Clinical trial results:
A Phase IIb multicentre, double-blind, dose-ranging, randomised, placebo-controlled study evaluating safety and efficacy of BGS649 in male obese subjects with hypogonadotropic hypogonadism

Summary

EudraCT number	2015-005760-42
Trial protocol	GB ES IT
Global end of trial date	15 February 2018

Results information

Result version number	v1 (current)
This version publication date	11 January 2022
First version publication date	11 January 2022

Trial information

Trial identification

Sponsor protocol code	MBGS205

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02730169
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Mereo BioPharma 2 Ltd
Sponsor organisation address	4th Floor, 1 Cavendish Place, London, United Kingdom, W1G 0QF
Public contact	William Moore, Mereo BioPharma 2 Ltd, +44 (0) 333 023 7300, enquiries@mereobiopharma.com
Scientific contact	Jackie Parkin, Mereo BioPharma 2 Ltd, +44 (0) 333 023 7300, enquiries@mereobiopharma.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	07 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 February 2018
Global end of trial reached?	Yes
Global end of trial date	15 February 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to demonstrate the efficacy of BGS649 to normalise total testosterone levels (300-1000 ng/dL [10.4-35 nmol/L]) in ≥ 75% of subjects after 24 weeks of treatment.

Protection of trial subjects:

This study was conducted in accordance with current applicable regulations, International Council for Harmonisation (ICH) guidelines, and local legal requirements. It complies with the ethical principles described in the 18th World Medical Assembly (Helsinki 1964) and amendments of the 29th (Tokyo 1975), 35th (Venice 1983), 41st (Hong Kong 1989), and 48th (South Africa 1996) World Medical Assemblies, Declaration of Helsinki. The risk to subjects in this study were minimised by compliance with the inclusion/exclusion criteria, close clinical monitoring, including signs and symptoms related to the potential risks of aromatase inhibitors for at least 25 weeks following the last dose of study medication. Additional stringent monitoring for inclusion in the study with specific observation for any class effects was performed throughout the study.

Background therapy:

No background therapy for obesity associated hypogonadotropic hypogonadism was given as there is no approved therapy available.

Evidence for comparator:

Not applicable, placebo control used.

Actual start date of recruitment	06 June 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	United States: 259
Worldwide total number of subjects	271
EEA total number of subjects	7

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	271
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited at 76 investigator centres in 5 countries worldwide.
The target population was obese male subjects with serum testosterone concentration below the normal range and at least t2 symptoms of sexual dysfunction.

Pre-assignment

Screening details:

Subjects were screened for up to 28 days before receiving their first dose of study treatment at the randomisation visit. Of the 2103 subjects screened for the study, 271 were randomised and received study treatment (BGS649 or placebo).

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Assessor

Blinding implementation details:

Matched placebo used.

Arms

Are arms mutually exclusive?	Yes
Arm title	BGS649 0.1 mg

Arm description:

Participants received 0.1 mg BGS649 orally on Day 1. Subsequent doses with 0.1 mg BGS649 were administered orally and taken once weekly to week 24.

Arm type	Experimental
Investigational medicinal product name	BGS649
Investigational medicinal product code	
Other name	Leflutrozole
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsules of BGS649 0.1 mg, 0.3 mg, 1.0 mg or BGS649 matching placebo were taken orally by the subject, with fluids, on a weekly basis at approximately the same time of day. Treatment was self administered except on Day 1 (Baseline) and at Week 12, when it was taken by the subject at the study site.

Arm title	BGS649 0.3 mg

Arm description:

Participants received 0.3 mg BGS649 orally on Day 1. Subsequent doses with 0.3 mg BGS649 were administered orally and taken once weekly to week 24.

Arm type	Experimental
Investigational medicinal product name	BGS649
Investigational medicinal product code	
Other name	Leflutrozole
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsules of BGS649 0.1 mg, 0.3 mg, 1.0 mg or BGS649 matching placebo were taken orally by the subject, with fluids, on a weekly basis at approximately the same time of day. Treatment was self administered except on Day 1 (Baseline) and at Week 12, when it was taken by the subject at the study site.

Arm title	BGS649 1.0 mg

Arm description:

Participants received 1.0 mg BGS649 orally on Day 1. Subsequent doses with 1.0 mg BGS649 were administered orally and taken once weekly to week 24.

Arm type	Experimental
Investigational medicinal product name	BGS649
Investigational medicinal product code	
Other name	Leflutrozole
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsules of BGS649 0.1 mg, 0.3 mg, 1.0 mg or BGS649 matching placebo were taken orally by the subject, with fluids, on a weekly basis at approximately the same time of day. Treatment was self administered except on Day 1 (Baseline) and at Week 12, when it was taken by the subject at the study site.

Arm title	BGS649 Placebo

Arm description:

Participants received BGS649 placebo orally on Day 1. Subsequent doses with BGS649 placebo were administered orally and taken once weekly to week 24.

Arm type	Experimental
Investigational medicinal product name	BGS649
Investigational medicinal product code	
Other name	Leflutrozole
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Capsules of BGS649 0.1 mg, 0.3 mg, 1.0 mg or BGS649 matching placebo were taken orally by the subject, with fluids, on a weekly basis at approximately the same time of day. Treatment was self administered except on Day 1 (Baseline) and at Week 12, when it was taken by the subject at the study site.

Number of subjects in period 1	BGS649 0.1 mg	BGS649 0.3 mg	BGS649 1.0 mg
Started	67	66	67
Completed	52	41	42
Not completed	15	25	25
Consent withdrawn by subject	5	11	5
Adverse event, non-fatal	6	8	13
Not Specified	2	-	2
Discontinuation criteria met as per protocol	1	1	-
Lost to follow-up	1	4	5
Protocol deviation	-	1	-

Number of subjects in period 1	BGS649 Placebo
Started	71
Completed	55
Not completed	16

Consent withdrawn by subject	7
Adverse event, non-fatal	2
Not Specified	1
Discontinuation criteria met as per protocol	-
Lost to follow-up	5
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial (overall period)

Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	271	271	
Age categorical Units: Subjects			
Adults (18-64 years)	271	271	
Age continuous Units: years			
arithmetic mean	50.8		
standard deviation	± 8.69	-	
Gender categorical Units: Subjects			
Male	271	271	

Subject analysis sets	
Subject analysis set title	BGS649 0.1 mg
Subject analysis set type	Full analysis

Subject analysis set description:

BGS649 0.1 mg weekly (1 BGS649 0.1 mg capsule and 2 indistinguishable placebo capsules)

BGS649: Capsules will be taken weekly for a maximum of 24 weeks

Subject analysis set title	BGS649 0.3 mg
Subject analysis set type	Full analysis

Subject analysis set description:

BGS649 0.3 mg weekly (3 BGS649 0.1 mg capsules)

BGS649: Capsules will be taken weekly for a maximum of 24 weeks

Subject analysis set title	BGS649 1.0 mg
Subject analysis set type	Full analysis

Subject analysis set description:

BGS649 1.0 mg weekly (1 BGS649 1.0 mg capsule and 2 indistinguishable placebo capsules)

BGS649: Capsules will be taken weekly for a maximum of 24 weeks

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo weekly (3 indistinguishable placebo capsules)

Placebo: Capsules will be taken weekly for a maximum of 24 weeks

Reporting group values	BGS649 0.1 mg	BGS649 0.3 mg	BGS649 1.0 mg
Number of subjects	67	66	67

Age categorical Units: Subjects			
Adults (18-64 years)	67	66	67
Age continuous Units: years			
arithmetic mean	51.4	51.6	49.6
standard deviation	± 8.39	± 7.31	± 9.72
Gender categorical Units: Subjects			
Male	67	66	67

Reporting group values	Placebo		
Number of subjects	71		
Age categorical Units: Subjects			
Adults (18-64 years)	71		
Age continuous Units: years			
arithmetic mean	50.9		
standard deviation	± 9.17		
Gender categorical Units: Subjects			
Male	71		

End points

End points reporting groups

Reporting group title	BGS649 0.1 mg

Reporting group description:

Participants received 0.1 mg BGS649 orally on Day 1. Subsequent doses with 0.1 mg BGS649 were administered orally and taken once weekly to week 24.

Reporting group title	BGS649 0.3 mg

Reporting group description:

Participants received 0.3 mg BGS649 orally on Day 1. Subsequent doses with 0.3 mg BGS649 were administered orally and taken once weekly to week 24.

Reporting group title	BGS649 1.0 mg

Reporting group description:

Participants received 1.0 mg BGS649 orally on Day 1. Subsequent doses with 1.0 mg BGS649 were administered orally and taken once weekly to week 24.

Reporting group title	BGS649 Placebo

Reporting group description:

Participants received BGS649 placebo orally on Day 1. Subsequent doses with BGS649 placebo were administered orally and taken once weekly to week 24.

Subject analysis set title	BGS649 0.1 mg
Subject analysis set type	Full analysis

Subject analysis set description:

BGS649 0.1 mg weekly (1 BGS649 0.1 mg capsule and 2 indistinguishable placebo capsules)

BGS649: Capsules will be taken weekly for a maximum of 24 weeks

Subject analysis set title	BGS649 0.3 mg
Subject analysis set type	Full analysis

Subject analysis set description:

BGS649 0.3 mg weekly (3 BGS649 0.1 mg capsules)

BGS649: Capsules will be taken weekly for a maximum of 24 weeks

Subject analysis set title	BGS649 1.0 mg
Subject analysis set type	Full analysis

Subject analysis set description:

BGS649 1.0 mg weekly (1 BGS649 1.0 mg capsule and 2 indistinguishable placebo capsules)

BGS649: Capsules will be taken weekly for a maximum of 24 weeks

Subject analysis set title	Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

Placebo weekly (3 indistinguishable placebo capsules)

Placebo: Capsules will be taken weekly for a maximum of 24 weeks

Primary: Normalisation of total testosterone levels in ≥ 75% of subjects at Week 24

End point title	Normalisation of total testosterone levels in ≥ 75% of subjects at Week 24

End point description:

End point type	Primary

End point timeframe:

Baseline to week 24

End point values	BGS649 0.1 mg	BGS649 0.3 mg	BGS649 1.0 mg	Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	67	66	67	71
Units: Number of subjects	59	62	63	7

Statistical analyses

Statistical analysis title	Comparison of active groups to placebo

Statistical analysis description:

Intention to Treat population using last observation carried forward imputation for missing data and analysed Fisher's exact test.

Comparison groups	Placebo v BGS649 0.1 mg v BGS649 0.3 mg v BGS649 1.0 mg
Number of subjects included in analysis	271
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	Fisher exact

Notes:

[1] - For all active groups versus placebo.

Secondary: Normalisation of total testosterone levels in ≥ 90% of subjects at Week 24

End point title	Normalisation of total testosterone levels in ≥ 90% of subjects at Week 24

End point description:

End point type	Secondary

End point timeframe:

Baseline to week 24

End point values	BGS649 0.1 mg	BGS649 0.3 mg	BGS649 1.0 mg	Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	67	66	67	71
Units: Number of subjects	59	62	63	7

Statistical analyses

Statistical analysis title	Comparison of active groups to placebo

Statistical analysis description:

Intention to Treat population using last observation carried forward imputation for missing data and analysed Fisher's exact test.

Comparison groups	BGS649 0.1 mg v BGS649 0.3 mg v BGS649 1.0 mg v Placebo
Number of subjects included in analysis	271
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	Fisher exact

Notes:

[2] - For all active groups versus placebo.

Secondary: Change of LH to 24 weeks

End point title	Change of LH to 24 weeks

End point description:

End point type	Secondary

End point timeframe:

Baseline to week 24

End point values	BGS649 0.1 mg	BGS649 0.3 mg	BGS649 1.0 mg	Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	67	66	67	71
Units: mIU/mL				
number (not applicable)	2.108	3.560	5.209	-0.043

Statistical analyses

Statistical analysis title	Comparison of active groups to placebo

Statistical analysis description:

A mixed model for repeated measures (MMRN) with change from baseline as the outcome and treatment, visit, treatment by visit interaction, baseline value and baseline by visit interaction as covariates.

Comparison groups	BGS649 0.1 mg v BGS649 0.3 mg v BGS649 1.0 mg v Placebo
Number of subjects included in analysis	271
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [3]
Method	Mixed models analysis

Notes:

[3] - P value for all active groups versus placebo.

Secondary: Change of FSH to 24 weeks

End point title	Change of FSH to 24 weeks

End point description: Change in FSH	
End point type	Secondary
End point timeframe: Baseline to week 24	

End point values	BGS649 0.1 mg	BGS649 0.3 mg	BGS649 1.0 mg	Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	67	66	67	71
Units: mIU/mL				
number (not applicable)	4.836	6.183	8.282	0.038

Statistical analyses

Statistical analysis title	Comparison of active groups to placebo
Comparison groups	BGS649 0.1 mg v BGS649 0.3 mg v BGS649 1.0 mg v Placebo
Number of subjects included in analysis	271
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [4]
Method	Mixed models analysis

Notes:
[4] - For all active groups versus placebo.

Secondary: Population PK analysis	
End point title	Population PK analysis
End point description: Population PK analysis (Week 12, pre-dose and 1 hour post-dose and EOT at Week 24).	
End point type	Secondary
End point timeframe: Week 12, pre-dose and 1 hour post-dose and EOT at Week 24.	

End point values	BGS649 0.1 mg	BGS649 0.3 mg	BGS649 1.0 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	64	59	65	
Units: ng/mL				
geometric mean (confidence interval 95%)				
Week 12 Pre-dose	0.73 (0.64 to 0.83)	2.55 (2.33 to 2.80)	8.93 (8.29 to 9.62)	
Week 12 1h Post-Dose	1.43 (1.24 to 1.65)	4.39 (3.89 to 4.97)	14.91 (13.52 to 16.45)	

Week 24 EOT	0.78 (0.64 to 0.97)	2.76 (2.14 to 3.57)	9.10 (7.61 to 10.89)	

Statistical analyses

No statistical analyses for this end point

Secondary: PK analysis of semen BGS649 concentrations

End point title	PK analysis of semen BGS649 concentrations
End point description:	
PK analysis of semen BGS649 concentrations at Visit 8 (EOT at Week 24).	
End point type	Secondary
End point timeframe:	
Visit 8 (EOT at Week 24).	

End point values	BGS649 0.1 mg	BGS649 0.3 mg	BGS649 1.0 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	64	59	65	
Units: ng/mL				
geometric mean (confidence interval 95%)				
Week 24 EOT	0.49 (0.42 to 0.58)	1.58 (1.19 to 2.08)	5.28 (4.16 to 6.71)	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time to first normal testosterone level

End point title	Time to first normal testosterone level
End point description:	
End point type	Other pre-specified
End point timeframe:	
Over study period to week 24	

End point values	BGS649 0.1 mg	BGS649 0.3 mg	BGS649 1.0 mg	Placebo
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	67	66	67	71
Units: Days				
number (not applicable)	7	7	7	111

Statistical analyses

Statistical analysis title	Comparison of active groups to placebo
Comparison groups	BGS649 0.1 mg v BGS649 0.3 mg v BGS649 1.0 mg v Placebo
Number of subjects included in analysis	271
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [5]
Method	Kaplan-Meier

Notes:

[5] - P less than 0.001 compared to placebo for all active arm

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were recorded from signing the informed consent to completion of the 90 day follow-up period after last administration of study drug.

Adverse event reporting additional description:

At each visit the investigator had to document any occurrence of adverse events and abnormal laboratory findings. Any event spontaneously reported by the participant or observed by the investigator was recorded, irrespective of the relation to study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	BGS649 0.1 mg

Reporting group description:

Participants received 0.1 mg BGS649 orally on Day 1. Subsequent doses with 0.1 mg BGS649 were administered orally and taken once weekly to week 24.

Reporting group title	BGS649 0.3 mg

Reporting group description:

Participants received 0.3 mg BGS649 orally on Day 1. Subsequent doses with 0.3 mg BGS649 were administered orally and taken once weekly to week 24.

Reporting group title	BGS649 1.0 mg

Reporting group description:

Participants received 1.0 mg BGS649 orally on Day 1. Subsequent doses with 1.0 mg BGS649 were administered orally and taken once weekly to week 24.

Reporting group title	Placebo

Reporting group description:

Participants received placebo orally on Day 1. Subsequent doses with placebo were administered orally and taken once weekly to week 24.

Serious adverse events	BGS649 0.1 mg	BGS649 0.3 mg	BGS649 1.0 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 67 (2.99%)	2 / 66 (3.03%)	5 / 67 (7.46%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Skull fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (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
Vascular disorders			

Hypertension			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (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
Cardiac disorders			
Cardiac arrest			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (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			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (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
General disorders and administration site conditions			
Chest pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Anaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Intestinal perforation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (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
Skin and subcutaneous tissue disorders			
Diabetic foot			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (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			
Back pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (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
Gouty arthritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Postoperative wound infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (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
Diverticulitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (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
Osteomyelitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (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
Pyelonephritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (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
Sepsis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 71 (7.04%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Skull fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac arrest			
alternative assessment type: Non-			

systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Syncope				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chest pain				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				

Intestinal perforation				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Respiratory failure				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Diabetic foot				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ureterolithiasis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
alternative assessment type: Non-systematic				

subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gouty arthritis				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Postoperative wound infection				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arthritis infective				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
alternative assessment type: Non-systematic				

subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	BGS649 0.1 mg	BGS649 0.3 mg	BGS649 1.0 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 67 (55.22%)	39 / 66 (59.09%)	47 / 67 (70.15%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Seborrhoeic keratosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Squamous cell carcinoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			

Hypertension			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 67 (2.99%)	2 / 66 (3.03%)	5 / 67 (7.46%)
occurrences (all)	2	2	5
Haematoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Hot flush			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	4 / 66 (6.06%)	1 / 67 (1.49%)
occurrences (all)	1	4	1
Chest pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	1 / 67 (1.49%)
occurrences (all)	0	1	1
Oedema peripheral			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	1	0	1
Influenza like illness			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	1	1	0
Asthenia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Chest discomfort			
alternative assessment type: Non-			

systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Cyst			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Energy increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Oedema			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Erectile dysfunction			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	1 / 67 (1.49%)
occurrences (all)	0	1	1
Gynaecomastia			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 67 (2.99%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	2	0	0
Testicular pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	1	1	0
Breast pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Erection increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Prostatic mass			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Prostatomegaly			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Spontaneous penile erection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Testicular hypertrophy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1

Respiratory, thoracic and mediastinal disorders			
Cough			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	3 / 67 (4.48%)
occurrences (all)	1	0	3
Nasal congestion			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 67 (2.99%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	2	0	0
Oropharyngeal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	1 / 67 (1.49%)
occurrences (all)	0	1	1
Asthma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Bronchial hyperreactivity			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Pickwickian syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Productive cough			
alternative assessment type: Non-			

systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Respiratory failure			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Sinus congestion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Sleep apnoea syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	2
Psychiatric disorders			
Insomnia			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 67 (2.99%)	0 / 66 (0.00%)	2 / 67 (2.99%)
occurrences (all)	2	0	2
Depression			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	3 / 66 (4.55%)	0 / 67 (0.00%)
occurrences (all)	0	3	0
Libido decreased			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 66 (1.52%)	1 / 67 (1.49%)
occurrences (all)	1	1	1
Irritability			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Adjustment disorder with depressed mood			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Agitation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Anxiety			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Apathy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Euphoric mood			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Loss of libido			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Mood altered			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Investigations			
Haematocrit increased			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 67 (1.49%)	4 / 66 (6.06%)	5 / 67 (7.46%)
occurrences (all)	2	5	6
Prostatic specific antigen increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 67 (2.99%)	1 / 66 (1.52%)	4 / 67 (5.97%)
occurrences (all)	2	1	4
Blood triglycerides increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	2 / 66 (3.03%)	1 / 67 (1.49%)
occurrences (all)	0	2	1
Weight increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	2 / 67 (2.99%)
occurrences (all)	0	1	2
Blood creatinine increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	1	0	1
Blood pressure increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	2 / 67 (2.99%)
occurrences (all)	0	1	2
Aspartate aminotransferase increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Alanine aminotransferase increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Hepatic enzyme increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	1	0	1

Blood bilirubin increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Blood insulin increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Blood pressure decreased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Blood prolactin increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Blood urine present			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
C-reactive protein increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Electrocardiogram QT prolonged			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Glycosylated haemoglobin increased			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Heart rate irregular			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Low density lipoprotein increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Back injury			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	1 / 67 (1.49%)
occurrences (all)	0	2	1
Contusion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Fall			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	2 / 67 (2.99%)
occurrences (all)	0	0	2
Limb injury			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	2 / 67 (2.99%)
occurrences (all)	0	0	2
Muscle strain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Animal bite			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Arthropod sting			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Excoriation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Laceration			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Radius fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Tendon rupture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Thermal burn			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0

Tooth fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Cyanosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Extrasystoles			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Left ventricular hypertrophy			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	7 / 67 (10.45%)	3 / 66 (4.55%)	4 / 67 (5.97%)
occurrences (all)	8	4	4
Dizziness			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 67 (4.48%)	0 / 66 (0.00%)	2 / 67 (2.99%)
occurrences (all)	3	0	2
Paraesthesia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	1 / 67 (1.49%)
occurrences (all)	0	1	1
Syncope			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Central nervous system lesion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Complex regional pain syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Facial paralysis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Lethargy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Metabolic encephalopathy			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Migraine			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Neuralgia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Presyncope			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Primary headache associated with sexual activity			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Sensory loss			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Tremor			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Polycythaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 67 (4.48%)	2 / 66 (3.03%)	0 / 67 (0.00%)
occurrences (all)	3	2	0
Ear and labyrinth disorders			
Tinnitus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Dry eye			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	2 / 67 (2.99%)
occurrences (all)	0	0	2
Blepharitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			

Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	2 / 66 (3.03%)	1 / 67 (1.49%)
occurrences (all)	1	2	1
Constipation			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	1	0	1
Nausea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	1	0	1
Vomiting			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	1 / 67 (1.49%)
occurrences (all)	0	1	1
Abdominal discomfort			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	1	0	1
Dry mouth			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	1 / 67 (1.49%)
occurrences (all)	0	1	1
Toothache			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	2
Abdominal distension			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 66 (1.52%)	2 / 67 (2.99%)
occurrences (all)	1	1	2
Dermatitis contact			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	2	1	0
Pruritus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	2 / 67 (2.99%)
occurrences (all)	0	0	2
Alopecia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Androgenetic alopecia			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Blister			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Dermatitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Diabetic foot			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Hidradenitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Night sweats			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Onycholysis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Penile ulceration			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Seborrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1

Renal and urinary disorders			
Pollakiuria			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 66 (1.52%)	1 / 67 (1.49%)
occurrences (all)	1	1	1
Nephrolithiasis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Bladder outlet obstruction			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Calculus urinary			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Chronic kidney disease			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Glycosuria			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Haematuria			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Micturition urgency			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Nocturia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Renal cyst			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Urinary tract obstruction			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 67 (4.48%)	3 / 66 (4.55%)	1 / 67 (1.49%)
occurrences (all)	3	3	1
Back pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 67 (2.99%)	2 / 66 (3.03%)	2 / 67 (2.99%)
occurrences (all)	2	2	2
Muscle spasms			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 67 (2.99%)	2 / 66 (3.03%)	0 / 67 (0.00%)
occurrences (all)	2	2	0
Myalgia			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 67 (1.49%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	1	1	0
Pain in extremity			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	3 / 67 (4.48%)
occurrences (all)	1	0	3
Osteopenia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Bursitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Groin pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Intervertebral disc protrusion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Osteoarthritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	3
Psoriatic arthropathy			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	2	0	0
Rotator cuff syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0

Spinal column stenosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Trigger finger			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 67 (4.48%)	3 / 66 (4.55%)	2 / 67 (2.99%)
occurrences (all)	4	4	2
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 67 (2.99%)	2 / 66 (3.03%)	1 / 67 (1.49%)
occurrences (all)	2	2	1
Sinusitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	1	1	0
Influenza			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	1 / 67 (1.49%)
occurrences (all)	0	1	1
Urinary tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	2 / 66 (3.03%)	0 / 67 (0.00%)
occurrences (all)	0	2	0
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Osteomyelitis			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Pneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Sepsis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Tooth abscess			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	1	1	0
Bacterial prostatitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Ear infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0

Folliculitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Furuncle			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Gastritis viral			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis norovirus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Oral herpes			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Otitis externa			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Otitis media			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Otitis media acute			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Rash pustular			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	2
Respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Tinea pedis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Vitamin D deficiency			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 67 (2.99%)	2 / 66 (3.03%)	1 / 67 (1.49%)
occurrences (all)	2	2	1
Diabetes mellitus			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	1 / 66 (1.52%)	1 / 67 (1.49%)
occurrences (all)	1	1	1
Hypertriglyceridaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	1	0	1
Type 2 diabetes mellitus			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 67 (1.49%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	1	1	0
Fluid retention			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Gout			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Hypochloraemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Hypoglycaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	1 / 66 (1.52%)	0 / 67 (0.00%)
occurrences (all)	0	1	0
Hyponatraemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 67 (1.49%)	0 / 66 (0.00%)	0 / 67 (0.00%)
occurrences (all)	1	0	0
Increased appetite			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 67 (0.00%)	0 / 66 (0.00%)	1 / 67 (1.49%)
occurrences (all)	0	0	1

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 71 (57.75%)		

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Seborrhoeic keratosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Squamous cell carcinoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Haematoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Hot flush			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Chest pain			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Oedema peripheral				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Influenza like illness				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Asthenia				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Chest discomfort				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Cyst				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Energy increased				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Feeling hot				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Non-cardiac chest pain				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			

Oedema				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Pain				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Pyrexia				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Reproductive system and breast disorders				
Erectile dysfunction				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Gynaecomastia				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Testicular pain				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Breast pain				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Erection increased				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Prostatic mass				
alternative assessment type: Non-				

systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Prostatomegaly			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Spontaneous penile erection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Testicular hypertrophy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Nasal congestion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Asthma			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Bronchial hyperreactivity			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Dyspnoea				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Epistaxis				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Pickwickian syndrome				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Productive cough				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Respiratory failure				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Rhinitis allergic				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Sinus congestion				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Sleep apnoea syndrome				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			

Psychiatric disorders			
Insomnia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Depression			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Libido decreased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Irritability			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	2		
Adjustment disorder with depressed mood			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Agitation			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Anxiety			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Apathy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Euphoric mood			
alternative assessment type: Non-			

systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Loss of libido				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Mood altered				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Investigations				
Haematocrit increased				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Prostatic specific antigen increased				
alternative assessment type: Non-systematic				
subjects affected / exposed	2 / 71 (2.82%)			
occurrences (all)	2			
Blood triglycerides increased				
alternative assessment type: Non-systematic				
subjects affected / exposed	2 / 71 (2.82%)			
occurrences (all)	2			
Weight increased				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Blood creatinine increased				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Blood pressure increased				
alternative assessment type: Non-systematic				

subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Aspartate aminotransferase increased				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	2			
Alanine aminotransferase increased				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Hepatic enzyme increased				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Blood bilirubin increased				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Blood glucose increased				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Blood insulin increased				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Blood pressure decreased				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Blood prolactin increased				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			

Blood urine present			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
C-reactive protein increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Electrocardiogram QT prolonged			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Glycosylated haemoglobin increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Heart rate irregular			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Low density lipoprotein increased			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Back injury			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Contusion			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Fall			
alternative assessment type: Non-			

systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Limb injury				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Muscle strain				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Animal bite				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Arthropod sting				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Excoriation				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Laceration				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Procedural pain				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Radius fracture				
alternative assessment type: Non-systematic				

subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Skin abrasion			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Tendon rupture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Thermal burn			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Tooth fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Cardiac disorders			
Atrial fibrillation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Cyanosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Extrasystoles			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Left ventricular hypertrophy			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	3		
Dizziness			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Paraesthesia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Syncope			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Central nervous system lesion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Complex regional pain syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Facial paralysis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Lethargy			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Metabolic encephalopathy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Migraine			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Neuralgia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Presyncope			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Primary headache associated with sexual activity			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Sensory loss			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Tremor			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Polycythaemia			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Tinnitus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Eye disorders			
Dry eye			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Blepharitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Constipation			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	2		
Nausea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Vomiting			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Abdominal discomfort			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Dry mouth			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Toothache			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Abdominal distension			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Dyspepsia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Food poisoning			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Haematochezia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Dermatitis contact				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Pruritus				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Alopecia				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Androgenetic alopecia				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Blister				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Dermatitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Diabetic foot				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Hidradenitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			

Night sweats				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Onycholysis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Penile ulceration				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Seborrhoea				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Renal and urinary disorders				
Pollakiuria				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Nephrolithiasis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Bladder outlet obstruction				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Calculus urinary				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Chronic kidney disease				
alternative assessment type: Non-systematic				

subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Glycosuria				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Haematuria				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Hydronephrosis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Micturition urgency				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Nocturia				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Renal cyst				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Urinary retention				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Urinary tract obstruction				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			

Musculoskeletal and connective tissue disorders			
Arthralgia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Back pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Muscle spasms			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Myalgia			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Pain in extremity			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Osteopenia			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Bursitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Groin pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Intervertebral disc protrusion			
alternative assessment type: Non-			

systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Osteoarthritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Psoriatic arthropathy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Rotator cuff syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Spinal column stenosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Trigger finger			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 71 (7.04%)		
occurrences (all)	5		
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Sinusitis			
alternative assessment type: Non-systematic			

subjects affected / exposed	2 / 71 (2.82%)			
occurrences (all)	2			
Influenza				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Urinary tract infection				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	2			
Gastroenteritis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Osteomyelitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Pneumonia				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Sepsis				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Tooth abscess				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Tooth infection				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			

Bacterial prostatitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Bronchitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Conjunctivitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Ear infection				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Folliculitis				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Furuncle				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Gastritis viral				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Gastroenteritis norovirus				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Lower respiratory tract infection				
alternative assessment type: Non-systematic				

subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Oral herpes				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Otitis externa				
alternative assessment type: Non-systematic				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences (all)	1			
Otitis media				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Otitis media acute				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Rash pustular				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Respiratory tract infection				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Tinea pedis				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			
Viral upper respiratory tract infection				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences (all)	0			

Metabolism and nutrition disorders			
Vitamin D deficiency			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Diabetes mellitus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Hypertriglyceridaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Type 2 diabetes mellitus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Fluid retention			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Gout			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Hypochloraemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Hypokalaemia			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Hyponatraemia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Increased appetite			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 March 2016	The purpose of this amendment was clarification of eligibility criteria and requirement of participants to refrain from sperm donation during the trial.
05 May 2016	The purpose of this amendment was a change to inclusion criteria to require two morning testosterone measurements of less than 300 ng/dL.
26 September 2016	The purpose of this amendment was a change to the interim analysis population to require approximately 100 participants.
03 November 2016	The purpose of this amendment was a change in the wash out period of topical testosterone treatments from six months prior to the first screening visit.
10 March 2017	The purpose of this amendment was to reduce the frequency of semen sampling.

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.

None reported

Notes: