



Clinical trial results:

Phase III trial comparing preoperative chemoradiotherapy with neoadjuvant Folfirinox chemotherapy followed by preoperative chemoradiotherapy for patients with locally advanced rectal cancer (PRODIGE-GERCOR-SFRO-GRECCAR trial).

Summary

EudraCT number	2011-004406-25
Trial protocol	FR
Global end of trial date	01 July 2023

Results information

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

Trial information

Trial identification

Sponsor protocol code	UC-0110/1005
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01804790
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UNICANCER
Sponsor organisation address	101 rue de Tolbiac, Paris, France, 75015
Public contact	Nourredine AIT-RAHMOUNE, UNICANCER, 33 01 71 93 67 04 , n.a-rahmoune@unicancer.fr
Scientific contact	Nourredine AIT-RAHMOUNE, UNICANCER, 33 01 71 93 67 04 , n.a-rahmoune@unicancer.fr

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 July 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 July 2023
Global end of trial reached?	Yes
Global end of trial date	01 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to compare Disease-Free Survival (DFS) after 3 years in the standard preoperative chemotherapy arm versus chemotherapy with Folfirinox followed by standard preoperative chemotherapy arm for patients with locally advanced rectal cancer.

Protection of trial subjects:

This study was conducted in accordance with the French national regulatory requirements and with:

- the European Clinical Trials Directive (2001/20/EC),
- the French Huriet law (No. 88-1138) dated 20 December 1988 relative to the protection of individuals taking part in biomedical research and amended by the French Public Health law (No. 2004-806) dated 9 August 2004,
- French data protection law No. 78-17 of 6 January 1978 amended by law No. 2004-801 of 6 August 2004 relating to the protection of persons with regard to personal data processing,
- French bio-ethics law No. 2004-800 dated 6 August 2004.
- Good Clinical Practices dated 24 November 2006.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 June 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	7 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 461
Worldwide total number of subjects	461
EEA total number of subjects	461

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	310
From 65 to 84 years	151
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 461 subjects were included from 05/06/2012 to 26/06/2017 by 35 participating centers (Only in France).

Pre-assignment

Screening details:

Patients with histologically confirmed rectal adenocarcinoma <15 cm from the anal verge and MRI-staged T3 at risk of local recurrence or cT4, N-any, M0 were included.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Patients included in this arm received:

- 1) Chemoradiotherapy (CRT) = Radiotherapy + Chemotherapy (50 Gy + Capecitabine; 25 fractions) for 5 weeks
- 2) Total Mesorectal Excision (TME) Surgery (or Partial Mesorectal Excision (PME) for tumours of the upper third) 6 to 8 weeks after CRT
- 3) Adjuvant Chemotherapy (adjuvant CT) = either FOLFOX6 or Capecitabine for 6 months

Arm type	Standart arm
No investigational medicinal product assigned in this arm	
Arm title	Arm B

Arm description:

Patients included in this arm received:

- 1- Neoadjuvant chemotherapy (mFolfirinox) for 2 months (6 cycles) = Oxaliplatin (85 mg/m²) + Irinotecan (180 mg/m²) + Folinic acid (400 mg/m²) + continuous infusion Fluorouracil (2400 mg/m²)
- 2- CRT = Radiotherapy + Chemotherapy (50 Gy + Capecitabine; 25 fractions) for 5 weeks
- 3- TME Surgery (or Partial Mesorectal Excision (PME) for tumours of the upper third) 6 to 8 weeks after CRT
- 4- Adjuvant CT = either FOLFOX6 or Capecitabine for 3 months

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

Dosage and administration details:

Patients received 85g/m² D1 over 2 hours.

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

Dosage and administration details:

Patients were received 180 mg/m² D1 over 90 minutes starting 30 minutes after the start of folinic acid

Investigational medicinal product name	Folinic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use
Dosage and administration details:	
Patients were received 400 mg/m ² D1 as a 2-hour infusion.	
Investigational medicinal product name	5-Fluorouracil (5FU)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Patients were received 2.4 g/m² as a continuous infusion over 46 hours (1,200 mg/m²/ day).

Number of subjects in period 1	Arm A	Arm B
Started	230	231
Completed	122	139
Not completed	108	92
Consent withdrawn by subject	11	10
Physician decision	32	30
Lost of follow-up	2	-
Toxicity	13	22
Protocol violation	1	1
Death	8	3
Other	9	2
Progression	22	7
Non compliance	2	5
Post surgery complication	8	9
Second cancer	-	1
Metastasis at inclusion	-	2

Baseline characteristics

Reporting groups

Reporting group title	Arm A
Reporting group description:	
Patients included in this arm received:	
1) Chemoradiotherapy (CRT) = Radiotherapy + Chemotherapy (50 Gy + Capecitabine; 25 fractions) for 5 weeks	
2) Total Mesorectal Excision (TME) Surgery (or Partial Mesorectal Excision (PME) for tumours of the upper third) 6 to 8 weeks after CRT	
3) Adjuvant Chemotherapy (adjuvant CT) = either FOLFOX6 or Capecitabine for 6 months	
Reporting group title	Arm B
Reporting group description:	
Patients included in this arm received:	
1- Neoadjuvant chemotherapy (mFolfirinox) for 2 months (6 cycles) = Oxaliplatin (85 mg/m2) + Irinotecan (180 mg/m2) + Folinic acid (400 mg/m2) + continuous infusion Fluorouracil (2400 mg/m2)	
2- CRT = Radiotherapy + Chemotherapy (50 Gy + Capecitabine; 25 fractions) for 5 weeks	
3- TME Surgery (or Partial Mesorectal Excision (PME) for tumours of the upper third) 6 to 8 weeks after CRT	
4- Adjuvant CT = either FOLFOX6 or Capecitabine for 3 months	

Reporting group values	Arm A	Arm B	Total
Number of subjects	230	231	461
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)	150	160	310
From 65-84 years	80	71	151
85 years and over	0	0	0
Age continuous			
Units: years			
median	62	61	
full range (min-max)	26 to 75	34 to 77	-
Gender categorical			
Units: Subjects			
Female	74	81	155
Male	156	150	306
WHO			
Units: Subjects			
WHO 0	182	178	360
WHO 1	44	51	95
Missing	4	2	6
Distance from the anal verge (TenAlea Data)			
Units: Subjects			
≤5cm	94	93	187

5.1-10cm	113	114	227
10.1-15cm	23	24	47
cN stage			
Units: Subjects			
N0	26	21	47
N+	194	200	394
NX	5	8	13
Missing	5	2	7
PI-MA: Anal verge distance to inferior edge of the tumour			
Units: mm			
arithmetic mean	54.55	49.51	
standard deviation	± 25.57	± 26.51	-
PI-SA: Distance between the lower pole of the tumour and the anal sphincter			
Units: mm			
median	28.03	30.05	
standard deviation	± 20.01	± 27.25	-

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
Patients included in this arm received:	
1) Chemoradiotherapy (CRT) = Radiotherapy + Chemotherapy (50 Gy + Capecitabine; 25 fractions) for 5 weeks	
2) Total Mesorectal Excision (TME) Surgery (or Partial Mesorectal Excision (PME) for tumours of the upper third) 6 to 8 weeks after CRT	
3) Adjuvant Chemotherapy (adjuvant CT) = either FOLFOX6 or Capecitabine for 6 months	
Reporting group title	Arm B
Reporting group description:	
Patients included in this arm received:	
1- Neoadjuvant chemotherapy (mFolfirinox) for 2 months (6 cycles) = Oxaliplatin (85 mg/m2) + Irinotecan (180 mg/m2) + Folinic acid (400 mg/m2) + continuous infusion Fluorouracil (2400 mg/m2)	
2- CRT = Radiotherapy + Chemotherapy (50 Gy + Capecitabine; 25 fractions) for 5 weeks	
3- TME Surgery (or Partial Mesorectal Excision (PME) for tumours of the upper third) 6 to 8 weeks after CRT	
4- Adjuvant CT = either FOLFOX6 or Capecitabine for 3 months	

Primary: Disease-Free Survival (DFS) at 3 years

End point title	Disease-Free Survival (DFS) at 3 years
End point description:	
DFS was defined as the time from randomization until the occurrence of the first oncological event, such as local or metastatic recurrence, the development of a second cancer or death, irrespective of cause. Patients without events at the time of the analysis were censored at the date of the last informational follow-up. Locoregional recurrence was defined as an anastomotic recurrence or a local recurrence in the sacral concavity.	
End point type	Primary
End point timeframe:	
at 3 years	

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	231		
Units: percent				
number (confidence interval 95%)	68.5 (61.9 to 74.2)	75.7 (69.4 to 80.8)		

Statistical analyses

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

Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.34
Method	Cox proportional-hazards
Parameter estimate	Hazard ratio (HR)
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	0.97

Secondary: Overall survival (OS)

End point title	Overall survival (OS)
End point description:	
Overall survival (OS) is defined as the interval between the randomization and the occurrence of death whatever the cause. Patients alive at the time of the analysis will be censored on the date of the last informative follow-up.	
End point type	Secondary
End point timeframe:	
At 7 years.	

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	231		
Units: percent				
number (confidence interval 95%)	80 (74.1 to 84.6)	86.9 (81.6 to 90.7)		

Statistical analyses

Statistical analysis title	OS analysis
Comparison groups	Arm A v Arm B
Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.08
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.73

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.09

Secondary: Specific Survival (SS)

End point title	Specific Survival (SS)
End point description:	
Specific Survival (SS) was defined as the period between the date of randomization and the date of death due to cancer or to treatment-related toxicity.	
End point type	Secondary
End point timeframe:	
At 5 years.	

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	231		
Units: percent				
number (confidence interval 95%)	82.4 (76.7 to 86.8)	88.1 (83.1 to 91.8)		

Statistical analyses

Statistical analysis title	SS analysis
Comparison groups	Arm A v Arm B
Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.07
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	1.05

Secondary: Metastasis-free Survival (MFS)

End point title	Metastasis-free Survival (MFS)
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End point description:

Metastasis-Free Survival (MFS) was defined as the period between the randomization and the occurrence of the first distant event at all sites of recurrence distant from the resection site (e.g. peritoneal, hepatic, pulmonary or lymph nodes). Locoregional events were ignored and patients alive without metastasis at the time of analysis were censored on the date of the last exam not having revealed this type of event. Metastatic recurrence rate was deduced from metastasis-free survival.

End point type	Secondary
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End point timeframe:

At 5 years.

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	231		
Units: Percent				
number (confidence interval 95%)	67.7 (61.2 to 73.4)	77.6 (71.5 to 82.5)		

Statistical analyses

Statistical analysis title	MFS analysis
Comparison groups	Arm A v Arm B
Number of subjects included in analysis	461
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.07
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	1.02

Secondary: Local recurrence rate

End point title	Local recurrence rate
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End point description:

Local recurrence rate was defined as the rate of anastomotic or local recurrence in the sacral concavity.

End point type	Secondary
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End point timeframe:

At 5 years.

End point values	Arm A	Arm B		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	231		
Units: percent				
number (confidence interval 95%)	6.4 (3.8 to 10.8)	4.7 (2.5 to 8.5)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were recorded from the date the patient signed the consent form until 28 days after administration of the last dose of product (90 days in the case of radiotherapy).

Adverse event reporting additional description:

For non serious adverse events only the main toxicities reported during chemoradiotherapy (CRT) were available.

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

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.0
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Reporting groups

Reporting group title	Arm A
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Reporting group description:

Patients included in this arm received:

1- Chemoradiotherapy (CRT) = Radiotherapy + Chemotherapy (50 Gy + Capecitabine; 25 fractions) for 5 weeks

2- Total Mesorectal Excision (TME) Surgery (or Partial Mesorectal Excision (PME) for tumours of the upper third) 6 to 8 weeks after CRT

3- Adjuvant Chemotherapy (adjuvant CT) = either FOLFOX6 or Capecitabine for 6 months

Reporting group title	Arm B
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Reporting group description:

Patients included in this arm received:

1- Neoadjuvant chemotherapy (mFolfirinox) for 2 months (6 cycles) = Oxaliplatin (85 mg/m²) + Irinotecan (180 mg/m²) + Folinic acid (400 mg/m²) + continuous infusion Fluorouracil (2400 mg/m²)

2- CRT = Radiotherapy + Chemotherapy (50 Gy + Capecitabine; 25 fractions) for 5 weeks

3- TME Surgery (or Partial Mesorectal Excision (PME) for tumours of the upper third) 6 to 8 weeks after CRT

4- Adjuvant CT = either FOLFOX6 or Capecitabine for 3 months

Serious adverse events	Arm A	Arm B	
Total subjects affected by serious adverse events			
subjects affected / exposed	88 / 230 (38.26%)	107 / 231 (46.32%)	
number of deaths (all causes)	56	42	
number of deaths resulting from adverse events	2	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma endometrial			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			

subjects affected / exposed	1 / 230 (0.43%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carcinoma vocal cord			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney cancer			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroendocrine tumour			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic neuroendocrine tumor			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary metastases			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			

subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urothelial carcinoma			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Squamous cell carcinoma of the hypopharynx			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cholecystectomy			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteral nutrition			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileostomy closure			
subjects affected / exposed	1 / 230 (0.43%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal abscess drainage			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (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				
Catheter related thrombosis				
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Chest pain				
subjects affected / exposed	0 / 230 (0.00%)	3 / 231 (1.30%)		
occurrences causally related to treatment / all	0 / 0	0 / 3		
deaths causally related to treatment / all	0 / 0	0 / 0		
Death				
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	1 / 1	0 / 0		
Disease progression				
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 1	0 / 0		
Fever				
subjects affected / exposed	1 / 230 (0.43%)	2 / 231 (0.87%)		
occurrences causally related to treatment / all	1 / 1	1 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
General physical health deterioration				
subjects affected / exposed	1 / 230 (0.43%)	2 / 231 (0.87%)		
occurrences causally related to treatment / all	0 / 1	1 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
Pain				
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 1	0 / 0		
Prolapse				
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Reaction febrile				

subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic pain			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Unknown cause of death			
subjects affected / exposed	1 / 230 (0.43%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 1	
Immune system disorders			
Allergic reaction			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug allergy			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hypertrophy			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fluid collection			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Perineal pain			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal hemorrhage			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chest pain			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism pulmonary			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumopathy			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 230 (0.43%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 230 (0.00%)	3 / 231 (1.30%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide			
subjects affected / exposed	2 / 230 (0.87%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	

Injury, poisoning and procedural complications			
Anastomotic fistula			
subjects affected / exposed	4 / 230 (1.74%)	5 / 231 (2.16%)	
occurrences causally related to treatment / all	0 / 4	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic leak			
subjects affected / exposed	1 / 230 (0.43%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic stenosis			
subjects affected / exposed	1 / 230 (0.43%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal stoma necrosis			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrostomy failure			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peristomal abscess NOS			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative abscess			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative complication			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Postoperative hernia			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
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 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound breakdown			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prolapse of intestinal stoma			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suture rupture			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trauma			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	2 / 230 (0.87%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute pericarditis			

subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation paroxysmal			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 230 (0.43%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Cardio-respiratory failure			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain - cardiac			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary spasm			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary spastic angina			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death sudden			

subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Myocardial infarct			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 230 (0.43%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tamponade cardiac			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cholinergic syndrome			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epileptic fit			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			

subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological disorder			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraplegia			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sensory neuropathy			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	0 / 230 (0.00%)	4 / 231 (1.73%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile aplasia			
subjects affected / exposed	0 / 230 (0.00%)	3 / 231 (1.30%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphopenia			

subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	2 / 230 (0.87%)	6 / 231 (2.60%)	
occurrences causally related to treatment / all	2 / 2	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal detachment			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (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 abscess			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 230 (0.43%)	2 / 231 (0.87%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess intestinal			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess perianal			

subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute pancreatitis			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal lesion			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal pain			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowel obstruction			
subjects affected / exposed	0 / 230 (0.00%)	2 / 231 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 230 (0.43%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic fistula			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colonic obstruction			

subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhea			
subjects affected / exposed	5 / 230 (2.17%)	5 / 231 (2.16%)	
occurrences causally related to treatment / all	6 / 6	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhea hemorrhagic			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epigastric pain			
subjects affected / exposed	0 / 230 (0.00%)	2 / 231 (0.87%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fecal vomiting			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula of small intestine			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastro-intestinal disorder NOS			

subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal toxicity			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoperitoneum			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernial eventration			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileitis			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus paralytic			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious colitis			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	4 / 230 (1.74%)	5 / 231 (2.16%)	
occurrences causally related to treatment / all	0 / 6	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction small intestine			

subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis ulcerative			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fluid collection			
subjects affected / exposed	4 / 230 (1.74%)	3 / 231 (1.30%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic pain			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 230 (0.43%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctalgia			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal bleeding			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectorrhagia			

subjects affected / exposed	0 / 230 (0.00%)	2 / 231 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectovaginal fistula			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	4 / 230 (1.74%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestine perforation			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subocclusive syndrome			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 230 (0.87%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 230 (0.43%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic pain			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			

Eczematous rash subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 230 (0.00%) 0 / 0 0 / 0	1 / 231 (0.43%) 1 / 1 0 / 0	
Renal and urinary disorders			
Acute renal failure subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	6 / 230 (2.61%) 3 / 6 0 / 1	2 / 231 (0.87%) 0 / 2 0 / 0	
Acute renal insufficiency subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 230 (0.00%) 0 / 0 0 / 0	1 / 231 (0.43%) 0 / 1 0 / 0	
Functional renal failure subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 230 (0.43%) 1 / 1 0 / 0	0 / 231 (0.00%) 0 / 0 0 / 0	
Renal failure acute subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 230 (0.00%) 0 / 0 0 / 0	1 / 231 (0.43%) 1 / 1 0 / 0	
Renal insufficiency subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	3 / 230 (1.30%) 2 / 3 0 / 0	2 / 231 (0.87%) 0 / 2 0 / 0	
Endocrine disorders			
Diabetes subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 230 (0.00%) 0 / 0 0 / 0	1 / 231 (0.43%) 0 / 1 0 / 0	
Diabetic metabolic decompensation subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 230 (0.43%) 0 / 1 0 / 0	0 / 231 (0.00%) 0 / 0 0 / 0	

Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain legs			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess			
subjects affected / exposed	0 / 230 (0.00%)	2 / 231 (0.87%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess perianal			
subjects affected / exposed	1 / 230 (0.43%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorectal infection			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial pyelonephritis			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Catheter infection			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometritis			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia coli infection			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious colitis			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pneumonitis			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 230 (0.43%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic abscess			
subjects affected / exposed	0 / 230 (0.00%)	4 / 231 (1.73%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			

subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Peritonitis perforative			
subjects affected / exposed	1 / 230 (0.43%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcal pneumonia			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	3 / 230 (1.30%)	5 / 231 (2.16%)	
occurrences causally related to treatment / all	1 / 3	1 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Septicemia			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Septicemia due to Escherichia coli (E. coli)			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin & subcutaneous tissue abscess			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary infection			

subjects affected / exposed	1 / 230 (0.43%)	2 / 231 (0.87%)	
occurrences causally related to treatment / all	0 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 230 (1.30%)	0 / 231 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalemia			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypocalcemia			
subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalemia			
subjects affected / exposed	0 / 230 (0.00%)	2 / 231 (0.87%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			

subjects affected / exposed	0 / 230 (0.00%)	1 / 231 (0.43%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Arm A	Arm B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	230 / 230 (100.00%)	231 / 231 (100.00%)	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	17 / 230 (7.39%)	39 / 231 (16.88%)	
occurrences (all)	1	1	
Aspartate aminotransferase increased			
subjects affected / exposed	13 / 230 (5.65%)	44 / 231 (19.05%)	
occurrences (all)	1	1	
Alkaline phosphatase increased			
subjects affected / exposed	8 / 230 (3.48%)	33 / 231 (14.29%)	
occurrences (all)	1	1	
GGT increased			
subjects affected / exposed	10 / 230 (4.35%)	67 / 231 (29.00%)	
occurrences (all)	1	1	
Vascular disorders			
Thromboembolic event			
subjects affected / exposed	2 / 230 (0.87%)	2 / 231 (0.87%)	
occurrences (all)	1	1	
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 230 (1.30%)	30 / 231 (12.99%)	
occurrences (all)	1	1	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	83 / 230 (36.09%)	148 / 231 (64.07%)	
occurrences (all)	1	1	
Neutropenia			

subjects affected / exposed	30 / 230 (13.04%)	75 / 231 (32.47%)	
occurrences (all)	1	1	
Thrombopenia			
subjects affected / exposed	36 / 230 (15.65%)	81 / 231 (35.06%)	
occurrences (all)	1	1	
Lymphopenia			
subjects affected / exposed	182 / 230 (79.13%)	182 / 231 (78.79%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	87 / 230 (37.83%)	79 / 231 (34.20%)	
occurrences (all)	1	1	
Fever			
subjects affected / exposed	3 / 230 (1.30%)	1 / 231 (0.43%)	
occurrences (all)	1	1	
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	128 / 230 (55.65%)	127 / 231 (54.98%)	
occurrences (all)	1	1	
Constipation			
subjects affected / exposed	39 / 230 (16.96%)	25 / 231 (10.82%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	44 / 230 (19.13%)	43 / 231 (18.61%)	
occurrences (all)	1	1	
Vomiting			
subjects affected / exposed	10 / 230 (4.35%)	10 / 231 (4.33%)	
occurrences (all)	1	1	
Abdominal pain			
subjects affected / exposed	23 / 230 (10.00%)	15 / 231 (6.49%)	
occurrences (all)	1	1	
Anorexia			
subjects affected / exposed	15 / 230 (6.52%)	12 / 231 (5.19%)	
occurrences (all)	1	1	
Stomatitis			

subjects affected / exposed occurrences (all)	8 / 230 (3.48%) 1	6 / 231 (2.60%) 1	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 230 (0.87%)	12 / 231 (5.19%)	
occurrences (all)	1	1	
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	12 / 230 (5.22%)	15 / 231 (6.49%)	
occurrences (all)	1	1	
Metabolism and nutrition disorders			
Weight loss			
subjects affected / exposed	16 / 230 (6.96%)	9 / 231 (3.90%)	
occurrences (all)	1	1	
Hyperglycemia			
subjects affected / exposed	12 / 230 (5.22%)	10 / 231 (4.33%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 June 2012	<ul style="list-style-type: none">- Correction of typographical errors on pages 6, 13 page 45 found in the protocol V2 from 26-Apr-2012.- Modification of the investigators list
12 December 2012	<ul style="list-style-type: none">- Correction of typographical errors found in the protocol V3 from 26-Apr-2012- Modifications of summary table of investigations (H) in the protocol V3 from 26-Apr-2012- Withdrawal of Annex 7 "Tumours evaluation classification" and modification of the numbers of the following annexes- Modification of the website address used for the randomization process (https://prod.tenalea.net/gso/dm/)- Main objective was disease-free survival not the evaluation of the tumour response according to RECIST (page 45)- The data owner was corrected- Correction of the study title- Modification of the investigators list
06 June 2013	<ul style="list-style-type: none">- Modification of the investigators list
05 September 2013	<ul style="list-style-type: none">- The investigators list was modified
22 October 2013	<ul style="list-style-type: none">- The cardiac assessment to be performed on inclusion before starting treatment to prevent the occurrence of a serious cardiac event under Fluorouracil was detailed- The collection of the quality of life questionnaires became mandatory- Clarification regarding radiotherapy- Homogeneization of the tummary table of investigations and examinations required in the protocol- Update of the contacts list- Modification of the investigators list
22 October 2013	<ul style="list-style-type: none">- The cardiac assessment to be performed on inclusion before starting treatment to prevent the occurrence of a serious cardiac event under Fluorouracil was detailed- The collection of the quality of life questionnaires became mandatory- Clarification regarding radiotherapy- Homogeneization of the tummary table of investigations and examinations required in the protocol- Update of the contacts list- Modification of the investigators list
03 February 2015	<ul style="list-style-type: none">- Inclusion period were extended- An assessment at the end of adjuvant chemotherapy was added (14 days after last adjuvant chemo cycle)- Withdrawal of the recommendation on the use of Calium Gluconate and Magnesium Sulfate to prevent neurotoxicity in patients receiving Oxaliplatin- Clarification of the protocol following the request of participating centres- Update of the contacts list- Modification of the investigators list
28 May 2015	<ul style="list-style-type: none">- Addition of a new biological study regarding the role of circulating miRNA as predictive biomarker in rectal cancers.- Update of the sampling and storage procedures for biological samples- Update of the contacts list- Modification of the investigators list

03 December 2015	- Modification of the investigators list
04 January 2017	- Modification of the coordinator of the study and addition of co-coordinators. - Modification of the investigator list
03 January 2020	- Modification of the coordinator of the study

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported