# 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 |

### 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 reasearch 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 |

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/m2 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/m2 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 |

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/m2 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/m2 p.o.
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Day 2-9: Capecitabine orally 1000 mg/m2 p.o.twice daily
Day 10, morning: Capecitabine orally 1000 mg/m2 p.o.
Days 11-14: no treatment

| **Number of subjects in period 1** | 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<br>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<br>Units: years | | | |
| median | 63 | | |
| inter-quartile range (Q1-Q3) | 56.5 to 70 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 16 | 16 | |
| Male | 44 | 44 | |
| ECOG performance status<br>Units: Subjects | | | |
| Zero | 55 | 55 | |
| One | 5 | 5 | |
| Type of primary tumour<br>Units: Subjects | | | |
| Adenocarcinoma | 60 | 60 | |
| Missing | 0 | 0 | |
| Rigid sigmoidoscopy<br>Units: Subjects | | | |
| Performed | 34 | 34 | |
| Not performed | 25 | 25 | |
| Unknown | 1 | 1 | |
| MRI-T stage<br>Units: Subjects | | | |
| T2 | 1 | 1 | |
| T3a | 17 | 17 | |
| T3b | 24 | 24 | |
| T3c | 14 | 14 | |
| T3d | 1 | 1 | |

| | | | |
|---|---|---|---|
| T4a | 3 | 3 | |
| MRI-N stage<br>Units: Subjects | | | |
| N0 | 7 | 7 | |
| N1 | 39 | 39 | |
| N2 | 14 | 14 | |
| MRI-CRM involvement<br>Units: Subjects | | | |
| Clear | 59 | 59 | |
| Missing data | 1 | 1 | |
| MRI-Extramural vascular invasion<br>Units: Subjects | | | |
| Positive | 25 | 25 | |
| Negative | 35 | 35 | |
| Missing | 0 | 0 | |
| Predominant differentiation of primary tumour<br>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+<br>Units: Subjects | | | |
| One | 35 | 35 | |
| Two | 14 | 14 | |
| Three | 11 | 11 | |
| Missing EMVI data | 0 | 0 | |
| Time from histopathological diagnosis to registration<br>Units: Days | | | |
| median | 34.5 | | |
| inter-quartile range (Q1-Q3) | 28.5 to 46.5 | - | |
| Rigid sigmoidoscopy-time from sigmoidoscopy to registration<br>Units: Days | | | |
| median | 44.5 | | |
| inter-quartile range (Q1-Q3) | 35 to 54 | - | |
| Rigid sigmoidoscopy-distance to anal verge of inferior aspect of tumour<br>Units: millimetres | | | |
| median | 80 | | |
| inter-quartile range (Q1-Q3) | 60 to 100 | - | |
| Time from MRI scan to registration<br>Units: Weeks | | | |
| median | 3.7 | | |
| inter-quartile range (Q1-Q3) | 2.6 to 4.6 | - | |
| MRI-Craniocaudal length<br>Units: millimetres | | | |
| arithmetic mean | 49.1 | | |
| standard deviation | ± 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[1] |
|---|---|

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

| End point values | 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

| End point values | 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) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

During neo-adjuvant chemotherapy

| End point values | 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 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

During adjuvant chemotherapy

| End point values | 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) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

During adjuvant chemotherapy

| End point values | 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) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

During neo-adjuvant chemotherapy

| End point values | 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

| End point values | 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

| End point values | 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) |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

During adjuvant chemotherapy

| End point values | 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 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

During radiotherapy

| End point values | 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

| End point values | 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

| End point values | 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

| End point values | 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 lumenal tumour cell density

| End point title | Resection lumenal tumour cell density |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Post-surgery

| End point values | 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

| End point values | 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

| End point values | 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

| End point values | 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

| End point values | 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 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Post-surgery

| End point values | 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 |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Overall

| End point values | 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 |
| **Dictionary used** | |
| Dictionary name | CTCAE |
| Dictionary version | 4 |
| **Reporting groups** | |
| Reporting group title | Neo-adjuvant |
| Reporting group description: - | |
| Reporting group title | Adjuvant |
| Reporting group description: Adjuvant chemotherapy after surgery | |
| Reporting group title | Post-surgery complications |
| 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 %

| **Non-serious adverse events** | 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

## 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 |

Notes: