



Clinical trial results:

A Phase 1/2, Open-Label, Dose-Escalation, Safety and Tolerability Study of INCAGN01949 in Subjects With Advanced or Metastatic Solid Tumors Summary

EudraCT number	2016-002079-93
Trial protocol	GB
Global end of trial date	26 March 2019

Results information

Result version number	v1 (current)
This version publication date	10 April 2020
First version publication date	10 April 2020

Trial information

Trial identification

Sponsor protocol code	INCAGN 1949-101
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02923349
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Incyte Biosciences International Sàrl
Sponsor organisation address	1110 Morges, , Rue Docteur-Yersin , Switzerland, 10
Public contact	call centre, Incyte Corporation, 1 8554633463, RA@INCYTE.COM
Scientific contact	call centre, Incyte Corporation, 1 8554633463, RA@INCYTE.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	26 March 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 March 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety, tolerability, and DLTs of INCAGN01949 and to define a MTD or PAD of INCAGN01949 in subjects with metastatic or advanced solid tumors.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles of Good Clinical Practice, according to the International Conference on Harmonisation Guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 October 2016
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	Spain: 10
Country: Number of subjects enrolled	United Kingdom: 17
Country: Number of subjects enrolled	United States: 55
Country: Number of subjects enrolled	Switzerland: 5
Worldwide total number of subjects	87
EEA total number of subjects	27

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)	59
From 65 to 84 years	28

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

The study was conducted at 4 different sites in US, 1 site in Switzerland, Spain and 2 sites in the United Kingdom

Pre-assignment

Screening details:

A total of 129 participants were screened for this study, of which 42 participants were screen failures and 87 participants were randomized to treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort1 - INCAGN1949 7mg

Arm description: -

Arm type	Experimental
Investigational medicinal product name	INCAGN01949
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

7mg of ICAGN 1949 is dosed as an IV infusion over 30minutes on Day 1 of each cycle

Arm title	Cohort2 - INCAGN1949 20mg
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	INCAGN01949
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

20mg of ICAGN 1949 is dosed as an IV infusion over 30minutes on Day 1 of each cycle

Arm title	Cohort3 - INCAGN1949 70mg
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	INCAGN01949
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

70mg of ICAGN 1949 is dosed as an IV infusion over 30minutes on Day 1 of each cycle

Arm title	Cohort4 - INCAGN1949 200 mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	INCAGN01949
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

200mg of ICAGN 1949 is dosed as an IV infusion over 30minutes on Day 1 of each cycle

Arm title	Cohort5 - INCAGN1949 350mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	INCAGN01949
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

350mg of ICAGN 1949 is dosed as an IV infusion over 30minutes on Day 1 of each cycle

Arm title	Cohort6 - INCAGN1949 700mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	INCAGN01949
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

700mg of ICAGN 1949 is dosed as an IV infusion over 30minutes on Day 1 of each cycle

Arm title	Cohort7 - INCAGN1949 1400mg
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	INCAGN01949
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

1400mg of ICAGN 1949 is dosed as an IV infusion over 30minutes on Day 1 of each cycle

Number of subjects in period 1	Cohort1 - INCAGN1949 7mg	Cohort2 - INCAGN1949 20mg	Cohort3 - INCAGN1949 70mg
Started	4	4	22
Completed	0	0	5
Not completed	4	4	17
Physician decision	-	-	-
Death	1	-	2
Unknown	1	2	4
Lost to follow-up	-	-	3
Withdrawal by subject	2	2	8

Number of subjects in period 1	Cohort4 - INCAGN1949 200 mg	Cohort5 - INCAGN1949 350mg	Cohort6 - INCAGN1949 700mg
Started	18	23	12
Completed	2	4	5
Not completed	16	19	7
Physician decision	1	1	-
Death	4	2	3
Unknown	1	3	-
Lost to follow-up	-	1	1
Withdrawal by subject	10	12	3

Number of subjects in period 1	Cohort7 - INCAGN1949 1400mg
Started	4
Completed	1
Not completed	3
Physician decision	2
Death	-
Unknown	1
Lost to follow-up	-
Withdrawal by subject	-

Baseline characteristics

Reporting groups

Reporting group title	Cohort1 - INCAGN1949 7mg
Reporting group description: -	
Reporting group title	Cohort2 - INCAGN1949 20mg
Reporting group description: -	
Reporting group title	Cohort3 - INCAGN1949 70mg
Reporting group description: -	
Reporting group title	Cohort4 - INCAGN1949 200 mg
Reporting group description: -	
Reporting group title	Cohort5 - INCAGN1949 350mg
Reporting group description: -	
Reporting group title	Cohort6 - INCAGN1949 700mg
Reporting group description: -	
Reporting group title	Cohort7 - INCAGN1949 1400mg
Reporting group description: -	

Reporting group values	Cohort1 - INCAGN1949 7mg	Cohort2 - INCAGN1949 20mg	Cohort3 - INCAGN1949 70mg
Number of subjects	4	4	22
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	2	14
From 65-84 years	1	2	8
85 years and over	0	0	0
Age continuous Units: years			
geometric mean	54.3	63.8	56.8
standard deviation	± 16.24	± 12.63	± 14.27
Gender categorical Units: Subjects			
Female	2	3	14
Male	2	1	8
Race Units: Subjects			
White/Caucasian	4	3	19
Asian	0	1	2
Other	0	0	1
Black/African American	0	0	0
Ethnicity Units: Subjects			

Hispanic or Latino	0	0	1
Not Hispanic or Latino	4	4	19
Not Reported	0	0	1
Other	0	0	1

Reporting group values	Cohort4 - INCAGN1949 200 mg	Cohort5 - INCAGN1949 350mg	Cohort6 - INCAGN1949 700mg
Number of subjects	18	23	12
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	12	17	8
From 65-84 years	6	6	4
85 years and over	0	0	0
Age continuous Units: years			
geometric mean	58.9	58.1	61.3
standard deviation	± 12.78	± 12.44	± 9.93
Gender categorical Units: Subjects			
Female	12	17	3
Male	6	6	9
Race Units: Subjects			
White/Caucasian	17	23	9
Asian	0	0	1
Other	1	0	0
Black/African American	0	0	2
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	16	22	11
Not Reported	1	1	0
Other	0	0	0

Reporting group values	Cohort7 - INCAGN1949 1400mg	Total	
Number of subjects	4	87	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	

Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	3	59	
From 65-84 years	1	28	
85 years and over	0	0	
Age continuous Units: years geometric mean standard deviation	52.8 ± 24.50	-	
Gender categorical Units: Subjects			
Female	2	53	
Male	2	34	
Race Units: Subjects			
White/Caucasian	4	79	
Asian	0	4	
Other	0	2	
Black/African American	0	2	
Ethnicity Units: Subjects			
Hispanic or Latino	1	4	
Not Hispanic or Latino	2	78	
Not Reported	1	4	
Other	0	1	

End points

End points reporting groups

Reporting group title	Cohort1 - INCAGN1949 7mg
Reporting group description: -	
Reporting group title	Cohort2 - INCAGN1949 20mg
Reporting group description: -	
Reporting group title	Cohort3 - INCAGN1949 70mg
Reporting group description: -	
Reporting group title	Cohort4 - INCAGN1949 200 mg
Reporting group description: -	
Reporting group title	Cohort5 - INCAGN1949 350mg
Reporting group description: -	
Reporting group title	Cohort6 - INCAGN1949 700mg
Reporting group description: -	
Reporting group title	Cohort7 - INCAGN1949 1400mg
Reporting group description: -	

Primary: To evaluate the safety, tolerability, and DLTs of INCAGN01949 and to define a MTD or PAD of INCAGN01949 in subjects with metastatic or advanced solid tumors

End point title	To evaluate the safety, tolerability, and DLTs of INCAGN01949 and to define a MTD or PAD of INCAGN01949 in subjects with metastatic or advanced solid tumors ^[1]
End point description:	To evaluate the safety, tolerability, and DLTs of INCAGN01949 and to define a MTD or PAD of INCAGN01949 in subjects with metastatic or advanced solid tumors
End point type	Primary
End point timeframe:	From screening through 60 days after end of treatment, up to 11 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: There is no hypothesis testing for this endpoint , descriptive analysis is provided.

End point values	Cohort1 - INCAGN1949 7mg	Cohort2 - INCAGN1949 20mg	Cohort3 - INCAGN1949 70mg	Cohort4 - INCAGN1949 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	22	18
Units: participants	4	4	21	17

End point values	Cohort5 - INCAGN1949 350mg	Cohort6 - INCAGN1949 700mg	Cohort7 - INCAGN1949 1400mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	12	4	
Units: participants	22	11	4	

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the preliminary efficacy of INCAGN01949 by assessing the objective response rate per RECIST v1.1 and mRECIST v1.1.

End point title	To evaluate the preliminary efficacy of INCAGN01949 by assessing the objective response rate per RECIST v1.1 and mRECIST v1.1.
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End point description:

End point type	Secondary
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End point timeframe:

Baseline and every 8 weeks, up to 11 months

End point values	Cohort1 - INCAGN1949 7mg	Cohort2 - INCAGN1949 20mg	Cohort3 - INCAGN1949 70mg	Cohort4 - INCAGN1949 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	22	18
Units: participants	0	0	0	0

End point values	Cohort5 - INCAGN1949 350mg	Cohort6 - INCAGN1949 700mg	Cohort7 - INCAGN1949 1400mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	12	4	
Units: participants	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the preliminary efficacy of INCAGN01949 by assessing the duration of response per RECIST v1.1 and mRECIST v1.1.

End point title	To evaluate the preliminary efficacy of INCAGN01949 by assessing the duration of response per RECIST v1.1 and mRECIST v1.1.
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End point description:

End point type	Secondary
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End point timeframe:

Baseline and every 8 weeks , up to 11 months

End point values	Cohort1 - INCAGN1949 7mg	Cohort2 - INCAGN1949 20mg	Cohort3 - INCAGN1949 70mg	Cohort4 - INCAGN1949 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[2]	0 ^[3]	0 ^[4]	0 ^[5]
Units: days				
median (full range (min-max))	(to)	(to)	(to)	(to)

Notes:

[2] - There were no responders in this group

[3] - There were no responders in this group

[4] - There were no responders in this group

[5] - There were no responders in this group

End point values	Cohort5 - INCAGN1949 350mg	Cohort6 - INCAGN1949 700mg	Cohort7 - INCAGN1949 1400mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0 ^[6]	1	0 ^[7]	
Units: days				
median (full range (min-max))	(to)	192 (192 to 192)	(to)	

Notes:

[6] - There were no responders in this group

[7] - There were no responders in this group

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the preliminary efficacy of INCAGN01949 by assessing the progression free survival per RECIST v1.1 and mRECIST v1.1.

End point title	To evaluate the preliminary efficacy of INCAGN01949 by assessing the progression free survival per RECIST v1.1 and mRECIST v1.1.
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End point description:

End point type	Secondary
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End point timeframe:

Baseline and every 8 weeks , up to 11 months

End point values	Cohort1 - INCAGN1949 7mg	Cohort2 - INCAGN1949 20mg	Cohort3 - INCAGN1949 70mg	Cohort4 - INCAGN1949 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	22	18
Units: days				
median (full range (min-max))	57 (55 to 59)	47.5 (29 to 112)	54 (23 to 216)	56 (26 to 281)

End point values	Cohort5 - INCAGN1949 350mg	Cohort6 - INCAGN1949 700mg	Cohort7 - INCAGN1949 1400mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	12	4	
Units: days				
median (full range (min-max))	52 (1 to 166)	125 (21 to 298)	46.5 (42 to 53)	

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the preliminary efficacy of INCAGN01949 by assessing the duration of disease control per RECIST v1.1 and mRECIST v1.1.

End point title	To evaluate the preliminary efficacy of INCAGN01949 by assessing the duration of disease control per RECIST v1.1 and mRECIST v1.1.
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End point description:

End point type	Secondary
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End point timeframe:

Baseline and every 8 weeks , up to 11 months

End point values	Cohort1 - INCAGN1949 7mg	Cohort2 - INCAGN1949 20mg	Cohort3 - INCAGN1949 70mg	Cohort4 - INCAGN1949 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	8	7
Units: days				
median (full range (min-max))	0 (0 to 0)	57 (57 to 57)	64 (1 to 160)	57 (1 to 225)

End point values	Cohort5 - INCAGN1949	Cohort6 - INCAGN1949	Cohort7 - INCAGN1949	
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	350mg	700mg	1400mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	7	0 ^[8]	
Units: days				
median (full range (min-max))	0 (0 to 0)	120 (1 to 249)	(to)	

Notes:

[8] - All subjects had a response of progressive disease

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the Tmax of INCAGN01949 in subjects with advanced or metastatic solid tumors

End point title	To evaluate the Tmax of INCAGN01949 in subjects with advanced or metastatic solid tumors
End point description:	
End point type	Secondary
End point timeframe:	
cycle 1	

End point values	Cohort1 - INCAGN1949 7mg	Cohort2 - INCAGN1949 20mg	Cohort3 - INCAGN1949 70mg	Cohort4 - INCAGN1949 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	21	17
Units: hr				
median (full range (min-max))	0.64 (0.6 to 4.4)	2.53 (0.55 to 4.5)	4.3 (0.50 to 25.2)	0.63 (0.5 to 4.5)

End point values	Cohort5 - INCAGN1949 350mg	Cohort6 - INCAGN1949 700mg	Cohort7 - INCAGN1949 1400mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	7	4	
Units: hr				
median (full range (min-max))	0.6 (0.0 to 194)	0.7 (0.53 to 4.2)	0.73 (0.0 to 2.43)	

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the Cmin of INCAGN01949 in subjects with advanced or

metastatic solid tumors. Cmin is the minimum observed concentration of INCAGN1949

End point title	To evaluate the Cmin of INCAGN01949 in subjects with advanced or metastatic solid tumors. Cmin is the minimum observed concentration of INCAGN1949
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End point description:

End point type	Secondary
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End point timeframe:

cycle 1

End point values	Cohort1 - INCAGN1949 7mg	Cohort2 - INCAGN1949 20mg	Cohort3 - INCAGN1949 70mg	Cohort4 - INCAGN1949 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	20	17
Units: ng/ml				
arithmetic mean (standard deviation)	303 (± 202)	1890 (± 1570)	3620 (± 1550)	8880 (± 4510)

End point values	Cohort5 - INCAGN1949 350mg	Cohort6 - INCAGN1949 700mg	Cohort7 - INCAGN1949 1400mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	18	7	3	
Units: ng/ml				
arithmetic mean (standard deviation)	17000 (± 8040)	41000 (± 13000)	117000 (± 19300)	

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the Cmax of INCAGN01949 in subjects with advanced or metastatic solid tumors.

End point title	To evaluate the Cmax of INCAGN01949 in subjects with advanced or metastatic solid tumors.
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End point description:

End point type	Secondary
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End point timeframe:

cycle 1

End point values	Cohort1 - INCAGN1949 7mg	Cohort2 - INCAGN1949 20mg	Cohort3 - INCAGN1949 70mg	Cohort4 - INCAGN1949 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	21	17
Units: ng/mL				
arithmetic mean (standard deviation)	1630 (± 735)	5820 (± 324)	22300 (± 32800)	39200 (± 10300)

End point values	Cohort5 - INCAGN1949 350mg	Cohort6 - INCAGN1949 700mg	Cohort7 - INCAGN1949 1400mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	7	4	
Units: ng/mL				
arithmetic mean (standard deviation)	84900 (± 76700)	207000 (± 45500)	347000 (± 130000)	

Statistical analyses

No statistical analyses for this end point

Secondary: To evaluate the AUC0-t of INCAGN01949 in subjects with advanced or metastatic solid tumors

End point title	To evaluate the AUC0-t of INCAGN01949 in subjects with advanced or metastatic solid tumors
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End point description:

End point type	Secondary
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End point timeframe:
cycle 1

End point values	Cohort1 - INCAGN1949 7mg	Cohort2 - INCAGN1949 20mg	Cohort3 - INCAGN1949 70mg	Cohort4 - INCAGN1949 200 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	4	21	17
Units: ug*hr/mL				
arithmetic mean (standard deviation)	185 (± 81.7)	904 (± 197)	2370 (± 841)	5400 (± 1820)

End point values	Cohort5 - INCAGN1949 350mg	Cohort6 - INCAGN1949 700mg	Cohort7 - INCAGN1949 1400mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	21	7	4	

Units: ug*hr/mL				
arithmetic mean (standard deviation)	10000 (± 5600)	28300 (± 7720)	61600 (± 9130)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From screening through 60 days after end of treatment, up to 11 months

Adverse event reporting additional description:

AE additional description

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19
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Reporting groups

Reporting group title	PART 1 Dose 1 (7 mg)
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Reporting group description:

PART 1 Dose 1 (7 mg)

Reporting group title	PART 1 Dose 2 (20 mg)
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Reporting group description:

PART 1 Dose 2 (20 mg)

Reporting group title	PART 1 Dose 3 (70 mg)
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Reporting group description:

PART 1 Dose 3 (70 mg)

Reporting group title	PART 1 Dose 4 (200 mg)
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Reporting group description:

PART 1 Dose 4 (200 mg)

Reporting group title	PART 1 Dose 5 (350 mg)
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Reporting group description:

PART 1 Dose 5 (350 mg)

Reporting group title	PART 1 Dose 6 (700 mg)
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Reporting group description:

PART 1 Dose 6 (700 mg)

Reporting group title	PART 1 Dose 7 (1400 mg)
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Reporting group description:

PART 1 Dose 7 (1400 mg)

Serious adverse events	PART 1 Dose 1 (7 mg)	PART 1 Dose 2 (20 mg)	PART 1 Dose 3 (70 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)	1 / 4 (25.00%)	8 / 22 (36.36%)
number of deaths (all causes)	1	0	2
number of deaths resulting from adverse events	1	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Tumour pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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			
Deep vein thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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			
General physical health deterioration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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			
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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			
Spinal fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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			
Ventricular tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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			
Ataxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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
Cauda equina syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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
Spinal cord compression			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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
Ascites			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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
Colitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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
Jaundice cholestatic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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			
Acute kidney injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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
Hydronephrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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 incontinence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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 pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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

Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
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			
Appendicitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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 bacterial			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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
Myelitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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 streptococcal			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 22 (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			
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (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
Serious adverse events			
	PART 1 Dose 4 (200 mg)	PART 1 Dose 5 (350 mg)	PART 1 Dose 6 (700 mg)
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 18 (50.00%)	9 / 23 (39.13%)	5 / 12 (41.67%)

number of deaths (all causes)	4	2	3
number of deaths resulting from adverse events	1	2	3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (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
Malignant neoplasm progression			
subjects affected / exposed	1 / 18 (5.56%)	2 / 23 (8.70%)	3 / 12 (25.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 3
Tumour pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (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			
Deep vein thrombosis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (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
Embolism			
subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (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
Oedema			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (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
Pain			

subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	0 / 12 (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
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Spinal fracture			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (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
Cardiac disorders			
Ventricular tachycardia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (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
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 18 (5.56%)	1 / 23 (4.35%)	0 / 12 (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
Cauda equina syndrome			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			

subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (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			
Abdominal pain			
subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	2 / 12 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (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
Colitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	0 / 12 (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
Diarrhoea			
subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	0 / 12 (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 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (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	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (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
Small intestinal obstruction			

subjects affected / exposed	2 / 18 (11.11%)	2 / 23 (8.70%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 18 (5.56%)	1 / 23 (4.35%)	0 / 12 (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
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (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
Jaundice cholestatic			
subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	0 / 12 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	0 / 12 (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
Hydronephrosis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	0 / 12 (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
Urinary incontinence			
subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	0 / 12 (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
Urinary tract pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Arthralgia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	0 / 12 (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
Back pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (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			
Appendicitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	0 / 12 (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 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection bacterial			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (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
Myelitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	0 / 12 (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
Pneumonia streptococcal			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (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
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	0 / 12 (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

Serious adverse events	PART 1 Dose 7 (1400 mg)		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 4 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant neoplasm progression			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Embolism			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General physical health deterioration			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oedema			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Spinal fracture			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Ventricular tachycardia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ataxia			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cauda equina syndrome			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal cord compression			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Jaundice cholestatic			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hydronephrosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary incontinence			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection bacterial			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myelitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pneumonia streptococcal subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 4 (0.00%) 0 / 0 0 / 0		
Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 4 (0.00%) 0 / 0 0 / 0		

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

Non-serious adverse events	PART 1 Dose 1 (7 mg)	PART 1 Dose 2 (20 mg)	PART 1 Dose 3 (70 mg)
Total subjects affected by non-serious adverse events subjects affected / exposed	4 / 4 (100.00%)	4 / 4 (100.00%)	21 / 22 (95.45%)
Vascular disorders Deep vein thrombosis subjects affected / exposed occurrences (all) Hypertension subjects affected / exposed occurrences (all) Thrombophlebitis superficial subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0	0 / 22 (0.00%) 0 0 / 22 (0.00%) 0 0 / 22 (0.00%) 0
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Chills subjects affected / exposed occurrences (all) Early satiety subjects affected / exposed occurrences (all) Fatigue	0 / 4 (0.00%) 0 0 / 4 (0.00%) 0 0 / 4 (0.00%) 0	0 / 4 (0.00%) 0 1 / 4 (25.00%) 1 0 / 4 (0.00%) 0	2 / 22 (9.09%) 2 1 / 22 (4.55%) 3 0 / 22 (0.00%) 0

subjects affected / exposed	2 / 4 (50.00%)	2 / 4 (50.00%)	6 / 22 (27.27%)
occurrences (all)	2	2	8
Gait disturbance			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Nodule			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Pyrexia			
subjects affected / exposed	0 / 4 (0.00%)	2 / 4 (50.00%)	1 / 22 (4.55%)
occurrences (all)	0	4	1
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	4 / 22 (18.18%)
occurrences (all)	0	1	5
Dyspnoea			

subjects affected / exposed	1 / 4 (25.00%)	2 / 4 (50.00%)	2 / 22 (9.09%)
occurrences (all)	1	2	2
Dyspnoea exertional			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Haemothorax			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Wheezing			

subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 4 (0.00%) 0	0 / 22 (0.00%) 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Hallucination			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Investigations			
Amylase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Lymph node palpable			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Platelet count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	2 / 4 (50.00%)	1 / 4 (25.00%)	0 / 22 (0.00%)
occurrences (all)	2	1	0
Weight increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Joint injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Meniscus injury			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Rib fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Spinal fracture			

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 1	0 / 22 (0.00%) 0
Tooth fracture subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	0 / 22 (0.00%) 0
Cardiac disorders Sinus bradycardia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 1	0 / 22 (0.00%) 0
Ventricular tachycardia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	0 / 22 (0.00%) 0
Nervous system disorders Ataxia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	0 / 22 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	1 / 22 (4.55%) 1
Dysgeusia subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 4 (0.00%) 0	1 / 22 (4.55%) 1
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	2 / 22 (9.09%) 2
Neuropathy peripheral subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	1 / 22 (4.55%) 1
Spinal cord compression subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 4 (0.00%) 0	0 / 22 (0.00%) 0
Tremor subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	0 / 22 (0.00%) 0
Blood and lymphatic system disorders			

Anaemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	4 / 22 (18.18%) 5
Ear and labyrinth disorders Tinnitus subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	0 / 22 (0.00%) 0
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 1	0 / 22 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 1	1 / 22 (4.55%) 1
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 4 (25.00%) 1	0 / 22 (0.00%) 0
Ascites subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	0 / 22 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 4 (25.00%) 1	4 / 22 (18.18%) 4
Diarrhoea subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 2	0 / 4 (0.00%) 0	3 / 22 (13.64%) 3
Dry mouth subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	0 / 22 (0.00%) 0
Dyspepsia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	0 / 22 (0.00%) 0
Dysphagia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 4 (0.00%) 0	0 / 22 (0.00%) 0
Epigastric discomfort			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	3 / 22 (13.64%)
occurrences (all)	0	1	5
Vomiting			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	5 / 22 (22.73%)
occurrences (all)	1	0	5
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Pruritus generalised			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Rash maculo-papular			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Tumour pruritus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Haemorrhage urinary tract			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nocturia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Urinary tract obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	3 / 4 (75.00%)	3 / 22 (13.64%)
occurrences (all)	0	4	3
Back pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	3 / 22 (13.64%)
occurrences (all)	1	0	3
Bone pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Fistula			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 4 (25.00%)	2 / 4 (50.00%)	0 / 22 (0.00%)
occurrences (all)	1	2	0
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Infectious pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Rash pustular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Wound infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 4 (25.00%)	3 / 4 (75.00%)	6 / 22 (27.27%)
occurrences (all)	1	3	6
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	1 / 22 (4.55%)
occurrences (all)	0	2	2
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 4 (25.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 4 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	PART 1 Dose 4 (200 mg)	PART 1 Dose 5 (350 mg)	PART 1 Dose 6 (700 mg)
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Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 18 (94.44%)	22 / 23 (95.65%)	10 / 12 (83.33%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Thrombophlebitis superficial			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	0 / 18 (0.00%)	2 / 23 (8.70%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Early satiety			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	7 / 18 (38.89%)	8 / 23 (34.78%)	4 / 12 (33.33%)
occurrences (all)	7	8	4
Gait disturbance			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Influenza like illness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nodule			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Non-cardiac chest pain			

subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1
Oedema peripheral subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 3	0 / 23 (0.00%) 0	2 / 12 (16.67%) 2
Peripheral swelling subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	2 / 23 (8.70%) 2	1 / 12 (8.33%) 1
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	2 / 23 (8.70%) 2	1 / 12 (8.33%) 1
Reproductive system and breast disorders Vaginal haemorrhage subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	5 / 18 (27.78%) 7	1 / 23 (4.35%) 1	1 / 12 (8.33%) 1
Dyspnoea subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 3	3 / 23 (13.04%) 3	2 / 12 (16.67%) 2
Dyspnoea exertional subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	2 / 12 (16.67%) 2
Epistaxis subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1
Haemothorax subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Hypoxia			

subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Pleural effusion			
subjects affected / exposed	0 / 18 (0.00%)	2 / 23 (8.70%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Productive cough			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pulmonary embolism			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Wheezing			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Hallucination			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Investigations			
Amylase increased			

subjects affected / exposed	2 / 18 (11.11%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	3
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 18 (0.00%)	1 / 23 (4.35%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Blood bilirubin increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Blood creatinine increased			
subjects affected / exposed	1 / 18 (5.56%)	2 / 23 (8.70%)	1 / 12 (8.33%)
occurrences (all)	1	2	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Blood urea increased			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Lipase increased			
subjects affected / exposed	1 / 18 (5.56%)	1 / 23 (4.35%)	1 / 12 (8.33%)
occurrences (all)	1	1	2
Lymph node palpable			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			

subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 23 (4.35%) 1	0 / 12 (0.00%) 0
Platelet count decreased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1
Weight decreased subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	2 / 23 (8.70%) 2	0 / 12 (0.00%) 0
Weight increased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 23 (4.35%) 1	0 / 12 (0.00%) 0
Joint injury subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Meniscus injury subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Rib fracture subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Spinal fracture subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Tooth fracture subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1
Cardiac disorders			
Sinus bradycardia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Ventricular tachycardia			

subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Nervous system disorders			
Ataxia			
subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Dizziness			
subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 23 (4.35%) 1	0 / 12 (0.00%) 0
Dysgeusia			
subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Hypoaesthesia			
subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 23 (4.35%) 1	0 / 12 (0.00%) 0
Neuropathy peripheral			
subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Spinal cord compression			
subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Tremor			
subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	1 / 23 (4.35%) 1	2 / 12 (16.67%) 2
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Abdominal pain			

subjects affected / exposed	3 / 18 (16.67%)	4 / 23 (17.39%)	0 / 12 (0.00%)
occurrences (all)	3	4	0
Abdominal pain upper			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	1 / 18 (5.56%)	1 / 23 (4.35%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Constipation			
subjects affected / exposed	6 / 18 (33.33%)	4 / 23 (17.39%)	1 / 12 (8.33%)
occurrences (all)	6	4	1
Diarrhoea			
subjects affected / exposed	4 / 18 (22.22%)	3 / 23 (13.04%)	1 / 12 (8.33%)
occurrences (all)	7	3	1
Dry mouth			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Epigastric discomfort			
subjects affected / exposed	2 / 18 (11.11%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	3 / 18 (16.67%)	6 / 23 (26.09%)	0 / 12 (0.00%)
occurrences (all)	3	7	0
Vomiting			
subjects affected / exposed	3 / 18 (16.67%)	4 / 23 (17.39%)	0 / 12 (0.00%)
occurrences (all)	3	6	0
Hepatobiliary disorders			

Cholangitis subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Skin and subcutaneous tissue disorders			
Erythema subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1
Night sweats subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	2 / 23 (8.70%) 2	0 / 12 (0.00%) 0
Pruritus generalised subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1
Rash subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	1 / 23 (4.35%) 1	0 / 12 (0.00%) 0
Rash maculo-papular subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 3	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Tumour pruritus subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Renal and urinary disorders			
Haematuria subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 23 (4.35%) 1	1 / 12 (8.33%) 1
Haemorrhage urinary tract subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Nocturia			

subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Urinary incontinence subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 23 (4.35%) 1	0 / 12 (0.00%) 0
Urinary retention subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Urinary tract obstruction subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	1 / 23 (4.35%) 1	0 / 12 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 23 (4.35%) 1	1 / 12 (8.33%) 1
Back pain subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 3	5 / 23 (21.74%) 5	1 / 12 (8.33%) 1
Bone pain subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Fistula subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1
Flank pain subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Groin pain subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	1 / 12 (8.33%) 1
Musculoskeletal chest pain			

subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	2
Pain in extremity			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Infectious pleural effusion			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Rash pustular			
subjects affected / exposed	1 / 18 (5.56%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 23 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Wound infection subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	4 / 18 (22.22%) 4	7 / 23 (30.43%) 8	3 / 12 (25.00%) 4
Dehydration subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	0 / 12 (0.00%) 0
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 23 (0.00%) 0	1 / 12 (8.33%) 2
Hypokalaemia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	1 / 23 (4.35%) 1	0 / 12 (0.00%) 0

Non-serious adverse events	PART 1 Dose 7 (1400 mg)		
Total subjects affected by non-serious adverse events subjects affected / exposed	4 / 4 (100.00%)		
Vascular disorders			
Deep vein thrombosis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Hypertension subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Thrombophlebitis superficial subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Early satiety			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	2		
Gait disturbance			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nodule			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Non-cardiac chest pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Oedema peripheral			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Immune system disorders			

Seasonal allergy subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Reproductive system and breast disorders Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Dyspnoea subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 2		
Dyspnoea exertional subjects affected / exposed occurrences (all)	2 / 4 (50.00%) 3		
Epistaxis subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Haemothorax subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Hypoxia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Nasal congestion subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0		
Pleural effusion subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1		
Productive cough			

subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Pulmonary embolism			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Rhinitis allergic			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Upper-airway cough syndrome			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Wheezing			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hallucination			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Investigations			
Amylase increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood urea increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
C-reactive protein increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Lipase increased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Lymph node palpable			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Lymphocyte count decreased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Platelet count decreased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Joint injury			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Meniscus injury			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Rib fracture			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Spinal fracture			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tooth fracture			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Ventricular tachycardia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Neuropathy peripheral			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Spinal cord compression			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tremor			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 4 (50.00%)		
occurrences (all)	3		
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Ascites			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Diarrhoea			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Dysphagia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Epigastric discomfort			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Night sweats			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pruritus generalised			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Tumour pruritus			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Haemorrhage urinary tract			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Nocturia			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Urinary incontinence			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Urinary retention			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Urinary tract obstruction			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Bone pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Fistula			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Groin pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Infections and infestations			

Cellulitis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Infectious pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Rash pustular			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Skin infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 4 (25.00%)		
occurrences (all)	1		
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Wound infection			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 4 (0.00%)		
occurrences (all)	0		

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