Clinical trial results:
A Multicenter, Randomized, Open-label Study in Patients with esophageal Cancer refractory or intolerant to Combination Therapy with Fluoropyrimidine and Platinum-based Drugs

Summary

EudraCT number	2015-003339-36
Trial protocol	DE DK GB IT
Global end of trial date	23 October 2020

Results information

Result version number	v1 (current)
This version publication date	06 December 2024
First version publication date	06 December 2024

Trial information

Trial identification

Sponsor protocol code	CA209-473

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	Chaussee de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@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	23 October 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare overall survival (OS) between the nivolumab group and control group (docetaxel or paclitaxel) in patients with esophageal cancer refractory or intolerant to combination therapy with fluoropyrimidine- and platinum-based drugs.

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 participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 December 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 274
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 59
Country: Number of subjects enrolled	Taiwan: 68
Country: Number of subjects enrolled	United States: 1
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Denmark: 4
Worldwide total number of subjects	419
EEA total number of subjects	17

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)	197
From 65 to 84 years	221
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

419 participants were randomized, 417 were treated

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Nivolumab Arm

Arm description:

Nivolumab 240 mg/body solution intravenously every 2 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends

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:

240 mg at 2-week intervals

Arm title	Active Comparator Arm Docetaxel/Paclitaxel

Arm description:

Docetaxel: Intravenously administered at a dose of 75 mg/m2 every 3 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends OR Paclitaxel: Intravenously administered at a dose of 100 mg/m2 weekly for 6 weeks followed by 2-week drug holiday until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends

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

Dosage and administration details:

100 mg/m2 weekly for 6 weeks in succession followed by a 2-week drug holiday

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

Dosage and administration details:

75 mg/m2 at 3-week intervals

Number of subjects in period 1	Nivolumab Arm	Active Comparator Arm Docetaxel/Paclitaxel
Started	210	209
Completed	209	208
Not completed	1	1
Adverse event, serious fatal	1	-
Consent withdrawn by subject	-	1

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Nivolumab Arm

Arm description:

Nivolumab 240 mg/body solution intravenously every 2 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends

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:

240 mg at 2-week intervals

Arm title	Active Comparator Arm Docetaxel/Paclitaxel

Arm description:

Docetaxel: Intravenously administered at a dose of 75 mg/m2 every 3 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends OR Paclitaxel: Intravenously administered at a dose of 100 mg/m2 weekly for 6 weeks followed by 2-week drug holiday until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends

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

Dosage and administration details:

100 mg/m2 weekly for 6 weeks in succession followed by a 2-week drug holiday

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

Dosage and administration details:

75 mg/m2 at 3-week intervals

Number of subjects in period 2	Nivolumab Arm	Active Comparator Arm Docetaxel/Paclitaxel
Started	209	208
Completed	0	0
Not completed	209	208
Other reasons	209	208

Baseline characteristics

Reporting groups	
Reporting group title	Nivolumab Arm
Reporting group description:	
Nivolumab 240 mg/body solution intravenously every 2 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends	
Reporting group title	Active Comparator Arm Docetaxel/Paclitaxel
Reporting group description:	
Docetaxel: Intravenously administered at a dose of 75 mg/m2 every 3 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends OR Paclitaxel: Intravenously administered at a dose of 100 mg/m2 weekly for 6 weeks followed by 2-week drug holiday until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends	

Reporting group values	Nivolumab Arm	Active Comparator Arm Docetaxel/Paclitaxel	Total
Number of subjects	210	209	419
Age Categorical Units: participants			
<=18 years	0	0	0
Between 18 and 65 years	112	85	197
>=65 years	98	124	222
Age Continuous Units: years			
arithmetic mean	64	67	
inter-quartile range (Q1-Q3)	57 to 69	57 to 72	-
Sex: Female, Male Units: participants			
Female	31	24	55
Male	179	185	364
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	201	200	401
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	9	9	18
More than one race	0	0	0
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Nivolumab Arm
Reporting group description:	
Nivolumab 240 mg/body solution intravenously every 2 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends	
Reporting group title	Active Comparator Arm Docetaxel/Paclitaxel
Reporting group description:	
Docetaxel: Intravenously administered at a dose of 75 mg/m2 every 3 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends OR Paclitaxel: Intravenously administered at a dose of 100 mg/m2 weekly for 6 weeks followed by 2-week drug holiday until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends	
Reporting group title	Nivolumab Arm
Reporting group description:	
Nivolumab 240 mg/body solution intravenously every 2 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends	
Reporting group title	Active Comparator Arm Docetaxel/Paclitaxel
Reporting group description:	
Docetaxel: Intravenously administered at a dose of 75 mg/m2 every 3 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends OR Paclitaxel: Intravenously administered at a dose of 100 mg/m2 weekly for 6 weeks followed by 2-week drug holiday until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends	

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
Overall survival (OS) is defined as the time from randomization to death from any cause. For participants lost to follow-up and participants who were alive at the time of data cutoff date, data was censored at the time the participant was last confirmed to be alive. Conducted using the Kaplan-Meier method.	
End point type	Primary
End point timeframe:	
From date of randomization until the date of death due to any cause (assessed up to approximately 58 months)	

End point values	Nivolumab Arm	Active Comparator Arm Docetaxel/Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	210	209		
Units: Months				
median (confidence interval 95%)	10.91 (9.23 to 13.34)	8.51 (7.29 to 9.86)		

Statistical analyses

Statistical analysis title	Hazard Ratio
Comparison groups	Nivolumab Arm v Active Comparator Arm Docetaxel/Paclitaxel
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0189
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.97

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)

End point description:

Progression-free survival (PFS) is the time from randomization until disease progression or worsening. Progressive Disease (PD): At least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. Conducted by using the Kaplan-Meier method

End point type	Secondary

End point timeframe:

From date of randomization until progressive disease or death due to any cause (assessed up to approximately 58 months)

End point values	Nivolumab Arm	Active Comparator Arm Docetaxel/Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	210	209		
Units: Months				
median (confidence interval 95%)	1.68 (1.51 to 2.73)	3.35 (2.99 to 4.21)		

Statistical analyses

Statistical analysis title	Hazard Ratio (HR)
Comparison groups	Nivolumab Arm v Active Comparator Arm Docetaxel/Paclitaxel
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.33

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)

End point description:

Objective response rate (ORR) is defined as the percentage of participants whose best overall response is assessed as either complete response (CR) or partial response (PR). Overall response and best overall response was determined solely by imaging assessment according to the RECIST Guideline Version 1.1 and did not take into account any clinical/symptomatic progression.
Complete Response (CR): Disappearance of all (non-lymph node) target lesions. Any pathological lymph nodes (whether
target or non-target) must have reduction in the short axis to <10 mm.
Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline
sum diameters.

End point type	Secondary

End point timeframe:

From randomization until progressive disease or death due to any cause (assessed up to approximately 58 months)

End point values	Nivolumab Arm	Active Comparator Arm Docetaxel/Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	210	209		
Units: Percent of Participants				
number (confidence interval 95%)	15.7 (11.1 to	16.3 (11.5 to		

21.4)	22.0)

Statistical analyses

Statistical analysis title	Odds Ratio (OR)
Comparison groups	Nivolumab Arm v Active Comparator Arm Docetaxel/Paclitaxel
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.62

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)

End point description:

Duration of response (DoR) measures the length of time that a tumor responds to treatment without growing or spreading i.e. the length of time a participant had either a complete response (CR) or partial response (PR) to study treatment.
Complete Response (CR): Disappearance of all (non-lymph node) target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in the short axis to <10 mm.
Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Conducted by using the Kaplan-Meier method.

End point type	Secondary

End point timeframe:

From randomization until progression or death due to any cause (assessed up to approximately 58 months)

End point values	Nivolumab Arm	Active Comparator Arm Docetaxel/Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	171	158		
Units: Months				
median (confidence interval 95%)	6.93 (5.39 to 11.14)	3.91 (2.79 to 4.17)		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)

End point description:

Disease control rate is defined as the percentage of participants whose best overall response is assessed as complete response (CR), partial response (PR) or stable disease (SD).
Complete Response (CR): Disappearance of all (non-lymph node) target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in the short axis to <10 mm.
Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.
Stable Disease (SD): Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameter while on study.

End point type	Secondary

End point timeframe:

From randomization until progressive disease or death due to any cause (assessed up to approximately 58 months)

End point values	Nivolumab Arm	Active Comparator Arm Docetaxel/Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	210	209		
Units: Percent of participants				
number (confidence interval 95%)	30.5 (24.3 to 37.2)	47.4 (40.4 to 54.4)		

Statistical analyses

Statistical analysis title	Odds Ratio (OR)
Comparison groups	Nivolumab Arm v Active Comparator Arm Docetaxel/Paclitaxel
Number of subjects included in analysis	419
Analysis specification	Pre-specified
Analysis type	
Method	Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.48

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	0.72

Secondary: Best Overall Response (BOR)

End point title	Best Overall Response (BOR)

End point description:

Best overall response (BOR) refers to the best response recorded from the start of the treatment until disease progression or recurrence.
Complete Response (CR): Disappearance of all (non-lymph node) target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in the short axis to <10 mm.
Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.
Progressive Disease (PD): At least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm.

End point type	Secondary

End point timeframe:

From randomization until progressive disease or death due to any cause (assessed up to approximately 58 months)

End point values	Nivolumab Arm	Active Comparator Arm Docetaxel/Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	210	209		
Units: Percent of participants				
number (not applicable)				
Complete Response (CR)	1.0	1.0		
Partial Response (PR)	14.8	15.3		
Progressive Disease (PD)	44.3	24.4		
Stable Disease (SD)	14.8	31.1		
Not Evaluable (NE)	25.2	28.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response (TTR)

End point title	Time to Response (TTR)

End point description:

Time to response (TTR) is the duration from the start of treatment to the first observation of a predefined clinical response.

Complete Response (CR): Disappearance of all (non-lymph node) target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in the short axis to <10 mm.
Partial Response (PR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

End point type	Secondary

End point timeframe:

From randomization until complete response or partial response (assessed up to approximately 58 months)

End point values	Nivolumab Arm	Active Comparator Arm Docetaxel/Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	210	209		
Units: Months				
arithmetic mean (full range (min-max))	2.66 (1.2 to 22.3)	1.48 (1.2 to 5.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Best Percent Reduction from Baseline in the Sum of Diameters of the Target Lesion

End point title	Best Percent Reduction from Baseline in the Sum of Diameters of the Target Lesion

End point description:

Best percent reduction from baseline in the sum of diameters of the target lesion was used to evaluate the effectiveness of treatment in reducing tumor size. The diameter data excludes that obtained after an overall response of progressive disease (PD) and after new treatment for cancer.

End point type	Secondary

End point timeframe:

From randomization until progressive disease or death due to any cause (assessed up to approximately 58 months)

End point values	Nivolumab Arm	Active Comparator Arm Docetaxel/Paclitaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	210	209		
Units: Percent reduction from baseline	100	100		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Monitoring for non-serious adverse events (AEs) continued until 28 days after the treatment phase ended. Serious AEs were tracked during the treatment period and for 100 days after the last dose.

Adverse event reporting additional description:

Serious AEs and non-serious AEs included participants who received at least one dose of study medicine.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Active Comparator Arm Docetaxel/Paclitaxel

Reporting group description:

Docetaxel: Intravenously administered at a dose of 75 mg/m2 every 3 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends OR Paclitaxel: Intravenously administered at a dose of 100 mg/m2 weekly for 6 weeks followed by 2-week drug holiday until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends.

Reporting group title	Nivolumab Arm

Reporting group description:

Nivolumab 240 mg/body solution intravenously every 2 weeks until documented disease progression, discontinuation due to toxicity, withdrawal of consent or the study ends.

Serious adverse events	Active Comparator Arm Docetaxel/Paclitaxel	Nivolumab Arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	78 / 208 (37.50%)	70 / 209 (33.49%)	
number of deaths (all causes)	186	178	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to lymph nodes			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cancer pain			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphangiosis carcinomatosa			

subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm progression			
subjects affected / exposed	0 / 208 (0.00%)	2 / 209 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tumour haemorrhage			
subjects affected / exposed	1 / 208 (0.48%)	3 / 209 (1.44%)	
occurrences causally related to treatment / all	0 / 1	3 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Skin cancer			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Jejunostomy			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 208 (0.48%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	1 / 208 (0.48%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 208 (0.48%)	6 / 209 (2.87%)	
occurrences causally related to treatment / all	0 / 1	6 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	1 / 208 (0.48%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Disease progression			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Stenosis			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Anaphylactic shock			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary embolism			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumothorax spontaneous			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	3 / 208 (1.44%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	3 / 208 (1.44%)	3 / 209 (1.44%)	
occurrences causally related to treatment / all	2 / 3	2 / 3	
deaths causally related to treatment / all	0 / 0	1 / 2	
Pneumonia aspiration			
subjects affected / exposed	2 / 208 (0.96%)	3 / 209 (1.44%)	
occurrences causally related to treatment / all	2 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pleural effusion			
subjects affected / exposed	3 / 208 (1.44%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	3 / 208 (1.44%)	4 / 209 (1.91%)	
occurrences causally related to treatment / all	3 / 3	4 / 4	
deaths causally related to treatment / all	1 / 1	1 / 1	
Dyspnoea			
subjects affected / exposed	1 / 208 (0.48%)	4 / 209 (1.91%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal fistula			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagobronchial fistula			
subjects affected / exposed	0 / 208 (0.00%)	2 / 209 (0.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			
subjects affected / exposed	3 / 208 (1.44%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Liver function test increased			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Radiation pneumonitis			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stoma site extravasation			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Tracheo-oesophageal fistula			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Pericarditis			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Bone marrow failure			

subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	16 / 208 (7.69%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	23 / 23	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	0 / 208 (0.00%)	2 / 209 (0.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 208 (0.96%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenitis			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	2 / 208 (0.96%)	2 / 209 (0.96%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ileus			
subjects affected / exposed	1 / 208 (0.48%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	2 / 208 (0.96%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 208 (0.48%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 208 (0.96%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	2 / 208 (0.96%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric fistula			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aorto-oesophageal fistula			

subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct obstruction			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Excessive granulation tissue			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stevens-Johnson syndrome			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Endocrine disorders			
Adrenocorticotropic hormone deficiency			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypopituitarism			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Fistula			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 208 (0.00%)	2 / 209 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			

subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	2 / 208 (0.96%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mediastinitis			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	13 / 208 (6.25%)	10 / 209 (4.78%)	
occurrences causally related to treatment / all	3 / 13	2 / 11	
deaths causally related to treatment / all	1 / 2	0 / 2	
Postoperative wound infection			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 208 (0.96%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Septic shock			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	0 / 208 (0.00%)	2 / 209 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle abscess			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess neck			
subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal infection			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			
subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 208 (0.48%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	5 / 208 (2.40%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	5 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord abscess			

subjects affected / exposed	1 / 208 (0.48%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	2 / 208 (0.96%)	0 / 209 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 208 (0.48%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 208 (0.48%)	2 / 209 (0.96%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	1 / 208 (0.48%)	4 / 209 (1.91%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 208 (0.00%)	2 / 209 (0.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 208 (0.48%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	6 / 208 (2.88%)	4 / 209 (1.91%)	
occurrences causally related to treatment / all	7 / 7	3 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 1 diabetes mellitus			

subjects affected / exposed	0 / 208 (0.00%)	1 / 209 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Active Comparator Arm Docetaxel/Paclitaxel	Nivolumab Arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	203 / 208 (97.60%)	165 / 209 (78.95%)	
Investigations			
Weight decreased			
subjects affected / exposed	11 / 208 (5.29%)	11 / 209 (5.26%)	
occurrences (all)	11	11	
Neutrophil count decreased			
subjects affected / exposed	76 / 208 (36.54%)	4 / 209 (1.91%)	
occurrences (all)	185	12	
Lymphocyte count decreased			
subjects affected / exposed	21 / 208 (10.10%)	5 / 209 (2.39%)	
occurrences (all)	39	19	
Aspartate aminotransferase increased			
subjects affected / exposed	7 / 208 (3.37%)	14 / 209 (6.70%)	
occurrences (all)	8	14	
Alanine aminotransferase increased			
subjects affected / exposed	7 / 208 (3.37%)	11 / 209 (5.26%)	
occurrences (all)	9	11	
White blood cell count decreased			
subjects affected / exposed	72 / 208 (34.62%)	2 / 209 (0.96%)	
occurrences (all)	173	2	
Nervous system disorders			
Neuropathy peripheral			
subjects affected / exposed	23 / 208 (11.06%)	0 / 209 (0.00%)	
occurrences (all)	23	0	
Dysgeusia			

subjects affected / exposed	14 / 208 (6.73%)	5 / 209 (2.39%)	
occurrences (all)	14	5	
Peripheral sensory neuropathy			
subjects affected / exposed	48 / 208 (23.08%)	1 / 209 (0.48%)	
occurrences (all)	50	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	61 / 208 (29.33%)	25 / 209 (11.96%)	
occurrences (all)	76	28	
Leukopenia			
subjects affected / exposed	18 / 208 (8.65%)	0 / 209 (0.00%)	
occurrences (all)	61	0	
Neutropenia			
subjects affected / exposed	40 / 208 (19.23%)	1 / 209 (0.48%)	
occurrences (all)	94	1	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	39 / 208 (18.75%)	29 / 209 (13.88%)	
occurrences (all)	51	40	
Malaise			
subjects affected / exposed	50 / 208 (24.04%)	13 / 209 (6.22%)	
occurrences (all)	72	16	
Fatigue			
subjects affected / exposed	52 / 208 (25.00%)	20 / 209 (9.57%)	
occurrences (all)	54	21	
Chest pain			
subjects affected / exposed	4 / 208 (1.92%)	13 / 209 (6.22%)	
occurrences (all)	5	15	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	17 / 208 (8.17%)	14 / 209 (6.70%)	
occurrences (all)	17	15	
Stomatitis			
subjects affected / exposed	26 / 208 (12.50%)	7 / 209 (3.35%)	
occurrences (all)	28	7	
Abdominal pain			

subjects affected / exposed	8 / 208 (3.85%)	13 / 209 (6.22%)	
occurrences (all)	9	15	
Constipation			
subjects affected / exposed	40 / 208 (19.23%)	36 / 209 (17.22%)	
occurrences (all)	42	36	
Diarrhoea			
subjects affected / exposed	34 / 208 (16.35%)	39 / 209 (18.66%)	
occurrences (all)	36	42	
Dysphagia			
subjects affected / exposed	3 / 208 (1.44%)	13 / 209 (6.22%)	
occurrences (all)	3	13	
Nausea			
subjects affected / exposed	40 / 208 (19.23%)	23 / 209 (11.00%)	
occurrences (all)	41	26	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	8 / 208 (3.85%)	13 / 209 (6.22%)	
occurrences (all)	12	13	
Cough			
subjects affected / exposed	25 / 208 (12.02%)	33 / 209 (15.79%)	
occurrences (all)	27	35	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	7 / 208 (3.37%)	12 / 209 (5.74%)	
occurrences (all)	8	12	
Pruritus			
subjects affected / exposed	15 / 208 (7.21%)	26 / 209 (12.44%)	
occurrences (all)	18	29	
Alopecia			
subjects affected / exposed	100 / 208 (48.08%)	3 / 209 (1.44%)	
occurrences (all)	100	3	
Rash			
subjects affected / exposed	40 / 208 (19.23%)	26 / 209 (12.44%)	
occurrences (all)	43	28	
Psychiatric disorders			

Insomnia			
subjects affected / exposed	13 / 208 (6.25%)	12 / 209 (5.74%)	
occurrences (all)	14	12	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	3 / 208 (1.44%)	21 / 209 (10.05%)	
occurrences (all)	3	21	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	22 / 208 (10.58%)	6 / 209 (2.87%)	
occurrences (all)	23	6	
Arthralgia			
subjects affected / exposed	25 / 208 (12.02%)	10 / 209 (4.78%)	
occurrences (all)	29	12	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	13 / 208 (6.25%)	15 / 209 (7.18%)	
occurrences (all)	17	34	
Nasopharyngitis			
subjects affected / exposed	10 / 208 (4.81%)	13 / 209 (6.22%)	
occurrences (all)	15	18	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	68 / 208 (32.69%)	40 / 209 (19.14%)	
occurrences (all)	79	42	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 May 2019	To include the timing of informed consent from subjects to enter the CA209-473 Extension phase and to set wash-out period before the first CA209-473 dose in the CA209-473 Extension phase.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported