor response

End point title	Tumor response

End point description:

The objective response rate (ORR) was defined as the percentage of patients with a complete response (CR) or partial response (PR) as assessed by the investigator using RECIST 1.1

End point type	Secondary

End point timeframe:

Until disease progression or date of death, assessed up until 128 weeks after randomization.

End point values	Arm A: Gemcitabine	Arm B: FOLFIRINOX		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	85		
Units: percent				
number (confidence interval 95%)				
Objective response	15.1 (8.3 to 24.5)	42.4 (31.7 to 53.6)		
Disease control	88.4 (79.7 to 94.3)	82.4 (72.6 to 89.8)		
Complete Response	2.3 (0.3 to 8.1)	9.4 (4.2 to 17.7)		
Partial Response	12.8 (6.6 to 21.7)	32.9 (23.1 to 44)		
Stable Disease	73.3 (62.6 to 82.2)	40 (29.5 to 51.2)		
Progressive Disease	11.6 (5.7 to 20.3)	17.6 (10.2 to 27.4)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Toxicity was evaluated during treatment, at the end of study visit (3-5 weeks after the last chemotherapy cycle) and at follow-up visits (every 8 weeks after chemotherapy for 2 years then every 12 weeks for the following 3 years.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	Arm A: Gemcitabine

Reporting group description:

Gemcitabine was administered at a dose of 1,000 mg/m2, by intravenous infusion (strictly) over 30 minutes. It could be administered on an outpatient basis (day hospital), but not at the patient's home. Gemcitabine administration had to be repeated once a week for 3 consecutive weeks (D1, D8 and D15 of a cycle), followed by a week without injection (1 cycle = 4 weeks) except during the first cycle, which includes an additional infusion of Gemcitabine on D22. Doses were adjusted before each administration of chemotherapy, depending on the patient's weight and individual tolerance to gemcitabine. The dose of gemcitabine was recalculated if the weight change was ≥ 10%.
Gemcitabine treatment was continued for 24 weeks (19 injections and 6 cycles).

Reporting group title	Arm B: FOLFIRINOX

Reporting group description:

Treatment started with oxaliplatin 85 mg/m2 as a 2-hour IV infusion, followed by simultaneous administration (via Y-line) of folinic acid 400 mg/m2 (racemic) (or 200 mg/m2 if L-folinic acid) as a 2-hour IV infusion, and then irinotecan 180 mg/m2 as a 90-min IV infusion. The irinotecan infusion was started 30 minutes after the start of the folinic acid infusion.
5-FU (2400 mg/m2/h) was administered as a continuous IV infusion over 46 hours after the end of the folinic acid infusion, i.e. 1200 mg/m2/day for the 2 days.
The next cycle started on D15. Treatment could be given on an outpatient basis (day hospital), but not at the patient's home.
Treatment was continued for 24 weeks (12 cycles).

Serious adverse events	Arm A: Gemcitabine	Arm B: FOLFIRINOX	
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 85 (35.29%)	35 / 84 (41.67%)	
number of deaths (all causes)	81	79	
number of deaths resulting from adverse events	1	1	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			

subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Thrombosis multiple			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Extravasation of drug			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile reaction			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	4 / 85 (4.71%)	3 / 84 (3.57%)	
occurrences causally related to treatment / all	0 / 4	2 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hyperthermia			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			

Acute pulmonary oedema			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 85 (0.00%)	2 / 84 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Biliary stent occlusion			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood electrolytes decreased			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endoscopic retrograde cholangiopancreatography			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 85 (1.18%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ischaemic stroke			

subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Loss of consciousness			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neurological disorder NOS			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischemic attack			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aplasia bone marrow			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile aplasia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			

subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 85 (1.18%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syndrome hemolytic uremic			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Thrombotic microangiopathy			
subjects affected / exposed	2 / 85 (2.35%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 85 (2.35%)	2 / 84 (2.38%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowel obstruction			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhea			
subjects affected / exposed	1 / 85 (1.18%)	6 / 84 (7.14%)	
occurrences causally related to treatment / all	1 / 1	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal obstruction			

subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fecal impaction (causing obstruction)			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric hemorrhage			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemorrhage of digestive tract			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemorrhoidal bleeding			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melena			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction colon			

subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain abdominal			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic cyst			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 85 (2.35%)	4 / 84 (4.76%)	
occurrences causally related to treatment / all	2 / 2	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute cholecystitis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	3 / 85 (3.53%)	3 / 84 (3.57%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cholestasis			
subjects affected / exposed	1 / 85 (1.18%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dilatation biliary tract			

subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrenous cholecystitis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cytolysis			
subjects affected / exposed	2 / 85 (2.35%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive jaundice			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute retention of urine			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nephrotic syndrome			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal insufficiency			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Infections and infestations			

Acute pyelonephritis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial translocation			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Obstructive pyelonephritis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SARS-CoV-2 infection			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes			

subjects affected / exposed	1 / 85 (1.18%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food intolerance			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hyperglycemia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalemia			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	0 / 85 (0.00%)	2 / 84 (2.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Arm A: Gemcitabine	Arm B: FOLFIRINOX	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 85 (100.00%)	82 / 84 (97.62%)	
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Hot flush			

subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Hypertensive crisis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Embolism			
subjects affected / exposed	5 / 85 (5.88%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Hypertension			
subjects affected / exposed	2 / 85 (2.35%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Hematoma			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Venous thrombosis			
subjects affected / exposed	3 / 85 (3.53%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Deep vein thrombosis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Cataract surgery			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Pacemaker implantation			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	5 / 85 (5.88%)	7 / 84 (8.33%)	
occurrences (all)	1	1	
Pain			
subjects affected / exposed	3 / 85 (3.53%)	2 / 84 (2.38%)	
occurrences (all)	1	1	
General physical health deterioration			

subjects affected / exposed	5 / 85 (5.88%)	3 / 84 (3.57%)	
occurrences (all)	1	1	
Extravasation at perfusion site			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	72 / 85 (84.71%)	66 / 84 (78.57%)	
occurrences (all)	1	1	
Chills			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Hyperthermia			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Inflammation			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Catheter site inflammation			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Mucosal inflammation			
subjects affected / exposed	6 / 85 (7.06%)	15 / 84 (17.86%)	
occurrences (all)	1	1	
Malaise			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Oedema			
subjects affected / exposed	2 / 85 (2.35%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Face oedema			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Peripheral oedema			
subjects affected / exposed	13 / 85 (15.29%)	4 / 84 (4.76%)	
occurrences (all)	1	1	
influenza-like syndrome			

subjects affected / exposed	6 / 85 (7.06%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Ulcer			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Xerosis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Breast cyst			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Prostatitis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	4 / 85 (4.71%)	2 / 84 (2.38%)	
occurrences (all)	1	1	
Dyspnoea exertional			
subjects affected / exposed	3 / 85 (3.53%)	2 / 84 (2.38%)	
occurrences (all)	1	1	
Pulmonary embolism			
subjects affected / exposed	2 / 85 (2.35%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Hiccups			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Laryngospasm			

subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Acute pulmonary edema			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	0 / 85 (0.00%)	3 / 84 (3.57%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	2 / 85 (2.35%)	3 / 84 (3.57%)	
occurrences (all)	1	1	
Productive cough			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	1 / 85 (1.18%)	4 / 84 (4.76%)	
occurrences (all)	1	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 85 (2.35%)	3 / 84 (3.57%)	
occurrences (all)	1	1	
Depression			
subjects affected / exposed	5 / 85 (5.88%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Mood altered			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	3 / 85 (3.53%)	2 / 84 (2.38%)	
occurrences (all)	1	1	
Libido disorder			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	2 / 85 (2.35%)	1 / 84 (1.19%)	
occurrences (all)	1	1	

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	64 / 85 (75.29%)	55 / 84 (65.48%)	
occurrences (all)	1	1	
Blood albumin decreased			
subjects affected / exposed	14 / 85 (16.47%)	10 / 84 (11.90%)	
occurrences (all)	1	1	
Aspartate aminotransferase increased			
subjects affected / exposed	58 / 85 (68.24%)	49 / 84 (58.33%)	
occurrences (all)	1	1	
Blood chloride normal			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Creatinine renal clearance abnormal			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Blood creatinine abnormal			
subjects affected / exposed	11 / 85 (12.94%)	7 / 84 (8.33%)	
occurrences (all)	1	1	
Blood creatine decreased			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Blood creatinine decreased			
subjects affected / exposed	2 / 85 (2.35%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Serum ferritin			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Blood fibrinogen			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	58 / 85 (68.24%)	59 / 84 (70.24%)	
occurrences (all)	1	1	
Blood glucose			

subjects affected / exposed	2 / 85 (2.35%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Blood lactate dehydrogenase			
subjects affected / exposed	2 / 85 (2.35%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Blood magnesium			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Blood magnesium decreased			
subjects affected / exposed	4 / 85 (4.71%)	4 / 84 (4.76%)	
occurrences (all)	1	1	
Monocyte count increased			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Neutrophil count			
subjects affected / exposed	51 / 85 (60.00%)	39 / 84 (46.43%)	
occurrences (all)	1	1	
Lymphocyte count			
subjects affected / exposed	46 / 85 (54.12%)	25 / 84 (29.76%)	
occurrences (all)	1	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	43 / 85 (50.59%)	57 / 84 (67.86%)	
occurrences (all)	1	1	
Platelet count			
subjects affected / exposed	56 / 85 (65.88%)	59 / 84 (70.24%)	
occurrences (all)	1	1	
Weight decreased			
subjects affected / exposed	40 / 85 (47.06%)	42 / 84 (50.00%)	
occurrences (all)	1	1	
Blood potassium increased			
subjects affected / exposed	8 / 85 (9.41%)	4 / 84 (4.76%)	
occurrences (all)	1	1	
Blood potassium decreased			
subjects affected / exposed	3 / 85 (3.53%)	6 / 84 (7.14%)	
occurrences (all)	1	1	
Blood sodium decreased			

subjects affected / exposed	1 / 85 (1.18%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Blood urea increased			
subjects affected / exposed	2 / 85 (2.35%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Blood urea decreased			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Hyperkalaemia			
subjects affected / exposed	6 / 85 (7.06%)	3 / 84 (3.57%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Device defective			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Head injury			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Device occlusion			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Perfusion related reaction			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Congenital, familial and genetic disorders			
Aplasia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Cardiac disorders			
Heart failure			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	

Palpitations			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Cardiac disorder			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Ageusia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Anosmia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Aphasia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Memory disorder			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	3 / 85 (3.53%)	2 / 84 (2.38%)	
occurrences (all)	1	1	
Dysesthesia			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Dysgeusia			
subjects affected / exposed	7 / 85 (8.24%)	12 / 84 (14.29%)	
occurrences (all)	1	1	
Taste disorder			

subjects affected / exposed	1 / 85 (1.18%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Hypogeusia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Peripheral neuropathy			
subjects affected / exposed	8 / 85 (9.41%)	70 / 84 (83.33%)	
occurrences (all)	1	1	
Paresthesia			
subjects affected / exposed	0 / 85 (0.00%)	4 / 84 (4.76%)	
occurrences (all)	0	1	
Parosmia			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
consciousness lost			
subjects affected / exposed	1 / 85 (1.18%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Syncope			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Cholinergic syndrome			
subjects affected / exposed	0 / 85 (0.00%)	2 / 84 (2.38%)	
occurrences (all)	0	1	
Tremor			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Essential tremor			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
speech disorder			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Nervous system disorder			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			

Anemia			
subjects affected / exposed	75 / 85 (88.24%)	66 / 84 (78.57%)	
occurrences (all)	1	1	
Bone marrow aplasia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Hyperleucocytosis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Leucopenia			
subjects affected / exposed	49 / 85 (57.65%)	27 / 84 (32.14%)	
occurrences (all)	1	1	
Lymphadenopathy			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Lymphopenia			
subjects affected / exposed	3 / 85 (3.53%)	2 / 84 (2.38%)	
occurrences (all)	1	1	
Thrombotic microangiopathy			
subjects affected / exposed	2 / 85 (2.35%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Febrile neutropenia			
subjects affected / exposed	2 / 85 (2.35%)	3 / 84 (3.57%)	
occurrences (all)	1	1	
Hemolytic syndrome			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Thrombopenia			
subjects affected / exposed	0 / 85 (0.00%)	4 / 84 (4.76%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Positional vertigo			

subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Visual field defect			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Eye haemorrhage			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Dry mouth			
subjects affected / exposed	1 / 85 (1.18%)	3 / 84 (3.57%)	
occurrences (all)	1	1	
Constipation			
subjects affected / exposed	28 / 85 (32.94%)	25 / 84 (29.76%)	
occurrences (all)	1	1	
Diarrhoea			
subjects affected / exposed	40 / 85 (47.06%)	67 / 84 (79.76%)	
occurrences (all)	1	1	
Abdominal distension			
subjects affected / exposed	2 / 85 (2.35%)	4 / 84 (4.76%)	
occurrences (all)	1	1	
Abdominal pain			
subjects affected / exposed	52 / 85 (61.18%)	60 / 84 (71.43%)	
occurrences (all)	1	1	
Upper abdominal pain			
subjects affected / exposed	8 / 85 (9.41%)	7 / 84 (8.33%)	
occurrences (all)	1	1	
Tooth pain			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			

subjects affected / exposed	2 / 85 (2.35%)	4 / 84 (4.76%)	
occurrences (all)	1	1	
Dysphagia			
subjects affected / exposed	1 / 85 (1.18%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Anal fistula			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Flatulence			
subjects affected / exposed	1 / 85 (1.18%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Fecaloma			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Abdominal discomfort			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Epigastric discomfort			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Inguinal hernia			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal hemorrhage			
subjects affected / exposed	2 / 85 (2.35%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Rectal hemorrhage			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Hemorrhoids			
subjects affected / exposed	0 / 85 (0.00%)	3 / 84 (3.57%)	
occurrences (all)	0	1	
Pancreatic cyst			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Nausea			

subjects affected / exposed	46 / 85 (54.12%)	67 / 84 (79.76%)	
occurrences (all)	1	1	
Duodenal occlusion			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Intestinal occlusion			
subjects affected / exposed	2 / 85 (2.35%)	2 / 84 (2.38%)	
occurrences (all)	1	1	
Gingival oedema			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Proctalgia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Ptyalisme			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Gastrooesophageal reflux			
subjects affected / exposed	2 / 85 (2.35%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Gingival retraction			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	1 / 85 (1.18%)	2 / 84 (2.38%)	
occurrences (all)	1	1	
Aphthous ulcer			
subjects affected / exposed	1 / 85 (1.18%)	2 / 84 (2.38%)	
occurrences (all)	1	1	
Duodenal ulcer			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	32 / 85 (37.65%)	44 / 84 (52.38%)	
occurrences (all)	1	1	
Hepatobiliary disorders			

Cholangitis			
subjects affected / exposed	3 / 85 (3.53%)	2 / 84 (2.38%)	
occurrences (all)	1	1	
Cholestasis			
subjects affected / exposed	1 / 85 (1.18%)	4 / 84 (4.76%)	
occurrences (all)	1	1	
Cholecystitis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Acute cholecystitis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Hepatic cytolysis			
subjects affected / exposed	2 / 85 (2.35%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 85 (0.00%)	2 / 84 (2.38%)	
occurrences (all)	0	1	
Jaundice			
subjects affected / exposed	4 / 85 (4.71%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Liver disorder			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Alopecia			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Angioedema			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Skin fissures			

subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	8 / 85 (9.41%)	3 / 84 (3.57%)	
occurrences (all)	1	1	
Rash			
subjects affected / exposed	0 / 85 (0.00%)	3 / 84 (3.57%)	
occurrences (all)	0	1	
Maculo-papular rash			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Skin reaction			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Night sweats			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Acral syndrome			
subjects affected / exposed	1 / 85 (1.18%)	9 / 84 (10.71%)	
occurrences (all)	1	1	
Skin toxicity			
subjects affected / exposed	1 / 85 (1.18%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Skin ulcer			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Vesical dilatation			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Dysuria			
subjects affected / exposed	3 / 85 (3.53%)	1 / 84 (1.19%)	
occurrences (all)	1	1	

Glycosuria			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Renal failure			
subjects affected / exposed	2 / 85 (2.35%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Nycturia			
subjects affected / exposed	1 / 85 (1.18%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Nephrolithiasis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Pollakiuria			
subjects affected / exposed	2 / 85 (2.35%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Proteinuria			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Nephrotic syndrome			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Arthropathy			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Cervical pain			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
muscle contractions			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Dorsal pain			

subjects affected / exposed	7 / 85 (8.24%)	11 / 84 (13.10%)	
occurrences (all)	1	1	
Jaw pain			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Flank pain			
subjects affected / exposed	2 / 85 (2.35%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Bone pain			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	2 / 85 (2.35%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Musculoskeletal discomfort			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Hypercreatinaemia			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	6 / 85 (7.06%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Sacral pain			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Trismus			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Infections and infestations			
Tooth abscess			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Liver abscess			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	

Bronchitis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Cholecystitis infective			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
COVID-19			
subjects affected / exposed	0 / 85 (0.00%)	3 / 84 (3.57%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis viral			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Infection			
subjects affected / exposed	5 / 85 (5.88%)	6 / 84 (7.14%)	
occurrences (all)	1	1	
Injection site infection			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Catheter site infection			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	2 / 85 (2.35%)	5 / 84 (5.95%)	
occurrences (all)	1	1	
Genital infection			
subjects affected / exposed	1 / 85 (1.18%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Viral infection			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	

Oral mycosis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Pyelonephritis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Pyelonephritis acute			
subjects affected / exposed	1 / 85 (1.18%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Erysipelas			
subjects affected / exposed	3 / 85 (3.53%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Synovial cyst			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Appetite decreased			
subjects affected / exposed	39 / 85 (45.88%)	39 / 84 (46.43%)	
occurrences (all)	1	1	
Diabetes			
subjects affected / exposed	1 / 85 (1.18%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Iron deficiency			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Malnutrition			
subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Dehydration			

subjects affected / exposed	0 / 85 (0.00%)	1 / 84 (1.19%)	
occurrences (all)	0	1	
Hypercalcaemia			
subjects affected / exposed	1 / 85 (1.18%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Hyperchloraemia			
subjects affected / exposed	1 / 85 (1.18%)	1 / 84 (1.19%)	
occurrences (all)	1	1	
Hyperglycaemia			
subjects affected / exposed	28 / 85 (32.94%)	30 / 84 (35.71%)	
occurrences (all)	1	1	
Hypernatraemia			
subjects affected / exposed	2 / 85 (2.35%)	0 / 84 (0.00%)	
occurrences (all)	1	0	
Hypoalbuminaemia			
subjects affected / exposed	3 / 85 (3.53%)	4 / 84 (4.76%)	
occurrences (all)	1	1	
Hypocalcaemia			
subjects affected / exposed	9 / 85 (10.59%)	10 / 84 (11.90%)	
occurrences (all)	1	1	
Hypochloraemia			
subjects affected / exposed	4 / 85 (4.71%)	4 / 84 (4.76%)	
occurrences (all)	1	1	
Hypoglycaemia			
subjects affected / exposed	2 / 85 (2.35%)	3 / 84 (3.57%)	
occurrences (all)	1	1	
Hypokalaemia			
subjects affected / exposed	9 / 85 (10.59%)	8 / 84 (9.52%)	
occurrences (all)	1	1	
Hypomagnesaemia			
subjects affected / exposed	1 / 85 (1.18%)	3 / 84 (3.57%)	
occurrences (all)	1	1	
Hyponatraemia			
subjects affected / exposed	14 / 85 (16.47%)	9 / 84 (10.71%)	
occurrences (all)	1	1	
Hypoproteinaemia			

subjects affected / exposed	0 / 85 (0.00%)	3 / 84 (3.57%)	
occurrences (all)	0	1	
Cell death			
subjects affected / exposed	3 / 85 (3.53%)	0 / 84 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 February 2015	- Modification of the investigators list
11 February 2016	- Modification of the investigators list
27 September 2016	- Modification of the investigators list - Update of the protocol - Update of the information and consent form
20 February 2017	- Modification of the investigators list
19 April 2017	- Modification of the investigators list
12 March 2018	- Modification of the investigators list
24 April 2019	- Modification of the investigators list - Preventive measure against severe toxicities in the context of fluoropyrimidine-based treatment: Modification of inclusion criteria (addition of inclusion criterion no. 12 in the protocol). - Addition of information required by the GDPR in the information and consent forms.
25 May 2020	- The investigators list was modified - Inclusion period were extended
09 December 2021	- The investigators list was modified
23 November 2023	The sponsor UNICANCER had decided to stop monitoring the last patients on 25-Sep-2023 (i.e. a follow-up of approximately 2 years after the inclusion of the last patient instead of the 5-year follow-up initially planned). Since the recruitment took longer than initially planned, and the results obtained with data collected up to 25-Sep-2023 were complete to assess the protocol objectives, the study was stopped before its planned end.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
04 April 2024	The NEOPAN study was terminated earlier than the planned date. The sponsor UNICANCER had decided to stop monitoring the last patients on 25-Sep-2023 (i.e. a follow-up of approximately 2 years after the inclusion of the last patient instead of the 5-year follow-up initially planned). Since the recruitment took longer than initially planned, and the results obtained with data collected up to 25-Sep-2023 were complete to assess the protocol objectives, the study was stopped before its planned end.	-

Notes:

Limitations and caveats

None reported