Clinical trial results:
A multicenter randomized phase II study to determine the optimal first-line chemotherapy regimen in patients with metastatic pancreatic cancer (FOOTPATH)

Summary

EudraCT number	2017-003496-54
Trial protocol	DE
Global end of trial date	24 October 2024

Results information

Result version number	v1 (current)
This version publication date	19 October 2026
First version publication date	19 October 2026

Trial information

Trial identification

Sponsor protocol code	FOOTPATH

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03487016
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	LMU Munich
Sponsor organisation address	Marchioninistrasse 15, Munich, Germany, 81377
Public contact	Study Secretary, Klinikum der Ludwig-Maximilian-Universität München, Klinikum Großhadern, 0049 89440072208, matthias.wolff@med.uni-muenchen.de
Scientific contact	Study Secretary, Klinikum der Ludwig-Maximilian-Universität München, Klinikum Großhadern, 0049 89440072208, matthias.wolff@med.uni-muenchen.de

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	25 September 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 October 2024
Global end of trial reached?	Yes
Global end of trial date	24 October 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the optimal first-line regimen in metastatic pancreatic cancer

Protection of trial subjects:

The trial was conducted in accordance with the German Medicinal Products Act (AMG), ICH-GCP and the Declaration of Helsinki. Protocol version 3.0 was approved by the German competent authority (BfArM) on 16 January 2019; all amendments (final version 7.0, approved 12 September 2022) were approved before implementation.

All patients gave written informed consent before any protocol-specific procedure; legal capacity to consent was an inclusion criterion. Eligibility required ECOG performance status 0 to 1 and adequate organ function; patients with severe concomitant disease, hypersensitivity to a study drug, strong CYP3A4 or UGT1A1 inhibitors, known glucuronidation deficiency or complete DPD deficiency were excluded. Women of childbearing potential required a negative pregnancy test and highly effective contraception during treatment and for 7 months after the last dose; men had to use condoms for 6 months.

All study drugs are authorised in Germany and were given at established doses and schedules. Treatment continued until progression or unacceptable toxicity, with protocol-defined dose reductions and delays.

Adverse events were recorded from informed consent until 28 days after the last dose or the end-of-treatment visit, whichever was longer, and graded according to NCI CTCAE. Serious adverse events had to be reported within 24 hours to the pharmacovigilance contractor of the sponsor (ClinAssess GmbH); related serious adverse events were reportable irrespective of the time since the last dose. S

afety data were monitored continuously; no data monitoring committee was installed.

Tumour assessments (RECIST 1.1) and CA 19-9 were performed every 8 weeks.

Patients were covered by clinical trial insurance as required by the AMG.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 April 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 274
Worldwide total number of subjects	274
EEA total number of subjects	274

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)	134
From 65 to 84 years	140
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited at 38 sites in Germany. The first patient gave informed consent and was randomised on 18 April 2019; the last patient was randomised on 13 July 2022. In total, 303 patients gave informed consent, of whom 274 were randomised 1:1:1 to the three treatment arms.

Pre-assignment

Screening details:

303 patients gave written informed consent and entered screening. 29 patients were not randomised: 28 did not meet the eligibility criteria (screening failure) and 1 withdrew consent because of clinical deterioration before randomisation. 274 patients were randomised (arm A 90, arm B 92, arm C 92). 9 randomised patients were not treated.

Period 1

Period 1 title	Treatment & follow-up (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Open-label trial; treatment allocation was known to patients, investigators and sponsor after randomisation.

Arms

Are arms mutually exclusive?	Yes
Arm title	ARM A

Arm description:

Gemcitabine plus nab-paclitaxel
Description: Nab-paclitaxel 125 mg/m2 as a 30-minute i.v. infusion followed by gemcitabine 1000 mg/m2 as a 30-minute i.v. infusion on days 1, 8 and 15 of a 28-day cycle, until disease progression or unacceptable toxicity.

Arm type	Active comparator
Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

1000 mg/m2 as a 30-minute i.v. infusion on days 1, 8 and 15 of a 28-day cycle, until disease progression or unacceptable toxicity.

Investigational medicinal product name	nab-paclitaxcel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Nab-paclitaxel 125 mg/m2 as a 30-minute on days 1, 8 and 15 of a 28-day cycle, until disease progression or unacceptable toxicity.

Arm title	ARM B

Arm description:

Liposomal irinotecan 70 mg/m2 (irinotecan free base; 80 mg/m2 as irinotecan hydrochloride trihydrate before protocol amendment 2) i.v. over 90 minutes, followed by folinic acid 400 mg/m2 i.v. over 30 minutes and 5-fluorouracil 2400 mg/m2 i.v. over 46 hours, on day 1 of a 14-day cycle, until disease

progression or unacceptable toxicity.

Arm type	Experimental
Investigational medicinal product name	Liposomal irinotecan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Liposomal irinotecan 70 mg/m2 (irinotecan free base; 80 mg/m2 as irinotecan hydrochloride trihydrate i.v. over 90 minutes until disease progression or unacceptable toxicity.

Investigational medicinal product name	Folinic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

folinic acid 400 mg/m2 i.v. over 30 minutes

Investigational medicinal product name	5-FU
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

2400 mg/m2 i.v. over 46 hours, on day 1 of a 14-day cycle, until disease progression or unacceptable toxicity.

Arm title	ARM C

Arm description:

Alternating 14-day cycles of NAPOLI (liposomal irinotecan 70 mg/m2, folinic acid 400 mg/m2, 5-fluorouracil 2400 mg/m2 over 46 hours) and mFOLFOX6 (oxaliplatin 85 mg/m2 i.v. over 2 to 6 hours, folinic acid 400 mg/m2, 5-fluorouracil 2400 mg/m2 over 46 hours), starting with NAPOLI, until disease progression or unacceptable toxicity.

Arm type	Experimental
Investigational medicinal product name	Liposomal irinotecan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Liposomal irinotecan 70 mg/m2 (irinotecan free base; 80 mg/m2 as irinotecan hydrochloride trihydrate i.v. over 90 minutes until disease progression or unacceptable toxicity.

Investigational medicinal product name	Folinic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

folinic acid 400 mg/m2 i.v. over 30 minutes

Investigational medicinal product name	5-FU
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

2400 mg/m2 i.v. over 46 hours, on day 1 of a 14-day cycle, until disease progression or unacceptable toxicity.

Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

85 mg/m2 i.v. over 2 to 6 hours

Number of subjects in period 1	ARM A	ARM B	ARM C
Started	90	92	92
Received at least one dose in study	89	86	90
Completed	85	82	83
Not completed	5	10	9
Consent withdrawn by subject	2	7	2
Physician decision	1	2	-
Lost to follow-up	2	1	6
Protocol deviation	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Treatment & follow-up

Reporting group description: -

Reporting group values	Treatment & follow-up	Total	
Number of subjects	274	274	
Age categorical Units: Subjects			
Adults (18-64 years)	134	134	
From 65-84 years	140	140	
Gender categorical Units: Subjects			
Female	137	137	
Male	137	137	

End points

End points reporting groups

Reporting group title	ARM A

Reporting group description:

Gemcitabine plus nab-paclitaxel
Description: Nab-paclitaxel 125 mg/m2 as a 30-minute i.v. infusion followed by gemcitabine 1000 mg/m2 as a 30-minute i.v. infusion on days 1, 8 and 15 of a 28-day cycle, until disease progression or unacceptable toxicity.

Reporting group title	ARM B

Reporting group description:

Liposomal irinotecan 70 mg/m2 (irinotecan free base; 80 mg/m2 as irinotecan hydrochloride trihydrate before protocol amendment 2) i.v. over 90 minutes, followed by folinic acid 400 mg/m2 i.v. over 30 minutes and 5-fluorouracil 2400 mg/m2 i.v. over 46 hours, on day 1 of a 14-day cycle, until disease progression or unacceptable toxicity.

Reporting group title	ARM C

Reporting group description:

Alternating 14-day cycles of NAPOLI (liposomal irinotecan 70 mg/m2, folinic acid 400 mg/m2, 5-fluorouracil 2400 mg/m2 over 46 hours) and mFOLFOX6 (oxaliplatin 85 mg/m2 i.v. over 2 to 6 hours, folinic acid 400 mg/m2, 5-fluorouracil 2400 mg/m2 over 46 hours), starting with NAPOLI, until disease progression or unacceptable toxicity.

Primary: Progression free survival

End point title	Progression free survival

End point description:

End point type	Primary

End point timeframe:

From randomisation until objective disease progression or death from any cause, whichever occurred first.
Tumour assessments every 8 weeks.
Final analysis at data extract 10 September 2025 (maximum observed time to event 49.0 months).

End point values	ARM A	ARM B	ARM C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	86	90	
Units: months				
median (confidence interval 86.6%)	4.6 (3.7 to 5.6)	3.1 (2.1 to 3.9)	6.2 (4.5 to 7.3)	

Statistical analyses

Statistical analysis title	Statistical analysis 1 (A vs B)

Statistical analysis description:

Two-sided log-rank test at alpha 0.134 (equivalent to the pre-specified one-sided alpha of 0.067 per comparison). Hazard ratio from a Cox proportional hazards model with arm A as reference; HR below 1 favours arm B. Full analysis set.
Comparison groups: Period 1 ARM A und Period 1 ARM B

Comparison groups	ARM A v ARM B
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1681
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.237
Confidence interval	
level	Other: 86.6 %
sides	2-sided
lower limit	0.98
upper limit	1.562

Statistical analysis title	Statistical analysis 2 (A vs C)

Statistical analysis description:

Two-sided log-rank test at alpha 0.134 (equivalent to the pre-specified one-sided alpha of 0.067 per comparison). Hazard ratio from a Cox proportional hazards model with arm A as reference; HR below 1 favours arm C. Full analysis set.

Comparison groups	ARM A v ARM C
Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0205
Method	Logrank
Confidence interval	
level	Other: 86.6 %
sides	2-sided
lower limit	0.553
upper limit	0.883

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events from first administration of study medication until 28 days after the last administration. Safety set: all randomised patients who received at least one dose (N=265). Data extract 10 September 2025.

Adverse event reporting additional description:

Adverse events were graded according to NCI CTCAE version 5.0 and coded by MedDRA preferred term and system organ class. Frequencies are patient-based: each preferred term is counted once per patient with the highest grade. Per protocol, progression of the underlying pancreatic cancer, including progression with fatal outcome, was not recorded as a

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	28

Reporting groups

Reporting group title	Arm A

Reporting group description:

Arm A: Gemcitabine plus nab-paclitaxel. Description: Patients randomised to arm A who received at least one dose of study treatment (safety set).

Reporting group title	Arm B

Reporting group description:

Arm B: NAPOLI. Description: Patients randomised to arm B who received at least one dose of study treatment (safety set).

Reporting group title	Arm C

Reporting group description:

Arm C: Sequential NAPOLI and mFOLFOX6. Description: Patients randomised to arm C who received at least one dose of study treatment (safety set).

Serious adverse events	Arm A	Arm B	Arm C
Total subjects affected by serious adverse events			
subjects affected / exposed	52 / 89 (58.43%)	51 / 86 (59.30%)	53 / 90 (58.89%)
number of deaths (all causes)	84	81	78
number of deaths resulting from adverse events	12	7	6
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bowen's disease			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cancer pain			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lymphangioma			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour associated fever			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	1 / 89 (1.12%)	1 / 86 (1.16%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Axillary vein thrombosis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jugular vein thrombosis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subclavian vein thrombosis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			

subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Coeliac plexus block			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	2 / 89 (2.25%)	1 / 86 (1.16%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	1 / 2	0 / 1	0 / 1
Fatigue			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	3 / 89 (3.37%)	4 / 86 (4.65%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	1 / 3	1 / 4	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Generalised oedema			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 89 (0.00%)	2 / 86 (2.33%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	2 / 90 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 2

Oedema mucosal			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 89 (2.25%)	1 / 86 (1.16%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 2	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute interstitial pneumonitis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Apnoea			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	2 / 89 (2.25%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Haemoptysis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	4 / 89 (4.49%)	4 / 86 (4.65%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disorientation			

subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device occlusion			
subjects affected / exposed	1 / 89 (1.12%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural fever			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 89 (1.12%)	1 / 86 (1.16%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 1
Cardiac failure			
subjects affected / exposed	1 / 89 (1.12%)	1 / 86 (1.16%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ventricular fibrillation			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nervous system disorders			
Basal ganglia haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disturbance in attention			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic stroke			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cerebral infarction			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Middle cerebral artery stroke			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebrobasilar insufficiency			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	3 / 89 (3.37%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coagulopathy			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 89 (1.12%)	1 / 86 (1.16%)	3 / 90 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute abdomen			

subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 89 (1.12%)	1 / 86 (1.16%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	3 / 89 (3.37%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	3 / 89 (3.37%)	5 / 86 (5.81%)	8 / 90 (8.89%)
occurrences causally related to treatment / all	2 / 3	5 / 5	6 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal stenosis			
subjects affected / exposed	0 / 89 (0.00%)	2 / 86 (2.33%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			

subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric perforation			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric stenosis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorder			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			

subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal haemorrhage			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mechanical ileus			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	3 / 89 (3.37%)	2 / 86 (2.33%)	2 / 90 (2.22%)
occurrences causally related to treatment / all	2 / 3	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstruction gastric			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic failure			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic artery aneurysm			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	2 / 90 (2.22%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			

subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 89 (1.12%)	2 / 86 (2.33%)	4 / 90 (4.44%)
occurrences causally related to treatment / all	1 / 1	1 / 2	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	3 / 89 (3.37%)	2 / 86 (2.33%)	4 / 90 (4.44%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholestasis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	3 / 90 (3.33%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Liver disorder			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ocular icterus			

subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Portal vein stenosis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 89 (1.12%)	3 / 86 (3.49%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	1 / 1	0 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Calculus urinary			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 89 (1.12%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 89 (0.00%)	2 / 86 (2.33%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract disorder			

subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Atypical pneumonia			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
COVID-19 pneumonia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Candida sepsis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site infection			
subjects affected / exposed	2 / 89 (2.25%)	1 / 86 (1.16%)	2 / 90 (2.22%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis infective			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epididymitis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			

subjects affected / exposed	2 / 89 (2.25%)	2 / 86 (2.33%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	2 / 2	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	3 / 89 (3.37%)	2 / 86 (2.33%)	2 / 90 (2.22%)
occurrences causally related to treatment / all	2 / 3	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral discitis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella infection			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella sepsis			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Liver abscess			
subjects affected / exposed	2 / 89 (2.25%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal candidiasis			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 89 (1.12%)	1 / 86 (1.16%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumocystis jirovecii pneumonia			

subjects affected / exposed	2 / 89 (2.25%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 89 (1.12%)	2 / 86 (2.33%)	4 / 90 (4.44%)
occurrences causally related to treatment / all	0 / 1	0 / 2	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Rotavirus infection			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	5 / 89 (5.62%)	1 / 86 (1.16%)	2 / 90 (2.22%)
occurrences causally related to treatment / all	2 / 5	1 / 1	1 / 2
deaths causally related to treatment / all	1 / 1	1 / 1	1 / 2
Spontaneous bacterial peritonitis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 89 (0.00%)	2 / 86 (2.33%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 89 (0.00%)	1 / 86 (1.16%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	1 / 89 (1.12%)	0 / 86 (0.00%)	0 / 90 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	4 / 90 (4.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	0 / 89 (0.00%)	0 / 86 (0.00%)	1 / 90 (1.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Arm A	Arm B	Arm C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	88 / 89 (98.88%)	77 / 86 (89.53%)	86 / 90 (95.56%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	5 / 89 (5.62%)	5 / 86 (5.81%)	2 / 90 (2.22%)
occurrences (all)	5	5	2
Hypertension			
subjects affected / exposed	4 / 89 (4.49%)	3 / 86 (3.49%)	11 / 90 (12.22%)
occurrences (all)	7	3	11
Hypotension			

subjects affected / exposed	1 / 89 (1.12%)	4 / 86 (4.65%)	5 / 90 (5.56%)
occurrences (all)	1	4	5
General disorders and administration site conditions			
Chills			
subjects affected / exposed	2 / 89 (2.25%)	0 / 86 (0.00%)	5 / 90 (5.56%)
occurrences (all)	2	0	5
Fatigue			
subjects affected / exposed	40 / 89 (44.94%)	36 / 86 (41.86%)	40 / 90 (44.44%)
occurrences (all)	57	51	60
General physical health deterioration			
subjects affected / exposed	4 / 89 (4.49%)	6 / 86 (6.98%)	3 / 90 (3.33%)
occurrences (all)	4	9	4
Localised oedema			
subjects affected / exposed	5 / 89 (5.62%)	1 / 86 (1.16%)	2 / 90 (2.22%)
occurrences (all)	11	1	2
Mucosal inflammation			
subjects affected / exposed	6 / 89 (6.74%)	10 / 86 (11.63%)	13 / 90 (14.44%)
occurrences (all)	9	21	20
Oedema			
subjects affected / exposed	6 / 89 (6.74%)	5 / 86 (5.81%)	7 / 90 (7.78%)
occurrences (all)	7	5	7
Oedema peripheral			
subjects affected / exposed	17 / 89 (19.10%)	10 / 86 (11.63%)	5 / 90 (5.56%)
occurrences (all)	22	11	5
Pain			
subjects affected / exposed	9 / 89 (10.11%)	11 / 86 (12.79%)	5 / 90 (5.56%)
occurrences (all)	13	13	7
Pyrexia			
subjects affected / exposed	14 / 89 (15.73%)	6 / 86 (6.98%)	9 / 90 (10.00%)
occurrences (all)	33	7	11
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 89 (11.24%)	3 / 86 (3.49%)	4 / 90 (4.44%)
occurrences (all)	10	4	4
Dyspnoea			

subjects affected / exposed	12 / 89 (13.48%)	5 / 86 (5.81%)	6 / 90 (6.67%)
occurrences (all)	13	5	6
Epistaxis			
subjects affected / exposed	19 / 89 (21.35%)	4 / 86 (4.65%)	4 / 90 (4.44%)
occurrences (all)	26	4	4
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	3 / 89 (3.37%)	2 / 86 (2.33%)	8 / 90 (8.89%)
occurrences (all)	3	2	8
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	9 / 89 (10.11%)	1 / 86 (1.16%)	5 / 90 (5.56%)
occurrences (all)	11	1	5
Aspartate aminotransferase increased			
subjects affected / exposed	8 / 89 (8.99%)	0 / 86 (0.00%)	5 / 90 (5.56%)
occurrences (all)	10	0	5
Blood alkaline phosphatase increased			
subjects affected / exposed	11 / 89 (12.36%)	5 / 86 (5.81%)	5 / 90 (5.56%)
occurrences (all)	14	5	7
C-reactive protein increased			
subjects affected / exposed	9 / 89 (10.11%)	3 / 86 (3.49%)	3 / 90 (3.33%)
occurrences (all)	12	4	3
Gamma-glutamyltransferase increased			
subjects affected / exposed	13 / 89 (14.61%)	6 / 86 (6.98%)	8 / 90 (8.89%)
occurrences (all)	17	6	10
Weight decreased			
subjects affected / exposed	5 / 89 (5.62%)	14 / 86 (16.28%)	6 / 90 (6.67%)
occurrences (all)	5	14	7
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 89 (5.62%)	1 / 86 (1.16%)	4 / 90 (4.44%)
occurrences (all)	5	1	13
Neuropathy peripheral			
subjects affected / exposed	36 / 89 (40.45%)	14 / 86 (16.28%)	36 / 90 (40.00%)
occurrences (all)	53	18	72
Peripheral sensory neuropathy			

subjects affected / exposed	5 / 89 (5.62%)	4 / 86 (4.65%)	4 / 90 (4.44%)
occurrences (all)	5	4	5
Taste disorder			
subjects affected / exposed	9 / 89 (10.11%)	2 / 86 (2.33%)	7 / 90 (7.78%)
occurrences (all)	9	2	7
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	37 / 89 (41.57%)	16 / 86 (18.60%)	15 / 90 (16.67%)
occurrences (all)	61	19	30
Leukopenia			
subjects affected / exposed	25 / 89 (28.09%)	3 / 86 (3.49%)	6 / 90 (6.67%)
occurrences (all)	55	3	7
Lymphopenia			
subjects affected / exposed	5 / 89 (5.62%)	1 / 86 (1.16%)	4 / 90 (4.44%)
occurrences (all)	7	1	4
Neutropenia			
subjects affected / exposed	31 / 89 (34.83%)	8 / 86 (9.30%)	15 / 90 (16.67%)
occurrences (all)	86	8	33
Thrombocytopenia			
subjects affected / exposed	33 / 89 (37.08%)	2 / 86 (2.33%)	7 / 90 (7.78%)
occurrences (all)	86	2	11
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 89 (2.25%)	3 / 86 (3.49%)	6 / 90 (6.67%)
occurrences (all)	2	3	6
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	8 / 89 (8.99%)	13 / 86 (15.12%)	18 / 90 (20.00%)
occurrences (all)	11	16	25
Abdominal pain upper			
subjects affected / exposed	3 / 89 (3.37%)	4 / 86 (4.65%)	6 / 90 (6.67%)
occurrences (all)	3	4	8
Ascites			
subjects affected / exposed	3 / 89 (3.37%)	6 / 86 (6.98%)	4 / 90 (4.44%)
occurrences (all)	4	6	4
Constipation			

subjects affected / exposed	19 / 89 (21.35%)	18 / 86 (20.93%)	20 / 90 (22.22%)
occurrences (all)	31	25	27
Diarrhoea			
subjects affected / exposed	34 / 89 (38.20%)	46 / 86 (53.49%)	41 / 90 (45.56%)
occurrences (all)	46	82	74
Dry mouth			
subjects affected / exposed	4 / 89 (4.49%)	7 / 86 (8.14%)	3 / 90 (3.33%)
occurrences (all)	4	7	3
Nausea			
subjects affected / exposed	36 / 89 (40.45%)	41 / 86 (47.67%)	42 / 90 (46.67%)
occurrences (all)	59	59	75
Stomatitis			
subjects affected / exposed	3 / 89 (3.37%)	6 / 86 (6.98%)	11 / 90 (12.22%)
occurrences (all)	6	8	17
Vomiting			
subjects affected / exposed	18 / 89 (20.22%)	26 / 86 (30.23%)	24 / 90 (26.67%)
occurrences (all)	30	34	32
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	41 / 89 (46.07%)	16 / 86 (18.60%)	19 / 90 (21.11%)
occurrences (all)	48	18	20
Dry skin			
subjects affected / exposed	4 / 89 (4.49%)	6 / 86 (6.98%)	10 / 90 (11.11%)
occurrences (all)	5	6	10
Rash			
subjects affected / exposed	14 / 89 (15.73%)	3 / 86 (3.49%)	6 / 90 (6.67%)
occurrences (all)	18	4	7
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 89 (6.74%)	4 / 86 (4.65%)	7 / 90 (7.78%)
occurrences (all)	7	4	8
Infections and infestations			
COVID-19			
subjects affected / exposed	6 / 89 (6.74%)	1 / 86 (1.16%)	9 / 90 (10.00%)
occurrences (all)	7	1	9
Infection			

subjects affected / exposed	6 / 89 (6.74%)	3 / 86 (3.49%)	2 / 90 (2.22%)
occurrences (all)	7	4	2
Urinary tract infection			
subjects affected / exposed	6 / 89 (6.74%)	0 / 86 (0.00%)	5 / 90 (5.56%)
occurrences (all)	6	0	5
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	15 / 89 (16.85%)	18 / 86 (20.93%)	16 / 90 (17.78%)
occurrences (all)	16	18	20
Hypoalbuminaemia			
subjects affected / exposed	4 / 89 (4.49%)	8 / 86 (9.30%)	3 / 90 (3.33%)
occurrences (all)	6	9	4
Hypokalaemia			
subjects affected / exposed	7 / 89 (7.87%)	16 / 86 (18.60%)	9 / 90 (10.00%)
occurrences (all)	7	22	14
Hyponatraemia			
subjects affected / exposed	5 / 89 (5.62%)	3 / 86 (3.49%)	4 / 90 (4.44%)
occurrences (all)	5	4	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 May 2019	Protocol V3.0 to V4.0 (10.05.2019) Synopse V3.0 (30.04.2019), Patient information V4.0 (30.04.2019)
19 December 2019	Protocol V4.0 to V5.0 (16.12.2019) Synopse V4.0 (16.12.2019)
31 August 2020	Protocol V5.0 to V6.0 (15.07.2020) Synopse V5.0 (15.07.2020) Patient information V6.0 (15.07.2020)
24 August 2022	Protocol V7.0 (27.05.2022) Patient information V7.0, Addendum 1.0 to patient information (27.05.2022)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported