



Clinical trial results:

A Phase II, Open-Label, Multicenter, Multi-Cohort Study to Investigate the Efficacy and Safety of Cobimetinib Plus Atezolizumab in Patients with Solid Tumors

Summary

EudraCT number	2017-000794-37
Trial protocol	DE HU GB BE GR ES
Global end of trial date	25 June 2020

Results information

Result version number	v1 (current)
This version publication date	08 January 2021
First version publication date	08 January 2021

Trial information

Trial identification

Sponsor protocol code	WO39760
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03264066
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.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	25 June 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	25 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main goal of the study was to evaluate the efficacy of cobimetinib plus atezolizumab in participants with advanced solid tumors including the following cohorts: squamous cell carcinoma of the head and neck (SCCHN), urothelial carcinoma (UC), and renal cell carcinoma (RCC).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Belgium: 7
Country: Number of subjects enrolled	United Kingdom: 24
Country: Number of subjects enrolled	Hungary: 12
Country: Number of subjects enrolled	Korea, Republic of: 24
Country: Number of subjects enrolled	United States: 18
Worldwide total number of subjects	86
EEA total number of subjects	44

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)	44
From 65 to 84 years	42
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Enrollment took place in 17 investigational sites across the following six countries: Republic of Korea, Belgium, Germany, United Kingdom, Hungary and United States. Seven cohorts were planned in the study. No participants were enrolled in Cohort 7.

Pre-assignment

Screening details:

Participants with advanced solid tumors were included in the study: squamous cell carcinoma of head and neck (SCCHN), urothelial carcinoma (UC), and renal cell carcinoma (RCC). One subject, who deteriorated after enrollment, did not receive study treatment due to no longer meeting inclusion criteria and is not included here (safety population).

Period 1

Period 1 title	Overall Period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 - SCCHN - Treatment Naive

Arm description:

In participants with recurrent or advanced / metastatic squamous cell carcinoma of the head and neck (SCCHN) who were anti-PD-1 and anti-PD-L1 treatment naive, cobimetinib was administered at the approved dose and schedule of 60 mg once daily (QD) for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by intravenous (IV) infusion on Days 1 and 15 of each 28-day cycle.

Arm type	Experimental
Investigational medicinal product name	Cobimetinib
Investigational medicinal product code	
Other name	Cotellic
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received cobimetinib 60 mg (3 tablets of 20 mg each) orally once a day on Days 1-21 of each 28-day cycle.

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

Dosage and administration details:

Atezolizumab were given a fixed dose of 840 mg by intravenous (IV) infusion on Days 1 and 15 of each 28-day cycle.

Arm title	Cohort 2 - UC - Treatment Naive
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Arm description:

In participants with advanced / metastatic urothelial carcinoma (UC) who were anti-PD-1 and anti-PD-L1 treatment naive, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.

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

Dosage and administration details:

Atezolizumab were given a fixed dose of 840 mg by intravenous (IV) infusion on Days 1 and 15 of each 28-day cycle.

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

Dosage and administration details:

Participants received cobimetinib 60 mg (3 tablets of 20 mg each) orally once a day on Days 1-21 of each 28-day cycle.

Arm title	Cohort 3 - RCC - Treatment Naive
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Arm description:

In participants with metastatic renal cell carcinoma (RCC) who were anti-PD-1 and anti-PD-L1 treatment naive, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.

Arm type	Experimental
Investigational medicinal product name	Cobimetinib
Investigational medicinal product code	
Other name	Cotellic
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received cobimetinib 60 mg (3 tablets of 20 mg each) orally once a day on Days 1-21 of each 28-day cycle.

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

Dosage and administration details:

Atezolizumab were given a fixed dose of 840 mg by intravenous (IV) infusion on Days 1 and 15 of each 28-day cycle.

Arm title	Cohort 4 - SCCHN - Previous Treatment Exposure
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Arm description:

In participants with SCCHN whose disease had progressed while receiving anti-PD-1 or anti-PD-L1 therapy, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.

Arm type	Experimental
Investigational medicinal product name	Cobimetinib
Investigational medicinal product code	
Other name	Cotellic
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received cobimetinib 60 mg (3 tablets of 20 mg each) orally once a day on Days 1-21 of each 28-day cycle.

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

Dosage and administration details:

Atezolizumab were given a fixed dose of 840 mg by intravenous (IV) infusion on Days 1 and 15 of each 28-day cycle.

Arm title	Cohort 5 - UC - Previous Treatment Exposure
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Arm description:

In participants with UC whose disease had progressed while receiving anti-PD-1 or anti-PD-L1 therapy, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.

Arm type	Experimental
Investigational medicinal product name	Cobimetinib
Investigational medicinal product code	
Other name	Cotellic
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received cobimetinib 60 mg (3 tablets of 20 mg each) orally once a day on Days 1-21 of each 28-day cycle.

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

Dosage and administration details:

Atezolizumab were given a fixed dose of 840 mg by intravenous (IV) infusion on Days 1 and 15 of each 28-day cycle.

Arm title	Cohort 6 - RCC - Previous Treatment Exposure
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Arm description:

In participants with RCC whose disease had progressed while receiving anti-PD-1 or anti-PD-L1 therapy, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.

Arm type	Experimental
Investigational medicinal product name	Cobimetinib
Investigational medicinal product code	
Other name	Cotellic
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received cobimetinib 60 mg (3 tablets of 20 mg each) orally once a day on Days 1-21 of each 28-day cycle.

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

Dosage and administration details:

Atezolizumab were given a fixed dose of 840 mg by intravenous (IV) infusion on Days 1 and 15 of each 28-day cycle.

Number of subjects in period 1	Cohort 1 - SCCHN - Treatment Naive	Cohort 2 - UC - Treatment Naive	Cohort 3 - RCC - Treatment Naive
Started	20	19	17
Completed	0	0	0
Not completed	20	19	17
Adverse event, serious fatal	12	11	8
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	1	1	-
Progressive Disease	-	2	1
Study Terminated by Sponsor	5	5	8
Lost to follow-up	1	-	-

Number of subjects in period 1	Cohort 4 - SCCHN - Previous Treatment Exposure	Cohort 5 - UC - Previous Treatment Exposure	Cohort 6 - RCC - Previous Treatment Exposure
Started	20	7	3
Completed	0	0	0
Not completed	20	7	3
Adverse event, serious fatal	10	6	1
Consent withdrawn by subject	5	-	-
Adverse event, non-fatal	-	-	-
Progressive Disease	-	-	-
Study Terminated by Sponsor	5	1	2
Lost to follow-up	-	-	-

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1 - SCCHN - Treatment Naive
Reporting group description: In participants with recurrent or advanced / metastatic squamous cell carcinoma of the head and neck (SCCHN) who were anti-PD-1 and anti-PD-L1 treatment naive, cobimetinib was administered at the approved dose and schedule of 60 mg once daily (QD) for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by intravenous (IV) infusion on Days 1 and 15 of each 28-day cycle.	
Reporting group title	Cohort 2 - UC - Treatment Naive
Reporting group description: In participants with advanced / metastatic urothelial carcinoma (UC) who were anti-PD-1 and anti-PD-L1 treatment naive, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.	
Reporting group title	Cohort 3 - RCC - Treatment Naive
Reporting group description: In participants with metastatic renal cell carcinoma (RCC) who were anti-PD-1 and anti-PD-L1 treatment naive, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.	
Reporting group title	Cohort 4 - SCCHN - Previous Treatment Exposure
Reporting group description: In participants with SCCHN whose disease had progressed while receiving anti-PD-1 or anti-PD-L1 therapy, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.	
Reporting group title	Cohort 5 - UC - Previous Treatment Exposure
Reporting group description: In participants with UC whose disease had progressed while receiving anti-PD-1 or anti-PD-L1 therapy, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.	
Reporting group title	Cohort 6 - RCC - Previous Treatment Exposure
Reporting group description: In participants with RCC whose disease had progressed while receiving anti-PD-1 or anti-PD-L1 therapy, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.	

Reporting group values	Cohort 1 - SCCHN - Treatment Naive	Cohort 2 - UC - Treatment Naive	Cohort 3 - RCC - Treatment Naive
Number of subjects	20	19	17
Age categorical Units: Subjects			
Age Continuous Units: years arithmetic mean standard deviation	61.8 ± 10.1	65.3 ± 10.3	60.3 ± 11.5
Sex: Female, Male Units: participants			
Male	18	11	11
Female	2	8	6

Reporting group values	Cohort 4 - SCCHN - Previous Treatment Exposure	Cohort 5 - UC - Previous Treatment Exposure	Cohort 6 - RCC - Previous Treatment Exposure
Number of subjects	20	7	3
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	62.4 ± 6.4	61.4 ± 15.8	68.3 ± 15.0
Sex: Female, Male Units: participants			
Male	19	5	1
Female	1	2	2

Reporting group values	Total		
Number of subjects	86		
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	-		
Sex: Female, Male Units: participants			
Male	65		
Female	21		

End points

End points reporting groups

Reporting group title	Cohort 1 - SCCHN - Treatment Naive
Reporting group description: In participants with recurrent or advanced / metastatic squamous cell carcinoma of the head and neck (SCCHN) who were anti-PD-1 and anti-PD-L1 treatment naive, cobimetinib was administered at the approved dose and schedule of 60 mg once daily (QD) for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by intravenous (IV) infusion on Days 1 and 15 of each 28-day cycle.	
Reporting group title	Cohort 2 - UC - Treatment Naive
Reporting group description: In participants with advanced / metastatic urothelial carcinoma (UC) who were anti-PD-1 and anti-PD-L1 treatment naive, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.	
Reporting group title	Cohort 3 - RCC - Treatment Naive
Reporting group description: In participants with metastatic renal cell carcinoma (RCC) who were anti-PD-1 and anti-PD-L1 treatment naive, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.	
Reporting group title	Cohort 4 - SCCHN - Previous Treatment Exposure
Reporting group description: In participants with SCCHN whose disease had progressed while receiving anti-PD-1 or anti-PD-L1 therapy, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.	
Reporting group title	Cohort 5 - UC - Previous Treatment Exposure
Reporting group description: In participants with UC whose disease had progressed while receiving anti-PD-1 or anti-PD-L1 therapy, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.	
Reporting group title	Cohort 6 - RCC - Previous Treatment Exposure
Reporting group description: In participants with RCC whose disease had progressed while receiving anti-PD-1 or anti-PD-L1 therapy, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.	
Subject analysis set title	Cohort 1 - SCCHN - Treatment Naive
Subject analysis set type	Intention-to-treat
Subject analysis set description: In participants with recurrent or advanced / metastatic squamous cell carcinoma of the head and neck (SCCHN) who were anti-PD-1 and anti-PD-L1 treatment naive, cobimetinib was administered at the approved dose and schedule of 60 mg once daily (QD) for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by intravenous (IV) infusion on Days 1 and 15 of each 28-day cycle.	
Subject analysis set title	Cohort 2 - UC - Treatment Naive
Subject analysis set type	Intention-to-treat
Subject analysis set description: In participants with advanced / metastatic urothelial carcinoma (UC) who were anti-PD-1 and anti-PD-L1 treatment naive, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.	
Subject analysis set title	Cohort 3 - RCC - Treatment Naive
Subject analysis set type	Intention-to-treat
Subject analysis set description: In participants with metastatic renal cell carcinoma (RCC) who were anti-PD-1 and anti-PD-L1 treatment naive, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7	

days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.

Subject analysis set title	Cohort 4 - SCCHN - Previous Treatment Exposure
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

In participants with SCCHN whose disease had progressed while receiving anti-PD-1 or anti-PD-L1 therapy, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.

Subject analysis set title	Cohort 5 - UC - Previous Treatment Exposure
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

In participants with UC whose disease had progressed while receiving anti-PD-1 or anti-PD-L1 therapy, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.

Subject analysis set title	Cohort 6 - RCC - Previous Treatment Exposure
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Subject analysis set type	Intention-to-treat
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Subject analysis set description:

In participants with RCC whose disease had progressed while receiving anti-PD-1 or anti-PD-L1 therapy, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.

Subject analysis set title	Cohorts 1-6
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

In all participants cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR) ^[1]
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End point description:

Objective response rate was defined as the percentage of participants with a complete response (CR) or a partial response (PR) on two consecutive tumor assessments ≥ 4 weeks apart, as determined by the investigators using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1). CR was defined as disappearance of all lesions. PR was defined as $\geq 30\%$ decrease in the sum of diameters of target lesions, in the absence of CR, new lesions, and unequivocal progression in non-target lesions. The intent-to-treat (ITT) population included all participants enrolled in the study.

End point type	Primary
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End point timeframe:

Up to approximately 31 months

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: Since all subjects in the study received the same treatments statistical analyses were not planned to be conducted.

End point values	Cohort 1 - SCCHN - Treatment Naive	Cohort 2 - UC - Treatment Naive	Cohort 3 - RCC - Treatment Naive	Cohort 4 - SCCHN - Previous Treatment Exposure
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	17	20
Units: percentage of participants				
number (confidence interval 95%)	20.0 (0.00 to 40.03)	30.0 (7.42 to 52.58)	17.6 (0.00 to 38.71)	0 (0.00 to 2.50)

End point values	Cohort 5 - UC - Previous Treatment Exposure	Cohort 6 - RCC - Previous Treatment Exposure		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	3		
Units: percentage of participants				
number (confidence interval 95%)	0 (0.00 to 7.14)	0 (0.00 to 16.67)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
Overall survival was defined as the time from enrollment to death from any cause. The ITT population included all participants enrolled in the study. 9.99999: not estimable	
End point type	Secondary
End point timeframe:	
Up to approximately 31 months	

End point values	Cohort 1 - SCCHN - Treatment Naive	Cohort 2 - UC - Treatment Naive	Cohort 3 - RCC - Treatment Naive	Cohort 4 - SCCHN - Previous Treatment Exposure
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	17	20
Units: months				
median (full range (min-max))	16.8 (2 to 26)	18.7 (2 to 26)	21.7 (1 to 29)	7.7 (1 to 18)

End point values	Cohort 5 - UC - Previous Treatment Exposure	Cohort 6 - RCC - Previous Treatment Exposure		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	3		
Units: months				
median (full range (min-max))	5.9 (2 to 12)	9.99999 (6 to 12)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)
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End point description:

PFS was defined as the time from enrollment to the first occurrence of disease progression as determined by the investigator(s), using RECIST v1.1, or to death from any cause, whichever occurs first. Disease progression was defined as $\geq 20\%$ increase in the sum of diameters of target lesions, unequivocal progression in non-target lesions, and/or appearance of new lesions. The ITT population included all participants enrolled in the study.

End point type	Secondary
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End point timeframe:

Up to approximately 31 months

End point values	Cohort 1 - SCCHN - Treatment Naive	Cohort 2 - UC - Treatment Naive	Cohort 3 - RCC - Treatment Naive	Cohort 4 - SCCHN - Previous Treatment Exposure
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	17	20
Units: months				
median (full range (min-max))	5.5 (2 to 26)	3.4 (2 to 26)	3.4 (1 to 28)	3.6 (0 to 9)

End point values	Cohort 5 - UC - Previous Treatment Exposure	Cohort 6 - RCC - Previous Treatment Exposure		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	3		
Units: months				
median (full range (min-max))	2.1 (1 to 4)	2.7 (1 to 4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)
End point description:	
DOR was defined as the time from the first occurrence of a documented, confirmed objective response to disease progression as determined by the investigator, using RECIST v1.1, or to death from any cause, whichever occurs first. Objective response was defined as a complete response (CR) or a partial response (PR) on two consecutive tumor assessments ≥ 4 weeks apart. CR was defined as disappearance of all lesions. PR was defined as $\geq 30\%$ decrease in the sum of diameters of target lesions, in the absence of CR, new lesions, and unequivocal progression in non-target lesions. Disease progression was defined as $\geq 20\%$ increase in the sum of diameters of target lesions, unequivocal progression in non-target lesions, and/or appearance of new lesions. The ITT population included all participants enrolled in the study.	
End point type	Secondary
End point timeframe:	
Up to approximately 31 months	

End point values	Cohort 1 - SCCHN - Treatment Naive	Cohort 2 - UC - Treatment Naive	Cohort 3 - RCC - Treatment Naive	Cohort 4 - SCCHN - Previous Treatment Exposure
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0 ^[2]	0 ^[3]	0 ^[4]	0 ^[5]
Units: months				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[2] - Median DOR was not estimable due to low number of events.

[3] - Median DOR was not estimable due to low number of events.

[4] - Median DOR was not estimable due to low number of events.

[5] - Median DOR was not estimable due to low number of events.

End point values	Cohort 5 - UC - Previous Treatment Exposure	Cohort 6 - RCC - Previous Treatment Exposure		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0 ^[6]	0 ^[7]		
Units: months				
median (full range (min-max))	(to)	(to)		

Notes:

[6] - Median DOR was not estimable due to low number of events.

[7] - Median DOR was not estimable due to low number of events.

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)
End point description:	
DCR was defined as the percentage of participants with a complete response (CR), a partial response (PR), or stable disease at 16 weeks as determined by the investigator using RECIST v1.1. CR was defined as disappearance of all lesions. PR was defined as $\geq 30\%$ decrease in the sum of diameters of target lesions, in the absence of CR, new lesions, and unequivocal progression in non-target lesions. Stable disease was defined as neither sufficient shrinkage to qualify for CR or PR nor sufficient increase to qualify for disease progression. Disease progression was defined as $\geq 20\%$ increase in the sum of	

diameters of target lesions, unequivocal progression in non-target lesions, and/or appearance of new lesions. The ITT population included all participants enrolled in the study.

End point type	Secondary
End point timeframe:	
At 16 weeks	

End point values	Cohort 1 - SCCHN - Treatment Naive	Cohort 2 - UC - Treatment Naive	Cohort 3 - RCC - Treatment Naive	Cohort 4 - SCCHN - Previous Treatment Exposure
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20	20	17	20
Units: percentage of participants				
number (confidence interval 95%)	50.0 (25.59 to 74.41)	40.0 (16.03 to 63.97)	23.5 (0.42 to 46.63)	25.0 (3.52 to 46.48)

End point values	Cohort 5 - UC - Previous Treatment Exposure	Cohort 6 - RCC - Previous Treatment Exposure		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	3		
Units: percentage of participants				
number (confidence interval 95%)	0 (0.00 to 7.14)	0 (0.00 to 16.67)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events

End point title	Number of Participants With Adverse Events
End point description:	
An adverse event is any untoward medical occurrence in a subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events.	
End point type	Secondary
End point timeframe:	
Up to approximately 31 months	

End point values	Cohort 1 - SCCHN - Treatment Naive	Cohort 2 - UC - Treatment Naive	Cohort 3 - RCC - Treatment Naive	Cohort 4 - SCCHN - Previous Treatment Exposure
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	17	20
Units: participants	20	19	17	20

End point values	Cohort 5 - UC - Previous Treatment Exposure	Cohort 6 - RCC - Previous Treatment Exposure		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	3		
Units: participants	7	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) of Cobimetinib

End point title	Maximum Plasma Concentration (Cmax) of Cobimetinib
End point description:	Cmax is the maximum (or peak) concentration that a study drug achieves in the body.
End point type	Secondary
End point timeframe:	Day 15 of Cycle 3 (cycle is 28 days): 2-4 hours after cobimetinib dose

End point values	Cohorts 1-6			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: nanogram per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)	285 (\pm 56.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Plasma Concentration (Cmin) of Cobimetinib

End point title	Minimum Plasma Concentration (Cmin) of Cobimetinib
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End point description:

Cmin is the minimum (or trough) concentration that a study drug achieves in the body.

End point type	Secondary
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End point timeframe:

: Day 15 of Cycle 3 (cycle is 28 days): prior to cobimetinib dose

End point values	Cohorts 1-6			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: ng/mL				
geometric mean (geometric coefficient of variation)	174 (\pm 152)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Serum Concentration (Cmax) of Atezolizumab

End point title	Maximum Serum Concentration (Cmax) of Atezolizumab
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End point description:

Cmax is the maximum (or peak) concentration that a study drug achieves in the body.

End point type	Secondary
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End point timeframe:

30 minutes following end of atezolizumab infusion on Day 1 of Cycle 1 (each cycle is 28 days) and Day 15 of Cycle 3

End point values	Cohorts 1-6			
Subject group type	Subject analysis set			
Number of subjects analysed	40			
Units: micrograms per milliliter (mcg/mL)				
geometric mean (geometric coefficient of variation)	417000 (\pm 50.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Serum Concentration (Cmin) of Atezolizumab

End point title	Minimum Serum Concentration (Cmin) of Atezolizumab
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End point description:

C_{min} is the minimum (or trough) concentration that a study drug achieves in the body.

End point type	Secondary
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End point timeframe:

Prior to atezolizumab infusion on Day 1 of Cycles (each cycle is 28 days) 2, 4, 8, 12, and 16, Day 15 of Cycle 3

End point values	Cohorts 1-6			
Subject group type	Subject analysis set			
Number of subjects analysed	61			
Units: mcg/mL				
geometric mean (geometric coefficient of variation)	112000 (± 219)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Anti-drug Antibodies (ADAs)

End point title	Number of Participants With Anti-drug Antibodies (ADAs)
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End point description:

Participants were considered to be ADA positive if they were missing data at baseline but developed an ADA response following study drug administration (treatment-induced ADA response), or if they were ADA positive at baseline and the titer of one or more post-baseline samples was at least 4-fold greater (i.e., ≥ 0.60 -titer units) than the titer of the baseline sample (treatment-enhanced ADA response). Participants were considered to be ADA negative if they were missing data at baseline, had a post-baseline ADA result, and all post-baseline samples were negative, or if they were ADA positive at baseline but did not have any post-baseline samples with a titer that was at least 4-fold greater than the titer of the baseline sample (treatment unaffected).

End point type	Secondary
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End point timeframe:

Day 1 of Cycles (each cycle is 28 days) 1, 2, 4, 8, 12, and 16; Day 15 of Cycle 3; at atezolizumab treatment discontinuation visit, and <90 days after last atezolizumab infusion (up to approximately 31 months)

End point values	Cohorts 1-6			
Subject group type	Subject analysis set			
Number of subjects analysed	75			
Units: participants	24			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 31 months

Adverse event reporting additional description:

The safety population included all enrolled participants who received at least one dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	Cohort 1 - SCCHN - Treatment Naive
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Reporting group description:

In participants with recurrent or advanced / metastatic squamous cell carcinoma of the head and neck (SCCHN) who were anti-PD-1 and anti-PD-L1 treatment naive, cobimetinib was administered at the approved dose and schedule of 60 mg once daily (QD) for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by intravenous (IV) infusion on Days 1 and 15 of each 28-day cycle.

Reporting group title	Cohort 2 - UC - Treatment Naive
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Reporting group description:

In participants with advanced / metastatic urothelial carcinoma (UC) who were anti-PD-1 and anti-PD-L1 treatment naive, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.

Reporting group title	Cohort 3 - RCC - Treatment Naive
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Reporting group description:

In participants with metastatic renal cell carcinoma (RCC) who were anti-PD-1 and anti-PD-L1 treatment naive, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.

Reporting group title	Cohort 4 - SCCHN - Previous Treatment Exposure
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Reporting group description:

In participants with SCCHN whose disease had progressed while receiving anti-PD-1 or anti-PD-L1 therapy, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.

Reporting group title	Cohort 5 - UC - Previous Treatment Exposure
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Reporting group description:

In participants with UC whose disease had progressed while receiving anti-PD-1 or anti-PD-L1 therapy, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.

Reporting group title	Cohort 6 - RCC - Previous Treatment Exposure
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Reporting group description:

In participants with RCC whose disease had progressed while receiving anti-PD-1 or anti-PD-L1 therapy, cobimetinib was administered at the approved dose and schedule of 60 mg QD for 21 days and 7 days off of each 28-day cycle; and atezolizumab 840 mg by IV infusion on Days 1 and 15 of each 28-day cycle.

Serious adverse events	Cohort 1 - SCCN - Treatment Naive	Cohort 2 - UC - Treatment Naive	Cohort 3 - RCC - Treatment Naive
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 20 (65.00%)	9 / 19 (47.37%)	8 / 17 (47.06%)
number of deaths (all causes)	12	12	8
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
TUMOUR HAEMORRHAGE			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
GASTROSTOMY			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (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
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHILLS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FACE OEDEMA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FATIGUE			

subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
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 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
DYSпноEA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	2 / 17 (11.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA ASPIRATION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (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
PNEUMONITIS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (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
RESPIRATORY TRACT OEDEMA			

subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
DEVICE DISLOCATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EJECTION FRACTION DECREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
HUMERUS FRACTURE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INFUSION RELATED REACTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTOPERATIVE RESPIRATORY FAILURE			

subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDITIS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
ALTERED STATE OF CONSCIOUSNESS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMMUNE-MEDIATED ENCEPHALITIS			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
COLITIS			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			

subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	2 / 17 (11.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPHAGIA			
subjects affected / exposed	2 / 20 (10.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROCOLITIS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (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
GASTRITIS EROSIVE			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEUS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (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
INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (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
LARGE INTESTINE PERFORATION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			

subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMATOSIS INTESTINALIS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (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
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (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
VOMITING			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
IMMUNE-MEDIATED HEPATITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
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 / 20 (0.00%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH MACULAR			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
NEPHRITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY RETENTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
DEVICE RELATED SEPSIS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (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
ENDOCARDITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
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	3 / 20 (15.00%)	2 / 19 (10.53%)	2 / 17 (11.76%)
occurrences causally related to treatment / all	1 / 3	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 1	1 / 1	0 / 0

SEPSIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	2 / 19 (10.53%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 4 - SCCHN - Previous Treatment Exposure	Cohort 5 - UC - Previous Treatment Exposure	Cohort 6 - RCC - Previous Treatment Exposure
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 20 (50.00%)	4 / 7 (57.14%)	1 / 3 (33.33%)
number of deaths (all causes)	12	6	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
TUMOUR HAEMORRHAGE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
GASTROSTOMY			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

CHILLS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FACE OEDEMA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FATIGUE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYREXIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
DYSпноEA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA ASPIRATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

PNEUMONITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PULMONARY EMBOLISM			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT OEDEMA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
DEVICE DISLOCATION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (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	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EJECTION FRACTION DECREASED			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
HUMERUS FRACTURE			

subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (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
INFUSION RELATED REACTION			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
POSTOPERATIVE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PERICARDITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
ALTERED STATE OF CONSCIOUSNESS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMMUNE-MEDIATED ENCEPHALITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
COLITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DYSPHAGIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENTEROCOLITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTRITIS EROSIVE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ILEUS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINAL OBSTRUCTION			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARGE INTESTINE PERFORATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMATOSIS INTESTINALIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER GASTROINTESTINAL HAEMORRHAGE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
IMMUNE-MEDIATED HEPATITIS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

RASH			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH MACULAR			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
NEPHRITIS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY RETENTION			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
DEVICE RELATED SEPSIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ENDOCARDITIS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (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
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (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

PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
SEPSIS			
subjects affected / exposed	1 / 20 (5.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cohort 1 - SCCHN - Treatment Naive	Cohort 2 - UC - Treatment Naive	Cohort 3 - RCC - Treatment Naive
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 20 (100.00%)	19 / 19 (100.00%)	17 / 17 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA OF COLON			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
CANCER PAIN			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
KERATOACANTHOMA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
TUMOUR HAEMORRHAGE			

subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 19 (0.00%) 0	0 / 17 (0.00%) 0
Vascular disorders			
FLUSHING			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
HYPERTENSION			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
HYPOTENSION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	2 / 17 (11.76%)
occurrences (all)	1	0	2
LYMPHOEDEMA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
ORTHOSTATIC HYPOTENSION			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	1 / 20 (5.00%)	3 / 19 (15.79%)	2 / 17 (11.76%)
occurrences (all)	1	3	2
CHEST PAIN			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
CHILLS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
FACE OEDEMA			
subjects affected / exposed	2 / 20 (10.00%)	2 / 19 (10.53%)	2 / 17 (11.76%)
occurrences (all)	3	2	2
FACIAL PAIN			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
FATIGUE			

subjects affected / exposed	6 / 20 (30.00%)	9 / 19 (47.37%)	5 / 17 (29.41%)
occurrences (all)	6	14	7
GENERALISED OEDEMA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	1 / 20 (5.00%)	3 / 19 (15.79%)	0 / 17 (0.00%)
occurrences (all)	1	3	0
LOCALISED OEDEMA			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
MALAISE			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
MUCOSAL INFLAMMATION			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	2 / 17 (11.76%)
occurrences (all)	1	1	2
OEDEMA			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	2 / 17 (11.76%)
occurrences (all)	0	1	2
OEDEMA PERIPHERAL			
subjects affected / exposed	3 / 20 (15.00%)	2 / 19 (10.53%)	3 / 17 (17.65%)
occurrences (all)	3	2	3
PAIN			
subjects affected / exposed	3 / 20 (15.00%)	2 / 19 (10.53%)	0 / 17 (0.00%)
occurrences (all)	3	2	0
PERIPHERAL SWELLING			
subjects affected / exposed	0 / 20 (0.00%)	2 / 19 (10.53%)	0 / 17 (0.00%)
occurrences (all)	0	3	0
PYREXIA			
subjects affected / exposed	2 / 20 (10.00%)	7 / 19 (36.84%)	5 / 17 (29.41%)
occurrences (all)	2	9	9
SWELLING FACE			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			

HYPERSENSITIVITY subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 19 (0.00%) 0	0 / 17 (0.00%) 0
Reproductive system and breast disorders			
SCROTAL OEDEMA subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 19 (5.26%) 2	0 / 17 (0.00%) 0
TESTICULAR SWELLING subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 19 (0.00%) 0	0 / 17 (0.00%) 0
VAGINAL DISCHARGE subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 19 (5.26%) 1	0 / 17 (0.00%) 0
VAGINAL HAEMORRHAGE subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	2 / 19 (10.53%) 2	0 / 17 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
CHRONIC OBSTRUCTIVE PULMONARY DISEASE subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 19 (0.00%) 0	0 / 17 (0.00%) 0
COUGH subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	4 / 19 (21.05%) 5	2 / 17 (11.76%) 2
DYSPHONIA subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 19 (5.26%) 1	0 / 17 (0.00%) 0
DYSPNOEA subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	4 / 19 (21.05%) 4	1 / 17 (5.88%) 1
DYSPNOEA EXERTIONAL subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 19 (5.26%) 1	0 / 17 (0.00%) 0
EPISTAXIS subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 19 (0.00%) 0	0 / 17 (0.00%) 0

HAEMOPTYSIS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
LARYNGEAL OEDEMA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
NASAL CONGESTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
NASAL OBSTRUCTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	2 / 20 (10.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	2	1	0
PNEUMONITIS			
subjects affected / exposed	2 / 20 (10.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
PRODUCTIVE COUGH			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
RALES			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
WHEEZING			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
ANGER			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
ANXIETY			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
CONFUSIONAL STATE			

subjects affected / exposed	2 / 20 (10.00%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences (all)	2	1	1
DEPRESSION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
DISORIENTATION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
INSOMNIA			
subjects affected / exposed	3 / 20 (15.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	2 / 19 (10.53%)	1 / 17 (5.88%)
occurrences (all)	0	2	1
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	3 / 19 (15.79%)	0 / 17 (0.00%)
occurrences (all)	0	3	0
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	4 / 20 (20.00%)	7 / 19 (36.84%)	3 / 17 (17.65%)
occurrences (all)	4	9	3
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 20 (5.00%)	4 / 19 (21.05%)	0 / 17 (0.00%)
occurrences (all)	1	4	0
BLOOD MAGNESIUM DECREASED			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
BLOOD POTASSIUM DECREASED			

subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
BLOOD PRESSURE DECREASED			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
BLOOD PRESSURE INCREASED			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
BLOOD THYROID STIMULATING HORMONE INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
BLOOD URIC ACID INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
BRAIN NATRIURETIC PEPTIDE INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
CYTOMEGALOVIRUS TEST POSITIVE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
EJECTION FRACTION DECREASED			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	2 / 17 (11.76%)
occurrences (all)	1	0	3
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
HAEMOGLOBIN DECREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
INTERNATIONAL NORMALISED RATIO INCREASED			

subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 19 (0.00%) 0	0 / 17 (0.00%) 0
PLATELET COUNT DECREASED subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 19 (5.26%) 1	0 / 17 (0.00%) 0
PLATELET COUNT INCREASED subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 19 (0.00%) 0	0 / 17 (0.00%) 0
VITAMIN B12 DECREASED subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 19 (5.26%) 1	0 / 17 (0.00%) 0
VITAMIN D DECREASED subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 19 (5.26%) 1	0 / 17 (0.00%) 0
WEIGHT DECREASED subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 3	3 / 19 (15.79%) 3	1 / 17 (5.88%) 1
Injury, poisoning and procedural complications			
CONTUSION subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 19 (5.26%) 1	0 / 17 (0.00%) 0
FACE INJURY subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 19 (0.00%) 0	0 / 17 (0.00%) 0
FALL subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 19 (0.00%) 0	0 / 17 (0.00%) 0
INFUSION RELATED REACTION subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	3 / 19 (15.79%) 4	1 / 17 (5.88%) 1
INJURY subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 19 (0.00%) 0	0 / 17 (0.00%) 0
LIMB INJURY			

subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
POST PROCEDURAL SWELLING			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
SKIN LACERATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
STRESS FRACTURE			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
WOUND COMPLICATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
ATRIOVENTRICULAR BLOCK FIRST DEGREE			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
CORONARY ARTERY DISEASE			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
PERICARDITIS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
SINUS BRADYCARDIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
SINUS TACHYCARDIA			

subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
TACHYCARDIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
VENTRICULAR DYSFUNCTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
APHASIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
CAUDA EQUINA SYNDROME			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
CEREBRAL INFARCTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
DIZZINESS			
subjects affected / exposed	0 / 20 (0.00%)	4 / 19 (21.05%)	2 / 17 (11.76%)
occurrences (all)	0	4	2
DIZZINESS POSTURAL			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
DYSARTHRIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
DYSGEUSIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
HEADACHE			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
LETHARGY			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

LUMBAR RADICULOPATHY			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
PARAESTHESIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
PRESYNCOPE			
subjects affected / exposed	0 / 20 (0.00%)	2 / 19 (10.53%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
RESTLESS LEGS SYNDROME			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
SCIATICA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
STATUS EPILEPTICUS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
SYNCOPE			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
TASTE DISORDER			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	8 / 20 (40.00%)	6 / 19 (31.58%)	4 / 17 (23.53%)
occurrences (all)	9	6	5
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
LEUKOCYTOSIS			

subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
LEUKOPENIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
LYMPH NODE PAIN			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
LYMPHADENITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
LYMPHOPENIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
NEUTROPENIA			
subjects affected / exposed	2 / 20 (10.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	7	0	0
THROMBOCYTOPENIA			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Ear and labyrinth disorders			
HYPOACUSIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
INNER EAR DISORDER			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
VERTIGO			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
CHORIORETINOPATHY			

subjects affected / exposed	2 / 20 (10.00%)	3 / 19 (15.79%)	2 / 17 (11.76%)
occurrences (all)	2	4	2
ENTROPION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
EYELID OEDEMA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
EYELID PTOSIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
GLAUCOMA			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
LACRIMATION INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
MACULAR OEDEMA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
OPTIC NERVE DISORDER			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
PERIORBITAL OEDEMA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
RETINAL OEDEMA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
RETINOPATHY			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
SUBRETINAL FLUID			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
SWELLING OF EYELID			

subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
TRICHIASIS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
VISION BLURRED			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
VISUAL IMPAIRMENT			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences (all)	1	1	1
VITREOUS FLOATERS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
ABDOMINAL PAIN			
subjects affected / exposed	0 / 20 (0.00%)	2 / 19 (10.53%)	2 / 17 (11.76%)
occurrences (all)	0	3	2
ANAL HAEMORRHAGE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
ANGULAR CHEILITIS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
ASCITES			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
CHEILITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

CONSTIPATION			
subjects affected / exposed	1 / 20 (5.00%)	5 / 19 (26.32%)	3 / 17 (17.65%)
occurrences (all)	1	7	3
DIAPHRAGMATIC HERNIA			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
DIARRHOEA			
subjects affected / exposed	7 / 20 (35.00%)	11 / 19 (57.89%)	9 / 17 (52.94%)
occurrences (all)	9	15	13
DRY MOUTH			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences (all)	1	1	1
DYSPEPSIA			
subjects affected / exposed	2 / 20 (10.00%)	4 / 19 (21.05%)	3 / 17 (17.65%)
occurrences (all)	2	4	3
DYSPHAGIA			
subjects affected / exposed	2 / 20 (10.00%)	2 / 19 (10.53%)	1 / 17 (5.88%)
occurrences (all)	2	3	1
FLATULENCE			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
GASTRIC ULCER			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
GASTRITIS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
GASTROESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
GINGIVAL BLEEDING			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
GLOSSITIS			

subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
GLOSSODYNIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
HAEMATEMESIS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
HAEMATOCHEZIA			
subjects affected / exposed	0 / 20 (0.00%)	2 / 19 (10.53%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
HAEMORRHOIDS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
LIP OEDEMA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
LIP PAIN			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
LIP SWELLING			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
MOUTH ULCERATION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
MUCOUS STOOLS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
NAUSEA			
subjects affected / exposed	6 / 20 (30.00%)	3 / 19 (15.79%)	5 / 17 (29.41%)
occurrences (all)	6	3	5
OESOPHAGITIS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
ORAL DISCHARGE			

subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
ORAL PAIN			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
RECTAL HAEMORRHAGE			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
STOMATITIS			
subjects affected / exposed	2 / 20 (10.00%)	5 / 19 (26.32%)	2 / 17 (11.76%)
occurrences (all)	3	5	2
TOOTHACHE			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
VOMITING			
subjects affected / exposed	7 / 20 (35.00%)	4 / 19 (21.05%)	3 / 17 (17.65%)
occurrences (all)	9	8	3
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
BLISTER			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
DERMATITIS			
subjects affected / exposed	3 / 20 (15.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	3	0	1
DERMATITIS ACNEIFORM			
subjects affected / exposed	0 / 20 (0.00%)	2 / 19 (10.53%)	3 / 17 (17.65%)
occurrences (all)	0	2	3
DERMATITIS PSORIASIFORM			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
DRY SKIN			
subjects affected / exposed	3 / 20 (15.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	3	0	1

ECZEMA			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
ERYTHEMA			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
INTERTRIGO			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
NIGHT SWEATS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
ONYCHOCLASIS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
PRURITUS			
subjects affected / exposed	2 / 20 (10.00%)	3 / 19 (15.79%)	1 / 17 (5.88%)
occurrences (all)	2	3	2
RASH			
subjects affected / exposed	9 / 20 (45.00%)	9 / 19 (47.37%)	12 / 17 (70.59%)
occurrences (all)	10	11	14
RASH ERYTHEMATOUS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
RASH PAPULAR			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
RASH PRURITIC			

subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
SKIN FISSURES			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	1	2	0
STASIS DERMATITIS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
URTICARIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	3
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
DYSURIA			
subjects affected / exposed	0 / 20 (0.00%)	2 / 19 (10.53%)	0 / 17 (0.00%)
occurrences (all)	0	2	0
HAEMATURIA			
subjects affected / exposed	0 / 20 (0.00%)	3 / 19 (15.79%)	0 / 17 (0.00%)
occurrences (all)	0	4	0
NOCTURIA			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
POLLAKIURIA			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
PROTEINURIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
RENAL FAILURE			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
RENAL IMPAIRMENT			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

URINARY RETENTION subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 19 (5.26%) 1	0 / 17 (0.00%) 0
URINARY TRACT OBSTRUCTION subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 19 (5.26%) 1	0 / 17 (0.00%) 0
URINARY TRACT PAIN subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 19 (0.00%) 0	0 / 17 (0.00%) 0
Endocrine disorders			
HYPERTHYROIDISM subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 19 (5.26%) 1	0 / 17 (0.00%) 0
HYPOTHYROIDISM subjects affected / exposed occurrences (all)	3 / 20 (15.00%) 4	1 / 19 (5.26%) 1	1 / 17 (5.88%) 1
THYROIDITIS subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 19 (5.26%) 1	0 / 17 (0.00%) 0
Musculoskeletal and connective tissue disorders			
ARTHRALGIA subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	2 / 19 (10.53%) 3	3 / 17 (17.65%) 3
BACK PAIN subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 19 (5.26%) 1	1 / 17 (5.88%) 1
BONE PAIN subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 19 (5.26%) 1	0 / 17 (0.00%) 0
FLANK PAIN subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 19 (0.00%) 0	1 / 17 (5.88%) 1
GROIN PAIN subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 19 (5.26%) 1	1 / 17 (5.88%) 1
JOINT SWELLING			

subjects affected / exposed	2 / 20 (10.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
MUSCLE SPASMS			
subjects affected / exposed	2 / 20 (10.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	2	1	0
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
MYALGIA			
subjects affected / exposed	0 / 20 (0.00%)	2 / 19 (10.53%)	1 / 17 (5.88%)
occurrences (all)	0	2	1
MYOSITIS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
NECK PAIN			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
OSTEONECROSIS OF JAW			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
PAIN IN EXTREMITY			
subjects affected / exposed	3 / 20 (15.00%)	2 / 19 (10.53%)	1 / 17 (5.88%)
occurrences (all)	3	2	1
SYNOVITIS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
TRISMUS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			

BRONCHITIS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
CANDIDA INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
CELLULITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
CONJUNCTIVITIS			
subjects affected / exposed	2 / 20 (10.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
CYSTITIS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
CYSTITIS BACTERIAL			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
DEVICE RELATED INFECTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
DIVERTICULITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
INFLUENZA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	3 / 20 (15.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	4	0	1
NASOPHARYNGITIS			

subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
ORAL CANDIDIASIS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
ORAL HERPES			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
OTITIS EXTERNA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
OTITIS MEDIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
RASH PUSTULAR			
subjects affected / exposed	2 / 20 (10.00%)	2 / 19 (10.53%)	0 / 17 (0.00%)
occurrences (all)	2	2	0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
RHINITIS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
SKIN INFECTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
TONGUE FUNGAL INFECTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
TOOTH INFECTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	4	0	0
UPPER RESPIRATORY TRACT			

INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	1 / 19 (5.26%)	2 / 17 (11.76%)
occurrences (all)	0	1	2
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	4 / 19 (21.05%)	2 / 17 (11.76%)
occurrences (all)	0	5	2
URINARY TRACT INFECTION STAPHYLOCOCCAL			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
VIRAL INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
CACHEXIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
DECREASED APPETITE			
subjects affected / exposed	4 / 20 (20.00%)	7 / 19 (36.84%)	3 / 17 (17.65%)
occurrences (all)	4	8	4
DEHYDRATION			
subjects affected / exposed	2 / 20 (10.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	2
HYPERCALCAEMIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
HYPERGLYCAEMIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
HYPERKALAEMIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
HYPOALBUMINAEMIA			
subjects affected / exposed	0 / 20 (0.00%)	3 / 19 (15.79%)	6 / 17 (35.29%)
occurrences (all)	0	4	7
HYPOCALCAEMIA			

subjects affected / exposed	2 / 20 (10.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
HYPOKALAEMIA			
subjects affected / exposed	2 / 20 (10.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	3	1	0
HYPOMAGNESAEMIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 19 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
HYPONATRAEMIA			
subjects affected / exposed	0 / 20 (0.00%)	3 / 19 (15.79%)	1 / 17 (5.88%)
occurrences (all)	0	3	1
HYPOPHOSPHATAEMIA			
subjects affected / exposed	1 / 20 (5.00%)	2 / 19 (10.53%)	0 / 17 (0.00%)
occurrences (all)	1	2	0
IRON DEFICIENCY			
subjects affected / exposed	1 / 20 (5.00%)	1 / 19 (5.26%)	0 / 17 (0.00%)
occurrences (all)	1	1	0

Non-serious adverse events	Cohort 4 - SCCHN - Previous Treatment Exposure	Cohort 5 - UC - Previous Treatment Exposure	Cohort 6 - RCC - Previous Treatment Exposure
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 20 (95.00%)	7 / 7 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA OF COLON			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CANCER PAIN			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
KERATOACANTHOMA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
TUMOUR HAEMORRHAGE			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			

FLUSHING			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HYPERTENSION			
subjects affected / exposed	3 / 20 (15.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	8	0	0
HYPOTENSION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LYMPHOEDEMA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ORTHOSTATIC HYPOTENSION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CHEST PAIN			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CHILLS			
subjects affected / exposed	1 / 20 (5.00%)	2 / 7 (28.57%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
FACE OEDEMA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
FACIAL PAIN			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
FATIGUE			
subjects affected / exposed	5 / 20 (25.00%)	5 / 7 (71.43%)	0 / 3 (0.00%)
occurrences (all)	5	5	0
GENERALISED OEDEMA			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
LOCALISED OEDEMA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
MALAISE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
MUCOSAL INFLAMMATION			
subjects affected / exposed	1 / 20 (5.00%)	1 / 7 (14.29%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
OEDEMA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	2 / 20 (10.00%)	2 / 7 (28.57%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
PAIN			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
PERIPHERAL SWELLING			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
subjects affected / exposed	1 / 20 (5.00%)	4 / 7 (57.14%)	0 / 3 (0.00%)
occurrences (all)	1	4	0
SWELLING FACE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
HYPERSENSITIVITY			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1

Reproductive system and breast disorders			
SCROTAL OEDEMA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
TESTICULAR SWELLING			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VAGINAL DISCHARGE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VAGINAL HAEMORRHAGE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
COUGH			
subjects affected / exposed	2 / 20 (10.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
DYSPHONIA			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
DYSPNOEA			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
DYSPNOEA EXERTIONAL			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
EPISTAXIS			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
HAEMOPTYSIS			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	1	0

LARYNGEAL OEDEMA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
NASAL CONGESTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
NASAL OBSTRUCTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
PNEUMONITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PRODUCTIVE COUGH			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
RALES			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
WHEEZING			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
ANGER			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ANXIETY			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
CONFUSIONAL STATE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DEPRESSION			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DISORIENTATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
INSOMNIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	2 / 20 (10.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	4	1	0
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	1 / 20 (5.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BLOOD CREATINE PHOSPHOKINASE INCREASED			
subjects affected / exposed	1 / 20 (5.00%)	3 / 7 (42.86%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BLOOD MAGNESIUM DECREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BLOOD POTASSIUM DECREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BLOOD PRESSURE DECREASED			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BLOOD PRESSURE INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BLOOD THYROID STIMULATING HORMONE INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BLOOD URIC ACID INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BRAIN NATRIURETIC PEPTIDE INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
C-REACTIVE PROTEIN INCREASED			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
CYTOMEGALOVIRUS TEST POSITIVE			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
EJECTION FRACTION DECREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
HAEMOGLOBIN DECREASED			
subjects affected / exposed	1 / 20 (5.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
INTERNATIONAL NORMALISED RATIO INCREASED			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
PLATELET COUNT DECREASED			

subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
PLATELET COUNT INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VITAMIN B12 DECREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VITAMIN D DECREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
WEIGHT DECREASED			
subjects affected / exposed	4 / 20 (20.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	5	0	1
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
FACE INJURY			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
FALL			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
INFUSION RELATED REACTION			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
INJURY			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LIMB INJURY			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
POST PROCEDURAL SWELLING			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SKIN LACERATION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
STRESS FRACTURE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
WOUND COMPLICATION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
ATRIOVENTRICULAR BLOCK FIRST DEGREE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CARDIAC FAILURE CONGESTIVE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CORONARY ARTERY DISEASE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PERICARDITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SINUS BRADYCARDIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SINUS TACHYCARDIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
TACHYCARDIA			

subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
VENTRICULAR DYSFUNCTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
APHASIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
CAUDA EQUINA SYNDROME			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CEREBRAL INFARCTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
DIZZINESS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
DIZZINESS POSTURAL			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DYSARTHRIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
DYSGEUSIA			
subjects affected / exposed	1 / 20 (5.00%)	2 / 7 (28.57%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
HEADACHE			
subjects affected / exposed	3 / 20 (15.00%)	2 / 7 (28.57%)	1 / 3 (33.33%)
occurrences (all)	3	2	1
LETHARGY			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LUMBAR RADICULOPATHY			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PARAESTHESIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PRESYNCOPE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
RESTLESS LEGS SYNDROME			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SCIATICA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
STATUS EPILEPTICUS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SYNCOPE			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
TASTE DISORDER			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	2 / 20 (10.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	4	1	0
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
LEUKOCYTOSIS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
LEUKOPENIA			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LYMPH NODE PAIN			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LYMPHADENITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LYMPHOPENIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
NEUTROPENIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
THROMBOCYTOPENIA			
subjects affected / exposed	1 / 20 (5.00%)	2 / 7 (28.57%)	1 / 3 (33.33%)
occurrences (all)	1	2	1
Ear and labyrinth disorders			
HYPOACUSIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
INNER EAR DISORDER			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VERTIGO			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CHORIORETINOPATHY			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
ENTROPION			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
EYELID OEDEMA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
EYELID PTOSIS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
GLAUCOMA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LACRIMATION INCREASED			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
MACULAR OEDEMA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
OPTIC NERVE DISORDER			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PERIORBITAL OEDEMA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
RETINAL OEDEMA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
RETINOPATHY			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SUBRETINAL FLUID			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SWELLING OF EYELID			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
TRICHIASIS			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VISION BLURRED			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
VISUAL IMPAIRMENT			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VITREOUS FLOATERS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
ABDOMINAL DISCOMFORT			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ABDOMINAL PAIN			
subjects affected / exposed	1 / 20 (5.00%)	2 / 7 (28.57%)	0 / 3 (0.00%)
occurrences (all)	3	3	0
ANAL HAEMORRHAGE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ANGULAR CHEILITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ASCITES			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CHEILITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
CONSTIPATION			
subjects affected / exposed	4 / 20 (20.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	4	2	0

DIAPHRAGMATIC HERNIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DIARRHOEA			
subjects affected / exposed	13 / 20 (65.00%)	5 / 7 (71.43%)	2 / 3 (66.67%)
occurrences (all)	16	6	2
DRY MOUTH			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DYSPEPSIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DYSPHAGIA			
subjects affected / exposed	3 / 20 (15.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
FLATULENCE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
GASTRIC ULCER			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
GASTRITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
GASTROESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
GINGIVAL BLEEDING			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
GLOSSITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
GLOSSODYNIA			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HAEMATEMESIS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
HAEMATOCHEZIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
HAEMORRHOIDS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LIP OEDEMA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
LIP PAIN			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
LIP SWELLING			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
MOUTH ULCERATION			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
MUCOUS STOOLS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	6 / 20 (30.00%)	4 / 7 (57.14%)	0 / 3 (0.00%)
occurrences (all)	8	5	0
OESOPHAGITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ORAL DISCHARGE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ORAL PAIN			

subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
STOMATITIS			
subjects affected / exposed	4 / 20 (20.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	4	0	1
TOOTHACHE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
VOMITING			
subjects affected / exposed	4 / 20 (20.00%)	1 / 7 (14.29%)	1 / 3 (33.33%)
occurrences (all)	4	2	1
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
BLISTER			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
DERMATITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DERMATITIS ACNEIFORM			
subjects affected / exposed	5 / 20 (25.00%)	2 / 7 (28.57%)	0 / 3 (0.00%)
occurrences (all)	5	3	0
DERMATITIS PSORIASIFORM			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DRY SKIN			
subjects affected / exposed	4 / 20 (20.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	5	2	0
ECZEMA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

ERYTHEMA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
INTERTRIGO			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
NIGHT SWEATS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ONYCHOCLASIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PALMAR-PLANTAR ERYTHRODYSAESTHESIA SYNDROME			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	4 / 20 (20.00%)	3 / 7 (42.86%)	0 / 3 (0.00%)
occurrences (all)	4	6	0
RASH			
subjects affected / exposed	5 / 20 (25.00%)	5 / 7 (71.43%)	1 / 3 (33.33%)
occurrences (all)	6	7	1
RASH ERYTHEMATOUS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
RASH MACULO-PAPULAR			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
RASH PAPULAR			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
RASH PRURITIC			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
SKIN FISSURES			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
STASIS DERMATITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
URTICARIA			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
DYSURIA			
subjects affected / exposed	0 / 20 (0.00%)	3 / 7 (42.86%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
HAEMATURIA			
subjects affected / exposed	0 / 20 (0.00%)	2 / 7 (28.57%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
NOCTURIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
POLLAKIURIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
PROTEINURIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
RENAL FAILURE			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
RENAL IMPAIRMENT			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
URINARY RETENTION			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	3	0

URINARY TRACT OBSTRUCTION subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
URINARY TRACT PAIN subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Endocrine disorders HYPERTHYROIDISM subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
HYPOTHYROIDISM subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
THYROIDITIS subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
Musculoskeletal and connective tissue disorders ARTHRALGIA subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
BACK PAIN subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
BONE PAIN subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
FLANK PAIN subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
GROIN PAIN subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
JOINT SWELLING subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
MUSCLE SPASMS			

subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
MUSCULAR WEAKNESS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
MYALGIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
MYOSITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
NECK PAIN			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
OSTEONECROSIS OF JAW			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 20 (5.00%)	2 / 7 (28.57%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
SYNOVITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
TRISMUS			
subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

CANDIDA INFECTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
CELLULITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CONJUNCTIVITIS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
CYSTITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
CYSTITIS BACTERIAL			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DEVICE RELATED INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
DIVERTICULITIS			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
NASOPHARYNGITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ORAL CANDIDIASIS			

subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
ORAL HERPES			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
OTITIS EXTERNA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
OTITIS MEDIA			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
RASH PUSTULAR			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
RHINITIS			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
SKIN INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
STAPHYLOCOCCAL INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
TONGUE FUNGAL INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
TOOTH INFECTION			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

URINARY TRACT INFECTION subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	4 / 7 (57.14%) 4	0 / 3 (0.00%) 0
URINARY TRACT INFECTION STAPHYLOCOCCAL subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
VIRAL INFECTION subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 7 (0.00%) 0	1 / 3 (33.33%) 1
Metabolism and nutrition disorders			
CACHEXIA subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
DECREASED APPETITE subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
DEHYDRATION subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
HYPERCALCAEMIA subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
HYPERGLYCAEMIA subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0
HYPERKALAEMIA subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
HYPOALBUMINAEMIA subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
HYPOCALCAEMIA subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0
HYPOKALAEMIA			

subjects affected / exposed	2 / 20 (10.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
HYPOMAGNESAEMIA			
subjects affected / exposed	2 / 20 (10.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
HYPONATRAEMIA			
subjects affected / exposed	1 / 20 (5.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
HYPOPHOSPHATAEMIA			
subjects affected / exposed	0 / 20 (0.00%)	1 / 7 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
IRON DEFICIENCY			
subjects affected / exposed	0 / 20 (0.00%)	0 / 7 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 October 2017	Guidelines for managing subjects who experienced atezolizumab-associated adverse events were revised to include guidelines for hypophysitis and myocarditis. Adverse events of special interest (AESIs) were updated to include suspected transmission of an infectious agent by the study drug.
29 March 2018	Additional Cohorts 4-7 (post-CPI progressors and biopsy cohort) were added to the protocol with rationale for the additional cohorts. Tumor specimen biopsies in the cancer-related inclusion criteria were revised to allow more flexibility. Primary analysis was changed from 24 weeks to 16 weeks and sample size adjusted.
18 September 2018	Updated the lists of risks for atezolizumab and guidelines for managing subjects who experience atezolizumab-associated adverse events to include nephritis. Cobimetinib dose modification was amended to allow for dose re-escalations on a case-by-case basis after discussion with the Medical Monitor or his designee.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported