Clinical trial results:
Title: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study of GBR 830 in Adult Subjects with Moderate to Severe Atopic Dermatitis.

Eligible subjects participated in a 54-week treatment period, which comprised a randomised, placebo-controlled treatment period with ISB 830 (also known as GBR 830) for 16 weeks, followed by an open-label treatment period for 38 weeks.
In the double-blind period, subjects were randomised 1:1:1:1:1:1 into 1 of 6 different dose groups: 4 dose groups in Part 1 (3 ISB 830; 1 placebo), and 2 dose groups in Part 2 (1 ISB 830; 1 placebo). Parts 1 and 2 of the study ran concurrently.
All subjects in Groups 1 through 4 received a loading dose consisting of 2 subcutaneous (SC) injections, followed by 7 maintenance doses consisting of 1 SC injection per dose. For Groups 5 and 6, all subjects received a loading dose consisting of 4 SC injections, followed by 7 maintenance doses consisting of 2 SC injections per dose.
The open-label treatment period comprised a 38-week treatment period during which each subject received an SC injection q2w from Week 16 to Week 52, or until subject withdrawal. All subjects who had been randomised to Groups 1-4 received 300 mg q2w, and subjects randomised to Groups 5-6 received 600 mg q2w.
The primary objective was to evaluate the efficacy of ISB 830 monotherapy in adults with moderate to severe atopic dermatitis (AD) compared with placebo, as measured by percentage change from baseline in eczema area and severity index (EASI) score at Week 16.

Summary

EudraCT number	2018-000783-29
Trial protocol	DE PL LT
Global end of trial date	03 August 2021
Results information	
Result version number	v1 (current)
This version publication date	19 August 2022
First version publication date	19 August 2022

Trial information

Trial identification

Sponsor protocol code	GBR830-204

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03568162
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Ichnos Sciences SA
Sponsor organisation address	Rte de la Corniche 5A, Epalinges, Switzerland, 1066
Public contact	Regulatory Services, TMC Pharma Services Ltd, +44 1252842255, regulatory.services@tmcpharma.com
Scientific contact	Regulatory Services, TMC Pharma Services Ltd, +44 1252842255, regulatory.services@tmcpharma.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	22 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 August 2021
Global end of trial reached?	Yes
Global end of trial date	03 August 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterise the efficacy of ISB 830 monotherapy in adults with moderate-to-severe AD compared with placebo as measured by percentage change from baseline in EASI score at Week 16.

Protection of trial subjects:

The study protocol and all study related documents were reviewed and approved by the institutional ethics committee (IEC) or institutional review board (IRB) at each Investigator site before starting the study. This study was designed, conducted, and monitored in accordance with Sponsor procedures, which complied with the ethical principles of GCP as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki.

Subjects were to be removed from the study if any of the following circumstances occurred:
1. Withdrawal of consent by the subject.
2. Development of a serious or intolerable adverse event (AE) that necessitated discontinuation.
3. Severe laboratory abnormalities.
4. At the discretion of the Investigator, when he/she believed continued participation was not in the best interest of the subject.
5. At the discretion of the Investigator, when the subject did not adhere to the study procedures.
6. A positive pregnancy test.
7. A female partner of a male study subject became pregnant.
8. A protocol deviation that, in the opinion of the Sponsor and Investigator, warranted discontinuation from the study

Background therapy:

The following medications and therapies not permitted during the study:
- Investigational biological agent
- Investigational drugs eg, phosphodiesterase type 4 (PDE4) inhibitors, Janus kinase inhibitors (JAK inhibitors)
- Phototherapy for AD
- Marketed drugs, including systemic corticosteroids, immunosuppressive/immunomodulatory drugs including, but not limited to cyclosporine, mycophenolate mofetil, IFN-γ, PDE4 inhibitors, JAK inhibitors, azathioprine, methotrexate
- Topical medications including crisaborole, corticosteroids, tacrolimus, and/or pimecrolimus
- Regular use (>2 visits/week) of a tanning booth/parlor
- Cell-depleting agents including but not limited to rituximab
- Infliximab, adalimumab, golimumab, certolizumab pegol, abatacept, etanercept, anakinra, dupilumab
- Other biologics (not listed above)
- Live (attenuated) vaccines

All restrictions on the medications listed above were applicable for the entire duration of the study. Other concomitant medications that the subject received on a regular basis were continued, if in the opinion of the Investigator, they did not put the subject at undue risk or did not interfere with the study evaluations.

Subjects who received rescue treatment with systemic corticosteroids, non-steroidal systemic immunosuppressive drugs, or biologics were discontinued temporarily. Administration of ISB 830 was to resume after the appropriate washout period (4 weeks or 5 half-lives, whichever was longer) and following discussion and upon obtaining written approval from the Sponsor's medical monitor.

Evidence for comparator:

There was no active comparator; all patients were treated with ISB 830 or placebo.

Actual start date of recruitment	22 November 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 151
Country: Number of subjects enrolled	Czechia: 87
Country: Number of subjects enrolled	Germany: 48
Country: Number of subjects enrolled	United States: 134
Country: Number of subjects enrolled	Canada: 40
Worldwide total number of subjects	460
EEA total number of subjects	286

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	437
From 65 to 84 years	22
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The first patient was enrolled on 22 Nov 2018 and the date of the last visit was 03 August 2021. Overall, 462 patients were enrolled into groups 1-4 in Part 1 and 5-6 in Part 2 (287 in Europe; 175 outside Europe). Results are presented for the full analysis set (N=460).

Pre-assignment

Screening details:

Screening occurred within 28 days prior to randomisation. During screening, treatments for AD were withdrawn or modified per protocol. Subjects could be re-screened once (within or outside of the screening period) if they failed the screening evaluation.

Period 1

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

Blinding implementation details:

Neither the subject nor Investigator/ Sponsor staff involved in the treatment or clinical evaluation of the subjects were aware of the treatment administered. Since ISB 830 and placebo were not indistinguishable, the study drug was handled/prepared by a designated unblinded study drug administrator on site and was administered by a designated unblinded study team member not involved in the management of study subjects. An unblinded clinical monitor performed the study drug accountability.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1 (ISB 830 300mg q2w) - Part 1

Arm description:

Randomised ISB 830 treatment group, during the 16-week double-blind treatment period of Part 1 of the study.

Arm type	Experimental
Investigational medicinal product name	ISB 830
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

600 mg dose of ISB 830 (2 SC injections) on Day 1. Thereafter, 300 mg ISB 830 (1 SC injection) every 2 weeks (q2w) starting at Day 15.

Arm title	Group 2 (ISB 830 300mg q4w) - Part 1

Arm description:

Randomised ISB 830 treatment group, during the 16-week double-blind treatment period of Part 1 of the study.

Arm type	Experimental
Investigational medicinal product name	ISB 830
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

600 mg dose of ISB 830 (2 SC injections) on Day 1. Thereafter, 300 mg ISB 830 (1 SC injection) every

4 weeks (q4w) starting at Day 29. To maintain blinding, placebo (1 SC injection) was administered q4w starting at Day 15.

Arm title	Group 3 (ISB 830 75mg q4w) - Part 1
Arm description:	
Randomised ISB 830 treatment group, during the 16-week double-blind treatment period of Part 1 of the study.	
Arm type	Experimental
Investigational medicinal product name	ISB 830
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
150 mg dose of ISB 830 (2 SC injections) on Day 1. Thereafter, 75 mg ISB 830 (1 SC injection) every 4 weeks (q4w) starting at Day 29. To maintain blinding, placebo (1 SC injection) was administered q4w starting at Day 15.	
Arm title	Group 4 (Placebo q2w) - Part 1
Arm description:	
Randomised ISB 830 treatment group, during the 16-week double-blind treatment period of Part 1 of the study.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
Placebo (2 SC injections) on Day 1, followed by q2w dosing with placebo (1 SC injection) starting at Day 15.	
Arm title	Group 5 (ISB 830 600mg q2w) - Part 2
Arm description:	
Randomised ISB 830 treatment group, during the 54-week open-label treatment period of Part 2 of the study.	
Arm type	Experimental
Investigational medicinal product name	ISB 830
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
1200 mg dose of ISB 830 (2 SC injections) on Day 1. Thereafter, 600 mg ISB 830 (1 SC injection) every 2 weeks (q2w) starting at Day 15.	
Arm title	Group 6 (Placebo q2w) - Part 2
Arm description:	
Randomised ISB 830 treatment group, during the 54-week open-label treatment period of Part 2 of the study.	
Arm type	Placebo

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

Dosage and administration details:

Placebo (4 SC injections) on Day 1, followed by q2w dosing with placebo (2 SC injection) starting at Day 15.

Number of subjects in period 1	Group 1 (ISB 830 300mg q2w) - Part 1	Group 2 (ISB 830 300mg q4w) - Part 1	Group 3 (ISB 830 75mg q4w) - Part 1
Started	76	78	77
Completed	54	57	42
Not completed	22	21	35
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	15	13	26
Physician decision	-	1	1
Adverse event, non-fatal	-	1	2
Subject decision	-	-	-
Other	3	4	1
Pregnancy	-	-	-
Lost to follow-up	3	2	4
Protocol deviation	1	-	1

Number of subjects in period 1	Group 4 (Placebo q2w) - Part 1	Group 5 (ISB 830 600mg q2w) - Part 2	Group 6 (Placebo q2w) - Part 2
Started	80	75	74
Completed	50	61	60
Not completed	30	14	14
Adverse event, serious fatal	-	1	-
Consent withdrawn by subject	21	6	8
Physician decision	-	1	-
Adverse event, non-fatal	-	-	1
Subject decision	1	-	1
Other	4	2	1
Pregnancy	1	-	-
Lost to follow-up	2	3	2
Protocol deviation	1	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Group 1 (ISB 830 300mg q2w) - Part 1
Reporting group description:	
Randomised ISB 830 treatment group, during the 16-week double-blind treatment period of Part 1 of the study.	
Reporting group title	Group 2 (ISB 830 300mg q4w) - Part 1
Reporting group description:	
Randomised ISB 830 treatment group, during the 16-week double-blind treatment period of Part 1 of the study.	
Reporting group title	Group 3 (ISB 830 75mg q4w) - Part 1
Reporting group description:	
Randomised ISB 830 treatment group, during the 16-week double-blind treatment period of Part 1 of the study.	
Reporting group title	Group 4 (Placebo q2w) - Part 1
Reporting group description:	
Randomised ISB 830 treatment group, during the 16-week double-blind treatment period of Part 1 of the study.	
Reporting group title	Group 5 (ISB 830 600mg q2w) - Part 2
Reporting group description:	
Randomised ISB 830 treatment group, during the 54-week open-label treatment period of Part 2 of the study.	
Reporting group title	Group 6 (Placebo q2w) - Part 2
Reporting group description:	
Randomised ISB 830 treatment group, during the 54-week open-label treatment period of Part 2 of the study.	

Reporting group values	Group 1 (ISB 830 300mg q2w) - Part 1	Group 2 (ISB 830 300mg q4w) - Part 1	Group 3 (ISB 830 75mg q4w) - Part 1
Number of subjects	76	78	77
Age categorical			
Units: Subjects			
≥ 18 - <65	71	74	70
≥ 65	5	4	7
Age continuous			
Units: years			
arithmetic mean	40.2	36.6	38.4
standard deviation	± 13.10	± 14.77	± 16.87
Gender categorical			
Units: Subjects			
Female	32	44	41
Male	44	34	36
Investigator's global assessment (IGA)			
The Investigator's global assessment (IGA) was an assessment scale used in clinical studies to determine severity of AD and clinical response to treatment based on a 5-point scale ranging from 0 (clear) to 4 (severe). 0 = Clear - No inflammatory signs of atopic dermatitis 4 = Severe disease - Severe erythema and severe papulation/infiltration and Deep/dark red erythema; marked and extensive elevation (papulation/infiltration)			
Units: Subjects			

0 = Clear	0	0	0
1 = Almost clear	0	0	0
2 = Mild disease	0	0	0
3 = Moderate disease	49	48	49
4 = Severe disease	27	30	28
Number of days with severe pruritus in the past 7 days			
Number of days with severe pruritus in the past 7 days. Severe pruritus is ≥ 7 on Pruritus NRS.			
Units: Subjects			
<3 days	22	17	17
3 days	5	9	4
4 days	10	9	10
5 days	4	4	9
6 days	11	16	17
7 days	24	23	20
Missing	0	0	0
Body surface area			
Body surface area (BSA) affected by AD was assessed for each section of the body (the possible highest score for each region was: head and neck [9%], anterior trunk [18%], back [18%], upper limbs [18%], lower limbs [36%], and genitals [1%]) and was reported as a percentage of all major body sections combined.			
Units: percent			
arithmetic mean	46.69	50.82	46.70
standard deviation	± 21.383	± 24.182	± 21.175
Pruritus Numerical Rating Scale			
Baseline Pruritus Numerical Rating Scale (NRS) average score for maximum itch intensity was determined based on the average of daily Pruritus NRS scores for maximum itch intensity (the daily score ranges from 0 to 10) during the 7 days immediately preceding) randomisation. A minimum of 3 daily scores out of the 7 days was required to calculate the baseline average score.			
Units: NRS score			
arithmetic mean	7.42	7.53	7.52
standard deviation	± 1.634	± 1.650	± 1.639
Eczema Area and Severity Index (EASI)			
The Eczema Area and Severity Index (EASI) was a validated measure used in clinical practice and clinical trials to assess the severity and extent of AD. Four AD disease characteristics were assessed for severity by the Investigator or designee on a scale of "0" (absent) through "3" (severe). In addition, the area of AD involvement was assessed as a percentage by body area of head, trunk, arms, and legs and converted to a score of 0 to 6.			
Units: EASI score			
arithmetic mean	30.42	33.84	28.42
standard deviation	± 14.110	± 14.910	± 11.602

Reporting group values	Group 4 (Placebo q2w) - Part 1	Group 5 (ISB 830 600mg q2w) - Part 2	Group 6 (Placebo q2w) - Part 2
Number of subjects	80	75	74
Age categorical			
Units: Subjects			
≥ 18 - <65	78	72	72
≥ 65	2	3	2
Age continuous			
Units: years			
arithmetic mean	36.3	37.9	36.0
standard deviation	± 13.05	± 13.31	± 13.75

Gender categorical Units: Subjects			
Female	44	37	47
Male	36	38	27
Investigator's global assessment (IGA)			
The Investigator's global assessment (IGA) was an assessment scale used in clinical studies to determine severity of AD and clinical response to treatment based on a 5-point scale ranging from 0 (clear) to 4 (severe). 0 = Clear - No inflammatory signs of atopic dermatitis 4 = Severe disease - Severe erythema and severe papulation/infiltration and Deep/dark red erythema; marked and extensive elevation (papulation/infiltration)			
Units: Subjects			
0 = Clear	0	0	0
1 = Almost clear	0	0	0
2 = Mild disease	0	0	0
3 = Moderate disease	52	48	47
4 = Severe disease	28	27	27
Number of days with severe pruritus in the past 7 days			
Number of days with severe pruritus in the past 7 days. Severe pruritus is ≥ 7 on Pruritus NRS.			
Units: Subjects			
<3 days	27	14	18
3 days	5	3	2
4 days	5	6	6
5 days	13	9	12
6 days	11	16	14
7 days	19	26	22
Missing	0	1	0
Body surface area			
Body surface area (BSA) affected by AD was assessed for each section of the body (the possible highest score for each region was: head and neck [9%], anterior trunk [18%], back [18%], upper limbs [18%], lower limbs [36%], and genitals [1%]) and was reported as a percentage of all major body sections combined.			
Units: percent			
arithmetic mean	48.43	48.43	52.92
standard deviation	± 22.415	± 21.011	± 24.786
Pruritus Numerical Rating Scale			
Baseline Pruritus Numerical Rating Scale (NRS) average score for maximum itch intensity was determined based on the average of daily Pruritus NRS scores for maximum itch intensity (the daily score ranges from 0 to 10) during the 7 days immediately preceding) randomisation. A minimum of 3 daily scores out of the 7 days was required to calculate the baseline average score.			
Units: NRS score			
arithmetic mean	7.25	7.44	7.42
standard deviation	± 1.827	± 1.486	± 1.698
Eczema Area and Severity Index (EASI)			
The Eczema Area and Severity Index (EASI) was a validated measure used in clinical practice and clinical trials to assess the severity and extent of AD. Four AD disease characteristics were assessed for severity by the Investigator or designee on a scale of "0" (absent) through "3" (severe). In addition, the area of AD involvement was assessed as a percentage by body area of head, trunk, arms, and legs and converted to a score of 0 to 6.			
Units: EASI score			
arithmetic mean	30.65	29.86	31.81
standard deviation	± 13.173	± 13.223	± 14.340

Reporting group values	Total		

Number of subjects	460		
Age categorical Units: Subjects			
≥ 18 - <65	437		
≥ 65	23		
Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	245		
Male	215		
Investigator's global assessment (IGA)			
The Investigator's global assessment (IGA) was an assessment scale used in clinical studies to determine severity of AD and clinical response to treatment based on a 5-point scale ranging from 0 (clear) to 4 (severe). 0 = Clear - No inflammatory signs of atopic dermatitis 4 = Severe disease - Severe erythema and severe papulation/infiltration and Deep/dark red erythema; marked and extensive elevation (papulation/infiltration)			
Units: Subjects			
0 = Clear	0		
1 = Almost clear	0		
2 = Mild disease	0		
3 = Moderate disease	293		
4 = Severe disease	167		
Number of days with severe pruritus in the past 7 days			
Number of days with severe pruritus in the past 7 days. Severe pruritus is ≥ 7 on Pruritus NRS.			
Units: Subjects			
<3 days	115		
3 days	28		
4 days	46		
5 days	51		
6 days	85		
7 days	134		
Missing	1		
Body surface area			
Body surface area (BSA) affected by AD was assessed for each section of the body (the possible highest score for each region was: head and neck [9%], anterior trunk [18%], back [18%], upper limbs [18%], lower limbs [36%], and genitals [1%]) and was reported as a percentage of all major body sections combined.			
Units: percent arithmetic mean standard deviation	- -		
Pruritus Numerical Rating Scale			
Baseline Pruritus Numerical Rating Scale (NRS) average score for maximum itch intensity was determined based on the average of daily Pruritus NRS scores for maximum itch intensity (the daily score ranges from 0 to 10) during the 7 days immediately preceding) randomisation. A minimum of 3 daily scores out of the 7 days was required to calculate the baseline average score.			
Units: NRS score arithmetic mean standard deviation	- -		

Eczema Area and Severity Index (EASI)			
The Eczema Area and Severity Index (EASI) was a validated measure used in clinical practice and clinical trials to assess the severity and extent of AD. Four AD disease characteristics were assessed for severity by the Investigator or designee on a scale of "0" (absent) through "3" (severe). In addition, the area of AD involvement was assessed as a percentage by body area of head, trunk, arms, and legs and converted to a score of 0 to 6.			
Units: EASI score arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	Group 1 (ISB 830 300mg q2w) - Part 1
Reporting group description:	
Randomised ISB 830 treatment group, during the 16-week double-blind treatment period of Part 1 of the study.	
Reporting group title	Group 2 (ISB 830 300mg q4w) - Part 1
Reporting group description:	
Randomised ISB 830 treatment group, during the 16-week double-blind treatment period of Part 1 of the study.	
Reporting group title	Group 3 (ISB 830 75mg q4w) - Part 1
Reporting group description:	
Randomised ISB 830 treatment group, during the 16-week double-blind treatment period of Part 1 of the study.	
Reporting group title	Group 4 (Placebo q2w) - Part 1
Reporting group description:	
Randomised ISB 830 treatment group, during the 16-week double-blind treatment period of Part 1 of the study.	
Reporting group title	Group 5 (ISB 830 600mg q2w) - Part 2
Reporting group description:	
Randomised ISB 830 treatment group, during the 54-week open-label treatment period of Part 2 of the study.	
Reporting group title	Group 6 (Placebo q2w) - Part 2
Reporting group description:	
Randomised ISB 830 treatment group, during the 54-week open-label treatment period of Part 2 of the study.	

Primary: Percentage change in EASI score

End point title	Percentage change in EASI score
End point description:	
Percentage change in EASI score from baseline to Week 16. This was analysed using a mixed-effect model for repeated measures (MMRM). This accounted for the variance-covariance structure between visits and missing data. This model included all scheduled visits for the response variable. The adjusted means for each treatment and the estimated treatment differences for the treatment comparisons were presented together with 95% confidence intervals (CIs), along with P-values for the treatment comparisons. The adjusted means and estimated treatment differences for the treatment comparisons (each ISB 830 group vs placebo group) were also determined with corresponding 95% CIs.	
End point type	Primary
End point timeframe:	
From baseline to Week 16	

End point values	Group 1 (ISB 830 300mg q2w) - Part 1	Group 2 (ISB 830 300mg q4w) - Part 1	Group 3 (ISB 830 75mg q4w) - Part 1	Group 4 (Placebo q2w) - Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	45	39	42
Units: percent				
arithmetic mean (standard deviation)	-57.589 (±	-56.734 (±	-38.099 (±	-42.142 (±

	36.2014)	32.5395)	39.6857)	38.1945)

End point values	Group 5 (ISB 830 600mg q2w) - Part 2	Group 6 (Placebo q2w) - Part 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	51		
Units: percent				
arithmetic mean (standard deviation)	-59.737 (± 27.1176)	-43.252 (± 41.2404)		

Statistical analyses

Statistical analysis title	Percentage change in EASI score (Group 1)

Statistical analysis description:

The percentage change from baseline (Group 1) in EASI at Week 16 compared to placebo (Group 4). This was an MMRM analysis.

The adjusted mean treatment differences for the treatment comparisons were presented together with 95% CIs, along with P-values for the treatment comparisons.

Comparison groups	Group 4 (Placebo q2w) - Part 1 v Group 1 (ISB 830 300mg q2w) - Part 1
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-20.192
Confidence interval	
level	95 %
sides	2-sided
lower limit	-34.944
upper limit	-5.439
Variability estimate	Standard error of the mean
Dispersion value	7.4781

Statistical analysis title	Percentage change in EASI score (Group 2)

Statistical analysis description:

The percentage change from baseline (Group 2) in EASI at Week 16 compared to placebo (Group 4). This was an MMRM analysis.

The adjusted mean treatment differences for the treatment comparisons were presented together with 95% CIs, along with P-values for the treatment comparisons.

Comparison groups	Group 4 (Placebo q2w) - Part 1 v Group 2 (ISB 830 300mg q4w) - Part 1

Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.061
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-14.439
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.552
upper limit	0.674
Variability estimate	Standard error of the mean
Dispersion value	7.6622

Statistical analysis title	Percentage change in EASI score (Group 3)

Statistical analysis description:

The percentage change from baseline (Group 3) in EASI at Week 16 compared to placebo (Group 4). This was an MMRM analysis.

The adjusted mean treatment differences for the treatment comparisons were presented together with 95% CIs, along with P-values for the treatment comparisons.

Comparison groups	Group 4 (Placebo q2w) - Part 1 v Group 3 (ISB 830 75mg q4w) - Part 1
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.691
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	3.144
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.41
upper limit	18.698
Variability estimate	Standard error of the mean
Dispersion value	7.8864

Statistical analysis title	Percentage change in EASI score (Group 5)

Statistical analysis description:

The percentage change from baseline (Group 5) in EASI at Week 16 compared to placebo (Group 6). This was an MMRM analysis.

The adjusted mean treatment differences for the treatment comparisons were presented together with 95% CIs, along with P-values for the treatment comparisons.

Comparison groups	Group 5 (ISB 830 600mg q2w) - Part 2 v Group 6 (Placebo q2w) - Part 2

Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	Mixed models analysis
Parameter estimate	LS Mean Difference
Point estimate	-17.199
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.895
upper limit	-4.503
Variability estimate	Standard error of the mean
Dispersion value	6.409

Secondary: EASI-75

End point title	EASI-75

End point description:

Proportion of subjects with EASI-75 (≥75% improvement from baseline) at Week 16. The analyses were based on the stratified Cochran-Mantel-Haenzsel (CMH) test where randomisation strata (region, disease severity) were used as stratification variables. Pairwise treatment comparisons were made based on the CMH test using the P-value for the general association. The odds ratio and associated CI based on Wald test were provided.

The subjects with ≥75% improvement in EASI from baseline at Week 16 were considered as Responders. Any subject who received protocol-specified rescue medication during the blinded treatment period or withdrew from the study before Week 16, was considered a Non-Responder. Also, any subject who was missing a Week 16 efficacy assessment was considered a Non-Responder.

End point type	Secondary

End point timeframe:

From baseline to Week 16.

End point values	Group 1 (ISB 830 300mg q2w) - Part 1	Group 2 (ISB 830 300mg q4w) - Part 1	Group 3 (ISB 830 75mg q4w) - Part 1	Group 4 (Placebo q2w) - Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	76	78	77	80
Units: Subjects	18	16	9	9

End point values	Group 5 (ISB 830 600mg q2w) - Part 2	Group 6 (Placebo q2w) - Part 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	74		
Units: Subjects	19	14		

Statistical analyses

Statistical analysis title	EASI-75 (Group 1)

Statistical analysis description:

The comparison between Group 1 and placebo (Group 4) were based on the stratified CMH test. Pairwise treatment comparisons were made based on the CMH test using the P-value for the general association. The odds ratio and associated CI based on Wald test were provided.

Comparison groups	Group 1 (ISB 830 300mg q2w) - Part 1 v Group 4 (Placebo q2w) - Part 1
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.492
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.029
upper limit	6.039

Statistical analysis title	EASI-75 (Group 2)

Statistical analysis description:

The comparison between Group 2 and placebo (Group 4) were based on the stratified CMH test. Pairwise treatment comparisons were made based on the CMH test using the P-value for the general association. The odds ratio and associated CI based on Wald test were provided.

Comparison groups	Group 4 (Placebo q2w) - Part 1 v Group 2 (ISB 830 300mg q4w) - Part 1
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.109
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.056
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.843
upper limit	5.012

Statistical analysis title	EASI-75 (Group 3)

Statistical analysis description:

The comparison between Group 3 and placebo (Group 4) were based on the stratified CMH test. Pairwise treatment comparisons were made based on the CMH test using the P-value for the general association. The odds ratio and associated CI based on Wald test were provided.

Comparison groups	Group 4 (Placebo q2w) - Part 1 v Group 3 (ISB 830 75mg q4w) - Part 1
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.921
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.051
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.392
upper limit	2.824

Statistical analysis title	EASI-75 (Group 5)

Statistical analysis description:

The comparison between Group 5 and placebo (Group 6) were based on the stratified CMH test. Pairwise treatment comparisons were made based on the CMH test using the P-value for the general association. The odds ratio and associated CI based on Wald test were provided.

Comparison groups	Group 5 (ISB 830 600mg q2w) - Part 2 v Group 6 (Placebo q2w) - Part 2
Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.372
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.444
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.649
upper limit	3.215

Secondary: IGA success and IGA reduction

End point title	IGA success and IGA reduction

End point description:

Proportion of subjects achieving IGA success with both IGA 0 or 1 (on a 5-point scale) and an IGA reduction from baseline of ≥2 points at Week 16. The analyses were based on the stratified CMH test where randomisation strata (region, disease severity) were used as stratification variables. Pairwise treatment comparisons were made based on the CMH test using the P-value for the general association. The odds ratio and associated CI based on Wald test were provided.

The subjects with both IGA 0 or 1 (on a 5-point scale) and IGA reduction from baseline of ≥2 points at Week 16 were considered as Responders. Any subject who received protocol-specified rescue medication during the Blinded Treatment period or withdrew from the study before Week 16, was considered a Non-Responder. Also, any subject who was missing a Week 16 efficacy assessment were considered a Non-Responder.

End point type	Secondary

End point timeframe:

From baseline to Week 16.

End point values	Group 1 (ISB 830 300mg q2w) - Part 1	Group 2 (ISB 830 300mg q4w) - Part 1	Group 3 (ISB 830 75mg q4w) - Part 1	Group 4 (Placebo q2w) - Part 1
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	76	78	77	80
Units: Subjects	10	8	5	4

End point values	Group 5 (ISB 830 600mg q2w) - Part 2	Group 6 (Placebo q2w) - Part 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	74		
Units: Subjects	9	4		

Statistical analyses

Statistical analysis title	IGA success and IGA reduction (Group 1)

Statistical analysis description:

The comparison between Group 1 and placebo (Group 4) were based on the stratified CMH test. Pairwise treatment comparisons were made based on the CMH test using the P-value for the general association. The odds ratio and associated CI based on Wald test were provided.

Comparison groups	Group 1 (ISB 830 300mg q2w) - Part 1 v Group 4 (Placebo q2w) - Part 1
Number of subjects included in analysis	156
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.073
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.892
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.867
upper limit	9.647

Statistical analysis title	IGA success and IGA reduction (Group 2)

Statistical analysis description:

The comparison between Group 2 and placebo (Group 4) were based on the stratified CMH test. Pairwise treatment comparisons were made based on the CMH test using the P-value for the general association. The odds ratio and associated CI based on Wald test were provided.

Comparison groups	Group 2 (ISB 830 300mg q4w) - Part 1 v Group 4 (Placebo q2w) - Part 1
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.206
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.225
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.635
upper limit	7.791

Statistical analysis title	IGA success and IGA reduction (Group 3)

Statistical analysis description:

The comparison between Group 3 and placebo (Group 4) were based on the stratified CMH test. Pairwise treatment comparisons were made based on the CMH test using the P-value for the general association. The odds ratio and associated CI based on Wald test were provided.

Comparison groups	Group 4 (Placebo q2w) - Part 1 v Group 3 (ISB 830 75mg q4w) - Part 1
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.659
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.362
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.346
upper limit	5.358

Statistical analysis title	IGA success and IGA reduction (Group 5)

Statistical analysis description:

The comparison between Group 5 and placebo (Group 6) were based on the stratified CMH test. Pairwise treatment comparisons were made based on the CMH test using the P-value for the general association. The odds ratio and associated CI based on Wald test were provided.

Comparison groups	Group 5 (ISB 830 600mg q2w) - Part 2 v Group 6 (Placebo q2w) - Part 2

Number of subjects included in analysis	149
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.155
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.451
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.695
upper limit	8.641

Adverse events information

Timeframe for reporting adverse events:

From baseline to Week 54.

Adverse event reporting additional description:

Adverse events (AEs) were coded using the MedDRA and summarised by system organ class (SOC), preferred term (PT) and treatment group. Subjects were counted only once for each SOC, PT.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Group 1 (ISB 830 300mg q2w) - Part 1

Reporting group description:

Blinded Treatment Phase: ISB 830 administered at dose of 600 mg via SC injection (2 × 300 mg) on Day 1,followed by ISB 830 administered at dose of 300 mg (1 × 300 mg) via SC injection every 2 weeks (q2w) starting from Day 15 (Week 2) up to Week 14.

Open-label Treatment Phase: ISB 830 administered at dose of 300 mg (1 × 300 mg) via SC injection q2w starting from Week 16 up to Week 52 (or until participant withdrawal). Participants were followed up for 12 weeks after treatment discontinuation, maximum up to Week 66.

Reporting group title	Group 2 (ISB 830 300mg q4w) - Part 1

Reporting group description:

Blinded Treatment Phase: ISB 830 administered at dose of 600 mg via SC injection (2 × 300 mg) on Day 1, followed by ISB 830 administered at dose of 300 mg (1 × 300 mg) via SC injection every 4 weeks (q4w) starting from Day 29 (Week 4) up to Week 12 and placebo administered via SC injection q4w starting from Day 15 (Week 2) up to Week 14.

Open-label Treatment Phase: ISB 830 administered at dose of 300 mg (1 × 300 mg) via SC injection q2w starting from Week 16 up to Week 52 (or until participant withdrawal). Participants were followed up for 12 weeks after treatment discontinuation, maximum up to Week 66.

Reporting group title	Group 3 (ISB 830 75mg q4w) - Part 1

Reporting group description:

Blinded Treatment Phase: ISB 830 administered at dose of 150 mg via SC injection (2 × 75 mg) on Day 1, followed by ISB 830 administered at dose of 75 mg (1 × 75 mg) via SC injection q4w starting from Day 29 (Week 4) up to Week 12 and placebo administered via SC injection q4w starting from Day 15 (Week 2) up to Week 14.

Open-label Treatment Phase: ISB 830 administered at dose of 300 mg (1 × 300 mg) via SC injection q2w starting from Week 16 up to Week 52 (or until participant withdrawal). Participants were followed up for 12 weeks after treatment discontinuation, maximum up to Week 66

Reporting group title	Group 4 (Placebo q2w) - Part 1 - blinded

Reporting group description:

Blinded Treatment Phase: Placebo administered via SC injection (2 injections) q2w starting from Day 1 up to Week 14.

Reporting group title	Group 5 (ISB 830 600mg q2w) - Part 2

Reporting group description:

Blinded Treatment Phase: ISB 830 administered at dose of 1200 mg via SC injection (4 × 300 mg) on Day 1, followed by ISB 830 administered at dose of 600 mg (2 × 300 mg) via SC injection q2w starting from Day 15 (Week 2) up to Week 14.

Open-label Treatment Phase: ISB 830 administered at dose of 600 mg (2 × 300 mg) via SC injection q2w starting from Week 16 up to Week 52 (or until participant withdrawal). Participants were followed up for 12 weeks after treatment discontinuation, maximum up to Week 66.

Reporting group title	Group 6 (Placebo q2w) - Part 2 - blinded

Reporting group description:

Blinded Treatment Phase: Placebo administered via SC injection (4 injections) q2w starting from Day 1

up to Week 14.

Reporting group title	Group 7 (placebo, open-label) - Part 1

Reporting group description:

Open-label Treatment Phase: ISB 830 administered at dose of 300 mg (1 × 300 mg) via SC injection q2w starting from Week 16 up to Week 52 (or until participant withdrawal). Participants were followed up for 12 weeks after treatment discontinuation, maximum up to Week 66.
Note, this is a subset of patients in Group 4.

Reporting group title	Group 8 (Placebo open-label) - Part 2

Reporting group description:

Open-label Treatment Phase: ISB 830 administered at dose of 600 mg (2 × 300 mg) via SC injection q2w starting from Week 16 up to Week 52 (or until participant withdrawal). Participants were followed up for 12 weeks after treatment discontinuation, maximum up to Week 66.
Note, this is a subset of patients in Group 6.

Serious adverse events	Group 1 (ISB 830 300mg q2w) - Part 1	Group 2 (ISB 830 300mg q4w) - Part 1	Group 3 (ISB 830 75mg q4w) - Part 1
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 76 (5.26%)	6 / 78 (7.69%)	4 / 77 (5.19%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Keratoacanthoma			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (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
Uterine leiomyoma			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (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
Adenocarcinoma of colon			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Gun shot wound			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (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
Ligament rupture			

subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous complete			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Eye complication associated with device			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Pernicious anaemia			

subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (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
Eye disorders			
Chorioretinopathy			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (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			
Dermatitis atopic			
subjects affected / exposed	2 / 76 (2.63%)	2 / 78 (2.56%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	2 / 2	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Viral infection			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Metabolic acidosis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (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	Group 4 (Placebo q2w) - Part 1 - blinded	Group 5 (ISB 830 600mg q2w) - Part 2	Group 6 (Placebo q2w) - Part 2 - blinded
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 80 (1.25%)	1 / 75 (1.33%)	0 / 74 (0.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Keratoacanthoma			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (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
Uterine leiomyoma			

subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (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
Adenocarcinoma of colon			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Gun shot wound			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (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
Ligament rupture			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (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
Femur fracture			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (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
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous complete			

subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Eye complication associated with device			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Pernicious anaemia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (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
Eye disorders			
Chorioretinopathy			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (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
Infections and infestations			
Viral infection			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Metabolic acidosis			

subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (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	Group 7 (placebo, open-label) - Part 1	Group 8 (Placebo open-label) - Part 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 60 (3.33%)	2 / 67 (2.99%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Keratoacanthoma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Gun shot wound			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			

subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous complete			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Eye complication associated with device			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Pernicious anaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

Chorioretinopathy			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Viral infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Metabolic acidosis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Group 1 (ISB 830 300mg q2w) - Part 1	Group 2 (ISB 830 300mg q4w) - Part 1	Group 3 (ISB 830 75mg q4w) - Part 1
Total subjects affected by non-serious adverse events			
subjects affected / exposed	68 / 76 (89.47%)	56 / 78 (71.79%)	64 / 77 (83.12%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign breast neoplasm			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Skin papilloma			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Uterine leiomyoma			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0

Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 76 (6.58%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	5	1	0
Flushing			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Thrombophlebitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 76 (2.63%)	5 / 78 (6.41%)	1 / 77 (1.30%)
occurrences (all)	2	8	1
Application site reaction			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	1	1	0
Chest discomfort			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	1 / 77 (1.30%)
occurrences (all)	0	1	1
Chills			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Facial pain			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Feeling cold			

subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Feeling hot			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	1 / 76 (1.32%)	3 / 78 (3.85%)	1 / 77 (1.30%)
occurrences (all)	1	5	1
Injection site bruising			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Injection site erythema			
subjects affected / exposed	1 / 76 (1.32%)	3 / 78 (3.85%)	0 / 77 (0.00%)
occurrences (all)	1	3	0
Injection site haematoma			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Injection site induration			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Injection site oedema			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Injection site pain			
subjects affected / exposed	1 / 76 (1.32%)	2 / 78 (2.56%)	1 / 77 (1.30%)
occurrences (all)	1	2	1
Injection site pruritus			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Injection site rash			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Injection site reaction			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	2 / 77 (2.60%)
occurrences (all)	0	0	5
Injection site swelling			

subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	1	1	0
Injection site urticaria			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	1 / 77 (1.30%)
occurrences (all)	0	1	1
Malaise			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	2 / 77 (2.60%)
occurrences (all)	1	0	2
Pain			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	2 / 76 (2.63%)	2 / 78 (2.56%)	1 / 77 (1.30%)
occurrences (all)	3	3	1
Pyrexia			
subjects affected / exposed	2 / 76 (2.63%)	1 / 78 (1.28%)	2 / 77 (2.60%)
occurrences (all)	2	1	2
Therapeutic response unexpected			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Allergy to animal			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	3	0
Allergy to arthropod bite			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Allergy to arthropod sting			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Drug hypersensitivity			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0

Food allergy			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	1	3	0
Seasonal allergy			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Breast inflammation			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Breast mass			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Breast pain			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Breast tenderness			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Cervix inflammation			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Dysmenorrhoea			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Menstrual disorder			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Ovarian cyst			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Ovarian disorder			

subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Premature menopause			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Sexual dysfunction			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Uterine cervix stenosis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Uterine haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 76 (2.63%)	4 / 78 (5.13%)	3 / 77 (3.90%)
occurrences (all)	2	6	4
Cough			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	4 / 77 (5.19%)
occurrences (all)	1	1	4
Catarrh			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Dysphonia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	1 / 77 (1.30%)
occurrences (all)	0	1	1
Epistaxis			

subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	1	1	0
Nasal congestion			
subjects affected / exposed	3 / 76 (3.95%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	3	0	0
Nasal septum disorder			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	2 / 76 (2.63%)	0 / 78 (0.00%)	2 / 77 (2.60%)
occurrences (all)	2	0	2
Productive cough			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Reflux laryngitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	2 / 77 (2.60%)
occurrences (all)	1	1	2
Rhinorrhoea			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	1 / 77 (1.30%)
occurrences (all)	0	1	1
Sinus congestion			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Throat irritation			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0

Anxiety			
subjects affected / exposed	2 / 76 (2.63%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	2	1	0
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Bipolar disorder			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	2 / 77 (2.60%)
occurrences (all)	1	1	2
Initial insomnia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 76 (0.00%)	2 / 78 (2.56%)	1 / 77 (1.30%)
occurrences (all)	0	3	1
Mixed anxiety and depressive disorder			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Nervousness			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Panic attack			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 76 (0.00%)	2 / 78 (2.56%)	0 / 77 (0.00%)
occurrences (all)	0	2	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Bacterial test positive			

subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Blood bicarbonate decreased			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	2 / 77 (2.60%)
occurrences (all)	1	0	2
Blood glucose increased			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Blood iron decreased			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	2 / 76 (2.63%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	2	0	0
Blood triglycerides increased			
subjects affected / exposed	2 / 76 (2.63%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	2	0	0
Blood urine present			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 76 (0.00%)	2 / 78 (2.56%)	0 / 77 (0.00%)
occurrences (all)	0	2	0
C-reactive protein increased			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Cardiac murmur			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase			

increased			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Glucose urine present			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Haemoglobin urine present			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	4	0	1
Liver function test increased			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	0 / 76 (0.00%)	2 / 78 (2.56%)	0 / 77 (0.00%)
occurrences (all)	0	2	0
Platelet count increased			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Protein urine present			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Red blood cell count decreased			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Red blood cells urine positive			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0

Streptococcus test positive			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Transaminases increased			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Urinary casts present			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Urine ketone body present			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Urine leukocyte esterase			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Urine leukocyte esterase positive			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1
White blood cell count increased			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
White blood cells urine positive			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	2 / 77 (2.60%)
occurrences (all)	0	0	4
Alcohol poisoning			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Arthropod bite			

subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1
Burns second degree			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Epicondylitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	2	0	0
Hand fracture			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Injection related reaction			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	4	0	0
Joint injury			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Ligament injury			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	2 / 77 (2.60%)
occurrences (all)	0	1	2
Limb injury			
subjects affected / exposed	3 / 76 (3.95%)	0 / 78 (0.00%)	2 / 77 (2.60%)
occurrences (all)	3	0	2
Meniscus injury			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Nail injury			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Muscle strain			

subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Overdose			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	1 / 77 (1.30%)
occurrences (all)	0	1	1
Rib fracture			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Road traffic accident			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Tooth fracture			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Transfusion related complication			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Vaccination complication			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Wrist fracture			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0

Left ventricular hypertrophy			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	2 / 77 (2.60%)
occurrences (all)	0	1	2
Ventricular extrasystoles			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 76 (10.53%)	7 / 78 (8.97%)	4 / 77 (5.19%)
occurrences (all)	10	14	4
Ageusia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Anosmia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Aphonia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	2 / 76 (2.63%)	2 / 78 (2.56%)	2 / 77 (2.60%)
occurrences (all)	2	2	2
Dysaesthesia			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	1	1	0
Hypoaesthesia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Loss of consciousness			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Migraine			

subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Nerve compression			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	2 / 77 (2.60%)
occurrences (all)	0	0	2
Presyncope			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	1 / 77 (1.30%)
occurrences (all)	0	1	1
Sinus headache			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Tension headache			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Thoracic spinal cord paralysis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Blood loss anaemia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0

Lymphadenopathy			
subjects affected / exposed	0 / 76 (0.00%)	2 / 78 (2.56%)	2 / 77 (2.60%)
occurrences (all)	0	2	2
Lymphopenia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Thrombocytosis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Ear pain			
subjects affected / exposed	2 / 76 (2.63%)	0 / 78 (0.00%)	2 / 77 (2.60%)
occurrences (all)	2	0	3
Ear swelling			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
External ear inflammation			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
External ear pain			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Middle ear inflammation			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Ear lobe infection			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Eye disorders			

Blepharitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Cataract			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Chalazion			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis allergic			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Conjunctival hyperaemia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Eye haemorrhage			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	2	0	0
Eye irritation			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Eyelid margin crusting			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Eyelid oedema			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Keratitis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Photophobia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Swelling of eyelid			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	2

Visual impairment			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 76 (1.32%)	3 / 78 (3.85%)	0 / 77 (0.00%)
occurrences (all)	1	3	0
Diarrhoea			
subjects affected / exposed	4 / 76 (5.26%)	2 / 78 (2.56%)	6 / 77 (7.79%)
occurrences (all)	6	2	6
Abdominal discomfort			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	1	1	0
Abdominal pain lower			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	1 / 77 (1.30%)
occurrences (all)	0	2	1
Aphthous ulcer			
subjects affected / exposed	0 / 76 (0.00%)	2 / 78 (2.56%)	1 / 77 (1.30%)
occurrences (all)	0	2	1
Cheilitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	2 / 77 (2.60%)
occurrences (all)	1	0	2
Dental caries			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			

subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	1 / 77 (1.30%)
occurrences (all)	0	1	1
Gastrointestinal inflammation			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal sphincter insufficiency			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	3 / 76 (3.95%)	3 / 78 (3.85%)	2 / 77 (2.60%)
occurrences (all)	3	5	3
Odynophagia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Reflux gastritis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0

Toothache			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1
Tooth impacted			
subjects affected / exposed	2 / 76 (2.63%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	3	0	0
Vomiting			
subjects affected / exposed	1 / 76 (1.32%)	3 / 78 (3.85%)	1 / 77 (1.30%)
occurrences (all)	1	4	1
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Hepatic steatosis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Hypertransaminasaemia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	17 / 76 (22.37%)	24 / 78 (30.77%)	21 / 77 (27.27%)
occurrences (all)	20	45	29
Pruritus			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	4 / 77 (5.19%)
occurrences (all)	0	1	5
Acne			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Actinic keratosis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	2 / 77 (2.60%)
occurrences (all)	1	1	2
Alopecia areata			

subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Angioedema			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Blister			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Dermatitis allergic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Dermatitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	1 / 77 (1.30%)
occurrences (all)	0	1	1
Dermatitis exfoliative generalised			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	1	1	0
Dyshidrotic eczema			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Ecchymosis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	2 / 76 (2.63%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	2	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Onycholysis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Photodermatosis			

subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Pityriasis rosea			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Pruritus allergic			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Psoriasis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Purpura			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Rash erythematous			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Rash follicular			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Rash papular			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	1 / 77 (1.30%)
occurrences (all)	0	1	1
Rosacea			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Skin burning sensation			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Skin exfoliation			

subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Skin induration			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Skin fissures			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Solar urticaria			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Haemoglobinuria			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Urine abnormality			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	6 / 76 (7.89%)	2 / 78 (2.56%)	4 / 77 (5.19%)
occurrences (all)	7	3	4
Arthritis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	3 / 76 (3.95%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	3	0	0
Bursitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Joint swelling			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	2 / 77 (2.60%)
occurrences (all)	0	0	2
Ligamentitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal stiffness			
subjects affected / exposed	2 / 76 (2.63%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	2	1	0
Muscle tightness			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0

Myalgia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	3	0	1
Neck pain			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	2 / 77 (2.60%)
occurrences (all)	0	0	3
Pain in jaw			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Scleroderma			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	1	2	0
Synovitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Tendon pain			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Tendonitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	3 / 77 (3.90%)
occurrences (all)	1	0	3
Influenza			

subjects affected / exposed	4 / 76 (5.26%)	5 / 78 (6.41%)	1 / 77 (1.30%)
occurrences (all)	5	5	2
Nasopharyngitis			
subjects affected / exposed	16 / 76 (21.05%)	15 / 78 (19.23%)	10 / 77 (12.99%)
occurrences (all)	19	21	15
Oral herpes			
subjects affected / exposed	2 / 76 (2.63%)	3 / 78 (3.85%)	6 / 77 (7.79%)
occurrences (all)	3	3	10
Upper respiratory tract infection			
subjects affected / exposed	12 / 76 (15.79%)	8 / 78 (10.26%)	13 / 77 (16.88%)
occurrences (all)	16	13	17
Urinary tract infection			
subjects affected / exposed	3 / 76 (3.95%)	4 / 78 (5.13%)	4 / 77 (5.19%)
occurrences (all)	4	4	4
Abscess limb			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Abscess oral			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Acarodermatitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Acne pustular			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Asymptomatic bacteriuria			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1
Asymptomatic COVID-19			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Bacterial blepharitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Bacterial vaginosis			

subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Bacterial vulvovaginitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Bacteriuria			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	1 / 77 (1.30%)
occurrences (all)	2	2	1
Chest wall abscess			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Chronic sinusitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	2	0	0
Conjunctivitis			
subjects affected / exposed	2 / 76 (2.63%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	2	1	0
Conjunctivitis bacterial			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1
Eczema herpeticum			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1
Eczema impetiginous			

subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	1	1	0
Eczema infected			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Enteritis infectious			
subjects affected / exposed	0 / 76 (0.00%)	2 / 78 (2.56%)	0 / 77 (0.00%)
occurrences (all)	0	2	0
Enterobiasis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Epiglottitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Erysipelas			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Eyelid infection			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Folliculitis			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	1	1	0
Furuncle			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1
Gastroenteritis			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	1	2	0
Gastroenteritis viral			
subjects affected / exposed	0 / 76 (0.00%)	2 / 78 (2.56%)	1 / 77 (1.30%)
occurrences (all)	0	3	1
Gastrointestinal infection			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal viral infection			

subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Genital herpes			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Genital infection female			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Herpes ophthalmic			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Herpes simplex			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	3 / 77 (3.90%)
occurrences (all)	0	1	4
Herpes zoster			
subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	1	1	0
Hordeolum			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Impetigo			
subjects affected / exposed	2 / 76 (2.63%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	2	0	1
Infection			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Localised infection			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Ophthalmic herpes simplex			

subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Otitis externa			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	3	0	0
Otitis externa bacterial			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Paronychia			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Peritonsillar abscess			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 76 (0.00%)	2 / 78 (2.56%)	0 / 77 (0.00%)
occurrences (all)	0	2	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Pulpitis dental			
subjects affected / exposed	3 / 76 (3.95%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	3	0	1
Pyuria			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Rash pustular			

subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	2 / 76 (2.63%)	2 / 78 (2.56%)	1 / 77 (1.30%)
occurrences (all)	2	3	1
Rhinitis			
subjects affected / exposed	0 / 76 (0.00%)	2 / 78 (2.56%)	1 / 77 (1.30%)
occurrences (all)	0	2	1
Sinusitis			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	2 / 77 (2.60%)
occurrences (all)	0	1	2
Skin bacterial infection			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	1 / 77 (1.30%)
occurrences (all)	0	1	1
Skin candida			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Skin infection			
subjects affected / exposed	2 / 76 (2.63%)	2 / 78 (2.56%)	1 / 77 (1.30%)
occurrences (all)	2	2	1
Staphylococcal infection			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Staphylococcal skin infection			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	2
Subcutaneous abscess			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1
Superinfection			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Superinfection bacterial			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Tinea pedis			

subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1
Testicular abscess			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Trichomoniasis			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Vaginal infection			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Varicella zoster virus infection			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	1 / 76 (1.32%)	2 / 78 (2.56%)	0 / 77 (0.00%)
occurrences (all)	1	2	0
Viral pharyngitis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	1	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 76 (3.95%)	1 / 78 (1.28%)	1 / 77 (1.30%)
occurrences (all)	3	2	1
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Vulvovaginal mycotic infection			

subjects affected / exposed	1 / 76 (1.32%)	1 / 78 (1.28%)	1 / 77 (1.30%)
occurrences (all)	1	2	1
Ear lobe infection			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Diabetes mellitus			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	1	0	0
Dyslipidaemia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	1 / 76 (1.32%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	2	0	0
Histamine intolerance			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	0 / 77 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 76 (0.00%)	1 / 78 (1.28%)	1 / 77 (1.30%)
occurrences (all)	0	1	1
Hypercholesterolaemia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Hyperlipidaemia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	2 / 76 (2.63%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	3	0	0

Hyperuricaemia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Increased appetite			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	1 / 77 (1.30%)
occurrences (all)	0	0	1
Vitamin B12 deficiency			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 76 (0.00%)	0 / 78 (0.00%)	0 / 77 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Group 4 (Placebo q2w) - Part 1 - blinded	Group 5 (ISB 830 600mg q2w) - Part 2	Group 6 (Placebo q2w) - Part 2 - blinded
Total subjects affected by non-serious adverse events			
subjects affected / exposed	57 / 80 (71.25%)	65 / 75 (86.67%)	37 / 74 (50.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign breast neoplasm			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Skin papilloma			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Uterine leiomyoma			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 80 (0.00%)	3 / 75 (4.00%)	1 / 74 (1.35%)
occurrences (all)	0	3	1
Flushing			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0

Thrombophlebitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	3	0
Application site reaction			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Chest discomfort			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Facial pain			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Feeling cold			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Feeling hot			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Influenza like illness			

subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Injection site bruising			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Injection site erythema			
subjects affected / exposed	0 / 80 (0.00%)	2 / 75 (2.67%)	1 / 74 (1.35%)
occurrences (all)	0	5	2
Injection site haematoma			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Injection site induration			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Injection site oedema			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Injection site pruritus			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Injection site rash			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Injection site reaction			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Injection site swelling			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Injection site urticaria			
subjects affected / exposed	1 / 80 (1.25%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	1	3	0
Malaise			

subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	1 / 74 (1.35%)
occurrences (all)	0	1	1
Pain			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	1 / 80 (1.25%)	1 / 75 (1.33%)	1 / 74 (1.35%)
occurrences (all)	1	1	1
Pyrexia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Therapeutic response unexpected			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Allergy to animal			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Allergy to arthropod bite			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Allergy to arthropod sting			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Drug hypersensitivity			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Food allergy			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Hypersensitivity			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0

Seasonal allergy			
subjects affected / exposed	1 / 80 (1.25%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	1	2	0
Reproductive system and breast disorders			
Breast inflammation			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Breast mass			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Breast pain			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Breast tenderness			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Cervix inflammation			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	1 / 80 (1.25%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	1	4	0
Menstrual disorder			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Ovarian cyst			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Ovarian disorder			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Premature menopause			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Sexual dysfunction			

subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Uterine cervix stenosis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Uterine haemorrhage			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 80 (1.25%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	1	2	0
Cough			
subjects affected / exposed	2 / 80 (2.50%)	3 / 75 (4.00%)	0 / 74 (0.00%)
occurrences (all)	2	4	0
Catarrh			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Dysphonia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	1 / 80 (1.25%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	1	1	0
Epistaxis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Nasal septum disorder			

subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 80 (1.25%)	3 / 75 (4.00%)	1 / 74 (1.35%)
occurrences (all)	1	3	2
Productive cough			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Reflux laryngitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 80 (0.00%)	3 / 75 (4.00%)	2 / 74 (2.70%)
occurrences (all)	0	4	2
Rhinorrhoea			
subjects affected / exposed	0 / 80 (0.00%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	0	2	0
Sinus congestion			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Throat irritation			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	2	0
Anxiety			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Attention deficit hyperactivity disorder			

subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Bipolar disorder			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	1 / 80 (1.25%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	1	1	0
Initial insomnia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Insomnia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Mixed anxiety and depressive disorder			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Nervousness			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Panic attack			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Bacterial test positive			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Blood bicarbonate decreased			

subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Blood glucose increased			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Blood iron decreased			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Blood pressure increased			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Blood triglycerides increased			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Blood urine present			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Body temperature increased			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
C-reactive protein increased			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Cardiac murmur			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0

Glucose urine present			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Haemoglobin urine present			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Hepatic enzyme increased			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Neutrophil count decreased			
subjects affected / exposed	1 / 80 (1.25%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	3	1	0
Platelet count increased			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	2
Protein urine present			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Red blood cell count decreased			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Red blood cells urine positive			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Streptococcus test positive			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0

Transaminases increased			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Urinary casts present			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Urine ketone body present			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Urine leukocyte esterase			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Urine leukocyte esterase positive			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
White blood cell count increased			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	2 / 74 (2.70%)
occurrences (all)	1	0	3
White blood cells urine positive			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Alcohol poisoning			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 80 (0.00%)	3 / 75 (4.00%)	0 / 74 (0.00%)
occurrences (all)	0	4	0
Burns second degree			

subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Epicondylitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Hand fracture			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Injection related reaction			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Ligament injury			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Ligament sprain			
subjects affected / exposed	1 / 80 (1.25%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	1	1	0
Limb injury			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Meniscus injury			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Nail injury			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Muscle strain			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Overdose			

subjects affected / exposed	1 / 80 (1.25%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	1	1	0
Procedural pain			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Rib fracture			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Transfusion related complication			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Vaccination complication			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Wrist fracture			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Left ventricular hypertrophy			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0

Tachycardia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Ventricular extrasystoles			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 80 (10.00%)	6 / 75 (8.00%)	5 / 74 (6.76%)
occurrences (all)	9	11	5
Ageusia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Anosmia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Aphonia			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	2 / 74 (2.70%)
occurrences (all)	0	0	2
Dysaesthesia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Loss of consciousness			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	1 / 80 (1.25%)	1 / 75 (1.33%)	1 / 74 (1.35%)
occurrences (all)	1	1	1
Nerve compression			

subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	1 / 74 (1.35%)
occurrences (all)	0	1	1
Sinus headache			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Tension headache			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Thoracic spinal cord paralysis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Blood loss anaemia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Lymphadenopathy			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0

Lymphopenia			
subjects affected / exposed	2 / 80 (2.50%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	2	0	0
Neutropenia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Thrombocytosis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	1 / 80 (1.25%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	1	1	0
Ear swelling			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	2	0	0
External ear inflammation			
subjects affected / exposed	2 / 80 (2.50%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	2	0	0
External ear pain			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Middle ear inflammation			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Ear lobe infection			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Cataract			

subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Chalazion			
subjects affected / exposed	2 / 80 (2.50%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	2	0	0
Conjunctivitis allergic			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Conjunctival hyperaemia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Eye haemorrhage			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Eyelid margin crusting			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Eyelid oedema			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Keratitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Swelling of eyelid			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	0 / 80 (0.00%)	4 / 75 (5.33%)	0 / 74 (0.00%)
occurrences (all)	0	4	0
Diarrhoea			
subjects affected / exposed	1 / 80 (1.25%)	3 / 75 (4.00%)	3 / 74 (4.05%)
occurrences (all)	1	3	3
Abdominal discomfort			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Aphthous ulcer			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	2	0
Cheilitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0

Gastrointestinal inflammation			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal sphincter insufficiency			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Haematochezia			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	2 / 80 (2.50%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	2	2	0
Odynophagia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Reflux gastritis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Stomatitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Tooth impacted			

subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Hepatic steatosis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Hypertransaminasaemia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	17 / 80 (21.25%)	26 / 75 (34.67%)	12 / 74 (16.22%)
occurrences (all)	20	39	15
Pruritus			
subjects affected / exposed	1 / 80 (1.25%)	2 / 75 (2.67%)	2 / 74 (2.70%)
occurrences (all)	2	3	2
Acne			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Actinic keratosis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Alopecia			
subjects affected / exposed	3 / 80 (3.75%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	3	1	0
Alopecia areata			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Angioedema			

subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Blister			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Dermatitis contact			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Dermatitis exfoliative generalised			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Dyshidrotic eczema			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Ecchymosis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 80 (0.00%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	0	2	0
Hyperhidrosis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Onycholysis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	3	0
Photodermatosis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Pityriasis rosea			

subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Pruritus allergic			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Purpura			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Rash erythematous			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Rash follicular			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Rosacea			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Skin burning sensation			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Skin induration			

subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Skin fissures			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Swelling face			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Solar urticaria			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	2 / 80 (2.50%)	2 / 75 (2.67%)	1 / 74 (1.35%)
occurrences (all)	2	2	1
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Haemoglobinuria			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Urine abnormality			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 80 (0.00%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	0	2	0
Arthritis			

subjects affected / exposed	0 / 80 (0.00%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	0	2	0
Back pain			
subjects affected / exposed	1 / 80 (1.25%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	1	2	0
Bursitis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Groin pain			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Ligamentitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Muscle tightness			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Neck pain			

subjects affected / exposed	0 / 80 (0.00%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	0	2	0
Pain in extremity			
subjects affected / exposed	1 / 80 (1.25%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	1	1	0
Pain in jaw			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Scleroderma			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Spinal pain			
subjects affected / exposed	2 / 80 (2.50%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	2	0	1
Synovitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Tendon pain			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Tendonitis			
subjects affected / exposed	0 / 80 (0.00%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 80 (0.00%)	4 / 75 (5.33%)	0 / 74 (0.00%)
occurrences (all)	0	4	0
Influenza			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	7 / 80 (8.75%)	12 / 75 (16.00%)	7 / 74 (9.46%)
occurrences (all)	8	14	10

Oral herpes			
subjects affected / exposed	2 / 80 (2.50%)	2 / 75 (2.67%)	2 / 74 (2.70%)
occurrences (all)	3	2	2
Upper respiratory tract infection			
subjects affected / exposed	4 / 80 (5.00%)	6 / 75 (8.00%)	5 / 74 (6.76%)
occurrences (all)	4	7	6
Urinary tract infection			
subjects affected / exposed	4 / 80 (5.00%)	3 / 75 (4.00%)	2 / 74 (2.70%)
occurrences (all)	4	5	2
Abscess limb			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Abscess oral			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Acarodermatitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Acne pustular			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Asymptomatic bacteriuria			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Asymptomatic COVID-19			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Bacterial blepharitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Bacterial vaginosis			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	2	0	0
Bacterial vulvovaginitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0

Bacteriuria			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	0 / 80 (0.00%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	0	2	0
Cellulitis			
subjects affected / exposed	1 / 80 (1.25%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	1	2	0
Chest wall abscess			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Chronic sinusitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			
subjects affected / exposed	0 / 80 (0.00%)	2 / 75 (2.67%)	1 / 74 (1.35%)
occurrences (all)	0	2	1
Conjunctivitis bacterial			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	1 / 74 (1.35%)
occurrences (all)	0	2	1
Ear infection			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	1	0	1
Eczema herpeticum			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Eczema impetiginous			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Eczema infected			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	1 / 74 (1.35%)
occurrences (all)	0	1	1

Enteritis infectious			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Enterobiasis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Epiglottitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Erysipelas			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Eyelid infection			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	2 / 80 (2.50%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	2	1	0
Furuncle			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 80 (1.25%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	1	2	0
Gastroenteritis viral			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal infection			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal viral infection			
subjects affected / exposed	2 / 80 (2.50%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	2	0	0
Genital herpes			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0

Genital infection female			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Gingivitis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Herpes ophthalmic			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Herpes simplex			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Impetigo			
subjects affected / exposed	1 / 80 (1.25%)	3 / 75 (4.00%)	0 / 74 (0.00%)
occurrences (all)	2	4	0
Infection			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Localised infection			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Ophthalmic herpes simplex			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0

Otitis externa			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Otitis externa bacterial			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Peritonsillar abscess			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	2 / 80 (2.50%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	2	2	0
Pharyngitis streptococcal			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Pulpitis dental			
subjects affected / exposed	1 / 80 (1.25%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	1	1	0
Pyuria			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	2 / 80 (2.50%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	2	2	0

Rhinitis			
subjects affected / exposed	0 / 80 (0.00%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	0	2	0
Sinusitis			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	1 / 74 (1.35%)
occurrences (all)	0	1	1
Skin bacterial infection			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	1 / 74 (1.35%)
occurrences (all)	0	1	1
Skin candida			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Staphylococcal skin infection			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	2	0	0
Subcutaneous abscess			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Superinfection			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Superinfection bacterial			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Tinea pedis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 80 (0.00%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	0	3	0

Testicular abscess			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Tooth abscess			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Trichomoniasis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Vaginal infection			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Varicella zoster virus infection			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Viral infection			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Viral pharyngitis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 80 (1.25%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	1	1	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	2 / 80 (2.50%)	0 / 75 (0.00%)	1 / 74 (1.35%)
occurrences (all)	2	0	1
Ear lobe infection			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0

Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Dyslipidaemia			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Histamine intolerance			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 80 (1.25%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	1	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Hyperkalaemia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Hyperlipidaemia			
subjects affected / exposed	1 / 80 (1.25%)	2 / 75 (2.67%)	0 / 74 (0.00%)
occurrences (all)	3	2	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Hyperuricaemia			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	1	0
Hypokalaemia			

subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 80 (0.00%)	0 / 75 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 80 (0.00%)	1 / 75 (1.33%)	0 / 74 (0.00%)
occurrences (all)	0	2	0

Non-serious adverse events	Group 7 (placebo, open-label) - Part 1	Group 8 (Placebo open-label) - Part 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 60 (71.67%)	38 / 67 (56.72%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign breast neoplasm			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Skin papilloma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Uterine leiomyoma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 60 (3.33%)	1 / 67 (1.49%)	
occurrences (all)	2	1	
Flushing			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Thrombophlebitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Application site reaction			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Asthenia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Chest discomfort			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Chest pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Chills			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Face oedema			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Facial pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Feeling cold			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Feeling hot			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Influenza like illness			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Injection site bruising			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	

Injection site erythema			
subjects affected / exposed	2 / 60 (3.33%)	1 / 67 (1.49%)	
occurrences (all)	3	1	
Injection site haematoma			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Injection site induration			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Injection site oedema			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Injection site pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Injection site pruritus			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Injection site rash			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Injection site reaction			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Injection site swelling			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Injection site urticaria			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Malaise			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Oedema peripheral			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	

Pain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Peripheral swelling			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Therapeutic response unexpected			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Allergy to animal			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Allergy to arthropod bite			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Allergy to arthropod sting			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Drug hypersensitivity			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Food allergy			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Hypersensitivity			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Seasonal allergy			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			

Breast inflammation				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Breast mass				
subjects affected / exposed	0 / 60 (0.00%)	2 / 67 (2.99%)		
occurrences (all)	0	2		
Breast pain				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Breast tenderness				
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)		
occurrences (all)	0	1		
Cervix inflammation				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Dysmenorrhoea				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Menstrual disorder				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Ovarian cyst				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Ovarian disorder				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Premature menopause				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Sexual dysfunction				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Uterine cervix stenosis				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		

Uterine haemorrhage			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Vaginal haemorrhage			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 60 (1.67%)	1 / 67 (1.49%)	
occurrences (all)	1	1	
Cough			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Catarrh			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Dysphonia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Dyspnoea			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Epistaxis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Nasal congestion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Nasal septum disorder			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	4 / 60 (6.67%)	1 / 67 (1.49%)	
occurrences (all)	4	2	
Productive cough			

subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Reflux laryngitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Rhinitis allergic			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Sinus congestion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Throat irritation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract inflammation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Anxiety			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Attention deficit hyperactivity disorder			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Bipolar disorder			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Depression			

subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Initial insomnia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Mixed anxiety and depressive disorder			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Nervousness			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Panic attack			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Bacterial test positive			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Blood bicarbonate decreased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Blood bilirubin increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Blood creatinine increased			

subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	2	0	
Blood glucose increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Blood iron decreased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Blood pressure increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Blood triglycerides increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Blood urine present			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Body temperature increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
C-reactive protein increased			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Cardiac murmur			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Glucose urine present			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Haemoglobin decreased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	

Haemoglobin urine present			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Hepatic enzyme increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Liver function test increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Lymphocyte count decreased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Neutrophil count decreased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Platelet count increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Protein urine present			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Red blood cell count decreased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Red blood cells urine positive			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Streptococcus test positive			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Transaminases increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Urinary casts present			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	

Urine ketone body present			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Urine leukocyte esterase			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Urine leukocyte esterase positive			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Weight increased			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
White blood cell count increased			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
White blood cells urine positive			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Alcohol poisoning			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Arthropod bite			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Burns second degree			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Epicondylitis			

subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Hand fracture			
subjects affected / exposed	1 / 60 (1.67%)	1 / 67 (1.49%)	
occurrences (all)	1	1	
Injection related reaction			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Joint injury			
subjects affected / exposed	0 / 60 (0.00%)	3 / 67 (4.48%)	
occurrences (all)	0	3	
Ligament injury			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Ligament sprain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Limb injury			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Meniscus injury			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Nail injury			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Muscle strain			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Overdose			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Procedural pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Rib fracture			

subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Road traffic accident			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Skin abrasion			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Skin laceration			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Tooth fracture			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Transfusion related complication			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Vaccination complication			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Wrist fracture			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Left ventricular hypertrophy			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Tachycardia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Ventricular extrasystoles			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	

Nervous system disorders			
Headache			
subjects affected / exposed	5 / 60 (8.33%)	7 / 67 (10.45%)	
occurrences (all)	7	8	
Ageusia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Anosmia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Aphonia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	1 / 60 (1.67%)	1 / 67 (1.49%)	
occurrences (all)	1	3	
Dysaesthesia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Hypoaesthesia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Loss of consciousness			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Migraine			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Nerve compression			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Paraesthesia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Presyncope			

subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Sciatica			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Sinus headache			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Somnolence			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Tension headache			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Thoracic spinal cord paralysis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Blood loss anaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Iron deficiency anaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Lymphadenopathy			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Lymphopenia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Neutropenia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	

Thrombocytosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Deafness unilateral			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Ear pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Ear swelling			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
External ear inflammation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
External ear pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Middle ear inflammation			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Ear lobe infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Blepharitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Cataract			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Chalazion			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	2	0	
Conjunctivitis allergic			

subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Conjunctival hyperaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Eye haemorrhage			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Eye irritation			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Eyelid margin crusting			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Eyelid oedema			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Keratitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Photophobia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Swelling of eyelid			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Visual impairment			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	

Abdominal discomfort				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Abdominal pain lower				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Abdominal pain upper				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Aphthous ulcer				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Cheilitis				
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)		
occurrences (all)	1	0		
Constipation				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Dental caries				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Dry mouth				
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)		
occurrences (all)	0	1		
Dyspepsia				
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)		
occurrences (all)	1	0		
Gastritis				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Gastrointestinal inflammation				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Gastrooesophageal reflux disease				
subjects affected / exposed	1 / 60 (1.67%)	1 / 67 (1.49%)		
occurrences (all)	1	1		

Gastrooesophageal sphincter insufficiency			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Haematochezia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Haemorrhoids			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Odynophagia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Reflux gastritis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Stomatitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Toothache			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Tooth impacted			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	2	0	
Hepatobiliary disorders			

Hepatic function abnormal			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Hepatic steatosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Hypertransaminasaemia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			
subjects affected / exposed	12 / 60 (20.00%)	11 / 67 (16.42%)	
occurrences (all)	12	13	
Pruritus			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Acne			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Actinic keratosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Alopecia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Alopecia areata			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Angioedema			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Blister			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Dermatitis allergic			

subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Dermatitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Dermatitis contact			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Dermatitis exfoliative generalised			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Dyshidrotic eczema			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Ecchymosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Hyperhidrosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Onycholysis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Photodermatosis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Pityriasis rosea			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Pruritus allergic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Psoriasis			

subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)		
occurrences (all)	0	1		
Purpura				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Rash				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Rash erythematous				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Rash follicular				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Rash papular				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Rosacea				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Seborrhoeic dermatitis				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Skin burning sensation				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Skin exfoliation				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Skin induration				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Skin fissures				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Swelling face				

subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Solar urticaria			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Urticaria			
subjects affected / exposed	0 / 60 (0.00%)	2 / 67 (2.99%)	
occurrences (all)	0	2	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Haemoglobinuria			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Urine abnormality			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Hypothyroidism			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 60 (5.00%)	0 / 67 (0.00%)	
occurrences (all)	3	0	
Arthritis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Bursitis			

subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Groin pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Joint swelling			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Ligamentitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Muscle tightness			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal discomfort			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Neck pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Pain in jaw			

subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Scleroderma			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Spinal osteoarthritis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Spinal pain			
subjects affected / exposed	1 / 60 (1.67%)	1 / 67 (1.49%)	
occurrences (all)	2	1	
Synovitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Tendon pain			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Tendonitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Influenza			
subjects affected / exposed	2 / 60 (3.33%)	0 / 67 (0.00%)	
occurrences (all)	2	0	
Nasopharyngitis			
subjects affected / exposed	9 / 60 (15.00%)	8 / 67 (11.94%)	
occurrences (all)	11	8	
Oral herpes			
subjects affected / exposed	4 / 60 (6.67%)	3 / 67 (4.48%)	
occurrences (all)	7	5	
Upper respiratory tract infection			
subjects affected / exposed	8 / 60 (13.33%)	1 / 67 (1.49%)	
occurrences (all)	9	2	

Urinary tract infection			
subjects affected / exposed	4 / 60 (6.67%)	1 / 67 (1.49%)	
occurrences (all)	5	1	
Abscess limb			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Abscess oral			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Acarodermatitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Acne pustular			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Asymptomatic bacteriuria			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Asymptomatic COVID-19			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Bacterial blepharitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Bacterial vaginosis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	2	0	
Bacterial vulvovaginitis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Bacteriuria			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
COVID-19			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	

Cellulitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Chest wall abscess			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Chronic sinusitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Conjunctivitis			
subjects affected / exposed	1 / 60 (1.67%)	1 / 67 (1.49%)	
occurrences (all)	1	1	
Conjunctivitis bacterial			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Cystitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Ear infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Eczema herpeticum			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Eczema impetiginous			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Eczema infected			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Enteritis infectious			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Enterobiasis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	

Epiglottitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Erysipelas			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Eyelid infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Folliculitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	2	0	
Furuncle			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Gastroenteritis viral			
subjects affected / exposed	2 / 60 (3.33%)	0 / 67 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal viral infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Genital herpes			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Genital infection female			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Gingivitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	

Herpes ophthalmic				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Herpes simplex				
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)		
occurrences (all)	0	1		
Herpes zoster				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Hordeolum				
subjects affected / exposed	1 / 60 (1.67%)	1 / 67 (1.49%)		
occurrences (all)	1	1		
Impetigo				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Infection				
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)		
occurrences (all)	0	1		
Laryngitis				
subjects affected / exposed	2 / 60 (3.33%)	0 / 67 (0.00%)		
occurrences (all)	2	0		
Localised infection				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Ophthalmic herpes simplex				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Oral candidiasis				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Otitis externa				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Otitis externa bacterial				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		

Paronychia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Peritonsillar abscess			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Periodontitis			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Pharyngitis streptococcal			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Pneumonia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Pulpitis dental			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Pyuria			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Rash pustular			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	3 / 60 (5.00%)	0 / 67 (0.00%)	
occurrences (all)	3	0	

Skin bacterial infection				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Skin candida				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Skin infection				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Staphylococcal infection				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Staphylococcal skin infection				
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)		
occurrences (all)	0	1		
Subcutaneous abscess				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Superinfection				
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)		
occurrences (all)	1	0		
Superinfection bacterial				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Tinea pedis				
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)		
occurrences (all)	0	1		
Tonsillitis				
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)		
occurrences (all)	0	1		
Testicular abscess				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		
Tooth abscess				
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)		
occurrences (all)	0	0		

Tooth infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Trichomoniasis			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Vaginal infection			
subjects affected / exposed	0 / 60 (0.00%)	2 / 67 (2.99%)	
occurrences (all)	0	3	
Varicella zoster virus infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Viral infection			
subjects affected / exposed	2 / 60 (3.33%)	0 / 67 (0.00%)	
occurrences (all)	2	0	
Viral pharyngitis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Ear lobe infection			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Diabetes mellitus			

subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Dyslipidaemia			
subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Gout			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Histamine intolerance			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Hyperglycaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Hypercholesterolaemia			
subjects affected / exposed	0 / 60 (0.00%)	1 / 67 (1.49%)	
occurrences (all)	0	1	
Hyperkalaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Hyperlipidaemia			
subjects affected / exposed	1 / 60 (1.67%)	1 / 67 (1.49%)	
occurrences (all)	1	1	
Hypertriglyceridaemia			
subjects affected / exposed	1 / 60 (1.67%)	1 / 67 (1.49%)	
occurrences (all)	1	1	
Hyperuricaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Increased appetite			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	
Vitamin B12 deficiency			

subjects affected / exposed	1 / 60 (1.67%)	0 / 67 (0.00%)	
occurrences (all)	1	0	
Vitamin D deficiency			
subjects affected / exposed	0 / 60 (0.00%)	0 / 67 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 April 2018	Major changes from Protocol v1.0 to Protocol v2.0 (Amendment 1) dated 06-Apr-2018 included: • Clarified that subjects who completed the treatment period had the opportunity to enter in a separate Open-label extension study (GBR 830-205). Subjects who were not entering the Open-label extension study were to enter the follow-up period for the GBR 830-204 study. Subjects continuing in the follow-up period had a follow-up phone call on Days 141 (Week 20) and 169 (Week 24) and a final clinic visit on Day 197 (Week 28). • Modified the schedule of assessments table- the follow-up was split into 2 columns; 1 for Days 141 and 169, and 1 for Day 197 (final follow-up visit). It was expected that only a small group of subjects would be completing the follow-up period, as the majority of subjects were likely to consent to participate in the Open-label extension study (subjects were only required to complete 16 weeks of treatment to be eligible). Therefore, efficacy and exploratory assessments were no longer needed to be performed at the follow-up visits; only safety was assessed. • Revised Schedule of Assessments to clarify that samples for immunogenicity would be collected only on Day 197 of follow-up period. Samples for biomarker analysis would not be collected during follow-up period. Also, it was clarified that photographs would not be taken during the follow-up period (Week 28). Revised to clarify that height would only be measured at screening and to clarify details regarding the follow-up period for subjects entering the Open-label extension study.
06 April 2018	Major changes from Protocol v1.0 to Protocol v2.0 (Amendment 1) dated 06-Apr-2018 continued: • Clarified in Section 11.4, Pruritus NRS that a minimum of 3 daily scores were required instead of 4 daily scores. • Clarified in Table 7: Pharmacodynamic (Biomarker), Pharmacokinetic, and Immunogenicity Blood Sampling Time Points: PD (Biomarker) blood sample would not be taken at Days 86 and 197. • Clarified in Section 12.2, Pharmacokinetic Assessments: a final sample would only be collected on Day 197 for subjects that enter the follow-up period. • Clarified in Section 14.1 Screening Period (Day -28 to Day -1): data would be entered into the electronic subject diary every day from start of screening period to Day 113 (Week 16) instead of Day 197 (final study visit). • Added in Section 14.2.4, End of Treatment/Early Discontinuation: #20-Daily electronic subject diary assessment/collect electronic subject diary device (as this would no longer be collected during follow-up period, but at EOT). • Clarified in Section 14.3, Follow-up Period: Day 141±5, Day 169±5 and Day 197±5: the follow-up period will only pertain to subjects not enrolling in the Open-label extension protocol. Clarified that Days 141 and 169 will be phone contacts only and that Day 197 will be an in-person visit. Clarified which assessments will be performed at what time points. Removed efficacy assessments from the post treatment follow-up period. • Clarified that information will be provided separately from the protocol.

07 November 2018	Major changes from Protocol v2.0 to Protocol v3.0 (Amendment 2), dated 07-Nov-2018 included the below points: • Study design was revised to include details of the Open-label Treatment Phase portion of the study. Added text the Blinded Treatment Phase consists of a randomised, placebo-controlled treatment with GBR 830 for 16 weeks at different dose levels. The Open-label Treatment Phase consists of a 38-week treatment phase where 300 mg of GBR 830 would be administered q2w SC. The primary endpoint of the study would be assessed at the end of the Blinded Treatment period at Week 16. • Clarification/revision to number of subjects randomised to treatment groups (changed from 98 to 78 subjects). • Revision study design and Section 10.1, Study Drug to reflect the number of total doses (from 8 to 27), frequency (added every 2 weeks [q2w]), and inclusion of description of Open-label dose and duration (Open-label dosing of 300 mg q2w from Week 16 until Week 52). • Revised study design to clarify study assessments to be conducted. The new text read: Safety assessments, clinical laboratory assessments, vital sign assessments, PK sampling, immunogenicity sampling, and clinical efficacy assessments (IGA and EASI) would be performed by the blinded Investigator and blinded study staff as defined in the Schedule of Assessments, or until the subject discontinued from the study.
07 November 2018	Major changes from Protocol v2.0 to Protocol v3.0 (Amendment 2), dated 07-Nov-2018 continued (1): • Revised study design to clarify - The EOT visits would be conducted on Day 113 (Week 16) for the Blinded Treatment Phase and at Day 379 (Week 54) for the Open-label Treatment Phase for all subjects. - Subjects continue into the follow-up period had a follow-up phone call 4 and 8 weeks after the EOT visit (Day 407 (Week 58) and Day 435 (Week 62) respectively) and a final clinic visit after the EOT (Day 463 [Week 66]) visit. - Subjects who withdrew consent from Blinded Treatment Phase prior to Week 1 would undergo the Blinded Treatment Phase EOT visit procedures and enter the follow-up period. - Subjects who withdrew consent from Open-label Treatment Phase prior to Week 52 would undergo the Open-label Treatment Phase EOT visit procedures and enter the follow-up period. - All subjects continued in the follow-up period had a follow-up phone call 4 and 8 weeks after the EOT visit and a on Days 141 (Week 20) and 169 (Week 24) and a final clinic visit 12 weeks after the EOT visit. • Clarified criteria for subjects who had completed the GBR 830-204 study prior to implementation of protocol amendment 2 or who were in the follow-up phase of the study at the time of implementation of protocol amendment 2, to be eligible to participate in the Open-label Treatment Phase following completion of the Blinded Treatment Phase. • Modified Section 15.3.2, Secondary Endpoints from 'Percentage change in pruritus NRS scored on a scale of 0–10 from baseline, and number and percent of subjects with improvement of NRS from baseline at each time point investigated through Week 16' to 'Proportion of subjects with improvement (reduction) of pruritus NRS ≥4 from baseline to Week 16' per Paul Ehrlich Institute (PEI) request • Revised secondary efficacy endpoint to include timeframe for assessment Week 16 for Change in SCORAD from baseline.

07 November 2018	Major changes from Protocol v2.0 to Protocol v3.0 (Amendment 2), dated 07-Nov-2018 continued (2): • Added Week 54 to include timeframe for assessment of safety endpoints. • Clarified in Section 15.3.2 Secondary Endpoints, that PK parameters would be determined from the data obtained in the Blinded Treatment groups. • Separated in Section 15.3.3 Exploratory Endpoints; the exploratory efficacy endpoints from exploratory biomarker endpoints for clarity. Also added three new exploratory efficacy endpoints - Proportion of subjects with both IGA 0 or 1 (on a 5-point scale) and an IGA reduction from baseline of ≥2 points at Week 54. - Proportion of subjects with EASI-75 (≥75% improvement from baseline) at Week 54. - Proportion of subjects who achieve an EASI 50 (≥50% improvement from baseline) response from baseline through Week 54. • Revised Section 7.1.4 Number of Subjects and Section 15.1 Sample Size: - Number of subjects resulting from changing power of the study from 90 to 80% as well as study design changes. Approximately 563 (from previous 446) subjects would be screened to randomise 392 (from previous 312) eligible subjects in a 1:1:1:1 ratio. - A sample size of 62 (from previous 78) completed subjects per group would provide 80% (from previous 90%) power to detect a difference of 23% between GBR 830 and placebo treatment in the percentage of subjects who achieved an IGA score of 0 or 1 at Week 16, assuming that the percentages were 35% and 12% for GBR 830 and placebo, respectively - Assuming a dropout rate of 20%, 78 (from previous 98) subjects per arm would be randomised for a total of 392 (from previous 312) subjects in a 1:1:1:1 ratio.
07 November 2018	Major changes from Protocol v2.0 to Protocol v3.0 (Amendment 2), dated 07-Nov-2018 continued (3): • Included in Section 8.2 Exclusion Criteria: #22- Known hypersensitivity to monoclonal antibodies or any of the excipients of the drug product. • Revised Section 7.1.3 Duration of Study Participation due to inclusion of Open-label Treatment Phase. Added the text 'This duration will consist of the screening period of up to 4 weeks, the Blinded Treatment period of up to 16 weeks (14 weeks of treatment, with a loading dose on Day 1 followed by maintenance dosing from Day 15 [Week 2] until the last dose at Week 14), the Open-label treatment period of up to 38 weeks, and the follow-up period of 12 weeks starting at the end of the treatment period. Subjects who consent to participate in the Open-label Treatment Phase of the study after they completed the GBR 830-204 study on protocol amendment 1, would have a study participation duration of up to 84 weeks.' • Revised Section 7.1.3 Duration of Study Participation: There was a 54-week (previous 16-week) treatment period (consisting of 52 weeks [previous 14 weeks] of dosing, including a blinded loading dose on Day 1 followed by Blinded Treatment dosing from Week 2 until Week 14, followed by Open-label treatment dosing from Week 16 to Week 52). • Revised safety assessments to include: Subjects would be clinically monitored for safety throughout the study, including anaphylactic reactions and/or ISRs, with special monitoring at the study site for 2 hours after the first dose on Day 1 (in the Blinded Treatment Phase) and on Day 113 (Week 16) (first dose in Open-label Treatment Phase) and for 1 hour after dosing at all other visits. • Revised Section 7.1 Overall Study Design to describe changes in study design - inclusion of Open-label phase, changes regarding dosing, EOT, Follow-up, criteria for entering the Open-label phase of the study.

07 November 2018	Major changes from Protocol v2.0 to Protocol v3.0 (Amendment 2), dated 07-Nov-2018 continued (4): • Revised Section 7.1 Overall Study Design to describe subjects who received concomitant therapy with a prohibited medication during the study may have GBR 830 administration temporarily stopped for the duration of the prohibited treatment, including a washout period after last dose of prohibited medication of 4 weeks or 5 half-lives, whichever was longer. Administration of GBR 830 could then be resumed after the appropriate washout period and following discussion and upon obtaining written approval from the Sponsor's medical monitor. • Revised Table 2, Schedule of Assessments (Blinded Treatment Phase) to remove Follow-up period from Blinded Treatment Phase, removal of unnecessary visits and made adjustments clarifying when procedures would be conducted. Revised to clarify criteria for subjects entering the Open-label phase of the study. Clarified days when procedures would be performed for PK subjects. Clarified nature of physical exams to be conducted at specific visits. Provided details regarding skin photography and biopsy procedures. Clarified how subjects would be monitored during study drug administration. • Added new Schedule of Assessments (Open-label Treatment Phase) with footnotes and Section 7.2 Treatment Assignment detailing the procedures and timing for the Open-label Treatment Phase, EOT phase and Follow-up phase of the study. • Revised Section 7.1.2 Dosing Rationale per PEI request to further justify the highest dose and the intended average steady state Ctrough which was almost the double of the RO max. • Clarified criteria #9 in Section 8.3 Subject Withdrawal Criteria for subjects who were treatment failures or who were able to continue in the study following administration of rescue therapy
07 November 2018	Major changes from Protocol v2.0 to Protocol v3.0 (Amendment 2), dated 07-Nov-2018 continued (5): • Clarified text in Section 9.2.2 Permitted Concomitant Medications and Therapies under which circumstances subjects would continue study treatment (or not) and clarifies how the decision would be made. Clarified how these subjects would be handled in the analysis of the efficacy endpoints. • Clarified text in Section 9.4.1 Unblinding in the Event of a Medical Emergency that in the Blinded Treatment Phase, in event of emergencies, the Investigator may contact the Sponsor's medical monitor for drug specific input prior to disclosure of the treatment allocation. However, the Investigator would make the decision to unblind the treatment assignment. Unblinding was not applicable for the Open-label Treatment Phase of the study. • Clarified in Section 9.5 Subject Completion-criteria for study completion for blinded and Open-label phases of the study. • Revised Section 12.1, Pharmacokinetic, Immunogenicity, and Pharmacodynamic (Biomarker) Blood Sampling Time Points and Allowed Windows and Table 8 to have PK, PD and ADA sampling time points and windows for both the blinded and Open- label phases of the study. • Modified in Section 12.4, Pharmacodynamic (Biomarker) Assessments: The following text was added 'One to 3 photographs should be taken from the skin area where the biopsy will be taken. Photographs should be taken before and after skin cleaning and disinfection procedures and after biopsy has been taken. Photograph margins should be approximately 10 cm to the left and 10 cm to the right from the biopsy site to show the surrounding area of the skin. Refer to the photography reference manual for additional details.'
07 November 2018	Major changes from Protocol v2.0 to Protocol v3.0 (Amendment 2), dated 07-Nov-2018 continued (6): • Revised Section 14 Timing of Study Assessments Revised to reflect actual order of assessments. Text included to describe procedure for subjects to enter the Open-label phase of the study. The individual sub-sections were also revised/updated describing the procedures and assessments for both the blinded and Open-label phases of the study in accordance with the SOAs • Change in Executive leadership and Glenmark Medical Monitor. The Sponsor signatory was changed from Fred Grossman, DO, FAPA to Mahboob Rahman, MD due to Change in Executive leadership and Glenmark Medical Monitor.

29 November 2018	Major changes from Protocol v3.0 to Protocol v4.0 (Amendment 3), dated 29-Nov-2018 included the below points: • Updated the criteria to be met for the subset of subjects who had completed the Follow-up phase of the study and would consent to participate in the Open-label Treatment phase of the study in Section 7.1 Study Design, Section 7.2 Treatment Assignment, and Table 2 Schedule of Assessment footnote. • Clarified timing of Week 16 predose (within 15 minutes of first Open-label dose), serum sample in Table 2 Schedule of Assessment footnote #13 and #14. • Clarified timing of Week 16 predose in Table 2 Schedule of Assessment footnote #7: All Blinded Treatment Phase assessment must be completed prior to Open-label treatment dosing. The first Open-label dose would be administered on Week 16 (Day 113). • Clarified in Table 8 Pharmacodynamic (Biomarker), Pharmacokinetic, and Immunogenicity Blood Sampling Time Points: Day 113±1 day (2688 h, (Predose Dose 1 of Open-Label Phase Treatment) was the predose sample occurring on Day 113, prior to Dose 1 of the Open-label phase.
29 November 2018	Major changes from Protocol v3.0 to Protocol v4.0 (Amendment 3), dated 29-Nov-2018 continued: • Added in Table 8 Pharmacodynamic (Biomarker), Pharmacokinetic, and Immunogenicity Blood Sampling Time Points to clarify the timing of the PK/ADA timepoint for the subset of subjects who would have completed the Follow-up phase of the study and would consent to participate in the Open-label Treatment Phase of the study: For the subset of subjects who had completed the GBR 830-204 study prior to implementation of protocol amendment 3, and provide informed consent to participate in the Open-label Treatment Phase of the study, a PK and immunogenicity sample must be collected on the start day of the open label phase within 15 minutes prior to the first dose • Added in Section 14.1 Screening Period (Day -28 to Day -1): Medical History, Serology, TB Testing, ACQ-5, Immunogenicity blood samples, PK blood samples to align with the rest of the protocol • Clarified in Section 14.2.5, Start of Open-label Treatment Phase Day 113 the procedures to be performed for subjects who had completed the Blinded Treatment Phase and consent to participate in the Open-label Treatment Phase.
26 June 2019	Major changes in Protocol v8.0 (Amendment 7), dated 26-Jun-2019 included the points mentioned below. It superseded v4.0, Amendment 3 (Global Amendment); v7.0, Amendment 6 (German and Czech Republic Only): • Section 7.1 Study Design, Section 10.1, Table 6: Treatment Groups and Dose Regimens - Clarified that the study would be conducted in 2 parts; Part 1 comprised the original treatment groups and Part 2 comprised the new treatment groups (inclusion of the higher 600 mg dose group). - Included the description of the new dosing groups. The study would be conducted in 2 Parts, with dosing Groups 1-4 comprising Part 1, and dosing Groups 5-6 comprising Part 2. Group 5: 1200 mg GBR 830 (4 SC injections each containing 300 mg in a 2 mL volume) on Day 1, followed by q2w dosing of 600 mg GBR 830 (2 SC injections containing 300 mg in a 2 mL volume), starting at Day 15 (Week 2). Group 6: Dose of placebo (4 SC injections of 2 mL volume) on Day 1, followed by q2w dosing with placebo (2 SC injections of 2 mL) starting at Day 15 (Week 2). - Revised description of treatments in the Blinded Treatment Phase and Open-label phase regarding loading dose, blinded phase maintenance dose and Open-label phase maintenance dose. - Revised PK sampling-Approximately 80 rich PK subjects would be randomised (in a 1:1:1:1 ratio) to the treatment groups 1-4 and approximately 40 rich PK subjects would be randomised (in a 1:1 ratio) to treatment groups 5 and 6. The remaining subjects in the study would be included in the sparse PK group. Blood samples were collected from the rich and sparse PK subjects according to the respective schedule described in Table 8 of the protocol.

26 June 2019	Major changes in Protocol v8.0 (Amendment 7), dated 26-Jun-2019 continued (1): • Clarified number of subjects screened and eligible for randomisation in Parts 1 and 2 of the study in Section 7.1.4 Number of Subjects. For Groups 1 through 4, a sufficient number of subjects would be screened to randomise approximately 312 eligible subjects in a 1:1:1:1 ratio. For Groups 5 and 6, a sufficient number of subjects were to be screened to randomise approximately 156 eligible subjects in a 1:1 ratio to either GBR 830 or placebo, therefore a total of 468 subjects were planned to be randomised in this study. • Clarified time period for diary completion for Baseline Pruritus NRS score in Section 8.1 Inclusion criteria #8 • Updated the number of weeks of study participation for subjects requiring a modified Screening visit entering the Open-label phase from 84 weeks to 86 weeks in Section 7.1.3, Duration of study participation • Clarified doses in the blinded and Open-label treatment groups in Investigational product, dosage and mode of administration. Dosage for Blinded Treatment Phase: See Groups 1, 2, 3, and 5 in the Treatment Groups and Dose Regimens table, in the Study Design section above. Dosage for Open-label Treatment Phase: All subjects in Groups 1-4 in the Open-label Treatment Phase would receive 300 mg of GBR 830 q2w. All subjects in Groups 5-6 in the Open-label Treatment Phase would receive 600 mg q2w. • Clarified the methods used to analyse the primary and secondary endpoints and the order to be followed for the dose group comparisons for parts 1 and 2 in Section 15.6 Efficacy Analyses.
26 June 2019	Major changes in Protocol v8.0 (Amendment 7), dated 26-Jun-2019 continued (2): • Revised the number of subjects randomised to Parts 1 and 2 of the study in Section 15.1, Determination of Sample Size. Assuming a dropout rate of 20%, 78 subjects per arm would be randomised for a total of 468 subjects (previous 312 subjects). For Groups 1-4, the randomisation scheme was 1:1:1:1 (Part 1 of the study); and the randomisation scheme was 1:1 for Groups 5-6 (Part 2 of the study). The 2 parts of the study were independent with separate randomisation schedules • Revised dose administration during the Blinded Treatment Phase and Open-label phase for Parts 1 and 2 of the study in Section 7.1 Overall Study Design. - Added the text 'For Groups 5 and 6, all subjects will receive a loading dose consisting of 4 SC injections, followed by 7 maintenance doses consisting of 2 SC injection per dose. - Added the text 'All subjects in Groups 1-4 in the Open-label Treatment Phase will receive 300 mg q2w. All subjects in Groups 5-6 in the Open-label Treatment Phase will receive 600 mg q2w.' - Updated text to reflect 'During the Open-label Treatment Phase each subject will receive a dose of GBR 830 SC injection (300 mg or 600 mg q2w) (consisting of 1 to 2 SC injection per dose, respectively) from Week 16 to Week 52 or until subject withdrawal.' • Added the SAE name 'left anterior descending coronary artery blockage' in Section 5.4 Clinical Experience • Updated to include dose Groups 5 and 6 in Section 7.1 Overall Study Design and Study Design Figure 1

26 June 2019	Major changes in Protocol v8.0 (Amendment 7), dated 26-Jun-2019 continued (3): • Updated Section 7.1 Overall Study Design and Table 2 Schedule of Assessments – Blinded Treatment Phase, Footnotes - Clarified versions of protocol with the Open-label phase in footnote#1 for subset of subjects who had completed the GBR 830-204 study - Included Rich PK sampling in footnote#2 for written ICF - Clarified that samples would be collected from all subjects in footnote#10 for immunogenicity. - Clarified that samples would be collected from subjects that had consented in footnote#11 for biomarker analysis - Revised number of subjects per arm where PK samples would be collected in footnote#14 for serum samples for the sparse PK group. - Clarified timeframe for obtaining diary information in footnote #16 • Updated Section 7.1 Overall Study Design and Table 2 Schedule of Assessments – Open-label Treatment Phase, Footnotes - Clarified versions of protocol with the Open-label phase for subset of subjects who had completed the GBR 830-204 study • Section 7.1.2 Dosing Rationale revised to include rationale for addition of higher dose group (600 mg) based on data from a recently completed phase 1 PK study and additional in vitro experiments. • Section 7.3, Dose Adjustment Criteria clarified to state that no dose modifications were allowed in Blinded Treatment Phase. Information regarding temporary discontinuation of study drug was moved to Section 8.3.1 where it was deemed more appropriate. • Clarified in Section 8.3 Subject Withdrawal Criteria that a subject who was withdrawn from blinded or Open-label study drug treatment would be asked to complete all procedures scheduled for the EOT visits at time of withdrawal (Week 16, or Week 54, respectively).
26 June 2019	Major changes in Protocol v8.0 (Amendment 7), dated 26-Jun-2019 continued (4): • Updated the neutrophil/platelet guidelines under which the study drug would be temporarily discontinued in Section 8.3.1, Temporary Discontinuation of Study Drug. - Grade 3 (previously 1) neutrophil count 100-500/µL (previously <lower limit of normal [LLN]-1.5 x 103/µL), per the NIH/NCI-CTCAE v4.03, 2010. - Grade 2 (previously 1) platelet count <7.5 - 5 x 104/µL (previously <LLN-75 x 103/µL), per NIH/NCI-CTCAE. • Section 9.2.4 Lifestyle and/or Dietary Restrictions: Text changed from Global Amendment 3 to clarify that use of emollients containing additives listed in Exclusion criterion 5 should not be initiated during the study and antihistamines may be used during the study. Revised to state that regular use of tanning both and topical steroids were prohibited through Week 66. • Text changed in Section 9.4.2 Unblinding in the event of a Medical Emergency from Global Amendment 3 to clarify that in the event of a medical emergency, during the Blinded Treatment Phase, the Investigator may unblind an individual subject's study drug allocation. • Clarifies treatments administered in treatment Groups 1-4 and 5 and 6 in Section 10.1 Study Drug. Subjects in treatment groups 5 and 6 would receive a loading dose consisting of 4 SC injections, and maintenance dosing consisting of 2 SC injections per dose, to maintain the blind. During the Open-label Treatment Phase each subject would receive 19 maintenance doses of either 300 mg or 600 mg GBR 830 SC injection q2w. • Clarified injection sites for single and multiple injections as well as dosing for consecutive dosing visits in Section 10.5 Administration.

26 June 2019	Major changes in Protocol v8.0 (Amendment 7), dated 26-Jun-2019 continued (5): • Clarified number of subjects randomised to the rich and sparse PK sampling in Parts 1 and 2 of the study in Section 12.2 Pharmacokinetic Assessments. An experimental population PK design was used for the PK blood sampling. The subjects in the rich PK group had additional blood sampling between Days 1 to 8 (Week 1), and Days 85 to 92 (Week 12). Approximately 80 rich PK subjects were randomised (in a 1:1:1:1 ratio) to treatment Groups 1-4, and approximately 40 rich PK subjects were randomised (in a 1:1 ratio) to treatment Groups 5 and 6. All subjects not participating in the rich PK group were included under the sparse PK group. Blood samples should be collected from rich and sparse subjects according to the respective schedules described in Table 8. The subjects in the sparse PK group had widespread sampling with fewer time points for each subject, compared to the rich PK subjects. • Anti-HBsAg testing was removed from Section 13.1.6.1Virus Serology Testing. • Removed text 'Unexpected therapeutic or clinical benefit from the study drug' from Section 13.2.1.1 Adverse Event. • Sponsor medical monitor changed from Kathleen Lomax to Andrea Acocella.
28 January 2020	Major changes from Protocol v8.0 to Protocol v9.0 (Amendment 8), dated 28-Jan-2020 included: • Replaced IGA with percentage change from baseline in EASI score at Week 16 in Section 6.1 Primary Objectives • Deleted Secondary Objective: To evaluate the proportion of subjects with EASI-75 (≥75% improvement from baseline) at Week 16 • Deleted the word 'monotherapy' from the Secondary Objective: To evaluate safety, tolerability, PK and immunogenicity of GBR 830 monotherapy in adults with moderate to severe AD. • Added 'IGA' in the Secondary Objective: 'To measure the effect of ISB 830 on disease activity in adult subjects with moderate to severe AD, as measured by validated tools (such as IGA, EASI response, SCORAD).' • Updated the Section 15.3 Endpoints with regards to changes in objectives • Added Exploratory efficacy endpoints: To assess qualitative changes in Photographs of skin lesions taken at time points specified in the schedule of assessments (Table 2 and Table 3).
28 January 2020	Major changes from Protocol v8.0 to Protocol v9.0 (Amendment 8), dated 28-Jan-2020 continued (1): • Updated Section 12.3 Pharmacodynamic (Biomarker) Assessments to include additional biomarker assessments - All subjects consented in Part 2 will provide required blood samples, including plasma, serum, whole blood, vfPBMCs and/or cell subsets, as specified at the listed time points in Table 2, Table 3, and Table 8. - These blood samples were collected at all sites (when and where biomarker sample kits were available). The collection of these samples was explained to the subject by the Investigator/site staff at the time of written informed consent. - These samples could be used for biomarker research during the trial and/or at future time points, after the study has been completed. Results of this biomarker research were not provided to the subject, and were not to be used for clinical decision-making, but could be used by the Sponsor to guide future research and/or drug development. - The samples could be used to examine disease activity, autoimmunity/inflammation, ISB 830 mechanism of action, and/or the effect of the study drug(s) on the course of disease. All samples collected (and their derivatives) will be destroyed no later than 15 years after the completion of the study (or as required by local regulations). Details of sample collection, processing, shipping and storage was to be provided to the study sites in a separate manual.

28 January 2020	Major changes from Protocol v8.0 to Protocol v9.0 (Amendment 8), dated 28-Jan-2020 continued (2): - Leukocyte Sub-population Cell Counts by Flow Cytometry: Blood samples (8.5 mL each) for vfPBMC and/or cell subsets were collected at appropriate time points defined in Table 2, Table 3, and Table 8. The details of sample collection, processing and storage were outlined in the laboratory manual. - Exploratory Photographs: Subjects who agree to participate in the main study, also agreed to allow photography of their skin (excluding pictures of the subject's face) during study participation at specified time points as per Table 2 and Table 3. Photographs of the subject's skin (with the exception of the face) could also be taken at additional time points, as per Investigator judgment. The photographs could be used to examine disease activity, autoimmunity/inflammation, ISB 830 mechanism of action, and/or the effect of the study drug(s) on the course of disease. Details of photograph collection, processing, shipping and storage were provided to the study sites in a separate manual. - Optional Genetic Research/Pharmacogenomics Assessments: Subjects who provide written consent for Optional Genetic Research agree to provide a blood sample (one sample could be collected at any visit during the study) to evaluate genetic sequences that may be involved in disease activity, inflammation, study drug mechanism of action, PK/metabolism, and/or the effect of the study drug(s) on the course of disease. Subjects could decline this optional research without effect on their participation in the main study.
28 January 2020	Major changes from Protocol v8.0 to Protocol v9.0 (Amendment 8), dated 28-Jan-2020 continued (3): • Section 15.1 Sample Size and Section 15.6 Efficacy Analyses were updated to align with the change in objectives and endpoints. • Clarified that biomarker analyses would not be part of the CSR in Section 15.7.3 Pharmacodynamic (Biomarker) Analyses • Blood collection for clinical laboratory assessment and pregnancy test frequency was reduced. The frequency for AD photography, and blood collection for biomarker was increased. Footnotes were also updated in Section 7.1, Schedule of Assessments; Table 2 and Table 3.
05 May 2020	Major changes from Protocol v9.0 to Protocol v10.0 (Amendment 9), dated 05-May-2020 included: • Added text in Section 7.1.4 Number of Subjects (Planned) and Section 15.1 Sample Size as enrollment of additional subjects was now allowed due to pandemic-related discontinuation or withdrawal up to Week 16 in Part 2 only: The actual number of subjects randomised in Groups 5 and 6 could be different than initially planned due to the impact of the SARS-CoV-2/COVID-19 pandemic (see Section 8.3.4). It was clarified that approximately 468 subjects were planned to be randomised in this study. • Considering the pandemic, an additional criterion of fever (>100.4°F or >38°C), suspected infection, or infection requiring oral antibiotics was included in the list of events that may result in temporary discontinuation of study drug in Section 8.3.1 Temporary Discontinuation of Study Drug.

05 May 2020	Major changes from Protocol v9.0 to Protocol v10.0 (Amendment 9), dated 05-May-2020 continued (1): • Added text in Section 8.3.4 Enrollment of Additional Subjects: - Special considerations were added to the protocol based on the issues arising from the SARS-CoV-2/COVID-19 pandemic. During the blinded dosing period for Part 2 (ie, prior to completion of the Week 16 visit), any randomised subject who terminated study participation or who misses 2 or more consecutive doses of study drug (even if continuing with study participation) or misses any part of the primary endpoint assessments at Week 16, as a result of pandemic-related reasons, was not to be counted against the total number of subjects targeted (N=156 for Part 2 of the study). For each of these cases, a new subject could be screened and randomised, to allow an evaluable number of subjects for the Week 16 primary endpoint. The new subjects in screening would receive new subject numbers and new treatment assignments as per the current randomisation schedule in the protocol. - Additional subjects would only be added in response to the number of subjects who meet the above criteria, as a result of pandemic-related issues. Randomised subjects who discontinued study participation or miss consecutive doses or the Week 16 primary endpoint assessments for non-pandemic related reasons, or who had study drug or study visit issues after completing their Week 16 visit, would not trigger the screening of additional subjects.
05 May 2020	Major changes from Protocol v9.0 to Protocol v10.0 (Amendment 9), dated 05-May-2020 continued (2): • Added in Section 9.4.1 Blinding and Unblinding Procedures, to include flexibility of dosing for the subject who could not come to the site in special circumstances: - In special circumstances (eg, during SARS-CoV-2/COVID-19 pandemic, which could prevent the subject from presenting to the site), the handling, preparation, and administration of the study drug (during blinded or Open-label periods of the study) could be performed by an unblinded, qualified healthcare provider who was not involved in study management, such as a home-visit nurse contracted by the Sponsor (if such service was available at the time and where permitted by local regulations) (see Section 10.5). • Added in Section 10.4 Study Drug Preparation, to include flexibility of dosing for the subject who may not come to the site in special circumstances: - In special circumstances, (eg, during SARS-CoV-2/COVID-19 pandemic, which may prevent the subject from presenting to the site), an unblinded, qualified healthcare provider may prepare study drug for injection (see Section 10.5).
05 May 2020	Major changes from Protocol v9.0 to Protocol v10.0 (Amendment 9), dated 05-May-2020 continued (3): • Added in Section 10.5 Administration, to include flexibility of dosing for the subject who may not come to the site in special circumstances: - In special circumstances, (eg, during SARS-CoV-2/COVID-19 pandemic, which may prevent the subject from presenting to the site), subjects could receive 'at home' dosing, performed by an unblinded, qualified healthcare provider (if such service was available at the time and where permitted by local regulations) who would perform vital sign measurements (ie, systolic and diastolic blood pressure [mmHg], pulse rate [beats per minute], respiratory rate [per minute] and oral or tympanic temperature [degrees in Celsius]) by standard methods prior to dosing, and who would conduct the protocol-specified observation post-injection. Women of childbearing potential would also be administered a monthly urine pregnancy test by the unblinded, qualified healthcare provider, and must have a negative pregnancy result prior to dosing. - Additional details were provided in the pharmacy manual and in a separate home healthcare provider manual.

05 May 2020	Major changes from Protocol v9.0 to Protocol v10.0 (Amendment 9), dated 05-May-2020 continued (4): • Added additional pandemic related safety assessments to ensure safety of subjects in the SARS-CoV-2/ COVID-19 pandemic in Section 13.1 Safety Parameters: To ensure the ongoing safety of subjects during the pandemic, study subjects who missed or were unable to attend scheduled clinic visits would be contacted by the site via a safety phone call that includes the collection of AEs/SAEs and concomitant medications. This phone call was to be performed for every missed visit that occurs during the pandemic. If the subject meets other criteria, eg, for withdrawal/discontinuation of the study drug, the site was to follow the protocol in regard to those criteria. • Section 15.6 Efficacy Analyses was updated to explain clearly the endpoints that would be conducted under the PPS. Updated to align with statistical analysis plan. Efficacy analyses for Part 2 was amended to include changes based on enrolment of additional subject due to pandemic-related issue. To assess the robustness of the results in the Part 2 of the study, the analyses on primary endpoint and secondary endpoints (IGA, EASI-75) would also be conducted excluding subjects who withdraw from the study or miss 2 or more consecutive doses prior to Week 16 or miss any part of the primary endpoint assessments at Week 16 due to the pandemic.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported