



## Clinical trial results:

### A Phase II study of neoadjuvant chemotherapy given before SCPRT as treatment for patients with MRI-staged operable rectal cancer at high risk of metastatic relapse

#### Summary

EudraCT number	2010-023083-40
Trial protocol	GB
Global end of trial date	29 November 2015

#### Results information

Result version number	v1 (current)
This version publication date	09 July 2017
First version publication date	09 July 2017
Summary attachment (see zip file)	COPERNICUS EudraCT final study report version1 (COPERNICUS EudraCT final study report version1.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	SPON830-10
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##### Additional study identifiers

ISRCTN number	ISRCTN10052456
ClinicalTrials.gov id (NCT number)	NCT01263171
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	Cardiff University
Sponsor organisation address	30-36 Newport Road, Cardiff, United Kingdom, CF24 0DE
Public contact	Martina Svodobova, Wales Cancer Trials Unit, 0044 2920687463, COPERNICUS@cardiff.ac.uk
Scientific contact	Chris Hurt, Wales Cancer Trials Unit, 0044 2920687463, COPERNICUS@cardiff.ac.uk

Notes:

##### Paediatric regulatory details

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

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 March 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 November 2015
Global end of trial reached?	Yes
Global end of trial date	29 November 2015
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The principal research question is whether in MRI-defined operable rectal cancer patients, it is feasible to treat for eight weeks with oxaliplatin/5-Fluorouracil chemotherapy and then give a short course of preoperative radiotherapy (SCPRT) immediately before surgical removal of the tumour. This will be measured by calculating the proportion of patients successfully completing surgery.

Protection of trial subjects:

IDMC

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	35
From 65 to 84 years	25
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

147 were assessed for eligibility. 60 registered.

Excluded (n=87)

Not meeting inclusion criteria (n=69)

Disease metastatic (n=25)

Other aspect of disease e.g. wrong stage, not measurable (n=22)

Patient fitness/co-morbidity (n=8)

Previous malignancy (n=4)

Clinician choice (n=4)

Other (n=4)

Unknown (n=2)

Declined to participate (n=18)

### Period 1

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

### Arms

Arm title	Single arm
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Arm description: -

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

Dosage and administration details:

Oxaliplatin is administered during neo-adjuvant (OxMdG) and adjuvant chemotherapy (OxMdG or OxCap).

Four 14-day cycles of OxMdG during neoadjuvant chemotherapy using Oxaliplatin/5-Fluorouracil (OxMdG).

Eight 14 day cycles of OxMdG during adjuvant chemotherapy or eight 14 day cycles of OxCap.

Day 1 of each cycle: oxaliplatin 85 mg/m<sup>2</sup> IV infusion, over 2 hours, in 250-500 mL 5% glucose.

Investigational medicinal product name	5-fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Four 14 day cycles during neo-adjuvant chemotherapy.

Eight 14 day cycles during adjuvant chemotherapy

Day 1 of each cycle: 5-FU 400 mg/m<sup>2</sup> IV bolus injection over 5 minutes

Investigational medicinal product name	5-fluorouracil
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous drip use

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Dosage and administration details:

Four 14 day cycles during neo-adjuvant chemotherapy

Eight 14 day cycles during adjuvant chemotherapy

Starting Day 1 of each cycle:

5-FU 2400 mg/m<sup>2</sup> IV infusion over 46 hours

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Eight 14 day cycles during adjuvant chemotherapy as alternative to 5-FU

Day 1, evening: Capecitabine 1000 mg/m<sup>2</sup> p.o.

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Day 2-9: Capecitabine orally 1000 mg/m<sup>2</sup> p.o. twice daily

Day 10, morning: Capecitabine orally 1000 mg/m<sup>2</sup> p.o.

Days 11-14: no treatment

<b>Number of subjects in period 1</b>	Single arm
Started	60
Completed	57
Not completed	3
Consent withdrawn by subject	1
Physician decision	1
Adverse event, non-fatal	1

## Baseline characteristics

### Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	60	60	
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	63		
inter-quartile range (Q1-Q3)	56.5 to 70	-	
Gender categorical			
Units: Subjects			
Female	16	16	
Male	44	44	
ECOG performance status			
Units: Subjects			
Zero	55	55	
One	5	5	
Type of primary tumour			
Units: Subjects			
Adenocarcinoma	60	60	
Missing	0	0	
Rigid sigmoidoscopy			
Units: Subjects			
Performed	34	34	
Not performed	25	25	
Unknown	1	1	
MRI-T stage			
Units: Subjects			
T2	1	1	
T3a	17	17	
T3b	24	24	
T3c	14	14	
T3d	1	1	

T4a	3	3	
MRI-N stage Units: Subjects			
N0	7	7	
N1	39	39	
N2	14	14	
MRI-CRM involvement Units: Subjects			
Clear	59	59	
Missing data	1	1	
MRI-Extramural vascular invasion Units: Subjects			
Positive	25	25	
Negative	35	35	
Missing	0	0	
Predominant differentiation of primary tumour Units: Subjects			
Well	5	5	
Moderate	49	49	
Poor	2	2	
Unknown	4	4	
Number of baseline MRI risk factors out of T>=3c or N1-2 or EMVI+ Units: Subjects			
One	35	35	
Two	14	14	
Three	11	11	
Missing EMVI data	0	0	
Time from histopathological diagnosis to registration Units: Days median inter-quartile range (Q1-Q3)	34.5 28.5 to 46.5	-	
Rigid sigmoidoscopy-time from sigmoidoscopy to registration Units: Days median inter-quartile range (Q1-Q3)	44.5 35 to 54	-	
Rigid sigmoidoscopy-distance to anal verge of inferior aspect of tumour Units: millimetres median inter-quartile range (Q1-Q3)	80 60 to 100	-	
Time from MRI scan to registration Units: Weeks median inter-quartile range (Q1-Q3)	3.7 2.6 to 4.6	-	
MRI-Craniocaudal length Units: millimetres arithmetic mean standard deviation	49.1 ± 11.9	-	
MRI-height from anal verge			

Units: millimetres			
arithmetic mean	78.7		
standard deviation	± 21.5	-	

## End points

### End points reporting groups

Reporting group title	Single arm
Reporting group description: -	

### Primary: Efficacy-proportion of patients having surgery

End point title	Efficacy-proportion of patients having surgery <sup>[1]</sup>
End point description:	

End point type	Primary
End point timeframe:	
Up to surgery	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: This is a single arm study and no comparison is being made

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Subjects				
Had surgery	57			
Did not have surgery	3			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Compliance-achieved total dose of 5FU/capecitabine (neo-adjuvant)

End point title	Compliance-achieved total dose of 5FU/capecitabine (neo-adjuvant)
End point description:	

End point type	Secondary
End point timeframe:	
During neo-adjuvant chemotherapy	



<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Percentage				
median (inter-quartile range (Q1-Q3))	100 (97 to 100)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Compliance-achieved dose intensity for 5FU/capecitabine (neo-adjuvant)

End point title	Compliance-achieved dose intensity for 5FU/capecitabine (neo-adjuvant)
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End point description:

End point type	Secondary
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End point timeframe:

During neo-adjuvant chemotherapy

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Percentage				
median (inter-quartile range (Q1-Q3))	100 (75 to 100)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Compliance-achieved total dose of 5FU/capecitabine during adjuvant chemotherapy

End point title	Compliance-achieved total dose of 5FU/capecitabine during adjuvant chemotherapy
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End point description:

End point type	Secondary
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End point timeframe:

During adjuvant chemotherapy

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: Percentage				
median (inter-quartile range (Q1-Q3))	80 (5 to 88)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Compliance-achieved dose intensity of 5FU/capecitabine (adjuvant)

End point title	Compliance-achieved dose intensity of 5FU/capecitabine (adjuvant)
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End point description:

End point type	Secondary
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End point timeframe:

During adjuvant chemotherapy

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: Percentage				
median (inter-quartile range (Q1-Q3))	63 (5 to 81)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Compliance-achieved total dose of oxaliplatin (neo-adjuvant)

End point title	Compliance-achieved total dose of oxaliplatin (neo-adjuvant)
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End point description:

End point type	Secondary
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End point timeframe:

During neo-adjuvant chemotherapy

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Percentage				
median (inter-quartile range (Q1-Q3))	100 (93 to 100)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Compliance-achieved dosse intensity of oxaliplatin (neo-adjuvant)

End point title	Compliance-achieved dosse intensity of oxaliplatin (neo-adjuvant)
End point description:	
End point type	Secondary
End point timeframe:	
During neo-adjuvant chemotherapy	

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Percentage				
median (inter-quartile range (Q1-Q3))	100 (75 to 100)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Compliance-achieved total dose of oxaliplatin (adjuvant)

End point title	Compliance-achieved total dose of oxaliplatin (adjuvant)
End point description:	
End point type	Secondary
End point timeframe:	
During adjuvant chemotherapy	

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: Percentage				
median (inter-quartile range (Q1-Q3))	58 (0 to 98)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Compliance-achieved dose intensity of oxaliplatin (adjuvant)

End point title	Compliance-achieved dose intensity of oxaliplatin (adjuvant)
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End point description:

End point type	Secondary
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End point timeframe:

During adjuvant chemotherapy

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: Percentage				
median (inter-quartile range (Q1-Q3))	45 (0 to 77)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Compliance-achieved planned dose for radiotherapy

End point title	Compliance-achieved planned dose for radiotherapy
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End point description:

End point type	Secondary
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End point timeframe:

During radiotherapy

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	58			
Units: percentage				
number (not applicable)	100			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Pathological complete regression

End point title	Pathological complete regression
End point description:	
End point type	Secondary
End point timeframe:	
Post-surgery	

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Number of patients	7			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Biopsy tumour cell density

End point title	Biopsy tumour cell density
End point description:	
End point type	Secondary
End point timeframe:	
Post-surgery	

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Density				
median (inter-quartile range (Q1-Q3))	37.2 (22.7 to 44.2)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Resection greatest tumour cell density

End point title	Resection greatest tumour cell density
End point description:	
End point type	Secondary
End point timeframe:	
Post-surgery	

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Density				
median (inter-quartile range (Q1-Q3))	21.4 (2.7 to 39.1)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Resection luminal tumour cell density

End point title	Resection luminal tumour cell density
End point description:	
End point type	Secondary
End point timeframe:	
Post-surgery	

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Density				
median (inter-quartile range (Q1-Q3))	17.6 (2.7 to 34.4)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Resection whole tumour cell density

End point title	Resection whole tumour cell density
End point description:	
End point type	Secondary
End point timeframe:	
Post-surgery	

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Density				
median (inter-quartile range (Q1-Q3))	8.7 (1.3 to 16.1)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Resction whole TCD as % of biopsy TCD

End point title	Resction whole TCD as % of biopsy TCD
End point description:	
End point type	Secondary
End point timeframe:	
Post-surgery	

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: percentage				
median (inter-quartile range (Q1-Q3))	19.4 (3.2 to 53.8)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Downstage of T-stage

End point title	Downstage of T-stage
End point description:	
End point type	Secondary
End point timeframe:	
Post neo-adjuvant chemotherapy	

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Number of patients	44			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Downstage of N stage

End point title	Downstage of N stage
End point description:	
End point type	Secondary
End point timeframe:	
Post neo-adjuvant chemotherapy	



<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Number of patients	36			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Tumour regression grade

End point title	Tumour regression grade
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End point description:

End point type	Secondary
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End point timeframe:

Post-surgery

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	57			
Units: Number of patients				
No regression	7			
Minimal regression	17			
Moderate regression	14			
Good regression	12			
Complete regression	7			
Unknown	0			

## Statistical analyses

No statistical analyses for this end point

### Secondary: Progression free survival

End point title	Progression free survival
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End point description:

End point type	Secondary
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End point timeframe:

Overall

<b>End point values</b>	Single arm			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: percent				
number (confidence interval 95%)	86.2 (74.3 to 92.9)			

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Overall

Assessment type	Systematic
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### Dictionary used

Dictionary name	CTCAE
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Dictionary version	4
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### Reporting groups

Reporting group title	Neo-adjuvant
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Reporting group description: -

Reporting group title	Adjuvant
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Reporting group description:

Adjuvant chemotherapy after surgery

Reporting group title	Post-surgery complications
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Reporting group description: -

Serious adverse events	Neo-adjuvant	Adjuvant	Post-surgery complications
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 60 (40.00%)	15 / 45 (33.33%)	0 / 57 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Thrombocytopenia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Anastomotic leak			
subjects affected / exposed	1 / 60 (1.67%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Thrombosis right arm			
subjects affected / exposed	0 / 60 (0.00%)	1 / 45 (2.22%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vascular access complication			
subjects affected / exposed	1 / 60 (1.67%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thromboembolic event			
subjects affected / exposed	1 / 60 (1.67%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 60 (1.67%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fever			
subjects affected / exposed	0 / 60 (0.00%)	1 / 45 (2.22%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 60 (0.00%)	1 / 45 (2.22%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			

subjects affected / exposed	0 / 60 (0.00%)	3 / 45 (6.67%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic/bowel obstruction			
subjects affected / exposed	0 / 60 (0.00%)	1 / 45 (2.22%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecal impaction			
subjects affected / exposed	0 / 60 (0.00%)	1 / 45 (2.22%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mechanical bowel obstruction			
subjects affected / exposed	0 / 60 (0.00%)	1 / 45 (2.22%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal anastomatic leak			
subjects affected / exposed	1 / 60 (1.67%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in right loin			
subjects affected / exposed	0 / 60 (0.00%)	1 / 45 (2.22%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal ascites			

subjects affected / exposed	1 / 60 (1.67%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucositis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laparotomy and small bowel resection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 45 (2.22%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anorectal infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory infection			
subjects affected / exposed	0 / 60 (0.00%)	2 / 45 (4.44%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary tract infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 45 (2.22%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	2 / 60 (3.33%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	1 / 60 (1.67%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Chest pain			
subjects affected / exposed	2 / 60 (3.33%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout (joint infection)			
subjects affected / exposed	1 / 60 (1.67%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Wound infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 45 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	Neo-adjuvant	Adjuvant	Post-surgery complications
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 60 (20.00%)	5 / 45 (11.11%)	10 / 57 (17.54%)
Investigations			
Neutrophil count decreased			
subjects affected / exposed	12 / 60 (20.00%)	5 / 45 (11.11%)	0 / 57 (0.00%)
occurrences (all)	12	5	0
Surgical and medical procedures			
Second operation required			
subjects affected / exposed	0 / 60 (0.00%)	0 / 45 (0.00%)	4 / 57 (7.02%)
occurrences (all)	0	0	4
Infections and infestations			
Pelvic infection/collection requiring draining			
subjects affected / exposed	0 / 60 (0.00%)	0 / 45 (0.00%)	10 / 57 (17.54%)
occurrences (all)	0	0	10
Serious infection-wound			
subjects affected / exposed	0 / 60 (0.00%)	0 / 45 (0.00%)	6 / 57 (10.53%)
occurrences (all)	0	0	6





## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

N/A
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Notes: