Clinical trial results:
PHASE 1/2 STUDY TO DETERMINE THE SAFETY, PHARMACOKINETICS, AND EFFICACY OF SINGLE AGENT CC-122 AND THE COMBINATIONS OF CC-122 AND IBRUTINIB AND CC-122 AND OBINUTUZUMAB IN SUBJECTS WITH CHRONIC LYMPHOCYTIC LEUKEMIA/SMALL LYMPHOCYTIC LYMPHOMA

Summary

EudraCT number	2014-003056-31
Trial protocol	DE ES
Global end of trial date	07 July 2020

Results information

Result version number	v1 (current)
This version publication date	23 July 2021
First version publication date	23 July 2021

Trial information

Trial identification

Sponsor protocol code	CC-122-CLL-001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 August 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 July 2020
Global end of trial reached?	Yes
Global end of trial date	07 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the study are: Determine the safety of single agent CC-122 in subjects with R/R CLL/SLL Determine the safety and tolerability of the combination of CC-122 and ibrutinib and determine the RP2D of the combination in ibrutinib-naive CLL/SLL subjects Determine the safety and tolerability of the combination of CC-122 and obinutuzumab and determine the RP2D of the combination in subjects with R/R CLL/SLL

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 May 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 29
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Austria: 7
Worldwide total number of subjects	46
EEA total number of subjects	17

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	23
From 65 to 84 years	23
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

46 participants treated

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

CC-122 single agent Dose Escalation starting at the 1.0 mg dose level up to a maximum of 4.0 mg

Arm type	Experimental
Investigational medicinal product name	CC-122
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 mg escalating up to 4mg

Arm title	Arm B

Arm description:

CC-122 in combination with ibrutinib Ascending fixed-dose cohorts of CC-122 starting at 0.5 mg up to a maximum of 4.0 mg or NTD, whichever occurs first, in combination with ibrutinib

Arm type	Experimental
Investigational medicinal product name	CC-122
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0.5 mg escalating up to 4mg

Investigational medicinal product name	Ibrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

420mg (140mg x 3)

Arm title	Arm C

Arm description:

CC-122 in combination with obinutuzumab

Ascending fixed-dose cohorts of CC-122 starting at 0.5 mg up to a maximum of 4.0 mg or NTD,

whichever occurs first, in combination with obinutuzumab.

Arm type	Experimental
Investigational medicinal product name	CC-122
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:
1 mg escalating up to 4mg

Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravascular use

Dosage and administration details:
6 cycles

Number of subjects in period 1	Arm A	Arm B	Arm C
Started	14	16	16
Completed	0	0	0
Not completed	14	16	16
Adverse event, serious fatal	1	-	-
Physician decision	1	2	1
Progression of Disease	5	1	6
Withdrawal by Participant	1	2	-
Adverse event, non-fatal	3	-	2
Other Reasons	1	11	5
Transition to other treatment	2	-	1
Lack of efficacy	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
CC-122 single agent Dose Escalation starting at the 1.0 mg dose level up to a maximum of 4.0 mg	
Reporting group title	Arm B
Reporting group description:	
CC-122 in combination with ibrutinib Ascending fixed-dose cohorts of CC-122 starting at 0.5 mg up to a maximum of 4.0 mg or NTD, whichever occurs first, in combination with ibrutinib	
Reporting group title	Arm C
Reporting group description:	
CC-122 in combination with obinutuzumab Ascending fixed-dose cohorts of CC-122 starting at 0.5 mg up to a maximum of 4.0 mg or NTD, whichever occurs first, in combination with obinutuzumab.	

Reporting group values	Arm A	Arm B	Arm C
Number of subjects	14	16	16
Age categorical Units: Subjects			
Adults (18-64 years)	5	8	10
From 65-84 years	9	8	6
Age Continuous Units: Years			
arithmetic mean	67.4	63.4	61.5
standard deviation	± 9.41	± 9.98	± 6.11
Sex: Female, Male Units: Participants			
Female	4	8	2
Male	10	8	14
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	1
White	12	16	14
More than one race	0	0	0
Unknown or Not Reported	0	0	1
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	0
Not Hispanic or Latino	14	15	16
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	46		

Age categorical Units: Subjects			
Adults (18-64 years)	23		
From 65-84 years	23		
Age Continuous Units: Years arithmetic mean standard deviation	 -		
Sex: Female, Male Units: Participants			
Female	14		
Male	32		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	1		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	2		
White	42		
More than one race	0		
Unknown or Not Reported	1		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1		
Not Hispanic or Latino	45		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
CC-122 single agent Dose Escalation starting at the 1.0 mg dose level up to a maximum of 4.0 mg	
Reporting group title	Arm B
Reporting group description:	
CC-122 in combination with ibrutinib Ascending fixed-dose cohorts of CC-122 starting at 0.5 mg up to a maximum of 4.0 mg or NTD, whichever occurs first, in combination with ibrutinib	
Reporting group title	Arm C
Reporting group description:	
CC-122 in combination with obinutuzumab Ascending fixed-dose cohorts of CC-122 starting at 0.5 mg up to a maximum of 4.0 mg or NTD, whichever occurs first, in combination with obinutuzumab.	

Primary: Number of participants and severity of AEs

End point title	Number of participants and severity of AEs[1]
End point description:	
Number and severity of adverse events using the NCI CTCAE criteria (version 4.03), including DLTs	
End point type	Primary
End point timeframe:	
Approximately 60 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: No Statistical Analysis done for this endpoint

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	16	16	
Units: Number				
Grade 3 AE	8	8	9	
Grade 4 AE	3	5	7	
DLTs	0	0	0	

Statistical analyses

No statistical analyses for this end point

Primary: Determination of Non tolerated dose (NTD) and Maximum tolerated dose (MTD)

End point title	Determination of Non tolerated dose (NTD) and Maximum tolerated dose (MTD)[2]
End point description:	
Determination of the NTD and MTD in CC-122 in combination with ibrutinib and CC-122 in combination with obinutuzumab	

9999 here represents the values as Not available (NA)

End point type	Primary

End point timeframe:

Approximately 60 Months

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No Statistical Analysis done for this endpoint

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[3]	16	16	
Units: mg				
arithmetic mean (full range (min-max))				
NTD	(to)	9999 (-9999 to 9999)	9999 (-9999 to 9999)	
MTD	(to)	9999 (-9999 to 9999)	9999 (-9999 to 9999)	

Notes:

[3] - This arm was not analyzed in this endpoint

Statistical analyses

No statistical analyses for this end point

Secondary: CC-122 plasma concentrations when administered alone or in combination with ibrutinib or obinutuzumab

End point title	CC-122 plasma concentrations when administered alone or in combination with ibrutinib or obinutuzumab

End point description:

CC-122 plasma concentrations when administered alone or in combination with ibrutinib or obinutuzumab

9999 here represents the values as Not available (NA)

End point type	Secondary

End point timeframe:

Approximately 60 Months

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	7	5	
Units: Percentage				
geometric mean (geometric coefficient of variation)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: CC-122 pharmacokinetic parameters when administered in combination with ibrutinib

End point title	CC-122 pharmacokinetic parameters when administered in combination with ibrutinib

End point description:

CC-122 pharmacokinetic parameters when administered in combination with ibrutinib

9999 here represents the values as Not available (NA)

End point type	Secondary

End point timeframe:

Approximately 60 Months

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	0[4]	0[5]	
Units: Percentage				
arithmetic mean (confidence interval 95%)	9999 (-9999 to 9999)	(to)	(to)	

Notes:

[4] - No subjects analyzed

[5] - No subjects analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Ibrutinib plasma concentrations and/or pharmacokinetic parameters when administered in combination with CC-122

End point title	Ibrutinib plasma concentrations and/or pharmacokinetic parameters when administered in combination with CC-122

End point description:

Ibrutinib plasma concentrations and /or pharmacokinetic parameters when administered in combination with CC-122

9999 here represents the values as Not available (NA)

End point type	Secondary

End point timeframe:

Approximately 60 Months

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	7	5	
Units: Percentage				
geometric mean (geometric coefficient of variation)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall Response (BOR)

End point title	Best overall Response (BOR)

End point description:

Best overall response [CR, CRi, nPR, PR, PRL (applicable to Arm B only)] CR = Complete Response CRi = Complete response with incomplete marrow recovery nPR = nodular Partial Response PR = Partial response PRL= Partial response with lymphocytosis

End point type	Secondary

End point timeframe:

Approximately 60 Months

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	16	16	
Units: Percentage				
number (confidence interval 95%)	7.1 (0.2 to 33.9)	87.5 (61.7 to 98.4)	62.5 (35.4 to 84.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Minimal Residual Disease Response Rate

End point title	Minimal Residual Disease Response Rate

End point description:

Minimal Residual Disease Response Rate in bone marrow and peripheral blood

End point type	Secondary

End point timeframe:

Approximately 60 Months

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	16	16	
Units: Percentage				
number (confidence interval 95%)				
Bone Marrow	0 (0.0 to 23.2)	0 (0.0 to 20.6)	0 (0.0 to 20.6)	
Peripheral Blood	0 (0.0 to 23.2)	0 (0.0 to 20.6)	18.8 (4.0 to 45.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response

End point description:

measured from the time the response is first met until the first date that progressive disease or death is documented. Participants who neither progress nor die or who withdrew consent or are lost to follow-up prior to documentation of progression will be censored at the date of their last adequate response assessment.

9999 here represents the values as Not available (NA)

End point type	Secondary

End point timeframe:

Approximately 60 Months

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1	14	10	
Units: Days				
median (confidence interval 95%)	113 (-9999 to 9999)	9999 (-9999 to 9999)	602.0 (-9999 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

will be calculated as the time from irst IP (i.e. any study drug) dose date to the first documented progression or death due to any cause during or after the treatment period, whichever occurs first.

9999 here represents the values as Not available (NA)

End point type	Secondary

End point timeframe:
Approximately 60 Months

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	16	16	
Units: Months				
median (confidence interval 95%)	6.47 (0.43 to 12.29)	9999 (-9999 to 9999)	22.57 (5.55 to 9999)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Approximately 60 Months	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.0
Reporting groups	
Reporting group title	A (CC-122)
Reporting group description: -	
Reporting group title	B (CC-122+Ibrutinib)
Reporting group description: -	
Reporting group title	C (CC-122+Obinutuzumab)
Reporting group description: -	

Serious adverse events	A (CC-122)	B (CC-122+Ibrutinib)	C (CC-122+Obinutuzumab)
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 14 (50.00%)	7 / 16 (43.75%)	4 / 16 (25.00%)
number of deaths (all causes)	2	0	1
number of deaths resulting from adverse events	0	0	0
Investigations			
Troponin increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (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
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung adenocarcinoma			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (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
Injury, poisoning and procedural complications			
Comminuted fracture			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Nervous system disorders			

Cerebral artery occlusion			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Ischaemic stroke			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Syncope			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolytic anaemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Stomatitis			

subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Vomiting			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (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
Candida sepsis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (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
Enterococcal sepsis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (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
Influenza			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumonia			
subjects affected / exposed	3 / 14 (21.43%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	1 / 4	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Tumour lysis syndrome			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	A (CC-122)	B (CC-122+Ibrutinib)	C (CC-122+Obinutuzumab)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)	16 / 16 (100.00%)	16 / 16 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	0	3	1
Benign neoplasm of skin			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Lipoma			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Lung adenocarcinoma			

subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tumour flare			
subjects affected / exposed	2 / 14 (14.29%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	3	3	1
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Flushing			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Haematoma			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Hot flush			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Hypertension			
subjects affected / exposed	2 / 14 (14.29%)	6 / 16 (37.50%)	3 / 16 (18.75%)
occurrences (all)	3	30	9
Systolic hypertension			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Thrombophlebitis superficial			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 14 (21.43%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	12	3	0
Catheter site bruise			

subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Fatigue			
subjects affected / exposed	3 / 14 (21.43%)	1 / 16 (6.25%)	5 / 16 (31.25%)
occurrences (all)	3	1	9
Feeling hot			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Injection site pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Non-cardiac chest pain			
subjects affected / exposed	1 / 14 (7.14%)	3 / 16 (18.75%)	1 / 16 (6.25%)
occurrences (all)	1	3	1
Oedema peripheral			
subjects affected / exposed	3 / 14 (21.43%)	7 / 16 (43.75%)	3 / 16 (18.75%)
occurrences (all)	3	11	4
Pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Peripheral swelling			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pyrexia			

subjects affected / exposed	5 / 14 (35.71%)	4 / 16 (25.00%)	3 / 16 (18.75%)
occurrences (all)	14	6	3
Immune system disorders			
Cytokine release syndrome			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Seasonal allergy			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Erectile dysfunction			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gynaecomastia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nipple pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Vaginal haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 14 (21.43%)	5 / 16 (31.25%)	3 / 16 (18.75%)
occurrences (all)	3	6	4
Dyspnoea			
subjects affected / exposed	1 / 14 (7.14%)	1 / 16 (6.25%)	3 / 16 (18.75%)
occurrences (all)	1	1	5
Dyspnoea exertional			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Epistaxis			

subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Haemoptysis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Oropharyngeal pain			
subjects affected / exposed	0 / 14 (0.00%)	8 / 16 (50.00%)	4 / 16 (25.00%)
occurrences (all)	0	9	4
Pleural effusion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Productive cough			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	2 / 16 (12.50%)
occurrences (all)	0	1	2
Pulmonary hypertension			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Pulmonary mass			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pulmonary oedema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Respiratory tract congestion			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Rhinalgia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Sinus congestion			

subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 14 (7.14%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Confusional state			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Insomnia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Irritability			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Libido decreased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Mood altered			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Product issues			
Device occlusion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 14 (7.14%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	1	3	0
Amylase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	2	0	0
Aspartate aminotransferase increased			

subjects affected / exposed	1 / 14 (7.14%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Blood bilirubin increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 14 (14.29%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	3	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Brain natriuretic peptide increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hepatic enzyme increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Lipase increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Occult blood positive			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	4 / 16 (25.00%)
occurrences (all)	0	4	4
Weight increased			
subjects affected / exposed	0 / 14 (0.00%)	6 / 16 (37.50%)	1 / 16 (6.25%)
occurrences (all)	0	12	1
Injury, poisoning and procedural complications			

Arthropod bite			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Arthropod sting			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Buttock injury			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Comminuted fracture			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 14 (0.00%)	4 / 16 (25.00%)	0 / 16 (0.00%)
occurrences (all)	0	7	0
Dental restoration failure			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Fall			
subjects affected / exposed	0 / 14 (0.00%)	6 / 16 (37.50%)	2 / 16 (12.50%)
occurrences (all)	0	14	6
Infusion related reaction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	7 / 16 (43.75%)
occurrences (all)	0	0	7
Ligament sprain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Limb injury			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Meniscus injury			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Muscle strain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0

Post-traumatic neck syndrome			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Procedural nausea			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Rib fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Skin laceration			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Spinal fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Subcutaneous haematoma			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Thermal burn			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Tooth fracture			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Urinary retention postoperative			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Atrial fibrillation			

subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Bradycardia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Bundle branch block right			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Cardiac valve disease			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Sinus bradycardia			
subjects affected / exposed	1 / 14 (7.14%)	4 / 16 (25.00%)	1 / 16 (6.25%)
occurrences (all)	1	8	1
Sinus tachycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Tricuspid valve incompetence			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Ventricular hypertrophy			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Carotid arteriosclerosis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0

Cerebral artery occlusion			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	1 / 14 (7.14%)	5 / 16 (31.25%)	1 / 16 (6.25%)
occurrences (all)	1	7	1
Dizziness postural			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	3 / 14 (21.43%)	2 / 16 (12.50%)	2 / 16 (12.50%)
occurrences (all)	3	3	2
Memory impairment			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Paraesthesia			
subjects affected / exposed	0 / 14 (0.00%)	4 / 16 (25.00%)	2 / 16 (12.50%)
occurrences (all)	0	4	2
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Presyncope			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Speech disorder			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	1 / 14 (7.14%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	8 / 14 (57.14%)	0 / 16 (0.00%)	4 / 16 (25.00%)
occurrences (all)	11	0	6
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Haemorrhagic disorder			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Leukocytosis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Leukopenia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	5 / 16 (31.25%)
occurrences (all)	0	0	18
Lymph node pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Lymphocytosis			
subjects affected / exposed	0 / 14 (0.00%)	3 / 16 (18.75%)	4 / 16 (25.00%)
occurrences (all)	0	3	7
Lymphopenia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	7 / 16 (43.75%)
occurrences (all)	0	1	18
Neutropenia			
subjects affected / exposed	5 / 14 (35.71%)	6 / 16 (37.50%)	13 / 16 (81.25%)
occurrences (all)	16	27	66
Splenomegaly			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Thrombocytopenia			
subjects affected / exposed	2 / 14 (14.29%)	2 / 16 (12.50%)	6 / 16 (37.50%)
occurrences (all)	2	8	12
Ear and labyrinth disorders			

Autophony			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Ear discomfort			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Ear disorder			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Ear pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypoacusis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Tinnitus			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Vertigo			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 14 (7.14%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	1	3	0
Chalazion			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Conjunctival haemorrhage			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis allergic			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Diplopia			

subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Dyschromatopsia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Eye haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Eye irritation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Eye pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Foreign body sensation in eyes			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Macular degeneration			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Maculopathy			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Meibomian gland dysfunction			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Photophobia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Photopsia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Vision blurred			

subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Visual impairment			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 14 (7.14%)	4 / 16 (25.00%)	1 / 16 (6.25%)
occurrences (all)	1	4	1
Abdominal pain lower			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Angular cheilitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Constipation			
subjects affected / exposed	2 / 14 (14.29%)	4 / 16 (25.00%)	2 / 16 (12.50%)
occurrences (all)	2	5	2
Dental caries			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	3 / 14 (21.43%)	7 / 16 (43.75%)	4 / 16 (25.00%)
occurrences (all)	4	9	7
Dry mouth			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Dyspepsia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Dysphagia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	0	2	1

Flatulence			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	2
Gastritis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal polyp			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Gingival bleeding			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Inguinal hernia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Large intestine polyp			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	1 / 14 (7.14%)	7 / 16 (43.75%)	5 / 16 (31.25%)
occurrences (all)	1	11	5
Noninfective gingivitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Oral mucosal erythema			
subjects affected / exposed	1 / 14 (7.14%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Oral pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Paraesthesia oral			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0

Stomatitis			
subjects affected / exposed	0 / 14 (0.00%)	7 / 16 (43.75%)	1 / 16 (6.25%)
occurrences (all)	0	15	1
Toothache			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Umbilical hernia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	1 / 14 (7.14%)	3 / 16 (18.75%)	2 / 16 (12.50%)
occurrences (all)	1	5	2
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Actinic keratosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Alopecia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Dermatitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Dermatitis contact			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Dry skin			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Ecchymosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Erythema			

subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Hair texture abnormal			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Hyperhidrosis			
subjects affected / exposed	1 / 14 (7.14%)	2 / 16 (12.50%)	2 / 16 (12.50%)
occurrences (all)	1	2	2
Hyperkeratosis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Nail discolouration			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Nail disorder			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Night sweats			
subjects affected / exposed	4 / 14 (28.57%)	3 / 16 (18.75%)	2 / 16 (12.50%)
occurrences (all)	4	3	2
Onychoclasis			
subjects affected / exposed	0 / 14 (0.00%)	3 / 16 (18.75%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Onychomadesis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Petechiae			
subjects affected / exposed	0 / 14 (0.00%)	3 / 16 (18.75%)	1 / 16 (6.25%)
occurrences (all)	0	3	1
Precancerous skin lesion			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	1 / 14 (7.14%)	1 / 16 (6.25%)	3 / 16 (18.75%)
occurrences (all)	1	1	4
Rash			

subjects affected / exposed	1 / 14 (7.14%)	3 / 16 (18.75%)	2 / 16 (12.50%)
occurrences (all)	2	3	2
Rash erythematous			
subjects affected / exposed	1 / 14 (7.14%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Rash macular			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Rash maculo-papular			
subjects affected / exposed	0 / 14 (0.00%)	3 / 16 (18.75%)	2 / 16 (12.50%)
occurrences (all)	0	4	2
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Skin haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Skin lesion			
subjects affected / exposed	0 / 14 (0.00%)	3 / 16 (18.75%)	2 / 16 (12.50%)
occurrences (all)	0	3	5
Skin mass			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Solar lentigo			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0

Nephrolithiasis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	2
Pollakiuria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Strangury			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Urethral haemorrhage			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Urinary retention			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Urinary tract obstruction			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 14 (14.29%)	5 / 16 (31.25%)	2 / 16 (12.50%)
occurrences (all)	3	12	2
Back pain			
subjects affected / exposed	1 / 14 (7.14%)	4 / 16 (25.00%)	4 / 16 (25.00%)
occurrences (all)	1	9	4
Flank pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Muscle contracture			

subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	1 / 14 (7.14%)	5 / 16 (31.25%)	4 / 16 (25.00%)
occurrences (all)	1	6	4
Muscular weakness			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Musculoskeletal chest pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	2 / 14 (14.29%)	5 / 16 (31.25%)	2 / 16 (12.50%)
occurrences (all)	2	6	3
Neck pain			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	0	5	1
Osteoporosis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	1 / 14 (7.14%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	1	2	2
Synovial cyst			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Arthritis infective			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Bacteraemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Balanitis candida			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Body tinea			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Cellulitis			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	0	3	1
Conjunctivitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Diverticulitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Fungal balanitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gingivitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Haematoma infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 14 (0.00%)	3 / 16 (18.75%)	0 / 16 (0.00%)
occurrences (all)	0	4	0

Nasal herpes			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 14 (7.14%)	4 / 16 (25.00%)	5 / 16 (31.25%)
occurrences (all)	1	4	8
Oral candidiasis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Oral herpes			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	4
Pharyngitis			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Pneumonia			
subjects affected / exposed	1 / 14 (7.14%)	2 / 16 (12.50%)	1 / 16 (6.25%)
occurrences (all)	1	3	1
Pseudomonal sepsis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Sinusitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	3 / 16 (18.75%)
occurrences (all)	0	1	6
Skin infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tinea cruris			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

Tinea infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	1 / 14 (7.14%)	6 / 16 (37.50%)	5 / 16 (31.25%)
occurrences (all)	2	10	7
Urinary tract infection			
subjects affected / exposed	0 / 14 (0.00%)	3 / 16 (18.75%)	4 / 16 (25.00%)
occurrences (all)	0	5	8
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Wound infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Dehydration			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Diabetes mellitus			

subjects affected / exposed	0 / 14 (0.00%)	3 / 16 (18.75%)	1 / 16 (6.25%)
occurrences (all)	0	4	2
Folate deficiency			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Gout			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hypercalcaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Hyperglycaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 16 (6.25%)	1 / 16 (6.25%)
occurrences (all)	0	2	2
Hyperkalaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hyperphosphataemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 16 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hyperuricaemia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 16 (6.25%)	2 / 16 (12.50%)
occurrences (all)	1	1	2
Hypocalcaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Hypokalaemia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 16 (12.50%)	2 / 16 (12.50%)
occurrences (all)	0	2	2
Hypomagnesaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Hypophosphataemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Iron deficiency			

subjects affected / exposed	1 / 14 (7.14%)	2 / 16 (12.50%)	3 / 16 (18.75%)
occurrences (all)	1	3	3
Polydipsia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 16 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported