Clinical trial results:
A Multi-Centre Randomised Clinical Trial of Biomarker-Driven Maintenance Treatment for First-Line Metastatic Colorectal Cancer (MODUL)

Summary

EudraCT number	2014-001017-61
Trial protocol	IT GB DE PT DK SK NL FR SE BE GR ES SI CY
Global end of trial date	

Results information

Result version number	v1
This version publication date	12 June 2020
First version publication date	12 June 2020

Trial information

Trial identification

Sponsor protocol code	MO29112

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02291289
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
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Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	31 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 May 2019
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study is to evaluate the progression free survival (PFS) within each cohort.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 April 2015
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	Argentina: 4
Country: Number of subjects enrolled	Belgium: 24
Country: Number of subjects enrolled	Bosnia and Herzegovina: 5
Country: Number of subjects enrolled	Brazil: 41
Country: Number of subjects enrolled	Denmark: 15
Country: Number of subjects enrolled	Egypt: 5
Country: Number of subjects enrolled	France: 50
Country: Number of subjects enrolled	Germany: 91
Country: Number of subjects enrolled	Greece: 36
Country: Number of subjects enrolled	Italy: 94
Country: Number of subjects enrolled	Mexico: 17
Country: Number of subjects enrolled	Netherlands: 16
Country: Number of subjects enrolled	Poland: 21
Country: Number of subjects enrolled	Portugal: 12
Country: Number of subjects enrolled	Korea, Republic of: 24
Country: Number of subjects enrolled	Russian Federation: 8
Country: Number of subjects enrolled	Serbia: 9
Country: Number of subjects enrolled	Slovakia: 1
Country: Number of subjects enrolled	Spain: 45
Country: Number of subjects enrolled	Sweden: 3
Country: Number of subjects enrolled	Turkey: 27
Country: Number of subjects enrolled	United Kingdom: 61
Worldwide total number of subjects	609
EEA total number of subjects	469

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)	364
From 65 to 84 years	243
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

To be eligible for the study, patients provided a primary tumour sample for biomarker assessment. This sample from the original diagnosis was used for the biomarker assessment which determined treatment assignment during the Maintenance Treatment Phase.

Period 1

Period 1 title	Induction Treatment
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

All participants will receive either eight 2-week cycles of 5-fluorouracil (5-FU)/ leucovorin calcium (LV) and oxaliplatin (FOLFOX) in combination with bevacizumab, or six 2-week cycles of FOLFOX in combination with bevacizumab, followed by two 2-week cycles of 5-FU/LV with bevacizumab.

Arm type	Induction Treatment
Investigational medicinal product name	5-fluorouracil (5-FU), leucovorin calcium (LV), and Oxaliplatin (FOLFOX)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered per the Investigator's discretion in accordance with locally approved prescribing information.

Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	Avastin
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5 mg/kg bevacizumab via 15-30 minute IV infusion on Day 1 of every 2-week cycle per local prescribing information

Investigational medicinal product name	5-FU/LV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1600-2400 mg/m^2 5-FU via 46-hour IV infusion in combination with 400 mg/m^2 LV via 2-hour infusion on Day 1 of every 2-week cycle until disease progression or death from any cause, whichever occurs first.

Arm title	Cohort 2

Arm description:

All participants will receive either eight 2-week cycles of 5-fluorouracil (5-FU)/ leucovorin calcium (LV) and oxaliplatin (FOLFOX) in combination with bevacizumab, or six 2-week cycles of FOLFOX in

combination with bevacizumab, followed by two 2-week cycles of 5-FU/LV with bevacizumab.

Arm type	Induction Treatment
Investigational medicinal product name	5-fluorouracil (5-FU), leucovorin calcium (LV), and Oxaliplatin (FOLFOX)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered per the Investigator's discretion in accordance with locally approved prescribing information.

Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	Avastin
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5 mg/kg bevacizumab via 15-30 minute IV infusion on Day 1 of every 2-week cycle per local prescribing information

Investigational medicinal product name	5-FU/LV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1600-2400 mg/m^2 5-FU via 46-hour IV infusion in combination with 400 mg/m^2 LV via 2-hour infusion on Day 1 of every 2-week cycle until disease progression or death from any cause, whichever occurs first.

Arm title	Cohort 3

Arm description:

All participants will receive either eight 2-week cycles of 5-fluorouracil (5-FU)/ leucovorin calcium (LV) and oxaliplatin (FOLFOX) in combination with bevacizumab, or six 2-week cycles of FOLFOX in combination with bevacizumab, followed by two 2-week cycles of 5-FU/LV with bevacizumab.

Arm type	Induction Treatment
Investigational medicinal product name	5-fluorouracil (5-FU), leucovorin calcium (LV), and Oxaliplatin (FOLFOX)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered per the Investigator's discretion in accordance with locally approved prescribing information.

Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	Avastin
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5 mg/kg bevacizumab via 15-30 minute IV infusion on Day 1 of every 2-week cycle per local prescribing information

Investigational medicinal product name	5-FU/LV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion

Routes of administration	Intravenous use

Dosage and administration details:

1600-2400 mg/m^2 5-FU via 46-hour IV infusion in combination with 400 mg/m^2 LV via 2-hour infusion on Day 1 of every 2-week cycle until disease progression or death from any cause, whichever occurs first.

Arm title	Cohort 4

Arm description:

All participants will receive either eight 2-week cycles of 5-fluorouracil (5-FU)/ leucovorin calcium (LV) and oxaliplatin (FOLFOX) in combination with bevacizumab, or six 2-week cycles of FOLFOX in combination with bevacizumab, followed by two 2-week cycles of 5-FU/LV with bevacizumab.

Arm type	Induction Treatment
Investigational medicinal product name	5-fluorouracil (5-FU), leucovorin calcium (LV), and Oxaliplatin (FOLFOX)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered per the Investigator's discretion in accordance with locally approved prescribing information.

Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	Avastin
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5 mg/kg bevacizumab via 15-30 minute IV infusion on Day 1 of every 2-week cycle per local prescribing information

Investigational medicinal product name	5-FU/LV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1600-2400 mg/m^2 5-FU via 46-hour IV infusion in combination with 400 mg/m^2 LV via 2-hour infusion on Day 1 of every 2-week cycle until disease progression or death from any cause, whichever occurs first.

Number of subjects in period 1	Cohort 1	Cohort 2	Cohort 3
Started	60	445	5
Completed	58	436	5
Not completed	2	9	0
Not Dosed	2	9	-

Number of subjects in period 1	Cohort 4
Started	99
Completed	98
Not completed	1

Not Dosed	1

Period 2

Period 2 title	Maintenance Treatment Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Cohort 1: 5-FU/LV,cetuximab,vemurafenib

Arm description:

Participants with v-raf murine sarcoma viral oncogene homolog B1 mutation positive (BRAFmut)/human epidermal growth factor receptor 2 negative (HER2-)/microsatellite stable (MSS)/rat sarcoma wild type (RASwt) will receive 1600-2400 milligrams per square meter (mg/m^2) 5-FU via 46-hour intravenous (IV) infusion in combination with 400 mg/m^2 LV via 2-hour infusion on Day 1 of every 2-week cycle with 500 mg/m^2 cetuximab via infusion on Day 1 of every 2-week cycle and 960 milligrams (mg) vemurafenib twice daily (BID) by mouth.

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

Dosage and administration details:

500 mg/m^2 via IV infusion on Day 1 of every 2-week cycle

Investigational medicinal product name	Vemurafenib
Investigational medicinal product code	
Other name	RO5185426
Pharmaceutical forms	Solution for infusion, Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

960 mg vermurafenib BID by mouth

Investigational medicinal product name	5-FU/LV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1600-2400 mg/m^2 5-FU via 46-hour IV infusion in combination with 400 mg/m^2 LV via 2-hour infusion on Day 1 of every 2-week cycle until disease progression per the Investigator's assessment using modified Response Evaluation Criteria in Solid Tumors or death from any cause, whichever occurs first.

Arm title	Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab

Arm description:

Per Investigator discretion, participants will receive fluoropyrimidine (5-FU/LV or capecitabine) at a dose and schedule per the Investigator's discretion in accordance with locally approved prescribing information and 5 mg/kg bevacizumab via 1-30 minute IV on Day 1 of every 2-week cycle.

Arm type	Active comparator
Investigational medicinal product name	5-FU/LV or capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Per Investigator's discretion: 1600-2400 mg/m^2 administered via 46-hour IV infusion on Day 1 of every 2-week cycle and LV 400 mg/m^2 administered via a 2-hour infusion on Day 1 every 2 weeks or 1000 mg/m^2 twice-daily capecitabine (BID) by mouth given days 1-14 every 2 weeks. The chosen fluoropyrimidine should be administered in accordance with local prescribing information.

Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	Avastin
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5 mg/kg bevacizumab via 15-30 minute IV infusion on Day 1 of every 2-week cycle per local prescribing information

Investigational medicinal product name	5-FU/LV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1600-2400 mg/m^2 5-FU via 46-hour IV infusion in combination with 400 mg/m^2 LV via 2-hour infusion on Day 1 of every 2-week cycle until disease progression per the Investigator's assessment using modified Response Evaluation Criteria in Solid Tumors or death from any cause, whichever occurs first.

Arm title	Cohort 2: 5-FU/LV or capecitabine,bevacizumab,atezolizumab

Arm description:

Participants with BRAFwt will receive fluoropyrimidine (1600-2400 mg/m^2 5-FU via 46-hour IV infusion in combination with 400 mg/m^2 LV via 2-hour infusion on Day 1 of every 2-week cycle or 1000 mg/m^2 twice-daily capecitabine BID by mouth on Days 1-14 every 2 weeks followed by a 1-week break) with 5 milligrams per kilogram (mg/kg) bevacizumab via 15-30 minute IV infusion on Day 1 of every 2-week cycle and 800 mg atezolizumab via 60-minute IV infusion on Day 1 of every 2-week cycle.

Arm type	Experimental
Investigational medicinal product name	5-FU/LV or capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Per Investigator's discretion: 1600-2400 mg/m^2 administered via 46-hour IV infusion on Day 1 of every 2-week cycle and LV 400 mg/m^2 administered via a 2-hour infusion on Day 1 every 2 weeks or 1000 mg/m^2 twice-daily capecitabine (BID) by mouth given days 1-14 every 2 weeks. The chosen fluoropyrimidine should be administered in accordance with local prescribing information.

Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	Avastin
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5 mg/kg bevacizumab via 15-30 minute IV infusion on Day 1 of every 2-week cycle per local prescribing information

Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

800 mg atezolizumab via 60-minute IV infusion on Day 1 of every 2-week cycle, or a fixed dose of 840 mg

Arm title	Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab

Arm description:

Per Investigator discretion, participants will receive fluoropyrimidine (5-FU/LV or capecitabine) at a dose and schedule per the Investigator's discretion in accordance with locally approved prescribing information and 5 mg/kg bevacizumab via 1-30 minute IV on Day 1 of every 2-week cycle.

Arm type	Active comparator
Investigational medicinal product name	5-FU/LV or capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Per Investigator's discretion: 1600-2400 mg/m^2 administered via 46-hour IV infusion on Day 1 of every 2-week cycle and LV 400 mg/m^2 administered via a 2-hour infusion on Day 1 every 2 weeks or 1000 mg/m^2 twice-daily capecitabine (BID) by mouth given days 1-14 every 2 weeks. The chosen fluoropyrimidine should be administered in accordance with local prescribing information.

Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	Avastin
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5 mg/kg bevacizumab via 15-30 minute IV infusion on Day 1 of every 2-week cycle per local prescribing information

Investigational medicinal product name	5-FU/LV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1600-2400 mg/m^2 5-FU via 46-hour IV infusion in combination with 400 mg/m^2 LV via 2-hour infusion on Day 1 of every 2-week cycle until disease progression per the Investigator's assessment using modified Response Evaluation Criteria in Solid Tumors or death from any cause, whichever occurs first.

Arm title	Cohort 3: capecitabine,trastuzumab,pertuzumab

Arm description:

Participants with human epidermal growth factor receptor 2 positive (HER2+) will receive 1000 mg/m^2 twice-daily capecitabine BID by mouth on Days 1-14 every 2 weeks followed by a 1-week break with trastuzumab by IV infusion on Day 1 of every 3-week treatment cycle at an initial loading dose of 8 mg/kg followed by 6 mg/kg for subsequent doses, and pertuzumab by IV infusion on Day 1 of each 3-week treatment cycle at an initial fixed loading dose of 840 mg followed by 420 mg for subsequent doses.

Arm type	Experimental

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

Dosage and administration details:

1000 mg/m^2 twice-daily capecitabine (BID) by mouth given days 1-14 every 2 weeks

Investigational medicinal product name	Trastuzumab
Investigational medicinal product code	
Other name	Herceptin; RO0452317
Pharmaceutical forms	Solution for infusion, Powder and solvent for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Initial loading dose of 8 mg/kg followed by 6 mg/kg for subsequent doses by IV infusion on Day 1 of every 3-week treatment cycle

Investigational medicinal product name	Pertuzumab
Investigational medicinal product code	
Other name	RO4368451
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Initial fixed loading dose of 840 mg followed by 420 mg for subsequent doses by IV infusion on Day 1 of each 3-week treatment cycle

Arm title	Cohort 3 Control: 5-FU/LV or capecitabin, bevacizumab

Arm description:

Per Investigator discretion, participants will receive fluoropyrimidine (5-FU/LV or capecitabine) at a dose and schedule per the Investigator's discretion in accordance with locally approved prescribing information and 5 mg/kg bevacizumab via 1-30 minute IV on Day 1 of every 2-week cycle.

Arm type	Active comparator
Investigational medicinal product name	5-FU/LV or capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Per Investigator's discretion: 1600-2400 mg/m^2 administered via 46-hour IV infusion on Day 1 of every 2-week cycle and LV 400 mg/m^2 administered via a 2-hour infusion on Day 1 every 2 weeks or 1000 mg/m^2 twice-daily capecitabine (BID) by mouth given days 1-14 every 2 weeks. The chosen fluoropyrimidine should be administered in accordance with local prescribing information.

Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	Avastin
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5 mg/kg bevacizumab via 15-30 minute IV infusion on Day 1 of every 2-week cycle per local prescribing information

Investigational medicinal product name	5-FU/LV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1600-2400 mg/m^2 5-FU via 46-hour IV infusion in combination with 400 mg/m^2 LV via 2-hour infusion on Day 1 of every 2-week cycle until disease progression per the Investigator's assessment using modified Response Evaluation Criteria in Solid Tumors or death from any cause, whichever occurs first.

Arm title	Cohort 4: Cobimetinib,atezolizumab

Arm description:

Participants with HER2-/high microsatellite instability (MSI-H); HER2-/MSS/v-raf murine sarcoma viral oncogene homolog B1 wild type (BRAFwt); HER2-/MSS/BRAFmut/rat sarcoma mutation positive (RASmut) will receive 60 mg cobimetinib orally for 3 weeks followed by a 1-week treatment break and atezolizumab at a fixed dose of 840 mg via 60-minute IV infusion on Day 1 of every 2-week cycle.

Arm type	Experimental
Investigational medicinal product name	Cobimetinib
Investigational medicinal product code	
Other name	RO5514041
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

60 mg orally once daily for 3 weeks followed by a 1-week treatment break

Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	RO5541267
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

800 mg atezolizumab via 60-minute IV infusion on Day 1 of every 2-week cycle, or a fixed dose of 840 mg

Arm title	Cohort 4 Control: 5-FU/LV or capecitabin, bevacizumab

Arm description:

Per Investigator discretion, participants will receive fluoropyrimidine (5-FU/LV or capecitabine) at a dose and schedule per the Investigator's discretion in accordance with locally approved prescribing information and 5 mg/kg bevacizumab via 1-30 minute IV on Day 1 of every 2-week cycle.

Arm type	Active comparator
Investigational medicinal product name	5-FU/LV or capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Per Investigator's discretion: 1600-2400 mg/m^2 administered via 46-hour IV infusion on Day 1 of every 2-week cycle and LV 400 mg/m^2 administered via a 2-hour infusion on Day 1 every 2 weeks or 1000 mg/m^2 twice-daily capecitabine (BID) by mouth given days 1-14 every 2 weeks. The chosen fluoropyrimidine should be administered in accordance with local prescribing information.

Investigational medicinal product name	Bevacizumab
Investigational medicinal product code	
Other name	Avastin
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

5 mg/kg bevacizumab via 15-30 minute IV infusion on Day 1 of every 2-week cycle per local prescribing information

Investigational medicinal product name	5-FU/LV
Investigational medicinal product code	
Other name	

Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1600-2400 mg/m^2 5-FU via 46-hour IV infusion in combination with 400 mg/m^2 LV via 2-hour infusion on Day 1 of every 2-week cycle until disease progression per the Investigator's assessment using modified Response Evaluation Criteria in Solid Tumors or death from any cause, whichever occurs first.

Number of subjects in period 2	Cohort 1: 5-FU/LV,cetuximab,vemurafenib	Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 2: 5-FU/LV or capecitabine,bevacizumab,atezolizumab
Started	40	20	297
Completed	16	4	45
Not completed	24	16	252
Adverse event, serious fatal	23	13	185
Consent withdrawn by subject	-	-	13
Physician decision	-	-	2
unknown	-	1	29
Adverse event, non-fatal	-	-	1
No Treatment Received	-	2	4
Multiple Reasons	-	-	4
Lost to follow-up	-	-	12
Protocol deviation	1	-	2

Number of subjects in period 2	Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 3: capecitabine,trastuzumab,pertuzumab	Cohort 3 Control: 5-FU/LV or capecitabin, bevacizumab
Started	148	3	2
Completed	19	1	0
Not completed	129	2	2
Adverse event, serious fatal	100	1	1
Consent withdrawn by subject	11	-	-
Physician decision	-	-	-
unknown	8	-	1
Adverse event, non-fatal	-	-	-
No Treatment Received	5	-	-
Multiple Reasons	1	-	-
Lost to follow-up	3	1	-
Protocol deviation	1	-	-

Number of subjects in period 2	Cohort 4: Cobimetinib,atezolizumab	Cohort 4 Control: 5-FU/LV or capecitabin, bevacizumab

Started	65	34
Completed	34	18
Not completed	31	16
Adverse event, serious fatal	26	11
Consent withdrawn by subject	2	3
Physician decision	-	1
unknown	-	-
Adverse event, non-fatal	-	-
No Treatment Received	1	-
Multiple Reasons	-	-
Lost to follow-up	2	1
Protocol deviation	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1
Reporting group description:	
All participants will receive either eight 2-week cycles of 5-fluorouracil (5-FU)/ leucovorin calcium (LV) and oxaliplatin (FOLFOX) in combination with bevacizumab, or six 2-week cycles of FOLFOX in combination with bevacizumab, followed by two 2-week cycles of 5-FU/LV with bevacizumab.	
Reporting group title	Cohort 2
Reporting group description:	
All participants will receive either eight 2-week cycles of 5-fluorouracil (5-FU)/ leucovorin calcium (LV) and oxaliplatin (FOLFOX) in combination with bevacizumab, or six 2-week cycles of FOLFOX in combination with bevacizumab, followed by two 2-week cycles of 5-FU/LV with bevacizumab.	
Reporting group title	Cohort 3
Reporting group description:	
All participants will receive either eight 2-week cycles of 5-fluorouracil (5-FU)/ leucovorin calcium (LV) and oxaliplatin (FOLFOX) in combination with bevacizumab, or six 2-week cycles of FOLFOX in combination with bevacizumab, followed by two 2-week cycles of 5-FU/LV with bevacizumab.	
Reporting group title	Cohort 4
Reporting group description:	
All participants will receive either eight 2-week cycles of 5-fluorouracil (5-FU)/ leucovorin calcium (LV) and oxaliplatin (FOLFOX) in combination with bevacizumab, or six 2-week cycles of FOLFOX in combination with bevacizumab, followed by two 2-week cycles of 5-FU/LV with bevacizumab.	

Reporting group values	Cohort 1	Cohort 2	Cohort 3
Number of subjects	60	445	5
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	39	254	5
From 65-84 years	21	189	0
85 years and over	0	2	0
Age Continuous Units: years			
arithmetic mean	59.2	60.6	49.6
standard deviation	± 11.0	± 12.3	± 7.4
Sex: Female, Male Units:			
Female	34	174	3
Male	26	271	2

Reporting group values	Cohort 4	Total	
Number of subjects	99	609	

Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	66	364	
From 65-84 years	33	243	
85 years and over	0	2	
Age Continuous Units: years			
arithmetic mean	59.5		
standard deviation	± 10.2	-	
Sex: Female, Male Units:			
Female	41	252	
Male	58	357	

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description:	
All participants will receive either eight 2-week cycles of 5-fluorouracil (5-FU)/ leucovorin calcium (LV) and oxaliplatin (FOLFOX) in combination with bevacizumab, or six 2-week cycles of FOLFOX in combination with bevacizumab, followed by two 2-week cycles of 5-FU/LV with bevacizumab.	
Reporting group title	Cohort 2
Reporting group description:	
All participants will receive either eight 2-week cycles of 5-fluorouracil (5-FU)/ leucovorin calcium (LV) and oxaliplatin (FOLFOX) in combination with bevacizumab, or six 2-week cycles of FOLFOX in combination with bevacizumab, followed by two 2-week cycles of 5-FU/LV with bevacizumab.	
Reporting group title	Cohort 3
Reporting group description:	
All participants will receive either eight 2-week cycles of 5-fluorouracil (5-FU)/ leucovorin calcium (LV) and oxaliplatin (FOLFOX) in combination with bevacizumab, or six 2-week cycles of FOLFOX in combination with bevacizumab, followed by two 2-week cycles of 5-FU/LV with bevacizumab.	
Reporting group title	Cohort 4
Reporting group description:	
All participants will receive either eight 2-week cycles of 5-fluorouracil (5-FU)/ leucovorin calcium (LV) and oxaliplatin (FOLFOX) in combination with bevacizumab, or six 2-week cycles of FOLFOX in combination with bevacizumab, followed by two 2-week cycles of 5-FU/LV with bevacizumab.	
Reporting group title	Cohort 1: 5-FU/LV,cetuximab,vemurafenib
Reporting group description:	
Participants with v-raf murine sarcoma viral oncogene homolog B1 mutation positive (BRAFmut)/human epidermal growth factor receptor 2 negative (HER2-)/microsatellite stable (MSS)/rat sarcoma wild type (RASwt) will receive 1600-2400 milligrams per square meter (mg/m^2) 5-FU via 46-hour intravenous (IV) infusion in combination with 400 mg/m^2 LV via 2-hour infusion on Day 1 of every 2-week cycle with 500 mg/m^2 cetuximab via infusion on Day 1 of every 2-week cycle and 960 milligrams (mg) vemurafenib twice daily (BID) by mouth.	
Reporting group title	Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab
Reporting group description:	
Per Investigator discretion, participants will receive fluoropyrimidine (5-FU/LV or capecitabine) at a dose and schedule per the Investigator's discretion in accordance with locally approved prescribing information and 5 mg/kg bevacizumab via 1-30 minute IV on Day 1 of every 2-week cycle.	
Reporting group title	Cohort 2: 5-FU/LV or capecitabine,bevacizumab,atezolizumab
Reporting group description:	
Participants with BRAFwt will receive fluoropyrimidine (1600-2400 mg/m^2 5-FU via 46-hour IV infusion in combination with 400 mg/m^2 LV via 2-hour infusion on Day 1 of every 2-week cycle or 1000 mg/m^2 twice-daily capecitabine BID by mouth on Days 1-14 every 2 weeks followed by a 1-week break) with 5 milligrams per kilogram (mg/kg) bevacizumab via 15-30 minute IV infusion on Day 1 of every 2-week cycle and 800 mg atezolizumab via 60-minute IV infusion on Day 1 of every 2-week cycle.	
Reporting group title	Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab
Reporting group description:	
Per Investigator discretion, participants will receive fluoropyrimidine (5-FU/LV or capecitabine) at a dose and schedule per the Investigator's discretion in accordance with locally approved prescribing information and 5 mg/kg bevacizumab via 1-30 minute IV on Day 1 of every 2-week cycle.	
Reporting group title	Cohort 3: capecitabine,trastuzumab,pertuzumab
Reporting group description:	
Participants with human epidermal growth factor receptor 2 positive (HER2+) will receive 1000 mg/m^2 twice-daily capecitabine BID by mouth on Days 1-14 every 2 weeks followed by a 1-week break with trastuzumab by IV infusion on Day 1 of every 3-week treatment cycle at an initial loading dose of 8 mg/kg followed by 6 mg/kg for subsequent doses, and pertuzumab by IV infusion on Day 1 of each 3-week treatment cycle at an initial fixed loading dose of 840 mg followed by 420 mg for subsequent doses.	
Reporting group title	Cohort 3 Control: 5-FU/LV or capecitabin, bevacizumab

Reporting group description:

Per Investigator discretion, participants will receive fluoropyrimidine (5-FU/LV or capecitabine) at a dose and schedule per the Investigator's discretion in accordance with locally approved prescribing information and 5 mg/kg bevacizumab via 1-30 minute IV on Day 1 of every 2-week cycle.

Reporting group title	Cohort 4: Cobimetinib,atezolizumab

Reporting group description:

Participants with HER2-/high microsatellite instability (MSI-H); HER2-/MSS/v-raf murine sarcoma viral oncogene homolog B1 wild type (BRAFwt); HER2-/MSS/BRAFmut/rat sarcoma mutation positive (RASmut) will receive 60 mg cobimetinib orally for 3 weeks followed by a 1-week treatment break and atezolizumab at a fixed dose of 840 mg via 60-minute IV infusion on Day 1 of every 2-week cycle.

Reporting group title	Cohort 4 Control: 5-FU/LV or capecitabin, bevacizumab

Reporting group description:

Per Investigator discretion, participants will receive fluoropyrimidine (5-FU/LV or capecitabine) at a dose and schedule per the Investigator's discretion in accordance with locally approved prescribing information and 5 mg/kg bevacizumab via 1-30 minute IV on Day 1 of every 2-week cycle.

Primary: Progression-Free Survival

End point title	Progression-Free Survival

End point description:

Progression-Free Survival (PFS) was evaluated according to response evaluation criteria in solid tumors version 1.1 (RECIST 1.1)

End point type	Primary

End point timeframe:

From randomization until disease progression or death from any cause, up to 5 years

End point values	Cohort 1: 5-FU/LV,cetuximab,vemurafenib	Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 2: 5-FU/LV or capecitabine,bevacizumab,atezolizumab	Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	20	297	148
Units: months				
median (confidence interval 95%)	9.99 (7.72 to 12.55)	11.60 (3.58 to 15.67)	7.13 (6.14 to 8.41)	7.36 (5.82 to 8.94)

End point values	Cohort 3: capecitabine,trastuzumab,pertuzumab	Cohort 3 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 4: Cobimetinib,atezolizumab	Cohort 4 Control: 5-FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	2	65	34
Units: months				
median (confidence interval 95%)	4.44 (3.55 to 14.69)	4.04 (4.04 to 5.39)	3.75 (3.42 to 3.91)	7.79 (3.98 to 9.46)

Statistical analyses

Statistical analysis title	Cohort 1 vs. Control
Comparison groups	Cohort 1: 5-FU/LV,cetuximab,vemurafenib v Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.872
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.82

Statistical analysis title	Cohort 2 vs. Control
Comparison groups	Cohort 2: 5-FU/LV or capecitabine,bevacizumab,atezolizumab v Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.666
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.18

Statistical analysis title	Cohort 4 vs. Control
Comparison groups	Cohort 4: Cobimetinib,atezolizumab v Cohort 4 Control: 5-FU/LV or capecitabin, bevacizumab
Number of subjects included in analysis	99
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.128
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.44

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	2.29

Secondary: Overall Survival

End point title	Overall Survival

End point description:

End point type	Secondary

End point timeframe:

From randomization until death from any cause, up to 5 years

End point values	Cohort 1: 5-FU/LV,cetuximab,vemurafenib	Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 2: 5-FU/LV or capecitabine,bevacizumab,atezolizumab	Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[1]	0[2]	0[3]	0[4]
Units: months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[1] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

[2] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

[3] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

[4] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

End point values	Cohort 3: capecitabine,trastuzumab,pertuzumab	Cohort 3 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 4: Cobimetinib,atezolizumab	Cohort 4 Control: 5-FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[5]	0[6]	0[7]	0[8]
Units: months				
median (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[5] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

[6] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

[7] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

[8] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response

End point title	Overall Response

End point description:

Calculated as the number of participants with a best overall response of CR or PR according to RECIST 1.1

End point type	Secondary

End point timeframe:

From randomization until disease progression, up to 5 years

End point values	Cohort 1: 5-FU/LV,cetuximab,vemurafenib	Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 2: 5-FU/LV or capecitabine,bevacizumab,atezolizumab	Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	20	297	148
Units: participants	20	5	49	22

End point values	Cohort 3: capecitabine,trastuzumab,pertuzumab	Cohort 3 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 4: Cobimetinib,atezolizumab	Cohort 4 Control: 5-FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	2	0[9]	0[10]
Units: participants	1	0		

Notes:

[9] - Target number of patients not enrolled and the target number of PFS events could not be reached

[10] - Target number of patients not enrolled and the target number of PFS events could not be reached

Statistical analyses

Statistical analysis title	Cohort 1 vs. Control
Comparison groups	Cohort 1: 5-FU/LV,cetuximab,vemurafenib v Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.064
Method	Chi-squared

Statistical analysis title	Cohort 2 vs. Control
Comparison groups	Cohort 2: 5-FU/LV or capecitabine,bevacizumab,atezolizumab v Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab

Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.658
Method	Chi-squared

Secondary: Disease Control Rate

End point title	Disease Control Rate

End point description:

Calculated as the proportion of participants with a best overall response of CR, PR or Stable Disease according to RECIST 1.1

End point type	Secondary

End point timeframe:

From randomization until disease progression, up to 5 years

End point values	Cohort 1: 5-FU/LV,cetuximab,vemurafenib	Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 2: 5-FU/LV or capecitabine,bevacizumab,atezolizumab	Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	20	297	148
Units: participants	36	15	227	111

End point values	Cohort 3: capecitabine,trastuzumab,pertuzumab	Cohort 3 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 4: Cobimetinib,atezolizumab	Cohort 4 Control: 5-FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	2	0[11]	0[12]
Units: participants	1	0		

Notes:

[11] - Target number of patients not enrolled and the target number of PFS events could not be reached

[12] - Target number of patients not enrolled and the target number of PFS events could not be reached

Statistical analyses

Statistical analysis title	Cohort 1 vs. Control
Comparison groups	Cohort 1: 5-FU/LV,cetuximab,vemurafenib v Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.125
Method	Chi-squared

Statistical analysis title	Cohort 2 vs. Control
Comparison groups	Cohort 2: 5-FU/LV or capecitabine,bevacizumab,atezolizumab v Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.739
Method	Chi-squared

Secondary: Time to Treatment Response

End point title	Time to Treatment Response

End point description:

Calculated as the time from randomization to the first Occurrence of a documented Objective Response (CR or PR) determined according to RECIST 1.1

End point type	Secondary

End point timeframe:

From randomization until disease progression or death from any cause, up to 5 years

End point values	Cohort 1: 5-FU/LV,cetuximab,vemurafenib	Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 2: 5-FU/LV or capecitabine,bevacizumab,atezolizumab	Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	20	297	148
Units: months				
median (full range (min-max))	3.943 (1.18 to 29.70)	5.552 (1.38 to 8.02)	5.224 (1.22 to 26.74)	4.616 (1.25 to 19.91)

End point values	Cohort 3: capecitabine,trastuzumab,pertuzumab	Cohort 3 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 4: Cobimetinib,atezolizumab	Cohort 4 Control: 5-FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	2	0[13]	0[14]
Units: months				
median (full range (min-max))	5.490 (5.490	0 (0 to 0)	(to)	(to)

	to 5.490)

Notes:

[13] - Target number of patients not enrolled and the target number of PFS events could not be reached

[14] - Target number of patients not enrolled and the target number of PFS events could not be reached

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response

End point description:

Defined as the time from the first assessment of CR or PR until disease progression or death from any cause, whichever occurs first

End point type	Secondary

End point timeframe:

From first objective response until disease progression or death from any cause, up to 5 years

End point values	Cohort 1: 5-FU/LV,cetuximab,vemurafenib	Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 2: 5-FU/LV or capecitabine,bevacizumab,atezolizumab	Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	20	297	148
Units: months				
median (confidence interval 95%)	11.50 (7.66 to 21.49)	8.74 (5.36 to 19.02)	9.30 (5.55 to 11.30)	7.59 (6.93 to 13.90)

End point values	Cohort 3: capecitabine,trastuzumab,pertuzumab	Cohort 3 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 4: Cobimetinib,atezolizumab	Cohort 4 Control: 5-FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	2	0[15]	0[16]
Units: months				
median (confidence interval 95%)	9.205 (9.205 to 9.205)	0 (0 to 0)	(to)	(to)

Notes:

[15] - Target number of patients not enrolled and the target number of PFS events could not be reached

[16] - Target number of patients not enrolled and the target number of PFS events could not be reached

Statistical analyses

Statistical analysis title	Cohort 1 vs. Control
Comparison groups	Cohort 1: 5-FU/LV,cetuximab,vemurafenib v Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.421
Method	Logrank

Statistical analysis title	Cohort 2 vs. Control
Comparison groups	Cohort 2: 5-FU/LV or capecitabine,bevacizumab,atezolizumab v Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab
Number of subjects included in analysis	445
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.495
Method	Logrank

Secondary: Change from Baseline in Eastern Cooperative Oncology Group Performance Status (ECOG PS)

End point title	Change from Baseline in Eastern Cooperative Oncology Group Performance Status (ECOG PS)

End point description:

End point type	Secondary

End point timeframe:

From baseline until end of study (up to 5 years)

End point values	Cohort 1: 5-FU/LV,cetuximab,vemurafenib	Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 2: 5-FU/LV or capecitabine,bevacizumab,atezolizumab	Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	20	297	148
Units: percentage of participants				
number (not applicable)				
Improved	10.0	5.0	10.4	5.4
Improved or stayed the same	75.0	85.0	76.7	82.5

End point values	Cohort 3: capecitabine,trastuzumab,pertuzumab	Cohort 3 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 4: Cobimetinib,atezolizumab	Cohort 4 Control: 5-FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	2	0[17]	0[18]

Units: percentage of participants				
number (not applicable)				
Improved	0	0		
Improved or stayed the same	100	100		

Notes:

[17] - Target number of patients not enrolled and the target number of PFS events could not be reached

[18] - Target number of patients not enrolled and the target number of PFS events could not be reached

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Adverse Events

End point title	Percentage of Participants with Adverse Events

End point description:

End point type	Secondary

End point timeframe:

From baseline until end of study (up to 5 years)

End point values	Cohort 1	Cohort 1: 5-FU/LV,cetuximab,vemurafenib	Cohort 2	Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[19]	0[20]	0[21]	0[22]
Units: percentage of participants				
number (not applicable)				

Notes:

[19] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

[20] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

[21] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

[22] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

End point values	Cohort 3	Cohort 2: 5-FU/LV or capecitabine,bevacizumab,atezolizumab	Cohort 4	Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[23]	0[24]	0[25]	0[26]
Units: percentage of participants				
number (not applicable)				

Notes:

[23] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

[24] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

[25] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

[26] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

End point values	Cohort 3: capecitabine,	Cohort 3 Control: 5-	Cohort 4: Cobimetinib,	Cohort 4 Control: 5-

	trastuzumab,pertuzumab	FU/LV or capecitabin, bevacizumab	atezolizumab	FU/LV or capecitabin, bevacizumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[27]	0[28]	0[29]	0[30]
Units: percentage of participants				
number (not applicable)				

Notes:

[27] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

[28] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

[29] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

[30] - Final Results will be provided at the time of final results disclosure (estimated July 2021).

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From baseline until end of study (up to 5 years)	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0
Reporting groups	
Reporting group title	Cohort 1 (Induction Treatment)
Reporting group description: -	
Reporting group title	Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab
Reporting group description: -	
Reporting group title	Cohort 1: 5-FU/LV,cetuximab, vemurafenib
Reporting group description: -	
Reporting group title	Cohort 2 (Induction Treatment)
Reporting group description: -	
Reporting group title	Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab
Reporting group description: -	
Reporting group title	Cohort 2: 5-FU/LV or capecitabine, bevacizumab, atezolizumab
Reporting group description: -	
Reporting group title	Cohort 3 (Induction Treatment)
Reporting group description: -	
Reporting group title	Cohort 3 Control: 5-FU/LV or capecitabin, bevacizumab
Reporting group description: -	
Reporting group title	Cohort 3: capecitabine, trastuzumab, pertuzumab
Reporting group description: -	
Reporting group title	Cohort 4 (Induction Treatment)
Reporting group description: -	
Reporting group title	Cohort 4 Control: 5-FU/LV or capecitabin, bevacizumab
Reporting group description: -	
Reporting group title	Cohort 4: Cobimetinib, atezolizumab
Reporting group description: -	

Serious adverse events	Cohort 1 (Induction Treatment)	Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 1: 5-FU/LV,cetuximab, vemurafenib
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 58 (15.52%)	8 / 18 (44.44%)	13 / 40 (32.50%)
number of deaths (all causes)	36	13	23
number of deaths resulting from adverse events	2	5	5
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Second primary malignancy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour perforation			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	0 / 18 (0.00%)	0 / 40 (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
Vascular disorders			
Arterial thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Ureteral stent removal			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Implant site dehiscence			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Implant site thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0

Infusion site extravasation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Dyspnoea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	1 / 1	0 / 0
Epistaxis			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Disorientation			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Investigations			
Blood creatine phosphokinase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood lactate dehydrogenase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood triglycerides increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Anastomotic ulcer			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pubis fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Rib fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Spinal fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Stoma site haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 58 (1.72%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Myocardial infarction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Restrictive cardiomyopathy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoaesthesia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral motor neuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Presyncope			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Febrile neutropenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Eye disorders			
Chorioretinopathy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Abdominal pain upper			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Faecaloma			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal obstruction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ileus alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Immune-mediated enterocolitis alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal stenosis alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Stomatitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	3 / 3
Hepatobiliary disorders			
Cholestasis			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 58 (3.45%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hepatic failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular injury			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatorenal failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypothyroidism			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall abscess			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Anal abscess			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Erysipelas			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis clostridial			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gingivitis alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hepatic infection alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Infection alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Labyrinthitis alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Large intestine infection alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Staphylococcal infection alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Upper respiratory tract infection alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Urinary tract infection alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (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
Metabolism and nutrition disorders Dehydration alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 2 (Induction Treatment)	Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 2: 5-FU/LV or capecitabine, bevacizumab, atezolizumab
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 436 (3.67%)	30 / 143 (20.98%)	90 / 293 (30.72%)
number of deaths (all causes)	292	100	185
number of deaths resulting from adverse events	3	20	46
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Second primary malignancy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Tumour perforation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Deep vein thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	2 / 293 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	4 / 293 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	4 / 4
Hypotension			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Superior vena cava syndrome			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Ureteral stent removal			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
General disorders and administration site conditions			
Asthenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 436 (0.23%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Gait disturbance			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 436 (0.23%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
General physical health deterioration			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hyperthermia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Implant site dehiscence			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Implant site thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infusion site extravasation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	2 / 143 (1.40%)	9 / 293 (3.07%)
occurrences causally related to treatment / all	0 / 0	1 / 3	3 / 9
deaths causally related to treatment / all	0 / 0	1 / 3	2 / 8
Immune system disorders			
Anaphylactic reaction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hypersensitivity			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 436 (0.23%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Dyspnoea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Epistaxis			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Interstitial lung disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pneumothorax			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	3 / 293 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	2 / 2
Respiratory failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Disorientation			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatine phosphokinase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood lactate dehydrogenase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood triglycerides increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	2 / 143 (1.40%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	3 / 3	0 / 0
Injury, poisoning and procedural complications			
Anastomotic ulcer			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Femur fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Post procedural haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pubis fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Stoma site haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Tracheal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Cardiac disorders			
Atrial fibrillation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiogenic shock			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 436 (0.23%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Myocardial ischaemia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 436 (0.23%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pericardial effusion			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Restrictive cardiomyopathy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Cerebrovascular accident			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoaesthesia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Peripheral motor neuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Blood and lymphatic system disorders			
Anaemia			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	5 / 293 (1.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	4 / 5
Neutropenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	2 / 143 (1.40%)	4 / 293 (1.37%)
occurrences causally related to treatment / all	0 / 0	4 / 4	5 / 5
deaths causally related to treatment / all	0 / 0	4 / 4	4 / 4
Ear and labyrinth disorders			
Vertigo			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Chorioretinopathy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 436 (0.46%)	1 / 143 (0.70%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	1 / 2	0 / 1	0 / 1
Abdominal pain upper			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Colitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	3 / 293 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Constipation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	4 / 293 (1.37%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 5
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	2 / 143 (1.40%)	7 / 293 (2.39%)
occurrences causally related to treatment / all	0 / 0	1 / 2	5 / 7
deaths causally related to treatment / all	0 / 0	1 / 1	4 / 5
Faecaloma			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Gastrointestinal obstruction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Gastrooesophageal reflux disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1

Ileus alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	4 / 293 (1.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Immune-mediated enterocolitis alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	2 / 143 (1.40%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Intestinal perforation alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Large intestinal obstruction alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal stenosis alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Large intestine perforation alternative assessment type: Systematic			

subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	1 / 1
Lower gastrointestinal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	2 / 293 (0.68%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 2
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	3 / 293 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	3 / 3
Oesophagitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	2 / 293 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	2 / 2
Proctalgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Stomatitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Subileus			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	2 / 293 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	5 / 293 (1.71%)
occurrences causally related to treatment / all	0 / 0	1 / 1	4 / 5
deaths causally related to treatment / all	0 / 0	1 / 1	3 / 4
Hepatobiliary disorders			
Cholestasis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	1 / 1
Hepatitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular injury			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatorenal failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Hepatotoxicity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Skin and subcutaneous tissue disorders			
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Renal and urinary disorders			
Acute kidney injury			
alternative assessment type: Systematic			

subjects affected / exposed	4 / 436 (0.92%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	1 / 4	0 / 1	0 / 0
Nephrolithiasis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypothyroidism			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	2 / 2
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 436 (0.23%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Abdominal infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 436 (0.23%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Abdominal wall abscess			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (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
Arthritis infective			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Bronchitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 436 (0.23%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 436 (0.23%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Diverticulitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 436 (0.23%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastroenteritis clostridial			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Gingivitis alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic infection alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 1
Labyrinthitis alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine infection alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Lung infection alternative assessment type: Systematic			

subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pneumonia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	3 / 293 (1.02%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 3
Pyelonephritis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sepsis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	3 / 293 (1.02%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Septic shock			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Staphylococcal infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	3 / 293 (1.02%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	1 / 1	1 / 2
Urosepsis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (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 device infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	2 / 143 (1.40%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 1
Metabolism and nutrition disorders			
Dehydration			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Diabetic ketoacidosis			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hypoglycaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hypokalaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	2 / 293 (0.68%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 2
Hyponatraemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 3 (Induction Treatment)	Cohort 3 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 3: capecitabine, trastuzumab, pertuzumab
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	2	1	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Second primary malignancy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour perforation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Ureteral stent removal			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Implant site dehiscence			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Implant site thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infusion site extravasation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Disorientation			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatine phosphokinase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood lactate dehydrogenase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood triglycerides increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Anastomotic ulcer			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pubis fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Stoma site haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Restrictive cardiomyopathy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoaesthesia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral motor neuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Chorioretinopathy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal obstruction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ileus alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated enterocolitis alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal stenosis alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Stomatitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholestasis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular injury			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatorenal failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypothyroidism			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall abscess			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis clostridial			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gingivitis alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic infection alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Labyrinthitis alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine infection alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Staphylococcal infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 4 (Induction Treatment)	Cohort 4 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 4: Cobimetinib, atezolizumab
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 98 (6.12%)	3 / 34 (8.82%)	25 / 64 (39.06%)
number of deaths (all causes)	38	11	26
number of deaths resulting from adverse events	2	3	9
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Second primary malignancy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour perforation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Arterial thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Hypertension			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Ureteral stent removal			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Gait disturbance			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Implant site dehiscence			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Implant site thrombosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infusion site extravasation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	2 / 64 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	2 / 64 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Disorientation			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatine phosphokinase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	3 / 64 (4.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	2 / 2
Blood lactate dehydrogenase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood triglycerides increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Anastomotic ulcer			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pubis fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Stoma site haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Coronary artery disease			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Restrictive cardiomyopathy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 98 (0.00%)	1 / 34 (2.94%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Haemorrhage intracranial			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoaesthesia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral motor neuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Syncope			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 98 (1.02%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Febrile neutropenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Chorioretinopathy			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 98 (2.04%)	1 / 34 (2.94%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Abdominal pain upper			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	1 / 34 (2.94%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	1 / 1
Constipation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecaloma			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal obstruction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ileus			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated enterocolitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	3 / 64 (4.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Intestinal perforation			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal obstruction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal stenosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Stomatitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholestasis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular injury			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatorenal failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Rash maculo-papular			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 98 (1.02%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Nephrolithiasis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Hypothyroidism			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	1 / 34 (2.94%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Back pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	1 / 34 (2.94%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Muscular weakness			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal abscess			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall abscess			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastroenteritis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis clostridial			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gingivitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Labyrinthitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pyelonephritis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Staphylococcal infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	2 / 64 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Urosepsis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Diabetic ketoacidosis			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1

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

Non-serious adverse events	Cohort 1 (Induction Treatment)	Cohort 1 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 1: 5-FU/LV,cetuximab, vemurafenib
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 58 (100.00%)	17 / 18 (94.44%)	39 / 40 (97.50%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Seborrhoeic keratosis			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	3
Vascular disorders			
Hypertension			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 58 (15.52%)	1 / 18 (5.56%)	1 / 40 (2.50%)
occurrences (all)	11	1	1
Hypotension			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 58 (3.45%)	0 / 18 (0.00%)	4 / 40 (10.00%)
occurrences (all)	2	0	4
General disorders and administration site conditions			
Asthenia			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 58 (18.97%)	1 / 18 (5.56%)	5 / 40 (12.50%)
occurrences (all)	12	2	9
Face oedema			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	17 / 58 (29.31%)	2 / 18 (11.11%)	9 / 40 (22.50%)
occurrences (all)	27	2	12
Influenza like illness			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	0 / 18 (0.00%)	3 / 40 (7.50%)
occurrences (all)	1	0	3
Mucosal inflammation			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 58 (8.62%)	2 / 18 (11.11%)	7 / 40 (17.50%)
occurrences (all)	6	4	8
Oedema peripheral			
alternative assessment type: Systematic			

subjects affected / exposed	3 / 58 (5.17%)	0 / 18 (0.00%)	3 / 40 (7.50%)
occurrences (all)	3	0	6
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	3 / 40 (7.50%)
occurrences (all)	0	0	3
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 58 (12.07%)	1 / 18 (5.56%)	9 / 40 (22.50%)
occurrences (all)	8	1	9
Immune system disorders			
Hypersensitivity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	3 / 40 (7.50%)
occurrences (all)	0	0	3
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Cough			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 58 (5.17%)	3 / 18 (16.67%)	5 / 40 (12.50%)
occurrences (all)	3	3	6
Dysphonia			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 58 (6.90%)	1 / 18 (5.56%)	1 / 40 (2.50%)
occurrences (all)	4	1	1
Dyspnoea			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 58 (5.17%)	2 / 18 (11.11%)	2 / 40 (5.00%)
occurrences (all)	3	2	2
Epistaxis			
alternative assessment type: Systematic			

subjects affected / exposed	7 / 58 (12.07%)	1 / 18 (5.56%)	5 / 40 (12.50%)
occurrences (all)	8	1	5
Hiccups			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Nasal dryness			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	1	1	0
Nasal ulcer			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Pulmonary embolism			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 58 (5.17%)	1 / 18 (5.56%)	1 / 40 (2.50%)
occurrences (all)	3	1	2
Psychiatric disorders			
Anxiety			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 58 (6.90%)	1 / 18 (5.56%)	1 / 40 (2.50%)
occurrences (all)	4	1	1
Insomnia			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 58 (12.07%)	1 / 18 (5.56%)	2 / 40 (5.00%)
occurrences (all)	7	1	2
Investigations			
Alanine aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 58 (3.45%)	0 / 18 (0.00%)	2 / 40 (5.00%)
occurrences (all)	3	0	3
Amylase increased			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 58 (5.17%)	1 / 18 (5.56%)	2 / 40 (5.00%)
occurrences (all)	5	1	2
Blood alkaline phosphatase increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences (all)	2	0	0
Blood bilirubin increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	1 / 18 (5.56%)	2 / 40 (5.00%)
occurrences (all)	1	1	3
Blood creatine phosphokinase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	3 / 40 (7.50%)
occurrences (all)	0	0	5
Ejection fraction decreased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	3 / 40 (7.50%)
occurrences (all)	0	0	3
Neutrophil count decreased			
alternative assessment type: Systematic			

subjects affected / exposed	10 / 58 (17.24%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences (all)	12	0	0
Platelet count decreased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 58 (3.45%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences (all)	3	0	1
Weight decreased			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 58 (5.17%)	2 / 18 (11.11%)	4 / 40 (10.00%)
occurrences (all)	3	2	4
Weight increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Infusion related reaction			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 58 (3.45%)	0 / 18 (0.00%)	2 / 40 (5.00%)
occurrences (all)	2	0	3
Nervous system disorders			
Dizziness			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 58 (5.17%)	1 / 18 (5.56%)	4 / 40 (10.00%)
occurrences (all)	5	2	4
Dysgeusia			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 58 (10.34%)	0 / 18 (0.00%)	4 / 40 (10.00%)
occurrences (all)	6	0	4
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 58 (6.90%)	0 / 18 (0.00%)	2 / 40 (5.00%)
occurrences (all)	4	0	2
Neuropathy peripheral			
alternative assessment type: Systematic			

subjects affected / exposed	6 / 58 (10.34%)	0 / 18 (0.00%)	2 / 40 (5.00%)
occurrences (all)	7	0	2
Neurotoxicity			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 58 (6.90%)	0 / 18 (0.00%)	3 / 40 (7.50%)
occurrences (all)	7	0	3
Paraesthesia			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 58 (20.69%)	0 / 18 (0.00%)	4 / 40 (10.00%)
occurrences (all)	17	0	4
Peripheral motor neuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	0 / 18 (0.00%)	2 / 40 (5.00%)
occurrences (all)	2	0	3
Peripheral sensory neuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 58 (24.14%)	1 / 18 (5.56%)	4 / 40 (10.00%)
occurrences (all)	19	1	5
Polyneuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 58 (3.45%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	2	1	0
Restless legs syndrome			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	1	1	0
Sensory loss			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	1	1	0
Somnolence			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2

Taste disorder			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 58 (5.17%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences (all)	3	0	0
Blood and lymphatic system disorders			
Anaemia			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 58 (13.79%)	2 / 18 (11.11%)	7 / 40 (17.50%)
occurrences (all)	9	3	10
Leukopenia			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 58 (6.90%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences (all)	4	0	0
Neutropenia			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 58 (22.41%)	2 / 18 (11.11%)	5 / 40 (12.50%)
occurrences (all)	15	2	5
Thrombocytopenia			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 58 (6.90%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences (all)	5	0	0
Eye disorders			
Cataract			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	3 / 40 (7.50%)
occurrences (all)	0	0	3
Conjunctival haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Lacrimation increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Periorbital oedema			

alternative assessment type: Systematic			
subjects affected / exposed	2 / 58 (3.45%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	2	1	0
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 58 (15.52%)	1 / 18 (5.56%)	7 / 40 (17.50%)
occurrences (all)	10	1	9
Abdominal pain upper			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 58 (12.07%)	3 / 18 (16.67%)	2 / 40 (5.00%)
occurrences (all)	8	3	2
Angular cheilitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	1 / 18 (5.56%)	1 / 40 (2.50%)
occurrences (all)	1	1	1
Constipation			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 58 (15.52%)	0 / 18 (0.00%)	5 / 40 (12.50%)
occurrences (all)	10	0	6
Dental cyst			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	26 / 58 (44.83%)	4 / 18 (22.22%)	16 / 40 (40.00%)
occurrences (all)	34	5	39
Dyspepsia			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 58 (5.17%)	1 / 18 (5.56%)	1 / 40 (2.50%)
occurrences (all)	4	1	1
Dysphagia			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 58 (3.45%)	0 / 18 (0.00%)	2 / 40 (5.00%)
occurrences (all)	3	0	4
Gingival bleeding			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	3
Haemorrhoids			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 58 (6.90%)	1 / 18 (5.56%)	1 / 40 (2.50%)
occurrences (all)	4	1	1
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	30 / 58 (51.72%)	0 / 18 (0.00%)	16 / 40 (40.00%)
occurrences (all)	60	0	23
Palatal ulcer			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Rectal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	2 / 40 (5.00%)
occurrences (all)	0	1	2
Stomatitis			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 58 (24.14%)	3 / 18 (16.67%)	5 / 40 (12.50%)
occurrences (all)	19	3	6
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 58 (24.14%)	1 / 18 (5.56%)	7 / 40 (17.50%)
occurrences (all)	18	1	11
Skin and subcutaneous tissue disorders			
Alopecia			
alternative assessment type: Systematic			

subjects affected / exposed	6 / 58 (10.34%)	2 / 18 (11.11%)	1 / 40 (2.50%)
occurrences (all)	6	2	1
Dermatitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	1	1	0
Dermatitis acneiform			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	11 / 40 (27.50%)
occurrences (all)	0	0	13
Dermatitis contact			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Dry skin			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 58 (3.45%)	3 / 18 (16.67%)	11 / 40 (27.50%)
occurrences (all)	2	3	12
Eczema			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	8 / 40 (20.00%)
occurrences (all)	0	4	10
Nail ridging			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Onychoclasis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	3 / 40 (7.50%)
occurrences (all)	0	0	3

Palmar-plantar erythrodysaesthesia syndrome			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 58 (5.17%)	4 / 18 (22.22%)	5 / 40 (12.50%)
occurrences (all)	4	5	5
Photosensitivity reaction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	9 / 40 (22.50%)
occurrences (all)	0	0	10
Pruritus			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	2 / 18 (11.11%)	4 / 40 (10.00%)
occurrences (all)	0	2	4
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 58 (3.45%)	0 / 18 (0.00%)	13 / 40 (32.50%)
occurrences (all)	2	0	17
Rash erythematous			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	3 / 40 (7.50%)
occurrences (all)	0	0	4
Rash macular			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	3
Skin disorder			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Skin fissures			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	6 / 40 (15.00%)
occurrences (all)	0	0	10
Skin toxicity			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 58 (1.72%)	0 / 18 (0.00%)	3 / 40 (7.50%)
occurrences (all)	1	0	4
Renal and urinary disorders			
Dysuria			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	1	1	0
Proteinuria			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	0	1
Endocrine disorders			
Hyperthyroidism			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Hypothyroidism			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 58 (5.17%)	3 / 18 (16.67%)	17 / 40 (42.50%)
occurrences (all)	6	4	29
Back pain			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 58 (10.34%)	2 / 18 (11.11%)	5 / 40 (12.50%)
occurrences (all)	6	2	5
Bone pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 58 (1.72%)	0 / 18 (0.00%)	2 / 40 (5.00%)
occurrences (all)	1	0	2
Muscle tightness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2
Musculoskeletal pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	1 / 40 (2.50%)
occurrences (all)	0	1	1
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 58 (6.90%)	1 / 18 (5.56%)	6 / 40 (15.00%)
occurrences (all)	4	1	8
Pain in extremity			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	0 / 18 (0.00%)	7 / 40 (17.50%)
occurrences (all)	1	0	10
Infections and infestations			
Bronchitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	1	2	0
Conjunctivitis			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 58 (3.45%)	1 / 18 (5.56%)	3 / 40 (7.50%)
occurrences (all)	2	1	3
Eye infection			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Folliculitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	6 / 40 (15.00%)
occurrences (all)	0	0	8
Gastroenteritis viral			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	1 / 18 (5.56%)	1 / 40 (2.50%)
occurrences (all)	1	1	1
Onychomycosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	2 / 18 (11.11%)	0 / 40 (0.00%)
occurrences (all)	0	2	0
Oral herpes			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	1 / 40 (2.50%)
occurrences (all)	0	1	1
Paronychia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	0 / 18 (0.00%)	5 / 40 (12.50%)
occurrences (all)	1	0	13
Rash pustular			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	3
Rhinitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	0 / 40 (0.00%)
occurrences (all)	0	0	0

Tracheitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	2 / 18 (11.11%)	3 / 40 (7.50%)
occurrences (all)	0	2	4
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	1 / 18 (5.56%)	1 / 40 (2.50%)
occurrences (all)	1	1	1
Metabolism and nutrition disorders			
Decreased appetite			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 58 (13.79%)	0 / 18 (0.00%)	8 / 40 (20.00%)
occurrences (all)	9	0	10
Food craving			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	1 / 40 (2.50%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	0 / 40 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	1 / 18 (5.56%)	2 / 40 (5.00%)
occurrences (all)	0	1	3
Hypokalaemia			
alternative assessment type: Systematic			

subjects affected / exposed	7 / 58 (12.07%)	1 / 18 (5.56%)	3 / 40 (7.50%)
occurrences (all)	8	1	6
Hypomagnesaemia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 58 (1.72%)	0 / 18 (0.00%)	6 / 40 (15.00%)
occurrences (all)	2	0	6
Hypophosphataemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 58 (0.00%)	0 / 18 (0.00%)	2 / 40 (5.00%)
occurrences (all)	0	0	2

Non-serious adverse events	Cohort 2 (Induction Treatment)	Cohort 2 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 2: 5-FU/LV or capecitabine, bevacizumab, atezolizumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	415 / 436 (95.18%)	118 / 143 (82.52%)	270 / 293 (92.15%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Seborrhoeic keratosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
alternative assessment type: Systematic			
subjects affected / exposed	90 / 436 (20.64%)	16 / 143 (11.19%)	49 / 293 (16.72%)
occurrences (all)	116	21	70
Hypotension			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 436 (0.92%)	1 / 143 (0.70%)	3 / 293 (1.02%)
occurrences (all)	4	1	3
General disorders and administration site conditions			
Asthenia			
alternative assessment type: Systematic			
subjects affected / exposed	73 / 436 (16.74%)	12 / 143 (8.39%)	39 / 293 (13.31%)
occurrences (all)	109	20	57
Face oedema			

alternative assessment type: Systematic			
subjects affected / exposed	2 / 436 (0.46%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences (all)	2	0	3
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	132 / 436 (30.28%)	23 / 143 (16.08%)	54 / 293 (18.43%)
occurrences (all)	202	28	78
Influenza like illness			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 436 (2.06%)	3 / 143 (2.10%)	8 / 293 (2.73%)
occurrences (all)	9	3	9
Mucosal inflammation			
alternative assessment type: Systematic			
subjects affected / exposed	31 / 436 (7.11%)	7 / 143 (4.90%)	19 / 293 (6.48%)
occurrences (all)	34	9	25
Oedema peripheral			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 436 (1.38%)	2 / 143 (1.40%)	6 / 293 (2.05%)
occurrences (all)	6	2	6
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 436 (0.69%)	2 / 143 (1.40%)	4 / 293 (1.37%)
occurrences (all)	3	2	4
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	43 / 436 (9.86%)	13 / 143 (9.09%)	31 / 293 (10.58%)
occurrences (all)	52	15	50
Immune system disorders			
Hypersensitivity			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 436 (2.29%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences (all)	10	0	1
Respiratory, thoracic and mediastinal disorders			

Chronic obstructive pulmonary disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	2 / 293 (0.68%)
occurrences (all)	0	1	2
Cough			
alternative assessment type: Systematic			
subjects affected / exposed	30 / 436 (6.88%)	10 / 143 (6.99%)	30 / 293 (10.24%)
occurrences (all)	32	12	38
Dysphonia			
alternative assessment type: Systematic			
subjects affected / exposed	25 / 436 (5.73%)	3 / 143 (2.10%)	15 / 293 (5.12%)
occurrences (all)	35	3	17
Dyspnoea			
alternative assessment type: Systematic			
subjects affected / exposed	17 / 436 (3.90%)	2 / 143 (1.40%)	12 / 293 (4.10%)
occurrences (all)	18	2	12
Epistaxis			
alternative assessment type: Systematic			
subjects affected / exposed	68 / 436 (15.60%)	15 / 143 (10.49%)	22 / 293 (7.51%)
occurrences (all)	74	19	27
Hiccups			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 436 (2.75%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences (all)	17	1	0
Nasal dryness			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 436 (0.23%)	0 / 143 (0.00%)	2 / 293 (0.68%)
occurrences (all)	1	0	2
Nasal ulcer			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
alternative assessment type: Systematic			

subjects affected / exposed	9 / 436 (2.06%)	1 / 143 (0.70%)	3 / 293 (1.02%)
occurrences (all)	9	1	3
Psychiatric disorders			
Anxiety			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 436 (2.06%)	1 / 143 (0.70%)	5 / 293 (1.71%)
occurrences (all)	9	1	5
Insomnia			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 436 (4.36%)	3 / 143 (2.10%)	10 / 293 (3.41%)
occurrences (all)	20	3	10
Investigations			
Alanine aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 436 (4.36%)	6 / 143 (4.20%)	8 / 293 (2.73%)
occurrences (all)	25	9	14
Amylase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	2 / 293 (0.68%)
occurrences (all)	0	0	2
Aspartate aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 436 (3.44%)	6 / 143 (4.20%)	11 / 293 (3.75%)
occurrences (all)	18	7	14
Blood alkaline phosphatase increased			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 436 (1.61%)	4 / 143 (2.80%)	5 / 293 (1.71%)
occurrences (all)	7	5	5
Blood bilirubin increased			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 436 (1.15%)	4 / 143 (2.80%)	8 / 293 (2.73%)
occurrences (all)	5	5	10
Blood creatine phosphokinase increased			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 436 (1.38%)	2 / 143 (1.40%)	4 / 293 (1.37%)
occurrences (all)	7	5	4
Ejection fraction decreased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences (all)	0	1	0
Lipase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	2 / 293 (0.68%)
occurrences (all)	0	0	2
Neutrophil count decreased			
alternative assessment type: Systematic			
subjects affected / exposed	46 / 436 (10.55%)	2 / 143 (1.40%)	6 / 293 (2.05%)
occurrences (all)	68	3	10
Platelet count decreased			
alternative assessment type: Systematic			
subjects affected / exposed	23 / 436 (5.28%)	3 / 143 (2.10%)	6 / 293 (2.05%)
occurrences (all)	35	4	19
Weight decreased			
alternative assessment type: Systematic			
subjects affected / exposed	32 / 436 (7.34%)	2 / 143 (1.40%)	11 / 293 (3.75%)
occurrences (all)	33	3	12
Weight increased			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 436 (1.61%)	1 / 143 (0.70%)	2 / 293 (0.68%)
occurrences (all)	7	1	3
Injury, poisoning and procedural complications			
Infusion related reaction			
alternative assessment type: Systematic			

subjects affected / exposed	7 / 436 (1.61%)	0 / 143 (0.00%)	9 / 293 (3.07%)
occurrences (all)	12	0	11
Nervous system disorders			
Dizziness			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 436 (3.44%)	1 / 143 (0.70%)	5 / 293 (1.71%)
occurrences (all)	17	1	6
Dysgeusia			
alternative assessment type: Systematic			
subjects affected / exposed	30 / 436 (6.88%)	3 / 143 (2.10%)	8 / 293 (2.73%)
occurrences (all)	39	3	8
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	38 / 436 (8.72%)	6 / 143 (4.20%)	23 / 293 (7.85%)
occurrences (all)	70	16	75
Neuropathy peripheral			
alternative assessment type: Systematic			
subjects affected / exposed	67 / 436 (15.37%)	10 / 143 (6.99%)	18 / 293 (6.14%)
occurrences (all)	95	10	21
Neurotoxicity			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 436 (3.21%)	2 / 143 (1.40%)	2 / 293 (0.68%)
occurrences (all)	20	3	3
Paraesthesia			
alternative assessment type: Systematic			
subjects affected / exposed	63 / 436 (14.45%)	10 / 143 (6.99%)	18 / 293 (6.14%)
occurrences (all)	75	11	21
Peripheral motor neuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 436 (1.15%)	0 / 143 (0.00%)	3 / 293 (1.02%)
occurrences (all)	5	0	3
Peripheral sensory neuropathy			
alternative assessment type: Systematic			

subjects affected / exposed	153 / 436 (35.09%)	15 / 143 (10.49%)	32 / 293 (10.92%)
occurrences (all)	233	16	38
Polyneuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 436 (3.67%)	1 / 143 (0.70%)	6 / 293 (2.05%)
occurrences (all)	18	2	6
Restless legs syndrome			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences (all)	0	1	0
Sensory loss			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences (all)	0	0	0
Somnolence			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	4 / 293 (1.37%)
occurrences (all)	0	0	5
Taste disorder			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 436 (2.06%)	1 / 143 (0.70%)	1 / 293 (0.34%)
occurrences (all)	9	1	1
Blood and lymphatic system disorders			
Anaemia			
alternative assessment type: Systematic			
subjects affected / exposed	35 / 436 (8.03%)	8 / 143 (5.59%)	19 / 293 (6.48%)
occurrences (all)	41	13	25
Leukopenia			
alternative assessment type: Systematic			
subjects affected / exposed	24 / 436 (5.50%)	3 / 143 (2.10%)	4 / 293 (1.37%)
occurrences (all)	32	3	8
Neutropenia			
alternative assessment type: Systematic			

subjects affected / exposed	96 / 436 (22.02%)	9 / 143 (6.29%)	11 / 293 (3.75%)
occurrences (all)	149	18	11
Thrombocytopenia			
alternative assessment type: Systematic			
subjects affected / exposed	27 / 436 (6.19%)	4 / 143 (2.80%)	10 / 293 (3.41%)
occurrences (all)	35	10	11
Eye disorders			
Cataract			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 436 (0.23%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences (all)	1	0	1
Conjunctival haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences (all)	0	1	0
Lacrimation increased			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 436 (1.38%)	5 / 143 (3.50%)	4 / 293 (1.37%)
occurrences (all)	6	5	5
Periorbital oedema			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	2 / 293 (0.68%)
occurrences (all)	0	0	2
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	51 / 436 (11.70%)	13 / 143 (9.09%)	39 / 293 (13.31%)
occurrences (all)	63	16	44
Abdominal pain upper			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 436 (4.36%)	12 / 143 (8.39%)	17 / 293 (5.80%)
occurrences (all)	22	16	21
Angular cheilitis			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 436 (0.46%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences (all)	2	0	0
Constipation			
alternative assessment type: Systematic			
subjects affected / exposed	81 / 436 (18.58%)	18 / 143 (12.59%)	36 / 293 (12.29%)
occurrences (all)	104	27	47
Dental cyst			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	158 / 436 (36.24%)	19 / 143 (13.29%)	74 / 293 (25.26%)
occurrences (all)	264	34	114
Dyspepsia			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 436 (3.21%)	3 / 143 (2.10%)	9 / 293 (3.07%)
occurrences (all)	17	3	11
Dysphagia			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 436 (2.52%)	1 / 143 (0.70%)	1 / 293 (0.34%)
occurrences (all)	18	1	1
Gingival bleeding			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 436 (0.69%)	0 / 143 (0.00%)	5 / 293 (1.71%)
occurrences (all)	3	0	5
Haemorrhoids			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 436 (2.29%)	1 / 143 (0.70%)	6 / 293 (2.05%)
occurrences (all)	11	2	6
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	177 / 436 (40.60%)	28 / 143 (19.58%)	60 / 293 (20.48%)
occurrences (all)	295	42	126

Palatal ulcer			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 436 (1.83%)	3 / 143 (2.10%)	5 / 293 (1.71%)
occurrences (all)	8	5	5
Stomatitis			
alternative assessment type: Systematic			
subjects affected / exposed	82 / 436 (18.81%)	11 / 143 (7.69%)	35 / 293 (11.95%)
occurrences (all)	111	19	48
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	82 / 436 (18.81%)	9 / 143 (6.29%)	38 / 293 (12.97%)
occurrences (all)	112	12	59
Skin and subcutaneous tissue disorders			
Alopecia			
alternative assessment type: Systematic			
subjects affected / exposed	40 / 436 (9.17%)	2 / 143 (1.40%)	8 / 293 (2.73%)
occurrences (all)	40	2	8
Dermatitis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 436 (0.23%)	1 / 143 (0.70%)	3 / 293 (1.02%)
occurrences (all)	1	1	3
Dermatitis acneiform			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 436 (0.92%)	0 / 143 (0.00%)	4 / 293 (1.37%)
occurrences (all)	5	0	4
Dermatitis contact			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences (all)	0	0	0
Dry skin			
alternative assessment type: Systematic			

subjects affected / exposed	24 / 436 (5.50%)	3 / 143 (2.10%)	19 / 293 (6.48%)
occurrences (all)	24	6	22
Eczema			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 436 (0.46%)	0 / 143 (0.00%)	2 / 293 (0.68%)
occurrences (all)	2	0	2
Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 436 (1.38%)	2 / 143 (1.40%)	12 / 293 (4.10%)
occurrences (all)	6	2	13
Nail ridging			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	3 / 143 (2.10%)	0 / 293 (0.00%)
occurrences (all)	0	3	0
Onychoclasis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences (all)	0	0	1
Palmar-plantar erythrodysaesthesia syndrome			
alternative assessment type: Systematic			
subjects affected / exposed	23 / 436 (5.28%)	25 / 143 (17.48%)	44 / 293 (15.02%)
occurrences (all)	30	40	64
Photosensitivity reaction			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 436 (0.69%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences (all)	3	0	0
Pruritus			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 436 (1.83%)	6 / 143 (4.20%)	19 / 293 (6.48%)
occurrences (all)	9	6	24
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 436 (3.44%)	0 / 143 (0.00%)	23 / 293 (7.85%)
occurrences (all)	16	0	28

Rash erythematous			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 436 (0.46%)	0 / 143 (0.00%)	3 / 293 (1.02%)
occurrences (all)	2	0	3
Rash macular			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences (all)	0	0	0
Skin disorder			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 436 (0.23%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences (all)	1	0	1
Skin fissures			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 436 (0.69%)	0 / 143 (0.00%)	2 / 293 (0.68%)
occurrences (all)	3	0	2
Skin toxicity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	3 / 293 (1.02%)
occurrences (all)	0	0	4
Renal and urinary disorders			
Dysuria			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 436 (2.06%)	1 / 143 (0.70%)	2 / 293 (0.68%)
occurrences (all)	9	1	2
Proteinuria			
alternative assessment type: Systematic			
subjects affected / exposed	17 / 436 (3.90%)	4 / 143 (2.80%)	17 / 293 (5.80%)
occurrences (all)	19	5	25
Endocrine disorders			
Hyperthyroidism			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 436 (0.23%)	0 / 143 (0.00%)	15 / 293 (5.12%)
occurrences (all)	1	0	16
Hypothyroidism			

alternative assessment type: Systematic			
subjects affected / exposed	2 / 436 (0.46%)	1 / 143 (0.70%)	24 / 293 (8.19%)
occurrences (all)	2	1	32
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 436 (2.29%)	6 / 143 (4.20%)	44 / 293 (15.02%)
occurrences (all)	11	7	53
Back pain			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 436 (2.98%)	9 / 143 (6.29%)	22 / 293 (7.51%)
occurrences (all)	14	9	32
Bone pain			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 436 (0.69%)	0 / 143 (0.00%)	7 / 293 (2.39%)
occurrences (all)	3	0	7
Muscle spasms			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 436 (2.06%)	0 / 143 (0.00%)	5 / 293 (1.71%)
occurrences (all)	9	0	5
Muscle tightness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	1 / 293 (0.34%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 436 (0.92%)	2 / 143 (1.40%)	5 / 293 (1.71%)
occurrences (all)	5	2	6
Musculoskeletal pain			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 436 (0.92%)	4 / 143 (2.80%)	14 / 293 (4.78%)
occurrences (all)	4	4	15
Myalgia			
alternative assessment type: Systematic			

subjects affected / exposed	8 / 436 (1.83%)	3 / 143 (2.10%)	15 / 293 (5.12%)
occurrences (all)	12	3	17
Pain in extremity			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 436 (3.44%)	8 / 143 (5.59%)	13 / 293 (4.44%)
occurrences (all)	19	9	18
Infections and infestations			
Bronchitis			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 436 (0.69%)	3 / 143 (2.10%)	5 / 293 (1.71%)
occurrences (all)	3	3	5
Conjunctivitis			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 436 (0.92%)	2 / 143 (1.40%)	5 / 293 (1.71%)
occurrences (all)	4	2	6
Eye infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	2 / 293 (0.68%)
occurrences (all)	0	1	3
Gastroenteritis viral			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 436 (3.44%)	10 / 143 (6.99%)	15 / 293 (5.12%)
occurrences (all)	17	12	20
Onychomycosis			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 436 (0.46%)	2 / 143 (1.40%)	2 / 293 (0.68%)
occurrences (all)	2	2	4
Oral herpes			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 436 (0.92%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences (all)	4	0	0
Paronychia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	1 / 293 (0.34%)
occurrences (all)	0	1	1
Rash pustular			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 436 (3.44%)	3 / 143 (2.10%)	5 / 293 (1.71%)
occurrences (all)	15	3	5
Tracheitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	1 / 143 (0.70%)	0 / 293 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 436 (2.75%)	2 / 143 (1.40%)	12 / 293 (4.10%)
occurrences (all)	13	2	20
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	21 / 436 (4.82%)	4 / 143 (2.80%)	11 / 293 (3.75%)
occurrences (all)	25	4	13
Metabolism and nutrition disorders			
Decreased appetite			
alternative assessment type: Systematic			

subjects affected / exposed	64 / 436 (14.68%)	15 / 143 (10.49%)	22 / 293 (7.51%)
occurrences (all)	84	16	24
Food craving			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 436 (0.00%)	0 / 143 (0.00%)	0 / 293 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
alternative assessment type: Systematic			
subjects affected / exposed	22 / 436 (5.05%)	2 / 143 (1.40%)	5 / 293 (1.71%)
occurrences (all)	29	5	6
Hypoalbuminaemia			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 436 (2.06%)	2 / 143 (1.40%)	2 / 293 (0.68%)
occurrences (all)	9	4	2
Hypocalcaemia			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 436 (2.75%)	6 / 143 (4.20%)	5 / 293 (1.71%)
occurrences (all)	16	10	10
Hypokalaemia			
alternative assessment type: Systematic			
subjects affected / exposed	34 / 436 (7.80%)	9 / 143 (6.29%)	6 / 293 (2.05%)
occurrences (all)	43	10	7
Hypomagnesaemia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 436 (0.23%)	0 / 143 (0.00%)	4 / 293 (1.37%)
occurrences (all)	1	0	4
Hypophosphataemia			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 436 (0.92%)	3 / 143 (2.10%)	2 / 293 (0.68%)
occurrences (all)	4	3	2

Non-serious adverse events	Cohort 3 (Induction Treatment)	Cohort 3 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 3: capecitabine, trastuzumab, pertuzumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 5 (100.00%)	2 / 2 (100.00%)	3 / 3 (100.00%)

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Seborrhoeic keratosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypotension			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	3 / 3 (100.00%)
occurrences (all)	0	0	3
General disorders and administration site conditions			
Asthenia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Face oedema			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 5 (60.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	1
Influenza like illness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
alternative assessment type: Systematic			

subjects affected / exposed	2 / 5 (40.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	2	0	1
Oedema peripheral			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Hypersensitivity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cough			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dysphonia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)	2 / 2 (100.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hiccups			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal ulcer			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Insomnia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Amylase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ejection fraction decreased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 5 (40.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Platelet count decreased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Infusion related reaction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Headache			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Neuropathy peripheral			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 5 (40.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Neurotoxicity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 5 (40.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Peripheral motor neuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 5 (40.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Polyneuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sensory loss			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Somnolence			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Angular cheilitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Constipation			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Dental cyst			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 5 (40.00%)	0 / 2 (0.00%)	2 / 3 (66.67%)
occurrences (all)	2	0	4
Dyspepsia			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	1 / 2 (50.00%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Palatal ulcer			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Skin and subcutaneous tissue disorders			
Alopecia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dermatitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry skin			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Eczema			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail ridging			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Onychoclasis			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	3 / 3 (100.00%)
occurrences (all)	1	0	5
Photosensitivity reaction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash macular			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin disorder			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Skin toxicity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hyperthyroidism			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Back pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Bone pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Muscle spasms			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Muscle tightness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bronchitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Eye infection			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Onychomycosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paronychia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Tracheitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 5 (20.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Food craving			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hypomagnesaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 5 (0.00%)	0 / 2 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 4 (Induction Treatment)	Cohort 4 Control: 5-FU/LV or capecitabin, bevacizumab	Cohort 4: Cobimetinib, atezolizumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	96 / 98 (97.96%)	27 / 34 (79.41%)	61 / 64 (95.31%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Seborrhoeic keratosis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 98 (19.39%)	5 / 34 (14.71%)	3 / 64 (4.69%)
occurrences (all)	27	7	4
Hypotension			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	3 / 64 (4.69%)
occurrences (all)	0	0	3
General disorders and administration site conditions			
Asthenia			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 98 (15.31%)	3 / 34 (8.82%)	11 / 64 (17.19%)
occurrences (all)	26	3	11
Face oedema			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	5 / 64 (7.81%)
occurrences (all)	0	0	5
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	34 / 98 (34.69%)	6 / 34 (17.65%)	12 / 64 (18.75%)
occurrences (all)	49	7	16
Influenza like illness			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 98 (2.04%)	1 / 34 (2.94%)	0 / 64 (0.00%)
occurrences (all)	2	1	0
Mucosal inflammation			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 98 (15.31%)	1 / 34 (2.94%)	3 / 64 (4.69%)
occurrences (all)	19	1	3
Oedema peripheral			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	1 / 34 (2.94%)	7 / 64 (10.94%)
occurrences (all)	0	1	9
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 98 (11.22%)	3 / 34 (8.82%)	17 / 64 (26.56%)
occurrences (all)	13	3	23
Immune system disorders			
Hypersensitivity			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			

Chronic obstructive pulmonary disease			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Cough			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 98 (6.12%)	3 / 34 (8.82%)	6 / 64 (9.38%)
occurrences (all)	6	3	6
Dysphonia			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 98 (4.08%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences (all)	4	0	1
Dyspnoea			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 98 (5.10%)	0 / 34 (0.00%)	2 / 64 (3.13%)
occurrences (all)	5	0	2
Epistaxis			
alternative assessment type: Systematic			
subjects affected / exposed	18 / 98 (18.37%)	3 / 34 (8.82%)	6 / 64 (9.38%)
occurrences (all)	19	4	6
Hiccups			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 98 (4.08%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Nasal dryness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	1 / 34 (2.94%)	0 / 64 (0.00%)
occurrences (all)	0	1	0
Nasal ulcer			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 98 (1.02%)	1 / 34 (2.94%)	0 / 64 (0.00%)
occurrences (all)	1	1	0
Psychiatric disorders			
Anxiety			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 98 (5.10%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences (all)	5	0	1
Insomnia			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 98 (3.06%)	0 / 34 (0.00%)	3 / 64 (4.69%)
occurrences (all)	3	0	3
Investigations			
Alanine aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 98 (2.04%)	0 / 34 (0.00%)	12 / 64 (18.75%)
occurrences (all)	2	0	13
Amylase increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	0 / 34 (0.00%)	4 / 64 (6.25%)
occurrences (all)	1	0	4
Aspartate aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 98 (2.04%)	0 / 34 (0.00%)	15 / 64 (23.44%)
occurrences (all)	2	0	15
Blood alkaline phosphatase increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	0 / 34 (0.00%)	6 / 64 (9.38%)
occurrences (all)	2	0	6
Blood bilirubin increased			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences (all)	0	0	4
Blood creatine phosphokinase increased			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	32 / 64 (50.00%)
occurrences (all)	0	0	39
Blood creatinine increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences (all)	1	0	1
Ejection fraction decreased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	0 / 34 (0.00%)	5 / 64 (7.81%)
occurrences (all)	1	0	6
Lipase increased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 98 (2.04%)	0 / 34 (0.00%)	5 / 64 (7.81%)
occurrences (all)	2	0	7
Neutrophil count decreased			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 98 (9.18%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	15	0	0
Platelet count decreased			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 98 (11.22%)	1 / 34 (2.94%)	5 / 64 (7.81%)
occurrences (all)	13	1	6
Weight decreased			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 98 (4.08%)	0 / 34 (0.00%)	5 / 64 (7.81%)
occurrences (all)	4	0	5
Weight increased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 98 (2.04%)	2 / 34 (5.88%)	3 / 64 (4.69%)
occurrences (all)	3	2	7
Injury, poisoning and procedural complications			
Infusion related reaction			
alternative assessment type: Systematic			

subjects affected / exposed	6 / 98 (6.12%)	0 / 34 (0.00%)	2 / 64 (3.13%)
occurrences (all)	11	0	2
Nervous system disorders			
Dizziness			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 98 (4.08%)	1 / 34 (2.94%)	4 / 64 (6.25%)
occurrences (all)	4	1	4
Dysgeusia			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 98 (6.12%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	7	0	0
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 98 (14.29%)	3 / 34 (8.82%)	6 / 64 (9.38%)
occurrences (all)	24	5	8
Neuropathy peripheral			
alternative assessment type: Systematic			
subjects affected / exposed	18 / 98 (18.37%)	5 / 34 (14.71%)	1 / 64 (1.56%)
occurrences (all)	25	5	2
Neurotoxicity			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 98 (8.16%)	1 / 34 (2.94%)	0 / 64 (0.00%)
occurrences (all)	15	1	0
Paraesthesia			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 98 (14.29%)	1 / 34 (2.94%)	0 / 64 (0.00%)
occurrences (all)	17	1	0
Peripheral motor neuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 98 (5.10%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences (all)	5	0	1
Peripheral sensory neuropathy			
alternative assessment type: Systematic			

subjects affected / exposed	28 / 98 (28.57%)	4 / 34 (11.76%)	3 / 64 (4.69%)
occurrences (all)	42	4	6
Polyneuropathy			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Restless legs syndrome			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Sensory loss			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Somnolence			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Taste disorder			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 98 (10.20%)	1 / 34 (2.94%)	6 / 64 (9.38%)
occurrences (all)	11	1	8
Leukopenia			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 98 (3.06%)	1 / 34 (2.94%)	0 / 64 (0.00%)
occurrences (all)	3	1	0
Neutropenia			
alternative assessment type: Systematic			

subjects affected / exposed	25 / 98 (25.51%)	3 / 34 (8.82%)	1 / 64 (1.56%)
occurrences (all)	40	4	1
Thrombocytopenia			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 98 (6.12%)	1 / 34 (2.94%)	4 / 64 (6.25%)
occurrences (all)	8	5	4
Eye disorders			
Cataract			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	0 / 34 (0.00%)	2 / 64 (3.13%)
occurrences (all)	1	0	2
Conjunctival haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 98 (2.04%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	2	0	0
Periorbital oedema			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 98 (11.22%)	5 / 34 (14.71%)	12 / 64 (18.75%)
occurrences (all)	13	5	15
Abdominal pain upper			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 98 (3.06%)	0 / 34 (0.00%)	4 / 64 (6.25%)
occurrences (all)	3	0	5
Angular cheilitis			
alternative assessment type: Systematic			

subjects affected / exposed	1 / 98 (1.02%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Constipation			
alternative assessment type: Systematic			
subjects affected / exposed	20 / 98 (20.41%)	2 / 34 (5.88%)	6 / 64 (9.38%)
occurrences (all)	23	2	7
Dental cyst			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	33 / 98 (33.67%)	8 / 34 (23.53%)	40 / 64 (62.50%)
occurrences (all)	68	11	84
Dyspepsia			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 98 (8.16%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences (all)	8	0	1
Dysphagia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	2 / 34 (5.88%)	1 / 64 (1.56%)
occurrences (all)	1	2	1
Gingival bleeding			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	2 / 64 (3.13%)
occurrences (all)	0	0	2
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	43 / 98 (43.88%)	5 / 34 (14.71%)	14 / 64 (21.88%)
occurrences (all)	90	21	18

Palatal ulcer			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 98 (16.33%)	3 / 34 (8.82%)	1 / 64 (1.56%)
occurrences (all)	21	3	1
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 98 (19.39%)	2 / 34 (5.88%)	11 / 64 (17.19%)
occurrences (all)	31	8	15
Skin and subcutaneous tissue disorders			
Alopecia			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 98 (6.12%)	1 / 34 (2.94%)	0 / 64 (0.00%)
occurrences (all)	6	1	0
Dermatitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences (all)	0	0	1
Dermatitis acneiform			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	2 / 34 (5.88%)	18 / 64 (28.13%)
occurrences (all)	1	2	20
Dermatitis contact			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Dry skin			
alternative assessment type: Systematic			

subjects affected / exposed	3 / 98 (3.06%)	1 / 34 (2.94%)	6 / 64 (9.38%)
occurrences (all)	3	1	6
Eczema			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences (all)	0	0	1
Nail ridging			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Onychoclasis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysaesthesia syndrome			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 98 (3.06%)	3 / 34 (8.82%)	0 / 64 (0.00%)
occurrences (all)	3	3	0
Photosensitivity reaction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Pruritus			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 98 (3.06%)	1 / 34 (2.94%)	7 / 64 (10.94%)
occurrences (all)	3	1	7
Rash			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 98 (3.06%)	0 / 34 (0.00%)	28 / 64 (43.75%)
occurrences (all)	3	0	32

Rash erythematous			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Rash macular			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Skin disorder			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	1 / 34 (2.94%)	1 / 64 (1.56%)
occurrences (all)	0	1	1
Skin toxicity			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 98 (3.06%)	0 / 34 (0.00%)	2 / 64 (3.13%)
occurrences (all)	4	0	2
Proteinuria			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	2 / 34 (5.88%)	1 / 64 (1.56%)
occurrences (all)	1	4	1
Endocrine disorders			
Hyperthyroidism			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences (all)	0	0	2
Hypothyroidism			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	3 / 64 (4.69%)
occurrences (all)	0	0	3
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	3 / 34 (8.82%)	7 / 64 (10.94%)
occurrences (all)	1	4	7
Back pain			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 98 (3.06%)	3 / 34 (8.82%)	5 / 64 (7.81%)
occurrences (all)	3	3	5
Bone pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences (all)	0	0	1
Muscle tightness			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 98 (4.08%)	1 / 34 (2.94%)	0 / 64 (0.00%)
occurrences (all)	4	1	0
Myalgia			
alternative assessment type: Systematic			

subjects affected / exposed	5 / 98 (5.10%)	2 / 34 (5.88%)	5 / 64 (7.81%)
occurrences (all)	9	3	5
Pain in extremity			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 98 (3.06%)	2 / 34 (5.88%)	5 / 64 (7.81%)
occurrences (all)	3	2	6
Infections and infestations			
Bronchitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	1 / 34 (2.94%)	1 / 64 (1.56%)
occurrences (all)	0	1	1
Eye infection			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 98 (3.06%)	1 / 34 (2.94%)	3 / 64 (4.69%)
occurrences (all)	3	1	4
Onychomycosis			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	1 / 34 (2.94%)	0 / 64 (0.00%)
occurrences (all)	0	1	0
Paronychia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	3 / 64 (4.69%)
occurrences (all)	0	0	3
Rhinitis			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 98 (2.04%)	3 / 34 (8.82%)	1 / 64 (1.56%)
occurrences (all)	2	3	1
Tracheitis			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 98 (4.08%)	3 / 34 (8.82%)	5 / 64 (7.81%)
occurrences (all)	5	3	2
Urinary tract infection			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 98 (3.06%)	1 / 34 (2.94%)	7 / 64 (10.94%)
occurrences (all)	3	1	10
Metabolism and nutrition disorders			
Decreased appetite			
alternative assessment type: Systematic			

subjects affected / exposed	14 / 98 (14.29%)	1 / 34 (2.94%)	10 / 64 (15.63%)
occurrences (all)	17	1	11
Food craving			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 98 (5.10%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences (all)	7	0	1
Hypoalbuminaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 98 (0.00%)	0 / 34 (0.00%)	1 / 64 (1.56%)
occurrences (all)	0	0	1
Hypocalcaemia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	0 / 34 (0.00%)	2 / 64 (3.13%)
occurrences (all)	1	0	2
Hypokalaemia			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 98 (2.04%)	1 / 34 (2.94%)	4 / 64 (6.25%)
occurrences (all)	2	1	4
Hypomagnesaemia			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 98 (1.02%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	1	0	0
Hypophosphataemia			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 98 (2.04%)	0 / 34 (0.00%)	0 / 64 (0.00%)
occurrences (all)	2	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2015	Changes include the replacement of terms "MPDL3280A" and "MPDL3280A (anti-PD-L1 antibody)" with "atezolizumab" (international, non-proprietary name); revision of study eligibility criteria to allow patients with cerebellar metastases, exclude patients with progression of CNS disease between last CNS-directed therapy and study baseline prior to baseline, exclude patients requiring steroid therapy for CNS disease; revision of Cohort 2 eligibility criteria to exclude patients continuing RANKL inhibitor therapy; clarifications and updates on drug products; updates to address any safety concerns or knowledge gaps; and other minor details.
11 April 2016	Changes include increasing the Cohort 2 target sample size from 330 to 405 patients to increase statistical power for Cohort 2 analyses and accommodate rapid accrual into Cohort 2. As a result of this change, the estimated duration of the study for Cohort 2 was increased from 17 to 22 months and the estimated overall study accrual was increased from 610 to 700 patients.
24 November 2016	Changes include Cohort 2 closure due to completion of accrual; incorporation of two new cohorts (Cohort 3: capecitabine/trastuzumab/pertuzumab vs fluoropyrimidine/bevacizumab in HER2+ patients; Cohort 4: cobimetinib/atezolizumab vs fluoropyrimidine/bevacizumab in HER2-/MSI-H; HER2-/MSS/BRAFwt or HER2-/MSS/BRAFmut/RASmut patients); adaptation of cohort assignment decision tree and study length estimates to accommodate new cohorts and Cohort 2 closure; removal of co-primary endpoint "early efficacy during the Maintenance Treatment Phase" based on advisory committees' advice (PFS remains as single primary efficacy endpoint); optional stool sample collection added to address a new exploratory microbiome biomarker evaluation objective; preliminary assessments of efficacy in each cohort removed based on advisory committees' advice; maximum allowable 5-FU dosing in Cohort 1 increased to 2,400 mg/m2 based on completion of safety run-in review by the iDMC; local ablation for liver metastases now allowed during the induction treatment phase; second-line treatment for BRAFmut early progressors modified to 5-FU/vemurafenib/cetuximab for BRAFmut/MSS patients and FP/bevacizumab/atezolizumab for BRAFmut/MSI-H patients; updates to cohort-specific exclusion criteria, safety monitoring, and treatment management based on current safety data. Country specific protocols versions introduced for Spain and France due to jurisdictional requirements for safety monitoring and for Egypt and the UK where Cohorts 3 and 4 were not opened (study enrolment closed in Egypt and UK).
08 August 2018	In accordance with independent Data Monitoring Committee recommendations following review of safety data, accrual into Cohort 4 was closed.
19 December 2019	Enrolment into study was closed. Cohort 4 (now closed due to iDMC recommendations) had broad biomarker eligibility criteria and was introduced to replace Cohort 2 (previously closed due to completion of accrual). No new or modified cohorts with broad eligibility criteria suitable for addition to protocol MO29112 were identified. Without a broad eligibility cohort to replace Cohort 4, the majority of patients eligible for study entry would not be eligible for any maintenance cohort assignment upon completion of study induction treatment. For this reason, the Sponsor decided to permanently discontinue enrolment.
18 February 2020	Changes include updates to safety information and treatment management for patients receiving atezolizumab; update to responsible Medical Monitor. Not Available - Will be provided at the time of final results disclosure.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
12 February 2018	Following the iDMC review of cohort 4 data a temporary recruitment halt to the whole study and a temporary halt to randomisation into cohort 4 was undertaken.	-

Notes:

Limitations and caveats

None reported