Clinical trial results:
A Randomized, Multicenter, Open-Label, Phase 3 Study of Nivolumab plus Ipilimumab or Nivolumab in Combination with Oxaliplatin plus Fluoropyrimidine versus Oxaliplatin plus Fluoropyrimidine in Subjects with Previously Untreated Advanced or Metastatic Gastric or Gastroesophageal Junction Cancer

Summary

EudraCT number	2016-001018-76
Trial protocol	ES GR PL HU DE PT FR CZ GB IT
Global end of trial date	06 June 2024

Results information

Result version number	v1 (current)
This version publication date	22 June 2025
First version publication date	22 June 2025

Trial information

Trial identification

Sponsor protocol code	CA209-649

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Global Submission Management, Clinical Trials, Bristol-Myers Squibb International Corporation, mg-gsm-ct@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, mg-gsm-ct@bms.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 June 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 June 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To compare OS in subjects with advanced or metastatic GC or GEJ cancer with PD-L1 CPS ≥ 5

To compare PFS, as assessed by BICR in subjects with advanced or metastatic GC or GEJ cancer with PD-L1 CPS ≥ 5

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 October 2016
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: 93
Country: Number of subjects enrolled	Australia: 53
Country: Number of subjects enrolled	Brazil: 76
Country: Number of subjects enrolled	Canada: 81
Country: Number of subjects enrolled	Chile: 162
Country: Number of subjects enrolled	China: 273
Country: Number of subjects enrolled	Colombia: 37
Country: Number of subjects enrolled	Czechia: 24
Country: Number of subjects enrolled	France: 73
Country: Number of subjects enrolled	Germany: 97
Country: Number of subjects enrolled	Greece: 46
Country: Number of subjects enrolled	Hong Kong: 7
Country: Number of subjects enrolled	Hungary: 31
Country: Number of subjects enrolled	Israel: 35
Country: Number of subjects enrolled	Italy: 64
Country: Number of subjects enrolled	Japan: 151
Country: Number of subjects enrolled	Korea, Republic of: 22
Country: Number of subjects enrolled	Mexico: 35
Country: Number of subjects enrolled	Peru: 51

Country: Number of subjects enrolled	Poland: 74
Country: Number of subjects enrolled	Portugal: 24
Country: Number of subjects enrolled	Romania: 74
Country: Number of subjects enrolled	Russian Federation: 24
Country: Number of subjects enrolled	Singapore: 24
Country: Number of subjects enrolled	Spain: 48
Country: Number of subjects enrolled	Taiwan: 8
Country: Number of subjects enrolled	Türkiye: 37
Country: Number of subjects enrolled	United Kingdom: 45
Country: Number of subjects enrolled	United States: 262
Worldwide total number of subjects	2031
EEA total number of subjects	555

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)	1248
From 65 to 84 years	775
85 years and over	8

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

2031 Participants Randomized and 1991 Treated

Period 1

Period 1 title	Pre-Treatment
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm 1: Nivolumab + Chemotherapy (XELOX or FOLFOX)

Arm description:

Nivolumab + Xelox: Nivolumab 360 mg IV over 30 minutes on Day 1 of each treatment cycle, every 3 weeks + Oxaliplatin 130 mg/m2 IV on Day 1 of each treatment cycle + capecitabine 1000 mg/m2 orally twice daily (ie, 1000 mg/m2 in the morning and 1000 mg/m2 in the evening) on Days 1 to 14 of each treatment cycle, every 3 weeks Nivolumab + Folfox: Nivolumab 240 mg IV over 30 minutes on Day 1 of each treatment cycle, every 2 weeks + Oxaliplatin 85 mg/m2 + leucovorin 400 mg/m2 + fluorouracil 400 mg/m2 IV on Day 1 of each treatment cycle, and fluorouracil 1200 mg/m2 IV continuous infusion over 24 hours (or per local standard) daily on Days 1 and 2 of each treatment cycle, every 2 weeks

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

Dosage and administration details:

100 mg (10 mg/mL)

Investigational medicinal product name	Leucovorin (Folfox)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

400 mg (50 mg/mL)

Investigational medicinal product name	Fluorouracil (Folfox)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

2500 mg (50 mg/ mL)

Investigational medicinal product name	capecitabine (xelox)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details: 150 mg and 500 mg tablets	
Investigational medicinal product name	oxaliplatin (xelox and folfox)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 100 mg (5 mg/mL)	
Arm title	Arm 2: Chemotherapy (XELOX or FOLFOX)

Arm description:

Chemotherapy (XELOX or FOLFOX): Xelox: Oxaliplatin 130 mg/m2 IV on Day 1 of each treatment cycle + capecitabine 1000 mg/m2 orally twice daily (ie, 1000 mg/m2 in the morning and 1000 mg/m2 in the evening) on Days 1 to 14 of each treatment cycle, every 3 weeks. Folfox: Oxaliplatin 85 mg/m2 + leucovorin 400 mg/m2 + fluorouracil 400 mg/m2 IV on Day 1 of each treatment cycle, and fluorouracil 1200 mg/m2 IV continuous infusion over 24 hours (or per local standard) daily on Days 1 and 2 of each treatment cycle, every 2 weeks. This chemotherapy group consists of the two comparison chemotherapy sub-groups. Arm 2a (792 participants) is the comparison group to Arm 1 and Arm 2b (404 participants) is the comparison group to Arm 3. Some participants were counted in both Arm 2a and Arm 2b.

Arm type	Active comparator
Investigational medicinal product name	oxaliplatin (xelox and folfox)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 100 mg (5 mg/mL)	
Investigational medicinal product name	Leucovorin (Folfox)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details: 400 mg (50 mg/mL)	
Investigational medicinal product name	Fluorouracil (Folfox)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details: 2500 mg (50 mg/ mL)	
Investigational medicinal product name	capecitabine (xelox)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 150 mg and 500 mg tablets	
Arm title	Arm 3: Nivolumab + Ipilimumab

Arm description:

1 mg/kg nivolumab administered IV over 30 minutes followed by ipilimumab 3 mg/kg administered IV over 30 minutes on Day 1 of each treatment cycle every 3 weeks for 4 doses (Cycles 1 to 4), followed by nivolumab 240 mg administered IV over 30 minutes on Day 1 of each treatment cycle every 2 weeks (Cycle 5 and beyond). Arm is closed to enrollment as of 05-June-2018.

Arm type	Experimental
Investigational medicinal product name	nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details: 100 mg (10 mg/mL)	
Investigational medicinal product name	ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use
Dosage and administration details: 200 mg (5 mg/mL)	

Number of subjects in period 1	Arm 1: Nivolumab + Chemotherapy (XELOX or FOLFOX)	Arm 2: Chemotherapy (XELOX or FOLFOX)	Arm 3: Nivolumab + Ipilimumab
Started	789	833	409
Completed	782	806	403
Not completed	7	27	6
withdrew consent	2	20	3
request to discontinue study treatment	-	2	-
Adverse event unrelated to study drug	-	2	1
Other reasons	1	2	2
no longer meets study criteria	4	-	-
Disease Progression	-	1	-

Period 2	
Period 2 title	Treatment
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded
Arms	
Are arms mutually exclusive?	Yes

Arm title	Arm 1: Nivolumab + Chemotherapy (XELOX or FOLFOX)

Arm description:

Nivolumab + Xelox: Nivolumab 360 mg IV over 30 minutes on Day 1 of each treatment cycle, every 3 weeks + Oxaliplatin 130 mg/m2 IV on Day 1 of each treatment cycle + capecitabine 1000 mg/m2 orally twice daily (ie, 1000 mg/m2 in the morning and 1000 mg/m2 in the evening) on Days 1 to 14 of each treatment cycle, every 3 weeks Nivolumab + Folfox: Nivolumab 240 mg IV over 30 minutes on Day 1 of each treatment cycle, every 2 weeks + Oxaliplatin 85 mg/m2 + leucovorin 400 mg/m2 + fluorouracil 400 mg/m2 IV on Day 1 of each treatment cycle, and fluorouracil 1200 mg/m2 IV continuous infusion over 24 hours (or per local standard) daily on Days 1 and 2 of each treatment cycle, every 2 weeks

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

Dosage and administration details:

100 mg (10 mg/mL)

Investigational medicinal product name	Leucovorin (Folfox)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

400 mg (50 mg/mL)

Investigational medicinal product name	Fluorouracil (Folfox)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

2500 mg (50 mg/ mL)

Investigational medicinal product name	capecitabine (xelox)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg and 500 mg tablets

Investigational medicinal product name	oxaliplatin (xelox and folfox)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100 mg (5 mg/mL)

Arm title	Arm 2: Chemotherapy (XELOX or FOLFOX)

Arm description:

Chemotherapy (XELOX or FOLFOX): Xelox: Oxaliplatin 130 mg/m2 IV on Day 1 of each treatment cycle + capecitabine 1000 mg/m2 orally twice daily (ie, 1000 mg/m2 in the morning and 1000 mg/m2 in the evening) on Days 1 to 14 of each treatment cycle, every 3 weeks. Folfox: Oxaliplatin 85 mg/m2 + leucovorin 400 mg/m2 + fluorouracil 400 mg/m2 IV on Day 1 of each treatment cycle, and fluorouracil 1200 mg/m2 IV continuous infusion over 24 hours (or per local standard) daily on Days 1 and 2 of each treatment cycle, every 2 weeks. This chemotherapy group consists of the two comparison chemotherapy sub-groups. Arm 2a (792 participants) is the comparison group to Arm 1 and Arm 2b (404 participants) is the comparison group to Arm 3. Some participants were counted in both Arm 2a and Arm 2b.

Arm type	Active comparator
Investigational medicinal product name	Leucovorin (Folfox)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

400 mg (50 mg/mL)

Investigational medicinal product name	Fluorouracil (Folfox)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

2500 mg (50 mg/ mL)

Investigational medicinal product name	capecitabine (xelox)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg and 500 mg tablets

Investigational medicinal product name	oxaliplatin (xelox and folfox)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100 mg (5 mg/mL)

Arm title	Arm 3: Nivolumab + Ipilimumab

Arm description:

1 mg/kg nivolumab administered IV over 30 minutes followed by ipilimumab 3 mg/kg administered IV over 30 minutes on Day 1 of each treatment cycle every 3 weeks for 4 doses (Cycles 1 to 4), followed by nivolumab 240 mg administered IV over 30 minutes on Day 1 of each treatment cycle every 2 weeks (Cycle 5 and beyond). Arm is closed to enrollment as of 05-June-2018.

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

Dosage and administration details:

100 mg (10 mg/mL)

Investigational medicinal product name	ipilimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

200 mg (5 mg/mL)

Number of subjects in period 2	Arm 1: Nivolumab + Chemotherapy (XELOX or FOLFOX)	Arm 2: Chemotherapy (XELOX or FOLFOX)	Arm 3: Nivolumab + Ipilimumab
Started	782	806	403
Completed	623	653	319
Not completed	159	153	84
Adverse event, serious fatal	122	94	68
Participant withdrew consent	20	40	8
Other reasons	12	12	5
Lost to follow-up	5	7	3

Baseline characteristics

Reporting groups

Reporting group title	Arm 1: Nivolumab + Chemotherapy (XELOX or FOLFOX)

Reporting group description:

Nivolumab + Xelox: Nivolumab 360 mg IV over 30 minutes on Day 1 of each treatment cycle, every 3 weeks + Oxaliplatin 130 mg/m2 IV on Day 1 of each treatment cycle + capecitabine 1000 mg/m2 orally twice daily (ie, 1000 mg/m2 in the morning and 1000 mg/m2 in the evening) on Days 1 to 14 of each treatment cycle, every 3 weeks Nivolumab + Folfox: Nivolumab 240 mg IV over 30 minutes on Day 1 of each treatment cycle, every 2 weeks + Oxaliplatin 85 mg/m2 + leucovorin 400 mg/m2 + fluorouracil 400 mg/m2 IV on Day 1 of each treatment cycle, and fluorouracil 1200 mg/m2 IV continuous infusion over 24 hours (or per local standard) daily on Days 1 and 2 of each treatment cycle, every 2 weeks

Reporting group title	Arm 2: Chemotherapy (XELOX or FOLFOX)

Reporting group description:

Chemotherapy (XELOX or FOLFOX): Xelox: Oxaliplatin 130 mg/m2 IV on Day 1 of each treatment cycle + capecitabine 1000 mg/m2 orally twice daily (ie, 1000 mg/m2 in the morning and 1000 mg/m2 in the evening) on Days 1 to 14 of each treatment cycle, every 3 weeks. Folfox: Oxaliplatin 85 mg/m2 + leucovorin 400 mg/m2 + fluorouracil 400 mg/m2 IV on Day 1 of each treatment cycle, and fluorouracil 1200 mg/m2 IV continuous infusion over 24 hours (or per local standard) daily on Days 1 and 2 of each treatment cycle, every 2 weeks. This chemotherapy group consists of the two comparison chemotherapy sub-groups. Arm 2a (792 participants) is the comparison group to Arm 1 and Arm 2b (404 participants) is the comparison group to Arm 3. Some participants were counted in both Arm 2a and Arm 2b.

Reporting group title	Arm 3: Nivolumab + Ipilimumab

Reporting group description:

1 mg/kg nivolumab administered IV over 30 minutes followed by ipilimumab 3 mg/kg administered IV over 30 minutes on Day 1 of each treatment cycle every 3 weeks for 4 doses (Cycles 1 to 4), followed by nivolumab 240 mg administered IV over 30 minutes on Day 1 of each treatment cycle every 2 weeks (Cycle 5 and beyond). Arm is closed to enrollment as of 05-June-2018.

Reporting group values	Arm 1: Nivolumab + Chemotherapy (XELOX or FOLFOX)	Arm 2: Chemotherapy (XELOX or FOLFOX)	Arm 3: Nivolumab + Ipilimumab
Number of subjects	789	833	409
Age categorical Units: Subjects			
Adults (18-64 years)	473	517	258
From 65-84 years	314	310	151
85 years and over	2	6	0
Age Continuous Units: Years			
arithmetic mean	60.3	59.8	59.4
standard deviation	± 11.9	± 12.1	± 11.7
Sex: Female, Male Units: Participants			
Female	249	246	131
Male	540	587	278
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	12	13	1
Asian	186	200	124
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	7	11	6
White	556	570	264
More than one race	0	0	0

Unknown or Not Reported	28	39	14

Reporting group values	Total		
Number of subjects	2031		
Age categorical Units: Subjects			
Adults (18-64 years)	1248		
From 65-84 years	775		
85 years and over	8		
Age Continuous Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	626		
Male	1405		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	26		
Asian	510		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	24		
White	1390		
More than one race	0		
Unknown or Not Reported	81		

End points reporting groups

Reporting group title	Arm 1: Nivolumab + Chemotherapy (XELOX or FOLFOX)

Reporting group description:

Nivolumab + Xelox: Nivolumab 360 mg IV over 30 minutes on Day 1 of each treatment cycle, every 3 weeks + Oxaliplatin 130 mg/m2 IV on Day 1 of each treatment cycle + capecitabine 1000 mg/m2 orally twice daily (ie, 1000 mg/m2 in the morning and 1000 mg/m2 in the evening) on Days 1 to 14 of each treatment cycle, every 3 weeks Nivolumab + Folfox: Nivolumab 240 mg IV over 30 minutes on Day 1 of each treatment cycle, every 2 weeks + Oxaliplatin 85 mg/m2 + leucovorin 400 mg/m2 + fluorouracil 400 mg/m2 IV on Day 1 of each treatment cycle, and fluorouracil 1200 mg/m2 IV continuous infusion over 24 hours (or per local standard) daily on Days 1 and 2 of each treatment cycle, every 2 weeks

Reporting group title	Arm 2: Chemotherapy (XELOX or FOLFOX)

Reporting group description:

Chemotherapy (XELOX or FOLFOX): Xelox: Oxaliplatin 130 mg/m2 IV on Day 1 of each treatment cycle + capecitabine 1000 mg/m2 orally twice daily (ie, 1000 mg/m2 in the morning and 1000 mg/m2 in the evening) on Days 1 to 14 of each treatment cycle, every 3 weeks. Folfox: Oxaliplatin 85 mg/m2 + leucovorin 400 mg/m2 + fluorouracil 400 mg/m2 IV on Day 1 of each treatment cycle, and fluorouracil 1200 mg/m2 IV continuous infusion over 24 hours (or per local standard) daily on Days 1 and 2 of each treatment cycle, every 2 weeks. This chemotherapy group consists of the two comparison chemotherapy sub-groups. Arm 2a (792 participants) is the comparison group to Arm 1 and Arm 2b (404 participants) is the comparison group to Arm 3. Some participants were counted in both Arm 2a and Arm 2b.

Reporting group title	Arm 3: Nivolumab + Ipilimumab

Reporting group description:

1 mg/kg nivolumab administered IV over 30 minutes followed by ipilimumab 3 mg/kg administered IV over 30 minutes on Day 1 of each treatment cycle every 3 weeks for 4 doses (Cycles 1 to 4), followed by nivolumab 240 mg administered IV over 30 minutes on Day 1 of each treatment cycle every 2 weeks (Cycle 5 and beyond). Arm is closed to enrollment as of 05-June-2018.

Reporting group title	Arm 1: Nivolumab + Chemotherapy (XELOX or FOLFOX)

Reporting group description:

Nivolumab + Xelox: Nivolumab 360 mg IV over 30 minutes on Day 1 of each treatment cycle, every 3 weeks + Oxaliplatin 130 mg/m2 IV on Day 1 of each treatment cycle + capecitabine 1000 mg/m2 orally twice daily (ie, 1000 mg/m2 in the morning and 1000 mg/m2 in the evening) on Days 1 to 14 of each treatment cycle, every 3 weeks Nivolumab + Folfox: Nivolumab 240 mg IV over 30 minutes on Day 1 of each treatment cycle, every 2 weeks + Oxaliplatin 85 mg/m2 + leucovorin 400 mg/m2 + fluorouracil 400 mg/m2 IV on Day 1 of each treatment cycle, and fluorouracil 1200 mg/m2 IV continuous infusion over 24 hours (or per local standard) daily on Days 1 and 2 of each treatment cycle, every 2 weeks

Reporting group title	Arm 2: Chemotherapy (XELOX or FOLFOX)

Reporting group description:

Chemotherapy (XELOX or FOLFOX): Xelox: Oxaliplatin 130 mg/m2 IV on Day 1 of each treatment cycle + capecitabine 1000 mg/m2 orally twice daily (ie, 1000 mg/m2 in the morning and 1000 mg/m2 in the evening) on Days 1 to 14 of each treatment cycle, every 3 weeks. Folfox: Oxaliplatin 85 mg/m2 + leucovorin 400 mg/m2 + fluorouracil 400 mg/m2 IV on Day 1 of each treatment cycle, and fluorouracil 1200 mg/m2 IV continuous infusion over 24 hours (or per local standard) daily on Days 1 and 2 of each treatment cycle, every 2 weeks. This chemotherapy group consists of the two comparison chemotherapy sub-groups. Arm 2a (792 participants) is the comparison group to Arm 1 and Arm 2b (404 participants) is the comparison group to Arm 3. Some participants were counted in both Arm 2a and Arm 2b.

Reporting group title	Arm 3: Nivolumab + Ipilimumab

Reporting group description:

1 mg/kg nivolumab administered IV over 30 minutes followed by ipilimumab 3 mg/kg administered IV over 30 minutes on Day 1 of each treatment cycle every 3 weeks for 4 doses (Cycles 1 to 4), followed by nivolumab 240 mg administered IV over 30 minutes on Day 1 of each treatment cycle every 2 weeks (Cycle 5 and beyond). Arm is closed to enrollment as of 05-June-2018.

Subject analysis set title	Arm 2a: Chemotherapy (XELOX or FOLFOX)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Chemotherapy (XELOX or FOLFOX): Xelox: Oxaliplatin 130 mg/m2 IV on Day 1 of each treatment cycle + capecitabine 1000 mg/m2 orally twice daily (ie, 1000 mg/m2 in the morning and 1000 mg/m2 in the evening) on Days 1 to 14 of each treatment cycle, every 3 weeks. Folfox: Oxaliplatin 85 mg/m2 + leucovorin 400 mg/m2 + fluorouracil 400 mg/m2 IV on Day 1 of each treatment cycle, and fluorouracil

1200 mg/m2 IV continuous infusion over 24 hours (or per local standard) daily on Days 1 and 2 of each treatment cycle, every 2 weeks. This arm is a subgroup of the chemotherapy group that acts as a comparison group to Arm 1.

Subject analysis set title	Arm 2b: Chemotherapy (XELOX or FOLFOX)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Chemotherapy (XELOX or FOLFOX): Xelox: Oxaliplatin 130 mg/m2 IV on Day 1 of each treatment cycle + capecitabine 1000 mg/m2 orally twice daily (ie, 1000 mg/m2 in the morning and 1000 mg/m2 in the evening) on Days 1 to 14 of each treatment cycle, every 3 weeks. Folfox: Oxaliplatin 85 mg/m2 + leucovorin 400 mg/m2 + fluorouracil 400 mg/m2 IV on Day 1 of each treatment cycle, and fluorouracil 1200 mg/m2 IV continuous infusion over 24 hours (or per local standard) daily on Days 1 and 2 of each treatment cycle, every 2 weeks. Comparison group to Arm 3.

Subject analysis set title	Arm 2b: Chemotherapy (XELOX or FOLFOX)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Chemotherapy (XELOX or FOLFOX): Xelox: Oxaliplatin 130 mg/m2 IV on Day 1 of each treatment cycle + capecitabine 1000 mg/m2 orally twice daily (ie, 1000 mg/m2 in the morning and 1000 mg/m2 in the evening) on Days 1 to 14 of each treatment cycle, every 3 weeks. Folfox: Oxaliplatin 85 mg/m2 + leucovorin 400 mg/m2 + fluorouracil 400 mg/m2 IV on Day 1 of each treatment cycle, and fluorouracil 1200 mg/m2 IV continuous infusion over 24 hours (or per local standard) daily on Days 1 and 2 of each treatment cycle, every 2 weeks. This arm is a subgroup of the chemotherapy group that acts as a comparison group to Arm 3.

Subject analysis set title	Arm 1: Nivo + Chem (PD-L1 CPS ≥ 5)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All Randomized Subjects with PD-L1 CPS ≥ 5

Subject analysis set title	Arm 2a: Chemo (PD-L1 CPS ≥ 5)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All Randomized Subjects with PD-L1 CPS ≥ 5

Subject analysis set title	Nivo + Chem (PD-L1 CPS ≥ 10)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All randomized subjects with PD-L1 CPS ≥ 10

Subject analysis set title	Nivo + Chem (PD-L1 CPS ≥ 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All Randomized Subjects with PD-L1 CPS ≥ 1

Subject analysis set title	Arm 2a: Chemotherapy (PD-L1 CPS ≥ 10)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All randomized subjects with PD-L1 CPS ≥ 10

Subject analysis set title	Arm 2a: Chemotherapy (PD-L1 CPS ≥ 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All randomized subjects with PD-L1 CPS ≥ 1

Primary: Overall Survival (OS) in participants treated with Nivolumab plus Chemotherapy vs Chemotherapy with PD-L1 CPS ≥ 5

End point title	Overall Survival (OS) in participants treated with Nivolumab plus Chemotherapy vs Chemotherapy with PD-L1 CPS ≥ 5

End point description:

Overall survival (OS), defined as the time from randomization to the time of death, in participants treated with Nivolumab plus Chemotherapy vs Chemotherapy with PD-L1 CPS (combined positive score) ≥ 5. CPS is defined as the number of PD-L1 staining cells (tumor cells, lymphocytes, macrophages) divided by the total number of viable tumor cells, multiplied by 100.

End point type	Primary

End point timeframe:

From the date of randomization up to the date of death, up to approximately 17 months

End point values	Arm 1: Nivo + Chem (PD-L1 CPS ≥ 5)	Arm 2a: Chemo (PD-L1 CPS ≥ 5)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	402	441		
Units: Months				
median (confidence interval 95%)	14.39 (13.11 to 16.23)	11.14 (10.05 to 12.12)		

Statistical analyses

Statistical analysis title	OS for PD-L1 CPS ≥ 5
Comparison groups	Arm 1: Nivo + Chem (PD-L1 CPS ≥ 5) v Arm 2a: Chemo (PD-L1 CPS ≥ 5)
Number of subjects included in analysis	843
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	0.81

Primary: Progression Free Survival (PFS) in participants treated with Nivolumab plus Chemotherapy vs Chemotherapy with PD-L1 CPS ≥ 5

End point title	Progression Free Survival (PFS) in participants treated with Nivolumab plus Chemotherapy vs Chemotherapy with PD-L1 CPS ≥ 5

End point description:

Progression Free Survival (PFS) is defined as the time from randomization to the date of the first documented PD or death due to any cause. PD is determined by blinded independent committee review (BICR) per RECIST1.1 criteria in participants treated with Nivolumab plus Chemotherapy vs Chemotherapy with PD-L1 CPS ≥ 5. Progressive disease (PD) is defined as at least a 20% increase in the sum of diameters of target lesions, taking in reference the smallest sum on study that also demonstrated an absolute increase of at least 5 mm. CPS is defined as the number of PD-L1 staining cells (tumor cells, lymphocytes, macrophages) divided by the total number of viable tumor cells, multiplied by 100.

End point type	Primary

End point timeframe:

From randomization to the date of the first documented progressive disease (PD) per BICR or death due to any cause (up to approximately 10 months)

End point values	Arm 1: Nivo + Chem (PD-L1 CPS ≥ 5)	Arm 2a: Chemo (PD-L1 CPS ≥ 5)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	366	376		
Units: Months				
median (confidence interval 95%)	8.31 (7.03 to 9.40)	6.14 (5.55 to 6.93)		

Statistical analyses

Statistical analysis title	PFS for PD-L1 CPS ≥ 5
Comparison groups	Arm 1: Nivo + Chem (PD-L1 CPS ≥ 5) v Arm 2a: Chemo (PD-L1 CPS ≥ 5)
Number of subjects included in analysis	742
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	0.82

Secondary: OS in participants treated with Nivolumab plus Chemotherapy vs Chemotherapy

End point title	OS in participants treated with Nivolumab plus Chemotherapy vs Chemotherapy[1]

End point description:

Overall survival (OS), defined as the time from randomization to the time of death, in participants treated with Nivolumab plus Chemotherapy vs Chemotherapy with PD-L1 CPS ≥ 1, 10, and all randomized participants. CPS is defined as the number of PD-L1 staining cells (tumor cells, lymphocytes, macrophages) divided by the total number of viable tumor cells, multiplied by 100.

End point type	Secondary

End point timeframe:

From the date of randomization up to the date of death, up to approximately 17 months

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No further statistical analysis done at this time

End point values	Arm 1: Nivolumab + Chemotherapy (XELOX or FOLFOX)	Arm 2a: Chemotherapy (XELOX or FOLFOX)	Nivo + Chem (PD-L1 CPS ≥ 10)	Nivo + Chem (PD-L1 CPS ≥ 1)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	697	727	316	561
Units: Months				
median (confidence interval 95%)				
All Randomized	13.73 (12.42 to 14.49)	11.63 (10.94 to 12.52)	15.01 (13.63 to 16.66)	13.80 (12.42 to 14.82)

End point values	Arm 2a: Chemotherapy (PD-L1 CPS ≥ 10)	Arm 2a: Chemotherapy (PD-L1 CPS ≥ 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	355	607		
Units: Months				
median (confidence interval 95%)				
All Randomized	10.94 (9.89 to 11.96)	11.37 (10.74 to 12.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: PFS in participants treated with Nivolumab plus Chemotherapy vs Chemotherapy

End point title	PFS in participants treated with Nivolumab plus Chemotherapy vs Chemotherapy[2]

End point description:

Progression free survival (PFS), defined as the time from randomization to the date of the first documented progressive disease (PD) or death due to any cause, in participants treated with Nivolumab plus Chemotherapy vs Chemotherapy by BICR per RECIST1.1 in participants with PD-L1 CPS ≥ 10, 1, or all randomized subjects. Progreessive disease (PD) is defined as at least a 20% increase in the sum of diameters of target lesions, taking in reference the smallest sum on study that also demonstrated an absolute increase of at least 5 mm. CPS is defined as the number of PD-L1 staining cells (tumor cells, lymphocytes, macrophages) divided by the total number of viable tumor cells, multiplied by 100.

End point type	Secondary

End point timeframe:

From randomization to the date of the first documented progressive disease (PD) per BICR or death due to any cause (up to approximately 10 months)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No further statistical analysis done at this time

End point values	Arm 1: Nivolumab + Chemotherapy (XELOX or FOLFOX)	Arm 2a: Chemotherapy (XELOX or FOLFOX)	Nivo + Chem (PD-L1 CPS ≥ 10)	Nivo + Chem (PD-L1 CPS ≥ 1)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	614	598	285	506
Units: Months				
median (confidence interval 95%)				
All Randomized	7.75 (7.10 to 8.57)	6.93 (6.67 to 7.16)	8.41 (7.00 to 9.79)	7.52 (7.03 to 8.51)

End point values	Arm 2a: Chemotherapy (PD-L1 CPS ≥ 10)	Arm 2a: Chemotherapy (PD-L1 CPS ≥ 1)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	307	510		
Units: Months				
median (confidence interval 95%)				
All Randomized	5.82 (5.45 to 6.90)	6.93 (6.21 to 7.06)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate in participants treated with Nivolumab plus Chemotherapy vs Chemotherapy

End point title	Objective Response Rate in participants treated with Nivolumab plus Chemotherapy vs Chemotherapy[3]

End point description:

Objective response rate (ORR) as assessed by BICR in participants with PD-L1 CPS ≥ 10, 5, 1, or all randomized participants. ORR is a percentage of participants determined by the number of participants with a best overall response (BOR) of complete response (CR) or partial response (PR) divided by the number of measurable participants with target lesion at baseline. BOR is defined as the best response designation as determined by the BICR, recorded between the date of randomization and the date of objectively documented progression (per RECIST 1.1 as determined by the BICR) or the date of subsequent anti-cancer therapy, whichever occurs first. CR is defined as the disappearance of all target lesions. PR is define as at 30% decrease in the sum of diameters of target lesions. The 806 chemotherapy treated participants are split into two separate arms (Arm 2a and Arm 2b) to act as comparison groups to the other treatment arms.

End point type	Secondary

End point timeframe:

From randomization to the date of objectively documented progression or the date of subsequent anti-cancer therapy, whichever occurs first (up to approximately 43 months)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No further statistical analysis done at this time

End point values	Arm 1: Nivolumab + Chemotherapy (XELOX or FOLFOX)	Arm 2a: Chemotherapy (XELOX or FOLFOX)	Arm 1: Nivo + Chem (PD-L1 CPS ≥ 5)	Arm 2a: Chemo (PD-L1 CPS ≥ 5)
Subject group type	Reporting group	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	789	792	473	482
Units: Percentage of Participants				
number (confidence interval 95%)				
All randomized participants	46.9 (43.4 to 50.4)	46.9 (43.4 to 50.4)	50.1 (45.5 to 54.7)	38.2 (33.8 to 42.7)

End point values	Nivo + Chem (PD-L1 CPS ≥ 10)	Nivo + Chem (PD-L1 CPS ≥ 1)	Arm 2a: Chemotherapy (PD-L1 CPS ≥ 10)	Arm 2a: Chemotherapy (PD-L1 CPS ≥ 1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	375	641	393	656
Units: Percentage of Participants				
number (confidence interval 95%)				
All randomized participants	48.8 (43.6 to 54.0)	48.8 (44.9 to 52.8)	37.7 (32.9 to 42.7)	38.0 (34.2 to 41.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Symptom Deterioration (TTSD) in participants treated with Nivolumab plus Chemotherapy vs Chemotherapy

End point title	Time to Symptom Deterioration (TTSD) in participants treated with Nivolumab plus Chemotherapy vs Chemotherapy[4]

End point description:

TTSD is defined as the the time from randomization until a clinically meaningful decline from baseline in Gastric Cancer Subscale (GaCS) score. A clinically meaningful deterioration is defined as a reduction of 8.2 points in the GaCS score. Subjects who do not deteriorate will be censored at the time of their last GACS assessment. Subjects without baseline GaCS assessment will be censored on the randomization date. Those with baseline GaCS, who do not have any GaCS assessments after randomization will be censored on the day after randomization.

Here "99999" means NA

End point type	Secondary

End point timeframe:

From randomization until a clinically meaningful decline from baseline in GaCS score

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No further statistical analysis done at this time

End point values	Arm 1: Nivolumab + Chemotherapy (XELOX or FOLFOX)			
Subject group type	Reporting group			
Number of subjects analysed	194			
Units: Months				
median (confidence interval 95%)	99999 (22.64 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: OS in participants treated with Nivolumab plus Ipilimumab vs Chemotherapy

End point title	OS in participants treated with Nivolumab plus Ipilimumab vs Chemotherapy[5]

End point description:

Overall survival (OS), defined as the time from randomization to the time of death, in participants treated with Nivolumab plus Ipilimumab vs Chemotherapy with PD-L1 CPS (combined positive score) ≥ 1, 5, 10, and all randomized participants. CPS is defined as the number of PD-L1 staining cells (tumor cells, lymphocytes, macrophages) divided by the total number of viable tumor cells, multiplied by 100.

End point type	Secondary

End point timeframe:

From the date of randomization up to the date of death, up to approximately 14 months

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No further statistical analysis done at this time

End point values	Arm 3: Nivolumab + Ipilimumab	Arm 2b: Chemotherapy (XELOX or FOLFOX)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	409	404		
Units: Months				
median (confidence interval 95%)				
All randomized participants	11.73 (9.56 to 13.54)	11.83 (10.97 to 12.71)		
Participants with CPS ≥ 1	11.73 (9.49 to 13.54)	11.47 (10.48 to 12.65)		
Participants with CPS ≥ 5	11.24 (9.17 to 13.40)	11.63 (10.05 to 12.71)		
Participants with CPS ≥ 10	11.63 (9.26 to 13.54)	11.33 (9.92 to 12.65)		

Statistical analyses

No statistical analyses for this end point

Secondary: PFS in participants treated with Nivolumab plus Ipilimumab vs Chemotherapy

End point title	PFS in participants treated with Nivolumab plus Ipilimumab vs Chemotherapy[6]

End point description:

Progression Free Survival (PFS) is defined as the time from randomization to the date of the first documented PD or death due to any cause. PD is determined by blinded independent committee review (BICR) per RECIST1.1 criteria in participants treated with Nivolumab plus Ipilumab vs Chemotherapy with PD-L1 CPS ≥ 10, 5, 1 or all randomized participants. Progressive disease (PD) is defined as at least a 20% increase in the sum of diameters of target lesions, taking in reference the smallest sum on study that also demonstrated an absolute increase of at least 5 mm. CPS is defined as the number of PD-L1 staining cells (tumor cells, lymphocytes, macrophages) divided by the total number of viable tumor cells, multiplied by 100.

End point type	Secondary

End point timeframe:

From randomization to the date of the first documented progressive disease (PD) per BICR or death due to any cause (up to approximately 9 months)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No further statistical analysis done at this time

End point values	Arm 3: Nivolumab + Ipilimumab	Arm 2b: Chemotherapy (XELOX or FOLFOX)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	409	404		
Units: Months				
median (confidence interval 95%)				
All randomized participants	2.83 (2.63 to 3.58)	7.06 (6.87 to 8.21)		
PD-L1 CPS ≥ 1	2.79 (2.60 to 3.91)	6.93 (5.98 to 7.26)		
PD-L1 CPS ≥ 5	2.83 (2.60 to 4.04)	6.28 (5.59 to 7.06)		
PD-L1 CPS ≥ 10	2.89 (2.63 to 4.24)	6.28 (5.52 to 7.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate in participants treated with Nivolumab plus Ipilimumab vs Chemotherapy

End point title	Objective Response Rate in participants treated with Nivolumab plus Ipilimumab vs Chemotherapy[7]

End point description:

Objective response rate (ORR) as assessed by BICR in participants with PD-L1 CPS ≥ 10, 5, 1, or all randomized participants. ORR is a percentage of participants determined by the number of participants with a best overall response (BOR) of complete response (CR) or partial response (PR) divided by the number of measurable participants with target lesion at baseline. BOR is defined as the best response designation as determined by the BICR, recorded between the date of randomization and the date of objectively documented progression (per RECIST 1.1 as determined by the BICR) or the date of

subsequent anti-cancer therapy, whichever occurs first. CR is defined as the disappearance of all target lesions. PR is define as at 30% decrease in the sum of diameters of target lesions. The 806 chemotherapy treated participants are split into two separate arms (Arm 2a and Arm 2b) to act as comparison groups to the other treatment arms.

End point type	Secondary

End point timeframe:

From randomization to the date of objectively documented progression or the date of subsequent anti-cancer therapy, whichever occurs first (up to approximately 43 months)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No further statistical analysis done at this time

End point values	Arm 3: Nivolumab + Ipilimumab	Arm 2b: Chemotherapy (XELOX or FOLFOX)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	409	404		
Units: Percentage of Participants				
number (confidence interval 95%)				
Participants with CPS ≥ 1	21.7 (17.4 to 26.6)	37.3 (32.0 to 42.9)		
Participants with CPS ≥ 5	23.1 (17.8 to 29.0)	37.7 (31.5 to 44.1)		
Participants with CPS ≥ 10	24.3 (18.3 to 31.2)	35.9 (29.2 to 43.0)		
All randomized participants	20.8 (17.0 to 25.0)	34.9 (30.3 to 39.8)		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality: from date of randomization to study completion (up to approximately 5 years).

Serious Adverse events and other adverse events: from date of first dose to 100 days post last dose (up to approximately 5 years).

Adverse event reporting additional description:

The number at Risk for All-Cause Mortality represents all Randomized Participants. The number at Risk for Serious Adverse Events and Other (Not Including Serious) Adverse Events represents all participants that received at least 1 dose of study medication

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Arm 1: Nivolumab + Chemotherapy (XELOX or FOLFOX)

Reporting group description:

Nivolumab + Xelox: Nivolumab 360 mg IV over 30 minutes on Day 1 of each treatment cycle, every 3 weeks + Oxaliplatin 130 mg/m2 IV on Day 1 of each treatment cycle + capecitabine 1000 mg/m2 orally twice daily (ie, 1000 mg/m2 in the morning and 1000 mg/m2 in the evening) on Days 1 to 14 of each treatment cycle, every 3 weeks

Nivolumab + Folfox: Nivolumab 240 mg IV over 30 minutes on Day 1 of each treatment cycle, every 2 weeks + Oxaliplatin 85 mg/m2 + leucovorin 400 mg/m2 + fluorouracil 400 mg/m2 IV on Day 1 of each treatment cycle, and fluorouracil 1200 mg/m2 IV continuous infusion over 24 hours (or per local standard) daily on Days 1 and 2 of each treatment cycle, every 2 weeks

Reporting group title	Arm 3: Nivolumab + Ipilimumab

Reporting group description:

1 mg/kg nivolumab administered IV over 30 minutes followed by ipilimumab 3 mg/kg administered IV over 30 minutes on Day 1 of each treatment cycle every 3 weeks for 4 doses (Cycles 1 to 4), followed by nivolumab 240 mg administered IV over 30 minutes on Day 1 of each treatment cycle every 2 weeks (Cycle 5 and beyond). Arm is closed to enrollment as of 05-June-2018.

Reporting group title	Arm 2: Chemotherapy (XELOX or FOLFOX)

Reporting group description:

Chemotherapy (XELOX or FOLFOX): Xelox: Oxaliplatin 130 mg/m2 IV on Day 1 of each treatment cycle + capecitabine 1000 mg/m2 orally twice daily (ie, 1000 mg/m2 in the morning and 1000 mg/m2 in the evening) on Days 1 to 14 of each treatment cycle, every 3 weeks. Folfox: Oxaliplatin 85 mg/m2 + leucovorin 400 mg/m2 + fluorouracil 400 mg/m2 IV on Day 1 of each treatment cycle, and fluorouracil 1200 mg/m2 IV continuous infusion over 24 hours (or per local standard) daily on Days 1 and 2 of each treatment cycle, every 2 weeks. This chemotherapy group consists of the two comparison chemotherapy sub-groups. Arm 2a (792 participants) is the comparison group to Arm 1 and Arm 2b (404 participants) is the comparison group to Arm 3. Some participants were counted in both Arm 2a and Arm 2b.

Serious adverse events	Arm 1: Nivolumab + Chemotherapy (XELOX or FOLFOX)	Arm 3: Nivolumab + Ipilimumab	Arm 2: Chemotherapy (XELOX or FOLFOX)
Total subjects affected by serious adverse events			
subjects affected / exposed	529 / 782 (67.65%)	307 / 403 (76.18%)	474 / 806 (58.81%)
number of deaths (all causes)	691	361	741
number of deaths resulting from adverse events	301	133	286

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic gastric cancer			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastasis			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to meninges			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Metastases to liver			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	3 / 782 (0.38%)	0 / 403 (0.00%)	4 / 806 (0.50%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to bone			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Malignant neoplasm progression			
subjects affected / exposed	248 / 782 (31.71%)	112 / 403 (27.79%)	246 / 806 (30.52%)
occurrences causally related to treatment / all	1 / 262	0 / 114	0 / 250
deaths causally related to treatment / all	1 / 238	0 / 97	0 / 232
Laryngeal squamous cell carcinoma			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastric neoplasm			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	2 / 782 (0.26%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Cancer pain			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Tumour pain			
subjects affected / exposed	2 / 782 (0.26%)	2 / 403 (0.50%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm malignant			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Neoplasm progression			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal adenocarcinoma			

subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Oesophageal cancer metastatic			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Rectal cancer			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Second primary malignancy			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Squamous cell carcinoma			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Squamous cell carcinoma of lung			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Tumour associated fever			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Tumour haemorrhage			
subjects affected / exposed	3 / 782 (0.38%)	2 / 403 (0.50%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour necrosis			

subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Tumour obstruction			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour ulceration			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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			
Obstructive shock			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Axillary vein thrombosis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Capillary leak syndrome			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Circulatory collapse			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Deep vein thrombosis			
subjects affected / exposed	2 / 782 (0.26%)	3 / 403 (0.74%)	3 / 806 (0.37%)
occurrences causally related to treatment / all	0 / 2	1 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			

subjects affected / exposed	6 / 782 (0.77%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	1 / 6	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Jugular vein thrombosis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral venous disease			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Peripheral artery occlusion			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Venous thrombosis			

subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Shock haemorrhagic			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Subclavian artery stenosis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Thrombosis			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic venous thrombosis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Euthanasia			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
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			
subjects affected / exposed	1 / 782 (0.13%)	3 / 403 (0.74%)	5 / 806 (0.62%)
occurrences causally related to treatment / all	0 / 1	2 / 3	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1

Malaise			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	3 / 806 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inflammation			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site haemorrhage			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Chest discomfort			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Complication associated with device			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 782 (0.13%)	2 / 403 (0.50%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 1
Disease progression			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Effusion			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Face oedema			

subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	3 / 782 (0.38%)	6 / 403 (1.49%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	3 / 3	2 / 6	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	5 / 782 (0.64%)	3 / 403 (0.74%)	7 / 806 (0.87%)
occurrences causally related to treatment / all	0 / 5	1 / 3	1 / 7
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Generalised oedema			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Catheter site extravasation			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Ulcer haemorrhage			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Sudden death			

subjects affected / exposed	2 / 782 (0.26%)	2 / 403 (0.50%)	3 / 806 (0.37%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 3
Pyrexia			
subjects affected / exposed	22 / 782 (2.81%)	9 / 403 (2.23%)	11 / 806 (1.36%)
occurrences causally related to treatment / all	8 / 24	11 / 13	3 / 12
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral swelling			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Performance status decreased			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	3 / 782 (0.38%)	0 / 403 (0.00%)	4 / 806 (0.50%)
occurrences causally related to treatment / all	0 / 3	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	3 / 782 (0.38%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
subjects affected / exposed	2 / 782 (0.26%)	2 / 403 (0.50%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 2	1 / 2	0 / 0
Mucosal inflammation			

subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	4 / 782 (0.51%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	3 / 4	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contrast media allergy			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Anaphylactic reaction			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vaginal haemorrhage			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Malignant pleural effusion			

subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Laryngeal haemorrhage			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Interstitial lung disease			
subjects affected / exposed	3 / 782 (0.38%)	2 / 403 (0.50%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	4 / 4	2 / 2	2 / 2
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Immune-mediated lung disease			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiccups			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mediastinal effusion			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			

subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Bronchospasm			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asphyxia			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Acute respiratory failure			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Dyspnoea			
subjects affected / exposed	0 / 782 (0.00%)	2 / 403 (0.50%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pulmonary embolism			
subjects affected / exposed	14 / 782 (1.79%)	10 / 403 (2.48%)	18 / 806 (2.23%)
occurrences causally related to treatment / all	1 / 14	1 / 10	2 / 19
deaths causally related to treatment / all	0 / 5	0 / 3	1 / 2
Pulmonary hypertension			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Pulmonary oedema			

subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	5 / 782 (0.64%)	2 / 403 (0.50%)	3 / 806 (0.37%)
occurrences causally related to treatment / all	1 / 5	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 3	0 / 2	0 / 1
Restrictive pulmonary disease			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Oropharyngeal discomfort			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	5 / 782 (0.64%)	6 / 403 (1.49%)	6 / 806 (0.74%)
occurrences causally related to treatment / all	0 / 6	0 / 7	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonitis			
subjects affected / exposed	19 / 782 (2.43%)	7 / 403 (1.74%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	22 / 22	9 / 9	0 / 1
deaths causally related to treatment / all	4 / 4	1 / 1	0 / 0
Pneumothorax			
subjects affected / exposed	3 / 782 (0.38%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary artery thrombosis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis aspiration			

subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Mental status changes			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Eating disorder			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Depression			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Bipolar disorder			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Stent malfunction			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device occlusion			
subjects affected / exposed	3 / 782 (0.38%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device leakage			

subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device dislocation			
subjects affected / exposed	3 / 782 (0.38%)	2 / 403 (0.50%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device breakage			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	0 / 782 (0.00%)	6 / 403 (1.49%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	6 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Bile duct stone			
subjects affected / exposed	3 / 782 (0.38%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stenosis			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute hepatic failure			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Hepatitis acute			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Hepatitis			

subjects affected / exposed	1 / 782 (0.13%)	5 / 403 (1.24%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	6 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	3 / 782 (0.38%)	5 / 403 (1.24%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	3 / 4	4 / 5	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hepatic failure			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Hepatic cyst ruptured			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Drug-induced liver injury			
subjects affected / exposed	1 / 782 (0.13%)	3 / 403 (0.74%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholestasis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis chronic			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			

subjects affected / exposed	5 / 782 (0.64%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis acute			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Cholangitis			
subjects affected / exposed	3 / 782 (0.38%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary obstruction			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis toxic			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Portal hypertension			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver injury			
subjects affected / exposed	0 / 782 (0.00%)	3 / 403 (0.74%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	7 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver disorder			
subjects affected / exposed	2 / 782 (0.26%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatorenal failure			

subjects affected / exposed	0 / 782 (0.00%)	2 / 403 (0.50%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Jaundice			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Immune-mediated hepatitis			
subjects affected / exposed	3 / 782 (0.38%)	3 / 403 (0.74%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	3 / 3	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hepatic disorder			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminasaemia			
subjects affected / exposed	0 / 782 (0.00%)	2 / 403 (0.50%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Hepatotoxicity			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	6 / 782 (0.77%)	2 / 403 (0.50%)	4 / 806 (0.50%)
occurrences causally related to treatment / all	0 / 6	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Suspected drug-induced liver injury			

subjects affected / exposed	0 / 782 (0.00%)	2 / 403 (0.50%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary cyst			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Lipase increased			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 782 (0.13%)	2 / 403 (0.50%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amylase increased			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Blood bilirubin increased			
subjects affected / exposed	6 / 782 (0.77%)	2 / 403 (0.50%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	2 / 6	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood corticotrophin decreased			

subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 782 (0.00%)	2 / 403 (0.50%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram ST segment elevation			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical condition abnormal			
subjects affected / exposed	2 / 782 (0.26%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Hepatitis C virus test positive			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Liver function test increased			
subjects affected / exposed	0 / 782 (0.00%)	2 / 403 (0.50%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	3 / 782 (0.38%)	0 / 403 (0.00%)	3 / 806 (0.37%)
occurrences causally related to treatment / all	5 / 5	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			

subjects affected / exposed	3 / 782 (0.38%)	1 / 403 (0.25%)	4 / 806 (0.50%)
occurrences causally related to treatment / all	2 / 3	0 / 1	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin increased			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Injury, poisoning and procedural complications			
Anastomotic stenosis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal stoma complication			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	3 / 782 (0.38%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Femur fracture			

subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis radiation			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Craniocerebral injury			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Procedural complication			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Skin laceration			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue injury			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			

subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Spinal fracture			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heat stroke			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Hip fracture			
subjects affected / exposed	3 / 782 (0.38%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	6 / 782 (0.77%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	7 / 7	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Lumbar vertebral fracture			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			

subjects affected / exposed	11 / 782 (1.41%)	0 / 403 (0.00%)	6 / 806 (0.74%)
occurrences causally related to treatment / all	0 / 11	0 / 0	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematoma			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Road traffic accident			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial rupture			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular access malfunction			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Afferent loop syndrome			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Congenital, familial and genetic disorders			
Microvillous inclusion disease			

subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Pyloric stenosis			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Tracheo-oesophageal fistula			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	4 / 782 (0.51%)	1 / 403 (0.25%)	4 / 806 (0.50%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 1
Angina pectoris			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arrhythmia			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Atrial fibrillation			

subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	2 / 782 (0.26%)	1 / 403 (0.25%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 2
Autoimmune myocarditis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	2 / 782 (0.26%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 1
Cardiac failure			
subjects affected / exposed	0 / 782 (0.00%)	2 / 403 (0.50%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	2 / 2	0 / 1
Cardiac failure acute			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac failure congestive			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			

subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Myocardial infarction			
subjects affected / exposed	2 / 782 (0.26%)	3 / 403 (0.74%)	5 / 806 (0.62%)
occurrences causally related to treatment / all	0 / 2	1 / 3	0 / 5
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 5
Pericardial effusion			
subjects affected / exposed	3 / 782 (0.38%)	1 / 403 (0.25%)	3 / 806 (0.37%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular extrasystoles			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Supraventricular tachycardia			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachyarrhythmia			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Tachycardia			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial injury			

subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Encephalopathy			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis autoimmune			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Dizziness			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic hyperosmolar coma			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Aphasia			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			

subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	2 / 782 (0.26%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 0
Cerebellar syndrome			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system lesion			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain stem infarction			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Brain oedema			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Cerebrovascular accident			
subjects affected / exposed	3 / 782 (0.38%)	1 / 403 (0.25%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 2
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 1
Seizure			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			

subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropathy peripheral			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuritis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paresis			
subjects affected / exposed	0 / 782 (0.00%)	2 / 403 (0.50%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial pressure increased			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Immune-mediated neuropathy			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokinesia			

subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Headache			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-Barre syndrome			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Transient ischaemic attack			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	9 / 782 (1.15%)	2 / 403 (0.50%)	4 / 806 (0.50%)
occurrences causally related to treatment / all	1 / 9	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Spinal cord compression			

subjects affected / exposed	2 / 782 (0.26%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic stroke			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	28 / 782 (3.58%)	13 / 403 (3.23%)	17 / 806 (2.11%)
occurrences causally related to treatment / all	13 / 33	1 / 16	4 / 17
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood loss anaemia			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	20 / 782 (2.56%)	1 / 403 (0.25%)	10 / 806 (1.24%)
occurrences causally related to treatment / all	17 / 21	0 / 1	6 / 10
deaths causally related to treatment / all	2 / 2	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Febrile bone marrow aplasia			
subjects affected / exposed	2 / 782 (0.26%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone marrow failure			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune thrombocytopenia			

subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Leukopenia			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenopathy			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Thrombotic microangiopathy			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Neutropenia			
subjects affected / exposed	4 / 782 (0.51%)	0 / 403 (0.00%)	3 / 806 (0.37%)
occurrences causally related to treatment / all	4 / 4	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Splenic haematoma			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Thrombocytopenia			

subjects affected / exposed	4 / 782 (0.51%)	2 / 403 (0.50%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	3 / 4	1 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myelosuppression			
subjects affected / exposed	4 / 782 (0.51%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	3 / 4	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Eye disorders			
Cataract			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Ocular vasculitis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual impairment			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal adhesions			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abdominal distension			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	6 / 782 (0.77%)	11 / 403 (2.73%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	6 / 6	15 / 15	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	3 / 782 (0.38%)	2 / 403 (0.50%)	3 / 806 (0.37%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cyclic vomiting syndrome			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	1 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	21 / 782 (2.69%)	13 / 403 (3.23%)	14 / 806 (1.74%)
occurrences causally related to treatment / all	17 / 22	10 / 15	13 / 16
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal obstruction			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Autoimmune colitis			
subjects affected / exposed	2 / 782 (0.26%)	3 / 403 (0.74%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	4 / 4	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspepsia			

subjects affected / exposed	0 / 782 (0.00%)	2 / 403 (0.50%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	13 / 782 (1.66%)	9 / 403 (2.23%)	23 / 806 (2.85%)
occurrences causally related to treatment / all	0 / 15	1 / 12	0 / 24
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Abdominal pain			
subjects affected / exposed	12 / 782 (1.53%)	4 / 403 (0.99%)	13 / 806 (1.61%)
occurrences causally related to treatment / all	0 / 12	0 / 4	1 / 14
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Abdominal pain lower			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	2 / 782 (0.26%)	2 / 403 (0.50%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	15 / 782 (1.92%)	6 / 403 (1.49%)	9 / 806 (1.12%)
occurrences causally related to treatment / all	1 / 16	0 / 6	0 / 10
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Duodenal perforation			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	1 / 782 (0.13%)	2 / 403 (0.50%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			

subjects affected / exposed	4 / 782 (0.51%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	4 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	3 / 782 (0.38%)	4 / 403 (0.99%)	11 / 806 (1.36%)
occurrences causally related to treatment / all	1 / 3	0 / 5	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 3
Gastric perforation			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	3 / 806 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric stenosis			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal fistula			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	13 / 782 (1.66%)	4 / 403 (0.99%)	9 / 806 (1.12%)
occurrences causally related to treatment / all	2 / 14	0 / 4	2 / 10
deaths causally related to treatment / all	1 / 3	0 / 1	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Gastrointestinal necrosis			

subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal obstruction			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal perforation			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal stenosis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Haematemesis			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Intestinal stenosis			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Intestinal obstruction			

subjects affected / exposed	3 / 782 (0.38%)	2 / 403 (0.50%)	7 / 806 (0.87%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Intestinal haemorrhage			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired gastric emptying			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated enterocolitis			
subjects affected / exposed	1 / 782 (0.13%)	11 / 403 (2.73%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	1 / 1	13 / 13	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Large intestinal haemorrhage			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Ileus			
subjects affected / exposed	4 / 782 (0.51%)	1 / 403 (0.25%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoperitoneum			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			

subjects affected / exposed	0 / 782 (0.00%)	2 / 403 (0.50%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal stenosis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Ileus paralytic			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malabsorption			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant gastrointestinal obstruction			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Melaena			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	8 / 782 (1.02%)	7 / 403 (1.74%)	10 / 806 (1.24%)
occurrences causally related to treatment / all	7 / 11	1 / 7	8 / 10
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Obstruction gastric			

subjects affected / exposed	4 / 782 (0.51%)	6 / 403 (1.49%)	6 / 806 (0.74%)
occurrences causally related to treatment / all	0 / 5	0 / 6	1 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Obstructive pancreatitis			
subjects affected / exposed	0 / 782 (0.00%)	2 / 403 (0.50%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal compression			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal fistula			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Oesophageal haemorrhage			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal obstruction			
subjects affected / exposed	4 / 782 (0.51%)	4 / 403 (0.99%)	3 / 806 (0.37%)
occurrences causally related to treatment / all	0 / 5	1 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal pain			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Oesophageal stenosis			
subjects affected / exposed	3 / 782 (0.38%)	2 / 403 (0.50%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 3	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal ulcer haemorrhage			

subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	29 / 782 (3.71%)	11 / 403 (2.73%)	23 / 806 (2.85%)
occurrences causally related to treatment / all	14 / 36	0 / 13	20 / 28
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Upper gastrointestinal haemorrhage			
subjects affected / exposed	17 / 782 (2.17%)	13 / 403 (3.23%)	10 / 806 (1.24%)
occurrences causally related to treatment / all	1 / 20	3 / 15	2 / 10
deaths causally related to treatment / all	0 / 2	1 / 3	0 / 0
Thrombosis mesenteric vessel			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 1	0 / 0
Subileus			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	4 / 782 (0.51%)	0 / 403 (0.00%)	5 / 806 (0.62%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Retroperitoneal haematoma			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctitis			

subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Prepyloric stenosis			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Peritoneal adhesions			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 782 (0.13%)	3 / 403 (0.74%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant ascites			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			

subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug eruption			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eczema asteatotic			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	2 / 782 (0.26%)	2 / 403 (0.50%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic skin ulcer			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Skin lesion			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic epidermal necrolysis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			

subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 782 (0.00%)	3 / 403 (0.74%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pemphigoid			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	6 / 782 (0.77%)	9 / 403 (2.23%)	4 / 806 (0.50%)
occurrences causally related to treatment / all	1 / 6	4 / 10	1 / 5
deaths causally related to treatment / all	0 / 4	0 / 1	0 / 0
Cystitis noninfective			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Dysuria			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 782 (0.00%)	2 / 403 (0.50%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Ureterolithiasis			

subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric dilatation			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	3 / 806 (0.37%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Prerenal failure			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Nephrolithiasis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephritis			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis			

subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Endocrine disorders			
Hypophysitis			
subjects affected / exposed	1 / 782 (0.13%)	4 / 403 (0.99%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Adrenal insufficiency			
subjects affected / exposed	3 / 782 (0.38%)	4 / 403 (0.99%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	3 / 3	3 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Autoimmune thyroiditis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthyroidism			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypopituitarism			
subjects affected / exposed	3 / 782 (0.38%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	2 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothalamo-pituitary disorder			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypothyroidism			

subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated hypophysitis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Secondary adrenocortical insufficiency			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroiditis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Back pain			
subjects affected / exposed	4 / 782 (0.51%)	1 / 403 (0.25%)	4 / 806 (0.50%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bone lesion			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Bone pain			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Mixed connective tissue disease			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			
subjects affected / exposed	0 / 782 (0.00%)	3 / 403 (0.74%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteolysis			

subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Pathological fracture			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Arthralgia			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Bronchitis viral			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary tract infection			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	4 / 782 (0.51%)	3 / 403 (0.74%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 4	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			

subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Appendicitis perforated			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Appendicitis			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amoebic colitis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal sepsis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal infection			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Abdominal abscess			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	1 / 782 (0.13%)	2 / 403 (0.50%)	3 / 806 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 2	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chorioretinitis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Cystitis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue fever			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	2 / 782 (0.26%)	1 / 403 (0.25%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Diarrhoea infectious			

subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Endophthalmitis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Enteritis infectious			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Enterocolitis infectious			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Epididymitis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			

subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Giardiasis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Hepatitis C			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex reactivation			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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 abscess			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Infection			
subjects affected / exposed	2 / 782 (0.26%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	2 / 2	1 / 1	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Intervertebral discitis			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine infection			

subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Localised infection			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Lower respiratory tract infection			
subjects affected / exposed	1 / 782 (0.13%)	2 / 403 (0.50%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Herpes virus infection			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphangitis			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mycobacterium avium complex infection			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic infection			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal candidiasis			

subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Osteomyelitis			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pneumococcal			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Peritonitis			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis bacterial			
subjects affected / exposed	2 / 782 (0.26%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	30 / 782 (3.84%)	14 / 403 (3.47%)	21 / 806 (2.61%)
occurrences causally related to treatment / all	6 / 35	0 / 15	2 / 21
deaths causally related to treatment / all	1 / 7	0 / 2	0 / 4
Pneumonia bacterial			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Pneumonia klebsiella			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parainfluenzae virus infection			

subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Pneumonia viral			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculous pleurisy			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Pyelonephritis			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
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			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Sepsis			
subjects affected / exposed	12 / 782 (1.53%)	3 / 403 (0.74%)	8 / 806 (0.99%)
occurrences causally related to treatment / all	1 / 12	1 / 3	0 / 8
deaths causally related to treatment / all	0 / 3	0 / 1	0 / 2
Septic shock			
subjects affected / exposed	1 / 782 (0.13%)	2 / 403 (0.50%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	1 / 1	0 / 2	0 / 1
Sialoadenitis			

subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Skin infection			
subjects affected / exposed	0 / 782 (0.00%)	2 / 403 (0.50%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Staphylococcal infection			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Stoma site infection			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Streptococcal bacteraemia			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Tonsillitis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Psoas abscess			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			

subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Urinary tract infection			
subjects affected / exposed	3 / 782 (0.38%)	6 / 403 (1.49%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 3	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	3 / 782 (0.38%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Viral infection			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Pneumonia aspiration			
subjects affected / exposed	3 / 782 (0.38%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Haematological infection			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Spontaneous bacterial peritonitis			

subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	8 / 782 (1.02%)	3 / 403 (0.74%)	7 / 806 (0.87%)
occurrences causally related to treatment / all	3 / 9	0 / 3	2 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Diabetic ketoacidosis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Electrolyte imbalance			
subjects affected / exposed	2 / 782 (0.26%)	1 / 403 (0.25%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Decreased appetite			

subjects affected / exposed	7 / 782 (0.90%)	6 / 403 (1.49%)	9 / 806 (1.12%)
occurrences causally related to treatment / all	5 / 10	2 / 6	10 / 12
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Gout			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Hypercalcaemia			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	0 / 782 (0.00%)	2 / 403 (0.50%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Hypernatraemia			
subjects affected / exposed	1 / 782 (0.13%)	0 / 403 (0.00%)	0 / 806 (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
Hypoalbuminaemia			
subjects affected / exposed	1 / 782 (0.13%)	3 / 403 (0.74%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 782 (0.13%)	2 / 403 (0.50%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			

subjects affected / exposed	3 / 782 (0.38%)	2 / 403 (0.50%)	5 / 806 (0.62%)
occurrences causally related to treatment / all	2 / 4	0 / 2	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	4 / 782 (0.51%)	3 / 403 (0.74%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	1 / 4	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophagia			
subjects affected / exposed	0 / 782 (0.00%)	0 / 403 (0.00%)	1 / 806 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoproteinaemia			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Malnutrition			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	2 / 806 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Metabolic acidosis			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (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
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 782 (0.00%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 782 (0.13%)	1 / 403 (0.25%)	0 / 806 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Arm 1: Nivolumab + Chemotherapy (XELOX or FOLFOX)	Arm 3: Nivolumab + Ipilimumab	Arm 2: Chemotherapy (XELOX or FOLFOX)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	763 / 782 (97.57%)	369 / 403 (91.56%)	756 / 806 (93.80%)
Vascular disorders			
Hypotension			
subjects affected / exposed	26 / 782 (3.32%)	21 / 403 (5.21%)	21 / 806 (2.61%)
occurrences (all)	31	29	24
Hypertension			
subjects affected / exposed	48 / 782 (6.14%)	17 / 403 (4.22%)	42 / 806 (5.21%)
occurrences (all)	66	25	61
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	40 / 782 (5.12%)	19 / 403 (4.71%)	41 / 806 (5.09%)
occurrences (all)	54	23	47
Mucosal inflammation			
subjects affected / exposed	77 / 782 (9.85%)	7 / 403 (1.74%)	47 / 806 (5.83%)
occurrences (all)	127	10	64
Oedema peripheral			
subjects affected / exposed	93 / 782 (11.89%)	44 / 403 (10.92%)	67 / 806 (8.31%)
occurrences (all)	122	46	70
Pyrexia			
subjects affected / exposed	143 / 782 (18.29%)	93 / 403 (23.08%)	95 / 806 (11.79%)
occurrences (all)	219	129	127
Fatigue			
subjects affected / exposed	273 / 782 (34.91%)	103 / 403 (25.56%)	235 / 806 (29.16%)
occurrences (all)	403	129	341
Asthenia			
subjects affected / exposed	119 / 782 (15.22%)	48 / 403 (11.91%)	130 / 806 (16.13%)
occurrences (all)	169	56	192
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	48 / 782 (6.14%)	4 / 403 (0.99%)	13 / 806 (1.61%)
occurrences (all)	57	4	15

Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	102 / 782 (13.04%)	51 / 403 (12.66%)	64 / 806 (7.94%)
occurrences (all)	138	64	76
Dyspnoea			
subjects affected / exposed	66 / 782 (8.44%)	37 / 403 (9.18%)	49 / 806 (6.08%)
occurrences (all)	82	50	53
Psychiatric disorders			
Insomnia			
subjects affected / exposed	61 / 782 (7.80%)	36 / 403 (8.93%)	69 / 806 (8.56%)
occurrences (all)	65	38	74
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	120 / 782 (15.35%)	76 / 403 (18.86%)	88 / 806 (10.92%)
occurrences (all)	177	94	128
Amylase increased			
subjects affected / exposed	91 / 782 (11.64%)	48 / 403 (11.91%)	45 / 806 (5.58%)
occurrences (all)	133	62	56
Aspartate aminotransferase increased			
subjects affected / exposed	165 / 782 (21.10%)	81 / 403 (20.10%)	115 / 806 (14.27%)
occurrences (all)	282	103	176
Blood bilirubin increased			
subjects affected / exposed	83 / 782 (10.61%)	30 / 403 (7.44%)	62 / 806 (7.69%)
occurrences (all)	169	32	96
Blood alkaline phosphatase increased			
subjects affected / exposed	107 / 782 (13.68%)	47 / 403 (11.66%)	69 / 806 (8.56%)
occurrences (all)	144	58	109
Blood creatinine increased			
subjects affected / exposed	42 / 782 (5.37%)	35 / 403 (8.68%)	22 / 806 (2.73%)
occurrences (all)	65	53	36
Lipase increased			
subjects affected / exposed	107 / 782 (13.68%)	52 / 403 (12.90%)	72 / 806 (8.93%)
occurrences (all)	149	66	87
Neutrophil count decreased			
subjects affected / exposed	171 / 782 (21.87%)	19 / 403 (4.71%)	140 / 806 (17.37%)
occurrences (all)	492	25	335

Platelet count decreased			
subjects affected / exposed	175 / 782 (22.38%)	21 / 403 (5.21%)	132 / 806 (16.38%)
occurrences (all)	338	25	238
Weight decreased			
subjects affected / exposed	139 / 782 (17.77%)	60 / 403 (14.89%)	128 / 806 (15.88%)
occurrences (all)	171	65	134
White blood cell count decreased			
subjects affected / exposed	124 / 782 (15.86%)	16 / 403 (3.97%)	92 / 806 (11.41%)
occurrences (all)	338	23	228
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	67 / 782 (8.57%)	12 / 403 (2.98%)	31 / 806 (3.85%)
occurrences (all)	85	14	43
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	45 / 782 (5.75%)	6 / 403 (1.49%)	42 / 806 (5.21%)
occurrences (all)	68	6	51
Headache			
subjects affected / exposed	89 / 782 (11.38%)	33 / 403 (8.19%)	53 / 806 (6.58%)
occurrences (all)	134	47	75
Dysgeusia			
subjects affected / exposed	48 / 782 (6.14%)	10 / 403 (2.48%)	43 / 806 (5.33%)
occurrences (all)	53	11	45
Dizziness			
subjects affected / exposed	57 / 782 (7.29%)	16 / 403 (3.97%)	59 / 806 (7.32%)
occurrences (all)	75	18	73
Peripheral sensory neuropathy			
subjects affected / exposed	146 / 782 (18.67%)	13 / 403 (3.23%)	129 / 806 (16.00%)
occurrences (all)	205	14	202
Paraesthesia			
subjects affected / exposed	72 / 782 (9.21%)	7 / 403 (1.74%)	78 / 806 (9.68%)
occurrences (all)	102	8	117
Neuropathy peripheral			
subjects affected / exposed	241 / 782 (30.82%)	7 / 403 (1.74%)	211 / 806 (26.18%)
occurrences (all)	356	8	320
Blood and lymphatic system disorders			

Thrombocytopenia			
subjects affected / exposed	172 / 782 (21.99%)	10 / 403 (2.48%)	161 / 806 (19.98%)
occurrences (all)	298	12	286
Neutropenia			
subjects affected / exposed	221 / 782 (28.26%)	18 / 403 (4.47%)	205 / 806 (25.43%)
occurrences (all)	503	28	415
Anaemia			
subjects affected / exposed	312 / 782 (39.90%)	132 / 403 (32.75%)	279 / 806 (34.62%)
occurrences (all)	511	179	387
Leukopenia			
subjects affected / exposed	76 / 782 (9.72%)	9 / 403 (2.23%)	65 / 806 (8.06%)
occurrences (all)	203	19	128
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	56 / 782 (7.16%)	26 / 403 (6.45%)	43 / 806 (5.33%)
occurrences (all)	63	31	44
Abdominal pain upper			
subjects affected / exposed	75 / 782 (9.59%)	37 / 403 (9.18%)	77 / 806 (9.55%)
occurrences (all)	97	44	98
Abdominal pain			
subjects affected / exposed	159 / 782 (20.33%)	66 / 403 (16.38%)	134 / 806 (16.63%)
occurrences (all)	209	83	169
Vomiting			
subjects affected / exposed	248 / 782 (31.71%)	72 / 403 (17.87%)	234 / 806 (29.03%)
occurrences (all)	488	114	442
Stomatitis			
subjects affected / exposed	68 / 782 (8.70%)	13 / 403 (3.23%)	57 / 806 (7.07%)
occurrences (all)	97	14	73
Nausea			
subjects affected / exposed	386 / 782 (49.36%)	101 / 403 (25.06%)	364 / 806 (45.16%)
occurrences (all)	765	137	643
Diarrhoea			
subjects affected / exposed	310 / 782 (39.64%)	112 / 403 (27.79%)	287 / 806 (35.61%)
occurrences (all)	523	171	503
Constipation			

subjects affected / exposed	201 / 782 (25.70%)	77 / 403 (19.11%)	177 / 806 (21.96%)
occurrences (all)	310	89	223
Dysphagia			
subjects affected / exposed	64 / 782 (8.18%)	32 / 403 (7.94%)	65 / 806 (8.06%)
occurrences (all)	73	34	74
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	28 / 782 (3.58%)	41 / 403 (10.17%)	7 / 806 (0.87%)
occurrences (all)	36	46	9
Rash			
subjects affected / exposed	90 / 782 (11.51%)	77 / 403 (19.11%)	22 / 806 (2.73%)
occurrences (all)	109	100	24
Pruritus			
subjects affected / exposed	79 / 782 (10.10%)	72 / 403 (17.87%)	19 / 806 (2.36%)
occurrences (all)	97	84	21
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	108 / 782 (13.81%)	0 / 403 (0.00%)	98 / 806 (12.16%)
occurrences (all)	137	0	123
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	82 / 782 (10.49%)	54 / 403 (13.40%)	13 / 806 (1.61%)
occurrences (all)	90	67	20
Hyperthyroidism			
subjects affected / exposed	30 / 782 (3.84%)	26 / 403 (6.45%)	2 / 806 (0.25%)
occurrences (all)	34	28	6
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	43 / 782 (5.50%)	9 / 403 (2.23%)	21 / 806 (2.61%)
occurrences (all)	50	12	21
Back pain			
subjects affected / exposed	87 / 782 (11.13%)	38 / 403 (9.43%)	69 / 806 (8.56%)
occurrences (all)	102	43	81
Arthralgia			
subjects affected / exposed	74 / 782 (9.46%)	30 / 403 (7.44%)	42 / 806 (5.21%)
occurrences (all)	94	33	47
Metabolism and nutrition disorders			

Hyponatraemia			
subjects affected / exposed	72 / 782 (9.21%)	53 / 403 (13.15%)	51 / 806 (6.33%)
occurrences (all)	110	75	61
Hypokalaemia			
subjects affected / exposed	93 / 782 (11.89%)	37 / 403 (9.18%)	74 / 806 (9.18%)
occurrences (all)	136	55	101
Hypocalcaemia			
subjects affected / exposed	53 / 782 (6.78%)	21 / 403 (5.21%)	37 / 806 (4.59%)
occurrences (all)	84	32	50
Hypoalbuminaemia			
subjects affected / exposed	109 / 782 (13.94%)	62 / 403 (15.38%)	72 / 806 (8.93%)
occurrences (all)	176	81	92
Decreased appetite			
subjects affected / exposed	237 / 782 (30.31%)	111 / 403 (27.54%)	226 / 806 (28.04%)
occurrences (all)	345	137	315
Hyperglycaemia			
subjects affected / exposed	82 / 782 (10.49%)	37 / 403 (9.18%)	64 / 806 (7.94%)
occurrences (all)	161	70	119

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 October 2016	• Provided reference to the newly-updated Nivolumab Investigator Brochure Version 15 in order to ensure the latest safety information is available, including updated algorithms for the management of side effects and contraception language • Clarified some study inclusion/exclusion criteria and procedures • Provided additional guidance on the implementation of RECIST 1.1 criteria
07 December 2016	• Added a new randomization arm, nivolumab-plus-chemotherapy (XELOX or FOLFOX) to the study • Added Blinded Independent Central Review (BICR) of tumor images • Clarified some study procedures, including limiting the treatment period with nivolumab to 2 years • Added safety recommendations for subjects receiving capecitabine
10 May 2017	• Modified inclusion value for albumin to 3.0 g/dL. • Added clarification for traditional Chinese medicines. • Clarified that PDL1 result must be evaluable in order to be randomized and that tumor sample must be submitted on positively charged slides if not sent as a tumor block. • Added instructions for the administration of nivolumab and chemotherapy when administered on the same day. • Specified that capecitabine should be taken with food. • Clarified that outcome research assessments schedule is independent of dosing schedule, and removed some wording that was leading to confusion regarding the safety visits schedule and treatment beyond disease progression.
05 January 2018	• Change the primary population to all comers in nivolumab in combination with oxaliplatin and fluoropyrimidine, • Add ORR by Blinded Independent Central Review (BICR) and PFS by BICR as primary endpoints in the nivolumab in combination with oxaliplatin and fluoropyrimidine and oxaliplatin plus fluoropyrimidine arms. • Clarify distal esophageal adenocarcinoma is eligible in the inclusion criteria. • Removal of the 28 day screening window, amylase and lipase removal from mandatory tests, clarification of procedures • Correction of minor formatting and typographical errors
29 May 2018	• Added that randomization of an additional 300 subjects beyond the originally planned 1349 subjects across the 3 study arms will allow for more robust analysis of the treatment effect of nivolumab in combination with ipilimumab or chemotherapy across different PD-L1 cutoffs in 1L GC/GEJ cancer.
11 June 2018	• Per recommendation of the Data Monitoring Committee (DMC), as of 05-June-2018, the nivolumab plus ipilimumab arm is now closed. Subjects randomized to this arm prior to or on 05-June-2018 will continue to receive treatment with study drugs per protocol, and the study data will remain blinded until planned primary analysis.

14 September 2018	• Incorporates the combined positive score (CPS) for PD-L1 expression into CA209649; the primary population is now subjects with PD-L1expression ≥5 by CPS rather than by the tumor proportion score (TPS) for subjects with nivolumab in combination with oxaliplatin and fluoropyrimidine compared to oxaliplatin and fluoropyrimidine. • The planned analysis of overall survival (OS) for nivolumab plus ipilimumab arm is changed to a secondary objective. • Objective response rate (ORR) has been changed to a secondary endpoint. • The primary, secondary, and exploratory objectives have been updated to reflect changes in subject population definition. • Second disease progression (PFS2) and time to secondary subsequent therapy (TSST) have been added as exploratory analyses. Information on subsequent treatment will be collected during follow-up period. • Statistical assumptions and considerations revised to reflect changes in study population and revised objectives. • Biomarker sampling has been adjusted based on new knowledge in this area of clinical research.
15 November 2018	Based on recent internal data, added approximately 356 subjects into randomization, in total of approximately 2005 subjects will be randomized to keep sample size for primary analyses of PFS and OS in PD-L1 CPS ≥5 subjects for nivolumab in combination with chemotherapy vs chemotherapy.
16 September 2019	Based on the data from the Keynote 062 study, PFS and OS Kaplan-Meier curves separation observed delay, the timing of PFS and OS analyses are updated with minimum follow up 12 and 24 months. In addition, to reduce variability of efficacy results, PFS population was expanded to all randomized subjects with PD-L1 CPS 5. Per Amendment 29, a 480 mg Q4W nivolumab dosing option for subjects who receive nivolumab alone after treatment with nivolumab in combination with ipilimumab or FOLFOX/XELOX is allowed.
11 May 2022	The primary purpose for this amendment is to incorporate changes from the approved Administrative Letters 12, 13, 14/15, 16, and 17 into the global protocol. Additional revisions include updates related to study governance considerations.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported