



Clinical trial results:

Perioperative Chemotherapy (FLOT Protocol) Compared To Neoadjuvant Chemoradiation (CROSS Protocol) in Patients With Adenocarcinoma of the Esophagus

Summary

EudraCT number	2015-001683-20
Trial protocol	DE
Global end of trial date	28 November 2023

Results information

Result version number	v1 (current)
This version publication date	12 November 2025
First version publication date	12 November 2025

Trial information

Trial identification

Sponsor protocol code	P000760
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02509286
WHO universal trial number (UTN)	-
Other trial identifiers	DRKS: DRKS00008008

Notes:

Sponsors

Sponsor organisation name	University Medical Center Schleswig-Holstein, Campus Lübeck
Sponsor organisation address	Ratzeburger Allee 160, Lübeck, Germany, 23538
Public contact	Coordinating Investigator: Prof. Jens Höppner, University Medical Center OWL - Campus Lippe, Bielefeld University, +49 5231-721151, jens.hoeppner@uni-bielefeld.de
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Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	03 April 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 November 2023
Global end of trial reached?	Yes
Global end of trial date	28 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary endpoint is the overall survival time of the patient. This will be calculated as time from start of study treatment to death due to any cause. After randomisation, patients will be followed up for a minimum duration of 36 months or until death. For patients alive at study end, the survival time will be censored at time of last known survival status.

Protection of trial subjects:

Before enrolment in the clinical trial, the patient was informed that participation in the clinical trial is voluntary and that he/she may withdraw from the clinical trial at any time without having to give reasons and without penalty or loss of benefits to which the patient is otherwise entitled. The treating physician provided the patient with information about the treatment methods to be compared and the possible risks involved. At the same time, the nature, significance, implications, expected benefits and potential risks of the clinical trial and alternative treatments were explained to the patient. During the informed consent discussion, the patient was also informed about the insurance cover that exists and the insured obligations. The patient was given ample time and opportunity to obtain answers to any open questions. All questions relating to the clinical trial should be answered to the satisfaction of the patient and/or his/her legal representative. In addition, the patient was given a patient information sheet that contains all the important information in writing.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 January 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 438
Worldwide total number of subjects	438
EEA total number of subjects	438

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	246
From 65 to 84 years	190
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

From February 2016 until April 2020, a total of 438 patients were randomized in 25 study centres in Germany.

Pre-assignment

Screening details: -

Pre-assignment period milestones

Number of subjects started	438
Number of subjects completed	438

Period 1

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

Blinding implementation details:

Blinding of patients and physicians performing the treatment was not possible as a matter of principle. Concealment of randomisation by online randomisation was guaranteed to minimize selection bias.

Arms

Are arms mutually exclusive?	Yes
Arm title	FLOT

Arm description:

4 cycles of chemotherapy prior to surgery and a further 4 cycles of chemotherapy post-surgery, each cycle lasted 14 days/2 weeks. The drugs used in the FLOT regimen include 5-FU, leucovorin, oxaliplatin and docetaxel.

Arm type	Experimental
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	Taxotere
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Concentrate for solution for infusion

Dosage and administration details:

50 mg/m² in 250 ml NaCl 0.9% over 1h, d1. Repetition every 2 weeks (d15, q2w) 4 cycles (8 weeks) preoperatively and 4 cycles (8 weeks) postoperatively

Investigational medicinal product name	Folinic acid
Investigational medicinal product code	
Other name	Leucovorin
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Infusion

Dosage and administration details:

200 mg/m² BSA in 250 mL NaCl 0.9% over 2 hours. Repetition every 2 weeks (d15, q2w) 4 cycles (8 weeks) preoperatively and 4 cycles (8 weeks) postoperatively

Investigational medicinal product name	5-FU
Investigational medicinal product code	
Other name	Fluorouracil
Pharmaceutical forms	Solution for injection
Routes of administration	Injection

Dosage and administration details: 2600 mg/m ² BSA over in NaCl 0,9% over 24 hours. Repetition every 2 weeks (d15, q2w) 4 cycles (8 weeks) preoperatively and 4 cycles (8 weeks) postoperatively	
Investigational medicinal product name	Oxaliplatin
Investigational medicinal product code	
Other name	Eloxatin
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Concentrate for solution for infusion
Dosage and administration details: 85 mg/m ² BSA in 500 mL Glucose 5% over 2 hours. Repetition every 2 weeks (d15, q2w) 4 cycles (8 weeks) preoperatively and 4 cycles (8 weeks) postoperatively	
Arm title	CROSS

Arm description:

Combination of chemotherapy including paclitaxel and carboplatin and radiotherapy prior to surgery. The patient received 5 weeks of radiation therapy and 5 weekly cycles of chemotherapy. Patients were radiated by external beam radiation, using 3D conformal radiation technique, starting the first day of the first cycle of chemotherapy.

Arm type	Active comparator
Investigational medicinal product name	Carboplatin
Investigational medicinal product code	
Other name	Axicarb, Carbo-cell, Carbomedac
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Dose-dependent; 2 mg/mL/min AUC in 500 ml glucose 5% over 1h

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	Abraxane, Celltaxel, NeoTaxan, Ribotax , Taxol, Taxomedac
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Infusion

Dosage and administration details:

50 mg/m² BSA in 500 mL NaCl 0.9% over 1 h.

Number of subjects in period 1	FLOT	CROSS
Started	221	217
Completed	221	217

Baseline characteristics

Reporting groups

Reporting group title	FLOT
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Reporting group description:

4 cycles of chemotherapy prior to surgery and a further 4 cycles of chemotherapy post-surgery, each cycle lasted 14 days/2 weeks. The drugs used in the FLOT regimen include 5-FU, leucovorin, oxaliplatin and docetaxel.

Reporting group title	CROSS
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Reporting group description:

Combination of chemotherapy including paclitaxel and carboplatin and radiotherapy prior to surgery. The patient received 5 weeks of radiation therapy and 5 weekly cycles of chemotherapy. Patients were radiated by external beam radiation, using 3D conformal radiation technique, starting the first day of the first cycle of chemotherapy.

Reporting group values	FLOT	CROSS	Total
Number of subjects	221	217	438
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)	125	121	246
From 65-84 years	94	96	190
85 years and over	2	0	2
Age continuous			
Units: years			
arithmetic mean	63.1	62.6	
standard deviation	± 8.59	± 9.75	-
Gender categorical			
Units: Subjects			
Female	24	23	47
Male	197	194	391

End points

End points reporting groups

Reporting group title	FLOT
Reporting group description: 4 cycles of chemotherapy prior to surgery and a further 4 cycles of chemotherapy post-surgery, each cycle lasted 14 days/2 weeks. The drugs used in the FLOT regimen include 5-FU, leucovorin, oxaliplatin and docetaxel.	
Reporting group title	CROSS
Reporting group description: Combination of chemotherapy including paclitaxel and carboplatin and radiotherapy prior to surgery. The patient received 5 weeks of radiation therapy and 5 weekly cycles of chemotherapy. Patients were radiated by external beam radiation, using 3D conformal radiation technique, starting the first day of the first cycle of chemotherapy.	

Primary: Overall survival time

End point title	Overall survival time
End point description:	
End point type	Primary
End point timeframe:	
Median follow-up time: 55 months	

End point values	FLOT	CROSS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	221	217		
Units: Time				
median (full range (min-max))	65.71 (0.00 to 81.74)	37.16 (0.00 to 80.43)		

Statistical analyses

Statistical analysis title	Effect of treatment on Overall Survival
Statistical analysis description: The regression model was stratified for study centre and included randomized treatment (FLOT vs. CROSS), baseline N stage (N0 vs. N+) and age as independent variables.	
Comparison groups	FLOT v CROSS
Number of subjects included in analysis	438
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0116
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	0.92

Primary: Overall survival rates

End point title	Overall survival rates
End point description:	
End point type	Primary
End point timeframe:	
year 1, 2, 3, 4, 5, 6	

End point values	FLOT	CROSS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	221	217		
Units: Rates				
number (confidence interval 95%)				
year 1	0.846 (0.789 to 0.888)	0.737 (0.671 to 0.793)		
year 2	0.659 (0.589 to 0.721)	0.593 (0.522 to 0.658)		
year 3	0.574 (0.501 to 0.640)	0.507 (0.435 to 0.575)		
year 4	0.529 (0.456 to 0.597)	0.399 (0.328 to 0.469)		
year 5	0.506 (0.432 to 0.576)	0.387 (0.315 to 0.459)		
year 6	0.460 (0.367 to 0.547)	0.336 (0.255 to 0.420)		

Statistical analyses

Statistical analysis title	Patients at risk (OS rate) at year 3
Comparison groups	FLOT v CROSS
Number of subjects included in analysis	438
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0116
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	0.92

Secondary: Progression-free survival

End point title	Progression-free survival
End point description:	
End point type	Secondary
End point timeframe:	
Time interval from randomisation to the first event of locoregional failure, metastatic progression or death.	

End point values	FLOT	CROSS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	221	217		
Units: Months				
median (full range (min-max))	38.44 (0.00 to 81.74)	15.87 (0.00 to 78.62)		

Statistical analyses

Statistical analysis title	Effect of treatment on PFS
Comparison groups	FLOT v CROSS
Number of subjects included in analysis	438
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.0014
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	0.85

Notes:

[1] - Censored (for 10 patients, 7 in FLOT arm and 3 in CROSS arm, who died without previous failure more than 6 months after the last follow-up visit, the death event was counted as event for the overall survival status but not for the progression-free survival status. For these patients, progression-free survival time was censored at the last follow-up visit.)

Secondary: Progression-free survival rates

End point title	Progression-free survival rates
End point description:	
End point type	Secondary
End point timeframe:	
year 1, 2, 3, 4, 5, 6	

End point values	FLOT	CROSS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	221	217		
Units: Rate				
number (confidence interval 95%)				
year 1	0.684 (0.615 to 0.744)	0.579 (0.508 to 0.644)		
year 2	0.560 (0.487 to 0.627)	0.409 (0.340 to 0.476)		
year 3	0.516 (0.443 to 0.584)	0.350 (0.284 to 0.417)		
year 4	0.463 (0.391 to 0.533)	0.309 (0.245 to 0.376)		
year 5	0.444 (0.370 to 0.515)	0.309 (0.245 to 0.376)		
year 6	0.418 (0.332 to 0.501)	0.291 (0.223 to 0.363)		

Statistical analyses

No statistical analyses for this end point

Secondary: Recurrence-free survival

End point title	Recurrence-free survival
End point description:	
End point type	Secondary
End point timeframe:	
Time interval from surgery to the first event of locoregional recurrence, metastatic progression or death.	

End point values	FLOT	CROSS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	179		
Units: Time to RFS [months]				
median (full range (min-max))	43.27 (0.00 to 78.82)	16.23 (0.00 to 75.70)		

Statistical analyses

Statistical analysis title	Effect of treatment on RFS
Comparison groups	FLOT v CROSS
Number of subjects included in analysis	371
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0056
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	0.89

Secondary: Recurrence-free survival rates

End point title	Recurrence-free survival rates
End point description:	
End point type	Secondary
End point timeframe:	
year 1, 2, 3 ,4, 5, 6	

End point values	FLOT	CROSS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	192	179		
Units: Rates				
number (confidence interval 95%)				
year 1	0.694 (0.622 to 0.754)	0.581 (0.504 to 0.651)		
year 2	0.582 (0.506 to 0.650)	0.420 (0.346 to 0.493)		
year 3	0.528 (0.451 to 0.598)	0.363 (0.291 to 0.436)		
year 4	0.489 (0.412 to 0.561)	0.342 (0.271 to 0.415)		
year 5	0.468 (0.390 to 0.542)	0.322 (0.246 to 0.401)		

year 6	0.468 (0.390 to 0.542)	0.322 (0.246 to 0.401)		
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Statistical analyses

No statistical analyses for this end point

Secondary: Tumor progression, status and site of failure

End point title	Tumor progression, status and site of failure
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End point description:

End point type	Secondary
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End point timeframe:

During study

End point values	FLOT	CROSS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	221	217		
Units: Number of patients				
Isolated locoregional failure	17	9		
Isolated distant failure	45	71		
Simultaneous locoregional and distant failure	26	27		
Distant metastases detected before start of therap	1	11		
Alive without failure	114	80		
Death without failure	18	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Resectional status

End point title	Resectional status
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End point description:

End point type	Secondary
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End point timeframe:

During study

End point values	FLOT	CROSS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	221	217		
Units: Number of patients				
R0	182	172		
R1	10	7		
R2	0	0		
No surgery	28	36		
No tumor resection	1	2		

Statistical analyses

Statistical analysis title	Resectional status – Rates (R0 vs. all other)
Comparison groups	FLOT v CROSS
Number of subjects included in analysis	438
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4157
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.97

Secondary: Histo-pathological Tumor Regression

End point title	Histo-pathological Tumor Regression
End point description:	
End point type	Secondary
End point timeframe:	
During study	

End point values	FLOT	CROSS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	221	217		
Units: Number of patients				
1a (no residual tumor)	36	24		
1b (>0 - <10% residual tumor)	47	71		
2 (10-50% residual tumor)	46	50		
3 (>50% residual tumor)	60	34		

No surgery	28	36		
No tumor resection	1	2		
Missing data	3	0		

Statistical analyses

Statistical analysis title	Tumor regression – Rates (1a/1b vs. all other)
Comparison groups	FLOT v CROSS
Number of subjects included in analysis	438
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1557
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	1.11

Statistical analysis title	Tumor regression – Rates (1a vs. all other)
Comparison groups	FLOT v CROSS
Number of subjects included in analysis	438
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0988
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	2.79

Secondary: Postoperative TNM Stage

End point title	Postoperative TNM Stage
End point description:	
End point type	Secondary
End point timeframe:	
After surgery	

End point values	FLOT	CROSS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	221	217		
Units: Number of patients				
ypT0	35	23		
ypTis	1	1		
ypT1	7	5		
ypT1a	4	9		
ypT1b	17	15		
ypT2	30	32		
ypT3	93	91		
ypT4	2	1		
ypT4a	2	1		
ypT4b	1	0		
ypTx	0	1		
No surgery	28	36		
No tumor resection	1	2		
ypT0ypN0	32	18		

Statistical analyses

Statistical analysis title	Effect of treatment on postoperative stage
Statistical analysis description:	
Postoperative TNM Stage – Rates (ypN0 vs. all other)	
Comparison groups	FLOT v CROSS
Number of subjects included in analysis	438
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7199
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.36

Statistical analysis title	Effect of treatment on postoperative stage
Statistical analysis description:	
Postoperative TNM Stage – Rates (ypT0ypN0 vs. all other)	
Comparison groups	FLOT v CROSS

Number of subjects included in analysis	438
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0396
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	3.51

Secondary: Hospitalisation time

End point title	Hospitalisation time
End point description:	
End point type	Secondary
End point timeframe:	
During study	

End point values	FLOT	CROSS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	207	196		
Units: Days				
arithmetic mean (standard deviation)				
Hospitalisation for neoadjuvant treatment	2.5 (± 5.0)	9.8 (± 11.4)		
Hospitalisation for surgery	19.7 (± 17.1)	20.2 (± 18.2)		
Hospitalisation for adjuvant treatment	2.0 (± 4.8)	0 (± 0)		
Total hospitalisation time for treatment	22.6 (± 18.4)	28.6 (± 20.9)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Complete study

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22
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Reporting groups

Reporting group title	CROSS
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Reporting group description:

CROSS protocol: radiation therapy (41.4Gy / 23fractions) and concurrent chemotherapy with Carboplatin and Paclitaxel (5 weeks) prior to surgery. Radiotherapy: days 1-5, days 8-12, days 15-19, days 22-26 and days 29-31. Chemotherapy: Paclitaxel 50mg/m² day 1, 8, 15, 22 and day 29. Carboplatin (2mg/ml/min AUC) day 1, 8, 15, 22 and day 29.

Reporting group title	FLOT
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Reporting group description:

FLOT protocol: 5-FU 2600 mg/m² (24 hours), d1 Leucovorin 200 mg/m², d1 Oxaliplatin 85 mg/m², d1 Docetaxel 50mg/m², d1 every two weeks (q2w), 4 neoadjuvant cycles (8 weeks) prior to surgery and 4 adjuvant cycles (8 weeks) postoperatively.

Serious adverse events	CROSS	FLOT	
Total subjects affected by serious adverse events			
subjects affected / exposed	82 / 196 (41.84%)	98 / 207 (47.34%)	
number of deaths (all causes)	121	97	
number of deaths resulting from adverse events	14	5	
Vascular disorders			
Aortic perforation			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Arterial haemorrhage			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			

subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphatic fistula			
subjects affected / exposed	1 / 196 (0.51%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Thrombosis			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Resuscitation			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	5 / 196 (2.55%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Fatigue			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	2 / 196 (1.02%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated hernia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion site extravasation			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	3 / 196 (1.53%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 196 (1.02%)	4 / 207 (1.93%)	
occurrences causally related to treatment / all	1 / 2	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			

Drug hypersensitivity			
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chylothorax			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial fistula			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	3 / 196 (1.53%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dyspnoea exertional			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epiglottic cyst			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemothorax			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	6 / 196 (3.06%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagobronchial fistula			
subjects affected / exposed	2 / 196 (1.02%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			

subjects affected / exposed	2 / 196 (1.02%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 196 (1.02%)	5 / 207 (2.42%)	
occurrences causally related to treatment / all	0 / 2	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic haemorrhage			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tracheal fistula			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Thrombosis in device			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device dislocation			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Weight decreased			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
Abdominal wound dehiscence			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic complication			
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic haemorrhage			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic leak			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic stenosis			
subjects affected / exposed	1 / 196 (0.51%)	3 / 207 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endotracheal intubation complication			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal procedural complication			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal stoma complication subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical ventilation complication subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative ileus subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative delirium subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural fistula subjects affected / exposed	2 / 196 (1.02%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural bile leak subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural haemorrhage subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation oesophagitis			

subjects affected / exposed	2 / 196 (1.02%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic rupture			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract procedural complication			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	4 / 196 (2.04%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	2 / 196 (1.02%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachyarrhythmia			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic cardiomyopathy			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral artery thrombosis			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			

subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial nerve disorder			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic seizure			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Presyncope			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	2 / 196 (1.02%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 196 (1.02%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	1 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile bone marrow aplasia			

subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	3 / 196 (1.53%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hilar lymphadenopathy			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	2 / 196 (1.02%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	2 / 196 (1.02%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute abdomen			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocutaneous fistula			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diaphragmatic hernia			
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 196 (0.51%)	9 / 207 (4.35%)	
occurrences causally related to treatment / all	0 / 1	8 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular perforation			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenogastric reflux			

subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	5 / 196 (2.55%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric dilatation			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal inflammation			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastropleural fistula			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Impaired gastric emptying			
subjects affected / exposed	0 / 196 (0.00%)	5 / 207 (2.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal atony			

subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical ileus			
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal strangulation			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 196 (0.51%)	4 / 207 (1.93%)	
occurrences causally related to treatment / all	0 / 1	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic colitis			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction gastric			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Odynophagia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	2 / 196 (1.02%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal stenosis			

subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pylorospasm			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic artery aneurysm			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	2 / 196 (1.02%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vomiting			
subjects affected / exposed	2 / 196 (1.02%)	10 / 207 (4.83%)	
occurrences causally related to treatment / all	0 / 3	10 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			

subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 196 (1.02%)	6 / 207 (2.90%)	
occurrences causally related to treatment / all	0 / 2	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric obstruction			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal sepsis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial sepsis			

subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candida infection			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon gangrene			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	3 / 196 (1.53%)	5 / 207 (2.42%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile infection			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 196 (0.51%)	9 / 207 (4.35%)	
occurrences causally related to treatment / all	1 / 1	3 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			

subjects affected / exposed	1 / 196 (0.51%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal candidiasis			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mediastinitis			
subjects affected / exposed	2 / 196 (1.02%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neutropenic infection			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	17 / 196 (8.67%)	11 / 207 (5.31%)	
occurrences causally related to treatment / all	3 / 19	1 / 12	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pneumonia fungal			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 196 (0.51%)	3 / 207 (1.45%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			

subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	1 / 196 (0.51%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Septic shock			
subjects affected / exposed	2 / 196 (1.02%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 1	1 / 1	
Sepsis			
subjects affected / exposed	4 / 196 (2.04%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 3	0 / 0	
Vascular device infection			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth infection			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 196 (0.51%)	2 / 207 (0.97%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Metabolism and nutrition disorders			
Cachexia			

subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 196 (0.51%)	6 / 207 (2.90%)	
occurrences causally related to treatment / all	0 / 1	6 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	CROSS	FLOT	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	183 / 196 (93.37%)	196 / 207 (94.69%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Vascular disorders			
Angiopathy			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Aortic aneurysm			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Arteriosclerosis			

subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Blood pressure fluctuation		
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)
occurrences (all)	0	2
Deep vein thrombosis		
subjects affected / exposed	2 / 196 (1.02%)	1 / 207 (0.48%)
occurrences (all)	2	1
Embolism		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Embolism venous		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Haematoma		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Hot flush		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Hypertension		
subjects affected / exposed	2 / 196 (1.02%)	1 / 207 (0.48%)
occurrences (all)	2	1
Hypotension		
subjects affected / exposed	8 / 196 (4.08%)	3 / 207 (1.45%)
occurrences (all)	8	3
Internal haemorrhage		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Jugular vein thrombosis		
subjects affected / exposed	2 / 196 (1.02%)	1 / 207 (0.48%)
occurrences (all)	2	1
Lymphatic fistula		
subjects affected / exposed	1 / 196 (0.51%)	3 / 207 (1.45%)
occurrences (all)	1	3
Peripheral coldness		

subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Peripheral embolism			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Superficial vein thrombosis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Thrombophlebitis			
subjects affected / exposed	2 / 196 (1.02%)	0 / 207 (0.00%)	
occurrences (all)	2	0	
Thrombosis			
subjects affected / exposed	0 / 196 (0.00%)	4 / 207 (1.93%)	
occurrences (all)	0	4	
Subclavian vein thrombosis			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Thoracic cavity drainage			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Tooth extraction			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 196 (2.04%)	5 / 207 (2.42%)	
occurrences (all)	4	5	
Catheter site inflammation			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Catheter site pain			
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences (all)	1	1	
Chest discomfort			

subjects affected / exposed	3 / 196 (1.53%)	1 / 207 (0.48%)
occurrences (all)	3	1
Chest pain		
subjects affected / exposed	6 / 196 (3.06%)	3 / 207 (1.45%)
occurrences (all)	10	3
Chills		
subjects affected / exposed	2 / 196 (1.02%)	4 / 207 (1.93%)
occurrences (all)	2	4
Discomfort		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Extravasation		
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)
occurrences (all)	0	2
Facial pain		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Fatigue		
subjects affected / exposed	54 / 196 (27.55%)	53 / 207 (25.60%)
occurrences (all)	58	70
Feeling abnormal		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Feeling cold		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
General physical health deterioration		
subjects affected / exposed	2 / 196 (1.02%)	13 / 207 (6.28%)
occurrences (all)	2	16
Generalised oedema		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Inflammation		
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)
occurrences (all)	1	1
Influenza like illness		

subjects affected / exposed	3 / 196 (1.53%)	1 / 207 (0.48%)
occurrences (all)	4	1
Mucosal inflammation		
subjects affected / exposed	21 / 196 (10.71%)	20 / 207 (9.66%)
occurrences (all)	21	22
Meteoropathy		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Medical device site necrosis		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Malaise		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Oedema peripheral		
subjects affected / exposed	1 / 196 (0.51%)	6 / 207 (2.90%)
occurrences (all)	1	6
Oedema		
subjects affected / exposed	1 / 196 (0.51%)	2 / 207 (0.97%)
occurrences (all)	1	2
Peripheral swelling		
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)
occurrences (all)	1	1
Pain		
subjects affected / exposed	7 / 196 (3.57%)	7 / 207 (3.38%)
occurrences (all)	7	7
Polyp		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Pyrexia		
subjects affected / exposed	7 / 196 (3.57%)	13 / 207 (6.28%)
occurrences (all)	7	14
Systemic inflammatory response syndrome		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1

Swelling subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Immune system disorders			
Anaphylactic shock subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Drug hypersensitivity subjects affected / exposed occurrences (all)	2 / 196 (1.02%) 2	1 / 207 (0.48%) 1	
Food allergy subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Hypersensitivity subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	5 / 207 (2.42%) 6	
Seasonal allergy subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Reproductive system and breast disorders			
Testicular oedema subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Respiratory, thoracic and mediastinal disorders			
Bronchospasm subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Atelectasis subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	2 / 207 (0.97%) 2	
Chylothorax subjects affected / exposed occurrences (all)	2 / 196 (1.02%) 2	0 / 207 (0.00%) 0	
Cough subjects affected / exposed occurrences (all)	6 / 196 (3.06%) 6	10 / 207 (4.83%) 10	

Dry throat		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Dysaesthesia pharynx		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Dysphonia		
subjects affected / exposed	3 / 196 (1.53%)	4 / 207 (1.93%)
occurrences (all)	3	4
Dyspnoea exertional		
subjects affected / exposed	4 / 196 (2.04%)	3 / 207 (1.45%)
occurrences (all)	4	3
Emphysema		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Epistaxis		
subjects affected / exposed	5 / 196 (2.55%)	22 / 207 (10.63%)
occurrences (all)	6	30
Dyspnoea		
subjects affected / exposed	3 / 196 (1.53%)	9 / 207 (4.35%)
occurrences (all)	4	9
Haemoptysis		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Hiccups		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Hypoventilation		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Laryngeal oedema		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Lung infiltration		
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)
occurrences (all)	0	2

Oropharyngeal pain		
subjects affected / exposed	2 / 196 (1.02%)	3 / 207 (1.45%)
occurrences (all)	2	3
Nasal mucosal disorder		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Oesophagobronchial fistula		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Pleural effusion		
subjects affected / exposed	6 / 196 (3.06%)	15 / 207 (7.25%)
occurrences (all)	7	17
Pleurisy		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Pneumonitis		
subjects affected / exposed	2 / 196 (1.02%)	1 / 207 (0.48%)
occurrences (all)	2	1
Pneumothorax		
subjects affected / exposed	9 / 196 (4.59%)	3 / 207 (1.45%)
occurrences (all)	10	3
Productive cough		
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)
occurrences (all)	0	2
Pulmonary artery thrombosis		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Pulmonary embolism		
subjects affected / exposed	6 / 196 (3.06%)	10 / 207 (4.83%)
occurrences (all)	6	11
Pulmonary mass		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Pulmonary oedema		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0

Respiratory failure subjects affected / exposed occurrences (all)	2 / 196 (1.02%) 2	3 / 207 (1.45%) 3	
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Thoracic haemorrhage subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Psychiatric disorders			
Alcohol withdrawal syndrome subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Anxiety disorder subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Delirium subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	4 / 207 (1.93%) 4	
Depression subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	2 / 207 (0.97%) 2	
Dysphemia subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Insomnia subjects affected / exposed occurrences (all)	2 / 196 (1.02%) 2	1 / 207 (0.48%) 1	
Listless subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Panic disorder subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Restlessness			

subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Sleep disorder subjects affected / exposed occurrences (all)	2 / 196 (1.02%) 2	3 / 207 (1.45%) 3	
Product issues			
Thrombosis in device subjects affected / exposed occurrences (all)	5 / 196 (2.55%) 5	1 / 207 (0.48%) 1	
Device breakage subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Blood creatine phosphokinase increased subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Blood creatinine increased subjects affected / exposed occurrences (all)	3 / 196 (1.53%) 3	0 / 207 (0.00%) 0	
Blood glucose abnormal subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Blood potassium abnormal subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Body temperature increased			

subjects affected / exposed	3 / 196 (1.53%)	0 / 207 (0.00%)
occurrences (all)	3	0
C-reactive protein increased		
subjects affected / exposed	10 / 196 (5.10%)	4 / 207 (1.93%)
occurrences (all)	10	4
Heart rate increased		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
General physical condition abnormal		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Inflammatory marker increased		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
International normalised ratio increased		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Myoglobin blood increased		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Neutrophil count increased		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Oxygen saturation		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Procalcitonin increased		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Pulmonary imaging procedure abnormal		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Weight decreased		

subjects affected / exposed	18 / 196 (9.18%)	36 / 207 (17.39%)	
occurrences (all)	18	38	
Transaminases increased			
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Abdominal wound dehiscence			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Anastomotic complication			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Anastomotic leak			
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences (all)	1	1	
Anastomotic stenosis			
subjects affected / exposed	2 / 196 (1.02%)	1 / 207 (0.48%)	
occurrences (all)	3	1	
Chemical peritonitis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Documented hypersensitivity to administered product			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Failure to anastomose			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal anastomotic stenosis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Gastrostomy tube site complication			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Gastrointestinal anastomotic leak			

subjects affected / exposed	2 / 196 (1.02%)	0 / 207 (0.00%)
occurrences (all)	2	0
Infusion related reaction		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Overdose		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Post procedural complication		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Post procedural haemorrhage		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Postoperative delirium		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Procedural pain		
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)
occurrences (all)	0	2
Rib fracture		
subjects affected / exposed	1 / 196 (0.51%)	2 / 207 (0.97%)
occurrences (all)	1	2
Scratch		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Skin laceration		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Radiation skin injury		
subjects affected / exposed	5 / 196 (2.55%)	0 / 207 (0.00%)
occurrences (all)	5	0
Stoma complication		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Toxicity to various agents		

subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Wound secretion subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Wound subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Wound dehiscence subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	2 / 207 (0.97%) 2	
Cardiac disorders			
Angina pectoris subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Arrhythmia subjects affected / exposed occurrences (all)	2 / 196 (1.02%) 2	0 / 207 (0.00%) 0	
Atrial fibrillation subjects affected / exposed occurrences (all)	7 / 196 (3.57%) 7	6 / 207 (2.90%) 7	
Atrial flutter subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Bradycardia subjects affected / exposed occurrences (all)	2 / 196 (1.02%) 2	0 / 207 (0.00%) 0	
Cardiac disorder subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Cardiac failure subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	1 / 207 (0.48%) 1	
Cardiomegaly subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	

Cardiovascular disorder			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Extrasystoles			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Pericardial effusion			
subjects affected / exposed	1 / 196 (0.51%)	2 / 207 (0.97%)	
occurrences (all)	1	2	
Pneumopericardium			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Sinus node dysfunction			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences (all)	1	1	
Tachyarrhythmia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	1 / 196 (0.51%)	2 / 207 (0.97%)	
occurrences (all)	1	2	
Nervous system disorders			
Akathisia			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Altered state of consciousness			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Anaesthesia			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Brachial plexopathy			

subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Dementia		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Cerebrovascular accident		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Disturbance in attention		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Dizziness		
subjects affected / exposed	2 / 196 (1.02%)	7 / 207 (3.38%)
occurrences (all)	2	7
Dysaesthesia		
subjects affected / exposed	2 / 196 (1.02%)	1 / 207 (0.48%)
occurrences (all)	2	1
Dysarthria		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Dysgeusia		
subjects affected / exposed	2 / 196 (1.02%)	10 / 207 (4.83%)
occurrences (all)	2	11
Headache		
subjects affected / exposed	2 / 196 (1.02%)	7 / 207 (3.38%)
occurrences (all)	2	7
Hyperaesthesia		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Hypoaesthesia		
subjects affected / exposed	1 / 196 (0.51%)	4 / 207 (1.93%)
occurrences (all)	1	4
Hypogeusia		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Hemiparesis		

subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)
occurrences (all)	0	2
Hypotonia		
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)
occurrences (all)	1	1
Lethargy		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Movement disorder		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Loss of consciousness		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Neurotoxicity		
subjects affected / exposed	1 / 196 (0.51%)	2 / 207 (0.97%)
occurrences (all)	1	2
Neuropathy peripheral		
subjects affected / exposed	1 / 196 (0.51%)	6 / 207 (2.90%)
occurrences (all)	1	6
Neurological symptom		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Peripheral sensory neuropathy		
subjects affected / exposed	2 / 196 (1.02%)	17 / 207 (8.21%)
occurrences (all)	3	26
Peroneal nerve palsy		
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)
occurrences (all)	1	1
Paraesthesia		
subjects affected / exposed	3 / 196 (1.53%)	24 / 207 (11.59%)
occurrences (all)	3	29
Paralysis recurrent laryngeal nerve		
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)
occurrences (all)	0	2
Paresis		

subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Polyneuropathy			
subjects affected / exposed	6 / 196 (3.06%)	57 / 207 (27.54%)	
occurrences (all)	6	71	
Restless legs syndrome			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	3 / 196 (1.53%)	2 / 207 (0.97%)	
occurrences (all)	3	2	
Taste disorder			
subjects affected / exposed	0 / 196 (0.00%)	3 / 207 (1.45%)	
occurrences (all)	0	3	
Tremor			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Vocal cord paresis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	30 / 196 (15.31%)	39 / 207 (18.84%)	
occurrences (all)	44	43	
Cytopenia			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Haematotoxicity			
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)	
occurrences (all)	0	2	
Lymphopenia			
subjects affected / exposed	2 / 196 (1.02%)	0 / 207 (0.00%)	
occurrences (all)	2	0	
Lymphadenopathy			
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences (all)	1	1	

Leukopenia			
subjects affected / exposed	64 / 196 (32.65%)	59 / 207 (28.50%)	
occurrences (all)	78	87	
Leukocytosis			
subjects affected / exposed	1 / 196 (0.51%)	4 / 207 (1.93%)	
occurrences (all)	1	4	
Neutropenia			
subjects affected / exposed	12 / 196 (6.12%)	78 / 207 (37.68%)	
occurrences (all)	12	122	
Pancytopenia			
subjects affected / exposed	2 / 196 (1.02%)	1 / 207 (0.48%)	
occurrences (all)	2	1	
Red blood cell abnormality			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	38 / 196 (19.39%)	14 / 207 (6.76%)	
occurrences (all)	44	19	
Thrombocytosis			
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)	
occurrences (all)	0	2	
Splenic infarction			
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences (all)	1	1	
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Vertigo			
subjects affected / exposed	3 / 196 (1.53%)	6 / 207 (2.90%)	
occurrences (all)	3	7	
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Eye inflammation			

subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Lacrimation increased subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Noninfective conjunctivitis subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Gastrointestinal disorders			
Abdominal hernia subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Abdominal distension subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	1 / 207 (0.48%) 1	
Abdominal pain upper subjects affected / exposed occurrences (all)	4 / 196 (2.04%) 4	7 / 207 (3.38%) 7	
Anal fissure subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Anal haemorrhage subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	1 / 207 (0.48%) 1	
Abdominal pain subjects affected / exposed occurrences (all)	3 / 196 (1.53%) 3	6 / 207 (2.90%) 6	
Ascites subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Constipation subjects affected / exposed occurrences (all)	25 / 196 (12.76%) 27	11 / 207 (5.31%) 14	
Diaphragmatic hernia subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	

Diarrhoea		
subjects affected / exposed	26 / 196 (13.27%)	75 / 207 (36.23%)
occurrences (all)	29	109
Dry mouth		
subjects affected / exposed	2 / 196 (1.02%)	0 / 207 (0.00%)
occurrences (all)	2	0
Dumping syndrome		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Dyspepsia		
subjects affected / exposed	5 / 196 (2.55%)	4 / 207 (1.93%)
occurrences (all)	5	4
Dysphagia		
subjects affected / exposed	36 / 196 (18.37%)	16 / 207 (7.73%)
occurrences (all)	40	16
Gastritis		
subjects affected / exposed	1 / 196 (0.51%)	2 / 207 (0.97%)
occurrences (all)	1	2
Flatulence		
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)
occurrences (all)	1	1
Gastric ulcer		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	2
Gastritis erosive		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Gastrointestinal disorder		
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)
occurrences (all)	0	2
Gastrointestinal motility disorder		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Gastrointestinal pain		
subjects affected / exposed	2 / 196 (1.02%)	1 / 207 (0.48%)
occurrences (all)	2	1

Gastrointestinal toxicity		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Gastrooesophageal reflux disease		
subjects affected / exposed	9 / 196 (4.59%)	10 / 207 (4.83%)
occurrences (all)	9	10
Gingival bleeding		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Haemorrhoids		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Ileus		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Impaired gastric emptying		
subjects affected / exposed	2 / 196 (1.02%)	3 / 207 (1.45%)
occurrences (all)	2	3
Incarcerated hiatus hernia		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Inguinal hernia		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Mouth ulceration		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Melaena		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Oesophagitis		
subjects affected / exposed	9 / 196 (4.59%)	0 / 207 (0.00%)
occurrences (all)	9	0
Oesophageal stenosis		
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)
occurrences (all)	0	2

Oesophageal pain		
subjects affected / exposed	5 / 196 (2.55%)	0 / 207 (0.00%)
occurrences (all)	5	0
Oesophageal fistula		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Odynophagia		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Obstruction gastric		
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)
occurrences (all)	1	1
Nausea		
subjects affected / exposed	48 / 196 (24.49%)	68 / 207 (32.85%)
occurrences (all)	53	86
Oral pain		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Pylorospasm		
subjects affected / exposed	5 / 196 (2.55%)	6 / 207 (2.90%)
occurrences (all)	5	6
Rectal tenesmus		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Regurgitation		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Toothache		
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)
occurrences (all)	0	3
Small intestinal perforation		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Stomatitis		
subjects affected / exposed	1 / 196 (0.51%)	3 / 207 (1.45%)
occurrences (all)	1	3

Vomiting subjects affected / exposed occurrences (all)	25 / 196 (12.76%) 32	31 / 207 (14.98%) 35	
Hepatobiliary disorders			
Cholangitis subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Portal vein thrombosis subjects affected / exposed occurrences (all)	3 / 196 (1.53%) 3	1 / 207 (0.48%) 1	
Skin and subcutaneous tissue disorders			
Angioedema subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Alopecia subjects affected / exposed occurrences (all)	10 / 196 (5.10%) 10	26 / 207 (12.56%) 27	
Alopecia areata subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Dermatitis allergic subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Dry skin subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	2 / 207 (0.97%) 2	
Dermatitis subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Erythema subjects affected / exposed occurrences (all)	5 / 196 (2.55%) 5	4 / 207 (1.93%) 4	
Hand dermatitis subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	2 / 207 (0.97%) 2	
Hyperhidrosis			

subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Nail ridging		
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)
occurrences (all)	0	2
Night sweats		
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)
occurrences (all)	0	2
Pain of skin		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Palmar-plantar erythrodysesthesia syndrome		
subjects affected / exposed	1 / 196 (0.51%)	5 / 207 (2.42%)
occurrences (all)	1	5
Penile ulceration		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Pruritus		
subjects affected / exposed	0 / 196 (0.00%)	6 / 207 (2.90%)
occurrences (all)	0	7
Skin reaction		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Rash		
subjects affected / exposed	6 / 196 (3.06%)	4 / 207 (1.93%)
occurrences (all)	6	5
Skin disorder		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Skin lesion		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Skin toxicity		
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)
occurrences (all)	1	1

Urticaria subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Renal and urinary disorders			
Acute kidney injury subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	3 / 207 (1.45%) 3	
Dysuria subjects affected / exposed occurrences (all)	4 / 196 (2.04%) 4	1 / 207 (0.48%) 1	
Haematuria subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Pollakiuria subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	1 / 207 (0.48%) 1	
Prerenal failure subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Renal cyst subjects affected / exposed occurrences (all)	0 / 196 (0.00%) 0	1 / 207 (0.48%) 1	
Renal failure subjects affected / exposed occurrences (all)	3 / 196 (1.53%) 3	1 / 207 (0.48%) 1	
Endocrine disorders			
Adrenal disorder subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Hyperparathyroidism subjects affected / exposed occurrences (all)	1 / 196 (0.51%) 1	0 / 207 (0.00%) 0	
Hypothyroidism subjects affected / exposed occurrences (all)	2 / 196 (1.02%) 2	1 / 207 (0.48%) 1	
Musculoskeletal and connective tissue disorders			

Arthralgia		
subjects affected / exposed	3 / 196 (1.53%)	0 / 207 (0.00%)
occurrences (all)	3	0
Back pain		
subjects affected / exposed	4 / 196 (2.04%)	6 / 207 (2.90%)
occurrences (all)	5	6
Foot deformity		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Intervertebral disc protrusion		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Myalgia		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Musculoskeletal chest pain		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Muscular weakness		
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)
occurrences (all)	0	2
Muscle spasms		
subjects affected / exposed	2 / 196 (1.02%)	3 / 207 (1.45%)
occurrences (all)	2	4
Osteoarthritis		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Pain in extremity		
subjects affected / exposed	2 / 196 (1.02%)	1 / 207 (0.48%)
occurrences (all)	2	1
Pain in jaw		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Trismus		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	2

Infections and infestations			
Abdominal abscess			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Abdominal infection			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Abdominal wall abscess			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Atypical pneumonia			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	3 / 196 (1.53%)	1 / 207 (0.48%)	
occurrences (all)	3	1	
Candida infection			
subjects affected / exposed	2 / 196 (1.02%)	1 / 207 (0.48%)	
occurrences (all)	2	1	
Device related infection			
subjects affected / exposed	4 / 196 (2.04%)	8 / 207 (3.86%)	
occurrences (all)	4	9	
Diverticulitis			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Fungal oesophagitis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Fungal skin infection			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Groin abscess			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Helicobacter gastritis			

subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Herpes zoster		
subjects affected / exposed	3 / 196 (1.53%)	2 / 207 (0.97%)
occurrences (all)	3	2
Infection		
subjects affected / exposed	4 / 196 (2.04%)	5 / 207 (2.42%)
occurrences (all)	4	5
Klebsiella bacteraemia		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Laryngitis		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Mediastinitis		
subjects affected / exposed	0 / 196 (0.00%)	3 / 207 (1.45%)
occurrences (all)	0	3
Mediastinal abscess		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Oral candidiasis		
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)
occurrences (all)	1	1
Oesophageal candidiasis		
subjects affected / exposed	8 / 196 (4.08%)	5 / 207 (2.42%)
occurrences (all)	8	5
Nasopharyngitis		
subjects affected / exposed	6 / 196 (3.06%)	7 / 207 (3.38%)
occurrences (all)	6	7
Peritonitis		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Pneumonia		
subjects affected / exposed	19 / 196 (9.69%)	24 / 207 (11.59%)
occurrences (all)	19	24
Paronychia		

subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Postoperative abscess			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences (all)	1	1	
Rhinitis			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Sepsis			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Septic shock			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Staphylococcal infection			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	7 / 196 (3.57%)	1 / 207 (0.48%)	
occurrences (all)	7	1	
Wound infection			
subjects affected / exposed	0 / 196 (0.00%)	3 / 207 (1.45%)	
occurrences (all)	0	3	
Metabolism and nutrition disorders			
Abnormal loss of weight			
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	2	
Decreased appetite			
subjects affected / exposed	15 / 196 (7.65%)	16 / 207 (7.73%)	
occurrences (all)	15	21	

Dehydration		
subjects affected / exposed	1 / 196 (0.51%)	2 / 207 (0.97%)
occurrences (all)	2	2
Diabetes mellitus inadequate control		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Gout		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Hypophagia		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Hyperbilirubinaemia		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Hypercalcaemia		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Hyperglycaemia		
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)
occurrences (all)	0	2
Hyperkalaemia		
subjects affected / exposed	3 / 196 (1.53%)	0 / 207 (0.00%)
occurrences (all)	3	0
Hypernatraemia		
subjects affected / exposed	0 / 196 (0.00%)	2 / 207 (0.97%)
occurrences (all)	0	2
Hypoalbuminaemia		
subjects affected / exposed	0 / 196 (0.00%)	1 / 207 (0.48%)
occurrences (all)	0	1
Hypocalcaemia		
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)
occurrences (all)	1	0
Hypokalaemia		
subjects affected / exposed	9 / 196 (4.59%)	10 / 207 (4.83%)
occurrences (all)	10	12

Hyponatraemia			
subjects affected / exposed	1 / 196 (0.51%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Iron deficiency			
subjects affected / exposed	1 / 196 (0.51%)	1 / 207 (0.48%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 October 2015	<p>Changes on request of BfArM:</p> <ul style="list-style-type: none">• All Adverse Events were documented independent of severity grade instead of only AEs of severity grade 3-4.• Duration of infusion was corrected to 2 hours.
10 December 2015	<p>Modification of inclusion criteria based on feedback from the trial sites:</p> <ul style="list-style-type: none">• Specification added to adequate cardiac and respiratory function (Synopsis and chapter 7.2). <p>Corrections in the Flow chart to modify some formal mistakes:</p> <ul style="list-style-type: none">• Flow chart: Specification which data must be available in the source data /case report form (page 42 and following)• Detail description of the visits: Corrections according to the Flow chart (chapter 10.2.1 to 10.3.2)• Trial Drug: Specification which medication can be used in the trial (chapter 12.1, FLOT arm).

30 November 2017	<p>Changes based on feedback and experience from the trial sites:</p> <ul style="list-style-type: none"> • Address changes in the responsibilities • Administrative correction (writing error) of the FEV1 values in the inclusion and exclusion criteria and specification of these values in percentage according to response of the Competent Authority • Administration time of Leucovorin changed from 2 hours to ≥ 30 min • Prohibited concomitant therapy: antibiotics deleted. <p>Additional changes regarding:</p> <ul style="list-style-type: none"> • Trial duration • Funding • Participating sites • German version of QoL and patient informed consent • Patient randomization • Time from end of neoadjuvant treatment to surgery • Follow-up 3 or 6 months in the first year according to clinical standard • Use of previous diagnostic • Change of used material for translational research • Correction of the timepoint for assessments during postoperative visits • Deletion of assessments of laboratory values and concomitant medication during follow-up • Clarification in section 11.3 Discontinuation criteria • Clarification in section Safety documentation criteria for patients who premature discontinued • Clarification in section 14.2.2, 14.3 and 14.4 Documentation CRF, data management and coding.
27 April 2018	<p>Changes as described above for Version V2.2. Additional changes regarding:</p> <ul style="list-style-type: none"> • Clarification in section 10.1, Table 2 and Table 3: Footnotes 3 and 4 and inclusion of Appendix 10.
04 November 2020	<p>Notification of administrative changes in the conduct of the study:</p> <ul style="list-style-type: none"> • Address changes in the responsibilities (Coordinating Investigator, Project Management and Medical trial coordinator) • Adaption of the time between end of neoadjuvant treatment and surgery from 4-6 weeks to 4-8 weeks: "6.2 Treatment arms" and "9.1 Dosing and treatment schedule" • Adaption of the legend in the flow chart regarding the time window for follow-up visits from ± 7 days to ± 14 days: "10.1 Visit schedule" (Table 2 and Table 3) • Adaption of documentation in CRF: "14.3 Data management" • Inserting the second support code: Synopsis and "21.1 Financing of the trial" • Update of Internet links in Appendix • Correction of typing errors in several sections of the CTP.

31 March 2021	Notification of the change of the sponsor of the study: <ul style="list-style-type: none"> • Change of Sponsor (Cover page and page 17, Chapter 3 Responsibilities) • Change of address of Prof. Lorenz, Steering Committee (Chapter 3 Responsibilities).
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Analyses of the evaluation of the patients quality of life (QoL) questionnaires are still ongoing and the results will be presented in an Addendum.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/39842010>

<http://www.ncbi.nlm.nih.gov/pubmed/27435280>