



Clinical trial results:

A Phase III randomized study evaluating gemcitabine and paclitaxel versus gemcitabine alone after FOLFIRINOX failure or intolerance in Metastatic Pancreatic Ductal Adenocarcinoma.

Summary

EudraCT number	2018-002886-21
Trial protocol	FR
Global end of trial date	11 May 2022

Results information

Result version number	v1 (current)
This version publication date	05 January 2025
First version publication date	05 January 2025

Trial information

Trial identification

Sponsor protocol code	UC-0110/1809
-----------------------	--------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03943667
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UNICANCER
Sponsor organisation address	101 rue de Tolbiac, Paris, France, 75015
Public contact	Nourredine AIT RAHMOUNE,, UNICANCER, 33 0171936704, n.ait-rahmoune@unicancer.fr
Scientific contact	Nourredine AIT RAHMOUNE,, UNICANCER, 33 0171936704, n.ait-rahmoune@unicancer.fr

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	10 June 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 May 2022
Global end of trial reached?	Yes
Global end of trial date	11 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the superiority in terms Overall Survival (OS) of gemcitabine + solvent-based (sb)-paclitaxel over gemcitabine alone in metastatic pancreatic ductal adenocarcinoma after FOLFIRINOX failure or intolerance.

Protection of trial subjects:

UNICANCER, the trial sponsor, certifies that the trial GEMPAX will be conducted in compliance with the protocol described in this document, and in accordance with the French national regulatory requirements:

- Declaration of Helsinki, as modified in 2008,
- Loi n°2012-300 du 5 mars 2012 relative aux recherches impliquant la personne humaine, as modified in 2016
- Regulation (EU) 2016/679 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation)
- Loi Informatique et Libertés n°78-17 du 6 janvier 1978 modifiée, relative à la protection des personnes physiques à l'égard des traitements de données à caractère personnel,
- Loi n° 2004-800 du 6 août 2004 modifiée, relative à la bioéthique,
- Décision du 24 novembre 2006 fixant les règles de Bonnes Pratiques Cliniques pour les recherches biomédicales portant sur des médicaments à usage humain
- Arrêté du 24 mai 2006 relatif au contenu et aux modalités de présentation d'un protocole de recherche biomédicale portant sur un médicament à usage humain
- Good Manufacturing Practices, in particular, Annex 13 on investigational medicinal products.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the ethics committee (EC) for review and approval. Approval of both the protocol and the consent form will be obtained before any participant is included. Any amendment to the protocol will require review and approval by the EC before the changes are implemented in the study. In addition, all changes to the consent form will be EC-approved. Depending on the consent form modifications a decision will be made whether a new consent is required for patients who have already given consent.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 June 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 211
--------------------------------------	-------------

Worldwide total number of subjects	211
EEA total number of subjects	211

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)	109
From 65 to 84 years	101
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Between June 2019 and March 2021, 211 patients were included by 31 French centers.

Pre-assignment

Screening details:

The study consisted of screening phase to establish patients' eligibility and document baseline measurements. Patients participating in the trial complied for a total number of 12 months after randomization, including an estimate of 6 months of treatment and 6 months of follow-up.

Period 1

Period 1 title	Overall periode (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

Arm description:

The patients randomized in this arm received:

- Paclitaxel 80 mg/m² in IV infusion over 60 minutes at D1, D8 and D15 followed by 1 week of rest, every 28 days.
- Gemcitabine 1000 mg/m² in IV infusion over 30-40 minutes at D1, D8, D15 followed by 1 week of rest, every 28 days.

A premedication to prevent hypersensitivity reactions (e.g., dexamethasone, diphenhydramine, H2 blockers) was applied according to the Summary of Products Characteristics. Initial antiemetic prophylaxis was also recommended.

Secondary prophylaxis of neutropenia (G-CSF) for weekly chemotherapy was not planned in EORTC recommendations. Center's practices was applied. Of note, the coordinator of the study was used to prescribe successfully pegylated G-CSF (pegfilgrastim=Neulasta®) on D1 and D15 of each cycle according to other published experience for weekly chemotherapy schedules.

At each infusion day, paclitaxel was administered before gemcitabine.

Arm type	Experimental
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

The patients received Paclitaxel 80 mg/m² in IV infusion over 60 minutes at D1, D8 and D15 followed by 1 week of rest, every 28 days.

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

Dosage and administration details:

The patients received Gemcitabine 1000 mg/m² in IV infusion over 30-40 minutes at D1, D8, D15 followed by 1 week of rest, every 28 days.

Arm title	Arm B
------------------	-------

Arm description:

The patients randomized in this arm received Gemcitabine 1000 mg/m² in IV infusion over 30-40 minutes at D1, D8, D15 followed by 1 week of rest, every 28 days.

Arm type	Control groupe
Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

The patients received Gemcitabine 1000 mg/m² in IV infusion over 30-40 minutes at D1, D8, D15 followed by 1 week of rest, every 28 days.

Number of subjects in period 1	Arm A	Arm B
Started	140	71
Completed	0	0
Not completed	140	71
Consent withdrawn by subject	1	-
Death	131	68
Sponsor decision	8	3

Baseline characteristics

Reporting groups

Reporting group title	Arm A
-----------------------	-------

Reporting group description:

The patients randomized in this arm received:

- Paclitaxel 80 mg/m² in IV infusion over 60 minutes at D1, D8 and D15 followed by 1 week of rest, every 28 days.

- Gemcitabine 1000 mg/m² in IV infusion over 30-40 minutes at D1, D8, D15 followed by 1 week of rest, every 28 days.

A premedication to prevent hypersensitivity reactions (e.g., dexamethasone, diphenhydramine, H2 blockers) was applied according to the Summary of Products Characteristics. Initial antiemetic prophylaxis was also recommended.

Secondary prophylaxis of neutropenia (G-CSF) for weekly chemotherapy was not planned in EORTC recommendations. Center's practices was applied. Of note, the coordinator of the study was used to prescribe successfully pegylated G-CSF (pegfilgrastim=Neulasta®) on D1 and D15 of each cycle according to other published experience for weekly chemotherapy schedules.

At each infusion day, paclitaxel was administered before gemcitabine.

Reporting group title	Arm B
-----------------------	-------

Reporting group description:

The patients randomized in this arm received Gemcitabine 1000 mg/m² in IV infusion over 30-40 minutes at D1, D8, D15 followed by 1 week of rest, every 28 days.

Reporting group values	Arm A	Arm B	Total
Number of subjects	140	71	211
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)	72	37	109
From 65-84 years	67	34	101
85 years and over	1	0	1
Age continuous			
Units: years			
median	65	64	
full range (min-max)	39 to 86	30 to 79	-
Gender categorical			
Units: Subjects			
Female	53	28	81
Male	87	43	130
ECOG at baseline			
Units: Subjects			
ECOG 0-1	122	63	185
ECOG 2	18	8	26
ECOG PS at baseline			
Units: Subjects			

ECOG PS 0-1	124	63	187
ECOG PS 2	16	8	24
PFS duration at first line therapy Units: Subjects			
Inferior to 6 months	59	33	92
Superior or equal to 6 months	81	38	119
CA 19-9 level at baseline Units: Subjects			
Inferior to 59XULN	76	37	113
Superior or equal to 59XULN	64	34	98
NLR at baseline Units: Subjects			
Inferior to 5	98	49	147
Superior or equal to 5	42	22	64

End points

End points reporting groups

Reporting group title	Arm A
-----------------------	-------

Reporting group description:

The patients randomized in this arm received:

- Paclitaxel 80 mg/m² in IV infusion over 60 minutes at D1, D8 and D15 followed by 1 week of rest, every 28 days.
- Gemcitabine 1000 mg/m² in IV infusion over 30-40 minutes at D1, D8, D15 followed by 1 week of rest, every 28 days.

A premedication to prevent hypersensitivity reactions (e.g., dexamethasone, diphenhydramine, H2 blockers) was applied according to the Summary of Products Characteristics. Initial antiemetic prophylaxis was also recommended.

Secondary prophylaxis of neutropenia (G-CSF) for weekly chemotherapy was not planned in EORTC recommendations. Center's practices was applied. Of note, the coordinator of the study was used to prescribe successfully pegylated G-CSF (pegfilgrastim=Neulasta®) on D1 and D15 of each cycle according to other published experience for weekly chemotherapy schedules.

At each infusion day, paclitaxel was administered before gemcitabine.

Reporting group title	Arm B
-----------------------	-------

Reporting group description:

The patients randomized in this arm received Gemcitabine 1000 mg/m² in IV infusion over 30-40 minutes at D1, D8, D15 followed by 1 week of rest, every 28 days.

Primary: Overall survival (OS)

End point title	Overall survival (OS)
-----------------	-----------------------

End point description:

The primary endpoint of the study is overall survival defined as the time from the date of randomization to the date of death due to any cause. Any patient not known to have died at the time of analysis was censored based on the last recorded date on which the patient was known to be alive.

End point type	Primary
----------------	---------

End point timeframe:

From the date of randomization to the date of death due to any cause.

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	140	71		
Units: Months				
median (confidence interval 95%)	6.4 (5.2 to 7.4)	5.9 (4.6 to 6.9)		

Statistical analyses

Statistical analysis title	OS analysis
Comparison groups	Arm A v Arm B

Number of subjects included in analysis	211
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4095
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.2

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)
End point description:	Progression Free Survival (PFS) is defined as the time from randomization until the date of event defined as the first documented progression, according to investigator assessment of RECIST version 1.1, or death (by any cause in the absence of progression). Patients who have not progressed or died at the time of analysis are censored at the time of the latest date of assessment from their last evaluable RECIST assessment.
End point type	Secondary
End point timeframe:	From randomization until the date of event defined as the first documented progression, according to investigator assessment of RECIST version 1.1, or death (by any cause in the absence of progression)

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	140	71		
Units: Months				
median (confidence interval 95%)	3.1 (2.2 to 4.3)	2.0 (1.9 to 2.3)		

Statistical analyses

Statistical analysis title	PSF analysis
Comparison groups	Arm A v Arm B
Number of subjects included in analysis	211
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0067
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.64

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	0.89

Secondary: Objective response rate (ORR)

End point title	Objective response rate (ORR)
End point description:	
Objective response rate (ORR) is defined as the proportion of patients with a complete or a partial response (CR or PR) as best overall response during the study.	
End point type	Secondary
End point timeframe:	
Objective Response rate according to RECIST v1.1 criteria	

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137 ^[1]	71		
Units: percent				
number (confidence interval 95%)	17.5 (11.6 to 24.9)	4.2 (0.9 to 11.9)		

Notes:

[1] - 3 missing data for objective response.

Statistical analyses

Statistical analysis title	ORR analysis
Comparison groups	Arm A v Arm B
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.007
Method	Chi-2

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Start at the date of the signature of the informed consent form to 30 days after the last administration of the investigational product.

Adverse event reporting additional description:

For this study, the safety population consist of 208 patients: 138 in arm A (GEMPAX) and 70 in arm B (gemcitabine).

For non serious adverse events only treatment-related adverse events (TRAEs) were available.

The number of occurrence are not available and will be always noted "1"

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
Dictionary version	25

Reporting groups

Reporting group title	Arm A
-----------------------	-------

Reporting group description: -

Reporting group title	Arm B
-----------------------	-------

Reporting group description: -

Serious adverse events	Arm A	Arm B	
Total subjects affected by serious adverse events			
subjects affected / exposed	71 / 138 (51.45%)	26 / 70 (37.14%)	
number of deaths (all causes)	122	65	
number of deaths resulting from adverse events	1	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Peritoneal carcinomatosis			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tumor progression			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vascular disorders			
Cerebral haemorrhage			

subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	3 / 138 (2.17%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Fever			
subjects affected / exposed	3 / 138 (2.17%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 138 (0.72%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hyperthermia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothermia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Mucositis			

subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary edema			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COPD exacerbation			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cryptogenic organizing pneumonia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 138 (0.00%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Interstitial lung disease			
subjects affected / exposed	1 / 138 (0.72%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pleural effusion			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			

Confusion			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Biliary stent occlusion			
subjects affected / exposed	2 / 138 (1.45%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fractured wrist			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral fracture			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac disorders			
Angina syndrome			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			

subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Coma			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyskinesia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischemic stroke			
subjects affected / exposed	1 / 138 (0.72%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neurological impairment			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Psychomotor regression syndrome			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
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	6 / 138 (4.35%)	2 / 70 (2.86%)	
occurrences causally related to treatment / all	4 / 6	1 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Anemia post chemotherapy			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (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	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bicytopenia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombopenia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	5 / 138 (3.62%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	5 / 5	0 / 0	
deaths causally related to treatment / all	0 / 4	0 / 0	
Acute pancreatitis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bleeding oesophageal varices			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal haemorrhage			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric hemorrhage			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastric ulcer hemorrhage			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal bleeding			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrojejunal ulcer, acute with perforation			

subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemorrhage of digestive tract			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intestinal obstruction			
subjects affected / exposed	6 / 138 (4.35%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Subocclusive syndrome			
subjects affected / exposed	3 / 138 (2.17%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Vomiting			
subjects affected / exposed	4 / 138 (2.90%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 5	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Biliary obstruction			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute acalculous cholecystitis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct obstruction			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stenosis			

subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiolitis			
subjects affected / exposed	0 / 138 (0.00%)	5 / 70 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	2 / 138 (1.45%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis acute			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Function liver abnormal			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Icterus			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			

subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal insufficiency			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Myositis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Biliary sepsis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract infection			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Catheter infection			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious colitis			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lung infection			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
SARS-CoV-2 infection			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 138 (1.45%)	1 / 70 (1.43%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary infection			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (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	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcemia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (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	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Arm A	Arm B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	138 / 138 (100.00%)	69 / 70 (98.57%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	70 / 138 (50.72%)	29 / 70 (41.43%)	
occurrences (all)	1	1	
Fatigue			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
General physical health deterioration			
subjects affected / exposed	3 / 138 (2.17%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hyperthermia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hypothermia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			
subjects affected / exposed	4 / 138 (2.90%)	0 / 70 (0.00%)	
occurrences (all)	1	0	

Mucosal inflammation subjects affected / exposed occurrences (all)	11 / 138 (7.97%) 1	0 / 70 (0.00%) 0	
Oedema subjects affected / exposed occurrences (all)	2 / 138 (1.45%) 0	0 / 70 (0.00%) 0	
Oedema peripheral subjects affected / exposed occurrences (all)	26 / 138 (18.84%) 1	4 / 70 (5.71%) 1	
Pain subjects affected / exposed occurrences (all)	3 / 138 (2.17%) 1	0 / 70 (0.00%) 0	
Pyrexia subjects affected / exposed occurrences (all)	11 / 138 (7.97%) 1	3 / 70 (4.29%) 1	
Xerosis subjects affected / exposed occurrences (all)	3 / 138 (2.17%) 1	0 / 70 (0.00%) 0	
Immune system disorders Anaphylactic shock subjects affected / exposed occurrences (all)	1 / 138 (0.72%) 1	0 / 70 (0.00%) 0	
Hypersensitivity subjects affected / exposed occurrences (all)	2 / 138 (1.45%) 1	1 / 70 (1.43%) 1	
Respiratory, thoracic and mediastinal disorders Chronic obstructive pulmonary disease subjects affected / exposed occurrences (all)	1 / 138 (0.72%) 1	0 / 70 (0.00%) 0	
Dyspnoea subjects affected / exposed occurrences (all)	3 / 138 (2.17%) 1	2 / 70 (2.86%) 1	
Epistaxis subjects affected / exposed occurrences (all)	8 / 138 (5.80%) 1	1 / 70 (1.43%) 1	
Hiccups			

subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Interstitial lung disease			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Laryngeal pain			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Organising pneumonia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Pulmonary embolism			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Pulmonary fibrosis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	6 / 138 (4.35%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Aspartate aminotransferase increased			
subjects affected / exposed	6 / 138 (4.35%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	4 / 138 (2.90%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Blood creatinine increased			
subjects affected / exposed	1 / 138 (0.72%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 138 (0.72%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Gamma-glutamyltransferase increased			

subjects affected / exposed	8 / 138 (5.80%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Haemoglobin decreased			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Lymphocyte count increased			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Neutrophil count increased			
subjects affected / exposed	3 / 138 (2.17%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Platelet count decreased			
subjects affected / exposed	12 / 138 (8.70%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Serum ferritin decreased			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Transaminases increased			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	2 / 138 (1.45%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Hyperkalaemia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hypoalbuminaemia			
subjects affected / exposed	3 / 138 (2.17%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Congenital, familial and genetic disorders			

Aplasia subjects affected / exposed occurrences (all)	1 / 138 (0.72%) 1	0 / 70 (0.00%) 0	
Cardiac disorders			
Atrial fibrillation subjects affected / exposed occurrences (all)	1 / 138 (0.72%) 1	0 / 70 (0.00%) 0	
Cardiac failure subjects affected / exposed occurrences (all)	2 / 138 (1.45%) 1	0 / 70 (0.00%) 0	
Nervous system disorders			
Ageusia subjects affected / exposed occurrences (all)	1 / 138 (0.72%) 1	0 / 70 (0.00%) 0	
Dizziness subjects affected / exposed occurrences (all)	1 / 138 (0.72%) 1	0 / 70 (0.00%) 0	
Dysaesthesia subjects affected / exposed occurrences (all)	2 / 138 (1.45%) 1	1 / 70 (1.43%) 1	
Dysgeusia subjects affected / exposed occurrences (all)	10 / 138 (7.25%) 1	0 / 70 (0.00%) 0	
Headache subjects affected / exposed occurrences (all)	4 / 138 (2.90%) 1	0 / 70 (0.00%) 0	
Hypoaesthesia subjects affected / exposed occurrences (all)	1 / 138 (0.72%) 1	0 / 70 (0.00%) 0	
Neuropathy peripheral subjects affected / exposed occurrences (all)	60 / 138 (43.48%) 1	3 / 70 (4.29%) 1	
Neurotoxicity subjects affected / exposed occurrences (all)	1 / 138 (0.72%) 1	1 / 70 (1.43%) 1	
Paraesthesia			

subjects affected / exposed	16 / 138 (11.59%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Peripheral sensory neuropathy			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Presyncope			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	78 / 138 (56.52%)	18 / 70 (25.71%)	
occurrences (all)	1	1	
Bicytopenia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Eosinophilia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Febrile neutropenia			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Leucocytosis			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Leucopenia			
subjects affected / exposed	5 / 138 (3.62%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Lymphopenia			
subjects affected / exposed	6 / 138 (4.35%)	3 / 70 (4.29%)	
occurrences (all)	1	1	
Neutropenia			
subjects affected / exposed	39 / 138 (28.26%)	13 / 70 (18.57%)	
occurrences (all)	1	1	

Thrombocytopenia subjects affected / exposed occurrences (all)	66 / 138 (47.83%) 1	18 / 70 (25.71%) 1	
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	1 / 138 (0.72%) 1	0 / 70 (0.00%) 0	
Eye disorders Conjunctival hyperaemia subjects affected / exposed occurrences (all) Eye disorder subjects affected / exposed occurrences (all) Lacrimation increased subjects affected / exposed occurrences (all) Vision blurred subjects affected / exposed occurrences (all)	1 / 138 (0.72%) 1 1 / 138 (0.72%) 1 1 / 138 (0.72%) 1 1 / 138 (0.72%) 1	0 / 70 (0.00%) 0 0 / 70 (0.00%) 0 0 / 70 (0.00%) 0 0 / 70 (0.00%) 0	
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Aphthous ulcer subjects affected / exposed occurrences (all) Ascites subjects affected / exposed occurrences (all) Constipation	1 / 138 (0.72%) 1 8 / 138 (5.80%) 1 1 / 138 (0.72%) 1 3 / 138 (2.17%) 1 1 / 138 (0.72%) 0 0	2 / 70 (2.86%) 1 1 / 70 (1.43%) 1 0 / 70 (0.00%) 0 0 / 70 (0.00%) 0 1 / 70 (1.43%) 0	

subjects affected / exposed	9 / 138 (6.52%)	8 / 70 (11.43%)
occurrences (all)	1	1
Diarrhoea		
subjects affected / exposed	38 / 138 (27.54%)	9 / 70 (12.86%)
occurrences (all)	1	1
Dyspepsia		
subjects affected / exposed	3 / 138 (2.17%)	0 / 70 (0.00%)
occurrences (all)	1	0
Dysphagia		
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)
occurrences (all)	1	0
Epigastric discomfort		
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)
occurrences (all)	0	1
Flatulence		
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)
occurrences (all)	1	0
Gastrointestinal disorder		
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)
occurrences (all)	1	0
Gastrointestinal toxicity		
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)
occurrences (all)	1	0
Gastrooesophageal reflux		
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)
occurrences (all)	1	0
Haemorrhoids		
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)
occurrences (all)	1	0
Mouth ulceration		
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)
occurrences (all)	1	0
Nausea		
subjects affected / exposed	53 / 138 (38.41%)	25 / 70 (35.71%)
occurrences (all)	1	1
Odynophagia		

subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Paraesthesia oral			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Stomatitis			
subjects affected / exposed	10 / 138 (7.25%)	2 / 70 (2.86%)	
occurrences (all)	1	1	
Vomiting			
subjects affected / exposed	22 / 138 (15.94%)	10 / 70 (14.29%)	
occurrences (all)	1	1	
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	3 / 138 (2.17%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Hepatic cytolysis			
subjects affected / exposed	8 / 138 (5.80%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	45 / 138 (32.61%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Cutaneous symptom			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Dry skin			
subjects affected / exposed	5 / 138 (3.62%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Nail disorder			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Night sweats			

subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Onycholysis			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	4 / 138 (2.90%)	4 / 70 (5.71%)	
occurrences (all)	1	1	
Rash			
subjects affected / exposed	6 / 138 (4.35%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Rash pruritic			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Skin disorder			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Skin fissures			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Skin toxicity			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Stasis dermatitis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Renal failure			

subjects affected / exposed occurrences (all)	0 / 138 (0.00%) 0	1 / 70 (1.43%) 1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 138 (5.07%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Muscle spasms			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	7 / 138 (5.07%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Myositis			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Cystitis			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Erysipelas			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Genital infection fungal			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	3 / 138 (2.17%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Localised infection			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Oral fungal infection			

subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Sepsis			
subjects affected / exposed	0 / 138 (0.00%)	1 / 70 (1.43%)	
occurrences (all)	0	1	
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Appetite decreased			
subjects affected / exposed	18 / 138 (13.04%)	7 / 70 (10.00%)	
occurrences (all)	1	1	
Hypercalcaemia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			
subjects affected / exposed	2 / 138 (1.45%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hypocalcaemia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	3 / 138 (2.17%)	1 / 70 (1.43%)	
occurrences (all)	1	1	
Hyponatraemia			
subjects affected / exposed	1 / 138 (0.72%)	0 / 70 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 December 2019	<ul style="list-style-type: none">- Modification of inclusion criterion #4 to introduce a time margin in the definition of progression on FOLFIRINOX- Rewording of non-inclusion criterion #6 concerning previous treatment to include a limitation to prior treatment with gemcitabine- Changes to the Glasgow score calculation method and the frequency with which this score must be determined- Changes to the neurological examination schedule- Changes to the hematological and biological examination schedule- Update of the list of investigators- Update of the patient information notice and creation of an addendum to the patient information notice
29 June 2020	Letter to ANSM for informing of the suspension of study inclusion during the COVID 19 pandemic
23 July 2020	<ul style="list-style-type: none">- Details for performing the Conjugated Bilirubin Assay (direct)- Modification of the schedule for clinical examinations, vital sign and performance index measurements performance index (ECOG-PS)- Correction of an error in the patient information notice, update of the schedule of visits, the section on data processing and creation of an addendum to the information notice- Update of the list of investigators
17 December 2021	<ul style="list-style-type: none">- Addition of collection of archived tumour material for patients randomised in the trial- Update of the list of investigators- Creation of an addendum to the patient information notice

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported