Clinical trial results:
A Randomized, Double-blind, Placebo-controlled, Phase 3 Study of Nivolumab or Nivolumab plus Cisplatin, in Combination with Radiotherapy in Participants with Cisplatin Ineligible and Cisplatin Eligible Locally Advanced Squamous Cell Carcinoma of the Head and Neck (SCCHN).

Summary

EudraCT number	2017-002676-87
Trial protocol	ES GB PL IT
Global end of trial date	14 October 2019

Results information

Result version number	v1 (current)
This version publication date	29 October 2020
First version publication date	29 October 2020

Trial information

Trial identification

Sponsor protocol code	CA209-9TM

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	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	14 October 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 October 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Following implementation of Revised Protocol 03, only safety assessments were conducted.

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	17 December 2017
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	France: 9
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Japan: 25
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Korea, Republic of: 8
Country: Number of subjects enrolled	Russian Federation: 4
Country: Number of subjects enrolled	Spain: 17
Country: Number of subjects enrolled	Taiwan: 6
Country: Number of subjects enrolled	Turkey: 1
Country: Number of subjects enrolled	United States: 36
Worldwide total number of subjects	111
EEA total number of subjects	31

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)	64
From 65 to 84 years	45
85 years and over	2

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

74 Randomized and 73 Treated

Period 1

Period 1 title	Randomized
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A (Cohort 1)

Arm description:

Nivolumab + Radiotherapy

Arm type	Active comparator
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravascular use

Dosage and administration details:

10 mg/mL – 100 mg fill volume, 240 mg IV x 1 dose then 360 mg IV x 3 doses then 480 mg IV x 6 doses

Investigational medicinal product name	Radiotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Radiopharmaceutical precursor, solution
Routes of administration	Intravenous bolus use

Dosage and administration details:

IMRT will be given in 35 fractions over 7 weeks beginning at Day 1 Cycle 3 for Cohort 1 or Day 1 Cycle 2 for Cohort 2, 5 fractions per week

Arm title	Arm B (Cohort 1)

Arm description:

Cetuximab + Radiotherapy

Arm type	Active comparator
Investigational medicinal product name	Radiotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Radiopharmaceutical precursor, solution
Routes of administration	Intravenous bolus use

Dosage and administration details:

IMRT will be given in 35 fractions over 7 weeks beginning at Day 1 Cycle 3 for Cohort 1 or Day 1 Cycle 2 for Cohort 2, 5 fractions per week

Investigational medicinal product name	Cetuximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

5 mg/mL - 500 mg fill volume, 400 mg/m2 IV x 1 dose then 250 mg/m2 IV x 7 doses

Arm title	Arm C (Cohort 2)

Arm description:

Cisplatin + Nivolumab + Radiotherapy

Arm type	Active comparator
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravascular use

Dosage and administration details:

10 mg/mL – 100 mg fill volume, 240 mg IV x 1 dose then 360 mg IV x 3 doses then 480 mg IV x 6 doses

Investigational medicinal product name	Radiotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Radiopharmaceutical precursor, solution
Routes of administration	Intravenous bolus use

Dosage and administration details:

IMRT will be given in 35 fractions over 7 weeks beginning at Day 1 Cycle 3 for Cohort 1 or Day 1 Cycle 2 for Cohort 2, 5 fractions per week

Investigational medicinal product name	Cisplastin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravascular use

Dosage and administration details:

1 mg/mL – 100 mg fill volume, 100 mg/m2 IV x 3 doses

Arm title	Arm D (Cohort 2)

Arm description:

Cisplatin + Radiotherapy

Arm type	Active comparator
Investigational medicinal product name	Cisplastin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravascular use

Dosage and administration details:

1 mg/mL – 100 mg fill volume, 100 mg/m2 IV x 3 doses

Investigational medicinal product name	Radiotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Radiopharmaceutical precursor, solution
Routes of administration	Intravenous bolus use

Dosage and administration details:

IMRT will be given in 35 fractions over 7 weeks beginning at Day 1 Cycle 3 for Cohort 1 or Day 1 Cycle 2

for Cohort 2, 5 fractions per week

Number of subjects in period 1[1]	Arm A (Cohort 1)	Arm B (Cohort 1)	Arm C (Cohort 2)
Started	12	10	27
Completed	12	10	27

Number of subjects in period 1[1]	Arm D (Cohort 2)
Started	25
Completed	25

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 74 Randomized and 73 Treated

Period 2

Period 2 title	Treatment Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A (Cohort 1)

Arm description:

Nivolumab + Radiotherapy

Arm type	Active comparator
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravascular use

Dosage and administration details:

10 mg/mL – 100 mg fill volume, 240 mg IV x 1 dose then 360 mg IV x 3 doses then 480 mg IV x 6 doses

Investigational medicinal product name	Radiotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Radiopharmaceutical precursor, solution

Routes of administration	Intravenous bolus use

Dosage and administration details:

IMRT will be given in 35 fractions over 7 weeks beginning at Day 1 Cycle 3 for Cohort 1 or Day 1 Cycle 2 for Cohort 2, 5 fractions per week

Arm title	Arm B (Cohort 1)

Arm description:

Cetuximab + Radiotherapy

Arm type	Active comparator
Investigational medicinal product name	Cetuximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

5 mg/mL - 500 mg fill volume, 400 mg/m2 IV x 1 dose then 250 mg/m2 IV x 7 doses

Investigational medicinal product name	Radiotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Radiopharmaceutical precursor, solution
Routes of administration	Intravenous bolus use

Dosage and administration details:

IMRT will be given in 35 fractions over 7 weeks beginning at Day 1 Cycle 3 for Cohort 1 or Day 1 Cycle 2 for Cohort 2, 5 fractions per week

Arm title	Arm C (Cohort 2)

Arm description:

Cisplatin + Nivolumab + Radiotherapy

Arm type	Active comparator
Investigational medicinal product name	Cisplastin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravascular use

Dosage and administration details:

1 mg/mL – 100 mg fill volume, 100 mg/m2 IV x 3 doses

Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravascular use

Dosage and administration details:

10 mg/mL – 100 mg fill volume, 240 mg IV x 1 dose then 360 mg IV x 3 doses then 480 mg IV x 6 doses

Investigational medicinal product name	Radiotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Radiopharmaceutical precursor, solution
Routes of administration	Intravenous bolus use

Dosage and administration details:

IMRT will be given in 35 fractions over 7 weeks beginning at Day 1 Cycle 3 for Cohort 1 or Day 1 Cycle 2 for Cohort 2, 5 fractions per week

Arm title	Arm D (Cohort 2)
Arm description: Cisplatin + Radiotherapy	
Arm type	Active comparator
Investigational medicinal product name	Cisplastin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravascular use
Dosage and administration details: 1 mg/mL – 100 mg fill volume, 100 mg/m2 IV x 3 doses	
Investigational medicinal product name	Radiotherapy
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Radiopharmaceutical precursor, solution
Routes of administration	Intravenous bolus use
Dosage and administration details: IMRT will be given in 35 fractions over 7 weeks beginning at Day 1 Cycle 3 for Cohort 1 or Day 1 Cycle 2 for Cohort 2, 5 fractions per week	

Number of subjects in period 2[2]	Arm A (Cohort 1)	Arm B (Cohort 1)	Arm C (Cohort 2)
Started	12	10	27
Completed	0	0	0
Not completed	12	10	27
Adverse event, serious fatal	-	-	1
completed	6	-	18
Adverse event unrelated to Study Drug	2	1	1
Other Reason	2	-	2
Study Drug Toxicity	1	-	1
admin reason by sponsor	-	7	-
Disease Progression	-	2	-
participant request to discontinue	-	-	4
participant withdrew consent	1	-	-

Number of subjects in period 2[2]	Arm D (Cohort 2)
Started	24
Completed	0
Not completed	24
Adverse event, serious fatal	-
completed	1
Adverse event unrelated to Study Drug	1

Other Reason	1
Study Drug Toxicity	1
admin reason by sponsor	19
Disease Progression	1
participant request to discontinue	-
participant withdrew consent	-

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 74 Randomized and 73 Treated

Baseline characteristics

Reporting groups	
Reporting group title	Arm A (Cohort 1)
Reporting group description: Nivolumab + Radiotherapy	
Reporting group title	Arm B (Cohort 1)
Reporting group description: Cetuximab + Radiotherapy	
Reporting group title	Arm C (Cohort 2)
Reporting group description: Cisplatin + Nivolumab + Radiotherapy	
Reporting group title	Arm D (Cohort 2)
Reporting group description: Cisplatin + Radiotherapy	

Reporting group values	Arm A (Cohort 1)	Arm B (Cohort 1)	Arm C (Cohort 2)
Number of subjects	12	10	27
Age categorical Units: Subjects			
Adults (18-64 years)	2	1	24
From 65-84 years	8	9	3
85 years and over	2	0	0
Age Continuous Units: Years			
arithmetic mean	74.5	74.7	59.0
standard deviation	± 8.3	± 6.5	± 6.6
Sex: Female, Male Units: participants			
Female	2	2	3
Male	10	8	24
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	4	6
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	2
White	8	5	16
More than one race	0	0	0
Unknown or Not Reported	1	1	3
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	5	4	9
Unknown or Not Reported	7	6	18

Reporting group values	Arm D (Cohort 2)	Total	
Number of subjects	25	74	

Age categorical Units: Subjects			
Adults (18-64 years)	19	46	
From 65-84 years	6	26	
85 years and over	0	2	
Age Continuous Units: Years			
arithmetic mean	60.8		
standard deviation	± 7.0	-	
Sex: Female, Male Units: participants			
Female	2	9	
Male	23	65	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	15	28	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	2	
White	7	36	
More than one race	0	0	
Unknown or Not Reported	3	8	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	2	20	
Unknown or Not Reported	23	54	

End points

End points reporting groups

Reporting group title	Arm A (Cohort 1)
Reporting group description: Nivolumab + Radiotherapy	
Reporting group title	Arm B (Cohort 1)
Reporting group description: Cetuximab + Radiotherapy	
Reporting group title	Arm C (Cohort 2)
Reporting group description: Cisplatin + Nivolumab + Radiotherapy	
Reporting group title	Arm D (Cohort 2)
Reporting group description: Cisplatin + Radiotherapy	
Reporting group title	Arm A (Cohort 1)
Reporting group description: Nivolumab + Radiotherapy	
Reporting group title	Arm B (Cohort 1)
Reporting group description: Cetuximab + Radiotherapy	
Reporting group title	Arm C (Cohort 2)
Reporting group description: Cisplatin + Nivolumab + Radiotherapy	
Reporting group title	Arm D (Cohort 2)
Reporting group description: Cisplatin + Radiotherapy	

Primary: Number of Participants with an Adverse Event (AE)

End point title	Number of Participants with an Adverse Event (AE)[1]
End point description: Number of Participants with an Adverse Event	
End point type	Primary
End point timeframe: 30 days	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis performed due to the type of endpoint

End point values	Arm A (Cohort 1)	Arm B (Cohort 1)	Arm C (Cohort 2)	Arm D (Cohort 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	10	27	24
Units: participants	12	10	27	24

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with an Serious Adverse Event (SAE)

End point title	Number of Participants with an Serious Adverse Event (SAE)[2]

End point description:

Number of Participants with an Serious Adverse Event (SAE)

End point type	Primary

End point timeframe:

30 days

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis performed due to the type of endpoint

End point values	Arm A (Cohort 1)	Arm B (Cohort 1)	Arm C (Cohort 2)	Arm D (Cohort 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	10	27	24
Units: participants	5	5	9	6

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with an Adverse Event Leading to Discontinuation

End point title	Number of Participants with an Adverse Event Leading to Discontinuation[3]

End point description:

Number of Participants with an Adverse Event Leading to Discontinuation

End point type	Primary

End point timeframe:

30 days

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis performed due to the type of endpoint

End point values	Arm A (Cohort 1)	Arm B (Cohort 1)	Arm C (Cohort 2)	Arm D (Cohort 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	10	27	24
Units: participants	2	3	8	4

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with an Adverse Event Leading to dose modification

End point title	Number of Participants with an Adverse Event Leading to dose modification[4]

End point description:

Number of Participants with an Adverse Event Leading to dose modification Here '9999' signifies data not available as does modification did not take place

End point type	Primary

End point timeframe:

30 days

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis performed due to the type of endpoint

End point values	Arm A (Cohort 1)	Arm B (Cohort 1)	Arm C (Cohort 2)	Arm D (Cohort 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	10	27	24
Units: participants	9999	9999	9999	9999

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with select adverse events

End point title	Number of Participants with select adverse events[5]

End point description:

Number of Participants with select adverse events. Select Adverse events include: gastrointestinal, hepatic, hypersensitivity/infusion reaction, pulmonary, renal, or skin.

End point type	Primary

End point timeframe:

30 days

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis performed due to the type of endpoint

End point values	Arm A (Cohort 1)	Arm B (Cohort 1)	Arm C (Cohort 2)	Arm D (Cohort 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	10	27	24
Units: participants				
Gastrointestinal	4	3	3	1
Hepatic	1	2	2	3
Hypersensitivity/Infusion Reaction	1	3	0	0
Pulmonary	0	0	0	0
Renal	2	1	13	6
Skin	7	7	12	11

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with an immune-mediated adverse event (IMAE)

End point title	Number of Participants with an immune-mediated adverse event (IMAE)[6]

End point description:

Number of Participants with an immune-mediated adverse event (IMAE)

End point type	Primary

End point timeframe:

100 days

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis performed due to the type of endpoint

End point values	Arm A (Cohort 1)	Arm B (Cohort 1)	Arm C (Cohort 2)	Arm D (Cohort 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	10	27	24
Units: participants				
Non-Endocrine related IMAE	1	0	3	0
Endocrine related IMAE	0	0	4	0

Statistical analyses

No statistical analyses for this end point

Primary: Time to onset and time to resolution of immune-related adverse events

End point title	Time to onset and time to resolution of immune-related adverse events[7]

End point description:

Time to onset and time to resolution of immune-related adverse events

End point type	Primary

End point timeframe:

100 days

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis performed due to the type of endpoint

End point values	Arm A (Cohort 1)	Arm B (Cohort 1)	Arm C (Cohort 2)	Arm D (Cohort 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[8]	0[9]	0[10]	0[11]
Units: Weeks				
arithmetic mean (confidence interval 95%)				
Endocrine IMAE	(to)	(to)	(to)	(to)
Non Endocrine IMAE	(to)	(to)	(to)	(to)

Notes:

[8] - Too few subjects, can risk subject identification

[9] - Too few subjects, can risk subject identification

[10] - Too few subjects, can risk subject identification

[11] - Too few subjects, can risk subject identification

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants who experienced death

End point title	Number of Participants who experienced death[12]

End point description:

Number of Participants who experienced death

End point type	Primary

End point timeframe:

100 days

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis performed due to the type of endpoint

End point values	Arm A (Cohort 1)	Arm B (Cohort 1)	Arm C (Cohort 2)	Arm D (Cohort 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	10	27	24
Units: participants	2	2	2	1

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with an abnormality in specific thyroid tests

End point title	Number of participants with an abnormality in specific thyroid tests[13]

End point description:

Number of participants with an abnormality in specific thyroid tests

End point type	Primary

End point timeframe:

30 Days

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis performed due to the type of endpoint

End point values	Arm A (Cohort 1)	Arm B (Cohort 1)	Arm C (Cohort 2)	Arm D (Cohort 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	10	27	23
Units: participants				
TSH > ULN	5	1	7	1
TSH > ULN WITH TSH <= ULN AT BASELINE	5	1	7	1
TSH >ULN WITH ATLEAST ONE FT3/FT4 TEST VALUE <LLN	4	0	4	0
TSH >ULN WITH ALL OTHER FT3/FT4 TEST VALUES >= LLN	0	0	2	1
TSH > ULN WITH FT3/FT4 TEST MISSING	1	1	1	0
TSH < LLN	4	3	16	13
TSH <LLN WITH TSH >= LLN AT BASELINE	3	3	13	13
TSH <LLN WITH ATLEAST ONE FT3/FT4 TEST VALUE > ULN	0	0	9	2
TSH <LLN WITH ALL OTHER FT3/FT4 TEST VALUES <= ULN	4	1	6	7
TSH < LLN WITH FT3/FT4 TEST MISSING	0	2	1	4

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with an abnormality in specific liver tests

End point title	Number of participants with an abnormality in specific liver tests[14]

End point description:

Number of participants with an abnormality in specific liver tests

End point type	Primary

End point timeframe:

30 days

Notes:

[14] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis performed due to the type of endpoint

End point values	Arm A (Cohort 1)	Arm B (Cohort 1)	Arm C (Cohort 2)	Arm D (Cohort 2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	10	27	24
Units: participants				
ALT OR AST > 3XULN	2	0	0	0
ALT OR AST> 5XULN	1	0	0	0
ALT OR AST> 10XULN	0	0	0	0

ALT OR AST > 20XULN	0	0	0	0
TOTAL BILIRUBIN > 2XULN	0	0	0	0
ALT/AST ELEV>3XULN;TOTAL BILIRUBIN>2XULN IN 1 DAY	0	0	0	0
ALT/AST ELEV>3XULN;TOTAL BILIRUBIN>2XULN IN 30DAYS	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from start of treatment up to 30 days after last treatment dose.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	RT + Nivo

Reporting group description:

Subjects who were ineligible for cisplatin chemotherapy received nivolumab 240 milligrams (mg) single dose on day 1 then 3 dose of 360 mg every 3 weeks followed by 6 dose of 480 mg every 4 weeks intravenously (IV) plus placebo cetuximab 400 milligrams per square meter (mg/m2) single dose and 250 mg/m2 every week for 7 weeks in combination with radiotherapy (RT). The infusion duration of nivolumab was 30 minutes.

Reporting group title	RT + Cetu

Reporting group description:

Subjects who were ineligible for cisplatin chemotherapy received placebo nivolumab 240 mg single dose on day 1 then 3 dose of 360 mg every 3 weeks followed by 6 dose of 480 mg every 4 weeks IV in plus cetuximab 400 mg/m2 single dose and 250 mg/m2 every week for 7 weeks in combination with RT. The infusion duration of nivolumab was 30 minutes. The infusion of cetuximab began at least 30 minutes after the completion of the nivolumab infusion.

Reporting group title	RT + Cis + Nivo

Reporting group description:

Subjects who were ineligible for cisplatin chemotherapy received nivolumab 240 mg single dose on day 1 then 3 dose of 360 mg every 3 weeks followed by 6 dose of 480 mg every 4 weeks IV in combination with 3 dose of cisplatin 100 mg/m2 and RT. The infusion duration of nivolumab was 30 minutes. The infusion of cisplatin began at least 30 minutes after the completion of the nivolumab infusion.

Reporting group title	RT + Cis

Reporting group description:

Subjects who were ineligible for cisplatin chemotherapy received placebo nivolumab 240 mg single dose on day 1 then 3 dose of 360 mg every 3 weeks followed by 6 dose of 480 mg every 4 weeks IV in combination with 3 dose of cisplatin 100 mg/m2 and RT. The infusion duration of nivolumab was 30 minutes. The infusion of cisplatin began at least 30 minutes after the completion of the nivolumab infusion.

Serious adverse events	RT + Nivo	RT + Cetu	RT + Cis + Nivo
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 12 (41.67%)	5 / 10 (50.00%)	9 / 27 (33.33%)
number of deaths (all causes)	2	1	2
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oropharyngeal squamous cell carcinoma			

subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (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	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (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
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 27 (3.70%)
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 disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Oedema peripheral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 27 (3.70%)
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, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (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
Pharyngeal necrosis			

subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (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
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (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
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (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
Myocardial infarction			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (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

Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (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			
Febrile neutropenia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 27 (3.70%)
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 disorders			
Dysphagia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	2 / 27 (7.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacillus bacteraemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (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
Septic shock			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Urinary tract infection bacterial			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			

subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (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
Hypokalaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	RT + Cis		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 24 (25.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oropharyngeal squamous cell carcinoma			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour haemorrhage			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypotension			

subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pharyngeal necrosis			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychotic disorder			

subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Platelet count decreased			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			

subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bacillus bacteraemia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile colitis			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mucosal infection			

subjects affected / exposed	1 / 24 (4.17%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 24 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	0 / 24 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection bacterial				
subjects affected / exposed	0 / 24 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
subjects affected / exposed	2 / 24 (8.33%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				
subjects affected / exposed	0 / 24 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypokalaemia				

subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malnutrition			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	RT + Nivo	RT + Cetu	RT + Cis + Nivo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	10 / 10 (100.00%)	26 / 27 (96.30%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Pyogenic granuloma			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Tumour haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Hypotension			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Lymphoedema			

subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences (all)	2	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	2 / 27 (7.41%)
occurrences (all)	3	0	2
Fatigue			
subjects affected / exposed	4 / 12 (33.33%)	5 / 10 (50.00%)	8 / 27 (29.63%)
occurrences (all)	5	5	12
Gait disturbance			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	2 / 12 (16.67%)	2 / 10 (20.00%)	7 / 27 (25.93%)
occurrences (all)	2	4	7
Oedema peripheral			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Pyrexia			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	4 / 27 (14.81%)
occurrences (all)	2	1	4
Xerosis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	1 / 27 (3.70%)
occurrences (all)	0	2	1
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	1	4	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	4 / 27 (14.81%)
occurrences (all)	3	1	4
Dysphonia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	2 / 27 (7.41%)
occurrences (all)	0	2	2
Dyspnoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	3 / 27 (11.11%)
occurrences (all)	1	0	3
Haemoptysis			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences (all)	2	0	1
Hiccups			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	4 / 27 (14.81%)
occurrences (all)	1	1	5
Laryngeal inflammation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	3 / 12 (25.00%)	3 / 10 (30.00%)	8 / 27 (29.63%)
occurrences (all)	3	3	8
Paranasal sinus hyposecretion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Pharyngeal inflammation			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	1 / 27 (3.70%)
occurrences (all)	2	1	1
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Delirium			

subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	3 / 12 (25.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	3	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	2 / 10 (20.00%)	2 / 27 (7.41%)
occurrences (all)	1	2	2
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	2 / 27 (7.41%)
occurrences (all)	1	1	2
Blood creatinine increased			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	8 / 27 (29.63%)
occurrences (all)	2	1	10
Blood electrolytes abnormal			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Blood magnesium decreased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Blood urea increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Lipase increased			

subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	2	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	4 / 27 (14.81%)
occurrences (all)	0	0	5
Neutrophil count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	9 / 27 (33.33%)
occurrences (all)	0	0	10
Platelet count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	3 / 27 (11.11%)
occurrences (all)	0	0	5
Protein total decreased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Weight decreased			
subjects affected / exposed	3 / 12 (25.00%)	2 / 10 (20.00%)	11 / 27 (40.74%)
occurrences (all)	5	2	13
White blood cell count decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	7 / 27 (25.93%)
occurrences (all)	0	0	8
C-Reactive protein increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Incision site inflammation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	3	0	0
Infusion related reaction			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Radiation skin injury			
subjects affected / exposed	3 / 12 (25.00%)	5 / 10 (50.00%)	8 / 27 (29.63%)
occurrences (all)	3	5	8
Recall phenomenon			

subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Stoma site inflammation			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	4	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Dysgeusia			
subjects affected / exposed	2 / 12 (16.67%)	2 / 10 (20.00%)	12 / 27 (44.44%)
occurrences (all)	2	2	12
Headache			
subjects affected / exposed	1 / 12 (8.33%)	2 / 10 (20.00%)	1 / 27 (3.70%)
occurrences (all)	1	2	1
Hemiparesis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	3	0
Neuralgia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Neuropathy peripheral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	3 / 27 (11.11%)
occurrences (all)	0	0	4
Taste disorder			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	3 / 27 (11.11%)
occurrences (all)	0	1	3
Tremor			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 12 (33.33%)	3 / 10 (30.00%)	12 / 27 (44.44%)
occurrences (all)	4	3	14
Leukocytosis			

subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Leukopenia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	2 / 27 (7.41%)
occurrences (all)	2	0	2
Lymphopenia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	2 / 27 (7.41%)
occurrences (all)	1	1	2
Neutropenia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	3 / 27 (11.11%)
occurrences (all)	1	0	3
Thrombocytopenia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Ear pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Tinnitus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	5 / 27 (18.52%)
occurrences (all)	0	0	5
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Vision blurred			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Cheilitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Constipation			

subjects affected / exposed	4 / 12 (33.33%)	2 / 10 (20.00%)	13 / 27 (48.15%)
occurrences (all)	7	3	14
Diarrhoea			
subjects affected / exposed	4 / 12 (33.33%)	3 / 10 (30.00%)	2 / 27 (7.41%)
occurrences (all)	5	3	3
Dry mouth			
subjects affected / exposed	4 / 12 (33.33%)	3 / 10 (30.00%)	12 / 27 (44.44%)
occurrences (all)	4	3	12
Dyspepsia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Dysphagia			
subjects affected / exposed	6 / 12 (50.00%)	3 / 10 (30.00%)	11 / 27 (40.74%)
occurrences (all)	6	3	12
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	1	1	0
Glossodynia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Lip dry			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	3 / 12 (25.00%)	1 / 10 (10.00%)	17 / 27 (62.96%)
occurrences (all)	5	1	24
Odynophagia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	7 / 27 (25.93%)
occurrences (all)	0	0	8
Oesophagitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	1 / 12 (8.33%)	2 / 10 (20.00%)	0 / 27 (0.00%)
occurrences (all)	1	2	0
Saliva altered			

subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	4 / 12 (33.33%)	4 / 10 (40.00%)	10 / 27 (37.04%)
occurrences (all)	6	4	12
Vomiting			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	6 / 27 (22.22%)
occurrences (all)	1	1	8
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	2 / 27 (7.41%)
occurrences (all)	0	0	2
Dermatitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	8 / 27 (29.63%)
occurrences (all)	0	1	8
Dermatitis acneiform			
subjects affected / exposed	0 / 12 (0.00%)	4 / 10 (40.00%)	0 / 27 (0.00%)
occurrences (all)	0	4	0
Dermatitis bullous			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	1 / 27 (3.70%)
occurrences (all)	0	1	1
Dry skin			
subjects affected / exposed	2 / 12 (16.67%)	2 / 10 (20.00%)	1 / 27 (3.70%)
occurrences (all)	2	2	1
Erythema			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	2	1	0
Lichen planus			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Pruritus			

subjects affected / exposed	3 / 12 (25.00%)	0 / 10 (0.00%)	3 / 27 (11.11%)
occurrences (all)	3	0	4
Rash			
subjects affected / exposed	4 / 12 (33.33%)	4 / 10 (40.00%)	3 / 27 (11.11%)
occurrences (all)	5	4	3
Rash papular			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences (all)	1	0	1
Skin exfoliation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Skin fissures			
subjects affected / exposed	0 / 12 (0.00%)	2 / 10 (20.00%)	0 / 27 (0.00%)
occurrences (all)	0	2	0
Skin reaction			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	3 / 27 (11.11%)
occurrences (all)	0	0	3
Anuria			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Dysuria			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	1	1	0
Urinary hesitation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hyperthyroidism			

subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	4 / 27 (14.81%)
occurrences (all)	0	1	4
Hypothyroidism			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	6 / 27 (22.22%)
occurrences (all)	0	0	6
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 10 (0.00%)	3 / 27 (11.11%)
occurrences (all)	0	0	3
Back pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	2 / 27 (7.41%)
occurrences (all)	1	0	3
Muscle spasms			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	4 / 12 (33.33%)	1 / 10 (10.00%)	2 / 27 (7.41%)
occurrences (all)	4	1	2
Pain in jaw			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Trismus			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Bacterial infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	1	2	0
Herpes simplex			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Infected dermal cyst			

subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Mucosal infection			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	5	1	0
Oral candidiasis			
subjects affected / exposed	2 / 12 (16.67%)	1 / 10 (10.00%)	2 / 27 (7.41%)
occurrences (all)	2	1	3
Paronychia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	0 / 27 (0.00%)
occurrences (all)	1	0	0
Pyoderma			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Skin infection			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Subcutaneous abscess			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	4 / 12 (33.33%)	2 / 10 (20.00%)	9 / 27 (33.33%)
occurrences (all)	4	2	11
Dehydration			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	2 / 27 (7.41%)
occurrences (all)	0	1	2
Diabetes mellitus			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	4 / 27 (14.81%)
occurrences (all)	2	1	4

Hypoalbuminaemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	0 / 27 (0.00%)
occurrences (all)	0	1	0
Hypocalcaemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 10 (0.00%)	1 / 27 (3.70%)
occurrences (all)	2	0	1
Hypokalaemia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	5 / 27 (18.52%)
occurrences (all)	1	1	6
Hypomagnesaemia			
subjects affected / exposed	0 / 12 (0.00%)	3 / 10 (30.00%)	4 / 27 (14.81%)
occurrences (all)	0	4	5
Hyponatraemia			
subjects affected / exposed	2 / 12 (16.67%)	0 / 10 (0.00%)	2 / 27 (7.41%)
occurrences (all)	2	0	2
Hypophosphataemia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 10 (10.00%)	1 / 27 (3.70%)
occurrences (all)	1	1	1
Malnutrition			
subjects affected / exposed	0 / 12 (0.00%)	1 / 10 (10.00%)	1 / 27 (3.70%)
occurrences (all)	0	2	1

Non-serious adverse events	RT + Cis		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 24 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Pyogenic granuloma			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Tumour haemorrhage			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Vascular disorders			

Hypertension			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Lymphoedema			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Gait disturbance			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Mucosal inflammation			
subjects affected / exposed	8 / 24 (33.33%)		
occurrences (all)	8		
Oedema peripheral			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	5		
Pain			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Xerosis			

subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Dysphonia			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Haemoptysis			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Hiccups			
subjects affected / exposed	7 / 24 (29.17%)		
occurrences (all)	7		
Laryngeal inflammation			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Paranasal sinus hyposecretion			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Pharyngeal inflammation			
subjects affected / exposed	5 / 24 (20.83%)		
occurrences (all)	5		
Psychiatric disorders			

Agitation			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Delirium			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Blood creatinine increased			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Blood electrolytes abnormal			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Blood magnesium decreased			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Blood thyroid stimulating hormone decreased			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Blood thyroid stimulating hormone increased			

subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Blood urea increased			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Lipase increased			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Neutrophil count decreased			
subjects affected / exposed	8 / 24 (33.33%)		
occurrences (all)	13		
Platelet count decreased			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Protein total decreased			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	7 / 24 (29.17%)		
occurrences (all)	8		
White blood cell count decreased			
subjects affected / exposed	7 / 24 (29.17%)		
occurrences (all)	13		
C-Reactive protein increased			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
Incision site inflammation			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Infusion related reaction			

subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Radiation skin injury			
subjects affected / exposed	11 / 24 (45.83%)		
occurrences (all)	11		
Recall phenomenon			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Stoma site inflammation			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Dysgeusia			
subjects affected / exposed	6 / 24 (25.00%)		
occurrences (all)	7		
Headache			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Hemiparesis			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Neuralgia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Neuropathy peripheral			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Taste disorder			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Tremor			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 24 (29.17%)		
occurrences (all)	7		
Leukocytosis			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Leukopenia			
subjects affected / exposed	4 / 24 (16.67%)		
occurrences (all)	5		
Lymphopenia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Neutropenia			
subjects affected / exposed	5 / 24 (20.83%)		
occurrences (all)	5		
Thrombocytopenia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Ear pain			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Tinnitus			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			

Cheilitis				
subjects affected / exposed	0 / 24 (0.00%)			
occurrences (all)	0			
Constipation				
subjects affected / exposed	12 / 24 (50.00%)			
occurrences (all)	13			
Diarrhoea				
subjects affected / exposed	1 / 24 (4.17%)			
occurrences (all)	1			
Dry mouth				
subjects affected / exposed	7 / 24 (29.17%)			
occurrences (all)	7			
Dyspepsia				
subjects affected / exposed	2 / 24 (8.33%)			
occurrences (all)	2			
Dysphagia				
subjects affected / exposed	5 / 24 (20.83%)			
occurrences (all)	5			
Gastrooesophageal reflux disease				
subjects affected / exposed	0 / 24 (0.00%)			
occurrences (all)	0			
Glossodynia				
subjects affected / exposed	0 / 24 (0.00%)			
occurrences (all)	0			
Lip dry				
subjects affected / exposed	0 / 24 (0.00%)			
occurrences (all)	0			
Nausea				
subjects affected / exposed	11 / 24 (45.83%)			
occurrences (all)	16			
Odynophagia				
subjects affected / exposed	5 / 24 (20.83%)			
occurrences (all)	5			
Oesophagitis				
subjects affected / exposed	2 / 24 (8.33%)			
occurrences (all)	2			

Oral pain			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Saliva altered			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	7 / 24 (29.17%)		
occurrences (all)	7		
Vomiting			
subjects affected / exposed	7 / 24 (29.17%)		
occurrences (all)	7		
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Dermatitis			
subjects affected / exposed	6 / 24 (25.00%)		
occurrences (all)	6		
Dermatitis acneiform			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Dermatitis bullous			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Lichen planus			

subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Rash papular			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Skin exfoliation			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Skin fissures			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Skin reaction			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Anuria			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Urinary hesitation			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		

Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Hypothyroidism			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Pain in jaw			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Trismus			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Bacterial infection			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Conjunctivitis			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Herpes simplex			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		

Infected dermal cyst			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Mucosal infection			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Oral candidiasis			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	4		
Paronychia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Pyoderma			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Skin infection			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Subcutaneous abscess			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	10 / 24 (41.67%)		
occurrences (all)	11		
Dehydration			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Diabetes mellitus			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Hyperkalaemia			

subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Hypocalcaemia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	3 / 24 (12.50%)		
occurrences (all)	3		
Hypomagnesaemia			
subjects affected / exposed	4 / 24 (16.67%)		
occurrences (all)	4		
Hyponatraemia			
subjects affected / exposed	2 / 24 (8.33%)		
occurrences (all)	2		
Hypophosphataemia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Malnutrition			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 November 2017	Update to questionnaire administration updated to align with dosing cycles. Outcome research assessment and endpoints redefined updated to align with analysis planned. TNM Staging clarified for high and intermediate risk definition. Other minor corrections, clarifications
21 February 2018	Added exclusion of participants with active interstitial lung disease (ILD) / pneumonitis or with a history of ILD / pneumonitis requiring steroids. Aligned thyroid testing to study visits. Added guidance for premedications for cetuximab if necessary.
16 November 2018	Enrollment in the study was closed as of 15-Oct-2018. Revised Protocol 03 covers the changes implemented to the protocol post study enrollment closure: study treatment unblinding, removal of placebo treatment, and removal of analysis of efficacy end-points and efficacy follow-up.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported