Clinical trial results:
A PHASE 2A, OPEN-LABEL, DOSE FINDING STUDY TO DETERMINE THE SAFETY AND TOLERABILITY OF SOTATERCEPT (ACE-011) IN ADULTS WITH BETA -THALASSEMIA

Summary

EudraCT number	2011-005659-15
Trial protocol	GB IT GR
Global end of trial date	24 May 2022

Results information

Result version number	v1 (current)
This version publication date	09 June 2023
First version publication date	09 June 2023

Trial information

Trial identification

Sponsor protocol code	ACE-011-B-THAL-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	Chaussee de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	25 October 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 May 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine a safe, tolerable and effective dose of sotatercept in adult subjects with RBC transfusion dependent beta-thalassemia major (including all subtypes) and beta-thalassemia intermedia, as well as non-transfusion dependent beta-thalassemia intermedia.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 October 2012
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	France: 4
Country: Number of subjects enrolled	Greece: 7
Country: Number of subjects enrolled	Italy: 26
Country: Number of subjects enrolled	United Kingdom: 9
Worldwide total number of subjects	46
EEA total number of subjects	37

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)	45

From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The protocol planned to enroll participants in the dose level 1.5 mg/kg and also open an expansion cohort once the potential recommended dose (PRD) was defined. Due to early termination, the 1.5 mg/kg dose level and expansion cohort were not enrolled.

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	Dose Level 1a: 0.1 mg/kg

Arm description:

Dose level 1a (starting dose) 0.1 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.

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

Dosage and administration details:

0.1 mg/kg Sotatercept subcutaneous injection once every 21 days

Arm title	Dose Level 1b: 0.3 mg/kg

Arm description:

Dose level 1b (starting dose) 0.3 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.

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

Dosage and administration details:

0.3 mg/kg Sotatercept subcutaneous injection once every 21 days

Arm title	Dose Level 2: 0.5 mg/kg

Arm description:

Dose level 2 (escalation dose) 0.5 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.

Arm type	Experimental

Investigational medicinal product name	Sotatercept
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

0.5 mg/kg Sotatercept subcutaneous injection once every 21 days

Arm title	Dose Level 3: 0.75 mg/kg

Arm description:

Dose level 3 (escalation dose) 0.75 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.

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

Dosage and administration details:

0.75 mg/kg Sotatercept subcutaneous injection once every 21 days

Arm title	Dose Level 4: 1 mg/kg

Arm description:

Dose level 4 (escalation dose) 1 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.

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

Dosage and administration details:

1 mg/kg Sotatercept subcutaneous injection once every 21 days

Number of subjects in period 1	Dose Level 1a: 0.1 mg/kg	Dose Level 1b: 0.3 mg/kg	Dose Level 2: 0.5 mg/kg
Started	8	9	8
Completed	2	1	1
Not completed	6	8	7
Adverse event, non-fatal	3	-	2
Study terminated by sponsor	-	4	1
Other reasons	2	1	2
Withdrew consent	1	1	2
Lack of efficacy	-	2	-

Number of subjects in period 1	Dose Level 3: 0.75 mg/kg	Dose Level 4: 1 mg/kg
Started	12	9
Completed	0	0
Not completed	12	9

Adverse event, non-fatal	3	5
Study terminated by sponsor	3	1
Other reasons	2	1
Withdrew consent	3	-
Lack of efficacy	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Dose Level 1a: 0.1 mg/kg
Reporting group description:	
Dose level 1a (starting dose) 0.1 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.	
Reporting group title	Dose Level 1b: 0.3 mg/kg
Reporting group description:	
Dose level 1b (starting dose) 0.3 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.	
Reporting group title	Dose Level 2: 0.5 mg/kg
Reporting group description:	
Dose level 2 (escalation dose) 0.5 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.	
Reporting group title	Dose Level 3: 0.75 mg/kg
Reporting group description:	
Dose level 3 (escalation dose) 0.75 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.	
Reporting group title	Dose Level 4: 1 mg/kg
Reporting group description:	
Dose level 4 (escalation dose) 1 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.	

Reporting group values	Dose Level 1a: 0.1 mg/kg	Dose Level 1b: 0.3 mg/kg	Dose Level 2: 0.5 mg/kg
Number of subjects	8	9	8
Age categorical Units: Subjects			
Adults (18-64 years)	8	9	8
From 65-84 years	0	0	0
Age Continuous Units: Years			
median	39.5	40.0	38.5
standard deviation	± 8.21	± 9.89	± 7.63
Sex: Female, Male Units: Participants			
Female	4	4	3
Male	4	5	5
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	0	0	0
White	7	9	6
More than one race	0	0	0
Unknown or Not Reported	0	0	2

Reporting group values	Dose Level 3: 0.75 mg/kg	Dose Level 4: 1 mg/kg	Total

Number of subjects	12	9	46
Age categorical Units: Subjects			
Adults (18-64 years)	11	9	45
From 65-84 years	1	0	1
Age Continuous Units: Years			
median	44.0	41.0	
standard deviation	± 10.29	± 10.36	-
Sex: Female, Male Units: Participants			
Female	8	3	22
Male	4	6	24
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	2	1	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	10	8	40
More than one race	0	0	0
Unknown or Not Reported	0	0	2

End points

End points reporting groups

Reporting group title	Dose Level 1a: 0.1 mg/kg
Reporting group description:	
Dose level 1a (starting dose) 0.1 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.	
Reporting group title	Dose Level 1b: 0.3 mg/kg
Reporting group description:	
Dose level 1b (starting dose) 0.3 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.	
Reporting group title	Dose Level 2: 0.5 mg/kg
Reporting group description:	
Dose level 2 (escalation dose) 0.5 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.	
Reporting group title	Dose Level 3: 0.75 mg/kg
Reporting group description:	
Dose level 3 (escalation dose) 0.75 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.	
Reporting group title	Dose Level 4: 1 mg/kg
Reporting group description:	
Dose level 4 (escalation dose) 1 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.	

Primary: Potential Recommended Dose as Determined by Number of Participants Experiencing Dose-Limiting Toxicities and Recommended Dose

End point title	Potential Recommended Dose as Determined by Number of Participants Experiencing Dose-Limiting Toxicities and Recommended Dose[1]
End point description:	
Number of participants with dose-limiting toxicities (DLT) are used to determine the potential recommended dose (PRD). PRD is defined as the highest dose with up to 1 out of 6 patients experiencing a DLT. DLT is defined as any side effects of the study treatment serious enough to prevent an increase in dose or level of treatment, including at least one of the following: Hypertension ≥ Grade 3 per National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.0; Hgb > 14 g/dL sustained for four weeks; any NCI CTCAE toxicity ≥ Grade 3. Grade 3 is defined as severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily life. PRD was identified as 1 mg/kg. Due to study termination, no patients were enrolled after 1 mg/kg cohort or in the Expansion Cohort. Thus, primary analyses to determine recommended dose (RD) were not conducted.	
End point type	Primary
End point timeframe:	
From first dose up to 28 days post the first dose	

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: Only summary statistics were planned for this endpoint

End point values	Dose Level 1a: 0.1 mg/kg	Dose Level 1b: 0.3 mg/kg	Dose Level 2: 0.5 mg/kg	Dose Level 3: 0.75 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	8	12
Units: Participants	0	0	0	0

End point values	Dose Level 4: 1 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Red Blood Cell Transfusion Burden Reduction from Baseline During Treatment

End point title	Number of Participants with Red Blood Cell Transfusion Burden Reduction from Baseline During Treatment

End point description:

Transfusion burden at baseline is defined as the total number of units of RBC transfusions that participants received within 168 days (24 weeks) prior to the first dose of study therapy. Transfusion burden during treatment is defined as the total number of RBC transfusion units that each participant received during the treatment divided by the treatment duration and multiplied by 168 days. The result is a 168-day transfusion burden average. Baseline measurement includes RBC transfusion history for transfusion dependent and non-transfusion dependent subjects, starting at 168 days prior to enrollment.

End point type	Secondary

End point timeframe:

From baseline to the last dose of study treatment (up to approximately 112 months)

End point values	Dose Level 1a: 0.1 mg/kg	Dose Level 1b: 0.3 mg/kg	Dose Level 2: 0.5 mg/kg	Dose Level 3: 0.75 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	3	2	5
Units: Participants				
≥ 25% reduction	0	0	2	4
≥ 33% reduction	0	0	2	3
≥ 50% reduction	0	0	1	2

End point values	Dose Level 4: 1 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	4			

Units: Participants				
≥ 25% reduction	3			
≥ 33% reduction	1			
≥ 50% reduction	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Hemoglobin Level Increase from Baseline in Non-Transfusion Dependent B-Thalassemia Intermedia Participants

End point title	Number of Participants With Hemoglobin Level Increase from Baseline in Non-Transfusion Dependent B-Thalassemia Intermedia Participants

End point description:

The Number of participants with a change in Hemoglobin levels will be listed for non-RBC transfusion dependent participants. Baseline assessments are the average of the last two measurements prior to the start of therapy.

End point type	Secondary

End point timeframe:

Measurements were taken in 9 and 12-week intervals, from baseline up to approximately 112 months

End point values	Dose Level 1a: 0.1 mg/kg	Dose Level 1b: 0.3 mg/kg	Dose Level 2: 0.5 mg/kg	Dose Level 3: 0.75 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	7
Units: Participants				
9-week Hgb ≥ 1.0 g/dl change from baseline	0	5	4	6
9-week Hgb ≥ 1.5 g/dl change from baseline	0	2	2	6
12-Week Hgb ≥ 1.0 g/dl change from baseline	0	4	4	6
12-WeekHgb ≥ 1.5 g/dl change from baseline	0	2	2	6

End point values	Dose Level 4: 1 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	5			
Units: Participants				
9-week Hgb ≥ 1.0 g/dl change from baseline	2			
9-week Hgb ≥ 1.5 g/dl change from baseline	1			
12-Week Hgb ≥ 1.0 g/dl change from baseline	1			

12-WeekHgb ≥ 1.5 g/dl change from baseline	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Adverse Events (AEs)

End point title	Number of Participants Experiencing Adverse Events (AEs)

End point description:

An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a pre-existing medical condition in a clinical investigation participant administered study treatment and that does not necessarily have a causal relationship with this treatment. Adverse events are graded on a scale from 1 to 5, with Grade 1 being mild and asymptomatic; Grade 2 is moderate requiring minimal, local or noninvasive intervention; Grade 3 is severe or medically significant but not immediately life-threatening; Grade 4 events are usually severe enough to require hospitalization; Grade 5 events are fatal. Treatment emergent adverse events (TEAE) are defined as an AE that began after the start of trial medication treatment; or if the event was continuous from baseline and was serious, trial medication-related, or resulted in death, discontinuation, or interruption or reduction of trial therapy.

End point type	Secondary

End point timeframe:

From first dose up to 112 days after the last dose of study treatment (up to 115 months)

End point values	Dose Level 1a: 0.1 mg/kg	Dose Level 1b: 0.3 mg/kg	Dose Level 2: 0.5 mg/kg	Dose Level 3: 0.75 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	8	12
Units: Participants				
Participants with at least one TEAE	8	9	8	12
TEAE leading to dose interruption	2	5	4	2
Participants with at least one serious TEAE	3	3	3	3
At least one grade 2/3/4 TEAE	7	9	6	11
At least one drug-related grade 2/3/4 TEAE	4	3	4	7
At least one serious drug- related TEAE	2	1	1	0
At least one TEAE leading to withdrawal	3	0	2	3

End point values	Dose Level 4: 1 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Participants				
Participants with at least one TEAE	9			
TEAE leading to dose interruption	5			

Participants with at least one serious TEAE	3			
At least one grade 2/3/4 TEAE	9			
At least one drug-related grade 2/3/4 TEAE	7			
At least one serious drug- related TEAE	1			
At least one TEAE leading to withdrawal	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Sotatercept in Serum

End point title	Concentrations of Sotatercept in Serum

End point description:

Sotatercept was administered as a subcutaneous injection every 21 days during the Treatment Period. Pharmacokinetic (PK) samples were collected at the pre-specified timepoints.

End point type	Secondary

End point timeframe:

Dose 1, Day 8; Dose 1, Day 15; Dose 2, Day 1; Dose 2, Day 8; Dose 3, Day 1; Dose 3, Day 8; Dose 4, Day 1; Dose 5, Day 1; Dose 6, Day 1

End point values	Dose Level 1a: 0.1 mg/kg	Dose Level 1b: 0.3 mg/kg	Dose Level 2: 0.5 mg/kg	Dose Level 3: 0.75 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	8	12
Units: ng/mL				
median (full range (min-max))				
Dose 1, Day 8	598.3 (289.2 to 1345.4)	1454.05 (1006.6 to 2768.3)	3045.45 (1586.7 to 4480)	5837.65 (3238.1 to 10590.5)
Dose 1, Day 15	388.7 (98.4 to 1046)	1150.1 (550.3 to 2158.4)	2329.75 (952 to 3005.5)	4279.65 (2107.8 to 6692)
Dose 2, Day 1	294.75 (112.9 to 547.1)	770.3 (317.2 to 1300.1)	1468.05 (682 to 2550.5)	2955.2 (1257.5 to 4450.8)
Dose 2, Day 8	683.1 (250.1 to 1210.6)	2065 (1363.7 to 3626.4)	4136.8 (1661.9 to 5573.8)	7753.35 (5046.4 to 8805.6)
Dose 3, Day 1	325.35 (228.8 to 790)	956.8 (380.6 to 1552.6)	2157.3 (422 to 3088.4)	3628.45 (653.5 to 6429.1)
Dose 3, Day 8	758.1 (444 to 1232)	2319.9 (1475.6 to 3667.4)	4507.3 (2077.8 to 5762.3)	8373.05 (5345.5 to 12177.8)
Dose 4, Day 1	334.85 (298 to 1014.9)	1022.3 (348.8 to 2096.9)	2441.6 (784 to 2845.3)	4137.1 (1447.1 to 6126.6)
Dose 5, Day 1	385.1 (287.5 to 467.5)	1473.9 (762.1 to 2764.4)	1618.8 (953.4 to 3440)	4449.7 (2340.4 to 5887.8)

Dose 6, Day 1	297.60 (227.80 to 484.40)	1368.10 (449.70 to 2363.20)	2266.40 (1115.20 to 3788.50)	4062.80 (1481.10 to 6584.00)

End point values	Dose Level 4: 1 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: ng/mL				
median (full range (min-max))				
Dose 1, Day 8	3874 (2264.9 to 7003)			
Dose 1, Day 15	2405.6 (1825.3 to 4605.5)			
Dose 2, Day 1	1701.5 (888.6 to 4267.9)			
Dose 2, Day 8	5148.1 (3537.4 to 10418.7)			
Dose 3, Day 1	2602.6 (822.2 to 5668.1)			
Dose 3, Day 8	6050.8 (3892.5 to 12139.6)			
Dose 4, Day 1	2869.2 (1478.9 to 4787.7)			
Dose 5, Day 1	3048 (1125.5 to 6529.3)			
Dose 6, Day 1	2780.80 (1479.20 to 7896.70)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Quality of Life (QOL) Change from Baseline

End point title	Number of Participants Experiencing Quality of Life (QOL) Change from Baseline

End point description:

The number of participants in the expansion cohort experiencing changes from baseline in Quality of Life. QOL was planned to be assessed at Day 168 (6 months) and Day 336 (12 months), after Dose 1 Day 1, independent of Dose Delay for participants enrolled in the Expansion Cohort only. QOL was planned to be calculated using the SF-36 and the FACT Anemia. The SF-36 is a Medical Outcomes Study (MOS) consisting of 36 questions developed to determine health status. The SF-36 measures eight scales: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health. The FACT Anemia measures fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) Measurement System.

Due to early study termination, no participants were enrolled in the expansion cohort and QOL was not assessed.

End point type	Secondary

End point timeframe:

From pre-dose up to Dose 8 (168 days/6months) and Dose 16 (336 days/12months) only

End point values	Dose Level 1a: 0.1 mg/kg	Dose Level 1b: 0.3 mg/kg	Dose Level 2: 0.5 mg/kg	Dose Level 3: 0.75 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[2]	0[3]	0[4]	0[5]
Units: Participants				

Notes:

[2] - No participants were assessed due to early study termination

[3] - No participants were assessed due to early study termination

[4] - No participants were assessed due to early study termination

[5] - No participants were assessed due to early study termination

End point values	Dose Level 4: 1 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	0[6]			
Units: Participants				

Notes:

[6] - No participants were assessed due to early study termination

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Anti-Drug Antibody (ADA)

End point title	Number of Participants with Anti-Drug Antibody (ADA)

End point description:

The number of participants with Anti–Sotatercept Antibody is a summary of antidrug antibody (ADA) status for ADA-evaluated participants. A participant is counted as 'positive' if there is any positive result captured during the study, a participant is counted as 'negative' if there is no positive result captured during the study. ADA data was collected Day 1 in dose schedules 1 through 6. Starting from Dose 7, ADA was measured at Day 1 every 3 Doses, then finally at the post-treatment follow-up visit at Month 2 and Month 4.

End point type	Secondary

End point timeframe:

From first dose up to 4 months after last dose (up to approximately 116 months)

End point values	Dose Level 1a: 0.1 mg/kg	Dose Level 1b: 0.3 mg/kg	Dose Level 2: 0.5 mg/kg	Dose Level 3: 0.75 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	8	12
Units: Participants				
Negative	8	8	8	10
Positive	0	1	0	2

End point values	Dose Level 4: 1 mg/kg			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: Participants				
Negative	9			
Positive	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Participants were assessed for all-cause mortality from their enrollment to study completion, (up to approximately 115 months). SAEs and Other AEs were assessed from first dose to 112 days following last dose (up to approximately 115 months)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Dose Level 1a: 0.1 mg/kg

Reporting group description:

Dose level 1a (starting dose) 0.1 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.

Reporting group title	Dose Level 1b: 0.3 mg/kg

Reporting group description:

Dose level 1b (starting dose) 0.3 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.

Reporting group title	Dose Level 4: 1 mg/kg

Reporting group description:

Dose level 4 (escalation dose) 1 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.

Reporting group title	Dose Level 3: 0.75 mg/kg

Reporting group description:

Dose level 3 (escalation dose) 0.75 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.

Reporting group title	Dose Level 2: 0.5 mg/kg

Reporting group description:

Dose level 2 (escalation dose) 0.5 mg/kg Sotatercept will be administered as an SC injection once every 21 days for up to six planned doses during the Treatment Period.

Serious adverse events	Dose Level 1a: 0.1 mg/kg	Dose Level 1b: 0.3 mg/kg	Dose Level 4: 1 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 8 (37.50%)	3 / 9 (33.33%)	3 / 9 (33.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
HEPATIC NEOPLASM			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (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			

UPPER LIMB FRACTURE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ULNA FRACTURE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (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
PUBIS FRACTURE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (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
PELVIC FRACTURE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FALL			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (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
FOREARM FRACTURE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (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
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (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			
THROMBOPHLEBITIS SUPERFICIAL			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
THROMBOSIS			

subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (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			
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (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			
SYNCOPE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
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 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
SPLENIC INFARCTION			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (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
EXTRAMEDULLARY HAEMOPOIESIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ANAEMIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (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			
PYREXIA			

subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (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
LOCAL SWELLING			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FATIGUE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
ANAPHYLACTIC REACTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (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 UPPER			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
SUBILEUS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (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			
BONE PAIN			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (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

Infections and infestations			
BACTERIAL PROSTATITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (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
CORONA VIRUS INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (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 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (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
PHARYNGOTONSILLITIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (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
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (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	Dose Level 3: 0.75 mg/kg	Dose Level 2: 0.5 mg/kg	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 12 (25.00%)	3 / 8 (37.50%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
HEPATIC NEOPLASM			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
UPPER LIMB FRACTURE			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ULNA FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PUBIS FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PELVIC FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FALL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
FOREARM FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
THROMBOPHLEBITIS SUPERFICIAL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
THROMBOSIS			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
SYNCOPE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SPINAL CORD COMPRESSION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
SPLENIC INFARCTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
EXTRAMEDULLARY HAEMOPOIESIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
PYREXIA			

subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOCAL SWELLING			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
FATIGUE			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
ANAPHYLACTIC REACTION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBILEUS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
BONE PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infections and infestations			
BACTERIAL PROSTATITIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CORONA VIRUS INFECTION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PHARYNGOTONSILLITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
SUBCUTANEOUS ABSCESS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Dose Level 1a: 0.1 mg/kg	Dose Level 1b: 0.3 mg/kg	Dose Level 4: 1 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 8 (100.00%)	9 / 9 (100.00%)	9 / 9 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HAEMANGIOMA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

HAEMANGIOMA OF LIVER			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
LIPOMA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
MELANOCYTIC NAEVUS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
THYROID NEOPLASM			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
HAEMATOMA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HOT FLUSH			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
HYPERTENSION			
subjects affected / exposed	1 / 8 (12.50%)	3 / 9 (33.33%)	2 / 9 (22.22%)
occurrences (all)	3	6	9
HYPOTENSION			
subjects affected / exposed	2 / 8 (25.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
PREHYPERTENSION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
THROMBOPHLEBITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
VENOUS RECANALISATION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

CHEST DISCOMFORT			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
ASTHENIA			
subjects affected / exposed	4 / 8 (50.00%)	4 / 9 (44.44%)	3 / 9 (33.33%)
occurrences (all)	4	7	5
MALAISE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
LOCALISED OEDEMA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
LOCAL SWELLING			
subjects affected / exposed	1 / 8 (12.50%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
IRRITABILITY			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
INJECTION SITE INFLAMMATION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
INJECTION SITE ERYTHEMA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	1 / 8 (12.50%)	4 / 9 (44.44%)	0 / 9 (0.00%)
occurrences (all)	1	5	0
GRANULOMA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
GENERALISED OEDEMA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
FATIGUE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	2 / 9 (22.22%)
occurrences (all)	0	2	3

CYST			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
CHILLS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
CHEST PAIN			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
MUCOSAL HYPERAEMIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
OEDEMA PERIPHERAL			
subjects affected / exposed	2 / 8 (25.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
PAIN			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
VACCINATION SITE WARMTH			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
VACCINATION SITE SWELLING			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
VACCINATION SITE PAIN			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
VACCINATION SITE LYMPHADENOPATHY			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
VACCINATION SITE ERYTHEMA			

subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PYREXIA			
subjects affected / exposed	3 / 8 (37.50%)	6 / 9 (66.67%)	4 / 9 (44.44%)
occurrences (all)	6	21	11
DEFICIT FOLATE			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
ALLERGY TO ARTHROPOD STING			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ALLOIMMUNISATION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
SEASONAL ALLERGY			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	7	4
HYPERSENSITIVITY			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
ANAPHYLACTIC REACTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Social circumstances			
MENOPAUSE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
EPIDIDYMITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ERECTILE DYSFUNCTION			

subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
CYSTOCELE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
BREAST CYST			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
AMENORRHOEA			
subjects affected / exposed	1 / 8 (12.50%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	5	4	0
DYSMENORRHOEA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
UTERINE PROLAPSE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PROSTATOMEGALY			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PELVIC PAIN			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
OVARIAN CYST			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
OLIGOMENORRHOEA			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
EPISTAXIS			
subjects affected / exposed	2 / 8 (25.00%)	1 / 9 (11.11%)	3 / 9 (33.33%)
occurrences (all)	4	1	3
DYSPNOEA EXERTIONAL			

subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
DYSPNOEA			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
DYSPHONIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
COUGH			
subjects affected / exposed	3 / 8 (37.50%)	4 / 9 (44.44%)	3 / 9 (33.33%)
occurrences (all)	6	26	6
BRONCHOSPASM			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
ASTHMATIC CRISIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
ASTHMA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ALLERGIC RESPIRATORY DISEASE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
HAEMOPTYSIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
YAWNING			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
WHEEZING			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SNEEZING			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
RHINORRHOEA			

subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
LUNG CYST			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PULMONARY MASS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PRODUCTIVE COUGH			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PNEUMONITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PLEURAL EFFUSION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
OROPHARYNGEAL PAIN			
subjects affected / exposed	4 / 8 (50.00%)	5 / 9 (55.56%)	2 / 9 (22.22%)
occurrences (all)	7	10	2
NASAL CONGESTION			
subjects affected / exposed	0 / 8 (0.00%)	4 / 9 (44.44%)	0 / 9 (0.00%)
occurrences (all)	0	4	0
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
STRESS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
LIBIDO DECREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

DEPRESSION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
BRUXISM			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
ANXIETY			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
INSOMNIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Investigations			
EJECTION FRACTION DECREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ELECTROCARDIOGRAM T WAVE ABNORMAL			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
CREATININE RENAL CLEARANCE DECREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
CARDIAC INDEX INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
BLOOD PRESSURE INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
BLOOD FOLLICLE STIMULATING HORMONE DECREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1

BLOOD FOLATE DECREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	2	2
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	1	2	2
ELECTROCARDIOGRAM QT SHORTENED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
CULTURE STOOL POSITIVE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
WEIGHT INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
WEIGHT DECREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
VITAMIN D DECREASED			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
URINE PROTEIN/CREATININE RATIO INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ULTRASOUND SCAN ABNORMAL			

subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ULTRASOUND LIVER ABNORMAL			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SERUM FERRITIN INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	3 / 9 (33.33%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
PLATELET COUNT INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PANCREATIC ENZYMES INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HEPATIC ENZYME INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
GLOMERULAR FILTRATION RATE DECREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
FIBRIN D DIMER INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ESCHERICHIA TEST POSITIVE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
ARTHROPOD BITE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
CHEST INJURY			

subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
CONTUSION			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	2	2	0
EPICONDYLITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
FALL			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
FOOT FRACTURE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
LIMB INJURY			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	2 / 9 (22.22%)
occurrences (all)	0	1	2
LIGAMENT SPRAIN			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
LACERATION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HUMERUS FRACTURE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
HAEMOLYTIC TRANSFUSION REACTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
FRACTURED SACRUM			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
FRACTURE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

ARTHROPOD STING			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
MENISCUS INJURY			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
MUSCLE STRAIN			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
NAIL INJURY			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
OVERDOSE			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
PATELLA FRACTURE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
POST-TRAUMATIC PAIN			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
REPETITIVE STRAIN INJURY			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
RIB FRACTURE			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
SOFT TISSUE INJURY			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
TENDON RUPTURE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
THERMAL BURN			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	0	3	0

TOOTH INJURY			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
TRANSFUSION REACTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
VACCINATION COMPLICATION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
WRIST FRACTURE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Congenital, familial and genetic disorders			
BENIGN FAMILIAL HAEMATURIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
SPLINTER HAEMORRHAGES			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
TACHYCARDIA			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	1 / 9 (11.11%)
occurrences (all)	0	5	1
VENTRICULAR ARRHYTHMIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
VENTRICULAR EXTRASYSTOLES			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PALPITATIONS			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
LEFT VENTRICULAR DYSFUNCTION			

subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
LEFT ATRIAL DILATATION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
EXTRASYSTOLES			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
SINUS HEADACHE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
SCIATICA			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
PRESYNCOPE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	2	1
MIGRAINE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HYPERAESTHESIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HEADACHE			
subjects affected / exposed	2 / 8 (25.00%)	6 / 9 (66.67%)	3 / 9 (33.33%)
occurrences (all)	7	27	4
FACIAL NEURALGIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
DYSGEUSIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
DYSARTHRIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0

DIZZINESS			
subjects affected / exposed	3 / 8 (37.50%)	3 / 9 (33.33%)	0 / 9 (0.00%)
occurrences (all)	4	6	0
CERVICOBRACHIAL SYNDROME			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
AGEUSIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
VISUAL FIELD DEFECT			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
TREMOR			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
SOMNOLENCE			
subjects affected / exposed	1 / 8 (12.50%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
Blood and lymphatic system disorders			
LYMPHADENOPATHY			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
ANAEMIA			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
BONE MARROW FAILURE			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
BONE MARROW OEDEMA SYNDROME			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
EXTRAMEDULLARY HAEMOPOIESIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	2 / 9 (22.22%)
occurrences (all)	0	1	2
LEUKOCYTOSIS			

subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
LYMPH NODE PAIN			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
SPLENOMEGALY			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
DEAFNESS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
VERTIGO			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
TINNITUS			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	2 / 9 (22.22%)
occurrences (all)	0	2	2
EXTERNAL EAR INFLAMMATION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
EAR PAIN			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Eye disorders			
CONJUNCTIVAL HAEMORRHAGE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
BLEPHARITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
CONJUNCTIVITIS			

subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
DACRYOSTENOSIS ACQUIRED			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
CONJUNCTIVITIS ALLERGIC			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
EYE PAIN			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
EYE SWELLING			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PTERYGIUM			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PINGUECULA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
OCULAR HYPERAEMIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
LACRIMATION INCREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
LACRIMAL DISORDER			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
DENTAL CARIES			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
CONSTIPATION			
subjects affected / exposed	0 / 8 (0.00%)	3 / 9 (33.33%)	1 / 9 (11.11%)
occurrences (all)	0	3	1

COLITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
ANAL PRURITUS			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
ABDOMINAL PAIN UPPER			
subjects affected / exposed	2 / 8 (25.00%)	5 / 9 (55.56%)	1 / 9 (11.11%)
occurrences (all)	5	6	1
ABDOMINAL PAIN LOWER			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
ABDOMINAL PAIN			
subjects affected / exposed	2 / 8 (25.00%)	3 / 9 (33.33%)	0 / 9 (0.00%)
occurrences (all)	2	5	0
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
DENTAL DISCOMFORT			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
LIP DISCOLOURATION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HYPERCHLORHYDRIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HAEMATOCHEZIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
GINGIVAL BLEEDING			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
GASTROOESOPHAGEAL REFLUX DISEASE			

subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
GASTROINTESTINAL DISORDER			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
GASTRITIS HAEMORRHAGIC			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
GASTRITIS EROSIVE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
FOOD POISONING			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
FAECALOMA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
DYSPEPSIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	2 / 9 (22.22%)
occurrences (all)	0	2	2
DUODENOGASTRIC REFLUX			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
DIARRHOEA			
subjects affected / exposed	2 / 8 (25.00%)	4 / 9 (44.44%)	1 / 9 (11.11%)
occurrences (all)	2	6	1
HAEMORRHOIDS			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
VOMITING			
subjects affected / exposed	1 / 8 (12.50%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
TEETHING			
subjects affected / exposed	1 / 8 (12.50%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
STOMATITIS			

subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
RECTAL HAEMORRHAGE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PAROTID GLAND ENLARGEMENT			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PARAESTHESIA ORAL			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
ORAL DISORDER			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
OESOPHAGITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ODYNOPHAGIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
NAUSEA			
subjects affected / exposed	1 / 8 (12.50%)	3 / 9 (33.33%)	1 / 9 (11.11%)
occurrences (all)	2	6	1
MOUTH ULCERATION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
MOUTH HAEMORRHAGE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
TOOTHACHE			
subjects affected / exposed	1 / 8 (12.50%)	4 / 9 (44.44%)	1 / 9 (11.11%)
occurrences (all)	1	8	2
Hepatobiliary disorders			
PORTAL HYPERTENSION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

HEPATOCELLULAR INJURY			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
GALLBLADDER POLYP			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
CHOLESTASIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
BILIARY DILATATION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SEBORRHOEIC DERMATITIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
RASH			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PURPURA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PRURITUS			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	1 / 9 (11.11%)
occurrences (all)	0	3	1
PETECHIAE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
PAPULE			

subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
NIGHT SWEATS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HYPERHIDROSIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
HIRSUTISM			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
HAIR TEXTURE ABNORMAL			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
ERYTHEMA			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
DERMATITIS			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
SKIN DISCOLOURATION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
DERMAL CYST			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SKIN HAEMORRHAGE			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
SKIN LESION			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
SKIN ULCER			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
SPIDER NAEVUS			

subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
URTICARIA			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Renal and urinary disorders			
LEUKOCYTURIA			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
HAEMATURIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
DYSURIA			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
CYSTITIS HAEMORRHAGIC			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
MICROALBUMINURIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
URINARY RETENTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
STRANGURY			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
RENAL CYST			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
RENAL COLIC			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
PROTEINURIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	1	1

POLYURIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
POLLAKIURIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
NEPHROPATHY			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
NEPHROLITHIASIS			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	2 / 9 (22.22%)
occurrences (all)	0	2	2
Endocrine disorders			
THYROIDITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
THYROID CYST			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HYPERTHYROIDISM			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
HYPERPROLACTINAEMIA			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
AUTOIMMUNE THYROIDITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
FLANK PAIN			
subjects affected / exposed	2 / 8 (25.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	2	1	0
COCCYDYNIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
BONE PAIN			

subjects affected / exposed	4 / 8 (50.00%)	6 / 9 (66.67%)	4 / 9 (44.44%)
occurrences (all)	10	13	12
BONE DISORDER			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
BACK PAIN			
subjects affected / exposed	3 / 8 (37.50%)	7 / 9 (77.78%)	3 / 9 (33.33%)
occurrences (all)	3	15	11
ARTHRITIS			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	1 / 9 (11.11%)
occurrences (all)	0	4	1
ARTHRALGIA			
subjects affected / exposed	5 / 8 (62.50%)	6 / 9 (66.67%)	2 / 9 (22.22%)
occurrences (all)	11	10	3
NECK PAIN			
subjects affected / exposed	1 / 8 (12.50%)	3 / 9 (33.33%)	0 / 9 (0.00%)
occurrences (all)	2	3	0
MYALGIA			
subjects affected / exposed	2 / 8 (25.00%)	2 / 9 (22.22%)	2 / 9 (22.22%)
occurrences (all)	2	2	3
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 8 (0.00%)	4 / 9 (44.44%)	0 / 9 (0.00%)
occurrences (all)	0	6	0
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	1 / 8 (12.50%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	2	2	0
MUSCLE SPASMS			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
LIGAMENT DISORDER			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
JOINT SWELLING			

subjects affected / exposed	1 / 8 (12.50%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	1	2	0
JOINT STIFFNESS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
JOINT RANGE OF MOTION DECREASED			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
JOINT EFFUSION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
INTERVERTEBRAL DISC DEGENERATION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
OSTEONECROSIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
GROIN PAIN			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
SPONDYLOLISTHESIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
TEMPOROMANDIBULAR JOINT SYNDROME			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
TENDON PAIN			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
TENDONITIS			

subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	3
OSTEOPENIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
OSTEOPOROSIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PAIN IN EXTREMITY			
subjects affected / exposed	3 / 8 (37.50%)	3 / 9 (33.33%)	3 / 9 (33.33%)
occurrences (all)	8	11	6
PAIN IN JAW			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	6	0	2
PERIARTHRITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
SENSATION OF HEAVINESS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
CYTOMEGALOVIRUS INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
CYSTITIS			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
CONJUNCTIVITIS VIRAL			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
BRONCHITIS			
subjects affected / exposed	0 / 8 (0.00%)	4 / 9 (44.44%)	1 / 9 (11.11%)
occurrences (all)	0	4	3
BODY TINEA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

EAR INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
ACUTE SINUSITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ACNE PUSTULAR			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ACUTE TONSILLITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	6
GASTROINTESTINAL INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
GINGIVAL INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
GINGIVITIS			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	0	2	0
HELICOBACTER INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
HORDEOLUM			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
INFECTED BITES			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
INFECTED SKIN ULCER			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
INFLUENZA			
subjects affected / exposed	0 / 8 (0.00%)	5 / 9 (55.56%)	1 / 9 (11.11%)
occurrences (all)	0	6	1

KLEBSIELLA INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
ESCHERICHIA URINARY TRACT INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	3
EYE INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
EYELID INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
FOLLICULITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
GASTROENTERITIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	1	2
GASTROENTERITIS VIRAL			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
PARAINFLUENZAE VIRUS INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
TINEA PEDIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
ORAL HERPES			
subjects affected / exposed	2 / 8 (25.00%)	4 / 9 (44.44%)	1 / 9 (11.11%)
occurrences (all)	2	5	1
ONYCHOMYCOSIS			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
NASOPHARYNGITIS			

subjects affected / exposed	2 / 8 (25.00%)	1 / 9 (11.11%)	2 / 9 (22.22%)
occurrences (all)	4	1	3
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	1 / 9 (11.11%)
occurrences (all)	0	3	1
PARONYCHIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
PERIODONTITIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
PHARYNGITIS			
subjects affected / exposed	1 / 8 (12.50%)	2 / 9 (22.22%)	2 / 9 (22.22%)
occurrences (all)	1	2	5
PNEUMONIA VIRAL			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
RHINITIS			
subjects affected / exposed	1 / 8 (12.50%)	3 / 9 (33.33%)	1 / 9 (11.11%)
occurrences (all)	1	4	2
SINUSITIS			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	1 / 9 (11.11%)
occurrences (all)	0	3	3
OTITIS EXTERNA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
UPPER RESPIRATORY TRACT INFECTION			

subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	2 / 9 (22.22%)
occurrences (all)	0	19	10
TROPICAL ULCER			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
TRACHEITIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
TOOTH INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
TOOTH ABSCESS			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	2 / 9 (22.22%)
occurrences (all)	0	3	2
TONSILLITIS			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	1 / 9 (11.11%)
occurrences (all)	0	2	2
VULVOVAGINAL MYCOTIC INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
VULVOVAGINAL CANDIDIASIS			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
VIRAL INFECTION			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
VAGINAL INFECTION			

subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
URINARY TRACT INFECTION FUNGAL			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
URINARY TRACT INFECTION BACTERIAL			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 8 (12.50%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	2	0	0
FOLATE DEFICIENCY			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
VITAMIN D DEFICIENCY			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
IRON OVERLOAD			
subjects affected / exposed	1 / 8 (12.50%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	1	1	0
HYPOMAGNESAEMIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 8 (0.00%)	1 / 9 (11.11%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
HYPERURICAEMIA			
subjects affected / exposed	0 / 8 (0.00%)	0 / 9 (0.00%)	2 / 9 (22.22%)
occurrences (all)	0	0	2
GOUT			
subjects affected / exposed	0 / 8 (0.00%)	2 / 9 (22.22%)	0 / 9 (0.00%)
occurrences (all)	0	5	0

Non-serious adverse events	Dose Level 3: 0.75 mg/kg	Dose Level 2: 0.5 mg/kg	
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	12 / 12 (100.00%)	8 / 8 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
HAEMANGIOMA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
HAEMANGIOMA OF LIVER			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
LIPOMA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
MELANOCYTIC NAEVUS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
THYROID NEOPLASM			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
HAEMATOMA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
HOT FLUSH			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
HYPERTENSION			
subjects affected / exposed	5 / 12 (41.67%)	3 / 8 (37.50%)	
occurrences (all)	10	3	
HYPOTENSION			
subjects affected / exposed	0 / 12 (0.00%)	2 / 8 (25.00%)	
occurrences (all)	0	3	
PREHYPERTENSION			

subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
THROMBOPHLEBITIS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
VENOUS RECANALISATION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
CHEST DISCOMFORT			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
ASTHENIA			
subjects affected / exposed	5 / 12 (41.67%)	4 / 8 (50.00%)	
occurrences (all)	8	4	
MALAISE			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
LOCALISED OEDEMA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
LOCAL SWELLING			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	
occurrences (all)	1	2	
IRRITABILITY			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
INJECTION SITE INFLAMMATION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
INJECTION SITE ERYTHEMA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
INFLUENZA LIKE ILLNESS			

subjects affected / exposed	1 / 12 (8.33%)	3 / 8 (37.50%)	
occurrences (all)	1	14	
GRANULOMA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
GENERALISED OEDEMA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
FATIGUE			
subjects affected / exposed	2 / 12 (16.67%)	4 / 8 (50.00%)	
occurrences (all)	2	6	
CYST			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
CHILLS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
CHEST PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
MUCOSAL HYPERAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
OEDEMA PERIPHERAL			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
PAIN			
subjects affected / exposed	1 / 12 (8.33%)	2 / 8 (25.00%)	
occurrences (all)	1	3	
VACCINATION SITE WARMTH			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
VACCINATION SITE SWELLING			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
VACCINATION SITE PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
VACCINATION SITE LYMPHADENOPATHY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
VACCINATION SITE ERYTHEMA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
PYREXIA			
subjects affected / exposed	3 / 12 (25.00%)	2 / 8 (25.00%)	
occurrences (all)	9	7	
DEFICIT FOLATE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
ALLERGY TO ARTHROPOD STING			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
ALLOIMMUNISATION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
SEASONAL ALLERGY			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
HYPERSENSITIVITY			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
DRUG HYPERSENSITIVITY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
ANAPHYLACTIC REACTION			

subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Social circumstances			
MENOPAUSE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
EPIDIDYMITIS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
ERECTILE DYSFUNCTION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
CYSTOCELE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
BREAST CYST			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
AMENORRHOEA			
subjects affected / exposed	2 / 12 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
DYSMENORRHOEA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
UTERINE PROLAPSE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
PROSTATOMEGALY			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
PELVIC PAIN			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
OVARIAN CYST			

subjects affected / exposed	2 / 12 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
OLIGOMENORRHOEA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
EPISTAXIS			
subjects affected / exposed	4 / 12 (33.33%)	1 / 8 (12.50%)	
occurrences (all)	4	1	
DYSPNOEA EXERTIONAL			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
DYSPNOEA			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
DYSPHONIA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
COUGH			
subjects affected / exposed	3 / 12 (25.00%)	5 / 8 (62.50%)	
occurrences (all)	8	12	
BRONCHOSPASM			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
ASTHMATIC CRISIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
ASTHMA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
ALLERGIC RESPIRATORY DISEASE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
HAEMOPTYSIS			

subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
YAWNING			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
WHEEZING			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
SNEEZING			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
RHINORRHOEA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
RHINITIS ALLERGIC			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
LUNG CYST			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
PULMONARY MASS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
PRODUCTIVE COUGH			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
PNEUMONITIS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
PLEURAL EFFUSION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
OROPHARYNGEAL PAIN			
subjects affected / exposed	4 / 12 (33.33%)	4 / 8 (50.00%)	
occurrences (all)	10	5	
NASAL CONGESTION			

subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	3	0	
RESPIRATORY TRACT CONGESTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
STRESS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
LIBIDO DECREASED			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
DEPRESSION			
subjects affected / exposed	0 / 12 (0.00%)	2 / 8 (25.00%)	
occurrences (all)	0	2	
BRUXISM			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
ANXIETY			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
INSOMNIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Investigations			
EJECTION FRACTION DECREASED			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
ELECTROCARDIOGRAM T WAVE ABNORMAL			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
CREATININE RENAL CLEARANCE DECREASED			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
CARDIAC INDEX INCREASED			

subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
BLOOD PRESSURE INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
BLOOD FOLLICLE STIMULATING HORMONE DECREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
BLOOD FOLATE DECREASED			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
ELECTROCARDIOGRAM QT SHORTENED			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
CULTURE STOOL POSITIVE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
WEIGHT INCREASED			

subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
WEIGHT DECREASED				
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)		
occurrences (all)	1	1		
VITAMIN D DECREASED				
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
URINE PROTEIN/CREATININE RATIO INCREASED				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
ULTRASOUND SCAN ABNORMAL				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
ULTRASOUND LIVER ABNORMAL				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
SERUM FERRITIN INCREASED				
subjects affected / exposed	2 / 12 (16.67%)	0 / 8 (0.00%)		
occurrences (all)	3	0		
PLATELET COUNT INCREASED				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		
PANCREATIC ENZYMES INCREASED				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		
HEPATIC ENZYME INCREASED				
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
GLOMERULAR FILTRATION RATE DECREASED				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		
FIBRIN D DIMER INCREASED				

subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
ESCHERICHIA TEST POSITIVE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
ARTHROPOD BITE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
CHEST INJURY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
CONTUSION			
subjects affected / exposed	0 / 12 (0.00%)	2 / 8 (25.00%)	
occurrences (all)	0	3	
EPICONDYLITIS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
FALL			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
FOOT FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
LIMB INJURY			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
LIGAMENT SPRAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
LACERATION			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
HUMERUS FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
HAEMOLYTIC TRANSFUSION REACTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
FRACTURED SACRUM			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
FRACTURE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
ARTHROPOD STING			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
MENISCUS INJURY			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
MUSCLE STRAIN			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
NAIL INJURY			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
OVERDOSE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
PATELLA FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
POST-TRAUMATIC PAIN			
subjects affected / exposed	0 / 12 (0.00%)	2 / 8 (25.00%)	
occurrences (all)	0	2	

REPETITIVE STRAIN INJURY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
RIB FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
SOFT TISSUE INJURY			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
TENDON RUPTURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
THERMAL BURN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
TOOTH INJURY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
TRANSFUSION REACTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
VACCINATION COMPLICATION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
WRIST FRACTURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Congenital, familial and genetic disorders			
BENIGN FAMILIAL HAEMATURIA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Cardiac disorders			
SPLINTER HAEMORRHAGES			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
TACHYCARDIA			

subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
VENTRICULAR ARRHYTHMIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
VENTRICULAR EXTRASYSTOLES			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
PERICARDIAL EFFUSION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
PALPITATIONS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
LEFT VENTRICULAR DYSFUNCTION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
LEFT ATRIAL DILATATION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
EXTRASYSTOLES			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
SINUS HEADACHE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
SCIATICA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	3	0	
PRESYNCOPE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
MIGRAINE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	

HYPERAESTHESIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
HEADACHE			
subjects affected / exposed	9 / 12 (75.00%)	5 / 8 (62.50%)	
occurrences (all)	43	26	
FACIAL NEURALGIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
DYSGEUSIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
DYSARTHRIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
DIZZINESS			
subjects affected / exposed	2 / 12 (16.67%)	3 / 8 (37.50%)	
occurrences (all)	2	7	
CERVICOBRACHIAL SYNDROME			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
AGEUSIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
VISUAL FIELD DEFECT			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
TREMOR			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
SOMNOLENCE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
LYMPHADENOPATHY			

subjects affected / exposed	2 / 12 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
ANAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
BONE MARROW FAILURE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
BONE MARROW OEDEMA SYNDROME			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
EXTRAMEDULLARY HAEMOPOIESIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
LEUKOCYTOSIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
LYMPH NODE PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
SPLENOMEGALY			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
DEAFNESS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
VERTIGO			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	
occurrences (all)	1	2	
TINNITUS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	

EXTERNAL EAR INFLAMMATION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
EAR PAIN			
subjects affected / exposed	2 / 12 (16.67%)	1 / 8 (12.50%)	
occurrences (all)	2	1	
Eye disorders			
CONJUNCTIVAL HAEMORRHAGE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
BLEPHARITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
CONJUNCTIVITIS			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
DACRYOSTENOSIS ACQUIRED			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
CONJUNCTIVITIS ALLERGIC			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
EYE PAIN			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
EYE SWELLING			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
PTERYGIUM			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
PINGUECULA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
OCULAR HYPERAEMIA			

subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
LACRIMATION INCREASED			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
LACRIMAL DISORDER			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
DENTAL CARIES			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
CONSTIPATION			
subjects affected / exposed	2 / 12 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	5	0	
COLITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
ANAL PRURITUS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	4 / 12 (33.33%)	1 / 8 (12.50%)	
occurrences (all)	6	1	
ABDOMINAL PAIN LOWER			
subjects affected / exposed	2 / 12 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	3	0	
ABDOMINAL PAIN			
subjects affected / exposed	1 / 12 (8.33%)	3 / 8 (37.50%)	
occurrences (all)	7	4	
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
DENTAL DISCOMFORT			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	

LIP DISCOLOURATION				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		
HYPERCHLORHYDRIA				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		
HAEMATOCHEZIA				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	4	0		
GINGIVAL BLEEDING				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		
GASTROOESOPHAGEAL REFLUX DISEASE				
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)		
occurrences (all)	2	1		
GASTROINTESTINAL DISORDER				
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
GASTRITIS HAEMORRHAGIC				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
GASTRITIS EROSIVE				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
FOOD POISONING				
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
FAECALOMA				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		
DYSPEPSIA				
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)		
occurrences (all)	1	1		
DUODENOGASTRIC REFLUX				

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
DIARRHOEA			
subjects affected / exposed	2 / 12 (16.67%)	1 / 8 (12.50%)	
occurrences (all)	5	2	
HAEMORRHOIDS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
VOMITING			
subjects affected / exposed	2 / 12 (16.67%)	2 / 8 (25.00%)	
occurrences (all)	5	3	
TEETHING			
subjects affected / exposed	0 / 12 (0.00%)	2 / 8 (25.00%)	
occurrences (all)	0	2	
STOMATITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
RECTAL HAEMORRHAGE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
PAROTID GLAND ENLARGEMENT			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
PARAESTHESIA ORAL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
ORAL DISORDER			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
OESOPHAGITIS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
ODYNOPHAGIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
NAUSEA			

subjects affected / exposed	3 / 12 (25.00%)	4 / 8 (50.00%)	
occurrences (all)	7	4	
MOUTH ULCERATION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
MOUTH HAEMORRHAGE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
TOOTHACHE			
subjects affected / exposed	1 / 12 (8.33%)	3 / 8 (37.50%)	
occurrences (all)	2	5	
Hepatobiliary disorders			
PORTAL HYPERTENSION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
HEPATOCELLULAR INJURY			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
GALLBLADDER POLYP			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
CHOLESTASIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
BILIARY DILATATION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
SEBORRHOEIC DERMATITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
RASH MACULO-PAPULAR			

subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
RASH			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
PURPURA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
PRURITUS			
subjects affected / exposed	2 / 12 (16.67%)	1 / 8 (12.50%)	
occurrences (all)	3	1	
PETECHIAE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
PAPULE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
NIGHT SWEATS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
HYPERHIDROSIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
HIRSUTISM			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
HAIR TEXTURE ABNORMAL			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
ERYTHEMA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
DERMATITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
SKIN DISCOLOURATION			

subjects affected / exposed	0 / 12 (0.00%)	2 / 8 (25.00%)	
occurrences (all)	0	2	
DERMAL CYST			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
SKIN HAEMORRHAGE			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
SKIN LESION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
SKIN ULCER			
subjects affected / exposed	0 / 12 (0.00%)	2 / 8 (25.00%)	
occurrences (all)	0	2	
SPIDER NAEVUS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
URTICARIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
LEUKOCYTURIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
HAEMATURIA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
DYSURIA			
subjects affected / exposed	2 / 12 (16.67%)	2 / 8 (25.00%)	
occurrences (all)	2	2	
CYSTITIS HAEMORRHAGIC			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
MICROALBUMINURIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	

URINARY RETENTION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
STRANGURY			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
RENAL CYST			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
RENAL COLIC			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
PROTEINURIA			
subjects affected / exposed	0 / 12 (0.00%)	2 / 8 (25.00%)	
occurrences (all)	0	2	
POLYURIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
POLLAKIURIA			
subjects affected / exposed	2 / 12 (16.67%)	2 / 8 (25.00%)	
occurrences (all)	3	2	
NEPHROPATHY			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
NEPHROLITHIASIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
THYROIDITIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
THYROID CYST			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
HYPERTHYROIDISM			

subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
HYPERPROLACTINAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
AUTOIMMUNE THYROIDITIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
FLANK PAIN			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
COCCYDYNIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
BONE PAIN			
subjects affected / exposed	4 / 12 (33.33%)	4 / 8 (50.00%)	
occurrences (all)	7	9	
BONE DISORDER			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
BACK PAIN			
subjects affected / exposed	5 / 12 (41.67%)	6 / 8 (75.00%)	
occurrences (all)	7	10	
ARTHRITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
ARTHRALGIA			
subjects affected / exposed	8 / 12 (66.67%)	7 / 8 (87.50%)	
occurrences (all)	12	13	
NECK PAIN			
subjects affected / exposed	5 / 12 (41.67%)	3 / 8 (37.50%)	
occurrences (all)	9	8	
MYALGIA			

subjects affected / exposed	2 / 12 (16.67%)	4 / 8 (50.00%)	
occurrences (all)	2	6	
MUSCULOSKELETAL STIFFNESS			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
MUSCULOSKELETAL PAIN			
subjects affected / exposed	4 / 12 (33.33%)	2 / 8 (25.00%)	
occurrences (all)	9	2	
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	3 / 12 (25.00%)	1 / 8 (12.50%)	
occurrences (all)	5	1	
MUSCLE SPASMS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
LIGAMENT DISORDER			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
JOINT SWELLING			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
JOINT STIFFNESS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
JOINT RANGE OF MOTION DECREASED			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
JOINT EFFUSION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
INTERVERTEBRAL DISC PROTRUSION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
INTERVERTEBRAL DISC DEGENERATION			

subjects affected / exposed	2 / 12 (16.67%)	0 / 8 (0.00%)		
occurrences (all)	2	0		
OSTEONECROSIS				
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
GROIN PAIN				
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
SPONDYLOLISTHESIS				
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
TEMPOROMANDIBULAR JOINT SYNDROME				
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
TENDON PAIN				
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
TENDONITIS				
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)		
occurrences (all)	1	1		
OSTEOPENIA				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		
OSTEOPOROSIS				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
PAIN IN EXTREMITY				
subjects affected / exposed	5 / 12 (41.67%)	5 / 8 (62.50%)		
occurrences (all)	9	9		
PAIN IN JAW				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		
PERIARTHRITIS				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		

SENSATION OF HEAVINESS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Infections and infestations			
CYTOMEGALOVIRUS INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
CYSTITIS			
subjects affected / exposed	2 / 12 (16.67%)	1 / 8 (12.50%)	
occurrences (all)	2	2	
CONJUNCTIVITIS VIRAL			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
BRONCHITIS			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	
occurrences (all)	1	1	
BODY TINEA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
EAR INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
ACUTE SINUSITIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
ACNE PUSTULAR			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
ACUTE TONSILLITIS			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
GASTROINTESTINAL INFECTION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
GINGIVAL INFECTION			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
GINGIVITIS				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
HELICOBACTER INFECTION				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		
HORDEOLUM				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	2		
INFECTED BITES				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		
INFECTED SKIN ULCER				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
INFLUENZA				
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)		
occurrences (all)	1	1		
KLEBSIELLA INFECTION				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		
ESCHERICHIA URINARY TRACT INFECTION				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
EYE INFECTION				
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)		
occurrences (all)	1	1		
EYELID INFECTION				
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
FOLLICULITIS				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		

GASTROENTERITIS				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	2		
GASTROENTERITIS VIRAL				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		
PARAINFLUENZAE VIRUS INFECTION				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
TINEA PEDIS				
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
ORAL HERPES				
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
ONYCHOMYCOSIS				
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
NASOPHARYNGITIS				
subjects affected / exposed	1 / 12 (8.33%)	4 / 8 (50.00%)		
occurrences (all)	1	5		
LOWER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)		
occurrences (all)	1	4		
PARONYCHIA				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
PERIODONTITIS				
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
PHARYNGITIS				
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		
PNEUMONIA VIRAL				

subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)		
occurrences (all)	1	0		
RESPIRATORY TRACT INFECTION				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
RESPIRATORY TRACT INFECTION VIRAL				
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
RHINITIS				
subjects affected / exposed	1 / 12 (8.33%)	5 / 8 (62.50%)		
occurrences (all)	1	6		
SINUSITIS				
subjects affected / exposed	0 / 12 (0.00%)	2 / 8 (25.00%)		
occurrences (all)	0	7		
OTITIS EXTERNA				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	1 / 12 (8.33%)	4 / 8 (50.00%)		
occurrences (all)	4	18		
TROPICAL ULCER				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
TRACHEITIS				
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)		
occurrences (all)	0	1		
TOOTH INFECTION				
subjects affected / exposed	0 / 12 (0.00%)	2 / 8 (25.00%)		
occurrences (all)	0	2		
TOOTH ABSCESS				
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)		
occurrences (all)	0	0		
TONSILLITIS				

subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 12 (8.33%)	2 / 8 (25.00%)	
occurrences (all)	1	3	
VULVOVAGINAL MYCOTIC INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
VULVOVAGINAL CANDIDIASIS			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	2	
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
VIRAL INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
VAGINAL INFECTION			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
URINARY TRACT INFECTION FUNGAL			
subjects affected / exposed	1 / 12 (8.33%)	0 / 8 (0.00%)	
occurrences (all)	1	0	
URINARY TRACT INFECTION BACTERIAL			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 12 (8.33%)	1 / 8 (12.50%)	
occurrences (all)	1	2	
FOLATE DEFICIENCY			
subjects affected / exposed	2 / 12 (16.67%)	0 / 8 (0.00%)	
occurrences (all)	2	0	
VITAMIN D DEFICIENCY			

subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
IRON OVERLOAD			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
HYPOMAGNESAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
HYPOGLYCAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	
HYPERURICAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 8 (12.50%)	
occurrences (all)	0	1	
GOUT			
subjects affected / exposed	0 / 12 (0.00%)	0 / 8 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 May 2012	Inclusion of beta-thalassemia intermedia population - transfusion and non-transfusion dependent population; modification in the Primary and Secondary objectives, as well as efficacy assessment parameters to include beta-thalassemia intermedia non-transfusion dependent population; revised subject eligibility criteria
11 February 2013	Revised subject eligibility criteria; revised timing of data review prior to opening of Dose Level 2 (0.5 mg/kg); clarification of the DLT definition with regards to the hemoglobin levels; increase the treatment duration to a maximum total treatment period of 22 months
20 June 2013	Implementation of 3 additional dose levels (0/75 mg/kg, 1.0 mg/kg, 1.5 mg/kg); revised subject eligibility criteria; revise timing of data review prior to opening higher Dose Levels; revised exploratory assessments; clarification on hemoglobin levels
27 February 2014	Revised secondary objectives to include Patient Reported Outcome instruments to assess Quality of Life for the Expansion Cohort; possibility to perform independent dose escalation for non-transfusion dependent versus transfusion dependent subjects; modification to the dose administration and dose delay guidelines; revised subject eligibility criteria; modifications in duration of the total treatment period and introduction of a long term treatment period; implementation of optional sperm sample collection, storage, and assessment; clarification in schedule of assessments; updated pre-clinical data in introduction; updated pre-clinical toxicity findings language; increased maximum number of patients; increased total number of sites
05 September 2014	Modification of the dose delay and dose reduction guidelines with respect to hypertension; clarification on the duration of the long term treatment period; retrospective collection of available iron metabolism data; modification in teh intra-patient dose escalation criteria to allow patients who have lost their response to treatment to be dose escalated; revised quality of life assessments to include 6 minute walking test for non transfusion dependent subjects; clarification at the protocol level on subject eligibility for long term treatment period; clarifications in schedule of assessments; clarification of injection site rotation in line with IP handling and administration guidelines
01 June 2017	Extension of treatment period until commercialization and availability of a similar class of therapy; introduction of an additional blood biomarker analysis; wording updated to clarify that change in hemoglobin should be calculated based on the predose HgB from last given dose; clarification of dose delay rule for sotatercept-related toxicities ongoing at day of dosing; update of toxicology wording according to Investigator's Brochure

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to early study termination, no patients were enrolled after 1 mg/kg cohort and no patients were enrolled in Expansion Cohort. Thus, primary analyses to determine RD and secondary analysis of QoL change from baseline were not conducted.

Notes: