



Clinical trial results:

Double-blind, randomized, placebo-controlled, phase II dose-finding study comparing different doses of ZED1227 capsules with placebo in the treatment of non-alcoholic fatty liver disease (NAFLD) with significant fibrosis

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2021-002253-29 |
| Trial protocol | ES PL DE BE |
| Global end of trial date | 05 July 2023 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 09 August 2024 |
| First version publication date | 09 August 2024 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | CEC-011/NAS |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT05305599 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Dr. Falk Pharma GmbH |
| Sponsor organisation address | Leinenweberstraße 5, Freiburg im Breisgau, Germany, 79108 |
| Public contact | Dept. of Clinical Research&Developm, Dr. Falk Pharma GmbH, +49 49761 1514 0, zentrale@drfalkpharma.de |
| Scientific contact | Dept. of Clinical Research&Developm, Dr. Falk Pharma GmbH, +49 0761 1514 0, zentrale@drfalkpharma.de |

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 | 29 August 2023 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 05 July 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 05 July 2023 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial is to evaluate the efficacy of three doses of ZED1227 versus (vs.) placebo for the 12-week treatment of patients with NAFLD with significant fibrosis

Protection of trial subjects:

Close supervision of subjects by implementing interim visits every 4 weeks during treatment and one follow up visit at weeks after end of treatment to guarantee their safety and wellbeing. Prior to recruitment of patients, all relevant documents of the clinical study were submitted and approved by the Independent Ethics Committees (IECs) responsible for the participating investigators. Written consent documents embodied the elements of informed consent as described in the Declaration of Helsinki, the ICH Guidelines for Good Clinical Practice (GCP) and were in accordance with all applicable laws and regulations. The informed consent form and patient information sheet described the planned and permitted uses, transfers and disclosures of the patient's personal data and personal health information for purposes of conducting the study. The informed consent form and the patient information sheet further explained the nature of the study, its objectives and potential risks and benefits as well as the date informed consent was given. Before being enrolled in the clinical trial, every patient was informed that participation in this trial was voluntary and that he/she could withdraw from the study at any time without giving a reason and without having to fear any loss in his/her medical care. The patient's consent was obtained in writing before the start of the study. By signing the informed consent, the patient declared that he/she was participating voluntarily and intended to follow the study protocol instructions and the instructions of the investigator and to answer the questions asked during the course of the trial.

Background therapy:

None

Evidence for comparator:

As there is no standard therapy, placebo was used as comparator

| | |
|---|---------------|
| Actual start date of recruitment | 05 April 2022 |
| 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: 58 |
| Country: Number of subjects enrolled | Spain: 38 |
| Country: Number of subjects enrolled | Belgium: 16 |
| Country: Number of subjects enrolled | France: 49 |
| Country: Number of subjects enrolled | Germany: 25 |
| Worldwide total number of subjects | 186 |
| EEA total number of subjects | 186 |

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) | 117 |
| From 65 to 84 years | 69 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

In total 186 patients were included in 5 countries (Germany, Poland, Spain, France and Belgium) from April 2022 to July 2023.

Pre-assignment

Screening details:

Screening criteria: Signed informed consent • male or female, 18 and 75 years of age • Diagnosed with NAFLD and significant fibroses (stages 2 or 3). 334 patients were screened. Thereof 186 patients were randomised. Of those 177 received study medication and were included in the safety analysis set (SAF). 174 were included in FAS.

Pre-assignment period milestones

| | |
|------------------------------|-----|
| Number of subjects started | 186 |
| Number of subjects completed | 174 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|---------------------------------|
| Reason: Number of subjects | Adverse event, non-fatal: 1 |
| Reason: Number of subjects | Randomized by mistake: 1 |
| Reason: Number of subjects | Consent withdrawn by subject: 7 |
| Reason: Number of subjects | Other: 2 |
| Reason: Number of subjects | Missing: 1 |

Period 1

| | |
|------------------------------|---|
| Period 1 title | Overall trial (treatment phase) (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:

Blinding was achieved by the application of the same number of capsule s(ZED1227 or placebo) to each patient. Placebo capsules matched verum capsules in size, taste, and appearance.

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|---------|
| Arm title | Group A |
|------------------|---------|

Arm description:

ZED1227 (low dose) 10 mg

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | ZED1227 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |

Dosage and administration details:

1 capsule twice a day: 1 capsule in the morning and 1 capsule in the evening

| | |
|------------------|---------|
| Arm title | Group B |
|------------------|---------|

Arm description:

ZED1227 (middle dose) 25 mg

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | ZED1227 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 1 capsule twice a day: 1 capsule in the morning and 1 capsule in the evening | |
| Arm title | Group C |
| Arm description: | |
| ZED1227 (high dose) 50 mg | |
| Arm type | Experimental |
| Investigational medicinal product name | ZED1227 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 1 capsule twice a day: 1 capsule in the morning and 1 capsule in the evening | |
| Arm title | Group D |
| Arm description: | |
| Placebo | |
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule, hard |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| 1 capsule twice a day: 1 capsule in the morning and 1 capsule in the evening | |

| Number of subjects in period 1^[1] | Group A | Group B | Group C |
|---|---------|---------|---------|
| Started | 41 | 43 | 45 |
| Completed | 40 | 42 | 43 |
| Not completed | 1 | 1 | 2 |
| Lack of Compliance | - | 1 | - |
| Physician decision | - | - | 1 |
| Consent withdrawn by subject | - | - | 1 |
| Adverse event, non-fatal | 1 | - | - |

| Number of subjects in period 1^[1] | Group D |
|---|---------|
| Started | 45 |
| Completed | 43 |
| Not completed | 2 |

| | |
|------------------------------|---|
| Lack of Compliance | - |
| Physician decision | - |
| Consent withdrawn by subject | 1 |
| Adverse event, non-fatal | 1 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: To meet the requirements of the system, the number of patients entered in the trial period reflects the FAS population. These are the patients, that were randomized, received study medication and at least one ample for analysis of the primary endpoint was available.

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------------------------|
| Reporting group title | Overall trial (treatment phase) |
|-----------------------|---------------------------------|

Reporting group description: -

| Reporting group values | Overall trial (treatment phase) | Total | |
|---------------------------------------|------------------------------------|-------|--|
| Number of subjects | 174 | 174 | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 111 | 111 | |
| From 65-75 years | 63 | 63 | |
| Age continuous Units: years | | | |
| median | 63.0 | | |
| full range (min-max) | 18 to 74 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 78 | 78 | |
| Male | 96 | 96 | |

Subject analysis sets

| | |
|----------------------------|-----|
| Subject analysis set title | FAS |
|----------------------------|-----|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

All randomized patients who received at least one dose of the IMP and had baseline serum levels of PRO-C3 collected.

| Reporting group values | FAS | | |
|---------------------------------------|----------|--|--|
| Number of subjects | 174 | | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 111 | | |
| From 65-75 years | 63 | | |
| Age continuous Units: years | | | |
| median | 63 | | |
| full range (min-max) | 18 to 74 | | |
| Gender categorical Units: Subjects | | | |
| Female | 78 | | |
| Male | 96 | | |

End points

End points reporting groups

| | |
|---|---------------|
| Reporting group title | Group A |
| Reporting group description: ZED1227 (low dose) 10 mg | |
| Reporting group title | Group B |
| Reporting group description: ZED1227 (middle dose) 25 mg | |
| Reporting group title | Group C |
| Reporting group description: ZED1227 (high dose) 50 mg | |
| Reporting group title | Group D |
| Reporting group description: Placebo | |
| Subject analysis set title | FAS |
| Subject analysis set type | Full analysis |
| Subject analysis set description: All randomized patients who received at least one dose of the IMP and had baseline serum levels of PRO-C3 collected. | |

Primary: Primary endpoint: relative change in PRO-C3

| | |
|---|---|
| End point title | Primary endpoint: relative change in PRO-C3 |
| End point description: The relative change (%) of serum levels of released N-terminal propeptide of type III collagen (PRO-C3) | |
| End point type | Primary |
| End point timeframe: Between baseline and the end-of-treatment (EOT)/withdrawal visit | |

| End point values | Group A | Group B | Group C | Group D |
|-------------------------------------|-------------------|--------------------|--------------------|-------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 41 | 43 | 45 | 45 |
| Units: Change of PRO-C3 | | | | |
| least squares mean (standard error) | 0.3 (\pm 3.56) | 10.2 (\pm 3.46) | -1.2 (\pm 3.48) | 6.8 (\pm 3.37) |

Statistical analyses

| | |
|----------------------------|-------------------------------|
| Statistical analysis title | Primary efficacy endpoint FAS |
| Comparison groups | Group A v Group D |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 86 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0921 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -6.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16.12 |
| upper limit | 3.1 |

| | |
|---|--------------------------------|
| Statistical analysis title | Primary efficacy endpoint FAS |
| Comparison groups | Group B v Group D |
| Number of subjects included in analysis | 88 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5863 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | 3.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.16 |
| upper limit | 12.92 |

| | |
|---|--------------------------------|
| Statistical analysis title | Primary efficacy endpoint FAS |
| Comparison groups | Group C v Group D |
| Number of subjects included in analysis | 90 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0479 |
| Method | ANOVA |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -1.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -17.57 |
| upper limit | 1.43 |

Secondary: Secondary Endpoint: relative change of ELF Score

| | |
|--|--|
| End point title | Secondary Endpoint: relative change of ELF Score |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| Between baseline and the end-of-treatment (EOT)/withdrawal visit | |

| End point values | Group A | Group B | Group C | Group D |
|--------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 40 | 43 | 45 | 45 |
| Units: % | | | | |
| arithmetic mean (standard deviation) | 0.70 (± 6.023) | 1.68 (± 5.431) | -0.98 (± 5.562) | 0.26 (± 5.514) |

| End point values | FAS | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 0 ^[1] | | | |
| Units: % | | | | |
| arithmetic mean (standard deviation) | () | | | |

Notes:

[1] - No determined for whole population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were assessed from BL visit, at interim visits (week 4 and week 8), at the end of treatment visit week 12 and at the Follow up visit week 16 .

Adverse event reporting additional description:

Treatment-Emergent and Post-Treatment Adverse Events

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 26.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Group A |
|-----------------------|---------|

Reporting group description:

ZED1227 (low dose) 10 mg

| | |
|-----------------------|---------|
| Reporting group title | Group B |
|-----------------------|---------|

Reporting group description:

ZED1227 (middle dose) 25 mg

| | |
|-----------------------|---------|
| Reporting group title | Group C |
|-----------------------|---------|

Reporting group description:

ZED1227 (high dose) 50 mg

| | |
|-----------------------|---------|
| Reporting group title | Group D |
|-----------------------|---------|

Reporting group description:

Placebo

| Serious adverse events | Group A | Group B | Group C |
|---|----------------|----------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 42 (4.76%) | 3 / 45 (6.67%) | 1 / 45 (2.22%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Cardiac disorders | | | |
| Dilated cardiomyopathy | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Hemorrhoidal hemorrhage | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anorectal varices | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (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 |
| Diverticulum intestinal | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (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 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (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 |
| Rectal hemorrhage | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Sleep apnea syndrome | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (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 | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Serious adverse events | Group D | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |

| | | | |
|---|----------------|--|--|
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Cardiac disorders | | | |
| Dilated cardiomyopathy | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Hemorrhoidal hemorrhage | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anorectal varices | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diverticulum intestinal | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rectal hemorrhage | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Sleep apnea syndrome | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|--|----------------------------------|--|--|
| Lumbar spinal stenosis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 45 (0.00%) 0 / 0 0 / 0 | | |
| Infections and infestations Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 45 (0.00%) 0 / 0 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 2 %

| Non-serious adverse events | Group A | Group B | Group C |
|--|---------------------|---------------------|---------------------|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 31 / 42 (73.81%) | 26 / 45 (57.78%) | 27 / 45 (60.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Fibroma subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 0 / 45 (0.00%) 0 | 0 / 45 (0.00%) 0 |
| Monoclonal gammopathy subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 0 / 45 (0.00%) 0 | 0 / 45 (0.00%) 0 |
| Vascular disorders Hypotension subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 0 / 45 (0.00%) 0 | 2 / 45 (4.44%) 2 |
| Hypertension subjects affected / exposed occurrences (all) | 1 / 42 (2.38%) 1 | 0 / 45 (0.00%) 0 | 0 / 45 (0.00%) 0 |
| Surgical and medical procedures Hyperhidrosis subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 1 / 45 (2.22%) 1 | 0 / 45 (0.00%) 0 |
| Skin burning sensation subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 0 / 45 (0.00%) 0 | 0 / 45 (0.00%) 0 |

| | | | |
|--|----------------|----------------|----------------|
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 2 / 45 (4.44%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Malaise | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Swelling face | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Reproductive system and breast disorders | | | |
| Heavy menstrual bleeding | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Postmenopausal haemorrhage | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epistaxis | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 2 / 42 (4.76%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Asthma | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Catarrh | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 1 | 1 |
| Depression | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Irritability | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipase increased | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 1 | 1 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood insulin increased | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chest X-ray abnormal | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Glutamate dehydrogenase increased | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| High density lipoprotein decreased | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Low density lipoprotein increased | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Prothrombin time shortened | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Smear cervix | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 0 / 45 (0.00%) 0 | 1 / 45 (2.22%) 1 |
| Transaminases increased subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 0 / 45 (0.00%) 0 | 0 / 45 (0.00%) 0 |
| Injury, poisoning and procedural complications | | | |
| Animal bite subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 0 / 45 (0.00%) 0 | 1 / 45 (2.22%) 1 |
| Arthropod bite subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 0 / 45 (0.00%) 0 | 1 / 45 (2.22%) 1 |
| Contusion subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 0 / 45 (0.00%) 0 | 0 / 45 (0.00%) 0 |
| Face injury subjects affected / exposed occurrences (all) | 1 / 42 (2.38%) 1 | 0 / 45 (0.00%) 0 | 0 / 45 (0.00%) 0 |
| Hand fracture subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 1 / 45 (2.22%) 1 | 0 / 45 (0.00%) 0 |
| Congenital, familial and genetic disorders | | | |
| Hydrocele subjects affected / exposed occurrences (all) | 1 / 42 (2.38%) 1 | 0 / 45 (0.00%) 0 | 0 / 45 (0.00%) 0 |
| Cardiac disorders | | | |
| Atrial Fibrillation subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 1 / 45 (2.22%) 1 | 0 / 45 (0.00%) 0 |
| Atrioventricular block first degree subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 0 / 45 (0.00%) 0 | 1 / 45 (2.22%) 1 |
| Dilated cardiomyopathy subjects affected / exposed occurrences (all) | 1 / 42 (2.38%) 1 | 0 / 45 (0.00%) 0 | 0 / 45 (0.00%) 0 |
| Nervous system disorders | | | |

| | | | |
|--------------------------------------|----------------|----------------|----------------|
| Headache | | | |
| subjects affected / exposed | 3 / 42 (7.14%) | 1 / 45 (2.22%) | 1 / 45 (2.22%) |
| occurrences (all) | 3 | 1 | 1 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Disturbance in attention | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Migraine | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Restless leg | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Eosinophilia | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Anaemia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Deafness | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Vertigo positional | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 42 (0.00%) 0 | 1 / 45 (2.22%) 1 | 0 / 45 (0.00%) 0 |
| Eye disorders | | | |
| Astigmatism | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blepharitis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Cataract | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye inflammation | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ocular hypertension | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Photophobia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ulcerative keratitis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Diarrhea | | | |
| subjects affected / exposed | 5 / 42 (11.90%) | 2 / 45 (4.44%) | 3 / 45 (6.67%) |
| occurrences (all) | 5 | 2 | 3 |
| Constipation | | | |
| subjects affected / exposed | 2 / 42 (4.76%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 3 / 45 (6.67%) |
| occurrences (all) | 1 | 0 | 3 |
| Abdominal distension | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 42 (2.38%) | 3 / 45 (6.67%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Nausea | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 2 / 45 (4.44%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Anorectal varices | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Breath odour | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Chronic gastritis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Defaecation urgency | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Diverticulum intestinal | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Duodenogastr | | | |

| | | | |
|----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eructation | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Faeces discoloured | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oesophageal ulcer | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pancreatitis chronic | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rectal tenesmus | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Regurgitation | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tongue discomfort | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Hepatobiliary disorders | | | |
| Hepatic steatosis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 3 / 42 (7.14%) | 1 / 45 (2.22%) | 1 / 45 (2.22%) |
| occurrences (all) | 3 | 2 | 1 |
| Rash | | | |
| subjects affected / exposed | 2 / 42 (4.76%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Acne | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis allergic | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Erythema | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash erythematous | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin irritation | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal colic | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 2 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pain in extremity | | | |

| | | | |
|-----------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 42 (2.38%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Intervertebral disc disorder | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Synovial cyst | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Torticollis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 5 / 42 (11.90%) | 1 / 45 (2.22%) | 2 / 45 (4.44%) |
| occurrences (all) | 5 | 1 | 2 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 1 / 45 (2.22%) | 3 / 45 (6.67%) |
| occurrences (all) | 1 | 1 | 3 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 1 / 45 (2.22%) | 1 / 45 (2.22%) |
| occurrences (all) | 1 | 1 | 1 |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| Bronchitis | | | |
| subjects affected / exposed | 3 / 42 (7.14%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 3 | 0 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 42 (4.76%) | 1 / 45 (2.22%) | 1 / 45 (2.22%) |
| occurrences (all) | 3 | 2 | 1 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 2 / 45 (4.44%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza | | | |
| subjects affected / exposed | 2 / 42 (4.76%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 2 / 42 (4.76%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 1 / 45 (2.22%) | 1 / 45 (2.22%) |
| occurrences (all) | 1 | 1 | 1 |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Infected bite | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|--------------------------------------|----------------|----------------|----------------|
| Lyme disease | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Periodontitis | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 2 / 45 (4.44%) |
| occurrences (all) | 0 | 0 | 2 |
| Diabetes | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diabetic metabolic decompensation | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Folate deficiency | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 1 / 45 (2.22%) |
| occurrences (all) | 0 | 0 | 1 |
| Gout | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 42 (2.38%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 0 / 45 (0.00%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Increased appetite | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 42 (0.00%) | 1 / 45 (2.22%) | 0 / 45 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|------------------|--|--|
| Non-serious adverse events | Group D | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 33 / 45 (73.33%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Fibroma | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Monoclonal gammopathy | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Surgical and medical procedures | | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin burning sensation | | | |

| | | | |
|---|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 45 (2.22%) 1 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Malaise | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Swelling face | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Reproductive system and breast disorders | | | |
| Heavy menstrual bleeding | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Postmenopausal haemorrhage | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 2 | | |

| | | | |
|-----------------------------|----------------|--|--|
| Epistaxis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Catarrh | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Depression | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Irritability | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sleep disorder | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Investigations | | | |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 2 | | |
| Lipase increased | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood insulin increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood triglycerides increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Chest X-ray abnormal | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Glutamate dehydrogenase increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| High density lipoprotein decreased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Low density lipoprotein increased | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Prothrombin time shortened | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Smear cervix | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Transaminases increased | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Injury, poisoning and procedural complications | | | |
| Animal bite | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Arthropod bite | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Contusion | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Face injury | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hand fracture | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Congenital, familial and genetic disorders | | | |
| Hydrocele | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cardiac disorders | | | |
| Atrial Fibrillation | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Atrioventricular block first degree | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dilated cardiomyopathy | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nervous system disorders | | | |

| | | | |
|--------------------------------------|----------------|--|--|
| Headache | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Sciatica | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Disturbance in attention | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Migraine | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Restless leg | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Eosinophilia | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 2 | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Ear and labyrinth disorders | | | |
| Deafness | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vertigo positional | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 45 (0.00%) 0 | | |
| Eye disorders | | | |
| Astigmatism | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Blepharitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cataract | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Eye inflammation | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Ocular hypertension | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Photophobia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ulcerative keratitis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Diarrhea | | | |
| subjects affected / exposed | 6 / 45 (13.33%) | | |
| occurrences (all) | 6 | | |
| Constipation | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 2 | | |
| Flatulence | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Abdominal distension | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nausea | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 2 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 2 | | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Anorectal varices | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Breath odour | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Chronic gastritis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Defaecation urgency | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Diverticulum intestinal | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Duodenogastr | | | |

| | | | |
|----------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Eructation | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Faeces discoloured | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oesophageal ulcer | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pancreatitis chronic | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rectal tenesmus | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Regurgitation | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tongue discomfort | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Toothache | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hepatobiliary disorders | | | |
| Hepatic steatosis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Rash | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Acne | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Alopecia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Dermatitis allergic | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Dry skin | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Erythema | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psoriasis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash erythematous | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash pruritic | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Skin irritation | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Proteinuria | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Renal colic | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 2 | | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pain in extremity | | | |

| | | | |
|-----------------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bursitis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Intervertebral disc disorder | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Synovial cyst | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Torticollis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 2 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 5 / 45 (11.11%) | | |
| occurrences (all) | 6 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 45 (6.67%) | | |
| occurrences (all) | 3 | | |

| | | | |
|-----------------------------|----------------|--|--|
| Bronchitis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cystitis | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 2 | | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 2 | | |
| Influenza | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 2 / 45 (4.44%) | | |
| occurrences (all) | 2 | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abscess limb | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infected bite | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|--------------------------------------|----------------|--|--|
| Lyme disease | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Otitis externa | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Periodontitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Metabolism and nutrition disorders | | | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Diabetes | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Diabetes mellitus inadequate control | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Diabetic metabolic decompensation | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Folate deficiency | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gout | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 45 (2.22%) | | |
| occurrences (all) | 1 | | |
| Increased appetite | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |
| Type 2 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 45 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 11 January 2023 | One global amendment dated 11 Jan 2023 was made to the original protocol, dated 11 Oct 2021 |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported