Clinical trial results:
Preoperative chemoradiotherapy and postoperative chemotherapy with capecitabine and oxaliplatin vs. capecitabine alone in locally advanced rectal cancer (PETACC-6)

Summary

EudraCT number	2006-006532-21
Trial protocol	BE GB FR DE
Global end of trial date	31 December 2015

Results information

Result version number	v1 (current)
This version publication date	18 May 2017
First version publication date	18 May 2017

Trial information

Trial identification

Sponsor protocol code	40054-22062

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00766155
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	European Organisation for Research and Treatment of Cancer
Sponsor organisation address	Avenue E. Mounier 83/11, Brussels, Belgium, 1200
Public contact	Project, Budget and Regulatory Dept, European Organisation for Research and Treatment of Cancer, +32 27441062, regulatory@eortc.be
Scientific contact	Project, Budget and Regulatory Dept, European Organisation for Research and Treatment of Cancer, +32 27441062, regulatory@eortc.be

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	31 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2015
Global end of trial reached?	Yes
Global end of trial date	31 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate whether the addition of oxaliplatin to preoperative fluoropyrimidine-based chemoradiation and postoperative fluoropyrimidine-based chemotherapy improves disease-free survival in patients with locally advanced rectal cancer.

Protection of trial subjects:

The responsible investigator ensured that this study was conducted in agreement with either the Declaration of Helsinki (available on the World Medical Association web site (http://www.wma.net)) and/or the laws and regulations of the country, whichever provides the greatest protection of the patient. The protocol had been written, and the study was conducted according to the ICH Harmonized Tripartite Guideline on Good Clinical Practice (ICH-GCP, available online at http://www.ema.europa.eu/pdfs/human/ich/013595en.pdf). The protocol was approved by the competent ethics committee(s) as required by the applicable national legislation.

Background therapy:

Reference therapy consists of
Preoperative treatment: capecitabine 825 mg/m² p.o. twice daily on days 1-33 (excluding weekends), radiotherapy: 45 Gy, 1.8 Gy on days 1-33 (excluding weekends)
Optional*: radiotherapy 5.4 Gy on days 36 to 38 using the same fields or as a boost to the primary tumour (3 fractions of 1.8 Gy) with capecitabine 825 mg/m² p.o. twice daily
Surgery (TME) 4-8 weeks after chemoradiation
Postoperative treatment (in patients achieving histopathological R0 or R1 resection): capecitabine 1000 mg/m² p.o. twice daily from the evening of day 1 to the morning of day 15, every three weeks, 6 cycles, (begin 6-8 weeks after surgery)
* If centers choose this option they have to adopt it for both arms during the entire study.

Evidence for comparator:

Over the last decades, important advances have been made in the treatment of rectal cancer. The standard of care has changed from surgery via postoperative multimodalities to the novel standard of preoperative (chemo) radiotherapy. In contrast to preoperative (chemo) radiation, postoperative treatment has no impact on sphincter preservation rates for low-lying lesions and does not allow downstaging of otherwise potentially unresectable T4 tumours. Therefore, preoperative radiation, that was developed since the 1980´s has become the preferred approach in most European countries. The benefit of a preoperative vs. a postoperative approach was confirmed by the German AIO/CAO/ARO-94 trial that compared postoperative to preoperative 5-FU based chemoradiation, followed by adjuvant 5-FU. The radiation dose was 50.4 Gy. Regarding the role of chemotherapy, several studies have indicated that the addition of at least single agent 5-FU to long-term radiation improves local control in both the postoperative and the preoperative setting. In view of these results, preoperative radio-chemotherapy was adopted as standard of care, if long-term preoperative radiation is chosen.

IV 5-FU is the present standard fluoropyrimidine in the treatment of rectal cancer in the pre- and postoperative treatment. The substitution of 5-FU by capecitabine is a promising option. Preoperative chemoradiation with capecitabine is well tolerated and shows at least similar effect on histopathological regression (pCR rates) in phase II trials. In adjuvant treatment of stage III colon cancer, capecitabine proved to be at least equivalent to 5-FU/FA in terms of disease-free survival and has become the standard of care if no oxaliplatin-based schedule may be used.

Actual start date of recruitment	27 November 2008
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 147
Country: Number of subjects enrolled	France: 53
Country: Number of subjects enrolled	Germany: 737
Country: Number of subjects enrolled	Israel: 30
Country: Number of subjects enrolled	Australia: 114
Country: Number of subjects enrolled	New Zealand: 13
Worldwide total number of subjects	1094
EEA total number of subjects	937

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)	635
From 65 to 84 years	458
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Between 27/11/2008 and 20/09/2011, patients with rectal adenocarcinoma within 12 cm from the anal verge, T3/4 and/or node-positive, with no evidence of metastatic disease and considered either resectable at the time of entry or expected to become resectable were recruited in 6 countries (Germany, Belgium, France, Israel, Australia and New Zealand).

Pre-assignment

Screening details:

Each patient considered by the Investigator to be a potential patient for the study underwent the informed consent process. If the patient agreed to participate in the study and an informed consent form was duly completed, dated and signed, then the Investigator assessed the patient's eligibility for the study.

Period 1

Period 1 title	Randomization (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	Cape+RT

Arm description:

Control Arm: capecitabine with radiotherapy before surgery, followed by capecitabine after surgery.
Preoperative treatment: capecitabine 825 mg/m² p.o. twice daily on days 1-33 (excluding weekends), radiotherapy: 45 Gy, 1.8 Gy on days 1-33 (excluding weekends)
Optional*: radiotherapy 5.4 Gy on days 36 to 38 using the same fields or as a boost to the primary tumour (3 fractions of 1.8 Gy) with capecitabine 825 mg/m² p.o. twice daily
Surgery (TME) 4-8 weeks after chemoradiation
Postoperative treatment (in patients achieving histopathological R0 or R1 resection): capecitabine 1000 mg/m² p.o. twice daily from the evening of day 1 to the morning of day 15, every three weeks, 6 cycles, (begin 6-8 weeks after surgery)
* If centers choose this option they have to adopt it for both arm during the entire study.

Arm type	Standard of care

No investigational medicinal product assigned in this arm

Arm title	Cape+Oxali+RT

Arm description:

Investigational Arm: capecitabine with oxaliplatin and radiotherapy before surgery, followed by capecitabine and oxaliplatin after surgery.
Preoperative treatment: capecitabine 825 mg/m² p.o. twice daily on days 1-33 (excluding weekends), radiotherapy: 45 Gy, 1.8 Gy on days 1-33 (excluding weekends), oxaliplatin 50 mg/m² IV on days 1, 8, 15, 22 and 29
Optional*: radiotherapy 5.4 Gy on days 36 to 38 using the same fields or as a boost to the primary tumour (3 fractions of 1.8 Gy) with capecitabine 825 mg/m² p.o. twice daily
Surgery (TME) 4-8 weeks after chemoradiation
Postoperative treatment (in patients achieving histopathological R0 or R1 resection): capecitabine 1000 mg/m² p.o. twice daily from the evening of day 1 to the morning of day 15 and oxaliplatin 130 mg/ m² IV on day 1, every three weeks, 6 cycles, (begin 6-8 weeks after surgery)
* If centers choose this option they have to adopt it for both arms during the entire study.

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:

Oxaliplatin was administered as a 1-hour and 2-hour intravenous infusion in the pre- and postoperative regimen of the investigational arm, respectively:
Preoperative treatment: oxaliplatin 50 mg/m² IV on days 1, 8, 15, 22 and 29
Postoperative treatment (in patients achieving histopathological R0 or R1 resection): oxaliplatin 130 mg/ m² IV on day 1, every three weeks, 6 cycles (begin 6-8 weeks after surgery)

Two forms are available: 10 or 20 mL of concentrate in a glass vial containing 50 or 100 mg oxaliplatin, respectively. Doses for oxaliplatin were administered on the basis of milligrams of drug per square meter of body surface area (BSA) as measured at baseline (mg/m2). The oxaliplatin dose was rounded to the nearest mg.

Number of subjects in period 1	Cape+RT	Cape+Oxali+RT
Started	547	547
Started allocated preop chemoradiation	543	525
Operated	533	511
Resected	532	507
Started allocated postop chemotherapy	419	334
Completed	367	283
Not completed	180	264
Adverse event, serious fatal	7	10
Consent withdrawn by subject	33	67
Physician decision	6	2
Adverse event, non-fatal	94	147
Second primary cancer	2	-
Lost to follow-up	4	3
Lack of efficacy	22	22
Protocol deviation	12	13

Baseline characteristics

Reporting groups	
Reporting group title	Cape+RT

Reporting group description:

Control Arm: capecitabine with radiotherapy before surgery, followed by capecitabine after surgery.
Preoperative treatment: capecitabine 825 mg/m² p.o. twice daily on days 1-33 (excluding weekends), radiotherapy: 45 Gy, 1.8 Gy on days 1-33 (excluding weekends)
Optional*: radiotherapy 5.4 Gy on days 36 to 38 using the same fields or as a boost to the primary tumour (3 fractions of 1.8 Gy) with capecitabine 825 mg/m² p.o. twice daily
Surgery (TME) 4-8 weeks after chemoradiation
Postoperative treatment (in patients achieving histopathological R0 or R1 resection): capecitabine 1000 mg/m² p.o. twice daily from the evening of day 1 to the morning of day 15, every three weeks, 6 cycles, (begin 6-8 weeks after surgery)
* If centers choose this option they have to adopt it for both arm during the entire study.

Reporting group title	Cape+Oxali+RT

Reporting group description:

Investigational Arm: capecitabine with oxaliplatin and radiotherapy before surgery, followed by capecitabine and oxaliplatin after surgery.
Preoperative treatment: capecitabine 825 mg/m² p.o. twice daily on days 1-33 (excluding weekends), radiotherapy: 45 Gy, 1.8 Gy on days 1-33 (excluding weekends), oxaliplatin 50 mg/m² IV on days 1, 8, 15, 22 and 29
Optional*: radiotherapy 5.4 Gy on days 36 to 38 using the same fields or as a boost to the primary tumour (3 fractions of 1.8 Gy) with capecitabine 825 mg/m² p.o. twice daily
Surgery (TME) 4-8 weeks after chemoradiation
Postoperative treatment (in patients achieving histopathological R0 or R1 resection): capecitabine 1000 mg/m² p.o. twice daily from the evening of day 1 to the morning of day 15 and oxaliplatin 130 mg/ m² IV on day 1, every three weeks, 6 cycles, (begin 6-8 weeks after surgery)
* If centers choose this option they have to adopt it for both arms during the entire study.

Reporting group values	Cape+RT	Cape+Oxali+RT	Total
Number of subjects	547	547	1094
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
median	62	62	
full range (min-max)	26 to 87	23 to 82	-
Gender categorical Units: Subjects			
Female	153	167	320
Male	394	380	774

T-stage Units: Subjects			
cT1	3	2	5
cT2	36	33	69
cT3	466	469	935
cT4	42	43	85
N-stage Units: Subjects			
cN0	118	120	238
cN1	295	296	591
cN2	98	93	191
cNX	36	38	74
TNM stage Units: Subjects			
Stage II	116	120	236
Stage III	392	386	778
cT3-4, cNX	35	38	73
Missing	4	3	7
Distance Tumor to anal verge Units: Subjects			
<=5cm	236	237	473
>5cm	311	310	621
MRI available at the center Units: Subjects			
No	66	56	122
Yes	481	491	972
Locoregional staging performed by Units: Subjects			
endorectal US + MRI	229	224	453
endorectal US + CT-scan	192	207	399
MRI alone	126	116	242
Performance status Units: Subjects			
PS0	420	432	852
PS1	126	108	234
PS2	1	7	8
Any concomitant non-malignant chronic disease Units: Subjects			
No	232	243	475
Yes	315	301	616
Unknown	0	3	3
Location of primary tumor Units: Subjects			
Upper third	69	63	132
Middle third	241	246	487
Lower third	190	178	368
Anorectal junction	33	40	73
Other	13	16	29
Unknown	1	4	5
Sphincter preservation according to the surgeon			

Units: Subjects			
Not sphincter-preserving	122	148	270
Sphincter-preserving	401	380	781
Unknown	24	19	43
Circumferential margins (by MRI) Units: Subjects			
Not involved (margins>1 mm)	171	180	351
Involved (margins<= 1mm)	167	152	319
Not applicable (MRI not done)	167	182	349
Unknown	42	33	75
Prior surgery for rectal cancer Units: Subjects			
No	501	508	1009
Yes, ileostomy	28	20	48
Yes, colostomy	14	15	29
Yes, other	4	0	4
Unknown	0	4	4
Complication related to primary tumor Units: Subjects			
None	413	433	846
Obstruction	30	23	53
Perforation	5	5	10
Obstruction and perforation	2	3	5
Other	81	70	151
Unknown	16	13	29

End points

End points reporting groups

Reporting group title	Cape+RT

Reporting group description:

Control Arm: capecitabine with radiotherapy before surgery, followed by capecitabine after surgery.
Preoperative treatment: capecitabine 825 mg/m² p.o. twice daily on days 1-33 (excluding weekends), radiotherapy: 45 Gy, 1.8 Gy on days 1-33 (excluding weekends)
Optional*: radiotherapy 5.4 Gy on days 36 to 38 using the same fields or as a boost to the primary tumour (3 fractions of 1.8 Gy) with capecitabine 825 mg/m² p.o. twice daily
Surgery (TME) 4-8 weeks after chemoradiation
Postoperative treatment (in patients achieving histopathological R0 or R1 resection): capecitabine 1000 mg/m² p.o. twice daily from the evening of day 1 to the morning of day 15, every three weeks, 6 cycles, (begin 6-8 weeks after surgery)
* If centers choose this option they have to adopt it for both arm during the entire study.

Reporting group title	Cape+Oxali+RT

Reporting group description:

Investigational Arm: capecitabine with oxaliplatin and radiotherapy before surgery, followed by capecitabine and oxaliplatin after surgery.
Preoperative treatment: capecitabine 825 mg/m² p.o. twice daily on days 1-33 (excluding weekends), radiotherapy: 45 Gy, 1.8 Gy on days 1-33 (excluding weekends), oxaliplatin 50 mg/m² IV on days 1, 8, 15, 22 and 29
Optional*: radiotherapy 5.4 Gy on days 36 to 38 using the same fields or as a boost to the primary tumour (3 fractions of 1.8 Gy) with capecitabine 825 mg/m² p.o. twice daily
Surgery (TME) 4-8 weeks after chemoradiation
Postoperative treatment (in patients achieving histopathological R0 or R1 resection): capecitabine 1000 mg/m² p.o. twice daily from the evening of day 1 to the morning of day 15 and oxaliplatin 130 mg/ m² IV on day 1, every three weeks, 6 cycles, (begin 6-8 weeks after surgery)
* If centers choose this option they have to adopt it for both arms during the entire study.

Subject analysis set title	Resected population - Cape+RT
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients randomized to the Cape+RT arm who have started the allocated pre-operative treatment, were operated and in whom surgical resection of the disease was performed.

Subject analysis set title	Resected population - Cape+Oxali+RT
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients randomized to the Cape+Oxali+RT arm who have started the allocated pre-operative treatment, were operated and in whom surgical resection of the disease was performed.

Subject analysis set title	Patients with sphincter preservation feasible - Cape+RT
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All patients randomized to the Cape+RT arm in whom sphincter preservation was judged feasible at entry on study.

Subject analysis set title	Patients with sphincter preservation feasible - Cape+Oxali+RT
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients randomized to the Cape+Oxali+RT arm in whom sphincter preservation was judged feasible at entry on study.

Primary: Disease-free survival (DFS) rate at 3 years

End point title	Disease-free survival (DFS) rate at 3 years

End point description:

Disease-free survival (DFS) is defined as the time interval from randomization to the first event of: loco-regional failure, metastatic recurrence, the appearance of a secondary colorectal cancer or death.
Patients with
R2 resection
a tumour that cannot be resected

distant metastases discovered at the time of surgery
will be considered as failures at the time of surgery.
Patients who have not had any such event at the time of data analysis will be censored at the last date they were known to be event-free. Patients with no follow-up records after baseline will be censored at day 1.

End point type	Primary

End point timeframe:

Tumor assessment was performed prior randomization, within 2 weeks before surgery, at surgery, every 6 months for the first three years after end of treatment and every 12 months in year 4 and 5. At time of analysis, median follow-up time was 54.7 months.

End point values	Cape+RT	Cape+Oxali+RT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	547[1]	547[2]		
Units: percent				
number (confidence interval 95%)	76.5 (72.6 to 79.9)	75.4 (71.4 to 79)		

Notes:

[1] - Primary analysis is intent-to-treat.

[2] - Primary analysis is intent-to-treat.

Attachments (see zip file)	DFS /DFS.jpg

Statistical analyses

Statistical analysis title	Primary analysis adjusted

Statistical analysis description:

The primary analysis of DFS was performed intention-to-treat (all randomized patients were analyzed in the arm they were allocated by randomization). DFS was compared between arms with the Cox's proportional hazards model adjusted for the stratification factors (except the center): clinical T category (T1-3 vs. T4), clinical nodal status (Nx vs. N0 vs. N1-2), distance from the tumor to the anal verge (≤5 cm vs. >5 cm), method of locoregional staging (EUS+MRI vs. EUS+CTscan vs. MRI alone).

Comparison groups	Cape+RT v Cape+Oxali+RT
Number of subjects included in analysis	1094
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.768
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.3

Statistical analysis title	Unadjusted analysis (secondary analysis)

Statistical analysis description:

This secondary analysis was not adjusted for stratification factors.

Comparison groups	Cape+RT v Cape+Oxali+RT
Number of subjects included in analysis	1094
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.744
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.31

Secondary: Pathological down-staging (ypT0-2N0) rate

End point title	Pathological down-staging (ypT0-2N0) rate

End point description:

The assessment was based on the review of the specimen and scoring by the local pathologist. Pathologic examination of the operative specimen was carried out including TNM classification according to the American Joint Committee on Cancer and International Union Against Cancer (sixth edition), the number of examined and involved lymph nodes, and the status of proximal, distal, and circumferential resection margins.

This endpoint is assessable only for the patients in whom a resection was performed. Therefore the patients not operated or not resected were scored as failures in the analysis of this endpoint.

End point type	Secondary

End point timeframe:

Histopathological response was assessed within 4-8 weeks after surgery.

End point values	Cape+RT	Cape+Oxali+RT	Resected population - Cape+RT	Resected population - Cape+Oxali+RT
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	547[3]	547[4]	534	508
Units: percent				
number (confidence interval 95%)	44.6 (40.4 to 48.9)	42.8 (38.6 to 47.1)	45.7 (41.4 to 50)	45.7 (41.3 to 50.1)

Notes:

[3] - The primary analysis of this endpoint was carried out in the intent-to-treat population.

[4] - The primary analysis of this endpoint was carried out in the intent-to-treat population.

Statistical analyses

Statistical analysis title	Primary analysis (intent-to-treat, adjusted)

Statistical analysis description:

The primary analysis was carried out in the intent-to-treat population by comparing the rates between treatment arms as estimated from fitting a logistic regression model to the data, with adjustment for all the stratification factors but center. The treatment effect was estimated as an odds ratio and its 95% confidence interval was estimated from the logistic model.

Comparison groups	Cape+RT v Cape+Oxali+RT

Number of subjects included in analysis	1094
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.549
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.929
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.731
upper limit	1.181

Statistical analysis title	Supportive analysis (resected population)

Statistical analysis description:

The analysis in the Resected population was performed as supportive analysis. The Resected population was defined as all randomized patients who started the allocated pre-operative treatment, were operated and in whom surgical resection of the disease was performed.

Comparison groups	Resected population - Cape+RT v Resected population - Cape+Oxali+RT
Number of subjects included in analysis	1042
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.968
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.995
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.779
upper limit	1.271

Secondary: Pathological complete remission (ypT0N0) rate

End point title	Pathological complete remission (ypT0N0) rate

End point description:

The assessment was based on the review of the specimen and scoring by the local pathologist. Pathologic examination of the operative specimen was carried out including TNM classification according to the American Joint Committee on Cancer and International Union Against Cancer (sixth edition), the number of examined and involved lymph nodes, and the status of proximal, distal, and circumferential resection margins.

This endpoint is assessable only for the patients in whom a resection was performed. Therefore the patients not operated or not resected were scored as failures in the analysis of this endpoint.

End point type	Secondary

End point timeframe:

Histopathological response was assessed within 4-8 weeks after surgery.

End point values	Cape+RT	Cape+Oxali+RT	Resected population - Cape+RT	Resected population - Cape+Oxali+RT
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	547[5]	547[6]	534	508
Units: percent				
number (confidence interval 95%)	11.5 (9 to 14.5)	13.5 (10.8 to 16.7)	11.8 (9.2 to 14.8)	14.4 (11.4 to 17.7)

Notes:

[5] - The primary analysis of this endpoint was carried out in the intent-to-treat population.
[6] - The primary analysis of this endpoint was carried out in the intent-to-treat population.

Statistical analyses

Statistical analysis title	Primary analysis (intent-to-treat, adjusted)

Statistical analysis description:

The primary analysis was carried out in the intent-to-treat population by comparing the rates between treatment arms as estimated from fitting a logistic regression model to the data, with adjustment for all the stratification factors but center. The treatment effect was estimated as an odds ratio and its 95% confidence interval was estimated from the logistic model.

Comparison groups	Cape+RT v Cape+Oxali+RT
Number of subjects included in analysis	1094
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.315
Method	Regression, Linear
Parameter estimate	Odds ratio (OR)
Point estimate	1.203
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.727

Statistical analysis title	Supportive analysis (resected population)

Statistical analysis description:

The analysis in the Resected population was performed as supportive analysis. The Resected population was defined as all randomized patients who started the allocated pre-operative treatment, were operated and in whom surgical resection of the disease was performed.

Comparison groups	Resected population - Cape+Oxali+RT v Resected population - Cape+RT

Number of subjects included in analysis	1042
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.227
Method	Regression, Linear
Parameter estimate	Odds ratio (OR)
Point estimate	1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.871
upper limit	1.8

Secondary: Tumor regression grade (Dworak)

End point title	Tumor regression grade (Dworak)

End point description:

The assessment was based on the review of the specimen and scoring by the local pathologist. The tumor regression was scored in 4 grades according the Dworak grade of regression.
0 – no regression detectable
1 – minimal regression: dominant tumour mass with obvious fibrosis and/or vasculopathy
2 – moderate regression: dominantly fibrotic changes with few tumour cells or groups
3 – good regression: very few (difficult to find microscopically) tumour cells in fibrotic tissue with or without mucin pools.
4 – total regression: no tumour cells detectable microscopically using standard procedures, only fibrotic mass or mucin pools.

Patients not operated or not resected were scored as failures in the analysis of this endpoint.

End point type	Secondary

End point timeframe:

Histopathological response was assessed within 4-8 weeks after surgery.

End point values	Cape+RT	Cape+Oxali+RT	Resected population - Cape+RT	Resected population - Cape+Oxali+RT
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	547[7]	547[8]	534	508
Units: Number of patients				
0 – no regression detectable	37	46	27	28
1 – minimal regression	116	81	115	79
2 – moderate regression	198	203	198	202
3 – good regression	105	114	105	114
4 – total regression	70	77	70	77
Missing	21	26	19	8

Notes:

[7] - The primary analysis of this endpoint was carried out in the intent-to-treat population.
[8] - The primary analysis of this endpoint was carried out in the intent-to-treat population.

Statistical analyses

Statistical analysis title	Primary analysis (intent-to-treat, adjusted)

Statistical analysis description:

Tumor regression grade was analyzed with two categories (No/minimal regression versus Moderate/Good/Total regression). The primary analysis was carried out in the intent-to-treat population by comparing the rates between treatment arms as estimated from fitting a logistic regression model to the data, with adjustment for all the stratification factors but center. The treatment effect was estimated as an odds ratio and its 95% confidence interval was estimated from the logistic model.

Comparison groups	Cape+RT v Cape+Oxali+RT
Number of subjects included in analysis	1094
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.087
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.272
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.966
upper limit	1.678

Statistical analysis title	Supportive analysis (resected population)

Statistical analysis description:

The analysis in the Resected population was performed as supportive analysis. The Resected population was defined as all randomized patients who started the allocated pre-operative treatment, were operated and in whom surgical resection of the disease was performed.

Comparison groups	Resected population - Cape+RT v Resected population - Cape+Oxali+RT
Number of subjects included in analysis	1042
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.023
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	1.872

Secondary: Histopathological R0 resection rate

End point title	Histopathological R0 resection rate

End point description:

The assessment was based on the review of the specimen and scoring by the local pathologist. The circumferential margin was considered involved if the tumour extended to within 1 mm of the circumferential resection margin (R1 resection).
R classification was defined as follows:

RX: Presence of residual tumor cannot be assessed
R0: No residual tumor
R1: Microscopic residual tumor
R2: Macroscopic residual tumor.
Patients not operated or not resected were scored as failures in the analysis of this endpoint.

End point type	Secondary

End point timeframe:

Histopathological response was assessed within 4-8 weeks after surgery.

End point values	Cape+RT	Cape+Oxali+RT	Resected population - Cape+RT	Resected population - Cape+Oxali+RT
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	547[9]	547[10]	534	508
Units: percent				
number (confidence interval 95%)	95.2 (93.1 to 96.9)	89.9 (87.1 to 92.3)	97.2 (95.4 to 98.4)	96.1 (94 to 97.6)

Notes:

[9] - The primary analysis of this endpoint was carried out in the intent-to-treat population.
[10] - The primary analysis of this endpoint was carried out in the intent-to-treat population.

Statistical analyses

Statistical analysis title	Primary analysis (intent-to-treat, adjusted)

Statistical analysis description:

The primary analysis was carried out in the intent-to-treat population by comparing the rates between treatment arms as estimated from fitting a logistic regression model to the data, with adjustment for all the stratification factors but center. The treatment effect was estimated as an odds ratio and its 95% confidence interval was estimated from the logistic model.

Comparison groups	Cape+RT v Cape+Oxali+RT
Number of subjects included in analysis	1094
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.442
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.268
upper limit	0.713

Statistical analysis title	Supportive analysis (resected population)

Statistical analysis description:

The analysis in the Resected population was performed as supportive analysis. The Resected population was defined as all randomized patients who started the allocated pre-operative treatment, were operated and in whom surgical resection of the disease was performed.

Comparison groups	Resected population - Cape+RT v Resected population - Cape+Oxali+RT
Number of subjects included in analysis	1042
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.316
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.702
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.346
upper limit	1.395

Secondary: Sphincter preservation rate

End point title	Sphincter preservation rate

End point description:

End point type	Secondary

End point timeframe:

It was noticed at baseline if according to the surgeon the sphincter can be preserved and after the operation if the sphincter has been preserved.

End point values	Cape+RT	Cape+Oxali+RT	Resected population - Cape+RT	Resected population - Cape+Oxali+RT
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	547[11]	547[12]	534	508
Units: percent				
number (confidence interval 95%)	70.6 (66.6 to 74.4)	66.9 (62.8 to 70.9)	72.1 (68.1 to 75.9)	71.7 (67.5 to 75.5)

Notes:

[11] - The primary analysis of this endpoint was carried out in the intent-to-treat population.

[12] - The primary analysis of this endpoint was carried out in the intent-to-treat population.

End point values	Patients with sphincter preservation feasible - Cape+RT	Patients with sphincter preservation feasible - Cape+Oxali+RT		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	401	380		
Units: percent				
number (confidence interval 95%)	86.8 (83.1 to 89.9)	84.2 (80.2 to 87.7)		

Statistical analyses

Statistical analysis title	Primary analysis (intent-to-treat, adjusted)

Statistical analysis description:

The primary analysis was carried out in the intent-to-treat population by comparing the rates between treatment arms as estimated from fitting a logistic regression model to the data, with adjustment for all the stratification factors but center. The treatment effect was estimated as an odds ratio and its 95% confidence interval was estimated from the logistic model.

Comparison groups	Cape+Oxali+RT v Cape+RT
Number of subjects included in analysis	1094
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.194
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.827
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.622
upper limit	1.101

Statistical analysis title	Supportive analysis (resected population)

Statistical analysis description:

The analysis in the Resected population was performed as supportive analysis. The Resected population was defined as all randomized patients who started the allocated pre-operative treatment, were operated and in whom surgical resection of the disease was performed.

Comparison groups	Resected population - Cape+RT v Resected population - Cape+Oxali+RT
Number of subjects included in analysis	1042
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.941
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.012
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.745
upper limit	1.375

Statistical analysis title	Supportive analysis (judged feasible at entry)

Statistical analysis description:

The endpoint of sphincter preservation rate was compared in the subset of patients in whom sphincter preservation was judged feasible at entry on study.

Comparison groups	Patients with sphincter preservation feasible - Cape+RT v Patients with sphincter preservation feasible - Cape+Oxali+RT
Number of subjects included in analysis	781
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.279
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.794
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.522
upper limit	1.205

Secondary: Perioperative complication rate

End point title	Perioperative complication rate

End point description:

The perioperative complications were defined as follows:
Any of the following events provided they are due to a severe surgery-related complication (i.e. wound infection, intra-abdominal infection, severe sepsis, …) requiring: prolongation of hospitalization (discharge >20 days after surgery), re-hospitalization within 30 days of surgery, reoperation under general anaesthesia within 30 days of surgery or death during surgery or within 30 days of surgery.
Other severe pre- or postoperative complications within 30 days of surgery.
>8 weeks delay of surgery due to study treatment-related toxicity; delay being measured between the end of preoperative chemoradiation and surgery.
Severe pre- or postoperative toxicity of study treatment leading to treatment discontinuation (all drugs discontinued) or death.

End point type	Secondary

End point timeframe:

Toxicity and adverse events were collected weekly during and at the end of preoperative treatment, within 2 weeks before surgery, within 4-8 weeks after surgery, before each cycle and at the end of postoperative CT, then 6-monthly for 5 years.

End point values	Cape+RT	Cape+Oxali+RT	Resected population - Cape+RT	Resected population - Cape+Oxali+RT
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	547[13]	547[14]	534	508
Units: percent				
number (confidence interval 95%)	30.5 (26.7 to 34.6)	39.3 (35.2 to 43.5)	30.9 (27 to 35)	40.9 (36.6 to 45.4)

Notes:

[13] - The primary analysis of this endpoint was carried out in the intent-to-treat population.

[14] - The primary analysis of this endpoint was carried out in the intent-to-treat population.

Statistical analyses

Statistical analysis title	Primary analysis (intent-to-treat, adjusted)

Statistical analysis description:

The primary analysis was carried out in the intent-to-treat population by comparing the rates between treatment arms as estimated from fitting a logistic regression model to the data, with adjustment for all the stratification factors but center. The treatment effect was estimated as an odds ratio and its 95% confidence interval was estimated from the logistic model.

Comparison groups	Cape+RT v Cape+Oxali+RT
Number of subjects included in analysis	1094
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.476
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.149
upper limit	1.899

Statistical analysis title	Supportive analysis (resected population)

Statistical analysis description:

The analysis in the Resected population was performed as supportive analysis. The Resected population was defined as all randomized patients who started the allocated pre-operative treatment, were operated and in whom surgical resection of the disease was performed.

Comparison groups	Resected population - Cape+RT v Resected population - Cape+Oxali+RT
Number of subjects included in analysis	1042
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.562
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.21
upper limit	2.02

Secondary: Overall survival (OS) rate at 3 years

End point title	Overall survival (OS) rate at 3 years

End point description:

Overall survival (OS) is defined as the time interval between the date of randomization and the date of death of any cause. Patients who were still alive when last traced were censored at the date of last follow-up.

End point type	Secondary

End point timeframe:

Each individual patient was to be followed up for survival for a minimum of 5 years after the end of treatment. At the time of analysis, median follow-up time was 55.39 months in the Cape+RT arm and 54.21 months in the Cape+Oxali+RT arm.

End point values	Cape+RT	Cape+Oxali+RT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	547	547		
Units: percent				
number (confidence interval 95%)	90.1 (87.1 to 92.4)	87.6 (84.4 to 90.2)		

Attachments (see zip file)	OS/OS.jpg

Statistical analyses

Statistical analysis title	Primary analysis adjusted

Statistical analysis description:

The primary analysis of OS was performed intention-to-treat (all randomized patients were analyzed in the arm they were allocated by randomization). OS was compared between arms with the Cox's proportional hazards model adjusted for the stratification factors (except the center): clinical T category (T1-3 vs. T4), clinical nodal status (Nx vs. N0 vs. N1-2), distance from the tumor to the anal verge (≤5 cm vs. >5 cm), method of locoregional staging (EUS+MRI vs. EUS+CTscan vs. MRI alone).

Comparison groups	Cape+RT v Cape+Oxali+RT
Number of subjects included in analysis	1094
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.229
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.62

Statistical analysis title	Unadjusted analysis (secondary analysis)

Statistical analysis description:

This secondary analysis was not adjusted for stratification factors.

Comparison groups	Cape+RT v Cape+Oxali+RT
Number of subjects included in analysis	1094
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.185
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.65

Secondary: Loco-regional failure rate at 3 years

End point title	Loco-regional failure rate at 3 years

End point description:

Loco-regional failure was defined as local or regional recurrence, a tumor that could not be resected or R2 resection at surgery. Local recurrence was defined as evidence of tumour in the anastomotic or perineal area. Regional recurrence was defined as evidence of tumour in the pelvic or retroperitoneal lymph nodes. Deaths prior to loco-regional failure were considered as a competing risk in the estimation of the cumulative incidence
of loco-regional failure.

End point type	Secondary

End point timeframe:

Patients were followed for loco-regional failure irrespective of metastatic recurrence or the appearance of a secondary colon cancer. At time of analysis, median follow-up time was 54.7 months.

End point values	Cape+RT	Cape+Oxali+RT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	547	547		
Units: percent				
number (confidence interval 95%)	6.95 (4.76 to 9.14)	5.35 (3.38 to 7.31)		

Attachments (see zip file)	Loco-regional failure/Loco-regional failure.jpg

Statistical analyses

Statistical analysis title	Primary analysis (death competing)

Statistical analysis description:

The primary analysis of loco-regional failure was performed using the competing risk methodology in the intent-to-treat population. The cumulative incidence of loco-regional failures was estimated and

compared between arms by means of an (unadjusted) Gray test. The 3-year cumulative incidence rates were estimated from the curve in each arm and their 95% confidence intervals were calculated.

Comparison groups	Cape+RT v Cape+Oxali+RT
Number of subjects included in analysis	1094
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.334
Method	Gray test

Statistical analysis title	Secondary analysis (death censored)

Statistical analysis description:

A Cox model adjusted for the stratification factors (but center) was also fitted, to obtain adjusted estimates of the hazard ratio and its 95% confidence interval. Patients who died prior to loco-regional failure were censored at the time of death.

Comparison groups	Cape+RT v Cape+Oxali+RT
Number of subjects included in analysis	1094
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.324
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	1.25

Secondary: Distant failure rate at 3 years

End point title	Distant failure rate at 3 years

End point description:

Distant failure was defined as the appearance of distant metastases. Deaths prior to distant failure were considered as a competing risk in the estimation of the cumulative incidence of distant metastases.

End point type	Secondary

End point timeframe:

Patients were followed for distant failure irrespective of the occurrence of loco-regional failure or absence of resection or incompleteness of the tumor resection. At time of analysis, median follow-up time was 54.7 months.

End point values	Cape+RT	Cape+Oxali+RT		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	547	547		
Units: percent				
number (confidence interval 95%)	18.2 (14.9 to 21.5)	17 (13.7 to 20.3)		

Attachments (see zip file)	Distant failure/Distant failure.jpg

Statistical analyses

Statistical analysis title	Primary analysis (death competing)

Statistical analysis description:

The primary analysis of distant failure was performed using the competing risk methodology in the intent-to-treat population. The cumulative incidence of distant failures was estimated and compared between arms by means of an (unadjusted) Gray test. The 3-year cumulative incidence rates were estimated from the curve in each arm and their 95% confidence intervals were calculated.

Comparison groups	Cape+RT v Cape+Oxali+RT
Number of subjects included in analysis	1094
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.369
Method	Gray test

Statistical analysis title	Secondary analysis (death censored)

Statistical analysis description:

A Cox model adjusted for the stratification factors (but center) was also fitted, to obtain adjusted estimates of the hazard ratio and its 95% confidence interval. Patients who died prior to distant failure were censored at the time of death.

Comparison groups	Cape+Oxali+RT v Cape+RT
Number of subjects included in analysis	1094
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.484
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.19

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected on a CRF to be submitted at pre-specified timepoint : at baseline, weekly during and at the end of preop CT, within 2 weeks before surgery, within 4-8 weeks post surgery, before each cycle and at the end of postop CT.

Adverse event reporting additional description:

CRF for AEs contains pre-specified items + additional boxes for all "other" AEs. AEs are evaluated using CTC grading (version 3.0), SAEs using MedDra (version 19.1). Grade 1-5 CTC AEs are reported. Hematological and biochemical abnormalities are not included. Non-SAEs has not been collected specifically, all AEs will be reported in non-SAE section.

Assessment type	Non-systematic

Dictionary used

Dictionary name	CTC
Dictionary version	3.0

Reporting groups

Reporting group title	Cape+RT

Reporting group description:

The analysis of the safety endpoints “Toxicity” were carried out in the safety population defined as all patients who have started their allocated treatment (at least one dose of the study drug(s) in chemotherapy trials).

Reporting group title	Cape+Oxali+RT

Reporting group description:

The analysis of the safety endpoints “Toxicity” were carried out in the safety population defined as all patients who have started their allocated treatment (at least one dose of the study drug(s) in chemotherapy trials).

Serious adverse events	Cape+RT	Cape+Oxali+RT	
Total subjects affected by serious adverse events			
subjects affected / exposed	188 / 545 (34.50%)	288 / 529 (54.44%)	
number of deaths (all causes)	80	88	
number of deaths resulting from adverse events	6	8	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
MENINGIOMA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL CELL CARCINOMA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TUMOUR PERFORATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
ARTERIAL OCCLUSIVE DISEASE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CIRCULATORY COLLAPSE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEEP VEIN THROMBOSIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	8 / 545 (1.47%)	5 / 529 (0.95%)	
occurrences causally related to treatment / all	6 / 8	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEMORAL ARTERY EMBOLISM			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMORRHAGE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	3 / 529 (0.57%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERTENSION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOTENSION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOVOLAEMIC SHOCK			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
ORTHOSTATIC HYPOTENSION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
PERIPHERAL ARTERY STENOSIS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
PERIPHERAL ISCHAEMIA				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 545 (0.37%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	1 / 2	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
SHOCK HAEMORRHAGIC				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
THROMBOPHLEBITIS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOSIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VENOUS THROMBOSIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
ILEOSTOMY			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
ASTHENIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	5 / 529 (0.95%)	
occurrences causally related to treatment / all	0 / 0	5 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHEST PAIN			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)		
occurrences causally related to treatment / all	0 / 1	1 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
CHILLS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	3 / 529 (0.57%)		
occurrences causally related to treatment / all	0 / 0	3 / 3		
deaths causally related to treatment / all	0 / 0	0 / 0		
DEATH				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	1 / 1		
DRUG INTOLERANCE				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 1	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
FATIGUE				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 545 (0.55%)	9 / 529 (1.70%)		
occurrences causally related to treatment / all	3 / 3	8 / 9		
deaths causally related to treatment / all	0 / 0	0 / 0		
FEELING COLD				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
GENERAL PHYSICAL HEALTH DETERIORATION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 545 (0.55%)	4 / 529 (0.76%)		
occurrences causally related to treatment / all	2 / 3	4 / 4		
deaths causally related to treatment / all	0 / 0	0 / 0		
IMPAIRED HEALING				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	8 / 545 (1.47%)	13 / 529 (2.46%)		
occurrences causally related to treatment / all	7 / 8	13 / 13		
deaths causally related to treatment / all	0 / 0	0 / 0		
INFLAMMATION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
MALAISE				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
MUCOSAL INFLAMMATION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				

subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
MULTIPLE ORGAN DYSFUNCTION SYNDROME			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	4 / 529 (0.76%)	
occurrences causally related to treatment / all	1 / 1	3 / 4	
deaths causally related to treatment / all	1 / 1	3 / 4	
NECROSIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
OEDEMA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAIN			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERFORMANCE STATUS DECREASED			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYREXIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	26 / 529 (4.91%)	
occurrences causally related to treatment / all	0 / 2	26 / 30	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUDDEN DEATH			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 545 (0.55%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	2 / 3	0 / 0	
SYSTEMIC INFLAMMATORY RESPONSE SYNDROME			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
ANAPHYLACTIC REACTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CYTOKINE RELEASE SYNDROME			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERSENSITIVITY			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	19 / 529 (3.59%)	
occurrences causally related to treatment / all	0 / 0	19 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
FEMALE GENITAL TRACT FISTULA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	2 / 2	4 / 4	
deaths causally related to treatment / all	0 / 0	1 / 1	
GENITAL ULCERATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PELVIC FLUID COLLECTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	3 / 529 (0.57%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PELVIC HAEMATOMA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROSTATITIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VAGINAL FISTULA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VULVOVAGINAL DISCOMFORT			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
ACUTE PULMONARY OEDEMA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ASPHYXIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	1 / 1		
ASPIRATION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	1 / 1	0 / 0		
BRONCHOSPASM				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
CHRONIC OBSTRUCTIVE PULMONARY DISEASE				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
DYSPNOEA				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)		
occurrences causally related to treatment / all	0 / 1	1 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
LARYNGOSPASM				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
PLEURAL EFFUSION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
PLEURISY				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
PNEUMONIA ASPIRATION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	1 / 1	1 / 1		
deaths causally related to treatment / all	0 / 0	1 / 1		
PNEUMOTHORAX				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 1	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
PULMONARY EMBOLISM				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				

subjects affected / exposed	13 / 545 (2.39%)	12 / 529 (2.27%)	
occurrences causally related to treatment / all	9 / 13	6 / 12	
deaths causally related to treatment / all	2 / 2	0 / 0	
RESPIRATORY FAILURE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 2	
Psychiatric disorders			
ANXIETY			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANXIETY DISORDER			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COMPLETED SUICIDE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
DEPRESSION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEPRESSION SUICIDAL			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
MAJOR DEPRESSION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
BLOOD CREATININE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD CREATININE INCREASED			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLOOD GLUCOSE INCREASED			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ELECTROCARDIOGRAM QT PROLONGED			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMOGLOBIN DECREASED			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATIC ENZYME INCREASED			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
WEIGHT DECREASED			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
ABDOMINAL WOUND DEHISCENCE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANASTOMOTIC COMPLICATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 545 (2.20%)	7 / 529 (1.32%)	
occurrences causally related to treatment / all	11 / 12	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANASTOMOTIC FISTULA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANASTOMOTIC LEAK			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 545 (3.49%)	18 / 529 (3.40%)	
occurrences causally related to treatment / all	19 / 19	17 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANASTOMOTIC ULCER			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANASTOMOTIC ULCER HAEMORRHAGE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLADDER INJURY			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEMORAL NECK FRACTURE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEMUR FRACTURE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FRACTURED SACRUM			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROENTERITIS RADIATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 545 (0.37%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL ANASTOMOTIC LEAK			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL STOMA COMPLICATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 545 (0.55%)	10 / 529 (1.89%)	
occurrences causally related to treatment / all	3 / 4	6 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL STOMA NECROSIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INCISIONAL HERNIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTESTINAL ANASTOMOSIS COMPLICATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	3 / 545 (0.55%)	3 / 529 (0.57%)	
occurrences causally related to treatment / all	3 / 3	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
POST PROCEDURAL BILE LEAK			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
POST PROCEDURAL HAEMORRHAGE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
POST PROCEDURAL URINE LEAK			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
POSTOPERATIVE DELIRIUM			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
POSTOPERATIVE ILEUS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROCEDURAL INTESTINAL PERFORATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROCEDURAL PAIN			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RADIATION PROCTITIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEROMA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPLENIC RUPTURE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
STOMA SITE HAEMORRHAGE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
STOMA SITE INFLAMMATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
STOMA SITE PAIN			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
STOMAL HERNIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUTURE RELATED COMPLICATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUTURE RUPTURE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
URETERIC INJURY			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
WOUND COMPLICATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
WOUND DECOMPOSITION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
WOUND DEHISCENCE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	6 / 529 (1.13%)	
occurrences causally related to treatment / all	1 / 1	6 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
WOUND NECROSIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
DIHYDROPYRIMIDINE DEHYDROGENASE DEFICIENCY			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
ACUTE CORONARY SYNDROME			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANGINA PECTORIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ARTERIOSPASM CORONARY			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FIBRILLATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 545 (0.73%)	6 / 529 (1.13%)	
occurrences causally related to treatment / all	2 / 4	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
CORONARY ARTERY DISEASE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EXTRASYSTOLES			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEFT VENTRICULAR DYSFUNCTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEFT VENTRICULAR FAILURE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MYOCARDIAL INFARCTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
MYOCARDIAL ISCHAEMIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RIGHT VENTRICULAR DYSFUNCTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RIGHT VENTRICULAR FAILURE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
SUPRAVENTRICULAR TACHYCARDIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
TACHYARRHYTHMIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
TACHYCARDIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VENTRICULAR TACHYCARDIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	3 / 529 (0.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
ATAXIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CAROTID ARTERY STENOSIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBRAL INFARCTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CEREBRAL ISCHAEMIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
CEREBROVASCULAR ACCIDENT			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIZZINESS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSARTHRIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSGEUSIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEMIPARESIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEMIPLEGIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTRACRANIAL ANEURYSM			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOENCEPHALOPATHY			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
NERVE COMPRESSION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
NEUROPATHY PERIPHERAL				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	4 / 529 (0.76%)		
occurrences causally related to treatment / all	0 / 0	4 / 4		
deaths causally related to treatment / all	0 / 0	0 / 0		
PERIPHERAL NERVE LESION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
PERIPHERAL SENSORY NEUROPATHY				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	3 / 529 (0.57%)		
occurrences causally related to treatment / all	0 / 0	3 / 3		
deaths causally related to treatment / all	0 / 0	0 / 0		
POLYNEUROPATHY				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PRESYNCOPE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SCIATICA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEIZURE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPEECH DISORDER			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SYNCOPE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 545 (0.37%)	5 / 529 (0.95%)	
occurrences causally related to treatment / all	1 / 2	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
TRANSIENT ISCHAEMIC ATTACK			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TREMOR			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
ANAEMIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	4 / 529 (0.76%)	
occurrences causally related to treatment / all	2 / 2	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
FEBRILE NEUTROPENIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPARIN-INDUCED THROMBOCYTOPENIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LEUKOPENIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUTROPENIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	1 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
PANCYTOPENIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
THROMBOCYTOPENIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
VERTIGO			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 545 (0.37%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
OPTIC ISCHAEMIC NEUROPATHY			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VISION BLURRED			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL ADHESIONS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 545 (0.92%)	11 / 529 (2.08%)	
occurrences causally related to treatment / all	3 / 5	9 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL PAIN UPPER			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	3 / 529 (0.57%)		
occurrences causally related to treatment / all	0 / 0	2 / 3		
deaths causally related to treatment / all	0 / 0	0 / 0		
ACUTE ABDOMEN				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
ANAL FISSURE				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
ANAL HAEMORRHAGE				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 1	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
ANAL INCONTINENCE				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
ASCITES				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLITIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	5 / 529 (0.95%)	
occurrences causally related to treatment / all	2 / 2	3 / 5	
deaths causally related to treatment / all	0 / 0	1 / 1	
CONSTIPATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 545 (0.92%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	2 / 5	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 545 (2.57%)	72 / 529 (13.61%)	
occurrences causally related to treatment / all	14 / 16	74 / 76	
deaths causally related to treatment / all	0 / 0	0 / 0	
DUODENAL PERFORATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DUODENAL ULCER PERFORATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENTERITIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 545 (0.55%)	3 / 529 (0.57%)	
occurrences causally related to treatment / all	3 / 3	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENTEROCOLITIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ENTEROVESICAL FISTULA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FAECALOMA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FREQUENT BOWEL MOVEMENTS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
GASTRIC ULCER				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)		
occurrences causally related to treatment / all	0 / 0	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
GASTRITIS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
GASTRITIS EROSIVE				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
GASTRODUODENITIS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
GASTROINTESTINAL NECROSIS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL PAIN			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GASTROINTESTINAL TRACT IRRITATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMATOCHEZIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMORRHAGIC ASCITES			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HAEMORRHOIDS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ILEUS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 545 (1.83%)	11 / 529 (2.08%)	
occurrences causally related to treatment / all	8 / 10	9 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
ILEUS PARALYTIC			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 545 (0.92%)	3 / 529 (0.57%)	
occurrences causally related to treatment / all	7 / 7	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTESTINAL OBSTRUCTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTESTINAL PERFORATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INTRA-ABDOMINAL FLUID COLLECTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
ISCHIORECTAL HERNIA				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
LARGE INTESTINE PERFORATION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
MECHANICAL ILEUS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
MELAENA				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
MOUTH ULCERATION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NAUSEA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 545 (0.55%)	21 / 529 (3.97%)	
occurrences causally related to treatment / all	3 / 3	23 / 23	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PANCREATITIS ACUTE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PAPILLA OF VATER STENOSIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROCTALGIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 545 (0.37%)	6 / 529 (1.13%)	
occurrences causally related to treatment / all	2 / 2	5 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROCTITIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	3 / 529 (0.57%)	
occurrences causally related to treatment / all	2 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PROCTITIS HAEMORRHAGIC			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RECTAL HAEMORRHAGE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RECTAL PROLAPSE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RECTAL STENOSIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
RECTAL TENESMUS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
SMALL INTESTINAL OBSTRUCTION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	3 / 529 (0.57%)		
occurrences causally related to treatment / all	1 / 1	3 / 3		
deaths causally related to treatment / all	0 / 0	0 / 0		
STOMATITIS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
SUBILEUS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	5 / 545 (0.92%)	4 / 529 (0.76%)		
occurrences causally related to treatment / all	1 / 5	3 / 4		
deaths causally related to treatment / all	0 / 0	0 / 0		
VOMITING				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				

subjects affected / exposed	9 / 545 (1.65%)	24 / 529 (4.54%)	
occurrences causally related to treatment / all	7 / 9	27 / 27	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
CHOLECYSTITIS ACUTE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLELITHIASIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GALLBLADDER OBSTRUCTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATOTOXICITY			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERBILIRUBINAEMIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
ACQUIRED EPIDERMOLYSIS BULLOSA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANGIOEDEMA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DECUBITUS ULCER			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DERMATITIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HIDRADENITIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PRURITUS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RASH GENERALISED			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SKIN IRRITATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SKIN TOXICITY			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 545 (1.47%)	8 / 529 (1.51%)	
occurrences causally related to treatment / all	5 / 9	5 / 9	
deaths causally related to treatment / all	0 / 0	1 / 1	
ACUTE PRERENAL FAILURE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLADDER OBSTRUCTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLADDER OUTLET OBSTRUCTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BLADDER SPASM			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CALCULUS BLADDER			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CALCULUS URINARY			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSURIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GLOMERULONEPHRITIS MINIMAL LESION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYDRONEPHROSIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUROGENIC BLADDER			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PRERENAL FAILURE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RENAL FAILURE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 545 (0.55%)	11 / 529 (2.08%)	
occurrences causally related to treatment / all	1 / 3	8 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
URETERIC OBSTRUCTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY RETENTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	3 / 545 (0.55%)	9 / 529 (1.70%)	
occurrences causally related to treatment / all	3 / 3	8 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT OBSTRUCTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ARTHRITIS REACTIVE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BACK PAIN			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COMPARTMENT SYNDROME			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
FISTULA				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 545 (0.37%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	1 / 2	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
FLANK PAIN				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
MUSCULAR WEAKNESS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)		
occurrences causally related to treatment / all	0 / 0	1 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
OSTEOARTHRITIS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
SPINAL PAIN				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
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			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL INFECTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABDOMINAL WALL ABSCESS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ABSCESS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 545 (2.39%)	20 / 529 (3.78%)	
occurrences causally related to treatment / all	13 / 13	17 / 21	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAL ABSCESS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	3 / 545 (0.55%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	5 / 5	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANORECTAL INFECTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CATHETER SITE INFECTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CHOLECYSTITIS INFECTIVE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CLOSTRIDIUM DIFFICILE COLITIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLONIC ABSCESS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
CYSTITIS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 545 (0.37%)	3 / 529 (0.57%)		
occurrences causally related to treatment / all	1 / 2	2 / 3		
deaths causally related to treatment / all	0 / 0	0 / 0		
DEVICE OCCLUSION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
DEVICE RELATED INFECTION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	1 / 1	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
DIABETIC GANGRENE				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)		
occurrences causally related to treatment / all	0 / 0	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
DIVERTICULITIS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
DOUGLAS' ABSCESS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
EMBOLIC PNEUMONIA				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
ENTEROBACTER INFECTION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
EPIDIDYMITIS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)		
occurrences causally related to treatment / all	0 / 0	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
ESCHERICHIA INFECTION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
ESCHERICHIA URINARY TRACT INFECTION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
GASTROENTERITIS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
GASTROENTERITIS NOROVIRUS				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)		
occurrences causally related to treatment / all	0 / 0	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
GASTROINTESTINAL INFECTION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
HAEMATOMA INFECTION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				

subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
HERPES OESOPHAGITIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HERPES SIMPLEX			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HERPES ZOSTER INFECTION NEUROLOGICAL			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HIV INFECTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFECTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	7 / 529 (1.32%)	
occurrences causally related to treatment / all	0 / 1	5 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
KLEBSIELLA SEPSIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOWER RESPIRATORY TRACT INFECTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
OESOPHAGEAL CANDIDIASIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PELVIC ABSCESS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 545 (0.55%)	3 / 529 (0.57%)	
occurrences causally related to treatment / all	4 / 4	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERINEAL ABSCESS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	3 / 545 (0.55%)	3 / 529 (0.57%)	
occurrences causally related to treatment / all	4 / 4	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERIRECTAL ABSCESS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERITONITIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 545 (0.92%)	7 / 529 (1.32%)	
occurrences causally related to treatment / all	4 / 5	6 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 545 (0.73%)	5 / 529 (0.95%)	
occurrences causally related to treatment / all	3 / 4	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA BACTERIAL			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
POSTOPERATIVE WOUND INFECTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PSEUDOMEMBRANOUS COLITIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYELITIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PYELONEPHRITIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RECTAL ABSCESS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	3 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
RETROPERITONEAL INFECTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPSIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 545 (0.55%)	6 / 529 (1.13%)	
occurrences causally related to treatment / all	3 / 3	6 / 6	
deaths causally related to treatment / all	1 / 1	1 / 1	
SEPTIC SHOCK			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	4 / 529 (0.76%)	
occurrences causally related to treatment / all	1 / 1	2 / 4	
deaths causally related to treatment / all	0 / 0	2 / 3	
STAPHYLOCOCCAL INFECTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
STAPHYLOCOCCAL SEPSIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
STOMA SITE ABSCESS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
STOMA SITE INFECTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBCUTANEOUS ABSCESS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUPERINFECTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUPERINFECTION FUNGAL			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
URINARY TRACT INFECTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	5 / 545 (0.92%)	4 / 529 (0.76%)	
occurrences causally related to treatment / all	4 / 6	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
UROGENITAL INFECTION BACTERIAL			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
UROSEPSIS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
WOUND ABSCESS			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
WOUND INFECTION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 545 (2.39%)	8 / 529 (1.51%)	
occurrences causally related to treatment / all	13 / 14	7 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
WOUND INFECTION STAPHYLOCOCCAL			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	3 / 545 (0.55%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	2 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DECREASED APPETITE			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	3 / 529 (0.57%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
DEHYDRATION			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 545 (1.65%)	20 / 529 (3.78%)	
occurrences causally related to treatment / all	7 / 10	17 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERGLYCAEMIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPERKALAEMIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOALBUMINAEMIA			
alternative dictionary used: MedDRA 19			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
HYPOCALCAEMIA				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
HYPOKALAEMIA				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 545 (0.37%)	4 / 529 (0.76%)		
occurrences causally related to treatment / all	1 / 2	4 / 4		
deaths causally related to treatment / all	0 / 0	0 / 0		
HYPONATRAEMIA				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 1	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
MALNUTRITION				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)		
occurrences causally related to treatment / all	0 / 1	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
TETANY				
alternative dictionary used: MedDRA 19				
alternative assessment type: Systematic				

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cape+RT	Cape+Oxali+RT	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	536 / 545 (98.35%)	529 / 529 (100.00%)	
Vascular disorders			
ARTERY			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	0 / 529 (0.00%)	
occurrences (all)	2	0	
CAROTID			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences (all)	1	1	
PERIPHERAL ARTERIAL ISCHEMIA			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	1 / 529 (0.19%)	
occurrences (all)	2	1	
PHLEBITIS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	13 / 529 (2.46%)	
occurrences (all)	1	19	
THROMBOSIS/THROMBUS/EMBOLISM			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			

subjects affected / exposed	40 / 545 (7.34%)	44 / 529 (8.32%)	
occurrences (all)	66	94	
VASCULAR DISORDERS - OTHER ADVERSE EVENT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 545 (0.92%)	11 / 529 (2.08%)	
occurrences (all)	9	17	
Surgical and medical procedures			
SURGICAL AND MEDICAL PROCEDURES - OTHER ADVERSE EVENT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 545 (0.92%)	2 / 529 (0.38%)	
occurrences (all)	9	5	
General disorders and administration site conditions			
ABDOMEN NOS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	36 / 545 (6.61%)	41 / 529 (7.75%)	
occurrences (all)	60	92	
DEATH NOS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
FATIGUE			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	294 / 545 (53.94%)	337 / 529 (63.71%)	
occurrences (all)	1264	1623	
FEVER			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			

subjects affected / exposed	39 / 545 (7.16%)	110 / 529 (20.79%)	
occurrences (all)	47	187	
FLU-LIKE SYNDROME			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences (all)	1	1	
GENERAL DISORDERS AND ADMINISTRATION - OTHER ADVERSE EVENT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	291 / 545 (53.39%)	307 / 529 (58.03%)	
occurrences (all)	1018	1094	
INSOMNIA			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	21 / 545 (3.85%)	34 / 529 (6.43%)	
occurrences (all)	79	105	
MULTI-ORGAN FAILURE			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)	
occurrences (all)	1	2	
OBESITY			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	2	
PAIN NOS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	4 / 529 (0.76%)	
occurrences (all)	1	5	
PELVIC			

alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	6 / 545 (1.10%)	5 / 529 (0.95%)		
occurrences (all)	7	8		
PELVIS				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	5 / 545 (0.92%)	4 / 529 (0.76%)		
occurrences (all)	11	4		
RADIATION				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 545 (0.55%)	3 / 529 (0.57%)		
occurrences (all)	5	5		
RIGORS/CHILLS				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)		
occurrences (all)	2	4		
SUDDEN DEATH				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 545 (0.37%)	0 / 529 (0.00%)		
occurrences (all)	2	0		
TUMOR PAIN				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 545 (0.37%)	2 / 529 (0.38%)		
occurrences (all)	3	8		
WEIGHT GAIN				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				

subjects affected / exposed	47 / 545 (8.62%)	33 / 529 (6.24%)	
occurrences (all)	150	128	
Immune system disorders			
ALLERGIC REACTION / HYPERSENSITIVITY			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 545 (2.57%)	95 / 529 (17.96%)	
occurrences (all)	16	164	
IMMUNE SYSTEM DISORDERS - OTHER ADVERSE EVENT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	7 / 529 (1.32%)	
occurrences (all)	0	14	
Reproductive system and breast disorders			
EJACULATORY DYSFUNCTION			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
ERECTILE DYSFUNCTION			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 545 (2.57%)	11 / 529 (2.08%)	
occurrences (all)	35	19	
LIBIDO			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	1	0	
PERINEUM			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 545 (0.37%)	5 / 529 (0.95%)		
occurrences (all)	5	9		
REPRODUCTIVE SYSTEM AND BREAST DISORDERS - OTHER ADVERSE EVENT				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	7 / 545 (1.28%)	5 / 529 (0.95%)		
occurrences (all)	16	14		
SCROTUM				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	5 / 545 (0.92%)	0 / 529 (0.00%)		
occurrences (all)	10	0		
TESTICLE				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)		
occurrences (all)	1	2		
TESTIS				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 545 (0.55%)	0 / 529 (0.00%)		
occurrences (all)	6	0		
URETER				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 545 (0.37%)	5 / 529 (0.95%)		
occurrences (all)	3	6		
URETHRA				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	5 / 545 (0.92%)	3 / 529 (0.57%)		
occurrences (all)	6	6		
VAGINA				

alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 545 (2.39%)	6 / 529 (1.13%)	
occurrences (all)	27	20	
VAGINAL DRYNESS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	1	0	
VAGINAL MUCOSITIS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
ASPIRATION			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	1	0	
BRONCHOSPASM, WHEEZING			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
CHEST/THORAX NOS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 545 (0.73%)	0 / 529 (0.00%)	
occurrences (all)	5	0	
COUGH			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			

subjects affected / exposed	28 / 545 (5.14%)	27 / 529 (5.10%)	
occurrences (all)	37	45	
DYSPNEA			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	34 / 545 (6.24%)	45 / 529 (8.51%)	
occurrences (all)	71	115	
EDEMA, LARYNX			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
LUNG (PNEUMONIA)			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 545 (1.28%)	5 / 529 (0.95%)	
occurrences (all)	8	6	
NASAL CAVITY/PARANASAL SINUS REACTIONS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	4	0	
PARANASAL			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
PLEURA			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	2 / 529 (0.38%)	
occurrences (all)	4	3	
PNEUMOTHORAX			

alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)	
occurrences (all)	2	2	
PULMONARY FIBROSIS (RADIOGRAPHIC CHANGES)			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	1	0	
RESPIRATORY, THORACIC AND MEDIASTINA - OTHER ADVERSE EVENT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	30 / 545 (5.50%)	40 / 529 (7.56%)	
occurrences (all)	37	60	
THORAX			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
Investigations			
WEIGHT LOSS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	209 / 545 (38.35%)	242 / 529 (45.75%)	
occurrences (all)	964	1132	
Cardiac disorders			
ASYSTOLE			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences (all)	0	2	
ATRIAL FIBRILLATION			
alternative dictionary used: CTC 3.0			

alternative assessment type: Systematic				
subjects affected / exposed	8 / 545 (1.47%)	9 / 529 (1.70%)		
occurrences (all)	10	26		
BIGEMINY				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)		
occurrences (all)	2	1		
CARDIAC DISORDERS - OTHER ADVERSE EVENT				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	23 / 545 (4.22%)	32 / 529 (6.05%)		
occurrences (all)	35	65		
CARDIAC ISCHEMIA/INFARCTION				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)		
occurrences (all)	1	1		
HYPERTENSION				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	48 / 545 (8.81%)	34 / 529 (6.43%)		
occurrences (all)	122	57		
HYPOTENSION				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	14 / 545 (2.57%)	19 / 529 (3.59%)		
occurrences (all)	15	37		
ISCHEMIA/INFARCTION				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	7 / 545 (1.28%)	4 / 529 (0.76%)		
occurrences (all)	19	4		

LEFT VENTRICULAR SYSTOLIC DYSFUNCTION				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences (all)	1	0		
PALPITATIONS				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 545 (0.37%)	3 / 529 (0.57%)		
occurrences (all)	3	4		
SINUS BRADYCARDIA				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences (all)	0	1		
SINUS TACHYCARDIA				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)		
occurrences (all)	3	1		
SUPRAVENTRICULAR TACHYCARDIA				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)		
occurrences (all)	0	2		
VASOVAGAL EPISODE				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	3 / 529 (0.57%)		
occurrences (all)	1	3		
VENTRICULAR TACHYCARDIA				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				

subjects affected / exposed	0 / 545 (0.00%)	3 / 529 (0.57%)	
occurrences (all)	0	5	
Nervous system disorders			
AGITATION			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 545 (0.73%)	1 / 529 (0.19%)	
occurrences (all)	4	1	
ANXIETY			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 545 (1.10%)	8 / 529 (1.51%)	
occurrences (all)	16	14	
CN I SMELL			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
CNS CEREBROVASCULAR ISCHEMIA			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	1 / 529 (0.19%)	
occurrences (all)	3	1	
CONFUSION			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)	
occurrences (all)	1	4	
DEPRESSION			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 545 (2.20%)	14 / 529 (2.65%)	
occurrences (all)	21	27	
DIZZINESS			

alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	41 / 545 (7.52%)	46 / 529 (8.70%)	
occurrences (all)	78	89	
ENCEPHALOPATHY			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	1	0	
MEMORY IMPAIRMENT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	2 / 529 (0.38%)	
occurrences (all)	8	2	
MENTAL STATUS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
NERVOUS SYSTEM DISORDERS - OTHER ADVERSE EVENT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	37 / 545 (6.79%)	64 / 529 (12.10%)	
occurrences (all)	144	156	
NEURALGIA/PERIPHERAL NERVE			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	7	0	
NEUROPATHY: MOTOR			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 545 (0.37%)	6 / 529 (1.13%)	
occurrences (all)	2	13	
NEUROPATHY: SENSORY			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	95 / 545 (17.43%)	334 / 529 (63.14%)	
occurrences (all)	246	1536	
SEIZURE			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)	
occurrences (all)	1	3	
TREMOR			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	4 / 529 (0.76%)	
occurrences (all)	7	5	
Blood and lymphatic system disorders			
BLOOD AND LYMPHATIC SYSTEM DISORDERS - OTHER ADVERSE EVENT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	125 / 545 (22.94%)	113 / 529 (21.36%)	
occurrences (all)	294	323	
HEMATOMA			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 545 (0.55%)	9 / 529 (1.70%)	
occurrences (all)	4	12	
PLATELETS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	3 / 529 (0.57%)	
occurrences (all)	0	3	

Ear and labyrinth disorders			
EAR AND LABYRINTH DISORDERS - OTHER ADVERSE EVENT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	5 / 529 (0.95%)	
occurrences (all)	2	15	
TINNITUS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
CATARACT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
EYE DISORDERS - OTHER ADVERSE EVENT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	29 / 545 (5.32%)	20 / 529 (3.78%)	
occurrences (all)	60	28	
EYE NOS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences (all)	1	1	
GLAUCOMA			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
RETINAL DETACHMENT			
alternative dictionary used: CTC 3.0			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
VISION-BLURRED VISION			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences (all)	0	6	
VISION-FLASHING LIGHTS/FLOATERS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
ABDOMEN			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	26 / 545 (4.77%)	36 / 529 (6.81%)	
occurrences (all)	45	59	
BILIARY TREE			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	1	0	
COLITIS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 545 (1.10%)	9 / 529 (1.70%)	
occurrences (all)	11	15	
CONSTIPATION			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			

subjects affected / exposed	91 / 545 (16.70%)	118 / 529 (22.31%)	
occurrences (all)	193	239	
DENTAL/TEETH/PERIDONTAL			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
DENTAL: TEETH			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	1	0	
DIARRHEA			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	372 / 545 (68.26%)	415 / 529 (78.45%)	
occurrences (all)	1274	1640	
ESOPHAGITIS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	6 / 529 (1.13%)	
occurrences (all)	2	8	
FISTULA, GI - ABDOMEN NOS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	1 / 529 (0.19%)	
occurrences (all)	2	10	
FISTULA, GI - ANUS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences (all)	0	2	
FISTULA, GI - ILEUM			
alternative dictionary used: CTC 3.0			

alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences (all)	1	0		
FISTULA, GI - RECTUM				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	7 / 545 (1.28%)	2 / 529 (0.38%)		
occurrences (all)	12	3		
FISTULA, GI - SMALL BOWEL NOS				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences (all)	0	1		
FLATULENCE				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	24 / 545 (4.40%)	19 / 529 (3.59%)		
occurrences (all)	52	34		
GASTROINTESTINAL DISORDERS - OTHER ADVERSE EVENT				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	182 / 545 (33.39%)	201 / 529 (38.00%)		
occurrences (all)	493	585		
GASTROINTESTINAL PAIN				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	213 / 545 (39.08%)	215 / 529 (40.64%)		
occurrences (all)	618	619		
HEARTBURN/DYSPEPSIA				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)		
occurrences (all)	1	2		

HEMORRHAGE, GI - ABDOMEN NOS				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 545 (0.37%)	2 / 529 (0.38%)		
occurrences (all)	2	2		
HEMORRHAGE, GI - ANUS				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 545 (0.37%)	5 / 529 (0.95%)		
occurrences (all)	4	10		
HEMORRHAGE, GI - LOWER GI NOS				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)		
occurrences (all)	1	3		
HEMORRHAGE, GI - PERITONEAL CAVITY				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences (all)	0	1		
HEMORRHAGE, GI - RECTUM				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	5 / 545 (0.92%)	8 / 529 (1.51%)		
occurrences (all)	10	10		
HEMORRHAGE, GI - STOMA				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 545 (0.37%)	2 / 529 (0.38%)		
occurrences (all)	2	3		
HEMORRHAGE, GI - VARICES (RECTAL)				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				

subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
HEMORRHOIDS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	1	0	
INCONTINENCE (ANAL)			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	31 / 545 (5.69%)	42 / 529 (7.94%)	
occurrences (all)	80	108	
INTESTINE			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	0 / 529 (0.00%)	
occurrences (all)	2	0	
JEJUNUM			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
LARGE BOWEL			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	0 / 529 (0.00%)	
occurrences (all)	2	0	
LEAK NOS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 545 (0.73%)	2 / 529 (0.38%)	
occurrences (all)	5	3	
LOWER GI NOS			
alternative dictionary used: CTC 3.0			

alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences (all)	0	1		
MUCOSA				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 545 (0.37%)	3 / 529 (0.57%)		
occurrences (all)	4	3		
MUCOSITIS/STOMATITIS (CLINICAL EXAM)				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	53 / 545 (9.72%)	55 / 529 (10.40%)		
occurrences (all)	87	101		
MUCOSITIS/STOMATITIS (FUNCTIONAL/SYMPTOMATI				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	34 / 545 (6.24%)	51 / 529 (9.64%)		
occurrences (all)	68	88		
NAUSEA				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	187 / 545 (34.31%)	318 / 529 (60.11%)		
occurrences (all)	477	978		
NECROSIS, GI - ILEUM				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)		
occurrences (all)	0	3		
NECROSIS, GI - RECTUM				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				

subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	1	0	
NECROSIS, GI - STOMA			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
OBSTRUCTION, GI - COLON			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	1	0	
OBSTRUCTION, GI - GALLBLADDER			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences (all)	2	1	
OBSTRUCTION, GI - ILEUM			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences (all)	1	1	
OBSTRUCTION, GI - SMALL BOWEL NOS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	3 / 529 (0.57%)	
occurrences (all)	2	3	
OBSTRUCTION, GI - STOMA			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences (all)	1	2	
PERFORATION, GI - COLON			

alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 545 (0.37%)	0 / 529 (0.00%)		
occurrences (all)	2	0		
PERFORATION, GI - DUODENUM				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)		
occurrences (all)	1	1		
PERFORATION, GI - RECTUM				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences (all)	1	0		
PERFORATION, GI - SMALL BOWEL NOS				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)		
occurrences (all)	0	2		
PERISTOMAL				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)		
occurrences (all)	1	2		
PHARYNX				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)		
occurrences (all)	1	1		
PROCTITIS				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				

subjects affected / exposed	110 / 545 (20.18%)	101 / 529 (19.09%)	
occurrences (all)	252	256	
PROLAPSE OF STOMA, GI			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 545 (0.55%)	5 / 529 (0.95%)	
occurrences (all)	12	7	
RECTUM			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	42 / 545 (7.71%)	52 / 529 (9.83%)	
occurrences (all)	111	114	
SMALL BOWEL			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)	
occurrences (all)	1	2	
SMALL BOWEL NOS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	3 / 529 (0.57%)	
occurrences (all)	1	4	
STOMACH			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	22 / 545 (4.04%)	34 / 529 (6.43%)	
occurrences (all)	41	52	
TASTE ALTERATION (DYSGEUSIA)			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences (all)	0	4	
ULCER, GI - RECTUM			
alternative dictionary used: CTC 3.0			

alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	1	0	
ULCER, GI - STOMACH			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences (all)	0	3	
ULCERATION			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	3 / 529 (0.57%)	
occurrences (all)	1	3	
VOMITING			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	82 / 545 (15.05%)	219 / 529 (41.40%)	
occurrences (all)	138	414	
Hepatobiliary disorders			
CHOLECYSTITIS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
HEPATIC			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences (all)	8	3	
HEPATOBILIARY DISORDERS - OTHER ADVERSE EVENT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	4 / 529 (0.76%)	
occurrences (all)	1	4	
PANCREATITIS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences (all)	1	1	
Skin and subcutaneous tissue disorders			
BREAST			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences (all)	0	2	
DERMATITIS ASSOCIATED WITH RT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	156 / 545 (28.62%)	119 / 529 (22.50%)	
occurrences (all)	341	253	
DRY SKIN			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	28 / 545 (5.14%)	8 / 529 (1.51%)	
occurrences (all)	67	8	
FACIAL			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences (all)	1	1	
FLUSHING			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)	
occurrences (all)	1	3	
HAIR LOSS/ALOPECIA			

alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	24 / 545 (4.40%)	23 / 529 (4.35%)		
occurrences (all)	60	48		
HAND-FOOT SKIN REACTION				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	180 / 545 (33.03%)	138 / 529 (26.09%)		
occurrences (all)	614	369		
HYPERPIGMENTATION				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 545 (0.37%)	1 / 529 (0.19%)		
occurrences (all)	7	2		
INJECTION SITE REACTION				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	4 / 545 (0.73%)	39 / 529 (7.37%)		
occurrences (all)	7	72		
NAIL CHANGES				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 545 (0.37%)	3 / 529 (0.57%)		
occurrences (all)	6	5		
RASH/DESQUAMATION				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)		
occurrences (all)	1	0		
SKIN AND SUBCUTANEOUS TISSUE DISORDERS - OTHER ADVERSE EVENT				
alternative dictionary used: CTC 3.0				
alternative assessment type: Systematic				

subjects affected / exposed	152 / 545 (27.89%)	118 / 529 (22.31%)	
occurrences (all)	327	262	
TONGUE			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	3 / 529 (0.57%)	
occurrences (all)	1	3	
WOUND COMPLICATION, NON-INFECTIOUS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	40 / 545 (7.34%)	34 / 529 (6.43%)	
occurrences (all)	58	59	
Renal and urinary disorders			
BLADDER			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 545 (2.02%)	11 / 529 (2.08%)	
occurrences (all)	28	13	
BLADDER (URINARY)			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	1 / 529 (0.19%)	
occurrences (all)	4	1	
BLADDER SPASMS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	3	0	
CYSTITIS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	75 / 545 (13.76%)	73 / 529 (13.80%)	
occurrences (all)	153	125	
FISTULA, GU - VAGINA			

alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	1 / 529 (0.19%)	
occurrences (all)	2	1	
HEMORRHAGE, GU - URINARY NOS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
INCONTINENCE (URINARY)			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	22 / 545 (4.04%)	27 / 529 (5.10%)	
occurrences (all)	55	66	
KIDNEY			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences (all)	2	1	
OBSTRUCTION, GU - URETER			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
PROSTATE			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	1 / 529 (0.19%)	
occurrences (all)	2	1	
RENAL AND URINARY DISORDERS - OTHER ADVERSE EVENT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			

subjects affected / exposed	100 / 545 (18.35%)	100 / 529 (18.90%)	
occurrences (all)	192	205	
RENAL FAILURE			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 545 (2.57%)	27 / 529 (5.10%)	
occurrences (all)	18	36	
URINARY FREQUENCY/URGENCY			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	0 / 529 (0.00%)	
occurrences (all)	3	0	
URINARY TRACT NOS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 545 (3.49%)	13 / 529 (2.46%)	
occurrences (all)	34	23	
Endocrine disorders			
ENDOCRINE DISORDERS - OTHER ADVERSE EVENT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 545 (1.65%)	7 / 529 (1.32%)	
occurrences (all)	14	18	
THYROID			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	2 / 529 (0.38%)	
occurrences (all)	10	6	
Musculoskeletal and connective tissue disorders			
BUTTOCK			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 545 (0.37%)	5 / 529 (0.95%)	
occurrences (all)	2	6	
EXTREMITY-LIMB			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
EXTREMITY-LOWER			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences (all)	0	3	
FRACTURE			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	3 / 529 (0.57%)	
occurrences (all)	5	6	
MUSCLE			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 545 (2.39%)	10 / 529 (1.89%)	
occurrences (all)	24	22	
MUSCULOSKELETAL AND CONNECTIVE TISSU - OTHER ADVERSE EVENT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 545 (2.02%)	13 / 529 (2.46%)	
occurrences (all)	21	20	
SEROMA			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 545 (0.37%)	1 / 529 (0.19%)	
occurrences (all)	4	1	
TENDON			

alternative dictionary used: CTC 3.0 alternative assessment type: Systematic subjects affected / exposed occurrences (all)	3 / 545 (0.55%) 5	0 / 529 (0.00%) 0	
Infections and infestations ANAL SPHINCTER alternative dictionary used: CTC 3.0 alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 545 (0.00%) 0	1 / 529 (0.19%) 2	
ANAL/PERIANAL alternative dictionary used: CTC 3.0 alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 545 (0.00%) 0	1 / 529 (0.19%) 1	
CATHETER-RELATED alternative dictionary used: CTC 3.0 alternative assessment type: Systematic subjects affected / exposed occurrences (all)	2 / 545 (0.37%) 2	4 / 529 (0.76%) 5	
DENTAL-TOOTH alternative dictionary used: CTC 3.0 alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 545 (0.18%) 1	0 / 529 (0.00%) 0	
ESOPHAGUS alternative dictionary used: CTC 3.0 alternative assessment type: Systematic subjects affected / exposed occurrences (all)	1 / 545 (0.18%) 4	0 / 529 (0.00%) 0	
FEBRILE NEUTROPENIA alternative dictionary used: CTC 3.0 alternative assessment type: Systematic			

subjects affected / exposed	1 / 545 (0.18%)	2 / 529 (0.38%)	
occurrences (all)	1	2	
INFECTIONS AND INFESTATIONS - OTHER ADVERSE EVENT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	129 / 545 (23.67%)	122 / 529 (23.06%)	
occurrences (all)	206	201	
MIDDLE EAR			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	1	0	
ORAL CAVITY			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	2	0	
PERITONEAL CAVITY			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 545 (0.73%)	8 / 529 (1.51%)	
occurrences (all)	5	15	
UPPER AIRWAY NOS			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
ALKALINE PHOSPHATASE			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 545 (0.18%)	0 / 529 (0.00%)	
occurrences (all)	6	0	
ANOREXIA			

alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	95 / 545 (17.43%)	142 / 529 (26.84%)	
occurrences (all)	201	336	
CREATININE			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	2 / 529 (0.38%)	
occurrences (all)	0	3	
DEHYDRATION			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 545 (2.57%)	29 / 529 (5.48%)	
occurrences (all)	19	37	
GLOMERULAR FILTRATION RATE			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	1	
LIPASE			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	2	
LYMPHOPENIA			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	1 / 529 (0.19%)	
occurrences (all)	0	3	
METABOLISM AND NUTRITION DISORDERS - OTHER ADVERSE EVENT			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			

subjects affected / exposed	34 / 545 (6.24%)	43 / 529 (8.13%)	
occurrences (all)	68	126	
PROTEINURIA			
alternative dictionary used: CTC 3.0			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 545 (0.00%)	3 / 529 (0.57%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 June 2011	The protocol was further amended on 28/06/2011 for urgent safety reasons to follow the recommendations of the Data Safety Monitoring Board and highlights the higher toxicity profile of the experimental arm in the informed consent form. In addition, several protocol modifications were done to make the timelines more close to clinical reality such as baseline evaluation and start of treatment after surgery. It was clarified that endorectal ultrasound at baseline is not necessary when high resolution MRI is also performed and there is also no need for an abdominal US when CT of the abdomen has already been performed for staging. The stratification factor 'availability of MRI at the center' was replaced by the method of locoregional staging (EUS+MRI vs. EUS+CTscan vs. MRI alone) in order to stratify randomization for the method actually used to stage the patient at the center (Amendment 5).
15 May 2012	Amendment 6 dated on 15/05/2012 resolved an existing inconsistency in the definition of the primary endpoint disease free survival with regards to patients achieving histopathological R1 resection. While patients achieving histopathological R0 or R1 resection had to receive postoperative protocol treatment, patients with R1 resection would have been considered as failures for the primary endpoint at the time of surgery. This amendment stipulated that patients with R1 resection will not be considered as failures at the time of surgery in alignment with medical judgment as they may benefit from the postoperative protocol treatment. Other minor clarifications to the definition of the trial endpoints have been given.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported